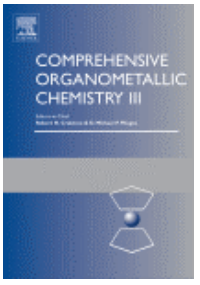

Comprehensive Organometallic Chemistry III

Elsevier, 2007

Volume 9: Applications I: Main Group Compounds in Organic Synthesis

9.01
Lithium

Due to reasons beyond the editors' control, the intended authors of the revised chapter on Lithium were not able to complete it, so the editors have instead provided a short list of the most important recent reviews in the area.

Selected reviews and monographs:

Clayden, J. In *Organolithiums: Selectiviy for Synthesis*; Baldwin J., Williams, R. M., Eds; Tetrahedron Organic Chemistry Series; Pergamon: Oxford, 2002; Vol. 23.

Guijarro, A.; Gomez, C.; Yus, M. I. Active metals in organic synthesis: recent advances. *Trends in Organic Chemistry* **2000**, *8*, 65–91.

Hodgson, D. M. *Organolithiums in Enantioselective Synthesis*; Topics in Organometallic Chemistry; Springer: Berlin, 2003; Vol. 5.

Majewski, M.; Snieckus, V. *Science of Synthesis*; Thieme: Stuttgart, 2005; Vols. 8a-b.

Najera, C.; Yus, M.; Eds. *Tetrahedron* Symposium-in-Print Number 111: Functionalised Organolithium Compounds. *Tetrahedron* **2005**, *61*, 3139–3176.

Najera, C.; Yus, M. Functionalized organolithium compounds: New synthetic adventures. *Current Organic Chemistry* **2003**, *7*(9), 867–926.

Najera, C.; Yus, M. Recent developments in the chemistry of functionalized organolithium compounds. *Recent Research Developments in Organic Chemistry* **1997**, *1*, 67–96.

Rappoport, Z.; Marek, I.; Eds. *The Chemistry of Organolithium Compounds*, Wiley: New York, 2004; Vols. 1-2.

Sapse A.-M.; Schleyer P. von R. *Lithium Chemistry*; Wiley: New York, 1995.

Tomooka, K.; Ito, M. Lithium in organic synthesis. *Main Group Metals in Organic Synthesis* **2004**, *1*, 1–34.

Wu, G.; Huang, M. *Organolithium in asymmetric processes*; Topics in Organometallic Chemistry; Springer: Berlin, 2004; Vol. 6, pp. 1–35.

9.02
Sodium and Potassium

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9.02.1 Introduction and Background

The chemistry of organosodium and organopotassium reagents has been reviewed in the two previous volumes of this series in 1982[1,2] and in 1995.[3] The more recent one[3] covers the literature up to 1994 and hence this chapter deals with the general aspects of the chemistry of organoalkali reagents mainly focusing on the achievements of the last decade. There are several books,[4–6] book chapters,[7–12] and reviews[13–17] dealing with the chemistry of organoalkali reagents but only three of them have been published after 1995.[8,11,11a,12]

Organosodium and organopotassium compounds have found a limited number of applications in organic synthesis mainly due to the difficulties in preparing and handling such reagents. Their use in the metallation of a large series of weakly acidic hydrocarbons was certainly a fundamental step in the development of organometallic chemistry; previously unreactive C–H bonds could finally be functionalized through a direct approach. However, the use of organosodium and -potassium reagents presents several drawbacks: the preparation of the organometallic species usually requires high-speed stirring and special equipment; despite the use of large excesses of substrates and long reaction times, yields are often unsatisfactory. This is the reason why organoalkali compounds were almost completely abandoned when in 1967 Schlosser discovered[18] that an equimolar mixture of butyllithium (LIC) and potassium *tert*-butoxide (KOR) constitutes a reagent (later called LIC-KOR) endowed with an exceptionally high metallating power together with a good stability even in ethereal solvents and, as discovered later, unusually high selectivity. Similar considerations hold for the alkyllithium and sodium alcoholates mixtures as well.

Since then, the preparation and use of organoalkali reagents in synthesis has been almost completely supplanted by the chemistry of superbases which are highly reactive organometallic species formed by mixing organolithium compounds and sodium or potassium alcoholates. Superbases have found many applications in the metallation of low acidic hydrocarbons.[19–21,7,3,8,10–12]

9.02.2 Superbases and their Constitution

Morton and his school were the first to use alkylmetal–metal alkoxide mixtures (mostly pentylsodium/sodium isopropoxide).[22–26] In these seminal studies the superbasic reagent butyllithium/potassium *tert*-butoxide was tested

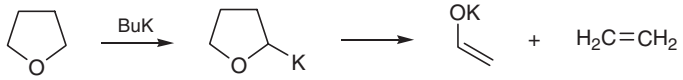
only as initiator of polymerization.[27,28] It was Schlosser who later independently conceived LIC-KOR and related superbases[18] and applied them for the first time to the high-efficacy metallation of low-acidity hydrocarbons.

Since the pioneering work of Morton,[22] the precise nature of the alcoholate/organometallic complexes has repeatedly been the subject of considerable speculation. However, little is known for sure. Despite a long and still open debate[20,7,3] concerning the constitution of the superbasic reagents, their real structural identity remains obscure. The superbasic reagent butyllithium/potassium *tert*-butoxide was conceived by Schlosser[18] as a mixed-metal reagent. He postulated a "mixed aggregate"[4,29] type interaction which strongly polarized the organometallic bonds, leading to an increase of reactivity compared to the neat organolithium reagent. It has been suggested that superbases may also exist as equilibria of several kinds of mixed aggregates having different stoichiometry and undergoing a morphological evolution in the course of the reaction.[20]

$$(RLi)_m + (KOR^1)_n \longrightarrow (R)_m(Li{+}K)_{m+n}(OR^1)$$

The existence of mixed organolithium/metal alkoxide aggregates is established beyond any doubt. For example, organolithiums (butyl-, isopropyl-, and *tert*-butyllithium) form 1 : 1 mixed aggregates with lithium *tert*-butoxide in hexane[30] and mixtures of alkyllithiums and lithium alkoxides with up to three alkoxide ligands have been detected in tetrahydrofuran solutions.[31,32] A variety of additional evidence[33] supports the idea that the formation of mixed aggregates is a general phenomenon occurring whenever metal species are mixed.

The simple metathetical exchange between lithium and a second alkali metal has been ruled out by comparative experiments. Butylpotassium, well studied since 1937,[34] is known to attack (like butylsodium) concomitantly allylic and vinylic protons from alkenes,[35,36] whereas the butyllithium/potassium *tert*-butoxide mixture offers a greater selectivity and higher yields.[37,38] The butyllithium/potassium *tert*-butoxide mixture and the butylpotassium reagent also exhibit striking differences in their stability toward ethereal solvents.[39] The mixture survives for hours in tetrahydrofuran at −50 °C, whereas neat butylpotassium reacts with tetrahydrofuran instantaneously, even below −100 °C, to give 2-tetrahydrofuryl potassium as the main product, which then decomposes at around −50 °C to ethylene and the potassium enolate of acetaldehyde.[39]



As a matter of fact a few safe conclusions can presently be drawn concerning the nature of superbasic reagents:

- when an alcoholate and an organolithium reagent are combined, a mixed aggregate is formed which contains strongly polarized organometallic species endowed with high reactivity;
- the metallation product after reaction with a superbasic reagent contains mainly, though not exclusively, the heavier alkali metal;
- the butyllithium/alkali metal alkoxide mixtures show different chemical behavior compared to simple butylsodium or butylpotassium and offer major practical advantages over the latter reagents.

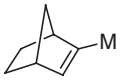
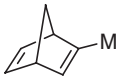
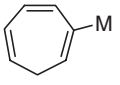
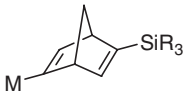
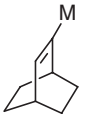
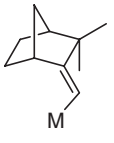
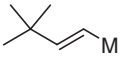
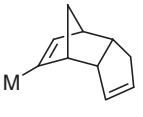
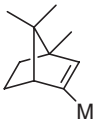
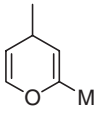
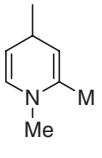
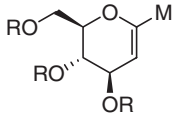
In the wake of the successful use of Schlosser's base, a variety of superbasic reagents have been studied, showing sometimes a modulated behavior. It must be pointed out, however, that the simple substitution of one component with a similar reagent (e.g., potassium *tert*-butoxide with another potassium alcoholate) affects the overall behavior of the base only to a small extent. In contrast, the use of different organolithium components (butyl-, *sec*-butyl, *tert*-butyl, and methyllithium) is often responsible for marked differences in the reactivity profiles.[40]

Most of the progress concerning organoalkali reagents in chemistry have been made using superbases. The following sections deal with the preparation and use of organoalkali compounds of vinyl, aryl, and benzyl type.

9.02.3 Metallation of Alkenes in the Vinylic Position

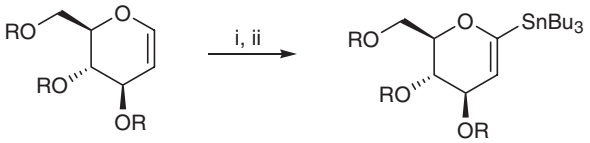
Alkenes lacking hydrogen atoms at allylic positions are much less acidic than ordinary unsaturated hydrocarbons. Superbases regioselectively exchange allylic protons in alkenes whenever there is a choice. However, a few examples of metallation of alkenic C–H bonds with superbases are known and a compilation of them is reported in Table 1. Ethylene itself has been deprotonated by the superbasic mixture constituted by butyllithium, potassium *tert*-butoxide, and TMEDA.[41]

Table 1 Metallation of alkenes in the vinylic position

Metallated alkene	*Superbase*	*References*
	LIC-NAOR	42,43
	LIC-NAOR	42,43
	LIC-NAOR	42,43
	LIC-NAOR	44
	NAC-KOR	37,38
	NAC-KOR	37,38
	NAC-NAOR	37,38
	NAC-KOR	45
	LIC-KOR	46
	LIC-KOR or $TMSCH_2K$	47
	LIC-KOR or $TMSCH_2K$	47
	LIC-KOR	48–50

While norbornene, norbornadiene, 2-triallkylsilylnorbornadiene, and 1,3,5-cycloheptatriene are selectively deprotonated by the LIC-NAOR mixture (butyllithium/sodium *tert*-butoxide), other less acidic substrates such as bicyclo[2.2.2]oct-2-ene, camphene, 3,3-dimethyl-1-butene, and *endo*-dicyclopentadiene require the use of stronger bases constituted by mixtures of pentylsodium/disodium pinacolate (NAC-NAOR) or pentylsodium/potassium *tert*-butoxide (NAC-KOR).

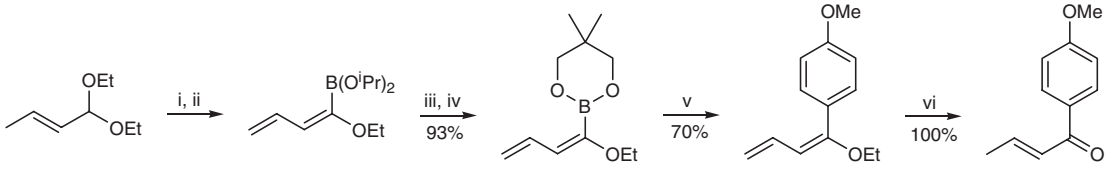
The presence of a heterosubstituent facilitates deprotonation. 4-Methyl-4H-pyran and 1,4-dimethyldihydropyridine are regioselectively metallated at the position next to the heteroatom by LIC-KOR or trimethylsilylmethylpotassium.[47] The metallation of cyclic vinyl ethers with Schlosser's base has been successfully used in the synthesis of C-glycosides[48–50] via metallation of the glucal followed by a reaction with tributyltin chloride to afford the corresponding tin derivative that could be submitted to coupling reactions with various electrophiles.[48]



R = $SiMe_2{}^tBu$

i, LIC-KOR, THF, –78 °C; ii, Bu_3SnCl

Quite recently, it has been reported that α,β-unsaturated acetals, when treated with the superbasic mixture butyllithium/potassium *tert*-butoxide, undergo a conjugate elimination to 1-alkoxy-1,3-dienes which, in the presence of a second equivalent of the superbase, are metallated in the vinylic position adjacent to the oxygen atom. The vinyl metallic intermediate thus formed, has been used in many reactions with electrophilic reagents.[51–54] In particular, reaction with trialkylboranes[55,56] and trialkylborates[57] affords the corresponding vinylboranes or boronates which have been successfully used in palladium-catalyzed cross-coupling processes.[57,58]



i, LIC-KOR 2 equiv., THF, –78 °C; ii, $B(O^iPr)_3$, –78 °C; to 25 °C iii, H_2O

iv,  , toluene, 25 °C

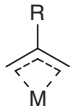
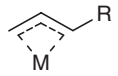
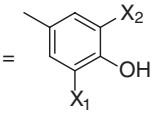
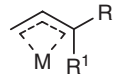
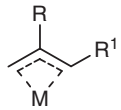
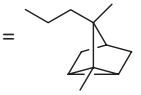
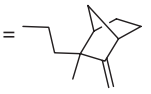
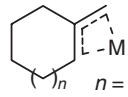
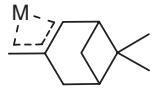
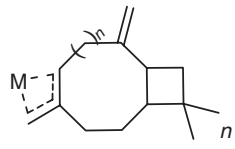
v, K_2CO_3 (2M in H_2O), *p*-$OMeC_6H_4I$, $Pd(PPh_3)_4$ (3%), toluene; vi, amberlyst 15, $CHCl_3$, 25 °C

9.02.4 Metallation of Alkenes, Dienes, and Polyenes at the Allylic Position

The selective and efficient metallation of alkenes in the allylic position by the Schlosser's base is certainly one of the major achievements in the field of superbase chemistry. A complete list of successful alkene metallations by superbases would be too long for the purpose of this chapter but some representative examples are shown in Tables 2 and 3 as a general trend for the unsubstituted and heterosubstituted alkenes, respectively.

Cis-olefins react faster than the corresponding *trans*-isomers.[59,60] The order of reactivity of allylic alkyl groups is methyl > methylene > methine.[21] LIC-KOR is, in general, able to exchange protons of the first two classes while the

Table 2 Metallation of propene and alkylsubstituted derivatives thereof at the allylic position

Compound	*R*	*References*
		62,63
	$R = CH_3$, C_2H_5, $CH(CH_3)_2$, $C(CH_3)_3$	64,65
	$R = CH{=}CH_2$, $C(CH_3){=}CH_2$	65,66
	$R = C_6H_5$, o–C_6H_4–C_6H_5	67
	$R = OCH_3$	68
	$R = CH_3$, C_3H_7–C_9H_{19}	63,69,70
	$R = C(CH_3)_3$	60,71
	$R = C(C_6H_5)_3$	72
	$R = C_6H_5$	21
	$R = (CH_2)_nCH_2CH{=}CH_2$ ($n = 0,2,3,4$)	73
	R =  $X_1 = X_2 = H$; $X_1 = OMe$; $X_2 = H$; $X_1 = H$; $X_2 = OMe$	74
	$R = R^1 = CH_3$, C_2H_5	61
	$R = CH_3$, $R' = C_2H_5$	65
	$R = R^1 = CH_3$; $R = CH_3$; $R^1 = C_2H_5$	65,75
	$R = CH_3$; $R^1 = C_4H_9$; $CH_2C(CH_3)_3$	21
	$R = CH_3$; R^1 = 	76
	$R = CH_3$, R^1 = 	77
	$R = C_2H_5$; $R^1 = C_4H_9$	21
	$R = CH(CH_3)_2$; $R^1 = CH_3$, C_2H_5	65
 $n = 1, 2, 3$		8,78
		70
 $n = 1, 2$		79

(*Continued*)

Table 2 (Continued)

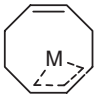
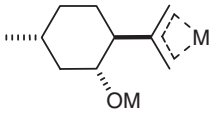
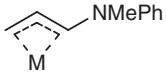
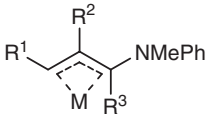
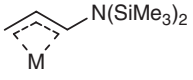
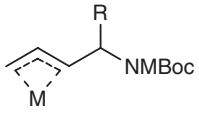
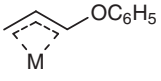
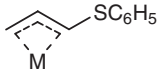
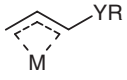
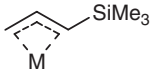
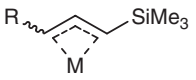
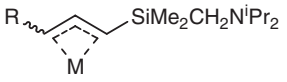
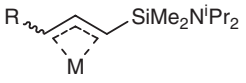
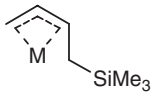
Compound	*R*	*References*
		37
		80
		81

Table 3 Metallation of heterosubstituted alkenes in the allylic position

Compound	*R*	*References*
		82,83
		84–86
		87
		88–90
		62,91
		62
 Y = O, S	R = 	92,93
		60,94,95

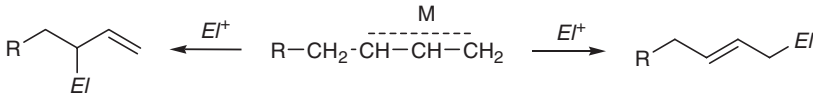
(*Continued*)

Table 3 (Continued)

Compound	*R*	*References*
	$R = CH_3$, C_3H_7, $C_2H_5(CH_3)CH$ $R = C_2H_5$, C_5H_{11}, C_9H_{19} $R = (CH_2)_3OM$, $(CH_2)_5OM$	96,97 63,97 98
		94,99
		100
		101

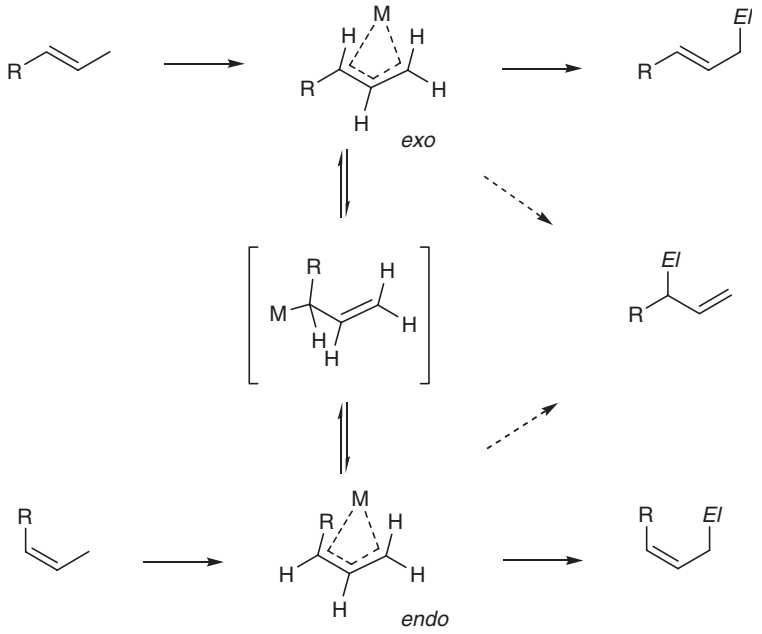
trimethylsilylmethyl potassium reagent (KQ) is required to deprotonate methine centers.[61] Metallation with superbases produce highly nucleophilic 2-alkenylmetal compounds from both 1- and 2-alkenes. They are essentially potassium derivatives, altough they still contain small amounts of lithium.[21]

Allylpotassium compounds have shown to be very useful organometallic intermediates for synthetic applications. In their reactions with electrophiles they behave in a highly regio- and stereoselective manner indeed. While allylmagnesium and allyllithium derivatives react with most electrophiles to preferentially give the branched product resulting from attack at the inner, more substituted position of the allyl unit,[20,21,61] allylpotassium species preferentially give the product carrying the substituent at the terminal position.



Such different behavior, even if not fully understood, has been attributed to a difference in the structure;[75,102–105] Grignard reagents have a monohapto (η^1) structure with the metal being tightly bound to the terminal carbon atom, inducing the attack of the electrophile on the highly negatively charged γ-carbon. On the other hand, allylpotassium reagents have a trihapto (η^3) π–bond with an almost equal charge distribution on the two allylic termini. Electrophilic attack then takes place on the less hindered terminal carbon atom giving the chain lengthened product.

Even more important for synthetic applications is the stereochemical control in the reaction of allylpotassium species with electrophiles. Once the allylic derivative of potassium is formed, it generally shows a high preference for adopting mainly one of the two possible conformations if the reaction mixture is submitted to torsional isomerization under thermal[59,60,69] or catalytic conditions.[106] Once the equilibrium is reached, the *endo*:*exo* distribution is strongly in favor of the former (125:1, 15:1, and 5:1 for 2-butenyl-, 2-pentenyl-, and 4-methy-2-pentenyl potassium, respectively).[21] As a consequence, if a 2-alkene is treated with LIC-KOR in THF at low temperature for a sufficiently long reaction time (usually 15–20 h) and then quenched with an electrophile, the functionalized *cis*-alkene is obtained almost exclusively. In addition, if the starting alkene is chosen either as a pure *cis*- or *trans*-stereoisomer and is then sequentially treated with LIC-KOR and an electrophile without equilibration of the allylpotassium intermediate, the pure *cis*- or *trans*-olefin is obtained, respectively. Such behavior of the allylpotassium reagents has been widely used in the synthesis of stereochemically pure alkenes.

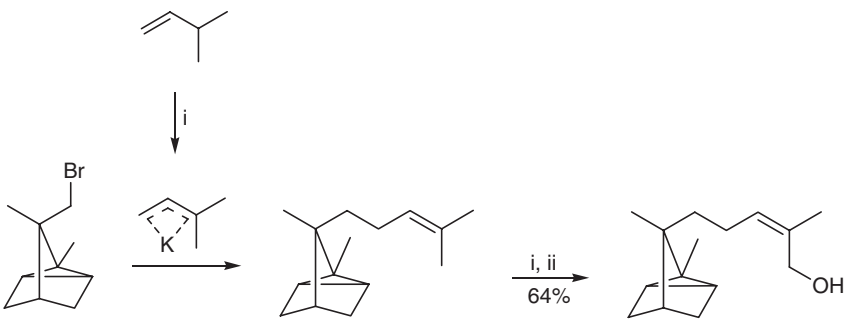


9.02.4.1 Trapping of Allylpotassium Reagents with Carbon Electrophiles

Many stereocontrolled carbon–carbon linking reactions have been described illustrating these principles. Natural insect pheromones have attracted considerable efforts[19–21] as shown by the synthesis of compounds listed in Table 4, all obtained as pure *Z*-isomer through a metallation–equilibration process.

The superbase metallation of alkenes in the allylic position followed by reaction with electrophiles is one of the best methods to access *Z*-alkenes with new functional groups.

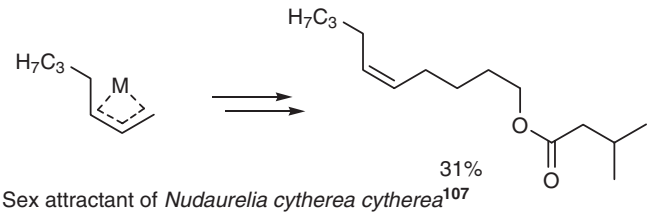
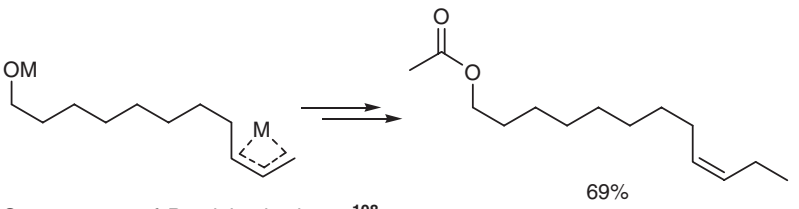
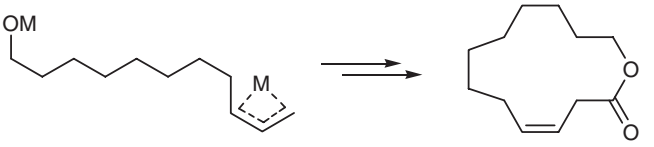
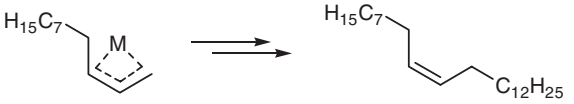
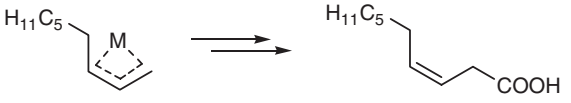
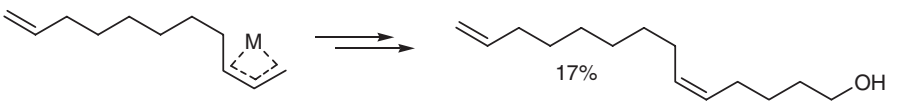
As an example, when phenylpotassium is allowed to react with 8-bromonortricyclene, α-santalene is produced which is then submitted again to metallation with LIC-KOR followed by borylation and oxidation.[76] The allowance for torsional equilibration produces the (*Z*)-α-santalol, one of the main constituents of the highly prized sandalwood oil, with no trace of the (*E*)-isomer. The entire sequence can also be contracted to a one-flask protocol still giving quite acceptable yields.[76]

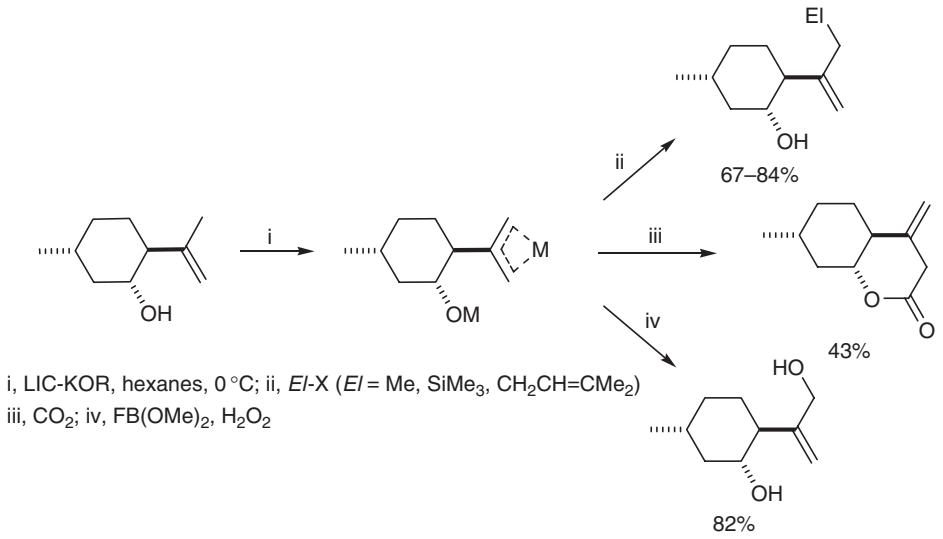


i, LIC-KOR, THF, –50 °C; ii, $FB(OMe)_2$, H_2O_2

A more recent example of alkene metallation by superbase followed by reaction with electrophiles is the functionalization of isopulegol which can be performed without protection of the hydroxy group.[81]

Table 4 Metallation of heterosubstituted alkenes in the allylic position

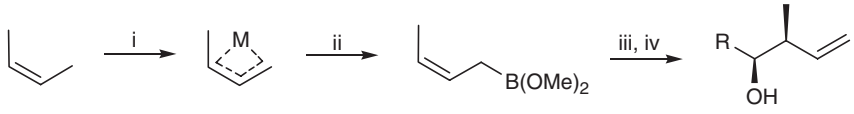
Reactions	*References*
 31% Sex attractant of *Nudaurelia cytherea cytherea*[107]	21
 69% Sex attractant of *Paralobesia viteana*[108]	21
 Pheromone component of *Cryptolestes pusillus*[109] 40%	21
 Sex attractant of *Musca domestica* 77%	110
 Pheromone of *Anthrenus flavipes*[111] 38%	21
 Mandibular secretion of *Cossus* larvae[73]	73



i, LIC-KOR, hexanes, 0 °C; ii, *El*-X (*El* = Me, $SiMe_3$, $CH_2CH{=}CMe_2$)
iii, CO_2; iv, $FB(OMe)_2$, H_2O_2

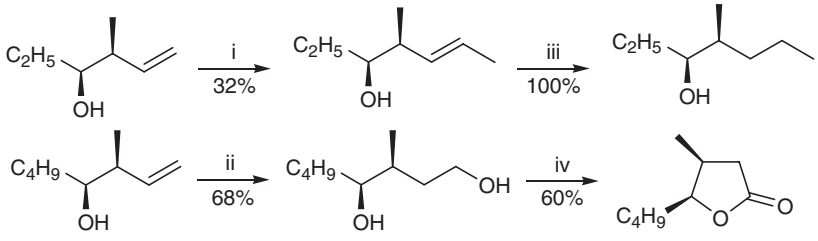
9.02.4.2 Stereoselective Preparation of Allylmetallic Reagents

One of the more interesting applications of allylpotassium reagents is the synthesis of other stereodefined allylmetallic intermediates. Stereochemically pure 2-alkene-boronates or boranes can be obtained via reaction of the alkenylpotassium species with a suitable boron electrophiles.[112–114,70] The corresponding 2-alkene boronates can then be oxidized with hydrogen peroxide in alkaline medium to give allylic alcohols[70] or used for the stereoselective allylation of aldehydes affording *syn*-homoallylic alcohols with high diastereoselectivities.[115,116]



i, LIC-KOR, THF, –50 °C; ii, $FB(OMe)_2$, THF, –75 °C
iii, RCHO (R = C_2H_5, C_5H_{11}, C_6H_5; iv, H_2O

Such a sequence has been successfully used[115] for the synthesis of 4-methyl-3-heptanol, the major constituent of the aggregation pheromone of the elm bark beetle (*Scolytus multistriatus* Marsham)[117] and *cis*-butyl-4-methyltetrahydro-2-furanone[118] known as "quercus lactone" or "oak lactone."

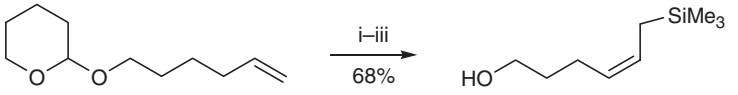


i, Me_3Al-$TiCl_4$, 0 °C, 30 min; ii, BH_3, H_2O_2; iii, H_2; iv, MnO_2, CH_3CN, 25 °C

Dialkylallyl boranes have also been prepared[119] by metallation of alkenes with trimethylsilylmethylpotassium followed by trapping of the allylpotassium species with dialkylchloroboranes. Such allylboranes have been then used

in reactions with carbonyl compounds,[120–123] deuterium oxide,[124] or water in order to effect an overall isomerization of the double bond as in the case of α-pinene,[125] 2-carene[126] and α-thujene.[126]

Stereochemically pure allylsilanes[63,75,98] and stannanes[127] can also be obtained by metallation of suitable olefins with the superbasic mixture of butyllithium and potassium *tert*-butoxide followed by reaction with trimethylchlorosilane and tributylchlorostannane, respectively. In a representative example, 6-(2-tetrahydropyranyloxy)hex-1-ene is transformed into *Z*-(6-hydroxyhex-2-enyl)trimethylsilane through metallation with trimethylsilylmethyl potassium followed by reaction with chlorotrimethylsilane and removal of the hydroxyl protective group.[98]

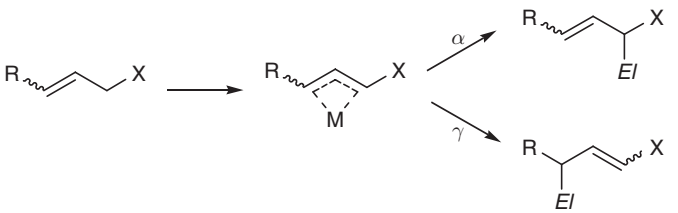


Z: *E* = 98 : 2

i, KCH_2SiMe_3, THF, –50 °C; ii, MeSiCl; iii, $BF_3{\cdot}OEt_2$, 25 °C

9.02.4.3 Reaction of Heterosubstituted Allylmetal Reagents with Electrophiles

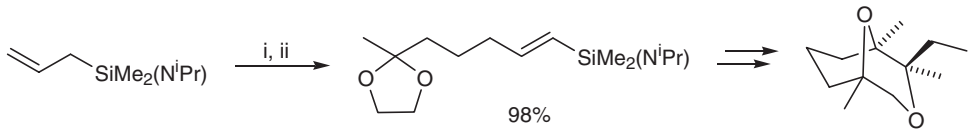
An important regiochemical issue arises when functional groups are present on the olefinic moiety; the electrophilic reagent can enter either the α- or the β-position with respect to the substituent.

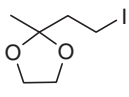


Organolithium reagents are usually basic enough to generate most of the heterosubstituted allylmetals, sometimes in conjunction with activators (e.g., TMEDA) or cosolvent (e.g., HMPA). However, as a change of the counterion may considerably influence the regio- and stereoselectivity of the reaction with electrophiles, many metallations with superbasic reagents have been reported indeed showing that this often allows a good tuning of the reactivity. Several examples have been already shown in Table 3.

Metallation of allylsilanes has been widely investigated[94] showing that the regiochemical outcome of the allylmetallic species is related to the base, the substrate, and the alkylation reagent used. Good level of γ-selectivity (attack on the unsubstituted terminus of the allylmetallic moiety) can be obtained with Schlosser's base[60,97] while deprotonation with TMEDA-activated butyllithium followed by reaction with alkyl halides produces 40 : 60 (α : γ) mixtures of regioisomers.[128,129] Increasing steric hindrance on silicon leads to a higher γ-selectivity, up to 99 : 1 level[94,100,130,131] with perfect (*E*)-stereocontrol. Good levels of α-selectivity are obtained only when the γ-position is substituted and the electrophile is not sterically hindered.[96]

The good γ-selectivity has been successfully applied in the first step of the synthesis of (±)-*exo*-brevicomin.[100]



i, LIC-KOR, Et_2O, –78 °C
ii,  I, –78 °C – 25 °C

9.02.4.4 Metallation of Dienes and Polyenes

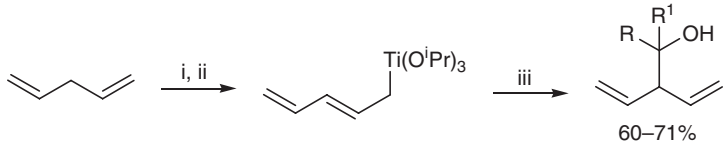
Conjugated and homoconjugated dienes can also be easily metallated by superbases at the activated allylic position, to give rise to pentadienyl type organopotassium species. Their conformation has been the object of careful NMR and synthetic studies as a function of the metal (lithium vs. potassium) and the substitution pattern of the pentadienyl moiety.[21]

The simplest member of the series, the 2,4-pentadienyl metallo species, has been shown by NMR studies,[132,133] to adopt either a W-shape or a U-shape conformation with the metal being lithium[132,133] or potassium, respectively, when both are dissolved in tetrahydrofuran.[134–136] The W-form is adopted by the 2,4-pentadienylpotassium when the organometallic species is generated in liquid ammonia[137] or in paraffinic suspension.[138] This has also been confirmed by the stereochemistry of the products formed after reaction with electrophiles.[134,135,138,139]

The situation becomes more complicated if the pentadienyl moiety carries substituents but it has been found that the potassium species prefers again the U-shape when alkyl substituents are located in position 1-,[140] 2-,[138] and 2,4-[138,141] while the W-shape is adopted by the 3-substitued member.[138]

Understandably, stereoselective reactions with electrophiles become less realistic under circumstances in which a large number of conformations are possible. Nevertheless, some applications have been reported[21,142] concerning the use of pentadienyl metallic species.

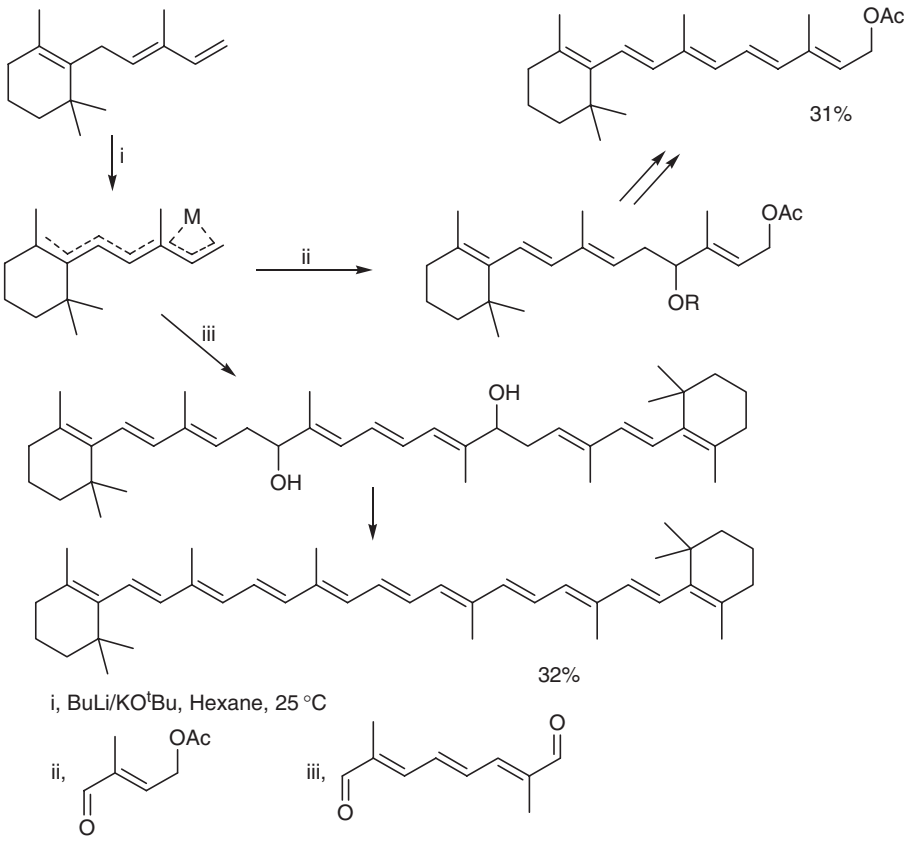
The regioselectivity of the electrophilic attack on the pentadienylpotassium species is related to the nature of the electrophile and the substitution pattern on the dienyl system. In general, halotrialkylsilanes,[139] fluorodimethoxyborane,[139] and chlorotri(isopropyloxy)titanium[143] show a marked preference for the terminal position, thus giving stereochemically pure dienyl derivatives. Carbonyl compounds and alkyl halides react with a lower regioselectivity giving both the conjugated and the non-conjugated dienes. The use of the dienylboron or dienyltitanium reagents prepared as described above circumvents the problem giving a perfect regiocontrol with allylic transposition in reaction with aldehydes.



i, LIC-KOR, THF, –75 °C; ii, $ClTi(O^iPr)_3$, THF, –75 °C; iii, RR^1CO, 25 °C

Heptatrienylpotassium compounds are formed when a triene having an allylic hydrogen atom is deprotonated with superbasic reagents. The number of possible conformations increases but the zigzag band form seems to prevail

often.[21] Such a stereopreference has been used, for example, in the synthesis of vitamin A and β-carotene.[144] The same heptatrienylpotassium intermediate is used and reacted either with (*E*)-formyl-2-butenyl acetate or with (2*E*,4*E*,6*E*)-2,7-dimethyl-2,4,6-octatrienedial to give vitamin A acetate and β-carotene in 31% and 32% yield, respectively.

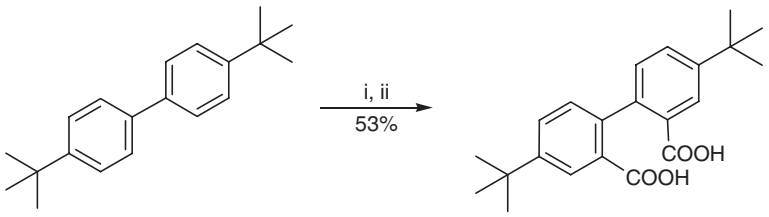


9.02.5 Metallation of Arenes

Benzene and many other aromatic hydrocarbons are readily metallated by superbasic reagents. Monometallation of benzene with butyllithium/potassium *tert*-butoxide (LIC-KOR) using the substrate as a co-solvent was the first revelation of the enormous reactivity of Schlosser's base.[18] According to a more recent study[145] clean monometallation can be accomplished with stoichiometric amounts of benzene only if the reaction is carried out in THF solution. Dimetallation appears to be inevitable in hexane suspension and it may even become predominant if the superbasic mixture is used in excess.[146] *Ortho*-isomers have only been identified in trace amounts, and the *meta*:*para* ratios are always somewhat smaller than unity.[145,147] *tert*-Butylbenzene[145] and (1-methylcyclopropyl)benzene[145] are converted by Schlosser's base into monometallated derivatives with *meta*:*para* ratios of approximately 1:1. Under the same reaction conditions, 1,3-di-*tert*-butylbenzene gives the *meta*-substituted compound[145,148] and 1,4-di-*tert*-butylbenzene is metallated in the highly hindered *ortho*-position[148] under more drastic reaction conditions (high concentration, 1.5 M, and 75 °C). Most of these "spiny" arenes are dimetallated when an excess of highly concentrated butyllithium/potassium *tert*-butoxide mixture in hydrocarbon media is used.[149]

Schlosser's base also metallates 1,1,3,3-tetramethylindane and 1,1,2,2,3,3-hexamethylindane, the *ortho*-analogs of the di-*tert*-butylbenzenes, in hexane at 25 °C.[148] 4,4′-Di-*tert*-butylbiphenyl is efficiently doubly metallated by the

superbasic mixture butyllithium/potassium *tert*-butoxide in hexane at 70 °C affording, after reaction with carbon dioxide, 4,4′-di-*tert*-butylbiphenyl-2,2′-dicarboxylic acid in 53% yield.



i, LIC-KOR, hexanes, 70 °C, 12 h; ii, CO_2

All the above-mentioned metallations of arenes with superbasic reagents are reported in Table 5.

Table 5 Metallation of arenes with superbases

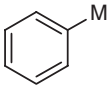
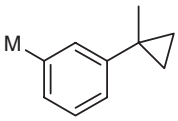
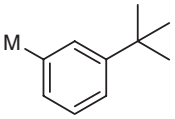
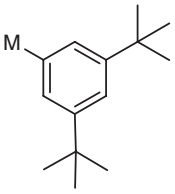
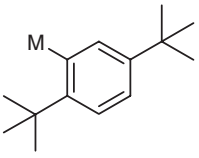
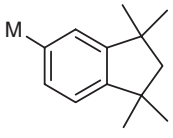
Compound	*References*
	18,145
	145
	145
	145
	148
	148

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Table 5 (Continued)

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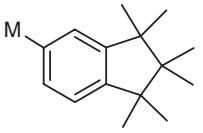
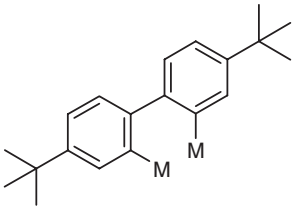
	148
	150

9.02.5.1 Metallation of Heterosubstituted Arenes

The activation provided by heterosubstituents is often strong enough to allow deprotonation of an aryl moiety with simple organolithium reagents. This concept has been largely applied, and the directed *ortho*-metallations (DOM) of aromatic derivatives have proved to be a powerful synthetic tool for functionalization.[151] The *ortho*-directing effect has been attributed either to the electronegativity of the heterosubstituent[152] or to the coordinating property of the electron-donor ligand particularly toward lithium atoms.[153] These two effects (inductive and coordinative) often operate simultaneously[8] and the higher contribution of one with respect to the other depends not only on the heterosusbstituent but also on the deprotonation reagent used. As a rule of thumb, weakly solvated organolithium compounds optimally exploit the coordinative capacities of a substituent, whereas diamine complexed butyllithium or the superbasic mixture butyllithium/potassium *tert*-butoxide preferentially deprotonate such positions where charge excess is most efficiently stabilized.[154] For this reason, even if simple organolithium reagents can be often basic enough to deprotonate heterosubstituted arenes, the use of a superbasic reagent may result in different regiochemical behavior.[155] This mechanism-based matching of neighboring groups and reagents has allowed the metallation of a large number of arenes carrying two different heterosubstituents, with the so-called "optional site selectivity."[8,154–156]

Table 6 reports some representative examples of superbase metallation of heterosubstituted arenes.

Table 6 Metallation of heterosubstituted arenes with superbases

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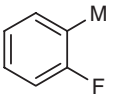
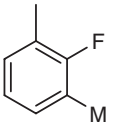
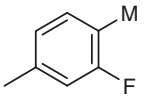
	157
	158
	158

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Table 6 (Continued)

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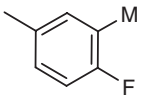
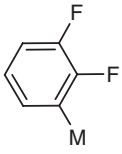
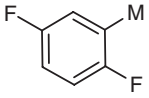
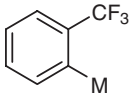
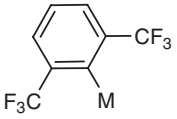
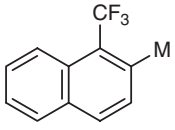
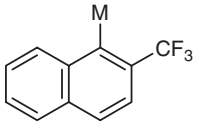
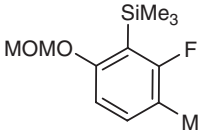
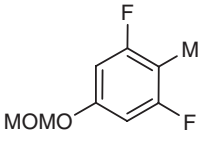
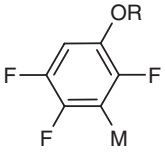
	158
	157
	157
	157,40
	157,40
	8
	159
	160
	161
	161

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Table 6 (Continued)

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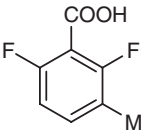
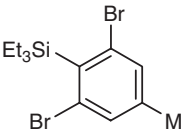
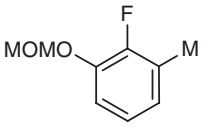
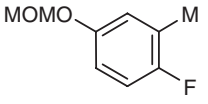
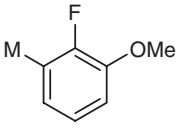
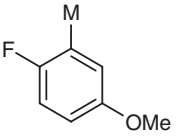
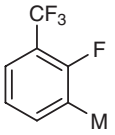
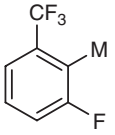
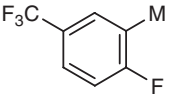
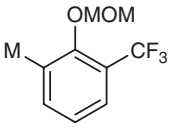
	162
	163
	164
	164
	165
	165
	157
	157
	157
	164

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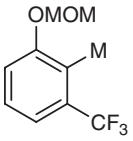
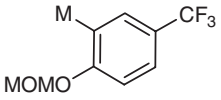
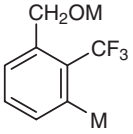
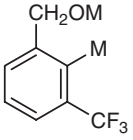
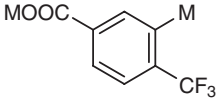
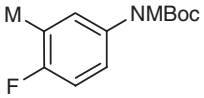
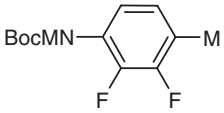
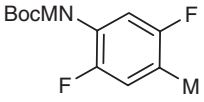
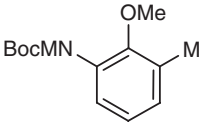
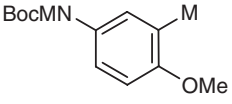
	164
	164
	166
	166
	166
	167
	168
	168
	154
	154

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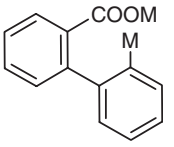
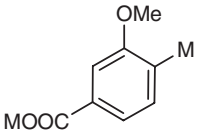
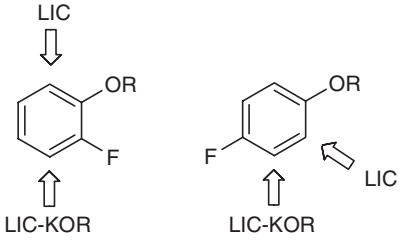
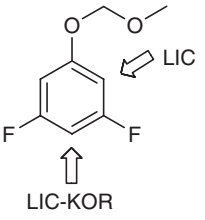
	169
	170

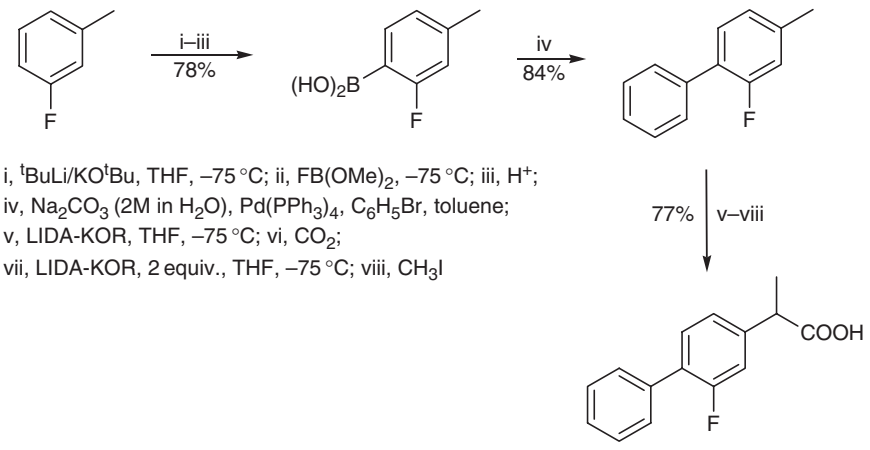
The concept of optional site selectivity is better illustrated by a few examples. Both 2- and 4-fluoroanisole undergo clean deprotonation of an oxygen-adjacent position[165] by butyllithium alone which takes advantage of the coordination by the methoxy group. On the contrary when butyllithium is first complexed with potassium *tert*-butoxide, the metallation occurs at the fluorine adjacent position.[165] The reagent being optimally coordinated this time from the beginning, the relative basicities of the organometallic intermediate now become the crucial factor.



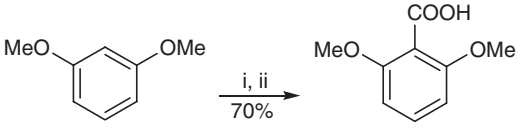
3,5-Difluorophenol offers another example of regioselectivity control through mechanism-matched choice of the reagent. When the methoxymethyl-protected substrate is treated with the superbasic reagent LIC-KOR, only the position adjacent to the two fluorine substituents is metallated and the arylpotassium then intercepted with electrophiles. The use of butyllithium alone in diethylether affords the intermediate, in which the metal has displaced a hydrogen *ortho* to the alkoxy group, even if it is contaminated by the other regioisomer (about 2.4%).[161]



The optional site selective metallation of fluorotoluenes[158] with the superbasic mixture of butyllithium and potassium *tert*-butoxide has been applied to the synthesis of the anti-inflammatory and analgesic drug Flurbiprofen.[171] 3-Fluorotoluene is selectively metallated in the 4-position with LIC-KOR in THF at −75 °C to afford, after reaction with fluorodimethoxyborane and hydrolysis, the corresponding boronic acid in 78% yield. A palladium-catalyzed coupling with bromobenzene gives the 2-fluoro-4-methylbiphenyl in 84% yield. This four-step sequence can also be contracted to a one-pot procedure with an overall yield of 79%. A double metallation with the superbasic mixture lithium diisopropylamide/potassium *tert*-butoxide (LIDA-KOR)[172,173] is then required to produce flurbiprofen.

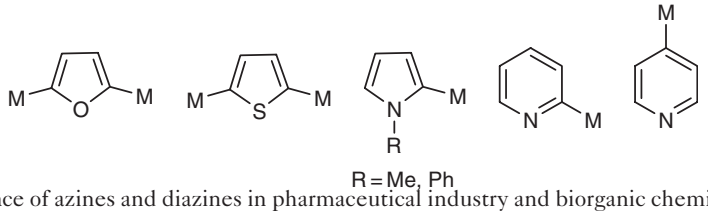


As outlined in the introduction, metallation with superbases is nowadays almost the only method to access organoalkali reagents in a synthetically useful way. However, a recent re-examination of alkylsodium chemistry has shown that an *in situ* procedure can be highly useful.[174] Octylsodium is generated by the treatment of 1-chlorooctane and sodium dispersion in toluene and in the presence of methoxy-substituted aromatic compounds which are efficiently deprotonated and functionalized. This procedure has the advantage of being economical and applicable to large-scale reactions, hence to industrial preparations.[175,176]



9.02.6 Metallation of Hetarenes

The metallation of five-membered heterocycles does not require superbases; it usually suffices the use of organolithium or lithium amide reagents. Furan and tiophene when treated with the superbasic mixture butyllithium/potassium *tert*-butoxide/tetramethylethylendiamine (TMEDA) undergo dimetallation in the 2,5-positions.[177] 1-Methylpyrrole is poorly metallated as compared to the oxygen and sulfur analogs; monometallation occurs using Schlosser's base in THF/hexane at −80 °C.[5,6] N-Phenylpyrrole is also monometallated by Schlosser's base while the use of TMEDA-activated butyllithium gives the *ortho*,α-dimetallated derivative.[178] Azines and diazines are more difficult to deprotonate. Pyridine itself has been monometallated using the Schlosser's base in THF at −100 °C[179,180] with a regioselectivity related to the reaction conditions. Polar medium favors the 4-metallated product, whereas in apolar solvent the 2-substituted product is formed preferentially.[179,180]

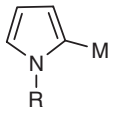
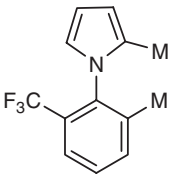
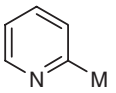
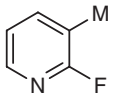
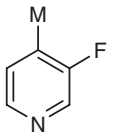
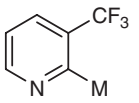
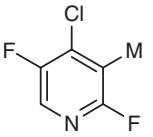
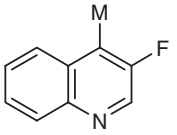


Due to the importance of azines and diazines in pharmaceutical industry and biorganic chemistry, the development of selective and efficient metallation protocols for substituted compounds has been the object of deep investigations.[181–183] The main difficulty in this context is that the π-deficient heteroaromatics undergo a facile nucleophilic addition to the azomethine bond with alkyllithiums.[184–186] For this reason sterically hindered non-nucleophilic lithium amides (lithium diisopropylamide and lithium 2,2,6,6-tetramethylpiperidide)[181,182] are usually employed in the selective deprotonation of heterocyclic compounds. In some cases the use of both unimetallic[183] and

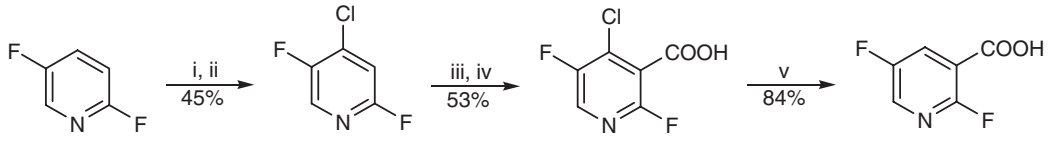
bimetallic superbases[8] is required to achieve a high level of selectivity. A compilation of some examples of superbase metallation of heterocyclic substrates is reported in Table 7.

The introduction of several different substituents on any vacant position of aromatic and heteroaromatic compounds ("regiochemically exhaustive functionalization"[155]) can be often done using a set of different organometallic reactions following the concept of mechanism-based matching of neighboring groups and reagents.[8,155] The superbase approach has been used, for example, in the selective functionalization of polyhalogenated pyridines. 2,5-Difluoropyridine can be monolithiated in position 4 and, after treatment with 1,1,2-trichloro-1,2,2-trifluoroethane,

Table 7 Metallation of heterocycles with superbases

Compound	*References*
 R = Me, Ph	178
	187
	179,180
	188
	188
	189
	190
	188

furnishes 4-chloro-2,5-difluoropyridine in 45% yield. In order to selectively introduce a further substituent on the pyridine ring, there are two options. Lithiation with LTMP in diethyl ether exchanges the hydrogen in position 6, whereas metallation with the superbasic mixture LTMP/KO^{t}Bu/PMDTA ("Faigl's mix") affords the 3-potassium species which can then be quenched with carbon dioxide to give the corresponding carboxylic acid in 53% yield. The final removal of chlorine by treatment with zinc in aqueous ammonia, produces 2,5-difluoropyridine-3-carboxylic acid that could not be obtained by direct lithiation–carbonation of 2,5-difluoropyridine.[190]

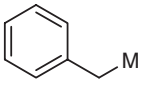
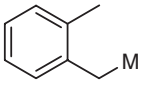
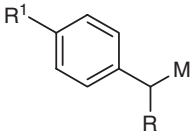
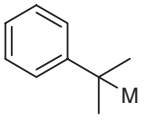
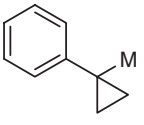


i, LIDA, THF, –75 °C; ii, Cl_2FCCF_2Cl, THF; iii, LTMP/KO^{t}Bu/PMDTA, THF, –75 °C; iv, CO_2; v, Zn, NH_3 (25% in H_2O)

9.02.7 Metallation of Alkylarenes and Alkyl-hetarenes

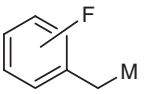
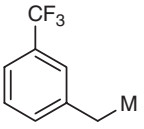
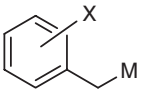
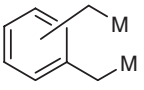
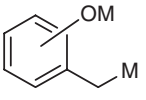
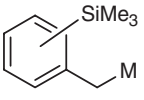
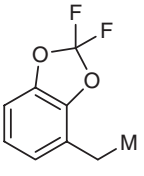
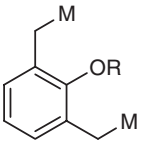
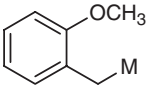
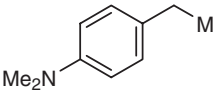
When alkylbenzene derivatives are submitted to metallation, the metal may displace either a benzylic (α) or a ring hydrogen atom (preferably at the sterically unhindered *meta* or *para* positions). To avoid contamination by the ring-metallated derivative, α-deprotonation of toluene needs to be done with Schlosser's base[18,191,192] while, for example, TMEDA-activated butyllithium gives rise to some contamination by ring-metallated products.[193,194] Examples of mono- and dimetallation of alkylbenzenes are reported in Table 8.

Table 8 Metallation of alkylarenes with superbases

Compound	*References*
	18,191,192
	195
	
$R = H$; $R^1 = CH_3$, C_2H_5	196,197
$R = CH_3$; $R^1 = C_2H_5$, $CH_2CH(CH_3)_2$	196
$R = C_2H_5$; $R^1 = H$	198
	37,199
	200

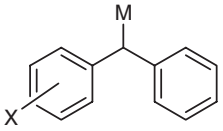
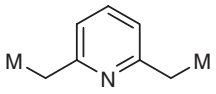
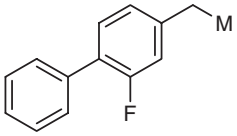
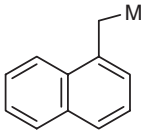
(*Continued*)

Table 8 (Continued)

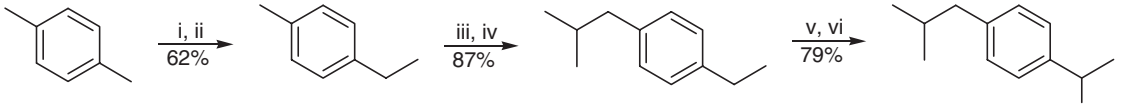
Compound	*References*
 *o*, *m*	158
	158
 *o*, *m*, *p* X = Cl, Br	201
 *o*, *m*, *p*	195,197
 *o*, *m*, *p*	202
 *o*, *m*, *p*	203
	204
	205
	206
	8

(*Continued*)

Table 8 (Continued)

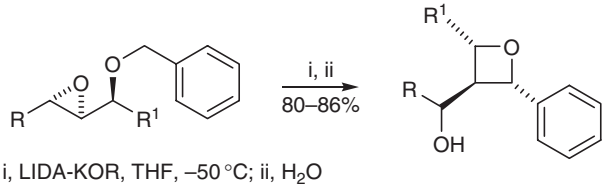
Compound	*References*
 *o*, *m*, *p*-F *p*-OCH_3	207,208
	195,197
	171
	64

The relative reactivity of different alkyl groups on a phenyl ring parallels the one encountered in alkenes: methyl > methylene > methine. This discrimination between benzylic position has been used to design a one-pot synthesis of "ibuprofene," an analgesic with both anti-inflammatory and anti-rheumatic properties. The synthesis has been accomplished[196] by sequential LIC-KOR deprotonation–alkylation starting with *para*-xylene.



i, LIC-KOR, THF, –75 °C; ii, CH_3I, THF; iii, LIC-KOR, hexane, 25 °C; iv, $(CH_3)_2CHBr$, –25 °C; v, LIC-KOR, hexane, 60 °C; vi, CO_2, THF

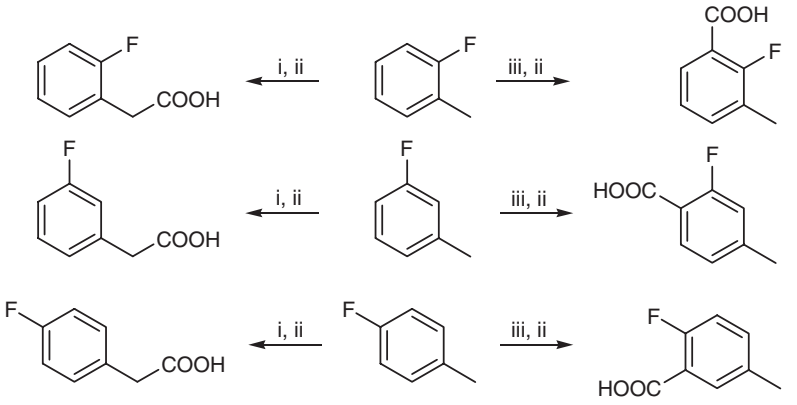
The efficiency of LIDA-KOR in promoting benzylic deprotonation has been employed in the stereoselective synthesis of di- and trisubstituted oxetanes.[209–213] Benzyl oxiranyl ethers are selectively metallated by LIDA-KOR and the resulting benzylmetallic species undergoes a 4-*exo* ring closure affording the corresponding oxetane in good yields and stereoselectivities.



i, LIDA-KOR, THF, –50 °C; ii, H_2O

The use of LIC-KOR and LIDA-KOR in the metallation of heterosubstituted toluenes constitutes a very clear example of mechanism-based matching of neighboring groups and reagents. *Ortho*-, *meta*-, and *para*-fluorotoluenes are exclusively *ortho*-metallated by LIC-KOR giving the corresponding 2-fluro-3-, 2-fluoro-4-, and 2-fluoro-5-methylbenzoic acids after carboxylation.[158] The benzylic positions can instead be selectively deprotonated by using LIDA-KOR under similar reaction conditions.[158,201] The isomeric 2-, 3-, and 4-fluorophenylacetic acids are obtained after

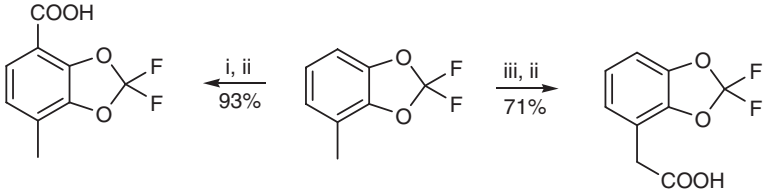
reaction with carbon dioxide in 37%, 62%, and 7% yields, the *ortho*- and *meta*-isomers isomerically pure and the *para*-isomer as a contaminant to the main product, 2-fluoro-5-methylbenzoic acid (53%), resulting from the metallation of an aromatic position.[158,201]



i, LIDA-KOR, THF, –75 °C; ii, CO_2; iii, LIC-KOR, THF, –75 °C

Analog results have been obtained in the metallation of fluoro-substituted diphenylmetanes.[207,208]

An additional example is constituted by 2,2-difluoro-4-methyl-1,3-benzodioxole which is deprotonated by *sec*-butyllithium exclusively at the 7-position, whereas only derivatives of the benzylmetal species are isolated after treatment with LIDA-KOR.[204]



i, LTMP/PMDTA/KO^{t}Bu, THF, –75 °C; ii; CO_2, THF, –75 °C; iii, LIDA-KOR, THF, –75 °C

9.02.8 Conclusion

In summary, as we have seen, neat polar organometallic reagents have been almost completely supplanted by superbase. The ease in their preparation and handling, their stability in most organic solvents at usual temperatures, and their high reactivity coupled with unusual selectivities make these reagents the best choice in most metallation processes to afford organosodium or organopotassium compounds which, in turn, show useful properties in their reaction with electrophiles.

Despite these outstanding features, superbases have not been exploited in full potential yet; future developments in this field are expected in the next years particularly concerning selective metallation of aromatic and hetero-aromatic compounds.

References

1. Wakefield, B. J. In *Comprehensive Organometallic Chemistry I*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 7, p 1.
2. Wardell, J. L. In *Comprehensive Organometallic Chemistry I*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 1, p 43.
3. Mordini, A. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11, p 93.
4. Schlosser, M. *Struktur und Reaktivität polarer Organometalle*; Springer: Berlin, 1973.
5. Brandsma, L.; Verkruijsse, H. D. *Preparative Polar Organometallic Chemistry 1*; Springer: Berlin, 1987.
6. Brandsma, L.; Verkruijsse, H. D. *Preparative Polar Organometallic Chemistry 2*; Springer: Berlin, 1990.
7. Mordini, A. In *Advances in Carbanion Chemistry*; Snieckus, V., Ed.; JAI Press: Greenwich, CT, 1992; Vol. 1, p 1.
8. Schlosser, M. In *Organometallics in Synthesis. A Manual*, 2nd ed.; Schlosser, M., Ed., Wiley: Chichester, 2002.

9. Ebel, H. F.; Lüttringhaus, A. In *Houben-Weyl, Methoden der organischen Chemie*; Müller, E., Ed.; Thieme: Stuttgart, 1970; Vol. 13/1, p 261.
10. Schlosser, M. In *Organometallics in Synthesis. A Manual*; Schlosser, M., Ed.; Wiley: London, 1994.
11. Mordini, A.; Valacchi, M. In *Science of Synthesis*; Majewski, M., Snieckus, V., Eds.; Georg Thieme Verlag: Stuttgart, 2006; Vol. 8b, pp 879–881.

11a. Mordini, A.; Valacchi, M. In *Science of Synthesis*; Majewski, M., Snieckus, V., Eds.; Georg Thieme Verlag: Sturttgart, 2006; Vol. 8b, pp 1197–1227.

12. Mordini, A.; Valacchi, M. In *Science of Synthesis*; Majewski, M., Snieckus, V., Eds.; Georg Thieme Verlag: Stuttgart - New York, 2006; Vol. 8b, pp 1437–1474.
13. Benkeser, R. A.; Foster, D. J.; Sauve, D. M.; Nobis, J. F. *Chem. Rev.* **1957**, *57*, 867.
14. Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 287.
15. Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 362.
16. Morton, A. A. *Chem. Rev.* **1944**, *35*, 1.
17. Schlosser, M.; Faigl, F.; Franzini, L.; Geneste, H.; Katsoulos, G.; Zhong, G.-F. *Pure Appl. Chem.* **1994**, *66*, 1423.
18. Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9.
19. Schlosser, M. *Pure Appl. Chem.* **1988**, *60*, 1627.
20. Schlosser, M. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Verlag Helvetica Chimica Acta: Basel, 1992; Vol. 6, p 227.
21. Schlosser, M.; Desponds, O.; Lehmann, R.; Moret, E.; Rauchschwalbe, G. *Tetrahedron* **1993**, *49*, 10175.
22. Morton, A. A.; Marsh, F. D.; Coombs, R. D.; Lyons, A. L.; Penner, S. E.; Ramsden, H. E.; Baker, V. B.; Little, E. L.; Letsinger, R. L. *J. Am. Chem. Soc.* **1950**, *72*, 3785.
23. Morton, A. A.; Holden, M. E. T. *J. Am. Chem. Soc.* **1947**, *69*, 1675.
24. Morton, A. A.; Claff, C. E.; Collins, F. W. *J. Org. Chem.* **1955**, *20*, 428.
25. Morton, A. A.; Eisenmann, J. L. *J. Org. Chem.* **1958**, *23*, 1469.
26. Benkeser, R. A.; Crimmins, T. F.; Tong, W.-H. *J. Am. Chem. Soc.* **1968**, *90*, 4366.
27. Wofford, C. F. (Phillips Petroleum Co.). U.S. Patent 3,294,768, **1963**.
28. Strobel, C. W. (Phillips Petroleum Co.). U.S. Patent 3,331,821, **1967**.
29. Caubère, P. *Rev. Heteroat. Chem.* **1991**, *4*, 78.
30. Lochmann, L.; Pospišil, J.; Vodnansky, J.; Trekoval, J.; Lím, D. *Collect. Czech. Chem. Commun.* **1965**, *30*, 2187.
31. McGarrity, J. F.; Ogle, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 1805.
32. Brown, T. L.; Ladd, J. A.; Newman, G. N. *J. Organomet. Chem.* **1965**, *3*, 1.
33. Caubère, P. *Chem. Rev.* **1993**, *93*, 2317.
34. Gilman, H.; Bailie, I. C. *J. Org. Chem.* **1937**, *2*, 84.
35. Broaddus, C. D. *J. Org. Chem.* **1964**, *29*, 2689.
36. Broaddus, C. D.; Logan, T. S.; Flautt, T. J. *J. Org. Chem.* **1963**, *28*, 1174.
37. Hartmann, J.; Schlosser, M. *Helv. Chim. Acta* **1976**, *59*, 453.
38. Schlosser, M.; Hartmann, J.; Stähle, M.; Kramar, J.; Walde, A.; Mordini, A. *Chimia* **1986**, *40*, 306.
39. Lehmann, R.; Schlosser, M. *Tetrahedron Lett.* **1984**, *25*, 745.
40. Schlosser, M.; Mongin, F.; Porwisiak, J.; Dmowski, W.; Büker, H. H.; Nibbering, N. M. M. *Chem. Eur. J.* **1998**, *4*, 1281.
41. Brandsma, L.; Verkruijsse, H. D.; Schade, C.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1986**, 260.
42. Stähle, M.; Lehmann, R.; Kramar, J.; Schlosser, M. *Chimia* **1985**, *39*, 229.
43. Verkruijsse, H. D.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 66.
44. Mordini, A.; Schlosser, M. *Chimia* **1986**, *40*, 309.
45. Kumagai, T.; Aga, M.; Okada, K.; Oda, M. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1428.
46. Nativi, C.; Ravidà, N.; Ricci, A.; Seconi, G.; Taddei, M. *J. Org. Chem.* **1991**, *56*, 1951.
47. Schlosser, M.; Schneider, P. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 489.
48. Hanessian, S.; Martin, M.; Desai, R. C. *J. Chem. Soc., Chem. Commun.* **1986**, 926.
49. Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 2572.
50. Schmidt, R. R.; Preuss, R.; Betz, R. *Tetrahedron Lett.* **1987**, *28*, 6591.
51. Venturello, P. *J. Chem. Soc., Chem. Commun.* **1992**, 1032.
52. Prandi, C.; Venturello, P. *J. Org. Chem.* **1994**, *59*, 3494.
53. Prandi, C.; Venturello, P. *J. Org. Chem.* **1994**, *59*, 5458.
54. Balma, T. P.; Deagostino, A.; Prandi, C.; Venturello, P. *J. Chem. Soc., Chem. Commun.* **2001**, 437.
55. Balma, T. P.; Deagostino, A.; Prandi, C.; Venturello, P. *J. Chem. Soc., Chem. Commun.* **2001**, 1536.
56. Deagostino, A.; Prandi, C.; Zavattaro, C.; Venturello, P. *Eur. J. Org. Chem.* **2003**, 2612.
57. Balma, T. P.; Deagostino, A.; Prandi, C.; Venturello, P. *Org. Lett.* **2002**, *4*, 1275.
58. Deagostino, A.; Migliardi, M.; Occhiato, E. G.; Prandi, C.; Zavattaro, C.; Venturello, P. *Tetrahedron* **2005**, *61*, 3429.
59. Thompson, T. B.; Ford, W. T. *J. Am. Chem. Soc.* **1979**, *101*, 5459.
60. Schlosser, M.; Hartmann, J. *J. Am. Chem. Soc.* **1976**, *98*, 4674.
61. Hartmann, J.; Schlosser, M. *Synthesis* **1975**, 328.
62. Hartmann, J.; Muthukrishnan, R.; Schlosser, M. *Helv. Chim. Acta* **1974**, *57*, 2261.
63. Desponds, O.; Franzini, L.; Schlosser, M. *Synthesis* **1997**, 150.
64. Schlosser, M.; Hartmann, J. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 508.
65. Giner, J. L.; Margot, C.; Djerassi, C. *J. Org. Chem.* **1989**, *54*, 2117.
66. Klusener, P. A. A.; Tip, L.; Brandsma, L. *Tetrahedron* **1991**, *47*, 2041.
67. Seyferth, D.; Jula, T. F. *J. Organomet. Chem.* **1974**, *66*, 195.
68. Taherirastgar, F.; Brandsma, L. *Chem. Ber.* **1997**, *130*, 45.
69. Schlosser, M.; Hartmann, J.; David, V. *Helv. Chim. Acta* **1974**, *57*, 1567.
70. Rauchschwalbe, G.; Schlosser, M. *Helv. Chim. Acta* **1975**, *58*, 1094.
71. Stähle, M.; Hartmann, J.; Schlosser, M. *Helv. Chim. Acta* **1977**, *60*, 1730.
72. Moret, E.; Furrer, J.; Schlosser, M. *Tetrahedron* **1988**, *44*, 3539.
73. Moret, E.; Desponds, O.; Schlosser, M. *J. Organomet. Chem.* **1991**, *409*, 83.
74. Rothen, L.; Schlosser, M. *Tetrahedron Lett.* **1991**, *32*, 2475.

75. Schlosser, M.; Dahan, R.; Cottens, S. *Helv. Chim. Acta* **1984**, *67*, 284.
76. Schlosser, M.; Zhong, G.-f *Tetrahedron Lett.* **1993**, *34*, 5441.
77. Zhong, G.-F.; Schlosser, M. *Synlett* **1994**, 173.
78. Moret, E.; Schneider, P.; Margot, C.; Stähle, M.; Schlosser, M. *Chimia* **1985**, *39*, 231.
79. Kotthaus, M.; Schlosser, M. *Tetrahedron Lett.* **1998**, *39*, 4031.
80. Revell, J. D.; Ganesan, A. *J. Org. Chem.* **2002**, *67*, 6250.
81. Schlosser, M.; Kotthaus, M. *Eur. J. Org. Chem.* **1999**, 459.
82. Ahlbrecht, H.; Eichler, J. *Synthesis* **1974**, 672.
83. Weston, J.; Ahlbrecht, H. *Tetrahedron* **1999**, *55*, 2289.
84. Ahlbrecht, H.; Sudheendranath, C. S. *Synthesis* **1982**, 717.
85. Ahlbrecht, H.; Simon, H. *Synthesis* **1983**, 58.
86. Ahlbrecht, H.; Simon, H. *Synthesis* **1983**, 61.
87. Degl'Innocenti, A.; Mordini, A.; Pinzani, D.; Reginato, G.; Ricci, A. *Synlett* **1991**, 712.
88. Franciotti, M.; Mordini, A.; Taddei, M. *Synlett* **1992**, 137.
89. Franciotti, M.; Mann, A.; Mordini, A.; Taddei, M. *Tetrahedron Lett.* **1993**, *34*, 1355.
90. Canali, C.; Mordini, A.; Pecchi, S.; Reginato, G.; Ricci, A. *Unpublished results, presented at OMCOS - VII*, Kobe, Japan, 1993.
91. Schlosser, M.; Strunk, S. *Tetrahedron* **1989**, *45*, 2649.
92. Zhong, G.-F.; Schlosser, M. *Tetrahedron Lett.* **1993**, *34*, 6265.
93. Mordini, A.; Pecchi, S.; Capozzi, G. *Tetrahedron* **1994**, *50*, 6029.
94. Chan, T. H.; Wang, D. *Chem. Rev.* **1995**, *95*, 1279.
95. Koumaglo, K.; Chan, T. H. *Tetrahedron Lett.* **1984**, *25*, 717.
96. Mordini, A.; Palio, G.; Ricci, A.; Taddei, M. *Tetrahedron Lett.* **1988**, *29*, 4991.
97. Schlosser, M.; Franzini, L. *Synthesis* **1998**, 707.
98. Moret, E.; Franzini, L.; Schlosser, M. *Chem. Ber.* **1997**, *130*, 335.
99. Horvath, R. F.; Chan, T. H. *J. Org. Chem.* **1989**, *54*, 317.
100. Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4412.
101. Degl'Innocenti, A.; Mordini, A.; Pagliai, L.; Ricci, A. *Synlett* **1991**, 155.
102. Stähle, M.; Schlosser, M. *J. Organomet. Chem.* **1981**, *220*, 277.
103. Schumann, U.; Weiss, E.; Dietrich, H.; Mahdi, W. *J. Organomet. Chem.* **1987**, *322*, 299.
104. Brownstein, S.; Bywater, S.; Worsfold, D. J. *J. Organomet. Chem.* **1980**, *199*, 1.
105. Whitesides, G. M.; Nordlander, J. E.; Roberts, J. D. *J. Am. Chem. Soc.* **1962**, *84*, 2010.
106. Franzini, L.; Moret, E.; Schlosser, M. *Chem. Ber.* **1997**, *130*, 83.
107. Henderson, H. E., *et al. J. Chem. Soc., Chem. Commun.* **1972**, 686.
108. Roelofs, W. L.; Tette, J. P.; Taschenberg, E. F.; Cameau, A. *Insect Physiol.* **1971**, *17*, 2235.
109. Millar, J. G.; Pierce, H. D.; Pierce, A. M.; Oehlschlager, A. C.; Borden, J. H.; Barak, A. V. *J. Chem. Ecol.* **1985**, *11*, 1053.
110. Moiseenkov, A. M.; Schaub, B.; Margot, C.; Schlosser, M. *Tetrahedron Lett.* **1985**, *26*, 305.
111. Fukui, H.; Matsumura, F.; Ma, M. C.; Burkholder, W. G. *Tetrahedron Lett.* **1974**, *15*, 3563.
112. Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 293.
113. Garcia, J.; Kim, B. M.; Masamune, S. *J. Org. Chem.* **1987**, *52*, 4831.
114. Roush, W. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1986**, *108*, 294.
115. Schlosser, M.; Fujita, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 309.
116. Fujita, K.; Schlosser, M. *Helv. Chim. Acta* **1982**, *65*, 1258.
117. Mori, K. *Tetrahedron* **1977**, *33*, 289.
118. Moret, E.; Schlosser, M. *Tetrahedron Lett.* **1984**, *25*, 4491.
119. Zaidlewicz, M. *J. Organomet. Chem.* **1985**, *293*, 139.
120. Zaidlewicz, M. *Tetrahedron Lett.* **1986**, *27*, 5135.
121. Zaidlewicz, M. *Synthesis* **1988**, 701.
122. Zaidlewicz, M. *J. Organomet. Chem.* **1991**, *409*, 103.
123. Zaidlewicz, M. Preparation of γ-damascone via a borane; PL 147742, **1989**.
124. Zaidlewicz, M.; Panda, C. S. *Synthesis* **1987**, 645.
125. Brown, H. C.; Zaidlewicz, M.; Bhat, K. S. *J. Org. Chem.* **1989**, *54*, 1764.
126. Zaidlewicz, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3847.
127. Desponds, O.; Schlosser, M. *J. Organomet. Chem.* **1991**, *409*, 93.
128. Corriu, R. J. P.; Masse, J.; Samate, D. *J. Organomet. Chem.* **1975**, *93*, 71.
129. Corriu, R. J. P.; Masse, J. *J. Organomet. Chem.* **1973**, *57*, C5.
130. Muchowski, J. M.; Naef, R.; Maddox, M. L. *Tetrahedron Lett.* **1985**, *26*, 5375.
131. Chan, T. H.; Koumaglo, K. *J. Organomet. Chem.* **1985**, *285*, 109.
132. Bates, R. B.; Gosselink, D. W.; Kaczynski, J. A. *Tetrahedron Lett.* **1967**, *8*, 205.
133. Ford, W. T.; Newcomb, M. *J. Am. Chem. Soc.* **1974**, *96*, 309.
134. Yasuda, H.; Yamauchi, M.; Ohnuma, Y.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1481.
135. Yasuda, H.; Ohnuma, Y.; Yamauchi, M.; Tani, H.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2036.
136. Schlosser, M.; Stähle, M. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 145.
137. Heiszwolf, G. J.; Kloosterziel, H. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 807.
138. Schlosser, M.; Rauchschwalbe, G. *J. Am. Chem. Soc.* **1978**, *100*, 3258.
139. Schlosser, M.; Zellner, A.; Leroux, F. *Synthesis* **2001**, 1830.
140. Bosshardt, H.; Schlosser, M. *Helv. Chim. Acta* **1980**, *63*, 2393.
141. Ernst, R. D.; Freeman, J. W.; Swepston, P. N.; Wilson, D. R. *J. Organomet. Chem.* **1991**, *402*, 17.
142. Schlosser, M.; Bosshardt, H.; Walde, A.; Stähle, M. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 303.
143. Zellner, A.; Schlosser, M. *Synlett* **2001**, 1016.
144. Rauchschwalbe, G.; Zellner, A.; Schlosser, M. *Eur. J. Org. Chem.* **2001**, 3903.

145. Schlosser, M.; Choi, J. H.; Takagishi, S. *Tetrahedron* **1990**, *46*, 5633.
146. Lochmann, L.; Fossatelli, M.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1990**, *109*, 529.
147. Lochmann, L. *Collect. Czech. Chem. Commun.* **1987**, *52*, 2710.
148. Baston, E.; Wang, Q.; Schlosser, M. *Tetrahedron Lett.* **2000**, *41*, 667.
149. Baston, E.; Maggi, R.; Friedrich, K.; Schlosser, M. *Eur. J. Org. Chem.* **2001**, 3985.
150. Schlosser, M.; Mangano, G.; Leroux, F. *Eur. J. Org. Chem.* **2004**, 1014.
151. Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.
152. Young, S.; Coblens, K. E.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 4887.
153. Morton, A. A. *J. Am. Chem. Soc.* **1947**, *69*, 969.
154. Maggi, R.; Schlosser, M. *J. Org. Chem.* **1996**, *61*, 5430.
155. Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **2005**, *44*, 376.
156. Mongin, F.; Maggi, R.; Schlosser, M. *Chimia* **1996**, *50*, 650.
157. Schlosser, M.; Katsoulos, G.; Takagishi, S. *Synlett* **1990**, 747.
158. Takagishi, S.; Schlosser, M. *Synlett* **1991**, 119.
159. Cottet, F.; Castagnetti, E.; Schlosser, M. *Synthesis* **2005**.
160. Marzi, E.; Bobbio, C.; Cottet, F.; Schlosser, M. *Eur. J. Org. Chem.* **2005**, 2116.
161. Marzi, E.; Gorecka, J.; Schlosser, M. *Synthesis* **2004**, 1609.
162. Rausis, T.; Schlosser, M. *Eur. J. Org. Chem.* **2002**, 3351.
163. Heiss, C.; Marzi, E.; Schlosser, M. *Eur. J. Org. Chem.* **2003**, 4625.
164. Marzi, E.; Schlosser, M. *Tetrahedron* **2005**, *61*, 3393.
165. Katsoulos, G.; Takagishi, S.; Schlosser, M. *Synlett* **1991**, 731.
166. Marzi, E.; Spitaleri, A.; Mongin, F.; Schlosser, M. *Eur. J. Org. Chem.* **2002**, 2508.
167. Takagishi, S.; Katsoulos, G.; Schlosser, M. *Synlett* **1992**, 360.
168. Andringa, H.; Verkruijsse, H. D.; Brandsma, L.; Lochmann, L. *J. Organomet. Chem.* **1990**, *393*, 307.
169. Tilly, D.; Samanta, S. S.; De, A.; Castanet, A.-S.; Mortier, J. *Org. Lett.* **2005**, *7*, 827.
170. Nguyen, T.-H.; Chau, N. T. T.; Castanet, A.-S.; Nguyen, K. P. P.; Mortier, J. *Org. Lett.* **2005**, *7*, 2445.
171. Schlosser, M.; Geneste, H. *Chem. Eur. J.* **1998**, *4*, 1969.
172. Margot, C.; Schlosser, M. *Tetrahedron* **1985**, *26*, 1035.
173. Mordini, A.; BenRayana, E.; Margot, C.; Schlosser, M. *Tetrahedron* **1990**, *46*, 2411.
174. Gissot, A.; Becht, J.-M.; Desmurs, J.-R.; Pevere, V.; Wagner, A.; Mioskowski, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 340–343.
175. Wagner, A.; Mioskowski, C.; Gissot, A.; Desmurs, J. R.; Jost, S. (Rhodia Chimie). WO 0064905, 2000.
176. Pévère, V.; Desmurs, J. R.; Mioskowski, C.; Wagner, A.; Gissot, A. (Rhodia Chimie). WO 9959941, 1999.
177. Feringa, B. L.; Hulst, R.; Rikers, R.; Brandsma, L. *Synthesis* **1988**, 316.
178. Faigl, F.; Schlosser, M. *Tetrahedron* **1993**, *49*, 10271.
179. Verbeek, J.; George, A. V. E.; de Jong, R. L. P.; Brandsma, L. *J. Chem. Soc., Chem. Commun.* **1984**, 257.
180. Verbeek, J.; Brandsma, L. *J. Org. Chem.* **1984**, *49*, 3857.
181. Mongin, F.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 4059.
182. Turck, A.; Plé, N.; Mongin, F.; Quéguiner, G. *Tetrahedron* **2001**, *57*, 4489.
183. Gros, P.; Fort, Y. *Eur. J. Org. Chem.* **2002**, 3375.
184. Ziegler, K.; Zeiser, H. *Ber. Dtsch. Chem. Ges.* **1930**, *63*, 1847.
185. Giam, C. S.; Stout, J. I. *J. Chem. Soc., Chem. Commun.* **1969**, 142.
186. Giam, C. S.; Knaus, E. E.; Pasutto, F. M. *J. Org. Chem.* **1974**, *39*, 3565.
187. Fogassy, K.; Harmat, V.; Böcskei, Z.; Tárkányi, G.; Toke, L.; Faigl, F. *Tetrahedron: Asymmetry* **2000**, *11*, 4771.
188. Shi, G.-Q.; Takagishi, S.; Schlosser, M. *Tetrahedron* **1994**, *50*, 1129.
189. Schlosser, M.; Marull, M. *Eur. J. Org. Chem.* **2003**, 1569.
190. Bobbio, C.; Schlosser, M. *J. Org. Chem.* **2005**, *70*, 3039.
191. Lochmann, L.; Trekoval, J. *J. Organomet. Chem.* **1987**, *326*, 1.
192. Lochmann, L.; Petranek, J. *Tetrahedron Lett.* **1991**, *32*, 1483.
193. Chalk, A. J.; Hoogeboom, T. J. *J. Organomet. Chem.* **1968**, *11*, 615.
194. Broaddus, C. D. *J. Org. Chem.* **1970**, *35*, 10.
195. Bach, R. D.; Klix, R. C. *Tetrahedron Lett.* **1986**, *27*, 1983.
196. Faigl, F.; Schlosser, M. *Tetrahedron Lett.* **1991**, *32*, 3369.
197. Bates, R. B.; Ogle, C. A. *J. Org. Chem.* **1982**, *47*, 3949.
198. Thurner, A.; Agai, B.; Faigl, F. *J. Chem. Res. (S)* **1998**, 158.
199. Schlosser, M.; Strunk, S. *Tetrahedron Lett.* **1984**, *25*, 741.
200. Schlosser, M.; Schneider, P. *Helv. Chim. Acta* **1980**, *63*, 2404.
201. Faigl, F.; Marzi, E.; Schlosser, M. *Chem. Eur. J.* **2000**, *6*, 771.
202. Bates, R. B.; Siahaan, T. J. *J. Org. Chem.* **1986**, *51*, 1432.
203. Masson, E.; Schlosser, M. *Org. Lett.* **2005**, *7*, 1923.
204. Schlosser, M.; Gorecka, J.; Castagnetti, E. *Eur. J. Org. Chem.* **2003**, 452.
205. Bates, R. B.; Gangwar, S.; Kane, V. V.; Suvannachut, K.; Taylor, S. R. *J. Org. Chem.* **1991**, *56*, 1696.
206. Schlosser, M.; Maccaroni, P.; Marzi, E. *Tetrahedron* **1998**, *54*, 2763.
207. Gualtieri, F.; Mordini, A.; Pecchi, S.; Scapecchi, S. *Synlett* **1996**, 447.
208. Gualtieri, F.; Mordini, A.; Pecchi, S.; Scapecchi, S. *Tetrahedron* **1998**, *54*, 2251.
209. Mordini, A.; Bindi, S.; Pecchi, S.; Degl'Innocenti, A.; Reginato, G.; Serci, A. *J. Org. Chem.* **1996**, *61*, 4374.
210. Mordini, A.; Bindi, S.; Pecchi, S.; Capperucci, A.; Degl'Innocenti, A.; Reginato, G. *J. Org. Chem.* **1996**, *61*, 4466.
211. Mordini, A.; Valacchi, M.; Nardi, C.; Bindi, S.; Poli, G.; Reginato, G. *J. Org. Chem.* **1997**, *62*, 8557.
212. Mordini, A.; Bindi, S.; Capperucci, A.; Nistri, D.; Reginato, G.; Valacchi, M. *J. Org. Chem.* **2001**, *66*, 3201.
213. Thurner, A.; Faigl, F.; Toke, L.; Mordini, A.; Valacchi, M.; Reginato, G.; Czira, G. *Tetrahedron* **2001**, *57*, 8173.

9.03
Magnesium

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9.03.1 Introduction

Organomagnesium reagents are used widely in all fields of organic synthesis. The rapid growth of the chemistry of Grignard reagents during the last decade is mostly connected with the availability of new methods for their preparation which are compatible with the presence of the functional groups. The recent developments in the field of organomagnesium chemistry have been reviewed in the last decade.[1,1a,1b] Transmetallation to less reactive and more chemoselective (zinc, copper, titanium, etc.,) organometallic species allows a fine-tuning of their reactivity pattern. Here, we consider mainly reactions of organomagnesium compounds in the presence (or absence) of catalysts. Although the structure of organomagnesium species was investigated for many years, the application of modern techniques gave new data concerning their constitution in solid phase and THF solution[2] and will not be emphasized herein.

9.03.2 Preparation of Grignard Reagents

9.03.2.1 Direct Oxidative Addition of Magnesium to Organic Halides

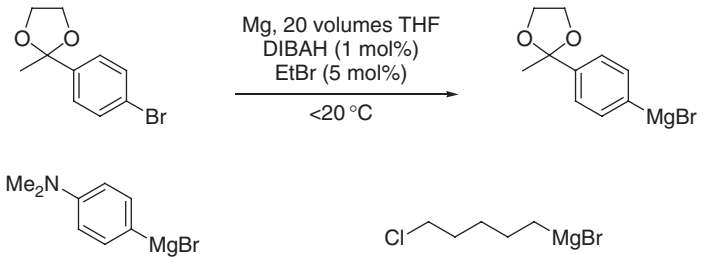
The oxidative addition of magnesium metal to organic halides is most widely used in industry and laboratory as the simplest route to a variety of unfunctionalized Grignard reagents. Solvents such as THF or diethyl ether are usually

used, although for safety reasons, they can be substituted by less flammable high-boiling glycol ethers. Use of non-ethereal solvents like toluene can offer some new applications.[3,4] The surface of magnesium is covered by an "oxide" layer that is actually mainly $Mg(OH)_2$.[5] The detailed mechanism of Grignard reagents formation is still being investigated.[6,7] The properties of the metal surface play an important role in this process and may lead to different reactivity patterns.[8] Due to the widespread use of organomagnesium compounds in industrial chemistry, safe and robust methods for plant scale performance of the magnesium insertion reaction are of high importance. Usually, activation of the magnesium surface is desired to shorten the induction period, and for the reproducibility of the reaction time. A new method of activation of Mg metal by the use of diisobutylaluminium hydride (DIBAH) allows running the reaction at 0–10 °C, which is crucial for the preparation of some reagents of lower stability (Scheme 1).[9]

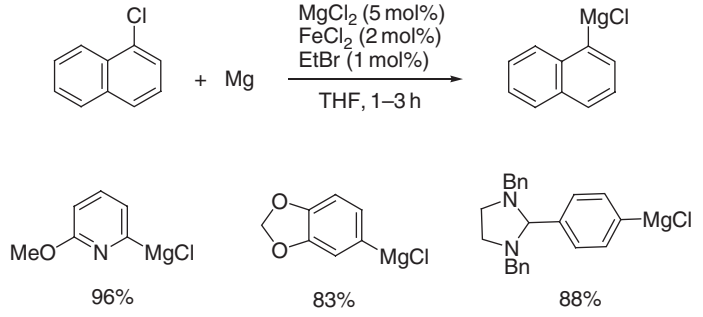
Transition metal catalysis has been applied in this process. In the presence of 2 mol% $FeCl_2$, low reactive aryl chlorides rapidly give aryl Grignard reagents in excellent yields (Scheme 2).[10]

A catalytic cycle, involving the formation of "inorganic Grignard" $Fe(MgX)_{0–2}$, and its oxidative addition to ArCl was postulated for this process. A highly reactive magnesium, developed by Rieke,[11,11a] can be used for the synthesis of Grignard reagents at low temperatures (−78 °C). Since organomagnesium compounds react in such conditions only with active electrophiles like aldehydes or ketones, a number of functional groups, not compatible with the usual methodology, are tolerated (Scheme 3).[12]

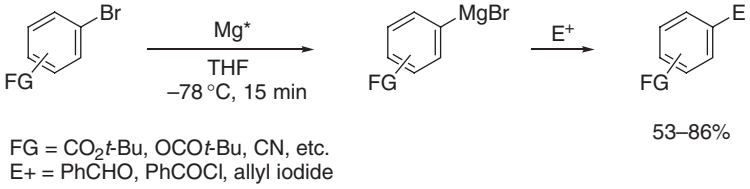
The reaction of heteroaryl halides with Rieke Mg, performed in the presence of electrophiles (Barbier conditions), affords sometimes better results than the usual stepwise method (Scheme 4).[13,14]



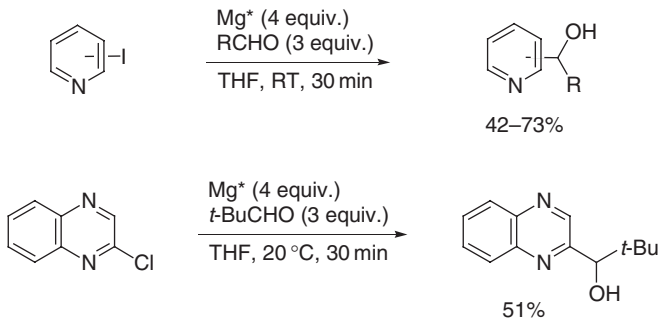
Scheme 1



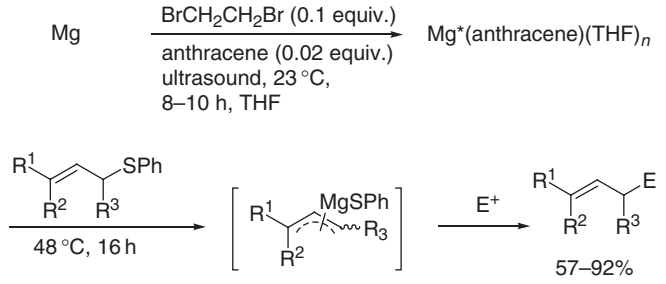
Scheme 2



Scheme 3



Scheme 4



Scheme 5

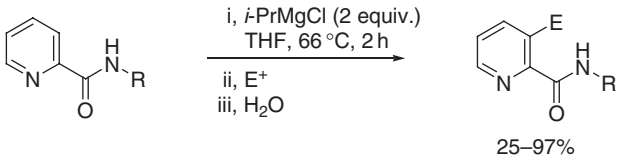
The reductive metallation of aryl sulfides allows the preparation of organolithium compounds. Cohen showed that soluble Mg–anthracene complex can be used instead of Li–naphthalenide for the reductive metallation of allyl phenyl sulfides (Scheme 5).[15]

9.03.2.2 Metallation Reactions with Magnesium Amides

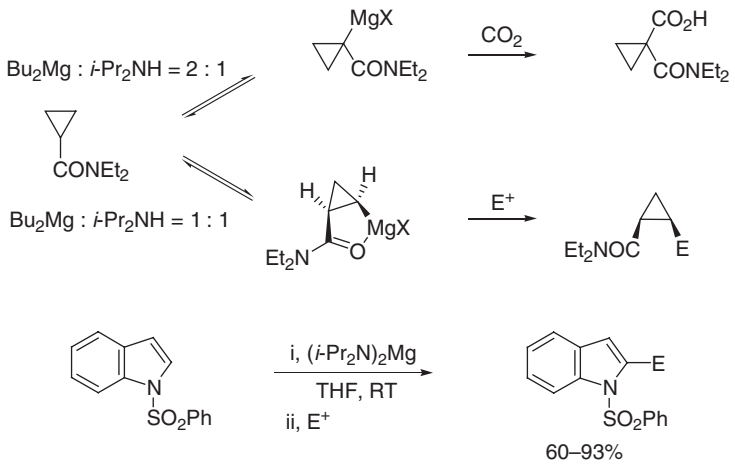
Alkylmagnesium reagents are strongly basic. Nevertheless, the slow rate of the direct metallation reaction makes this reaction often impractical. Alkylmagnesium compounds can be used as metallating agents for some heterocyclic compounds bearing an activating group although metallation often competes with the addition reactions (Scheme 6).[16]

3-Substituted pyridines undergo exclusively 1,4-addition and 4-substituted pyridines give a mixture of products.[16] The reaction of alkylmagnesium reagents with sterically hindered amines leads to the formation of magnesium amides (bis-amides or alkyl-monoamides, depending on the ratio of the reagents and their nature), reacting much faster than the parent alkylmagnesiums with C–H acidic substrates. These reagents, studied mostly by Eaton, allow the direct magnesiation of acidic compounds like cyclopropanes[17] and heterocyclic[18,19] derivatives under mild conditions (Scheme 7).

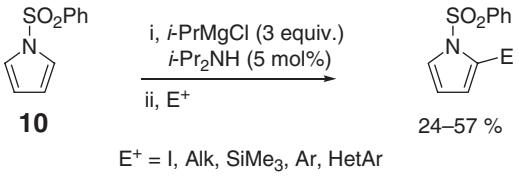
An amine can also be used in catalytic quantities, allowing a simple functionalization of a pyrrole (Scheme 8).[20]



Scheme 6



Scheme 7



Scheme 8

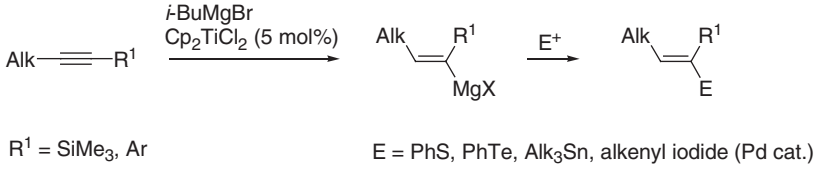
The chemistry of magnesium bis-amides has been reviewed.[21] Magnesium bis-amides have been used for the region- and stereoselective formation of enolates.[22,22a] Enantioselective enolization with chiral magnesium amides has been applied in asymmetric synthesis.[23,23a]

9.03.2.3 Hydromagnesiation of Olefins and Acetylenes

The addition reaction of MgH_2 to olefins leading to Grignard reagents was developed by Bogdanović.[24] The reaction of Mg metal with 1,4-diarylbutadienes gives complexes which mostly behave as usual Grignard reagents.[25]

The hydromagnesiation of acetylenes, catalysed by titano- and zirconocenes is well known. A regioselective reaction occurs only if one of the substituents on the triple bond is silicon or an aryl group. Studies on its mechanism were reported by Sato.[26,27] Cai has applied this reaction for the synthesis of a number of polysubstituted alkenes (Scheme 9).[28,28a–28c]

Uncatalyzed hydromagnesiation of 1,3-alkadienes with *i*-PrMgCl gives a mixture of magnesiated alkenes.[29] Reaction of 2-alkyl-1,3-butadienes with *n*-PrMgX in the presence of Cp_2TiCl_2 affords allyl Grignard reagents as a single regioisomer in excellent yields.[30]



Scheme 9

9.03.2.4 The Halogen–Magnesium Exchange Reaction

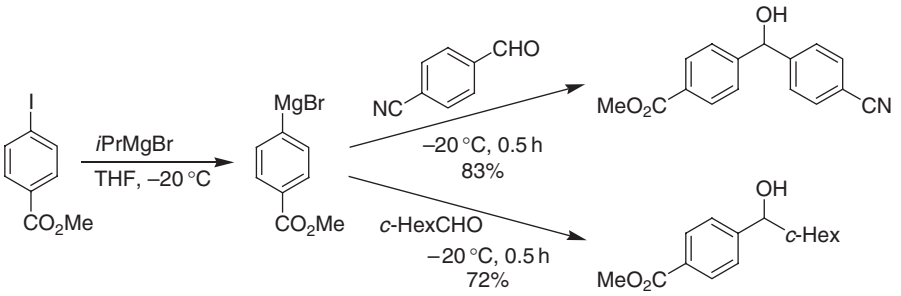
The halogen–lithium exchange suffers from the drawback of low functional group compatibility. In contrast, the halogen–magnesium exchange has been found as an excellent method for the preparation of polyfunctionalized organomagnesium reagents.[31] The reactivity order (I > Br >> Cl) is dictated by the bond strength, electronegativity, and polarizability of the halide. Only for very electron-poor systems like perfluorobenzenes the exchange of a chlorine atom is possible. For these reasons, aryl iodides are the most common substrates, although aryl bromides are more advantageous from the economical point of view. Preparation of Grignard compounds by a halogen/magnesium exchange reaction between alkyl (usually isopropyl) magnesium and aryl-, vinyl-, or cyclopropyl halogenide has found a great impact in the last decade, and a broad scope of substrates have been involved in this reaction.

Functionalized iodoarenes react readily with *i*PrMgCl or *i*PrMgBr in THF already below 0 °C, sometimes even at −78 °C, affording a range of functionalized arylmagnesium iodides.[32] Thus, treatment of methyl 4-iodobenzoate with *i*PrMgBr in THF at −20 °C provides after 30 min the corresponding Grignard reagent, which smoothly reacts with aldehydes at this temperature (Scheme 10).[33]

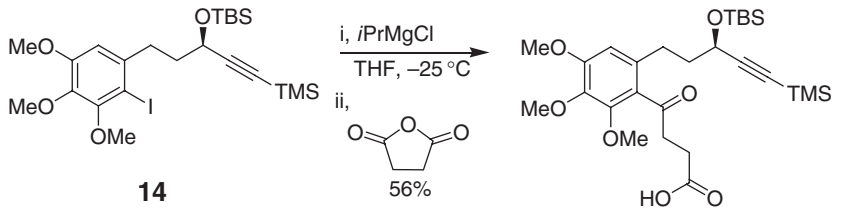
Aromatic iodides, bearing electron-donating groups usually require higher temperatures and prolonged reaction time. Although, even a highly electron-rich system possessing three methoxy groups was successfully subjected to iodine–magnesium exchange reaction in a total synthesis of colchicines (Scheme 11).[34]

Nickel catalyzes the halogen–magnesium exchange between aryl Grignard reagents and aryl halides.[35] The magnesium exchange reaction tolerates an impressive number of functional groups. The amino function can be protected in various ways. In some cases, iodoanilines can be directly used in the exchange reaction (Scheme 12).[36]

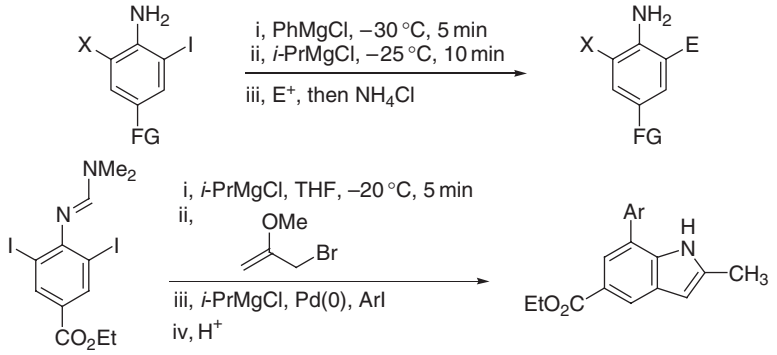
Aryl iodides, bearing an aldehyde function, can be subjected to an I/Mg- exchange reaction after conversion of the aldehyde to an imine.[37] A nitro group is rather reactive toward organomagnesium reagents. Nevertheless, the exchange reaction is facile in case of *ortho*-nitroaryl iodides if less reactive phenylmagnesium chloride is used instead of *i*-PrMgCl for performing the exchange reaction. For nitro-containing substrates, bearing an additional coordinating group or with blocked *ortho*-positions, the exchange of *meta*- and *para*-iodine is also possible (Scheme 13).[38]



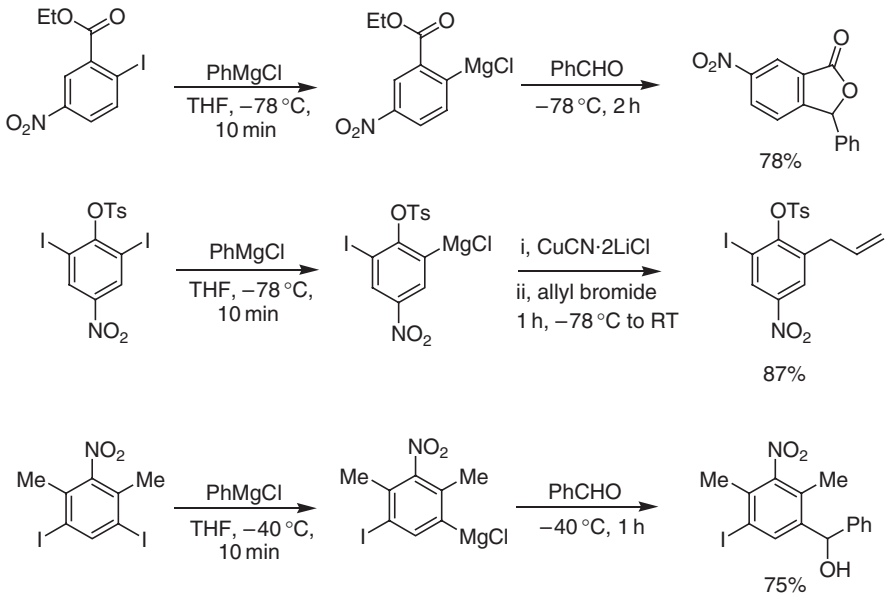
Scheme 10



Scheme 11



Scheme 12



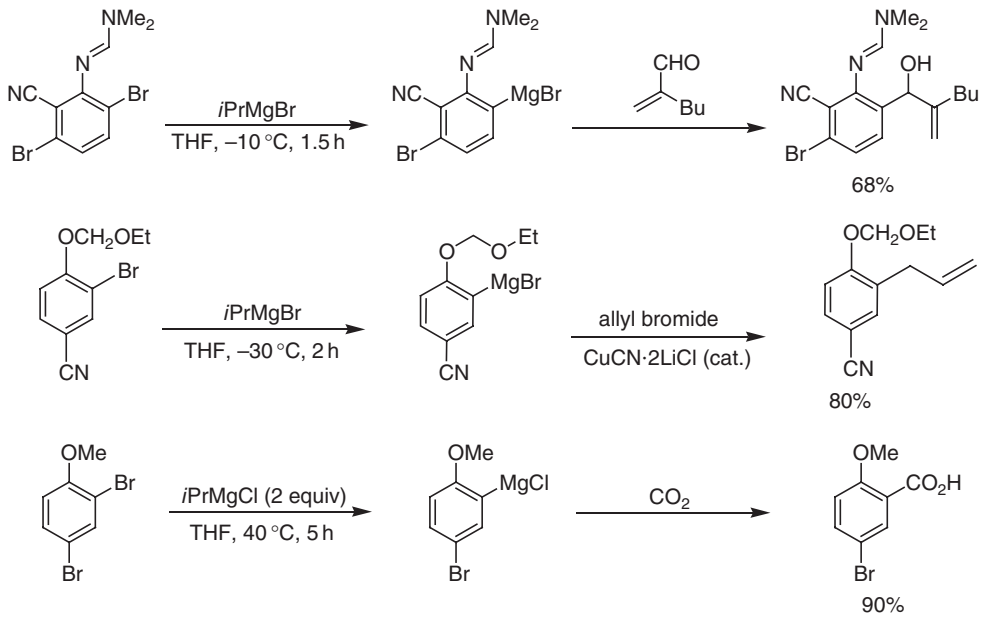
Scheme 13

Polyfunctional aryl bromides, bearing a chelating function *ortho* to bromine readily undergo a bromine–magnesium exchange.[39,40,40a] Even the less effective methoxy group directs the substitution in the case of 2,4-dibromoanisole (Scheme 14).[41]

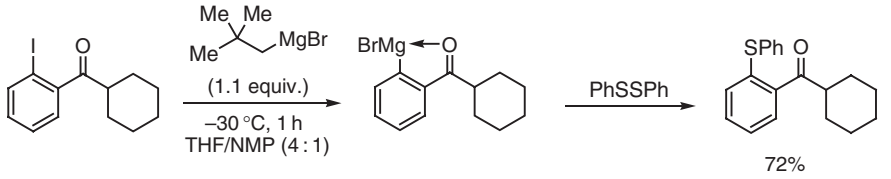
The Br/Mg exchange reaction of 3,5-bis(trifluoromethyl)bromobenzene is the method of choice in the large-scale production of 3,5-bis(trifluoromethyl)acetophenone for safety and reliability, in comparison with the usual Mg insertion process.[42] By tuning the reaction conditions, the preparation of ketone-containing arylmagnesium species group can be achieved. To avoid side-reactions, a sterically hindered but reactive Grignard reagent was used. *neo*-Pentylmagnesium bromide (NpMgBr) in conjunction with *N*-methylpyrrolidinone (NMP) as a polar co-solvent increases the rate of the iodine–magnesium exchange and leads to a complete reaction at −30 °C within 1 h (Scheme 15) (for the utility of neopentyl organometallics in zinc and copper chemisty, see Refs: 43, 43a, and 43b).

ortho-Iodobenzyl chlorides undergo the I/Mg- exchange reaction, leading after the reaction with electrophiles to substituted benzoannulated heterocycles (Scheme 16).[44]

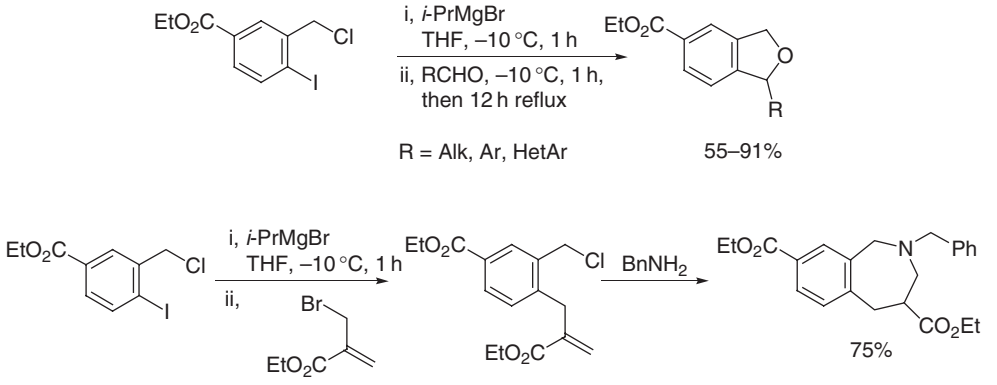
The iodine–magnesium exchange on *ortho*-iodoaryl sulfonates leads, after warming up, to the formation of functionalized arynes, which can be trapped by dienes or nucleophiles (Scheme 17).[45,46] Hetaryl iodides react with *i*-PrMgCl in THF giving the corresponding magnesium compounds in excellent yields (Scheme 18).[47,47a,47b]



Scheme 14

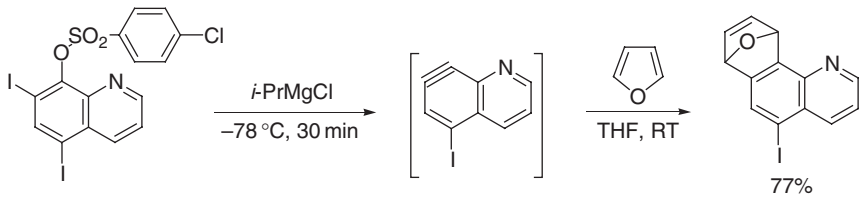


Scheme 15

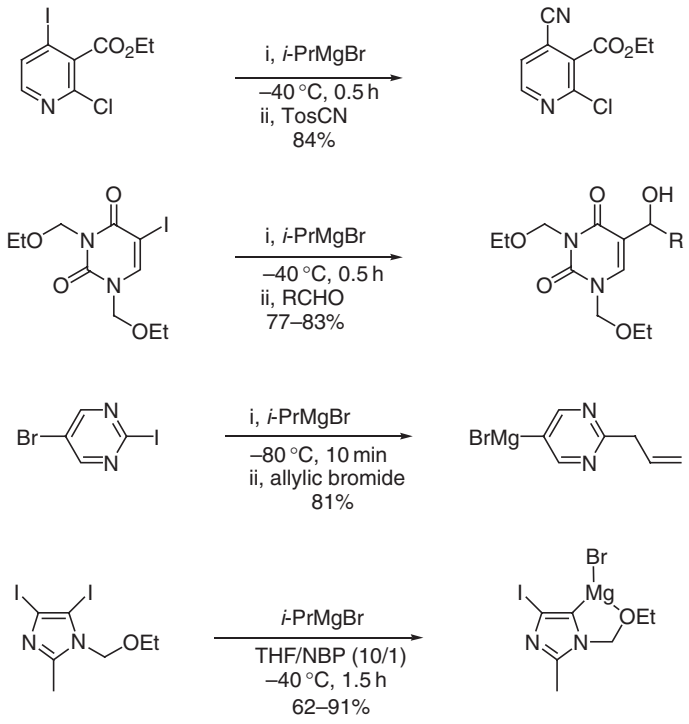


Scheme 16

Iodo-substituted pyridines,[48,49] uracils,[48,50] purines,[51] imidazoles,[48,52] quinolines,[53] imidazo[1,2-a]-pyridines,[54] pyrroles,[55,55a] and isoxazoles[56] undergo readily an I/Mg exchange reaction. At the temperatures required for the exchange, functional groups like an ester or a nitrile are tolerated. Bromopyridines are reactive enough to undergo the exchange with *i*-PrMgCl at room temperature.[57] The selective formation of 2- or 3-substituted bromothiophenes can



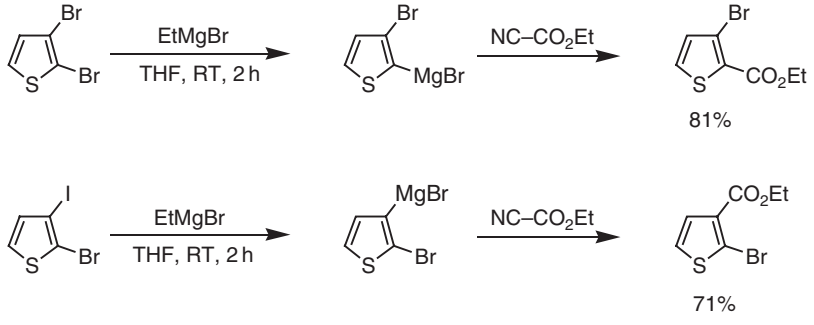
Scheme 17



Scheme 18

also be achieved by a halogen–magnesium exchange. Treatment of 2,3-dibromothiophene with EtMgBr gives only the 2-magnesiated product, whereas 2-bromo-3-iodothiophene exchanges selectively the iodine atom (Scheme 19).[58]

Bach has used the selective exchange reaction on 2,4-dibromothiazole for the synthesis of substituted 4-bromothiazoles.[59,59a] Lithium magnesiates, prepared by the reaction of an organolithium reagent (2 equiv.) and an



Scheme 19

alkylmagnesium halide (1 equiv.), are substantially more reactive than usual Grignard reagents and allow a Br/Mg exchange on various aryl bromides.[60] Even 0.5 equiv. of the lithium dibutylmagnesiate relative to the aromatic halide is sometimes sufficient (Scheme 20).

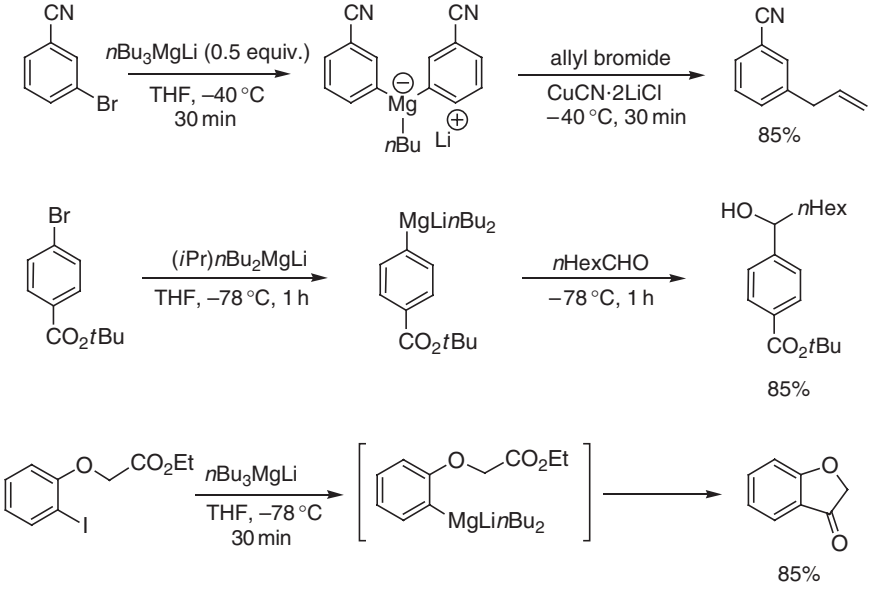
The exchange reaction on functionalized alkenyl halides was limited to reactions on systems bearing either an electron-withdrawing group in α-position[61] or a coordinating substituent in β-position (Scheme 21).[62]

In the case of β-dibromoacrylic esters, the halogen, placed *cis*- to the ester function, is exchanged selectively due to the strong intramolecular coordination (Scheme 21).[63]

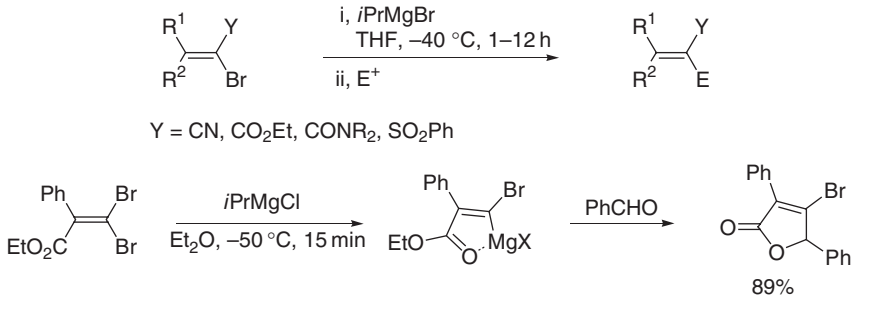
The aryl sulfoxide moiety may serve as a good leaving group in the exchange reaction. Thus, 1-haloalkenyl sulfoxides undergo exchange at −78 °C to give carbenoid compounds which can be trapped by electrophiles or further converted to acetylenes (Scheme 22).[64]

The iodine–magnesium exchange of allenyl iodides takes place by the action of *i*PrMgBr in ether. Subsequent reaction with aldehydes and ketones gives homopropargylic alcohols with high regioselectivity.[65] Exchange on chloroalkyl phenyl sulfoxides was also performed successfully.[66,67,68] It was applied to the synthesis of various olefins[69] as well as for the preparation of a chiral Grignard reagent, starting from a chiral sulfoxide (Scheme 23).[70,71]

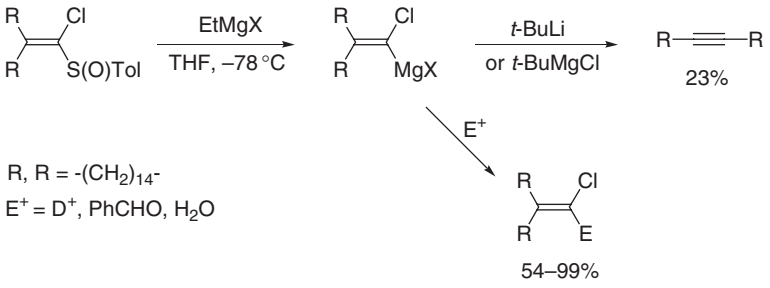
Exchange reactions of alkyl halides are synthetically useful mostly in the case of alkyl iodides bearing an α-halogen or α-acyloxy substituent. The resulting Grignard reagents react smoothly with various electrophiles (Scheme 24).[69,72,72a,72b]



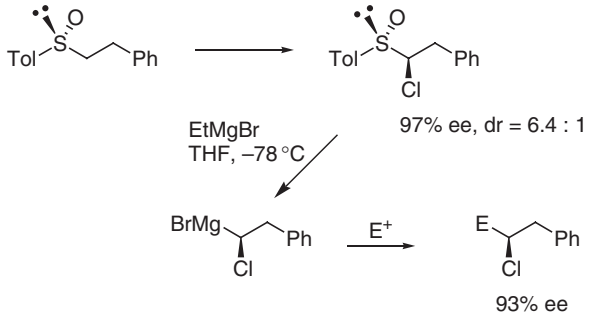
Scheme 20



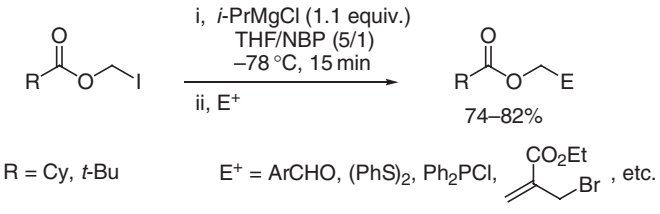
Scheme 21



Scheme 22



Scheme 23

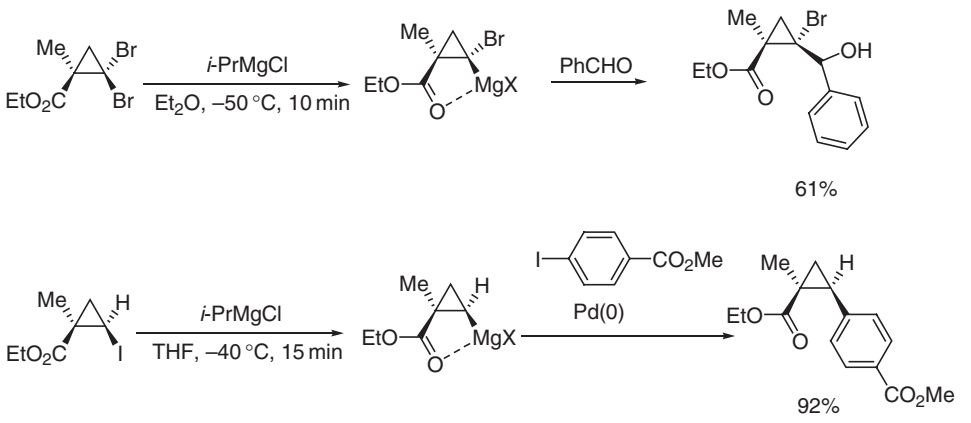


Scheme 24

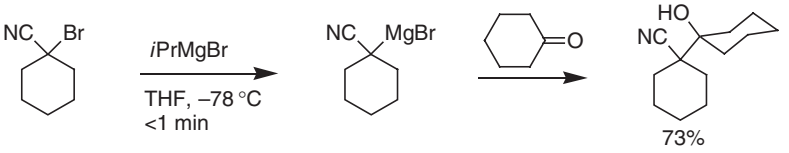
Exchange on iodoacetaldehyde allyl acetals in DME gave tetrahydrofurane derivatives by an intramolecular radical cyclization. In THF the mixture of open-chain and cyclized products is produced.[73] Cyclopropyl iodides and bromides are good substrates for the exchange reaction.[69,74,75,75a] The reaction is stereoselective and sufficiently fast at low temperatures, thus allowing the preparation of highly functionalized compounds. If a coordinating group like an ester is present in a *gem*-dihalocyclopropane, the *cis*-halogen substituent is exchanged selectively in ether (Scheme 25).[75,75a]

Magnesium cyclopropylidenes were generated by an exchange reaction on 1-chlorocyclopropyl phenyl sulfoxides with EtMgCl or *i*PrMgCl. They are conformationally stable below −60 °C.[76] Azyridinyl magnesium species are prepared by a sulfoxide–magnesium exchange and trapped by alkyl halides in the presence of a copper catalyst.[77] Although α-metallated aliphatic nitriles are usually generated by a deprotonation reaction, the halogen–magnesium exchange on α-bromonitriles can be used successfully.[78] The exchange is instantaneous at −78 °C, and reactions with electrophiles proceed smoothly (Scheme 26).

Treatment of (dibromomethyl)methyldiphenylsilane with Bu_3MgLi at −78 °C leads to a smooth exchange reaction. Addition of CuCN–LiCl causes migration of the butyl group affording α-silyl substituted magnesium species. They react with allyl bromide, acyl chlorides, or α,β-enones in the presence of a copper catalyst.[79,79a]



Scheme 25

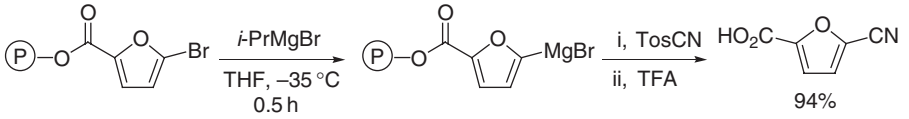


Scheme 26

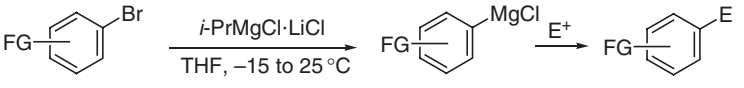
The halogen–magnesium exchange reaction can be easily applied to solid-phase synthesis,[72a,80,81] affording polymer-bound Grignard reagent, otherwise unavailable (Scheme 27).

Unactivated aryl bromides do not react with *i*-PrMgCl even at room temperature in a sufficient rate. Recently, Knochel and Krasovskiy found that the presence of 1 equiv. of LiCl in the reaction mixture enhances the exchange rate, thus allowing even the use of electron-rich aryl bromides in this reaction (Scheme 28).[82]

The yields of the resulting arylmagnesium reagents with electrophiles are substantially higher than in the absence of LiCl. Besides, LiCl ensures a very good solubility of the reaction products such as magnesium alcoholates in the reaction mixture, making the whole process much easier to handle. In the presence of LiCl, *ortho*-iodophenols can be converted to the corresponding Grignard reagent without protection of the hydroxyl function (Scheme 29).[83]

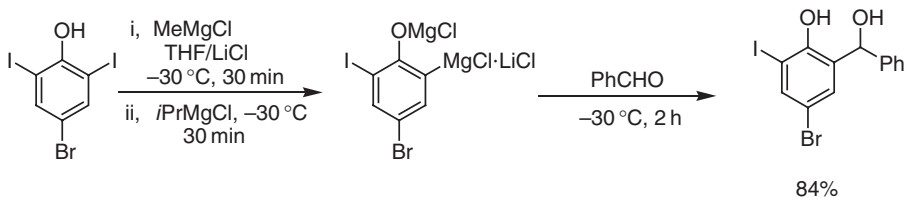


Scheme 27



FG = F, Cl, Br, CN, CO_2R, OMe

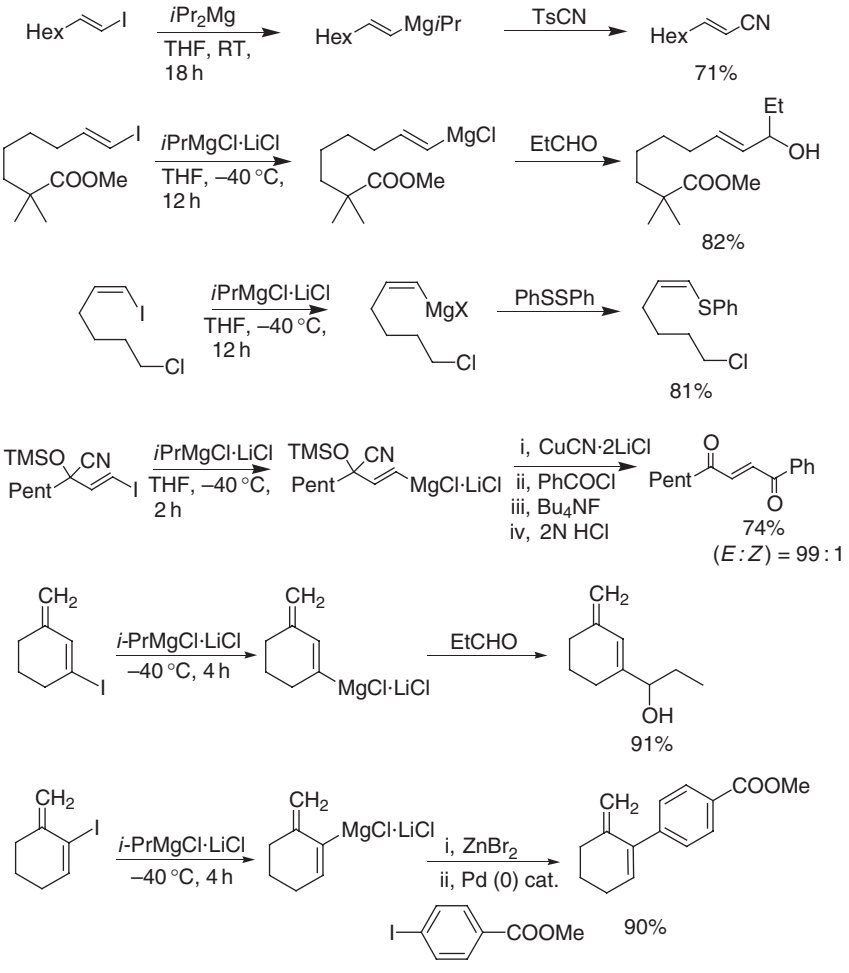
Scheme 28



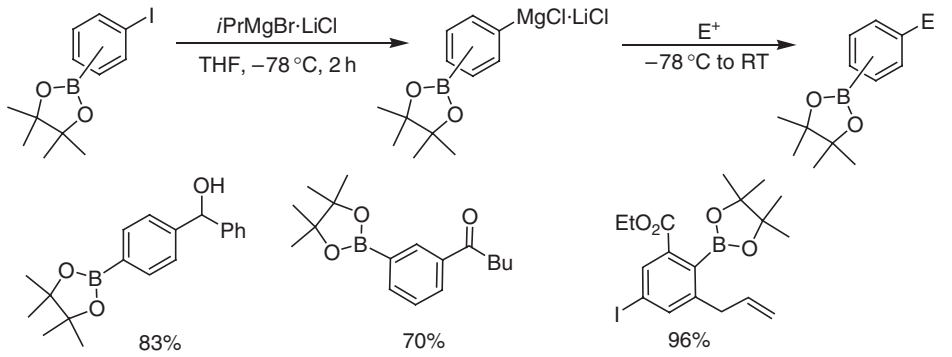
Scheme 29

The exchange in the presence of LiCl can be successfully used for the functionalization of *ortho*-dibromo- and tribromobenzenes, since the low temperatures permit the generation of unstable *o*-bromoarylmagnesium species. Although unfuctionalized alkenyl iodides react with *i*PrMgCl or $i\text{Pr}_2\text{Mg}$, the reaction proceeds only at 25 °C or even at higher temperatures, thus precluding the presence of sensitive groups. The use of *i*-PrMgCl·LiCl makes the exchange reaction possible on unactivated alkenyl iodides bearing functional groups. Complete retention of the double bond configuration was observed. Also, a number of iododienes have been used as substrates (Scheme 30).[84]

High activity of *i*-PrMgCl·LiCl in the exchange reaction allows the preparation of highly functionalized aryl- and hetaryl pinacolborates by the exchange reaction in the presence of boronic ester (Scheme 31).[85]



Scheme 30



Scheme 31

9.03.2.5 Miscellaneous Methods

Triple bond of arynes is highly reactive toward reactions with nucleophiles. Functionalized arynes, prepared from *ortho*-iodoaryl sulfonates by iodine–magnesium exchange followed by the elimination reaction of *ortho*-magnesio-aryl sulfonates, react with a number of heteroatomic nucleophiles, like R_2NMgX, RSMgX, RSeMgX, and partially with R_2PMgX, generating novel Grignard species. These species can be successfully trapped by electrophiles (Scheme 32).[45,46]

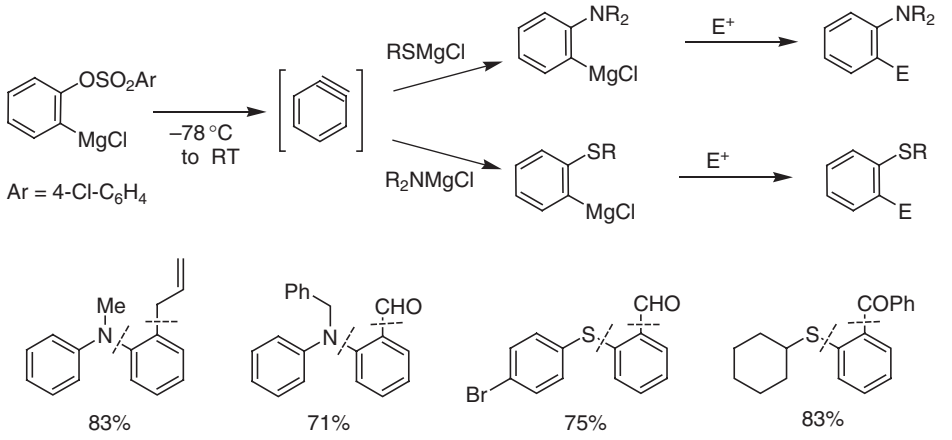
Similarly, the reaction of aryl Grignard reagents with arynes, prepared *in situ* from 2-fluorophenyllithium, gave after iodolysis sterically encumbered substituted 2-iodobiphenyls.[86]

Some alkyl or alkenylmagnesium compounds were obtained via carbometallation or ring-opening reactions with other Grignard reagents. These methods are described in the sections dedicated to the addition to multiple bonds or substitution reactions.

9.03.3 Reactivity of Grignard Reagents

9.03.3.1 Scope and Classification

Due to the versatility of the reactions of organomagnesium reagents we have divided them into two major groups: substitution and addition reactions. Cross-coupling reactions of all kinds, allylic substitutions, and ring opening of aziridines will be considered in the section dedicated to substitution reactions, whereas carbomagnesiation and 1,4-addition reactions will be discussed in the section dealing with addition reactions. Addition–elimination reactions will



Scheme 32

be discussed in the substitution section. Substitution reactions are subdivided into three groups according to the degree of unsaturation at the electrophilic center of the substrate. Reactions of allylic electrophiles usually give mixtures of S_N2 and S_N2' products. For convenience, these reactions are considered in Section 9.03.3.2.2.(ii) at the sp^2-carbon center.

9.03.3.2 Substitution Reactions

9.03.3.2.1 Substitution at sp^3 center

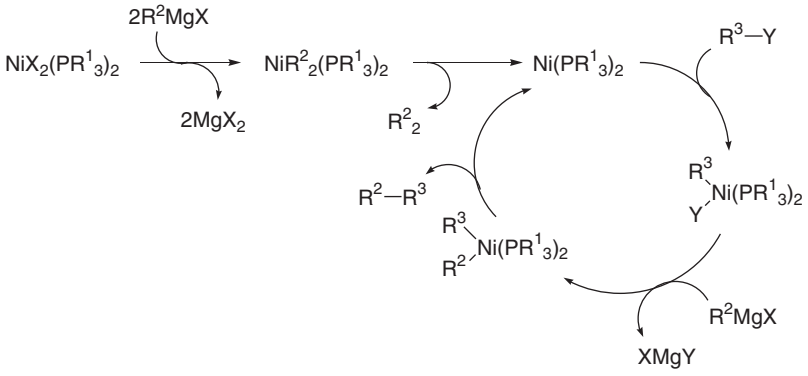
9.03.3.2.1.(i) Transition metal-catalyzed cross-coupling reactions of alkyl halides and sulfonates

In comparison with sp^2–sp^2 bond formation, sp^3–sp^2 couplings in the presence of Pd or Ni salts are more difficult to perform. As for unactivated alkyl electrophiles, oxidative addition to a metal center is slow and β-hydride elimination is generally a fast competing process. Kambe showed that in the presence of 1,3-butadiene *n*-alkyl bromides and tosylates can be coupled with aryl- and alkylmagnesium reagents using 3% $Pd(acac)_2$ as a catalyst.[87] Nickel catalysts are somewhat more effective and the reactions are completed already at 0 °C with 1% mol $NiCl_2$ and 30% mol of butadiene.[88] Arylmagnesium bromides undergo Pd-catalyzed cross-couplings with primary alkyl chlorides in the presence of strong electron-donating ligands (PCy_3, IMes).[89,90] The widely accepted mechanism for Ni- (or Pd)-catalyzed reaction is described in Scheme 33.

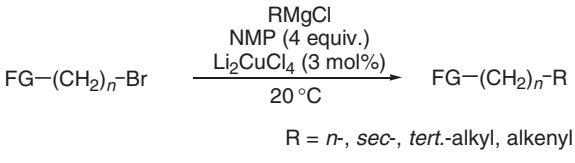
Li_2CuCl_4 in THF–NMP efficiently catalyzes the reaction of alkenyl Grignard reagents with primary alkyl bromides. Functional groups (ketone, ester, nitrile, sulfonate) are tolerated in this reaction (Scheme 34).[91]

Cyclizations can be achieved if an organomagnesium reagent bears a remote leaving group. A stereoselective substitution without erosion of the optical purity was observed by using copper catalysis (Scheme 35).[92]

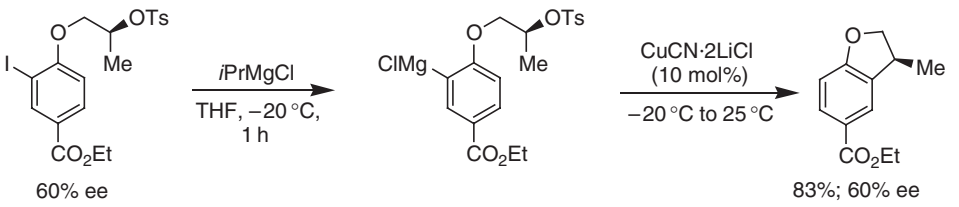
Copper thiophenolate–LiBr in THF is found to be a superior catalyst for the reaction of various organomagnesium reagents, including aryl, with primary alkyl tosylates and *n*-AlkMgBr with secondary tosylates.[93] In the presence of $CuCl_2$ (3% mol), primary alkyl fluorides react smoothly with tertiary alkyl Grignard reagents. Primary and secondary alkyl Grignard compounds require the addition of butadiene, whereas aryl magnesium derivatives react only at elevated temperatures.[94] 1,3-Butadienyl-2-magnesium chloride, derived from chloroprene, is easily alkylated by alkyl ω-bromonitriles in the presence of 5 mol% CuBr.[95] An amino–organomanganese complex in the presence of copper efficiently catalyzes the reaction of various alkylmagnesium chlorides with alkyl bromides (Scheme 36).[96]



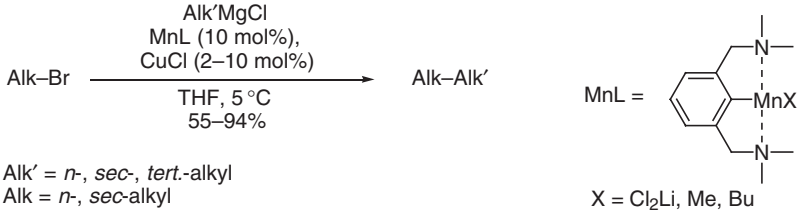
Scheme 33



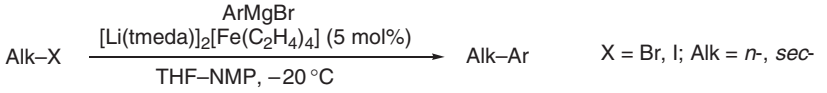
Scheme 34



Scheme 35



Scheme 36



Scheme 37

Cobalt-bis-(1,3-diphenylphosphino)-propane complex is a suitable catalyst for the reaction of various alkyl bromides with allylmagnesium reagents in THF.[97] In the presence of a suitably placed double bond, cyclization products were obtained in good yields.[98] Iron(III) salts were found to be superior catalysts for coupling reactions of various organomagnesium reagents with alkyl electrophiles. Aryl Grignard reagents were coupled with primary and secondary alkyl bromides in the presence of $FeCl_3$ and TMEDA[99] in THF or $Fe(acac)_3$ in ether.[100] The active catalyst is believed to be $Fe(MgX)_2$, formed in *situ* by the reduction of Fe(III) salts with the magnesium organometallics.[101] Fürstner showed that an Fe(-II) complex $[Li(TMEDA)]_2[Fe(C_2H_4)_4]$ is effective as a catalyst for the cross-coupling reaction,[101] affording complete conversion in minutes even at −20 °C (Scheme 37).

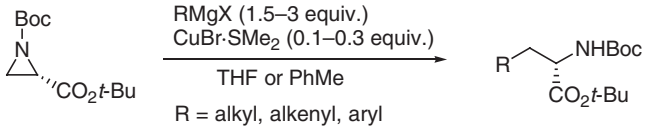
9.03.3.2.1.(ii) Ring opening of small cycles, acetals, and thioacetals

Organomagnesium reagents react in the presence of catalytic amount of copper(I) salts with aziridines bearing phosphinoyl, sulfonyl, or carbamate on the nitrogen, giving ring-opening products.[102,102a,102b] This method was used for the synthesis of chiral β-(het)arylalkylamines[103] and α-amino acids (Scheme 38).[104]

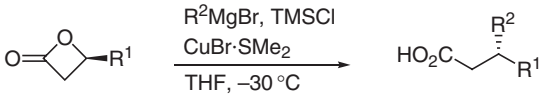
Substituted β-propiolactones, easily available in chiral form, undergo similar ring-opening reactions under these conditions, thus offering an alternative to enantioselective 1,4-addition (Scheme 39).[105]

Terminal epoxides undergo deprotonation at 0 °C with lithium tetramethylpiperidide. The anion reacts with alkyl and alkenyl Grignard reagents, opening the ring, and finally eliminates Li_2O, giving alkenes (Scheme 40).[106] Reaction of ketone dithioacetals with Grignard reagents investigated by Luh opens synthetic routes to a variety of polysubstituted alkenes.[107] Simple aliphatic dithioacetals react only in the presence of an Ni–trialkylphosphine catalyst (Scheme 41).[108]

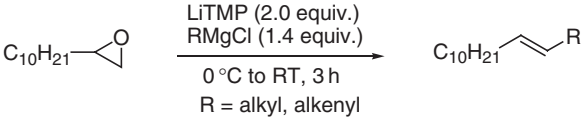
Chiral acetals undergo diastereoselective ring opening with Grignard reagents in toluene.[109,110] Ketals derived from ω-bromoketones react with $Mg/MgBr_2$, giving cycloalkanol ethers after Lewis acid-assisted ring opening and intramolecular quench of the alkylmagnesium species. Some substituted cyclopropanes and cyclobutanes were obtained by this method.[111] The reaction of α-aminonitriles with alkenylmagnesium reagents (Bruylant reaction) leading to allylamines was greatly improved by performing the reaction at low temperatures in the presence of $AgBF_4$.[112]



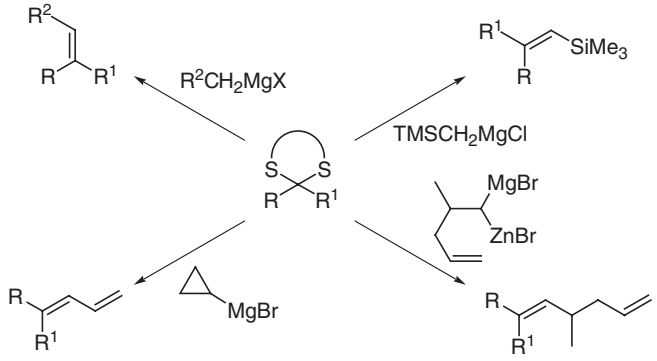
Scheme 38



Scheme 39



Scheme 40

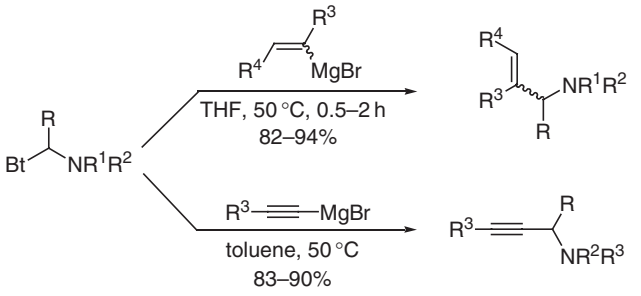


Scheme 41

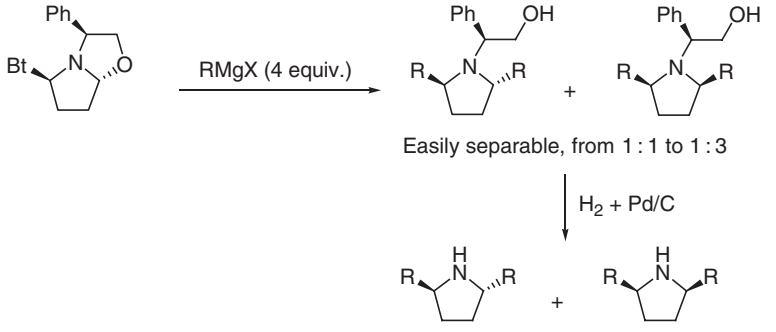
9.03.3.2.1.(iii) Miscellaneous reactions

Benzotriazole (Bt) may serve as a leaving group in reactions with organometallic species.[113] Benzotriazolyl-1,3-dioxolane has been used as a masked formyl equivalent to form dioxolanes from Grignard compound.[114] Polysubtituted α-aminobenzotriazoles react with Grignard reagents as imine equivalents. Thus, alkenylic and propargylic Grignard reagents give allyl- and propargylamines in good yields (Scheme 42).[115,115a]

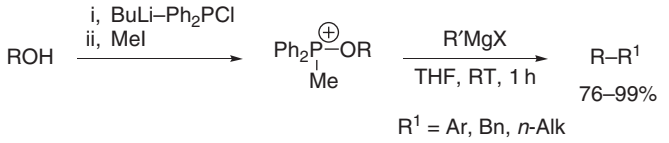
This reaction, applied on a readily available chiral aminal, afforded an easy route to optically pure *trans*-2,5-pyrrolidines (Scheme 43).[116] Ring opening of similar chiral alkyl substituted 1,3-oxazolidines with Grignard reagents was used in the enantioselective synthesis of substituted piperidines.[117] Chiral oxazolidines, obtained from (*S*)-phenylglycinol, react with organomagnesium compounds, giving ring-opening products in high yields and diastereoselectivity. A number of optically pure secondary amines were prepared by this method. It was also applied for the synthesis of bis(1,3-oxazolydinyl)alkanes, allowing an enantioselective route to C_2-symmetrical chiral 1,4- and 1,5-diamines. Stereoselective α-amidoalkylation reaction of organomagnesium reagents by phenylglycinol-derived bicyclic lactam gave enantiopure 5-substituted valerolactams.[118,118a] Tertiary allyl- and propargylamines were prepared from Grignard reagents and the corresponding aminals after their conversion into iminium triflates by the reaction with Tf_2O. The resulting diallylamines were deprotected into primary amines.[119] Some functionalities other



Scheme 42



Scheme 43



Scheme 44

than halides and sulfonates can serve as leaving groups in substitution reactions with organomagnesium reagents. Easily available benzylic α-azidoethers react with Grignard reagents with the substitution of the azide group.[120] An interesting method for the activation of alcohols for the substitution reaction was developed by Mukaiyama. Primary and benzylic diphenylphosphinites after quaternization with MeI were easily reacted with alkyl-, benzyl-, and arylmagnesium compounds producing the corresponding coupling products (Scheme 44).[121]

Transmetallation of alkylmagnesium reagents to Cu(I), Mn(II), and Zn(II) was investigated by Hoffmann, using an optically enriched Grignard reagent. Transmetallation to zinc proceeds with complete retention of configuration (concerted mechanism), whereas for copper and manganese a rather complicated process is observed. Seemingly, it occurs along two routes, including concerted processes and single-electron transfer depending on the reagents used.[122] Both reaction pathways were also proposed for the reaction of organomagnesium reagents with trialkyltin halides.[123]

9.03.3.2.2 Substitution at sp^2 center

9.03.3.2.2.(i) Transition metal-catalyzed cross-coupling reactions

9.03.3.2.2.(i).(a) Substituted aryl and hetaryl derivatives as electrophiles

Transition metal-catalyzed cross-coupling reaction has become the most important method for the formation of aryl–aryl bonds. The reaction of aryl halides and sulfonates with organomagnesium compounds is usually referred

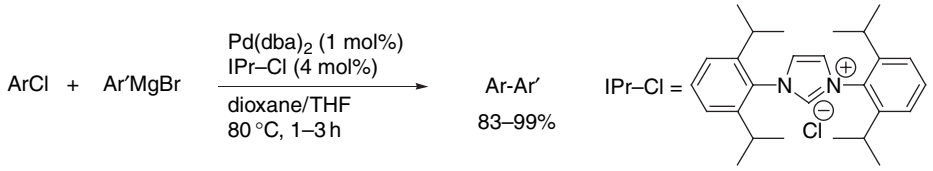
to as Kumada or Kumada–Tamao–Corriu reaction. Halogens are mostly used as a leaving group in the electrophile partner. Due to the availability and relatively low price of aryl and hetaryl chlorides efforts were put on the development of methods, which allow their use in cross-coupling reactions. Oxidative addition of the metal in aryl chlorides is relatively difficult. It requires in the case of Pd and Ni catalyst the presence of electron-rich ligands, typically bulky trialkylphosphines or stable carbenes. In the presence of $Pd(dba)_2$ (1 mol%) and of stable N-heterocyclic carbene (NHC, 4 mol%), aryl chlorides react with arylmagnesium compounds to form biaryls in good yields (Scheme 45).[124]

Dialkylphosphine oxides as ligands for Pd are sometimes even more effective.[125] Complexes of Ni with N-heterocyclic carbenes are efficient catalysts for the coupling of aryl chlorides. In this case the reaction proceeds at room temperature.[126] These compounds are active enough to promote cross-coupling of even less reactive aryl fluorides.[127] Electron-poor fluoroazines and -diazines react already in the presence of $NiCl_2$(dppp).[128] Hindered and electron-rich $P(t\text{Bu})_3$[126] and $t\text{Bu}_2\text{P(S)H}$[129] are good catalysts for the coupling of inactivated aryl chlorides in the presence of nickel. Transmetallation of organomagnesium compounds to zinc derivatives allows using conventional Ph_3P and $(i\text{PrO})_3P$ as ligands for Ni, provided that a reducing agent like CH_3MgCl or Vitride is used for forming of the active Ni(0) species.[130] For aryl chlorides bearing an *ortho*-coordinating group, like an imine, an oxazoline or even a nitrile, manganese salts in the presence of NMP are very effective catalysts for their coupling with alkyl, alkenyl, and aryl Grignard reagents. Other halogens or even methoxy-substituents can successfully serve as leaving groups (Scheme 46).[131]

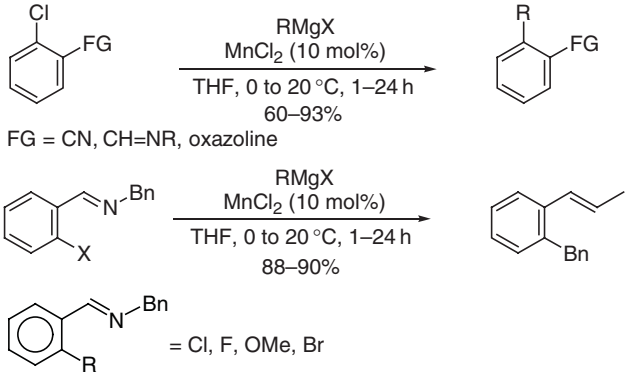
By using this method, 4-methyl-2′-cyanobiphenyl, an important intermediate for the synthesis of the antihypertensive drug Losartan, can be easily prepared.[132] 2-(*o*-Chlorophenyl)-oxazoline reacts with excess of arylmagnesium halide without catalysis, as it was shown by Meyers for 2-(*o*-methoxyphenyl)-oxazolines.[133] Cobalt(II) salts catalyze the coupling of Grignard reagents with α-chloroazines at −40 °C in ether (Scheme 47).[134,135]

Substituted pyridines, quinolines, and diazines react with polyfunctionalized aryl Grignard reagents, obtained by iodine–magnesium exchange under very mild conditions in the presence of $PdCl_2$(dppf) as a catalyst (Scheme 48).[136,137]

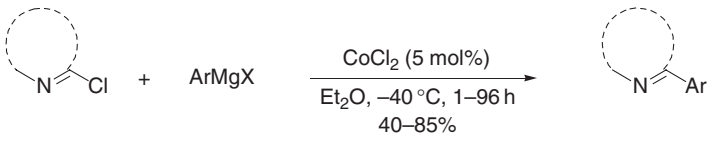
Bromo- and iodoanilines, -phenols and -benzoic acids, after *in situ* deprotonation by the excess of the reagent, can be coupled ($PdCl_2$(dppf), 1 mol%, THF, RT, 3 h) with organomagnesium halides, thus avoiding protection–deprotection steps.[138]



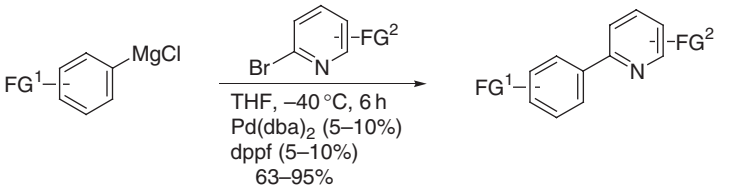
Scheme 45



Scheme 46



Scheme 47



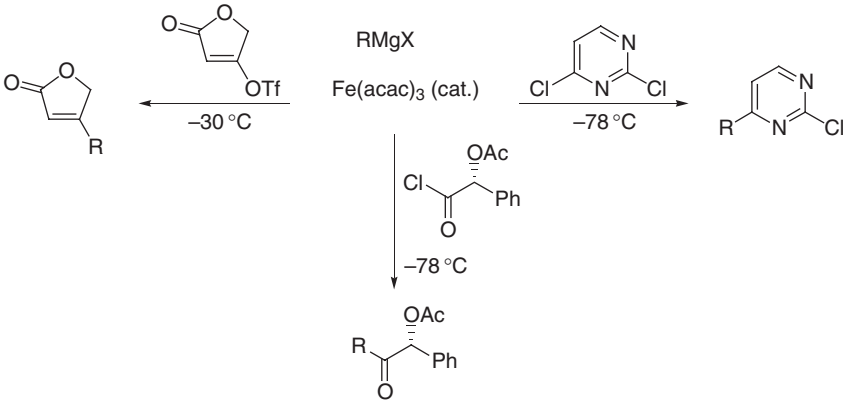
Scheme 48

Iron(III) salts are effective catalysts for sp^3–sp^2 coupling, which catalyze the reaction of alkylmagnesium compounds with aryl chlorides, triflates and tosylates as well as hetaryl chlorides in THF–NMP at 0 °C (Scheme 49, 50).[139,139a–139d]

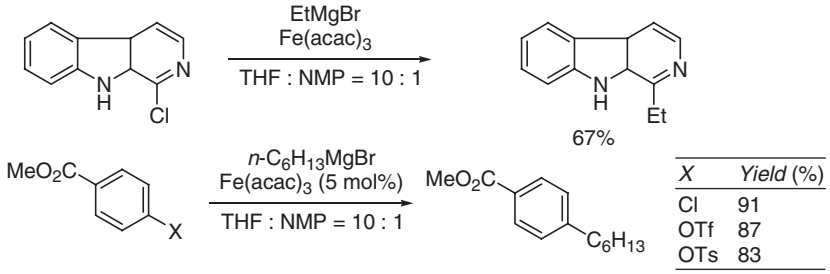
In few instances, aryl Grignard reagents are also used in this reaction, although the yields are not high.[140] Use of iron(III) salts for cross-coupling reactions is very advantageous due to the lack of toxicity, very high activity, low price, and their environmentally friendly nature. So far, unfortunately, no general methods for iron(III)-catalyzed sp^2–sp^2 carbon–carbon bond formation, covering more or less sufficient scope of substrates, have been developed. The main problem here is the occurrence of an extensive homocoupling reaction, leading to poor yields of the desired products. 2-Aryl-1,1-dibromoalkenes react in the presence of $Fe(acac)_3$ (5 mol%) with AlkMgBr (1 equiv.) being reduced to *trans*-2-aryl-1-bromoalkenes. They can be coupled *in situ* with the excess of Grignard reagent, leading to *trans*-2-aryl-1-alkyl substituted ethylenes in good to moderate yields.[141] Nickel catalysis has been applied to the large-scale synthesis of α-terthienyl, an important material for the preparation of conducting polymers.[142] Nickel on charcoal has been proposed as a cheap and easily removable catalyst for several Kumada coupling reactions.[143,144]

Selectivity of the coupling of an electrophilic reagent bearing several leaving groups can be achieved by tuning the nature of the ligand. Although iodide is almost always the most reactive leaving group in this reaction, the choice between bromide and a triflate strongly depends on the catalyst used (Scheme 51).[145]

Alkynyl and aryl Grignard reagents can be effectively coupled with aryl triflates, including highly sterically congested compounds, in the presence of palladium and the amino acid-derived P, N-ligand (2-dimethylamino)propyldiphenylphosphine (alaphos).[146,146a,146b] Aryl tosylates readily react with aryl Grignard reagents in the presence

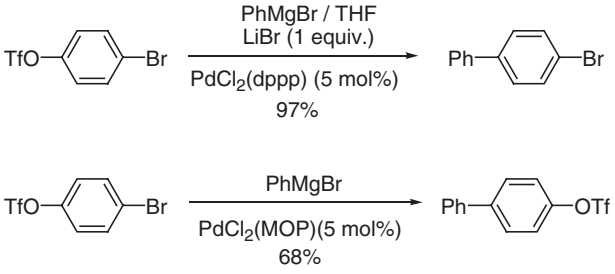


Scheme 49



X	*Yield* (%)
Cl	91
OTf	87
OTs	83

Scheme 50



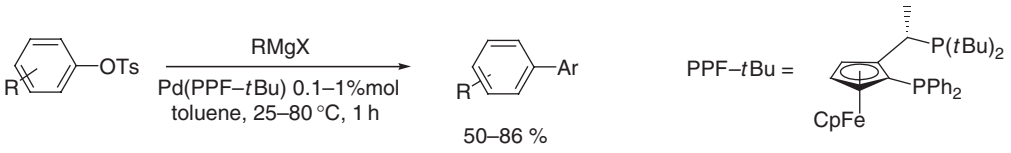
MOP= 2-diphenylphosphino-2′-methoxy-1,1′-binaphtyl

Scheme 51

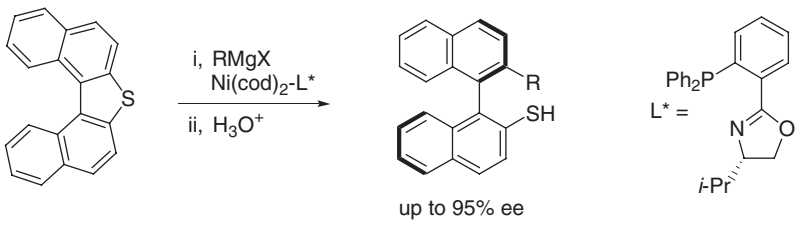
of the complex Pd(PPF–*t*Bu) (0.1 mol%), developed by Hartwig,[147] yielding coupling products under mild conditions (Scheme 52).

Sulfones,[148] some sulfonates,[149] and sulfonamides[150] react with Grignard reagents in the presence of nickel catalysts. The sulfonamide group can be reductively removed from a phenyl ring under similar conditions by the reaction with *i*PrMgCl–Ni(acac)$_2$.[150] Substituted dibenzothiophenes react with Grignard reagents, forming products of the thiophene ring cleavage. With a chiral Ni catalyst, axially chiral biaryls were obtained with excellent enantioselectivity (Scheme 53).[151]

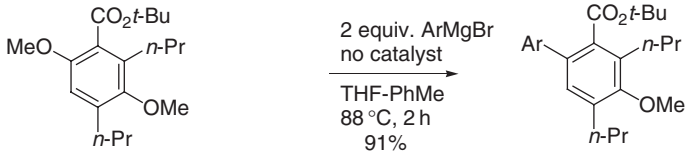
Diaryliodonium tetrafluoroborates undergo cross-coupling reactions with organomagnesium compounds in the presence of zinc salts and a Pd catalyst.[152] 5-Aryloxy-1-phenyl-1*H*-tetrazoles react under Ni catalysis with Grignard reagents and other organometallic reagents. Here, 1-phenyltetrazol-5-one serves as a leaving group, thus offering an alternative route for the activation of a phenolic hydroxyl for the substitution.[153] (Trisopropoxysilyl)methyl-magnesium chlorides react with aryl-, alkenyl-, and allylic bromides in the presence of nickel salts giving the coupling products which can be easily oxidized to primary alcohols.[154] Aryl- and heteroaryl nitriles react in the presence of Ni(PMe$_3$)$_2$Cl$_2$ with Grignard reagents giving cross-coupling products with the loss of cyanide. This is a rare and interesting case of C–C bond activation. Other tested ligands were proved ineffective in this reaction.[155,155a,155b] Use of Ni(PCy$_3$)$_2$Cl$_2$ under relatively harsh conditions (90 °C, 15 h) allows coupling of simple aromatic ethers.[156] Such ethers, possessing an electron-withdrawing substituent like an alkoxycarbonyl, 2-(1,3-oxazolinyl), benzaldimine, or nitro group in *ortho*-position, react with Grignard reagents even without transition metal catalysis (Scheme 54). In this case, the reaction proceeds via a nucleophilic aromatic substitution mechanism.[157] If the alkoxy substituent is optically active



Scheme 52



Scheme 53

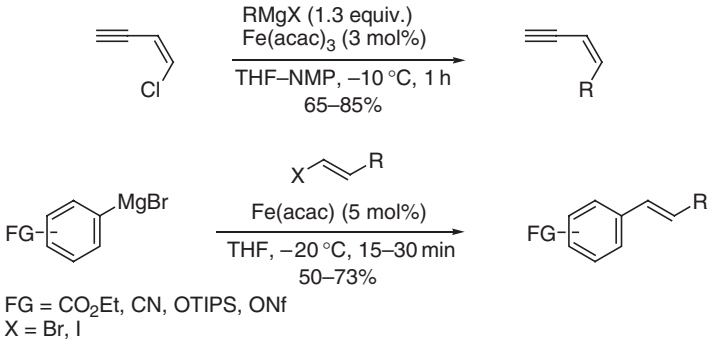


Scheme 54

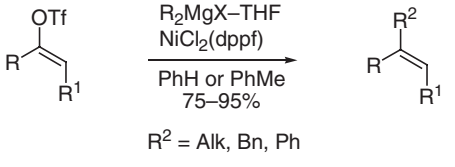
(e.g., like menthyloxy), the axially chiral products are obtained with high enantioselectivity. This chemistry was applied to the synthesis of pyrrolophenantridine alkaloids[158] and a number of new pharmacological agents.[159]

9.03.3.2.2.(i).(b) Substituted alkenes as electrophiles in cross-coupling reactions

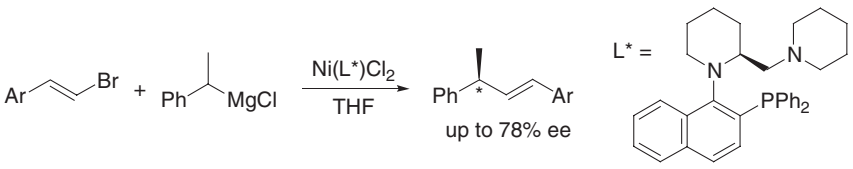
Chloroenynes and chlorodienes react with Grignard reagents with the retention of stereochemistry using palladium,[160] manganese,[161] and iron[162] catalysis. Iron seems to be the metal of choice for this transformation providing good yields and the mildest conditions (Scheme 55).[163,163a,163b] 1,3-Dienyl triflates[164] and enol triflates derived from β-ketoesters[165] undergo cross-coupling with Grignard reagents, catalyzed by copper(I) species. Dienyl phosphates give products in good yields only in the presence of nickel salts.[166] Simple enol triflates have been successfully coupled, with $NiCl_2$(dppp) as a catalyst (Scheme 56).[167]



Scheme 55



Scheme 56



Scheme 57

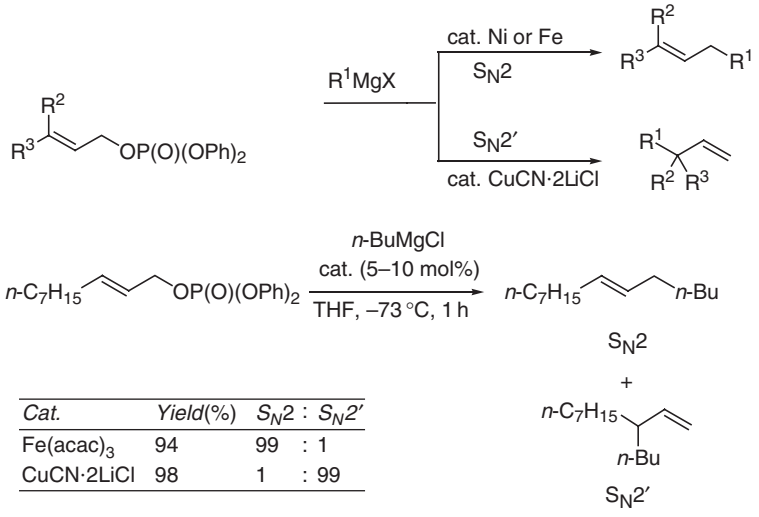
(*Z*)-alkenyl diisopropylcarbamates react with organomagnesium halides, yielding (*Z*)-alkenes. In some cases, full stereocontrol was achieved.[168] Enol phosphates can be derived *in situ* from ketones, using sterically hindered mesitylmagnesium bromide for the deprotonation followed by quench with chlorophosphates. They undergo cross-coupling with arylmagnesium species in the presence of a palladium catalyst.[169] 2,6-Dimethylphenylmagnesium bromide and its tri-, tetra-, and pentamethyl analogs react with *trans*-dibromoalkenes in the presence of a Pd catalyst, surprisingly giving exclusively polymethylsubstituted *cis*-stilbenes.[170] 2-Bromostyrenes react with 1-ethylphenylmagnesium chloride in the presence of a Ni catalyst yielding 1,3-diphenyl-1-butenes. When chiral complexes of nickel are used, the products are obtained with good enantiomeric excess (Scheme 57).[171,172]

9.03.3.2.2.(ii) Allylic substitution reactions

Reaction of organomagnesium compounds with allylic electrophiles usually requires transition metal catalysis in order to achieve good regio- and stereoselectivity. The regioselectivity depends on many factors and is often difficult to predict in each particular case. Usually, copper (I) salts are used as catalysis. In this case, increased temperature and amount of catalyst as well as slow addition of the Grignard reagent favor the formation of the γ-adduct.[173] On the contrary, iron catalysis for the reaction of Grignard reagents with allyl diphenylphosphates leads almost exclusively to the products of α-attack (Scheme 58).[174]

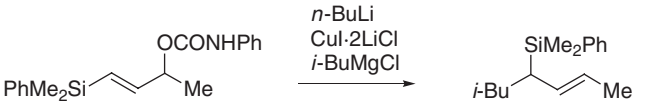
The presence of a diphenylphosphine moiety in the substrate[175] or the use of a strongly complexing *o*-diphenylphosphinobenzoate as the leaving group[176] affords very good level of stereoselectivity. Allylic carbamates[177,178] as well as allylic cyclic carbonates[179] are good substrates for regio- and diastereoselective reaction with Grignard reagents in the presence of $NiCl_2$(dppe) leading to (*E*)-allylic alcohols (Scheme 59).

Allylic substitution reaction is an important tool of enantioselective synthesis. Starting from readily available chiral allylic alcohols, products with tertiary and quaternary chiral centers can be obtained highly diastereoselectively,[180,180a,181,181a,181b] thus allowing an enantioselective new C–C bond formation (Scheme 60).



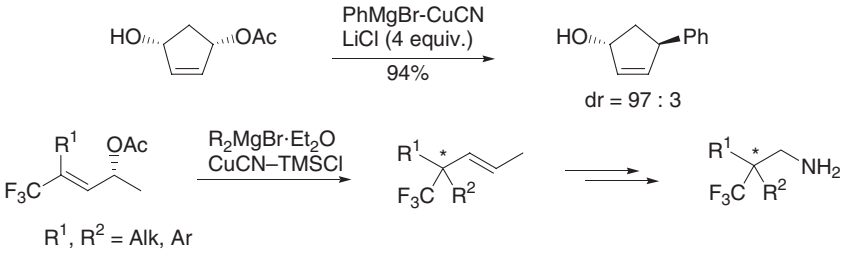
Cat.	*Yield*(%)	S_N2 : S_N2'
$Fe(acac)_3$	94	99 : 1
CuCN·2LiCl	98	1 : 99

Scheme 58



E : *Z* (reactant)	*Yield*(%)	*E* : *Z* (product)
98 : 2	90	6 : 94
2 : 98	93	97 : 3

Scheme 59

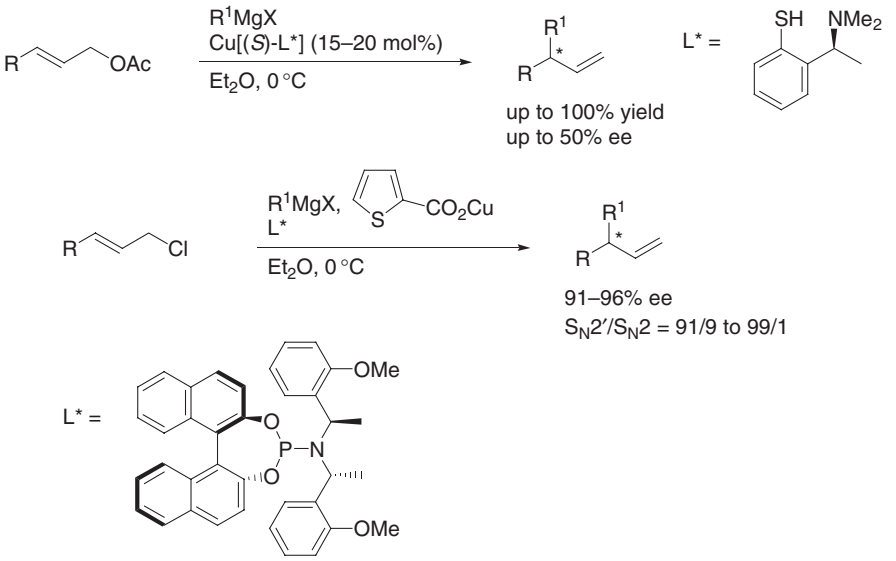


Scheme 60

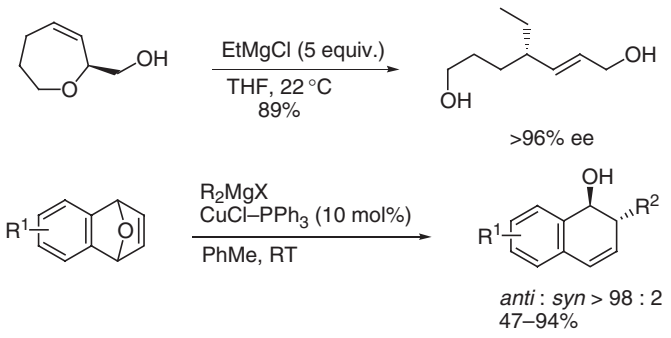
Another approach is to use achiral allylic substrates and a chiral ligand for metal catalyst. A number of ligands have been investigated for this reaction.[181,181a,181b,182,182a] In case of chiral binaphthol-derived phosphoramidites, introduced by Feringa, excellent regio- and enantioselectivity has been achieved (Scheme 61).[183,183a,183b]

Unsaturated cyclic acetals react with Grignard reagents in the presence of a chiral Ni catalyst, giving 3-substituted cycloalkanones in good yields and enantioselectivity up to 85% ee.[184] Ring-opening reaction of oxacyclo- and oxabicycloalkenes, possessing an allylic ether group, leads to synthetically useful polysubstituted alkenols (Scheme 62).[185,185a,185b]

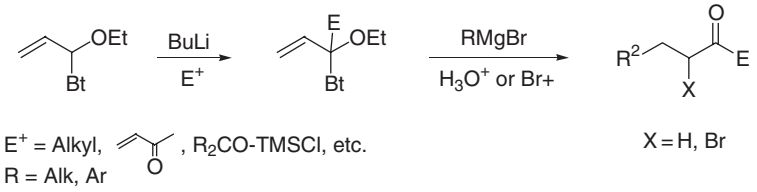
Chiral α-carbamoyloxy-2-alkenylboronates react with Grignard reagents with complete α- and diastereoselectivity through rearrangement of an intermediate "ate"-complex, yielding chiral allylboronates, which were oxidized to enantioenriched allylic alcohols.[186] Highly selective S_N2' reaction of Grignard reagents with substituted allylbenzotriazoles gives enol ethers, which can be converted into various substituted ketones (Scheme 63).[187]



Scheme 61



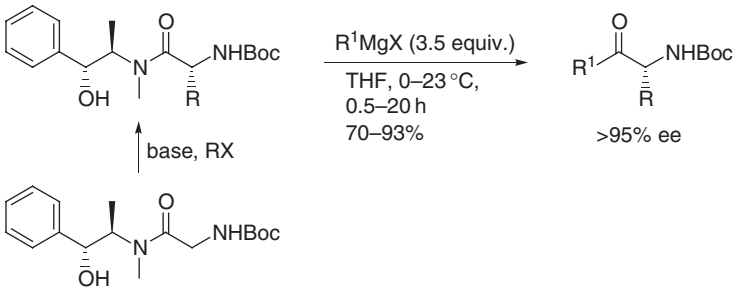
Scheme 62



Scheme 63

9.03.3.2.2.(iii) Synthesis of carbonyl compounds using Grignard reagents

The acylation of organometallic reagents with acyl chlorides has been reviewed by Dieter.[188] Acyl morpholides give good yields of ketones by the reaction with organomagnesium compounds.[189] N-*tert*-butoxy-N-methyl amides were used instead of Weinreb amides in order to avoid some side-reactions.[190] Acyl chlorides react with Grignard reagents in the presence of 5% $Fe(acac)_3$ already at −78 °C. At this temperature undesired side-reactions like the attack on the resulting ketone are completely suppressed. The reaction proceeds with the same mechanism as transition metal-catalysed cross-couplings.[139a] Aroyl cyanides have also been coupled with arylmagnesium compounds in the presence of $Fe(acac)_3$ to prepare benzophenones.[191] Alternatively, acyl halides first react with tri-*n*-butylphosphine to form acylphosphonium salts. These salts react smoothly with Grignard reagents giving ketones in good yields.[192,193] Various carboxylic acids form quantitatively activated esters with 2-chloro-4,6-dimethoxy-1,3,5-triazine, which react *in situ* with Grignard reagents in the presence of copper iodide.[194] A number of methods were developed for the conversion of α-amino acids into α-amino ketones avoiding epimerization at the chiral center.[195,196] Thus, a protected pseudoephedrine glycinamide is first diastereoselectively alkylated in the presence of a base. Further treatment of the product with organomagnesium compounds gives protected α-aminoketones in good yields with complete retention of configuration at the α-carbon (Scheme 64).[197]



Scheme 64

Symmetrical α-diones,[198,199] carboxylates,[200] tertiary amides,[201] and thioamides[202,203] are obtained from Grignard reagents in one-pot syntheses. betha-Enaminones give substituted α,β-enones by an addition–elimination mechanism.[204] Ethyl 2,3-epoxypropanoate, available in enantiopure form from serine, reacts at −85 °C with Grignard reagents yielding α,β-epoxyketones in good yields without epimerization.[205]

9.03.3.2.3 Substitution at *sp* center

Reactions, where an *sp* carbon is subjected to the attack of a Grignard reagent, are relatively rare. Usually, allenes are the resulting products of this transformation. Propargylic dithioacetals react with organomagnesium compounds to yield substituted allenes.[206,207] Alkynyl oxiranes lead to 2,3-allenols with good chirality transfer in the presence of an iron catalyst (Scheme 65).[208] Arylbenzotriazolylacetylenes, prepared in one pot from $BtCH_2SiMe_3$ and aroyl chlorides, react with aryl, alkyl, and allylmagnesium halides, giving good yields of disubstituted acetylenes.[209]

9.03.3.3 Addition to Multiple Bonds

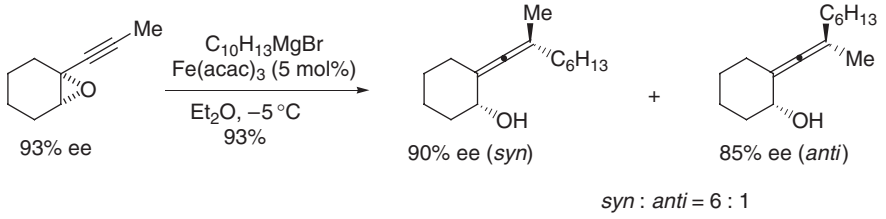
9.03.3.3.1 Addition to carbon–carbon multiple bonds

9.03.3.3.1.(i) Catalyzed addition to non-activated C═C bonds

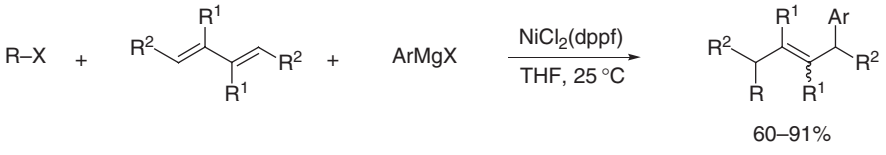
Uncatalyzed reactions of Grignard reagents with non-activated double bonds are generally difficult, with the exception of the reaction of allylmagnesium derivatives conjugated dienes. Recently, a number of synthetically useful methods involving transition metal catalysis were developed. Stereoselective addition of Grignard reagents to alkenes, mostly catalyzed by nickel and zirconium complexes, has been reviewed by Hoveyda.[210] Thus, the complex of nickel chloride and bis(diphenylphosphino)ferrocene efficiently catalyzes the three-component coupling of alkyl halides, butadienes, and arylmagnesium halides (Scheme 66).[211]

The reaction presumably goes through the addition of a radical (formed from RX) to the diene, followed by the reaction of the formed allyl radical with $[NiL_2Ar]$ complex. A combination of $CoCl_2$ and 1,6-bis(diphenylphosphino)hexane catalyzes a similar reaction of an alkyl bromide with a 1,3-diene and trimethylsilylmethylmagnesium chloride, yielding homoallylic silanes in good to excellent yields.[212] For both cases, the same catalytic cycle was proposed (Scheme 67).

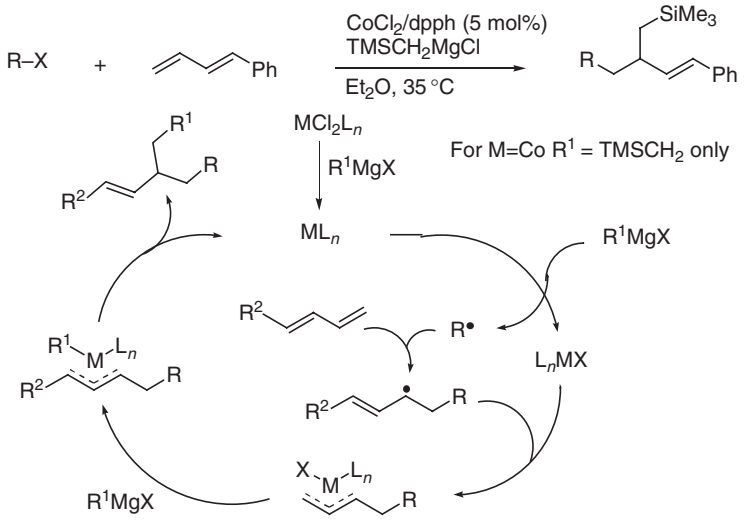
Similarly, nickel salts catalyze the dimerization and carbosilylation of 1,3-butadienes in the presence of chlorosilanes and Grignard reagents leading to 1,6-dienes bearing allylsilane unit.[213] Titanocene and zirconocene dichlorides efficiently catalyze the addition of Grignard reagents to unactivated alkenes. Hoveyda found that alkylmagnesium compounds react with monosubstituted alkenes and alkyl tosylates in the presence of Cp_2ZrCl_2 (5% mol.) forming, depending on the substrates involved, three different types of products. In many cases, the reaction is highly



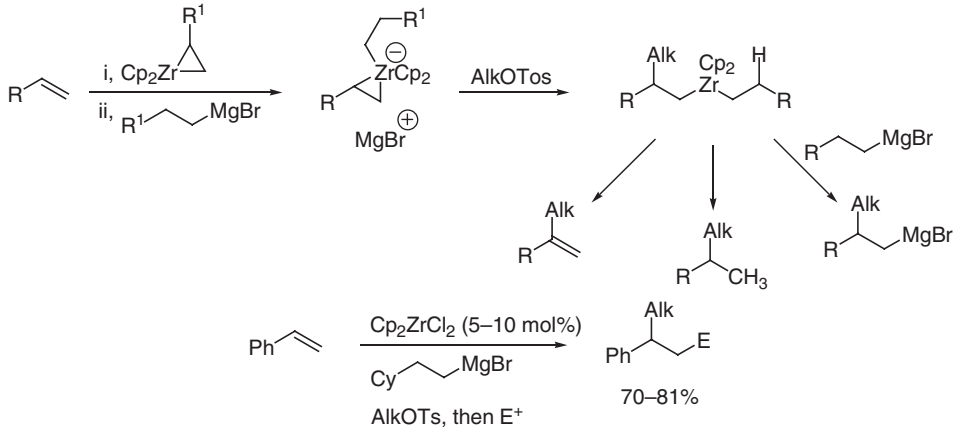
Scheme 65



Scheme 66



Scheme 67



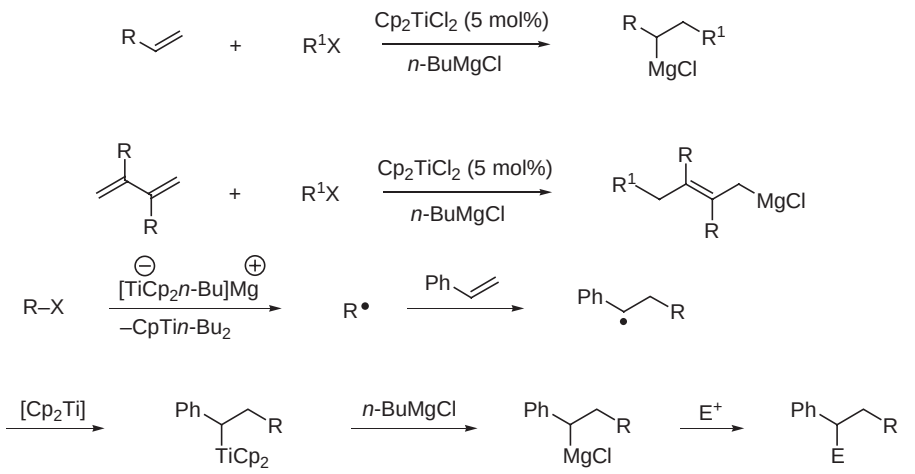
Scheme 68

selective. It has been applied to a sequential functionalization of styrenes by the attachment of two different electrophiles (Scheme 68).[214]

Titanocene dichloride catalyzes a regioselective carbomagnesiation of alkenes and dienes. The reaction proceeds at 0 °C in THF in the presence of Cp_2TiCl_2, an organic halide and *n*-BuMgCl to form the catalytic species, affording benzyl, allyl, or α-silyl alkyl Grignard compounds, which react with various electrophiles (Scheme 69).[215] Kambe has reported a dimerization reaction of alkenyl Grignard reagents in the presence of chlorosilanes, catalyzed by Cp_2TiCl_2 furnishing 1,4-disilyl-2-butenes.[216]

9.03.3.3.1.(ii) 1,4-Addition to α,β-unsaturated carbonyl compounds

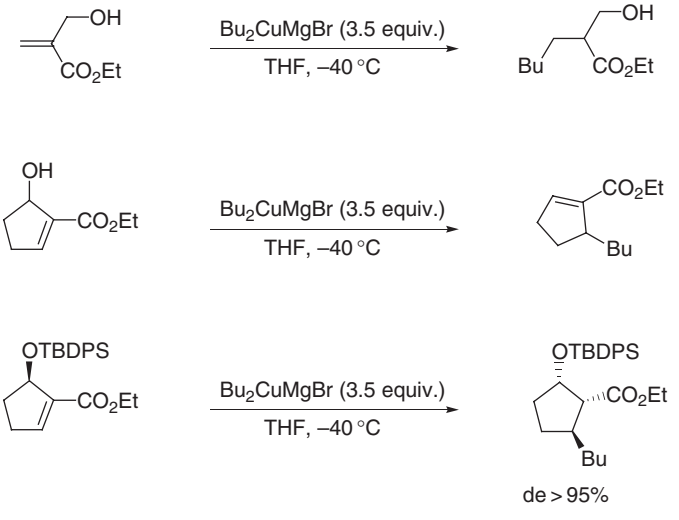
Michael addition of Grignard reagents to various unsaturated carbonyl compounds has been extensively studied. Copper-catalyzed conjugate addition reactions have been reviewed.[217] Highly functionalized organomagnesium reagents, obtained by the low-temperature iodine–magnesium exchange, give good yields of 1,4-addition products in the reaction with α,β-enones with a copper catalyst (CuCN·2LiCl, 5–10 mol%).[218] Homoallylic ketones are obtained in 26–77% yield on treatment of aromatic, aliphatic, and α-aminomethyl carboxylates with excess of an alkenylmagnesium bromide and a catalytic amount of copper salts in THF at −45 °C. The reaction proceeds as a



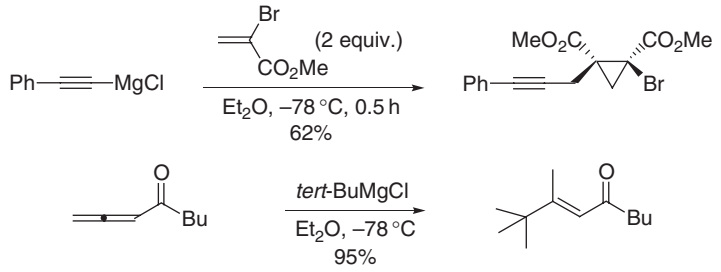
Scheme 69

sequence of Grignard acylation and 1,4-addition.[219] 3-Substituted glutarate diesters are easily obtained in good yields by the reaction of various Grignard reagents with dimethyl 1,3-propenedicarboxylate.[220] Addition of BuMgBr–CuBr to α-hydroxymethyl ethyl acrylate gives exclusively 1,4-adducts, although on cyclic systems allylic substitution takes place. If the alcohol function is properly protected, 1,4-addition occurs diastereoselectively in the presence of TMSCl (Scheme 70).[221,222] Two equivalents of an α-haloacrylic ester react with organomagnesium compounds, leading to various substituted halocyclopropane-*cis*-dicarboxylic acids.[223] Conjugated allenyl ketones react smoothly with Grignard reagents in ether at $-78\,^{\circ}C$ without catalyst, yielding α,β-enones in excellent yields and with complete (*E*)-selectivity (Scheme 71).[224]

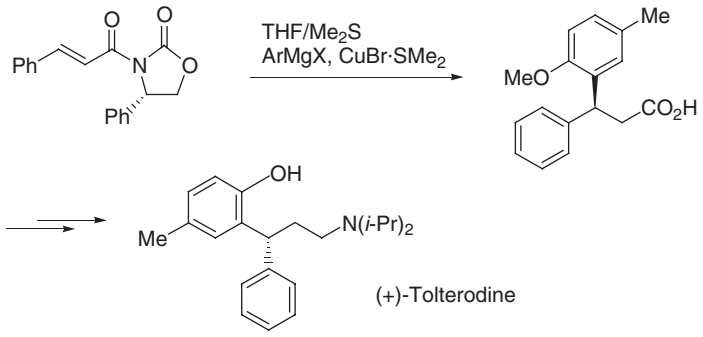
A number of chiral auxiliaries have been developed for performing 1,4-addition enantioselectively. Chiral oxazolidinones are often highly effective, affording the products with up to 99% ee. Optically active amidoacrylates, prepared from acryloyl oxazolidinone in four steps, react with Grignard reagents in the presence of a catalytic amount of copper. The reaction was applied by Hegedus for the synthesis of α-amino acids. Enantioselectivities up to 97% were obtained.[225] Asymmetric conjugate addition of an arylmagnesium reagent to cinnamoyloxazolidinone is the key step of the synthesis of (+)-tolterodine,[226] a pharmacologically important muscarinic receptor agonist (Scheme 72).



Scheme 70



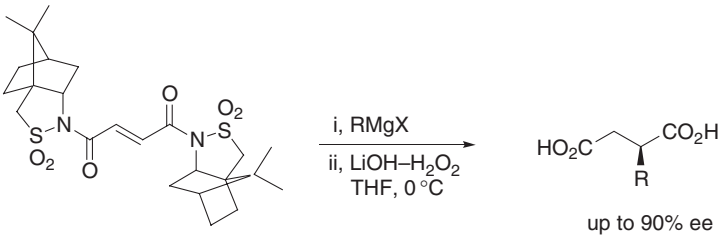
Scheme 71



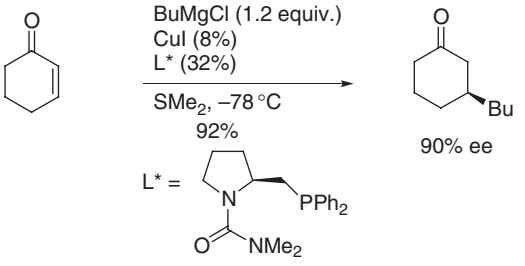
Scheme 72

Similar acryloyl imidazolidinones have been used in the asymmetric 1,4-addition of organomagnesium compounds in the presence of a Lewis acid. The diastereoselectivity is variable and was found to be highly depending on the nature of all the reaction participants.[227] A symmetric fumaramide, obtained from the camphor-derived Oppolzer sultam, adds Grignard reagents, yielding after hydrolysis monosubstituted succinic acids with up to 90% ee (Scheme 73).[228]

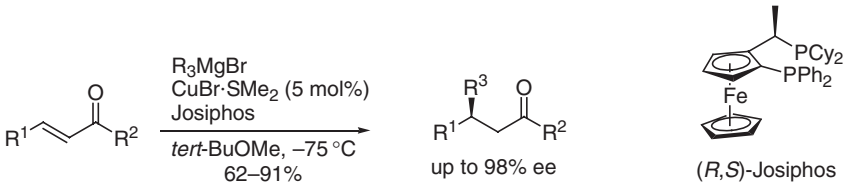
Grignard reagents with or without copper catalysts react with α-amidoacrylates, having mandelic esters as an auxiliary, although with modest de's.[229] Application of an asymmetric catalyst for the enantioselective 1,4-addition is advantageous due to the simplification of the overall process and lower costs. Some S,N- and P,N-ligands have been investigated. Benzalacetone reacts with a Grignard reagent in the presence of copper aminoarenethiolate (9% mol.), yielding the 1,4-addition product with 76% ee. 2-(1-Dimethylaminoethyl)thiolatocopper was found to be the optimal catalyst.[230] A proline-derived carbamoylphosphine catalyzes asymmetric 1,4-addition of Grignard reagents to 2-cyclohexenone although higher catalyst loadings are required in this case. Changing the solvent for diethyl ether and the catalyst loading to 3% mol leads to the product with 67% ee and slightly lower yield (Scheme 74).[231]



Scheme 73



Scheme 74



Scheme 75

Recently, Feringa found that ferrocene-derived ligand (*R*,*S*)-Josiphos, widely used for catalytic asymmetric hydrogenation, is also a good catalyst for asymmetric copper-catalyzed 1,4-addition. Reaction in *tert*-BuOMe in the presence of 6% mol of the ligand gave products with up to 98% ee (Scheme 75).[232,232a]

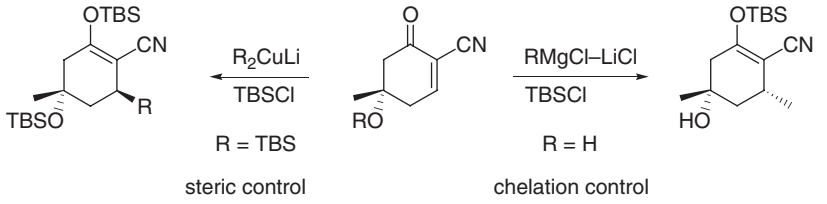
9.03.3.3.1.(iii) Addition to other activated alkenes

Addition to α,β-unsaturated nitriles has been reviewed by Fleming.[233] Addition to cyclic oxo-nitriles, bearing a hydroxy group, can be controlled depending on the protecting group, either sterically or by chelation (Scheme 76).

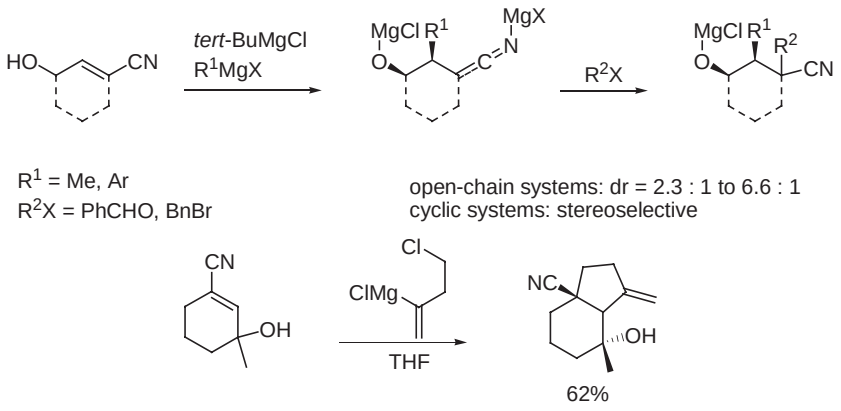
Hydroxy alkenyl and alkynyl nitriles can be subjected to a one-pot addition–alkylation sequence, leading to polysubstituted products. In the case of open-chain systems, diastereoselectivity from 2.3 : 1 to 6.6 : 1 was achieved. Cyclic systems may lead to a highly diastereoselective reaction.[234,234a–234c] ω-Chloroalkenylmagnesium bromides give bicyclic products (Scheme 77).[235,236]

Interestingly, unsaturated nitriles can be obtained from β-hydroxynitriles (prepared by reaction between aldehydes and aliphatic nitriles) by elimination of MgO in the presence of MeMgCl (2.1 equiv.).[237] 2-Pyridyldimethylsilyl alkenes undergo easily the addition of organomagnesium reagents on the double bond. The resulting organomagnesium species react *in situ* with electrophiles yielding trisubstituted alkylsilanes.[238] 2-Pyridyldimethylsilyl group can be further removed or easily substituted for a number of different functionalities.[239] Copper-catalyzed addition of Grignard reagents to the substituted cyclopropenes, bearing a coordinating substituent, occurs with high facial selectivity, giving polysubstituted cyclopropanes after quenching with an electrophile (Scheme 78).[240]

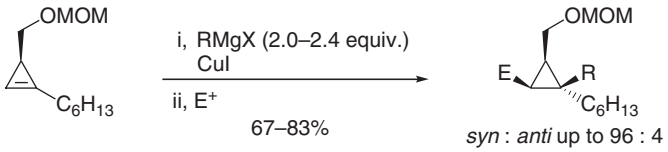
Reaction of nitroalkenes with Grignard reagents gives *aci*-salts, which, depending on the hydrolysis conditions and substrate structure, can be transformed into nitroalkanes, hydroxymoyl halides, or carboxylic acids.[241] Reaction of



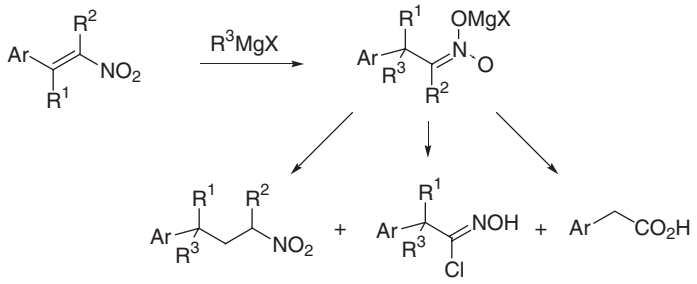
Scheme 76



Scheme 77



Scheme 78



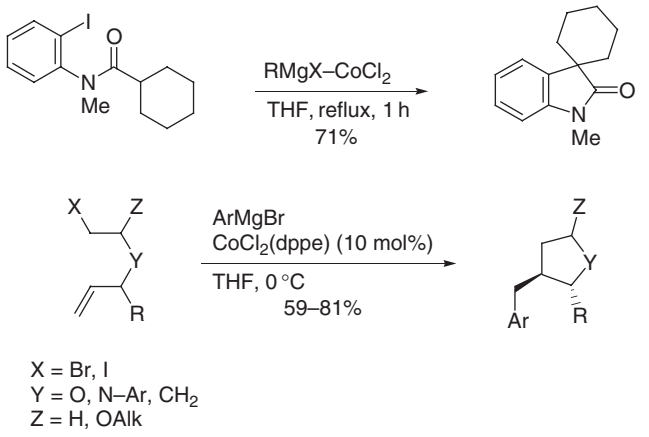
Scheme 79

RMgX with nitroalkenes in the presence of $CeCl_3$, followed by treatment with 100% AcOH was developed as an efficient synthesis of complex nitroalkanes (Scheme 79).[242]

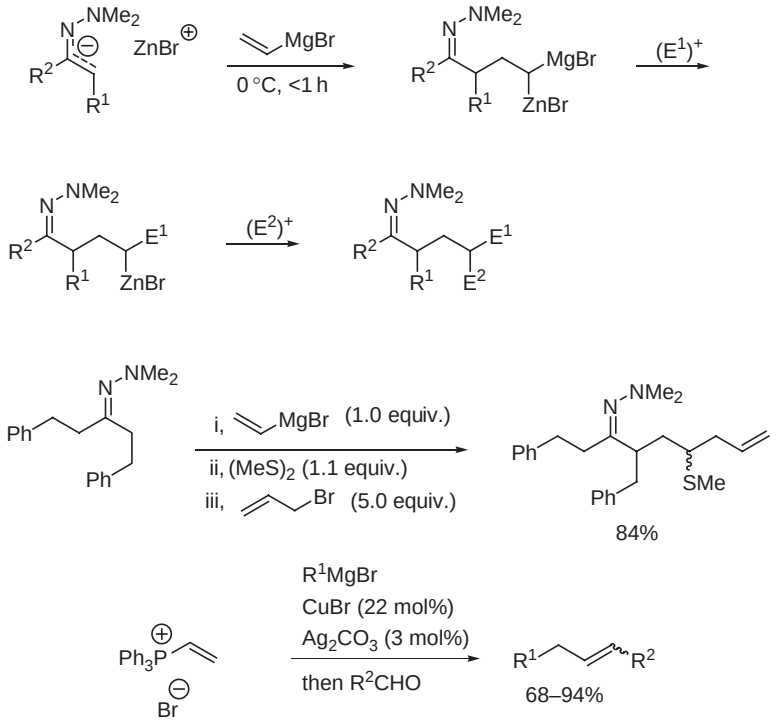
Imines derived from 3-methoxy-2-naphthaldehydes react with organomagnesium compounds by a 1,4-addition mechanism. This reaction can be performed with high diastereoselectivity by using an apropriate chiral auxiliary. The method was applied for the synthesis of optically pure β-tetralones.[243]

Reaction of aryl Grignard compounds, obtained *in situ* by iodine–magnesium exchange, with $CoCl_2$, presumably generates aryl radicals. In the presence of a double bond or aromatic ring an intramolecular radical cyclization may take place. This reaction was used for the synthesis of spiro-indolines.[244] Oshima has applied cobalt-mediated tandem radical cyclization-cross-coupling reaction for the synthesis of benzyl-substituted heterocycles (Scheme 80).[245]

Vinylmagnesium bromide reacts as a Michael acceptor with a zincated hydrazone, yielding a 1,1-bimetallic species, which in some cases can be sequentially trapped with two different electrophiles.[246,246a] The reaction proceeds via metalla-aza-Claisen rearrangement. The dimethyl hydrazone anion behaves as an "azaallylic" system (Scheme 81).[247] Vinylphosphonium salts add Grignard reagents, forming alkylphosphonium ylides. These ylides



Scheme 80

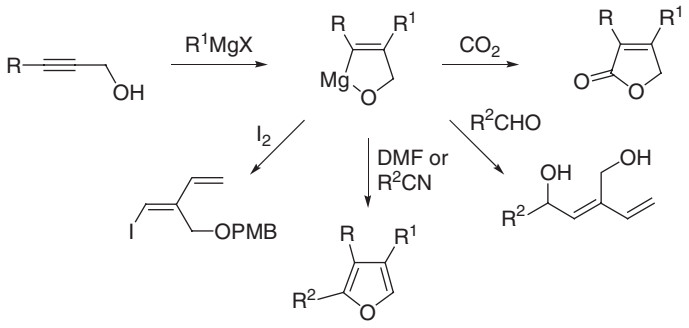


Scheme 81

react with aldehydes, yielding alkenes in one-pot sequence, catalyzed by copper and silver salts. Both metals are essential for the catalysis (Scheme 81).[248]

9.03.3.3.1.(iv) Addition to triple carbon–carbon bonds

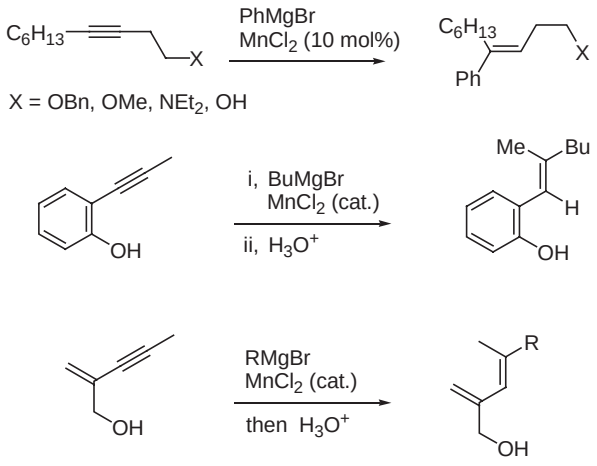
The addition of Grignard reagents to an unactivated triple bond usually requires the presence of a coordinating group and/or transition metal catalysis. Propargyl alcohols react with RMgX regioselectively. A number of synthetically useful transformations are possible using this synthetic method (Scheme 82).[249,249a,249b] Homopropargylic alcohols or



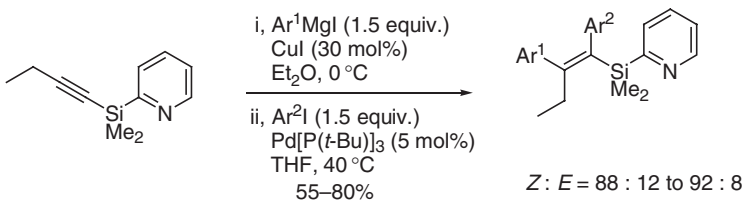
Scheme 82

ortho-ethynyl-phenols and -benzylic alcohols react with Grignard compounds using manganese salt catalysis. The corresponding propargylic alcohols give, under these conditions, allenes (Scheme 83).[250,251]

Acetylenes bearing a 2-pyridyldimethysilyl group add arylmagnesium halides in the presence of copper catalysts. The resulting alkenylmagnesium species can be further coupled *in situ* with aryl iodides. Pyridyldimethylsilyl group may also act as a leaving group in the subsequent cross-coupling reaction[252] affording triaryl-substituted alkenes. This method has been applied for the synthesis of Tamoxifen analogs, important as anti-cancer drugs (Scheme 84).[253]



Scheme 83



Scheme 84

9.03.3.3.2 Addition to carbon–oxygene double bonds

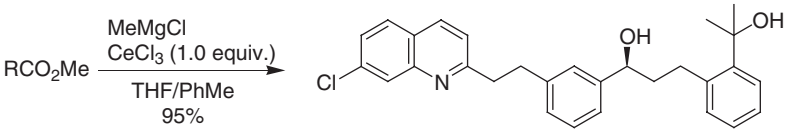
The reaction of organomagnesium species with carbonyl compounds is usually complicated by side reactions like reduction or enolization. Often, these reactions are even predominant. Much efforts were made for developing selective reactions. The use of rare earth metal chlorides, that form highly nucleophilic species with low basicity like cerium(III) chloride, was developed by Imamoto.[254] Enantioselective addition of organomagnesium species is usually performed by using chiral complexes of organomagnesium derivatives.[255] A computational study of the 1,2-addition of Grignard compounds to carbonyl compounds gives useful insights of this reaction.[256]

The addition of MeMgCl to an ester in the presence of $CeCl_3$ giving a tertiary alcohol was needed in the course of the synthesis of the antiasthmatic drug Singulair.[257] It was found that the formation of a specific form of $CeCl_3$–THF solvate is crucial for the reaction selectivity (Scheme 85).

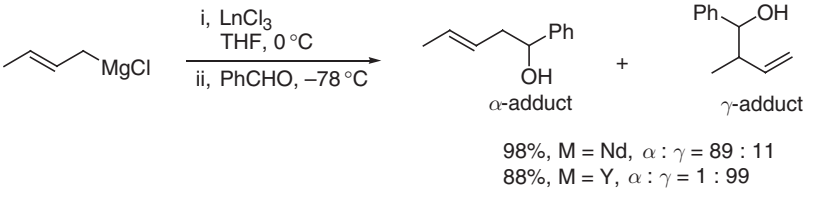
The selectivity of the reaction of crotylmagnesium chloride with benzaldehyde in the presence of various rare earth metal chlorides was studied by Imamoto. Interestingly, the ratio of α to γ products can be switched to the opposite simply by using of another rare earth metal salt. Yttrium gives exclusively γ-product, whereas neodymium leads to 89% of α-attack (with 92% of (*E*)-isomer).[258] Scandium behaves like yttrium, other lanthanides give intermediate results (Scheme 86).

In the presence of $InCl_3$ (5 mol%) Grignard reagents react with α,β-enones, giving improved 1,2/1,4 product ratio, although not as good as for $CeCl_3$.[259] The diastereoselectivity of the addition of 2-chloro-1-phenylethylmagnesium chloride with benzaldehyde was studied by Hoffmann. In the presence of Me_2AlCl, a *syn*/*anti* ratio between 86 : 14 and 96 : 4 was obtained. Interestingly, the corresponding Grignard reagent, bearing a thiophenyl group instead of chlorine gives exclusively the *syn*-addition product.[260]

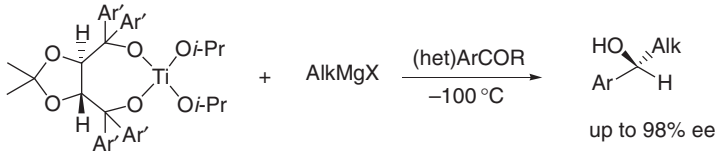
The enantioselective addition of organomagnesium compound to ketones can be performed by using either chiral reagent or chiral auxiliary in the substrate. Primary alkylmagnesium reagents add to aryl- and heteroaryl ketones in the presence of magnesium TADDOLate at −100 °C yielding products with up to 98% ee (Scheme 87).[261] Chiral α-ketoacetals, prepared in two steps from α-substituted cinnamic aldehydes, add organomagnesium species with up to 98% diastereoselectivity (Scheme 88).



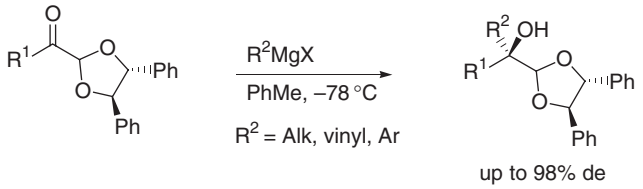
Scheme 85



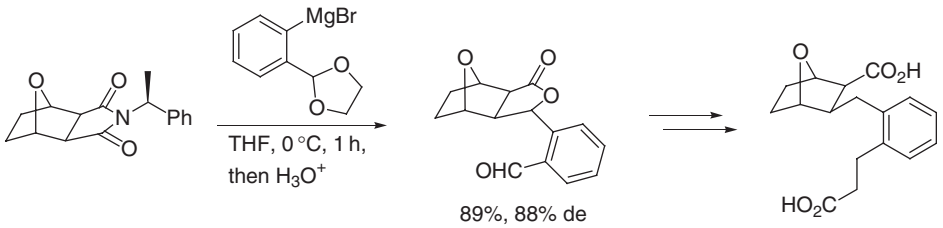
Scheme 86



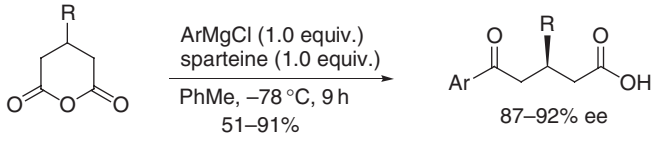
Scheme 87



Scheme 88



Scheme 89



Scheme 90

The aldehyde group of phenyl- and *tert*-butylglyoxals forms a cyclic aminoacetal with (*R*)-piperidin-3-ol. The remaining free keto group reacts with organomagnesium reagents with up to 96% de. Hydrolysis gives enantiopure α-hydroxy aldehydes.[262] N-Boc-leucinal reacts with allyl- and alkenylmagnesium halides giving *syn*- and *anti*-products in about 9 : 1 ratio. This method was used for the asymmetric synthesis of important amino acids like statine and norstatine.[263] Diastereoselective addition of a Grignard reagent to a chiral imide was used in an elegant enantioselective large-scale synthesis of a tromboxane A2 antagonist Ifetroban (Scheme 89).[264]

Reaction of succinylhydrazide derived from (*S*)-amino-2-methoymethylpyrrolidine (SAMP) with benzylmagnesium chlorides allows us to prepare a number of enantiopure 5-arylmethyl-pyrrolidones and -pyrrolidines.[265] An enantioselective desymmetrization of anhydrides was reported by Fu. Arylmagnesium chlorides react in toluene in the presence of 1 equiv. of (−)-sparteine with 3-substituted glutaric anhydrides, giving aryl ketones with 87–92% ee (Scheme 90).[266]

Ynals can be selectively hydrosilylated in the presence of Pt salts leading to α-triethylsilyl enals, which undergo 1,2-addition of Grignard reagents followed by Peterson elimination from the intermediate alcohol. This method offers a simple synthetic route from ynals to the corresponding allenes.[267]

9.03.3.3.3 Addition to the carbon–nitrogen multiple bonds

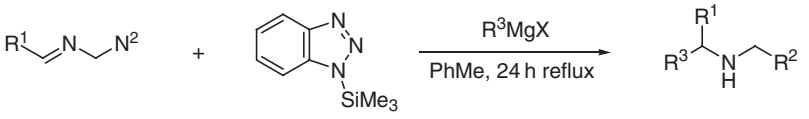
Reaction of Grignard reagents with imines and nitriles is an important method for preparing primary amines. In comparison with organolithium reagents, the reaction of RMgX with imines shows a complex behavior which depends on the nature of the reagents. A directing group on the aldimine facilitates the reaction. A stoichiometric amount of a Lewis acid can be added to enhance the rate and 1,2-selectivity.[268] The addition reaction of organometallic reagents to imines has been reviewed.[269,270]

Grignard reagents add with difficulty to imines derived from enolizable carbonyl compounds. Improvements such as the activation of the C═N bond can be achieved either by attachment of an electron-withdrawing group or

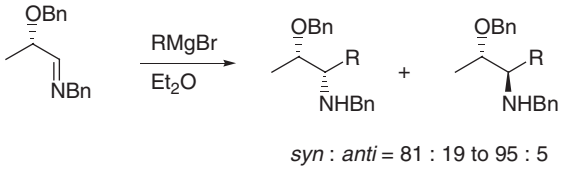
N-coordination with a Lewis acid, complexing the organometallic reagent, or the use of a ligand or a less basic organometallic species.[269] Activation of the C═N moiety of the aldimines by 1-benzotriazolyltrimethylsilane minimizes the risk of side reactions. The mechanism involves reversible addition of BtTMS to the imine followed by displacement of benzotriazolyl group by a Grignard reagent (Scheme 91).[271] Imines, derived from *O*-benzyllactaldehyde and benzylamine, react with non-stabilized Grignard reagents in ether yielding amino alcohols with excellent de's (Scheme 92).[272]

Addition of organomagnesium reagents to the N-benzylimine derived from 2-*O*-benzyl-L-threitol, afforded the *threo*-adduct with very good selectivity.[273] Similarly, PhMgBr or MeMgBr adds to the benzylimine from protected glyceraldehydes giving a single *syn*-diastereomer, supposedly via a five-membered chelate.[274] In contrast, for the cyclic substrate, the formation of a six-membered chelate was suggested, since in this case, a unique *anti*-adduct is obtained (Scheme 93).[275]

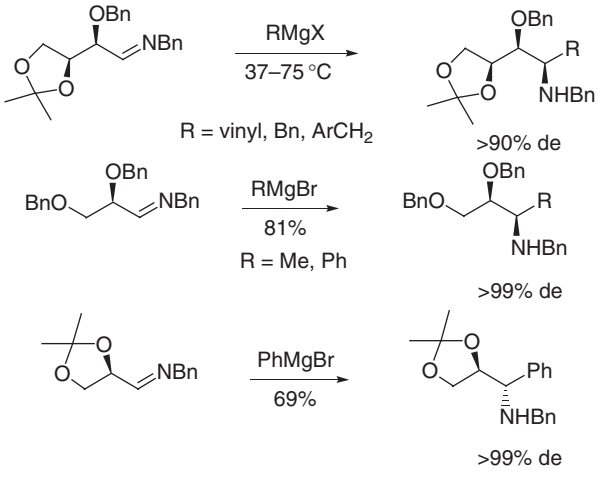
Very good yields and diastereoselectivities have been observed for the addition of RMgBr to imines derived from phenylglycinol which are existing in equilibria with cyclic 1,3-oxazolidines. Methoxyacetone imine reacts with Grignard reagents with excellent de's. The addition of Lewis acids (usually $MgBr_2$) has strong influence on the yields and selectivity. This approach was used for the asymmetric synthesis of 5-HT reuptake inhibitor Cericlamine (Scheme 94).[276]



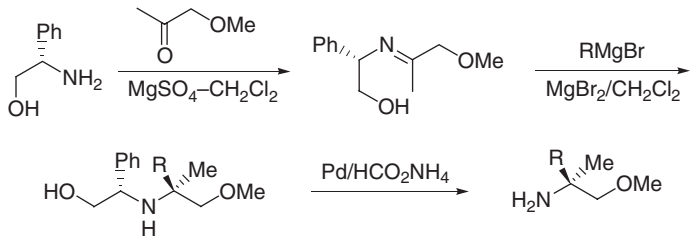
Scheme 91



Scheme 92



Scheme 93



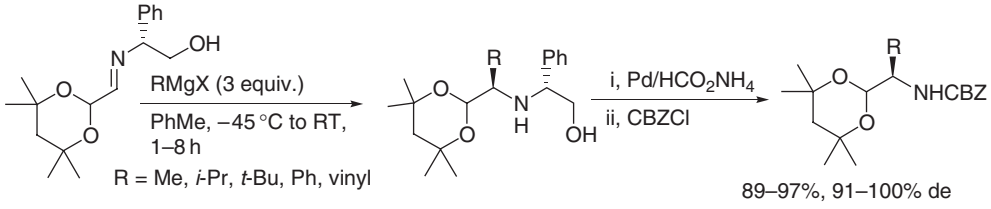
Scheme 94

Hemiacetals derived from fluoral and phenylglycinol react with excess of Grignard reagents, giving adducts with 90–95% de. They can be converted to optically pure 1-substituted-2,2,2-trifluoroethylamines by $Pb(OAc)_4$.[277] Imines derived from glyoxal acetals react with various organomagnesium compounds with excellent diastereoselectivity.[278] The resulting products were converted to protected enantiopure amino aldehydes. Although THF is usually the solvent of choice for this addition reaction, in this case, toluene turned out to be superior (Scheme 95).

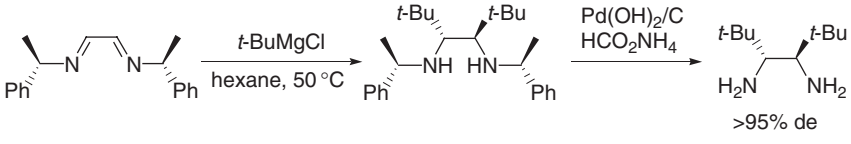
Interestingly, all other diols, tried as a protecting group on the acetal, led to lower diastereoselectivity of the addition. This synthetic strategy was used in the synthesis of indolizidine alkaloids,[279] bis(1-arylethyl)amines,[280] a protease inhibitor.[281] The addition reaction of 1,2-bisimines, easily available from glyoxal and chiral α-phenylethylamine, gives under optimized conditions a diastereomerically pure product, that was converted to a chiral 1,2-diamine. Interestingly, decrease of the temperature below the optimum (50 °C) leads to a sharp drop of the stereoselectivity (Scheme 96).[282]

Nitrones possess a highly polarized C═N bond, which is responsible for their good reactivity as electrophiles. Reactions of nitrones with organometallic compounds have been reviewed.[283] The reaction of organomagnesium compounds with α-alkoxynitrones gives a mixture of diastereomeric hydroxylamines in good yields. The diastereoselectivity of this reaction can be switched by precomplexation with Et_2AlCl.[284] Nitrones derived from L-serine give adducts with Grignard reagents in THF at −50 °C with high diastereoselectivity (Scheme 97).[285]

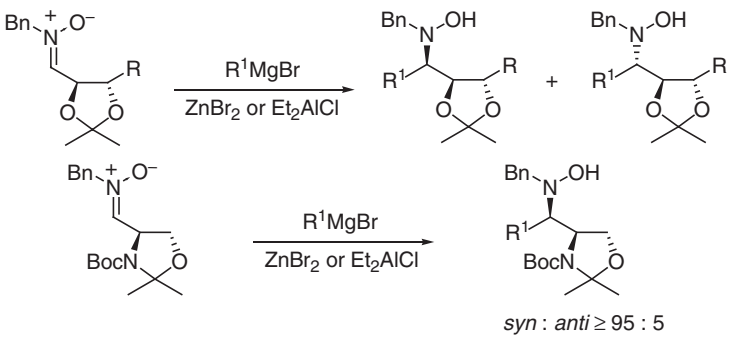
Chiral oxime ethers of (*R*)- and (*S*)-*O*-(1-phenylbutyl)-hydroxylamine (ROPHy/SOPHy) add Grignard reagents in the presence of BF_3 in toluene at −78 °C with good to very high diastereoselectivity.[286] The products were converted enantioselectively to primary amines, or in case of R = allyl to β-aminoacids (Scheme 98). For hydrazones, the C═N double bond is sufficiently reactive toward a nucleophilic attack of an organomagnesium compound. Although the reaction is relatively sluggish, high level of diastereoselectivity can be achieved. Reactions of a dimethylhydrazone-aminal



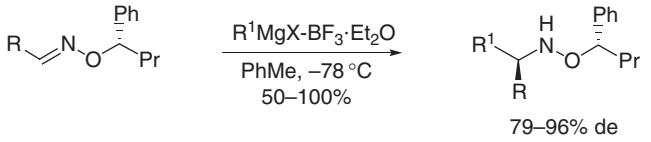
Scheme 95



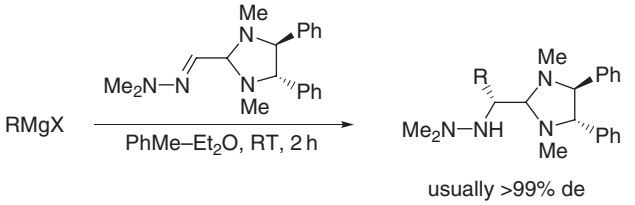
Scheme 96



Scheme 97



Scheme 98



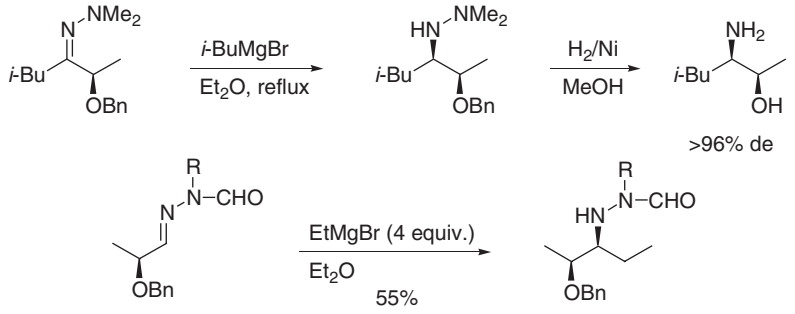
Scheme 99

of glyoxal led to the products such as single diastereomers. They were further converted to enantiomerically pure α-amino aldehydes (Scheme 99).[287]

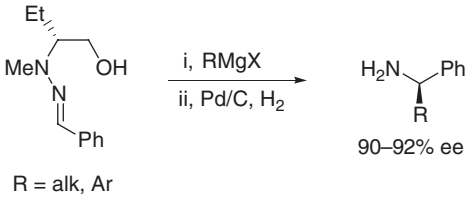
A structurally simple dimethylhydrazone of O-benzyllactaldehyde gives an excellent level of substrate control in the organomagnesium addition reaction, leading almost exclusively to the *syn*-isomer.[288] The addition product can be reduced to the corresponding *syn*-aminoalcohol on Raney Ni. Stereoselective Grignard addition to a similar N-formyl hydrazone proceeds with 92% diastereoselectivity, but the silylation of the amide nitrogen by TMSCl leads exclusively to the formation of a *syn*-adduct. This compound was synthesized as a side chain of the perspective antifungal drug Noxafil (Scheme 100).[289]

Hydrazones can be easily cleaved after the diastereoselective addition reaction and may bear a chiral auxiliary. According to these lines, hydrazones, derived from (*R*)-2-aminobutan-1-ol, were used for the synthesis of α-arylalkanamines with good optical purity (Scheme 101).[290,290a] Imines, bearing an acyl or phosphoryl moiety on the nitrogen atom, are suitable substrates for the addition of Grignard compounds. N-(diethoxyphosphoryl)benzaldimines give good yields of α-arylalkylamines after the reaction with organomagnesium halides followed by hydrolysis with 20% HCl.[291] N-diphenylphosphinoyl ketimines, derived from α-amino acids, react with Grignard reagents with very high de's. The diphenylphosphinoyl group can be cleaved after P═O bond reduction with $HSiCl_3$ giving optically active trisubstituted 1,2-ethylenediamines (Scheme 102).[292]

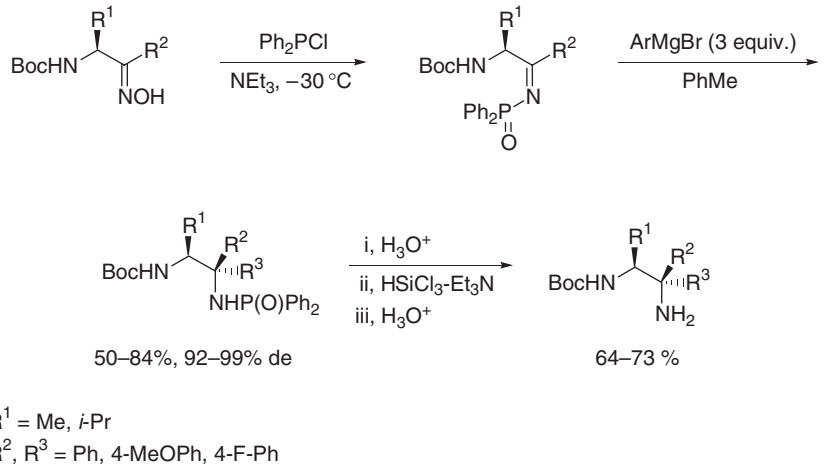
A convenient synthesis of aryl glycines from Grignard reagents, prepared via iodine–magnesium exchange, was performed by the reaction with N-Boc-iminomalonate (from diethyl mesoxalate and BocN═PPh_3). The reaction



Scheme 100



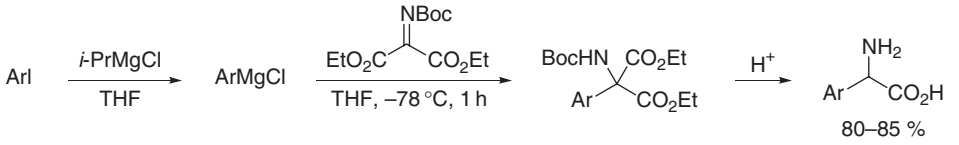
Scheme 101



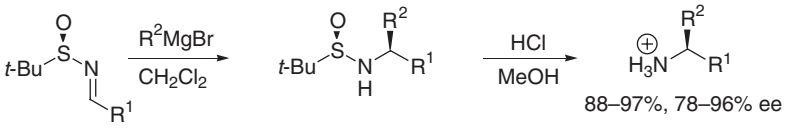
Scheme 102

proceeds smoothly at low temperatures, thus tolerating many functional groups in the Grignard reagent, and gives high yields of products (Scheme 103).[293] Chiral sulfinimines, developed by Ellman,[294,294a,294b] are very useful intermediates for the synthesis of optically pure primary amines. Both enantiomers of *tert*-butanesulfinamide are easily available by a simple reaction sequence (Scheme 104).[294b]

This reaction has also been applied to the synthesis of α-amino acids.[295,295a,295b] In the case of the sulfinimines derived from simple ketones, lithium reagents are preferable for the addition,[294a] although for cyclic ketones, organomagnesium compounds gave better results. The addition of alkyl and aryl Grignard compounds to



Scheme 103

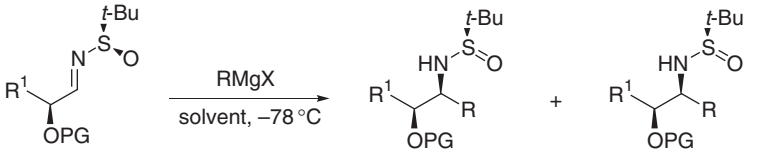


Scheme 104

sulfinyl imines derived from 3- and 4-substituted cyclohexanones proceeds with excellent diastereoselectivity, which is dependent on the stereochemistry of the ring substituents rather than on the sulfinyl group.[296] N-*t*-Butylsulfinyl α-alkoxyaldimines can be readily prepared from protected (*S*)-lactals. Addition of ethyl or phenyl Grignard compounds furnishes 1,2-disubstituted β-aminoalcohols in good yields (73–98%) and with high ee's. Depending on the protecting group and reaction conditions, either *syn*- or *anti*-alcohol can be prepared (Scheme 105).[297]

The presence of a coordinating group in the sulfinimine may strongly influence the selectivity of the reaction with Grignard derivatives. In the case of 2-pyridyl *tert*-butylsulfinimines, the diastereoselectivity of the addition is reversed due to the coordination with the pyridine nitrogen.[298,298a–298c] Attempts have been made to prepare sulfinyl chiral auxiliary based on the chiral natural pool. A sulfinamide auxiliary available from naturally occurring (+)-pulegone in four steps provides better diastereoselectivities than Ellman's sulfinimine.[299] A camphor-derived mercapto chiral auxiliary can be transformed into sulfen- and sulfin-amides after the reaction with Grignard compounds. After the reduction and hydrolysis, amines were obtained with up to 99% ee.[300]

The addition of organomagnesium reagents to chiral 2*H*-azirine 2-carboxylate esters was used for the synthesis of optically active quaternary β-amino acids (60–94% ee).[301] The nucleophilic attack of Grignard reagents on nitriles usually stops after the formation of magnesium salts of imines. ω-Bromonitriles give cyclic imines in 33–84% yields after the intramolecular alkylation reaction. Substituted benzophenonimines from aryl Grignard compounds and benzonitriles can be reduced *in situ* by sodium borohydride to benzhydrylamines.[302] A one-pot synthesis of (1*R*,2*S*)-1-aryl-2-alkylaminoalcohols from (*R*)-cyanohydrines[303] was accomplished by the reaction with MeMgX, transamination of the resulting magnesium imide, and diastereoselective reduction with $NaBH_4$. Addition of titanium(IV) isopropoxide to the imide, formed from a nitrile and an organomagnesium halide, allows the addition of a second Grignard reagent yielding primary amines. This approach has been used for the preparation of disubstituted α-amino acids from cyanohydrines.[304] 2-Substituted quinolines were obtained from quinoline-N-oxide by reaction with chloroformates followed by the addition of a Grignard reagent.[305]



PG = Bn, R = Et, THF/TMEDA, dr = 2 : 98
PG = TBS, R = Et, PhMe, dr = 92 : 8

Scheme 105

9.03.3.4 Diverse Reactions with Electrophiles

9.03.3.4.1 Electrophilic amination and reactions with nitroarenes

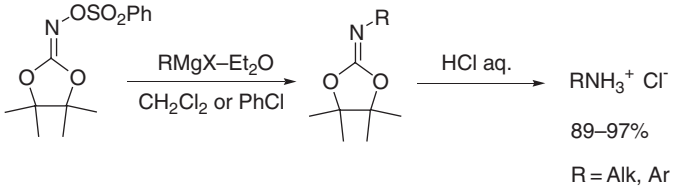
A number of methods were developed for the electrophilic amination of Grignard reagents[306,306a] to prepare primary amines. One of the recent examples uses 1,3-dioxolan-2-one *O*-sulfonyloxime.[307] The reaction gives imine, which affords primary amine after hydrolysis (Scheme 106). By using acetone *O*-(mesitylsulfonyl)-oxime the amination can be performed under Barbier conditions from aryl bromide and magnesium.[308]

Reaction of organic azides with Grignard reagents gives triazenes, which can be hydrolyzed into anilines (from aryl Grignard reagents and allyl azide[309]) or mono-N-alkylanilines (from aryl azides and alkyl Grignard reagents[310]). Arylmagnesium halides add to arylazosulfonates (from sodium phenylsulfinate and aryldiazonium fluoroborates) yielding diarylamines after reduction (Scheme 107).[311]

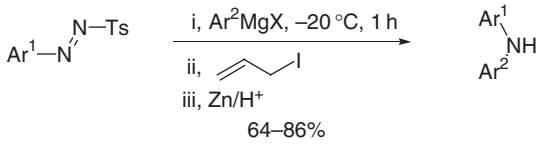
Nitrosoarenes give unstable diaryl hydroxylamines with aryl Grignard reagents, which can be reduced directly to diarylamines.[312] Since arylmagnesium halides reduce nitroarenes to nitroso compounds, readily available nitroarenes and nitrohetarenes can be involved in this reaction allowing a simple preparation of polyfunctionalized diaryl- and heteroarylamines (Scheme 108).[313]

Alkylmagnesium reagents react with 4-nitroanisole by different mechanisms, giving in THF at −70 °C a number of products. Oxidation by $KMnO_4$ in liquid NH_3 affords, depending on the alkyl chain, mixtures of nitrosoanisol and 2-alkyl-4-nitroanisol.[314]

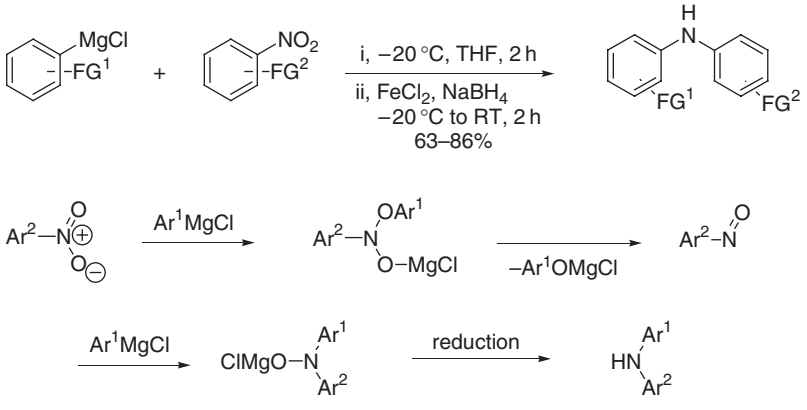
The synthesis of 7-substituted indoles from *ortho*-substituted nitroarenes and alkenylmagnesium halides is known as the Bartoli reaction.[315] Usually, *ortho*-unsubstituted nitroarenes give complex mixtures of products. In some cases



Scheme 106



Scheme 107



Scheme 108

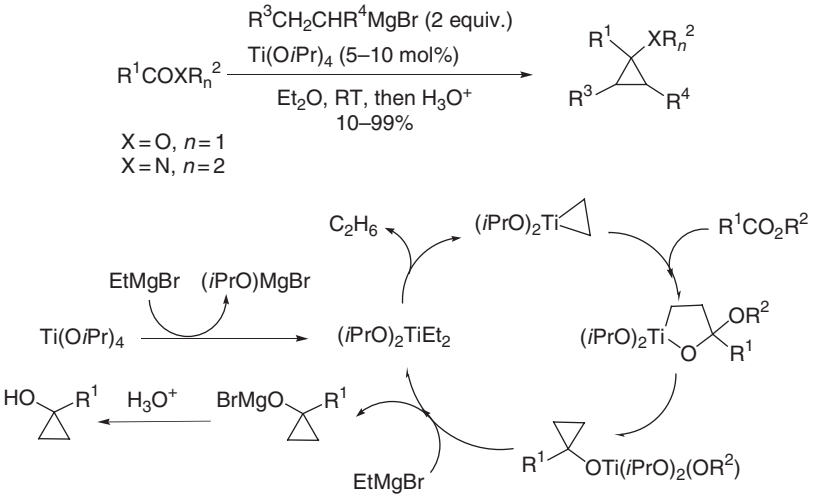
though, substituted nitroarenes with both free *ortho*-positions were converted into indoles in good yields.[316] The Bartoli reaction can be successfully used for the synthesis of substituted 4- and 6-azaindoles from 3-nitropyridines.[317] The reaction between organomagnesium reagents and nitroarenes was reviewed.[318]

9.03.3.4.2 Synthesis of cyclopropanes

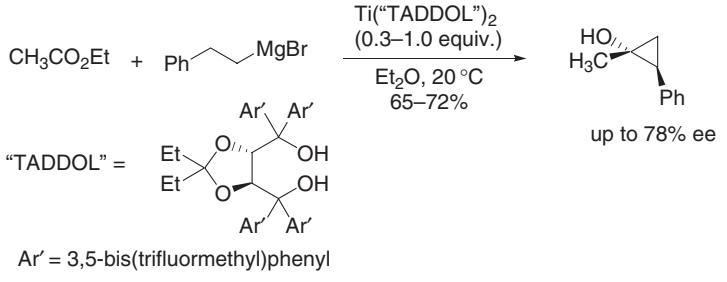
Formation of cyclopropylamines and cyclopropanols from alkylmagnesium halides and esters, amides, or nitriles, catalyzed by titanium alcoholates, was discovered by Kulinkovich in 1989. The reaction mechanism includes the formation of dialkoxytitanacyclopropanes, which reacts with a carbonyl compound or a nitrile (Scheme 109).

If an alkene is present in the reaction mixture the intermediate, titanacyclopropane, undergoes facile ligand exchange, giving new titanium species, which react further in the catalytic cycle. Thus, various alkenes can be involved in this reaction, inter- or intramolecularly, allowing the preparation of numerous cyclopropane derivatives. In the presence of a chiral titanium alcoholate the reaction can be performed with good enantioselectivity (Scheme 110).[319]

An extensive review of this reaction was published by Kulinkovich and de Meijere.[320] Titanium-mediated synthesis of cyclopropylamines from Grignard reagents and nitriles has been also reviewed.[321] The treatment of allylic alcohols with organomagnesium reagents in the presence of *gem*-alkyl dihalides affords substituted cyclopropyl alcohols.[322] Iodine–magnesium exchange occurs upon treatment of 3-iodomethyl-1-oxacyclopentanes with alkyl Grignard reagents. The resulting organomagnesium compounds undergo intramolecular nucleophilic substitution in ether affording cyclopropanes.[323]



Scheme 109



Scheme 110

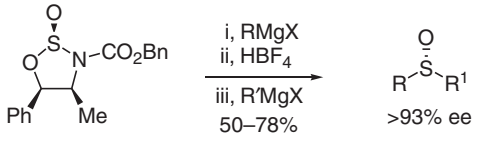
9.03.3.4.3 Synthesis of chiral sulfoxides

Chiral sulfoxides are useful intermediates in asymmetric synthesis. A number of methods for their preparation were developed in the last decade. An interesting displacement of dimethylphosphonylmethyl moiety, a carbon leaving group, from sulfur by Grignard reagents was used to obtain enantiomerically pure *p*-tolyl sulfoxides.[324] Optically pure methyl 4-bromophenyl sulfinate was subjected to a one-pot sequence yielding unsymmetrical dialkyl sulfoxides in 60–97% yield and >98% ee.[325,325a,325b] A simple one-pot synthesis of chiral sulfoxides from norephedrine-derived sulfamidites in high optical purity was developed (Scheme 111).[326,327]

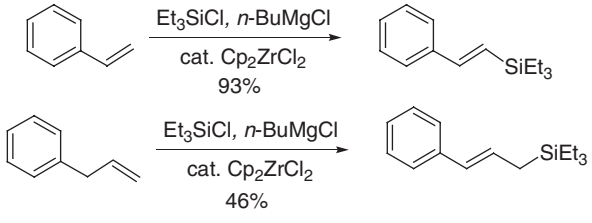
9.03.3.5 Various Reactions of Grignard Reagents

Styrene reacts with Et_3SiCl in the presence of *n*-BuMgCl and a catalytic amount of Cp_2ZrCl_2 to give (*E*)-isomer of β-triethylsilylstyrene in 93% yield with greater than 99% regio- and stereoselectivity.[328] From allylbenzene, cinnamyltriethylsilane was obtained in 46% yield (Scheme 112).

Oxidative homocoupling of alkyl, aryl, alkenyl, and allylic Grignard reagents occurs by the reaction with trifluoromethanesulfonic anhydride in 20–30 min at room temperature.[329] Arylmagnesium compounds dimerize by treatment with $TiCl_4$ (1.5 equiv.) at low temperatures.[330] Aryl chlorides are dechlorinated by Grignard reagents in the presence of an iron catalyst.[331] 1,1-Dibromocyclopropanes are subsequently reduced to monobromo derivatives or dehalogenated by treatment with EtMgBr and $Ti(OiPr)_4$ (5–10%) mol. at room temperature.[332] Reaction of arylmagnesium halides with diphenyl sulfoxide and TMSCl yields triarylsulfonium salts.[333] Aryl Grignard reagents react with SO_2 to form sulfinates, which are converted in a one-pot procedure to sulfonamides by treatment with SO_2Cl_2 and amines.[334] Reaction of acetophenone α,α-dibromooxime ethers with alkyl, alkenyl, and arylmagnesium compounds yields trisubstituted pyrimidines.[335] Reaction of lithium aralkylamides with carbenoid-type α-chloroalkylmagnesium halides gives α-lithiated tertiary amine, which can be trapped by electrophiles as a result of a nucleophilic attack on the carbene. Lithium dialkylamides give exclusively products of carbene dimerization.[336] The direct conversion of Grignard reagents to nitriles can be performed by the reaction with phenyl cyanate or, better, with 2-pyridyl cyanate.[337] Unsymmetrical diazenes were obtained by the reaction of Grignard reagents with arenediazonium *o*-benzenedisulfonimides.[338] Aryltrialkoxysilanes which are useful for cross-coupling reactions and for the production of silicone materials were obtained from arylmagnesium halides and tetraalkylorthosilicates.[339] Reaction of benzyl Grignard reagents with α-oxoketene dithioacetals followed by treatment with $BF_3{\cdot}Et_2O$ leads to substituted naphthalenes as a result of intramolecular electrophilic cyclization.[340,341] Treatment of furfural tosylhydrazone with arylmagnesium halides (2.5 equiv.) gave good yields of (*E*,*E*)-5-aryl-2,4-pentadienals. Alkylmagnesium compounds gave in this reaction 2-alkylfurans as products.[342]



Scheme 111



Scheme 112

9.03.4 Conclusion

The development of organomagnesium chemistry for organic synthesis has been accelerated by the extensive use of transition metal catalysis and by the finding of new preparations of polyfunctional Grignard reagents, using the I/Mg and Br/Mg exchange reactions. The Grignard reagents remain 100 years after their discovery by Victor Grignard key reagents for the organic synthesis. Further fascinating developments may be anticipated.

References

1. Wakefield, B. J. *Organomagnesium Methods in Organic Synthesis*; Academic: London, 1995.
1a. Silverman, G. S.; Rakita, P. E. *Handbook of Grignard Reagents*; Marcel Decker: New York, 1996.
1b. Richey, H. G., Jr. *Grignard Reagents: New Developments*; Wiley: Chichester, 2000.
2. Sakamoto, S.; Imamoto, T.; Yamaguchi, K. *Org. Lett.* **2001**, *3*, 1793–1795.
3. Tuulmets, A.; Marvi, M.; Panov, D. *J. Organomet. Chem.* **1996**, *523*, 133–138.
4. Sassian, M.; Panov, D.; Tuulmets, A. *Appl. Organomet. Chem.* **2002**, *16*, 525–529.
5. Garst, J. F.; Seriaga, M. P. *Coord. Chem. Rev.* **2004**, *248*, 623.
6. Walbovsky, H. M.; Topolski, M. *J. Am. Chem. Soc.* **1992**, *114*, 3455–3459.
7. Péralez, E.; Négrel, J.-C.; Chanon, M. *Tetrahedron* **1995**, *51*, 12601–12610.
8. Teerlinck, C. E.; Bowyer, W. J. *J. Org. Chem.* **1996**, *61*, 1059–1064.
9. Tilstam, U.; Weinmann, H. *Org. Process Res. Dev.* **2002**, *6*, 906–910.
10. Bogdanović, B.; Schwickardi, M. *Angew. Chem. Int. Ed.* **2000**, *39*, 4610–4612.
11. Rieke, R. D.; Hanson, M. V. *Tetrahedron* **1997**, *53*, 1925–1956.
11a. Rieke, R. D.; Sell, M. S.; Klein, W. R.; Chen, T.-A.; Brown, J. D.; Hanson, M. V. In *Active Metals. Preparation, Characterization, Application*; Fürstner, A., Ed.; Wiley-VCH: Weinheim, 1996; p 1.
12. Lee, J.; Velarde-Ortiz, R.; Guijarro, A.; Wurst, J. R.; Rieke, R. D. *J. Org. Chem.* **2000**, *65*, 5428–5430.
13. Sugimoto, O.; Yamada, S.; Tanji, K. *Tetrahedron Lett.* **2002**, *43*, 3355–3357.
14. Sugimoto, O.; Yamada, S.; Shigeru, K. *J. Org. Chem.* **2003**, *68*, 2054–2057.
15. Cheng, D.; Zhu, S.; Yu, Z.; Cohen, T. *J. Am. Chem. Soc.* **2001**, *123*, 30–34.
16. Bonnet, V.; Mongin, F.; Trécourt, F.; Quéguiner, G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4245–4249.
17. Eaton, P. E.; Zhang, M.-X. *Angew. Chem. Int. Ed.* **2002**, *41*, 2169–2171.
18. Schlecker, W.; Huth, A.; Ottow, E.; Mülzer, J. *J. Org. Chem.* **1995**, *60*, 8414–8416.
19. Kondo, Y.; Yoshida, A.; Sakamoto, T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2331–2332.
20. Dinsmore, A.; Billing, D. G.; Mandy, K.; Michael, J. P.; Mogano, D.; Patil, S. *Org. Lett.* **2004**, *6*, 293–296.
21. Henderson, K. W.; Kerr, W. J. *Chem. Eur. J.* **2001**, *7*, 3431–3437.
22. Bonafoux, D.; Bordeau, M.; Biran, C.; Dunogues, J. *J. Organomet. Chem.* **1995**, *993*, 27.
22a. Lessene, G.; Tripoli, R.; Cazeau, P.; Biran, C.; Bordeau, M. *Tetrahedron Lett.* **1999**, *40*, 4037.
23. Evans, D. A.; Nelson, S. G. *J. Am. Chem. Soc.* **1997**, *119*, 6452.
23a. Hendersson, K. W.; Kerr, W. J.; Mair, J. H. *Tetrahedron* **2002**, *58*, 4573.
24. Bogdanović, B.; Bons, P.; Konstantinović, S.; Schwickardi, M.; Westeppe, U. *Chem. Ber.* **1993**, *126*, 1371–1383.
25. Braun, L. F.; Dreier, T.; Christy, M.; Petersen, J. L. *Inorg. Chem.* **2004**, *43*, 3976–3987.
26. Gao, Y.; Sato, F. *J. Chem. Soc., Chem. Commun.* **1995**, 659–660.
27. Cai, M.; Xia, J.; Chen, G. *J. Organomet. Chem.* **2004**, *689*, 2531–2534.
28. Cai, M.; Xia, J.; Hao, W. *Heteroatom. Chem.* **2005**, *16*, 65–68.
28a. Cai, M.; Hao, W.; Zhao, H.; Xia, J. *J. Organomet. Chem.* **2004**, *689*, 3593–3597.
28b. Cai, M.; Xia, J.; Chen, G. *J. Organomet. Chem.* **2004**, *689*, 1714–1717.
28c. Shinokubo, H.; Miki, H.; Yokoo, T.; Oshima, K.; Utimoto, K. *Tetrahedron* **1995**, *51*, 11681–11692.
29. Victorov, N. B.; Zubritskii, L. M. *Russ. J. Org. Chem.* **1997**, *33*, 1706.
30. Sato, F.; Vrade, H. Hydromagnesation of alkenes and alkynes. In *Grignard Reagents – New Developments*; Richey, H. G., Jr., Ed.; Wiley: New York, 2000; pp 65–105.
31. Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 4414–4435.
32. Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem. Int. Ed.* **1998**, *37*, 1701.
33. Jensen, A. E.; Dohle, W.; Sapountzis, I.; Lindsay, D. M.; Vu, V. A.; Knochel, P. *Synthesis* **2002**, 565.
34. Graening, T.; Friedrichsen, W.; Lex, J.; Schmalz, H.-G. *Angew. Chem. Int. Ed.* **2002**, *41*, 1524–1526.
35. Wang, J.; Pomerantz, M. *Tetrahedron Lett.* **1995**, *36*, 2571–2574.
36. Varchi, G.; Kofink, C.; Lindsay, D. M.; Ricci, A.; Knochel, P. *Chem. Commun.* **2003**, *3*, 396–397.
37. Murafuji, T.; Nishio, K.; Nagasue, M.; Tanabe, A.; Aomo, M.; Sugihara, V. *Synthesis* **2000**, 1208.
38. Sapountzis, I.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 1610.
39. Varchi, G.; Jensen, A. E.; Dohle, W.; Ricci, A.; Cahiez, G.; Knochel, P. *Synlett* **2001**, 477.
40. Abarbri, M.; Dehmel, F.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7449.
40a. Abarbri, M.; Thibonnet, J.; Bérillon, L.; Dehmel, F.; Rottländer, M.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 4618.
41. Nishiyama, H.; Isaka, K.; Itoh, K.; Ohno, K.; Nagase, H.; Matsumoto, K.; Yoshiwara, H. *J. Org. Chem.* **1992**, *57*, 407.
42. Leazer, J. L., Jr.,; Cvetovich, R.; Tsay, F.-R.; Dolling, U.; Vickery, T.; Bachert, D. *J. Org. Chem.* **2003**, *68*, 3695–3698.
43. Jones, P.; Reddy, C. K.; Knochel, P. *Tetrahedron* **1998**, *54*, 1471.
43a. Jones, P.; Knochel, P. *J. Chem. Soc., Perkin Trans 1* **1997**, 3117.
43b. Kneisel, F. F.; Knochel, P. *Synlett* **2002**, *11*, 1799.
44. Delacroix, T.; Bérillon, L.; Cahiez, G.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 8108–8110.

45. Sapountzis, I.; Lin, W.; Fischer, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 4364–4366.
46. Lin, W.; Sapountzis, I.; Knochel, P. *Angew. Chem. Int. Ed.* **2005**, *44*, 4258–4261.
47. Abarbri, M.; Thibonnet, J.; Bérillon, L.; Dehmel, F.; Rottländer, M.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 4618–4634.
47a. Knochel, P.; Hupe, E.; Dohle, W.; Lindsay, D. M.; Bonnet, V.; Quéguiner, G.; Boudier, A.; Kopp, F.; Demay, S., Seidel, N., *et al. Pure Appl. Chem.* **2002**, *74*, 11–17.
47b. Jensen, A. E.; Dohle, W.; Sapountzis, I.; Lindsay, D. M.; Vu, V. A.; Knochel, P. *Synthesis* **2002**, *4*, 565–569.
48. Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem. Int. Ed.* **2003**, *42*, 4302–4320.
49. Bérillon, L.; Lepretre, A.; Turck, A.; Ple, N.; Quéguiner, G.; Cahiez, G.; Knochel, P. *Synlett* **1998**, 1359–1360.
50. Abarbri, M.; Knochel, P. *Synlett* **1999**, 1577–1578.
51. Tobrman, T.; Dvorak, D. *Org. Lett.* **2003**, *5*, 4289–4291.
52. Dehmel, F.; Abarbri, M.; Knochel, P. *Synlett* **2000**, 345–346.
53. Staubitz, A.; Dohle, W.; Knochel, P. *Synthesis* **2003**, *2*, 233.
54. Jaramillo, C.; Carretero, J. C.; de Diego, J. E.; del Prado, M.; Hamdouchi, C.; Roldán, J. L.; Sánchez-Martínez, C. *Tetrahedron Lett.* **2002**, *43*, 9051.
55. Bergauer, M.; Gmeiner, P. *Synthesis* **2001**, 2281.
55a. Felding, J.; Kristensen, J.; Bjerregaard, T.; Sander, L.; Vedsø, P.; Begtrup, M. *J. Org. Chem.* **1999**, *64*, 4196.
56. Kromann, H.; Slok, F. A.; Johansen, T. N.; Krogsgaard-Larsen, P. *Tetrahedron* **2001**, *57*, 2195.
57. Trécourt, F.; Breton, G.; Bonnet, V.; Mongin, F.; Marsais, F.; Quéguiner, G. *Tetrahedron Lett.* **1999**, *40*, 4339–4342.
58. Christophersen, C.; Begtrup, M.; Ebdrup, S.; Petersen, H.; Vedsø, P. *J. Org. Chem.* **2003**, *68*, 9513–9516.
59. Spiess, A.; Heckmann, G.; Bach, T. *Synlett* **2004**, 131.
59a. Abarbri, M.; Thibonnet, J.; Bérillon, L.; Dehmel, F.; Rottländer, M.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 4618.
60. Kitagawa, K.; Inoue, A.; Shinokubo, H.; Oshima, K. *Angew. Chem. Int. Ed.* **2000**, *39*, 2481–2483.
61. Thibonnet, J.; Vu, V. A.; Bérillon, L.; Knochel, P. *Tetrahedron* **2000**, *58*, 4787–4799.
62. Sapountzis, I.; Dohle, W.; Knochel, P. *Chem. Commun.* **2001**, 2068–2069.
63. Vu, V. A.; Marek, I.; Knochel, P. *Synthesis* **2003**, *12*, 1797–1802.
64. Satoh, T.; Takano, K.; Ota, H.; Someya, H.; Matsuda, K.; Koyama, M. *Tetrahedron* **1998**, *54*, 5557–5574.
65. Shinokubo, H.; Miki, H.; Yokoo, T.; Oshima, K.; Utimoto, K. *Tetrahedron* **1995**, *51*, 11681–11692.
66. Satoh, T.; Kondo, A.; Musashi, J. *Tetrahedron* **2004**, *60*, 5453–5460.
67. Hoffmann, R. W.; Hölzer, B.; Knopff, O.; Harms, K. *Angew. Chem. Int. Ed.* **2000**, *39*, 3072–3074.
68. Hoffmann, R. W.; Nell, P. G. *Angew. Chem. Int. Ed.* **1999**, *38*, 338–340.
69. Inoue, A.; Kondo, J.; Shinokubo, H.; Oshima, K. *Chem. Eur. J.* **2002**, *8*, 1730–1740.
70. Hoffmann, R. W.; Knopff, O.; Kusche, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 1462–1464.
71. Knopff, O.; Stiasny, H. C.; Hoffmann, R. W. *Organometallics* **2004**, *23*, 705–710.
72. Hoffmann, R. W.; Kusche, A. *Chem. Ber.* **1994**, *127*, 1311–1316.
72a. Rottländer, M.; Boymond, L.; Bérillon, L.; Lepretre, A.; Varchi, G.; Avolio, S.; Laaziri, H.; Quéguiner, G.; Ricci, A., Cahiez, G., *et al. Chem. Eur. J.* **2000**, *6*, 767–770.
72b. Avolio, S.; Malan, C.; Marek, I.; Knochel, P. *Synlett* **1999**, 1820.
73. Inoue, A.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2000**, *2*, 651–653.
74. Baird, M. S.; Nizovtsev, A. V.; Bolesov, I. G. *Tetrahedron* **2002**, *58*, 1581–1593.
75. Vu, V. A.; Marek, I.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 351–352.
75a. Kondo, J.; Inoue, A.; Shinokubo, H.; Oshima, K. *Angew. Chem. Int. Ed.* **2001**, *40*, 2085–2087.
76. Satoh, T.; Kurihara, T.; Fujita, K. *Tetrahedron* **2001**, *57*, 5369–5375.
77. Satoh, T.; Matsue, R.; Fujii, T.; Marikawa, S. *Tetrahedron* **2001**, *57*, 3891–3898.
78. Fleming, F. F.; Zhang, Z.; Knochel, P. *Org. Lett.* **2004**, *6*, 501–503.
79. Inoue, A.; Kondo, J.; Shinokubo, H.; Oshima, K. *Chem. Eur. J.* **2002**, *8*, 1730–1740.
79a. Inoue, A.; Shinokubo, H.; Oshima, K. *Angew. Chem. Int. Ed.* **2001**, *40*, 2085–2087.
80. Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem. Int. Ed.* **1998**, *37*, 1701–1703.
81. Franzen, R. G. *Tetrahedron* **2000**, *56*, 685–691.
82. Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 3333–3336.
83. Kopp, F.; Krasovskiy, A.; Knochel, P. *Chem. Commun.* **2004**, 2288–2289.
84. Ren, H.; Krasovskiy, A.; Knochel, P. *Org. Lett.* **2004**, *6*, 4215–4217.
85. Baron, O.; Knochel, P. *Angew. Chem. Int. Ed.* **2005**, *44*, 3133–3135.
86. Hartmann, N.; Niemeyer, M. *Synth. Commun.* **2001**, *31*, 3839–3845.
87. Terao, J.; Naitoh, Y.; Kuniyasu, H.; Kambe, N. *Chem. Lett.* **2003**, *32*, 890–891.
88. Terao, J.; Hideyuki, H.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2002**, *124*, 4222–4223.
89. Frisch, A. C.; Shaikh, N.; Zapf, A.; Beller, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 4056–4059.
90. Frisch, A. C.; Rataboul, F.; Zapf, A.; Beller, M. *J. Organomet. Chem.* **2003**, *687*, 403–409.
91. Cahiez, G.; Chaboche, C.; Jezequel, M. *Tetrahedron* **2000**, *56*, 2733–2737.
92. Kneisel, F. F.; Monguchi, Y.; Knapp, K. M.; Zipse, H.; Knochel, P. *Tetrahedron Lett.* **2002**, *43*, 4875.
93. Burns, D. H.; Miller, J. D.; Chan, H.-K.; Delaney, M. O. *J. Am. Chem. Soc.* **1997**, *119*, 2125–2133.
94. Terao, J.; Ikumi, A.; Kuniyasu, H.; Kambe, N. *J. Am. Chem. Soc.* **2003**, *125*, 5646–5647.
95. Fraser, F. F.; Jiang, T. *J. Org. Chem.* **1997**, *62*, 7890–7891.
96. Donkervoort, J. G.; Vicario, J. L.; Jastrzebski, J. T. B. H.; Gossage, R. A.; Cahiez, G.; van Koten, G. *J. Organomet. Chem.* **1998**, *558*, 61–69.
97. Tsuji, T.; Yorimitsu, H.; Oshima, K. *Angew. Chem. Int. Ed.* **2002**, *41*, 4137–4139.
98. Ohmiya, H.; Tsuji, T.; Yorimitsu, H.; Oshima, K. *Chem. Eur. J.* **2004**, *10*, 5640–5648.
99. Nakamura, M.; Matsuo, K.; Ito, S.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 3686–3687.
100. Nagano, T.; Hayashi, T. *Org. Lett.* **2004**, *6*, 1297–1299.
101. Ruben, M.; Fürstner, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 3955–3957.
102. Osborn, H. M. I.; Sweeney, J. B.; Howson, W. *Tetrahedron Lett.* **1994**, *35*, 2739–2742.

102a. Gajda, T.; Napieraj, A.; Osowska-Pacewicka, K.; Zawadzki, S.; Zwierzak, A. *Tetrahedron* **1997**, *53*, 4935–4946.
102b. Osowska-Pacewicka, K.; Zwierzak, A. *Synthesis* **1996**, 333–335.
103. Nenajdenko, V. G.; Karpov, A. S.; Balenkova, E. S. *Tetrahedron: Asymmetry* **2001**, *12*, 2517–2527.
104. Baldwin, J. E.; Farthing, C. N.; Russell, A. T.; Schofield, C. J.; Spivey, A. C. *Tetrahedron Lett.* **1996**, *37*, 3761–3764.
105. Nelson, S. G.; Wan, Z.; Stan, M. A. *J. Org. Chem.* **2002**, *67*(14), 4680–4683.
106. Hodgson, D. M.; Fleming, M. J.; Stanway, S. J. *J. Am. Chem. Soc.* **2004**, *126*, 12250–12251.
107. Luh, T.-Y. *J. Organomet. Chem.* **2002**, *653*, 209–214, and reference therein.
108. Huang, L.-F.; Huang, C.-H.; Stulgies, B.; de Meijere, A.; Luh, T.-Y. *Org. Lett.* **2003**, *5*, 4489–4491.
109. Yuan, T.-M.; Yeh, S.-M.; Hsieh, Y.-T.; Luh, T.-Y. *J. Org. Chem.* **1994**, *59*, 8192–8196.
110. Cheng, W.-L.; Shaw, Y.-J.; Yeh, S.-M.; Kanakamma, P. P.; Chen, Y.-H.; Chen, C.; Shieu, J.-C.; Yin, S.-J.; Lee, G.-H., Wang, Y., *et al. J. Org. Chem.* **1999**, *64*, 532–539.
111. Huang, J.-W.; Chen, C.-D.; Leung, M.-K. *Tetrahedron Lett.* **1999**, *40*, 8647–8650.
112. Agami, C.; Couty, F.; Evano, G. *Org. Lett.* **2000**, *2*, 2085–2088.
113. Katritzky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. *Chem. Rev.* **1998**, *98*, 409–548.
114. Katritzky, A. R.; Odens, H. H.; Voronkov, M. V. *J. Org. Chem.* **2000**, *65*, 1886–1888.
115. Katritzky, A. R.; Nair, S. K.; Qiu, G. *Synthesis* **2002**, 199–202.
115a. Review of the chemistry of benzotriazoles: Katritzky, A. R.; Lan, X.; Yang, Y. Z.; Denisko, O. V. *Chem. Rev.* **1998**, *98*, 409–548.
116. Katritzky, A. R.; Cui, X.-L.; Yang, B.; Steel, P. J. *Tetrahedron Lett.* **1998**, *39*, 1698–1700.
117. Poerwono, H.; Higashiyama, K.; Takahashi, H. *J. Org. Chem.* **1998**, *63*, 2711–2714.
118. Yamaguchi, T.; Higashiyama, K.; Kubo, H.; Ohmiya, S. *Tetrahedron: Asymmetry* **2000**, *11*, 3003–3015.
118a. Amat, M.; Escolano, C.; Llor, N.; Huguet, M.; Perez, M.; Bosch, J. *Tetrahedron: Asymmetry* **2003**, *14*, 1679–1683.
119. Gommermann, N.; Koradin, C.; Knochel, P. *Synthesis* **2002**, *14*, 2143–2149.
120. Baruah, M.; Bols, M. *J. Chem. Soc., Perkin Trans. 1* **2002**, 509–512.
121. Shintou, T.; Kikuchi, W.; Mukaiyama, T. *Chem. Lett.* **2003**, *32*, 676–677.
122. Hoffmann, R. W.; Hölzer, B. *J. Am. Chem. Soc.* **2002**, *124*, 4204–4205.
123. Dakternieks, D.; Dunn, K.; Henry, D. J.; Schiesser, C. H.; Tiekink, E. R. *Organometallics* **1999**, *18*, 3342–3347.
124. Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* **1999**, *121*, 9889–9890.
125. Li, G. Y. *J. Organomet. Chem.* **2002**, *653*, 63–68.
126. Bohm, V. P. W.; Weskamp, T.; Gstottmayr, C. W. K.; Herrmann, W. A. *Angew. Chem. Int. Ed.* **2000**, *39*, 1602–1604.
127. Herrmann, W. A.; Bohm, V. P. W.; Gstottmayr, C. W. K.; Grosche, M.; Reisinger, C.-P.; Weskamp, T. *J. Organomet. Chem.* **2001**, *617–618*, 616–628.
128. Mongin, F.; Mojović, L.; Guillamet, B.; Trécourt, F.; Quéguiner, G. *J. Org. Chem.* **2002**, *67*(25), **2002**, 8991–8994.
129. Li, G. Y.; Marshall, W. J. *Organometallics* **2002**, *21*, 590–591.
130. Miller, J.; Farrell, R. P. *Tetrahedron Lett.* **1998**, *39*, 7275–7278.
131. Cahiez, G.; Lepifre, F.; Ramiandrasoa, P. *Synthesis* **1999**, 2138–2144.
132. Goubet, D.; Meric, P.; Dormay, J.-R.; Mareau, P. *J. Org. Chem.* **1999**, *64*, 4516.
133. Astley, D.; Saygi, H.; Gezer, S.; Astley, S. T. *Tetrahedron Lett.* **2004**, *45*, 7315–7317.
134. Korn, T. J.; Cahiez, G.; Knochel, P. *Synlett* **2003**, 1892–1894.
135. Ohmiya, H.; Yorimitsu, H.; Oshima, K. *Chem. Lett.* **2004**, *33*, 1240–1241.
136. Bonnet, V.; Mongin, F.; Trécourt, F.; Quéguiner, G.; Knochel, P. *Tetrahedron Lett.* **2001**, *42*, 5717–5719.
137. Bonnet, V.; Mongin, F.; Trécourt, F.; Quéguiner, G.; Knochel, P. *Tetrahedron* **2002**, *58*, 4429–4438.
138. Bumagin, N. A.; Luzikova, E. V. *J. Organomet. Chem.* **1997**, *532*, 271–273.
139. Fürstner, A.; Leitner, A.; Mendez, M.; Krause, H. *J. Am. Chem. Soc.* **2002**, *124*, 13856–13863.
139a. Scheiper, B.; Bonnekessel, M.; Krause, H.; Fürstner, A. *J. Org. Chem.* **2004**, *69*, 3943–3949.
139b. Fürstner, A.; Leitner, A. *Angew. Chem. Int. Ed.* **2002**, *41*, 609–612.
139c. Seidel, G.; Laurich, D.; Fürstner, A. *J. Org. Chem.* **2004**, *69*, 3950–3952.
139d. Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177.
140. Quintin, J.; Franck, X.; Hocquemiller, R.; Figadére, B. *Tetrahedron Lett.* **2002**, *43*, 3547–3549.
141. Fakhfakh, M. A.; Franck, X.; Hocquemiller, R.; Figadere, B. *J. Organomet. Chem.* **2001**, *624*, 131–135.
142. Smeets, B. J. J.; Meijer, R. H.; Meuldijk, J.; Vekemans, J. A. J. M.; Hulshof, L. A. *Org. Process Res. Dev.* **2003**, *7*, 10–16.
143. Tasler, S.; Lipshutz, B. H. *J. Org. Chem.* **2003**, *68*, 1190–1199.
144. Lipshutz, B. H.; Tasler, S.; Chrisman, W.; Spliethoff, B.; Tesche, B. *J. Org. Chem.* **2003**, *68*, 1177–1189.
145. Kamikawa, T.; Hayashi, T. *Tetrahedron Lett.* **1997**, *38*, 7087–7090.
146. Hayashi, T.; Niizuma, S.; Kamikawa, T.; Suzuki, N.; Uozumi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9101–9102.
146a. Kamikawa, T.; Hayashi, T. *Synlett* **1997**, 163–164.
146b. Kamikawa, T.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 8922–8925.
147. Roy, A. M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 8704–8705.
148. Clayden, J.; Cooney, J. J. A.; Julia, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 7–14.
149. Cho, C.-H.; Yun, H.-S.; Park, K. *J. Org. Chem.* **2003**, *68*, 3017–3025.
150. Milburn, R. R.; Snieckus, V. *Angew. Chem. Int. Ed.* **2004**, *43*, 888–891.
151. Cho, Y.-H.; Kina, A.; Shimada, T.; Hayashi, T. *J. Org. Chem.* **2004**, *69*, 3811–3823.
152. Wang, L.; Chen, Z.-C. *Synth. Commun.* **2000**, *30*, 3607–3612.
153. Brigas, A. F.; Johnstone, R. A. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1735–1739.
154. Brondani, D. J.; Corriu, R. J. P.; El Ayoubi, S.; Moreau, J. J. E.; Wong Chi Man, M. *J. Organomet. Chem.* **1993**, *451*, C1–C3.
155. Miller, J. A. *Tetrahedron Lett.* **2001**, *42*, 6991–6993.
155a. Miller, J. A.; Dankwardt, J. W. *Tetrahedron Lett.* **2003**, *44*, 1907–1910.
155b. Miller, J. A.; Dankwardt, J. W.; Penney, J. M. *Synthesis* **2003**, 1643–1648.
156. Dankwardt, J. W. *Angew. Chem. Int. Ed.* **2004**, *43*, 2428–2432.
157. Hattori, T.; Takeda, A.; Yamabe, O.; Miyano, S. *Tetrahedron* **2002**, *58*, 233–238.
158. Hutchings, R. H.; Meyers, A. I. *J. Org. Chem.* **1996**, *61*, 1004–1013.

159. Aki, S.; Haraguchi, Y.; Sakikawa, H.; Ishigami, M.; Fujioka, T.; Furuta, T.; Minamikawa, J. *Org. Process Res. Dev.* **2001**, *5*, 535–538.
160. Ramiandrasoa, P.; Bréhon, B.; Thivet, A.; Alami, M.; Cahiez, G. *Tetrahedron Lett.* **1997**, *38*, 2447–2450.
161. Alami, M.; Ramiandrasoa, P.; Cahiez, G. *Synlett* **1998**, 325–327.
162. Seck, M.; Franck, X.; Hocquemiller, R.; Figadère, B.; Peyrat, J.-F.; Provot, O.; Brion, J.-D.; Alami, M. *Tetrahedron Lett.* **2004**, *45*, 1881–1884.
163. Dohle, W.; Kopp, F.; Cahiez, G.; Knochel, P. *Synlett* **2001**, 1901–1904.
163a. Cahiez, G.; Avedissian, H. *Synthesis* **1998**, 1199–1205.
163b. Dos Santos, M.; Franck, X.; Hocquemiller, R.; Figadère, B.; Peyrat, J.-F.; Provot, O.; Brion, J.-D.; Alami, M. *Synlett* **2004**, 2697–2700.
164. Karlström, A. S. E.; Roenn, M.; Thorarensen, A.; Bäckvall, J.-E. *J. Org. Chem.* **1998**, *63*, 2517–2522.
165. Die, M.; Nakata, M. *Synlett* **2001**, 1511–1515.
166. Karlström, A. S. E.; Itami, K.; Bäckvall, J.-E. *J. Org. Chem.* **1999**, *64*, 1745–1749.
167. Busacca, C. A.; Erikkson, M. C.; Fiaschisi, R. *Tetrahedron Lett.* **1999**, *40*, 3101–3104.
168. Poree, F.-H.; Clavel, A.; Betzer, J.-F.; Pancrazi, A.; Ardisson, J. *Tetrahedron Lett.* **2003**, *44*, 7553–7556.
169. Miller, J. A. *Tetrahedron Lett.* **2002**, *43*, 7111–7114.
170. Rathore, R.; Deselnicu, M. I.; Burns, C. L. *J. Am. Chem. Soc.* **2002**, *124*, 14832–14833.
171. Lloyd-Jones, G. C.; Butts, C. P. *Tetrahedron* **1998**, *54*, 901–914.
172. Horibe, H.; Kazuta, K.; Kotoku, M.; Kondo, K.; Okuno, H.; Murakami, Y.; Aoyama, T. *Synlett* **2003**, 2047–2051.
173. Bäckvall, J.-E.; Persson, E. S. M.; Brombrun, A. *J. Org. Chem.* **1994**, *59*, 4126–4130.
174. Yanagisawa, A.; Nomura, N.; Yamamoto, H. *Tetrahedron* **1994**, *50*, 6017–6028.
175. Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7273–7274.
176. Breit, B.; Demel, P.; Studte, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 3786–3789.
177. Smitrovich, J. H.; Wörpel, K. A. *J. Am. Chem. Soc.* **1998**, *120*, 12998–12999.
178. Smitrovich, J. H.; Wörpel, K. A. *J. Org. Chem.* **2000**, *65*, 1601–1614.
179. Kang, S.-K.; Cho, D.-G.; Park, C.-H.; Namkoong, E.-Y.; Shin, J.-S. *Synth. Commun.* **1995**, *25*, 1659–1667.
180. Kobayashi, Y.; Nakata, K.; Ainai, T. *Org. Lett.* **2005**, *7*, 183–186.
180a. Ito, M.; Matsuumi, M.; Murugesh, M. G.; Kobayashi, Y. *J. Org. Chem.* **2001**, *66*, 5881–5889.
181. Kimura, M.; Yamazaki, T.; Kitazume, T.; Kubota, T. *Org. Lett.* **2004**, *6*, 4651–4654.
181a. Meuzelaar, G. J.; Karlström, A. S. E.; Van Klaveren, M.; Persson, E.; Del Villar, A.; Van Koten, G.; Bäckvall, J.-E. *Tetrahedron* **2000**, *56*, 2895–2903.
181b. Heckmann, B.; Mioskowski, C.; Bhatt, R. K.; Falck, J. R. *Tetrahedron Lett.* **1996**, *37*, 1421–1424.
182. Alexakis, A.; Malan, C.; Lea, L.; Benhaim, C.; Fournioux, X. *Synlett* **2001**, 927–930.
182a. Chung, K.-G.; Miyake, Y.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2725–2729.
183. Tissot-Croset, K.; Polet, D.; Alexakis, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 2426–2428.
183a. Tissot-Croset, K.; Alexakis, A. *Tetrahedron Lett.* **2004**, *45*, 7375–7378.
183b. Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346–353.
184. Gomez-Bengoa, E.; Heron, N. M.; Didiuk, M. T.; Luchaco, C. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1998**, *120*, 7649–7650.
185. Lautens, M.; Ma, S. *J. Org. Chem.* **1996**, *61*, 7246–7247.
185a. Heron, N. M.; Adams, J. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, *119*, 6205–6206.
185b. Arrayas, R. G.; Cabrera, S.; Carretero, J. C. *Org. Lett.* **2003**, *5*, 1333–1336.
186. Beckmann, E.; Desai, V.; Hoppe, D. *Synlett* **2004**, 2275–2280.
187. Katritzky, A. R.; Zhang, G.; Jiang, J. *J. Org. Chem.* **1995**, *60*, 7605–7611.
188. Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177–4236.
189. Martin, R.; Romea, P.; Tey, C.; Urpi, F.; Vilarrasa, J. *Synlett* **1997**, 1414–1416.
190. Labeeuw, O.; Phansavath, P.; Genet, J.-P. *Tetrahedron Lett.* **2004**, *45*, 7107–7110.
191. Duplais, C.; Bures, F.; Sapountzis, I.; Korn, T. J.; Cahiez, G.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 2968–2970.
192. Maeda, H.; Takahashi, K.; Ohmori, H. *Tetrahedron* **1998**, *54*, 12233–12242.
193. Maeda, H.; Hino, N.; Yamauchi, Y.; Ohmori, H. *Chem. Pharm. Bull.* **2000**, *48*, 1196–1199.
194. De Luca, L.; Giacomelli, G.; Porcheddu, A. *Org. Lett.* **2001**, *3*, 1519–1521.
195. Klix, R. C.; Chamberlin, S. A.; Bhatia, A. V.; Davis, D. A.; Hayes, T. K.; Rojas, F. G.; Koops, R. W. *Tetrahedron Lett.* **1995**, *36*, 1791–1794.
196. Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mozzanti, G.; Ricci, A.; Varchi, G. *Synlett* **1998**, 1013–1015.
197. Myers, A. G.; Yoon, T. *Tetrahedron Lett.* **1995**, *36*, 9429–9432.
198. Michell, R. H.; Iyer, V. S. *Tetrahedron Lett.* **1993**, *34*, 3683–3686.
199. Babudri, F.; Fiadanese, V.; Marchese, G.; Punzi, A. *Tetrahedron Lett.* **1995**, *36*, 7305–7308.
200. Kashima, C.; Tsuruoka, S.; Mizuhara, S. *Tetrahedron* **1998**, *54*, 14679–14688.
201. Lemoucheux, L.; Rouden, J.; Lasne, M.-C. *Tetrahedron Lett.* **2000**, *41*, 9997–10001.
202. Babudri, F.; Fiandanese, V.; Marchese, G.; Punzi, A. *Synlett* **1994**, 719–720.
203. Katritzky, A. R.; Moutou, J.-L.; Yang, Z. *Synthesis* **1995**, 1497–1505.
204. Fontenas, C.; Ait-Haddou, H.; Bejan, E.; Balavoine, G. G. A. *Synth. Commun.* **1998**, *28*, 1743–1753.
205. Pégorier, L.; Petit, Y.; Mambu, A.; Larchevéque, M. *Synthesis* **1994**, *12*, 1403–1405.
206. Tseng, H.-R.; Luh, T.-Y. *J. Org. Chem.* **1996**, *61*, 8685–8686.
207. Tseng, H.-R.; Lee, C.-F.; Yang, L.-M.; Luh, T.-Y. *J. Org. Chem.* **1999**, *64*, 8582–8587.
208. Fürstner, A.; Mendez, M. *Angew. Chem. Int. Ed.* **2003**, *42*, 5355–5357.
209. Katritzky, A. R.; Abdel-Fattah, A. A. A.; Wang, M. *J. Org. Chem.* **2002**, *67*, 7526–7529.
210. Hoveyda, A. H.; Heron, N. M.; Adams, J. A. *Grignard Reagents;* Wiley: Chichester, 2000; pp 107–137.
211. Terao, J.; Nii, S.; Chowdhury, F. A.; Nakamura, A.; Kambe, N. *Adv. Synth. Cat.* **2004**, *346*, 905–908.
212. Mizutani, K.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2003**, *5*, 3959–3961.
213. Terao, J.; Ikumi, A.; Nakamura, A.; Kuniyasu, H.; Kambe, N. *Angew. Chem. Int. Ed.* **2003**, *42*, 3412–3414.
214. de Armas, J.; Hoveyda, A. H. *Org. Lett.* **2001**, *3*, 2097–2100.
215. Nii, S.; Terao, J.; Kambe, N. *J. Org. Chem.* **2004**, *69*, 573–576.
216. Watabe, H.; Terao, J.; Kambe, N. *Org. Lett.* **2001**, *3*, 1733–1735.
217. Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, *19*, 3221–3236.

218. Varchi, G.; Ricci, A.; Cahiez, G.; Knochel, P. *Tetrahedron* **2000**, *56*, 2727–2731.
219. Hansford, K. A.; Dettwiler, J. E.; Lubell, W. D. *Org. Lett.* **2003**, *5*, 4887–4890.
220. Leotta, G. J.; Overman, L. E.; Welmaker, G. S. *J. Org. Chem.* **1994**, *59*, 1946.
221. Dambrin, V.; Villiéras, M.; Janvier, P.; Toupet, L.; Amri, H.; Lebreton, J.; Villieras, J. *Tetrahedron* **2001**, *57*, 2155–2170.
222. Dambrin, V.; Villieras, M.; Lebreton, J.; Toupet, L.; Amri, H.; Villieras, J. *Tetrahedron Lett.* **1999**, *40*, 871–874.
223. Chen, C.; Xi, C.; Jiang, Y.; Hong, X. *Tetrahedron Lett.* **2004**, *45*, 6067–6069.
224. Chinkov, N.; Morlender-Vais, N.; Marek, I. *Tetrahedron Lett.* **2002**, *43*, 6009–6010.
225. Lander, P. A.; Hegedus, L. S. *J. Am. Chem. Soc.* **1994**, *116*, 8126–8132.
226. Andersson, P. G.; Schink, H. E.; Österlund, K. *J. Org. Chem.* **1998**, *63*, 8067–8070.
227. Bongini, A.; Cardillo, G.; Mingardi, A.; Tomasini, C. *Tetrahedron: Asymmetry* **1996**, *7*, 1457–1466.
228. Reid, G. P.; Brear, K. W.; Robins, D. J. *Tetrahedron: Asymmetry* **2004**, *15*, 793–801.
229. Cardillo, G.; Gentilucci, L.; Tolomelli, A.; Tomasini, C. *Tetrahedron* **1999**, *55*, 6231–6242.
230. Arink, A. M.; Braam, T. W.; Keeris, R.; Jastrzebski, J. T. B. H.; Benhaim, C.; Rosset, S.; Alexakis, A.; Van Koten, G. *Org. Lett.* **2004**, *6*, 1959–1962.
231. Kanai, M.; Tomioka, K. *Tetrahedron Lett.* **1995**, *36*, 4275–4278.
232. Lopez, F.; Harutyunyan, S. R.; Minaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2004**, *126*, 12784–12785.
232a. Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, *19*, 3221–3236.
233. Fleming, F. F.; Wang, Q. *Chem. Rev.* **2003**, *103*, 2035–2077.
234. Fleming, F. F.; Gudipati, V.; Steward, O. W. *Org. Lett.* **2002**, *4*, 659–661.
234a. Fleming, F. F.; Gudipati, V.; Steward, O. W. *Tetrahedron* **2003**, *59*, 5585–5593.
234b. Fleming, F. F.; Wang, Q.; Steward, O. W. *J. Org. Chem.* **2003**, *68*, 4235–4238.
234c. Fleming, F. F.; Wang, Q.; Steward, O. W. *Org. Lett.* **2000**, *2*, 1477–1479.
235. Fleming, F. F.; Zhang, Z.; Wang, Q.; Steward, O. W. *Angew. Chem. Int. Ed.* **2004**, *43*, 1126–1129.
236. Fleming, F. F.; Zhang, Z.; Wang, Q.; Steward, O. W. *J. Org. Chem.* **2003**, *68*, 7646–7650.
237. Fleming, F. F.; Shook, B. C. *J. Org. Chem.* **2002**, *67*, 3668–3672.
238. Itami, K.; Mitsudo, K.; Yoshida, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 2337–2339.
239. Itami, K.; Mitsudo, K.; Nokamil, T.; Kamei, T.; Koike, T.; Yoshida, J. *J. Organomet. Chem.* **2001**, *653*(1–2), 105–113.
240. Liao, L.; Fox, J. M. *J. Am. Chem. Soc.* **2002**, *124*, 14322–14323.
241. Yao, C.-F.; Kao, K.-H.; Liu, T.-J.; Chu, C.-M.; Wang, Y.; Chen, W.-C.; Lin, Y.-M.; Lin, W.-W.; Yan, M.-C., Liu, J.-Y., *et al. Tetrahedron* **1998**, *54*, 791–822.
242. Bartoli, G.; Bosco, M.; Sembri, L.; Marcantoni, E. *Tetrahedron Lett.* **1994**, *35*, 8651–8654.
243. Kolotuchin, S. V.; Meyers, A. I. *J. Org. Chem.* **2000**, *65*, 3018–3026.
244. Clark, A. J.; Davies, D. I.; Jones, K.; Millbanks, C. *J. Chem. Soc., Chem. Commun.* **1994**, *1*, 41–42.
245. Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, *123*, 5374–5375.
246. Nakamura, E.; Kubota, K.; Sakata, G. *J. Am. Chem. Soc.* **1997**, *119*, 5457–5458.
246a. Marek, I.; Normant, J.-F. *Chem. Rev.* **1996**, *96*, 3241–3267.
247. Sapountzis, I.; Lin, W.; Fischer, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 4364.
248. Shen, Y.; Yao, J. *J. Org. Chem.* **1996**, *61*, 8659–8661.
249. Forgione, P.; Fallis, A. G. *Tetrahedron Lett.* **2000**, *41*, 11–15 and 17–20.
249a. Tessier, P. E.; Penwell, A. J.; Souza, F. E. S.; Fallis, A. G. *Org. Lett.* **2003**, *5*, 2989–2992.
249b. Fallis, A. G. *Acc. Chem. Res.* **1999**, *32*, 464.
250. Yorimitsu, H.; Tang, J.; Okada, K.; Shinokubo, H.; Oshima, K. *Chem. Lett.* **1998**, 11–12.
251. Nishimae, S.; Inoue, R.; Shinokubo, H.; Oshima, K. *Chem. Lett.* **1998**, 785–787.
252. Itami, K.; Ushiogi, Y.; Nokami, T.; Ohashi, Y.; Yoshida, J. *Org. Lett.* **2004**, *6*(21), **2004**, 3695–3698 and references therein.
253. Tami, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2003**, *125*, 14670–14671.
254. Liu, H.-J.; Shia, K.-S.; Shang, X.; Zhu, B.-Y. *Tetrahedron* **1999**, *55*, 3803–3830.
255. Yus, M.; Ramon, D. J. *Recent Res. Dev. Org. Chem.* **2002**, *6*(1), **2002**, 297–378.
256. Yamazaki, S.; Yamabe, S. *J. Org. Chem.* **2002**, *67*, 9346–9353.
257. Conlon, D. A.; Kumke, D.; Moeder, C.; Hardiman, M.; Hutson, G.; Sailer, L. *Adv. Synth. Cat.* **2004**, *346*, 1307–1315.
258. Matsukawa, S.; Funabashi, Y.; Imamoto, T. *Tetrahedron Lett.* **2003**, *44*, 1007–1010.
259. Kelly, B. G.; Gilheany, D. G. *Tetrahedron Lett.* **2002**, *43*, 887–890.
260. Schulze, V.; Nell, P. G.; Burton, A.; Hoffmann, R. W. *J. Org. Chem.* **2003**, *68*, 4546–4548.
261. Weber, B.; Seebach, D. *Tetrahedron* **1994**, *50*, 6117–6128.
262. Choi, I.-Y.; Lee, H. G.; Chung, H.-K. *J. Org. Chem.* **2001**, *66*, 2484–2486.
263. Verresha, G.; Datta, A. *Tetrahedron Lett.* **1997**, *38*, 5223–5224.
264. Mueller, R. H.; Wang, S.; Pansegrau, P. D.; Janotti, J. Q.; Poss, M. A.; Boyhan, B. *Org. Process Res. Dev.* **1997**, *1*, 14–19.
265. Lebrun, S.; Couture, A.; Deniau, E.; Grandclaudon, P. *Tetrahedron: Asymmetry* **2003**, *14*, 2625–2632.
266. Shintani, R.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 1057–1059.
267. Tius, M. A.; Pal, S. K. *Tetrahedron Lett.* **2001**, *42*, 2605–2608.
268. Denmark, S. E.; Nakajama, N.; Nicaise, O. J.-C. *J. Am. Chem. Soc.* **1994**, *116*, 8797.
269. Bloch, R. *Chem. Rev.* **1998**, *98*, 1407.
270. Denmark, S. E.; Nicaise, O. J.-C. *Chem. Commun.* **1996**, 999.
271. Katritzky, A. R.; Hong, Q.; Yang, Z. *J. Org. Chem.* **1995**, *60*, 3405–3408.
272. Franz, T.; Hein, M.; Veith, U.; Jäger, V.; Peters, E.-M.; Peters, K.; von Schnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1298–1300.
273. Veith, U.; Schwardt, O.; Jäger, V. *Synlett* **1996**, 1181–1183.
274. Cativiela, C.; Diaz-de-Villegas, M. D.; Galvez, J. A. *Tetrahedron: Asymmetry* **1996**, *7*, 529–536.
275. Badorrey, R.; Cativiela, C.; Díaz-de-Villegas, M. D.; Gálvez, J. A. *Tetrahedron* **1997**, *53*, 1411–1416.
276. Steinig, A. G.; Spero, D. M. *J. Org. Chem.* **1999**, *64*, 2406–2410.
277. Ishii, A.; Higashiyama, K.; Mikami, K. *Synlett* **1997**, 1381–1382.
278. Muralidharan, K. R.; Mokhallalati, M. K.; Pridgen, L. N. *Tetrahedron Lett.* **1994**, *35*, 7489–7492.

279. Higashiyama, K.; Nakahata, K.; Takahashi, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 351.
280. Higashiyama, K.; Inoue, H.; Kamamuchi, T.; Takahashi, H. *J. Chem. Soc., Perkin Trans. 1* 111–115.
281. Pridgen, L. N.; Mokhallalafi, M. K.; McGuire, M. A. *Tetrahedron Lett.* **1997**, *38*, 1275–1278.
282. Roland, S.; Mangeney, P. *Eur. J. Org. Chem.* **2000**, 611–616.
283. Lombardo, M.; Trombini, C. *Curr. Org. Chem.* **2002**, *6*, 695–713.
284. Merino, P.; Castillo, E.; Merchan, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1997**, *8*, 1725–1729.
285. Merino, P.; Lanaspa, A.; Merchan, F. L.; Tejero, T. *Tetrahedron: Asymmetry* **1998**, *9*, 629–646.
286. Hunt, J. C. A.; Lloyd, C.; Moody, C. J.; Slawin, A. M. Z.; Takle, A. K. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3443–3454.
287. Alexakis, A.; Lensen, N.; Tranchier, J.-P.; Mangency, P.; Fenau-Dupont, J.; Declercq, J. P. *Synthesis* **1995**, 1038–1050.
288. Solladié-Cavallo, A.; Bonne, F. *Tetrahedron: Asymmetry* **1996**, *7*, 171–180.
289. Saksena, A. K.; Girijavallabhan, V. M.; Wang, H.; Lovey, R. G.; Guenter, F.; Mergelsberg, I.; Puar, M. S. *Tetrahedron Lett.* **2004**, *45*, 8249–8251.
290. Bataille, P.; Paterne, M.; Brown, E. *Tetrahedron: Asymmetry* **1998**, *9*, 2181–2182.
290a. Bataille, P.; Paterne, M.; Brown, E. *Tetrahedron: Asymmetry* **1999**, *10*, 1579–1588.
291. Zwierzak, A.; Napieraj, A. *Synthesis* **1999**, 930–934.
292. Kohmura, Y.; Mase, T. *J. Org. Chem.* **2004**, *69*, 6329–6334.
293. Cali, P.; Begtrup, M. *Synthesis* **2002**, 63–66.
294. Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *38*, 984–995.
294a. Ellman, J. A. *Pure Appl. Chem.* **2003**, *75*, 39–46.
294b. Liu, G.; Cogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1997**, *119*, 9913–9914.
295. Davis, F. A.; McCoull, W. *J. Org. Chem.* **1999**, *64*, 3396–3397.
295a. Cogan, D. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 268–269.
295b. Cogan, D. A.; Liu, G.; Ellman, J. A. *Tetrahedron* **1999**, *55*, 8883–8904.
296. McMahon, J. P.; Ellman, J. A. *Org. Lett.* **2004**, *6*, 1645–1647.
297. Evans, J. W.; Ellman, J. A. *J. Org. Chem.* **2003**, *68*, 9948–9957.
298. Kuduk, S. D.; DiPardo, R. M.; Chang, R. K.; Ng, C.; Bock, M. G. *Tetrahedron Lett.* **2004**, *45*, 6641–6643.
298a. Ellman, J. A.; Owens, T. D.; Tang, T. P. *Acc. Chem. Res.* **2002**, *35*, 984–995.
298b. Ellman, J. A. *Pure Appl. Chem.* **2003**, *75*, 39–46.
298c. Liu, G.; Cogan, D.; Owens, T. D.; Tang, T. P.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 1278–1284.
299. Kawecki, R. *Tetrahedron* **2003**, *14*, 2827–2832.
300. Yang, T.-K.; Chen, R.-Y.; Lee, D.-S.; Peng, W.-S.; Jiang, Y.-Z.; Mi, A.-Q.; Jong, T.-T. *J. Org. Chem.* **1994**, *59*, 914–921.
301. Davis, F. A.; Deng, J.; Zhang, Y.; Haltiwanger, R. C. *Tetrahedron* **2002**, *58*, 7135.
302. Dejaegher, Y.; Mangelinck, S.; De Kimpe, N. *Synlett* **2002**, 113–115.
303. Effenberger, F.; Gutterer, B.; Jäger, J. *Tetrahedron : Asymmetry* **1997**, *8*, 459–467.
304. Charette, A. B.; Gagnon, A.; Janes, M.; Mellon, C. *Tetrahedron Lett.* **1998**, *39*, 5147–5150.
305. Fry, D. F.; Fowler, C. B.; Dieter, R. K. *Synlett* **1994**, 836–838.
306. Askani, R.; Taber, D. F. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1996; Vol. 7, 1881.
306a. Askani, R.; Taber, D. F. In *Modern Amination Methods*; Ricci, A., Ed.; Wiley-VCH: Weinheim, 2000.
307. Kitamura, M.; Suga, T.; Chiba, S.; Narasaka, K. *Org. Lett.* **2004**, *6*, 4619–4621.
308. Erdik, E.; Daşkapan, T. *Tetrahedron Lett.* **2002**, *43*, 6237–6239.
309. Kabalka, G. W.; Li, G. *Tetrahedron Lett.* **1997**, *38*, 5777–5778.
310. Kumar, H. M. S.; Reddy, B. V. S.; Anjaneyulu, S.; Yadav, J. S. *Tetrahedron Lett.* **1999**, *40*, 8305–8306.
311. Sapountzis, I.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 897–900.
312. Kopp, F.; Sapountzis, I.; Knochel, P. *Synlett* **2003**, 885–887.
313. Sapountzis, I.; Knochel, P. *J. Am. Chem. Soc.* **2002**, *124*, 9390–9391.
314. Makosza, M.; Surowiec, M. *J. Organomet. Chem.* **2001**, *624*, 167–171.
315. Bosco, M.; Dalpozzo, R.; Bartoli, G.; Palmiero, G.; Petrini, M. *J. Chem. Soc., Perkin Trans. 2* **1991**, 633–657.
316. Dobbs, A. P.; Voyle, M.; Whittall, N. *Synlett* **1999**, 1594–1596.
317. Zhang, Z.; Yang, Z.; Meanwell, N. A.; Kadow, J. F.; Wang, T. *J. Org. Chem.* **2002**, *67*, 2345–2347.
318. Ricci, A.; Fochi, M. *Angew. Chem. Int. Ed.* **2003**, *42*, 1444–1446.
319. Corey, E. J.; Rao, S. A.; Noe, M. C. *J. Am. Chem. Soc.* **1994**, *116*, 9345–9346.
320. Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789–2834.
321. de Meijere, A.; Kozhushkov, S. I.; Savchenko, A. I. *J. Organomet. Chem.* **2004**, *689*, 2033–2055.
322. Bolm, C.; Pupowicz, D. *Tetrahedron Lett.* **1997**, *38*, 7349–7352.
323. Tsuji, T.; Nakamura, T.; Yorimitsu, H.; Hideki, S.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2004**, *60*, 973–978.
324. Cardellicchio, C.; Iacuone, A.; Naso, F.; Tortorella, P. *Tetrahedron Lett.* **1996**, *37*, 6017–6020.
325. Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Spina, G.; Tortorella, P. *J. Org. Chem.* **2001**, *66*, 5933–5936.
325a. Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Tortorella, P. *J. Org. Chem.* **2000**, *65*, 2843–2846.
325b. Capozzi, M. A. M.; Cardellicchio, C.; Naso, F.; Rosito, V. *J. Org. Chem.* **2002**, *67*, 7289–7294.
326. Garcia Ruano, J. L.; Alemparte, C.; Teresa Aranda, M.; Zarzuelo, M. M. *Org. Lett.* **2003**, *5*, 75–78.
327. Han, Z.; Krishnamurthy, D.; Grover, P.; Wilkinson, H. S.; Fang, Q. K.; Su, X.; Lu, Z.-H.; Magiera, D.; Senanayake, C. H. *Angew. Chem. Int. Ed.* **2003**, *42*, 2032–2035.
328. Terao, J.; Torü, K.; Saito, K.; Kambe, N.; Baba, A.; Sonoda, N. *Angew. Chem. Int. Ed.* **1998**, *37*, 2653–2656.
329. Nishiyama, T.; Seshita, T.; Shodai, H.; Aoki, K.; Kameyama, H.; Komura, K. *Chem. Lett.* **1996**, 549–550.
330. Inoue, A.; Kitagawa, K.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2000**, *56*, 9601–9605.
331. Guo, H.; Kanno, K.; Takahashi, T. *Chem. Lett.* **2004**, *33*, 1356–1357.
332. Al Dulayymi, J. R.; Baird, M. S.; Bolesov, I. G.; Nizovtsev, A. V.; Tverezovsky, V. V. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1603–1618.
333. Imazeki, S.; Sumino, M.; Fukasawa, K.; Ishihara, M.; Akiyama, T. *Synthesis* **2004**, 1648–1654.
334. Pandya, R.; Murashima, T.; Tedeschi, L.; Barrett, A. G. M. *J. Org. Chem.* **2003**, *68*, 8274–8276.
335. Kakiya, H.; Yagi, K.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc.* **2002**, *124*, 9032–9033.

336. Satoh, T.; Osawa, A.; Kondo, A. *Tetrahedron Lett.* **2004**, *45*, 6703–6707.
337. Koo, J. S.; Lee, J. I. *Synth. Commun.* **1996**, *26*, 3709–3713.
338. Barbero, M.; Degani, I.; Sughera, S.; Fochi, R.; Perracino, P. *Synthesis* **1998**, 1235–1237.
339. Manoso, A. S.; Ahn, C.; Soheili, A.; Handy, C. J.; Correia, R.; Seganish, W. M.; DeShong, P. *J. Org. Chem.* **2004**, *69*, 8305–8314.
340. Ila, H.; Junjappa, H.; Barun, O. *J. Organomet. Chem.* **2001**, *624*, 34–40.
341. Mehta, B. K.; Nandi, S.; Ila, H.; Junjappa, H. *Tetrahedron* **1999**, *55*, 12843–12852.
342. Chandrasekhar, S.; Venkat Reddy, M.; Srinivasa Reddy, R.; Ramarao, C. *Tetrahedron Lett.* **2000**, *41*, 2667–2670.

9.04
Zinc and Cadmium

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9.04.1 Zinc Reagents in Organic Synthesis

9.04.1.1 Introduction

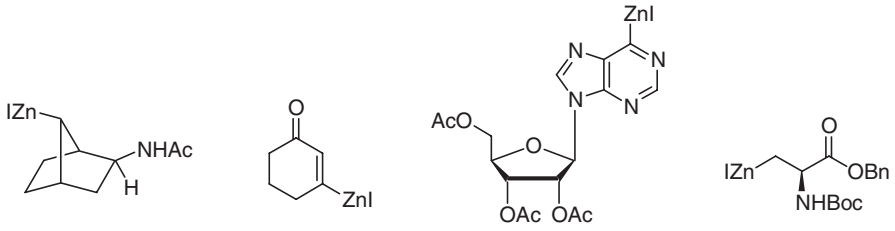
Organozinc compounds occupy a central position in organic chemistry. Since the discovery of the preparation of diethylzinc by Frankland in 1849,[1,1a] organozincs have been used for forming new carbon–carbon bonds.[2] Reformatsky reported in 1887 the preparation of zinc enolates,[3–6] and the cyclopropanation of alkenes using zinc carbenoids became possible after the work of Simmons and Smith.[7–12] The discovery by Grignard of a general preparation of organomagnesium reagents led many organic chemists to prefer these reagents due to their enhanced reactivity. However, the realization that organozincs can be readily transmetallated to several more reactive organometallic species led to the rebirth of organozinc chemistry. Especially important from the practical point of view were the transmetallation to palladium intermediates as shown by Negishi and co-workers,[13–18] as well as the conversion to organocopper species.[19,19a–19e] Within the last 10 years, a number of new synthetic methods involving organozincs have been developed and this chapter accounts for the most significant contributions over this period of time.

9.04.1.2 Preparation of Organozinc Compounds

9.04.1.2.1 The direct insertion of zinc metal

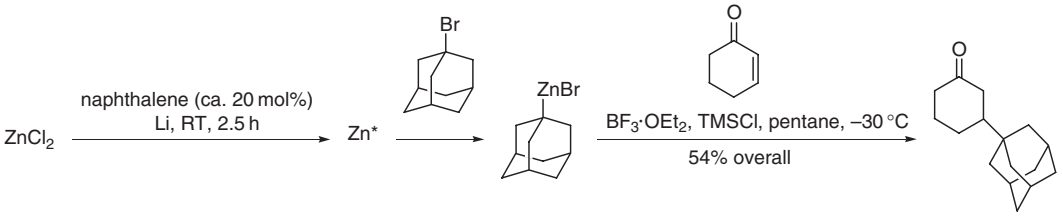
The oxidative addition of zinc dust to functionalized organic halides allows the preparation of a broad range of polyfunctional organozinc iodides, such as **1**–**4**.[20–23] Several functional groups such as nitro or azide group inhibit the radical transfer reaction leading to the zinc reagent. On another hand, hydroxyl groups form zinc alkoxides, which coat

the zinc surface and therefore hamper the reaction (a similar behavior was observed for other acidic hydrogen atoms, such as carboxylic acids, imidazoles). As a general rule, the nature of the zinc dust is less important than its activation. Finely cut zinc foil or zinc dust (commercially available source (ca. 325 mesh)) can be used. Zinc slowly oxidizes in air and is covered by an oxide layer. Its activation is of great importance; this is done by removing the oxide layer via chemical methods.

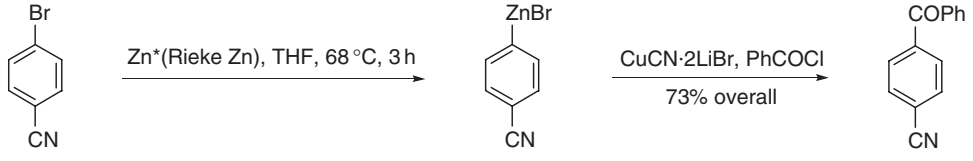


1 **2** **3** **4**

Under these conditions, a broad range of polyfunctional alkyl iodides are converted to the corresponding organozinc halides in high yields.[19,19a–19e,24,24a] In the case of primary alkyl iodides, the insertion occurs at 40–50 °C, whereas secondary alkyl iodides already react at 25–30 °C. Secondary alkyl bromides also react under these conditions,[25,25a] but primary alkyl bromides are usually inert with this type of activation and much better results are obtained by using Rieke zinc.[26–28a] Thus, the reduction of zinc chloride with finely cut lithium and naphthalene produces highly reactive zinc (Rieke zinc). This activated zinc[26g] readily inserts in secondary and tertiary alkyl bromides (Equation (1)). Rieke zinc proves also to be very useful for preparing aryl- and heteroarylzinc halides (Equation (2)).[25]

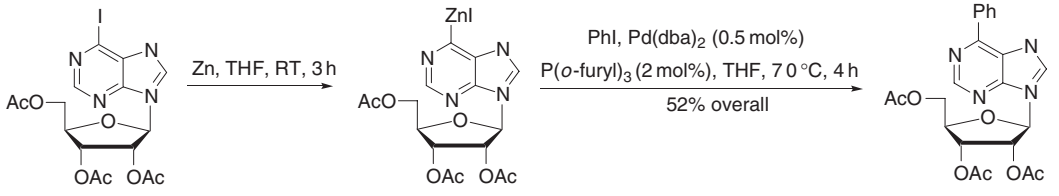


(1)

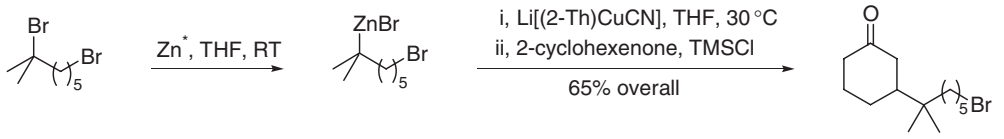


(2)

Iodinated nucleosides can be converted to the corresponding zinc reagents under mild conditions using either DMAC or THF as solvent depending on the solubility of the substrate. After a palladium(0)-catalyzed cross-coupling reaction with an aryl iodide, arylated nucleosides are obtained in satisfactory yields (Equation (3)).[22,22a] Secondary and tertiary alkyl bromides react even more readily, leading to the desired zinc reagents under mild conditions.[27,26g–26i] Remarkable chemoselectivity is observed with dibromoalkanes that bear both a primary and a tertiary alkyl bromide function. Only zinc insertion into the tertiary carbon–bromine bond is observed (Equation (4)).[26j] Functionalized secondary zinc reagents are obtained from secondary bromides in this way.

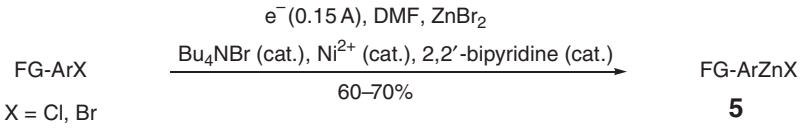


(3)



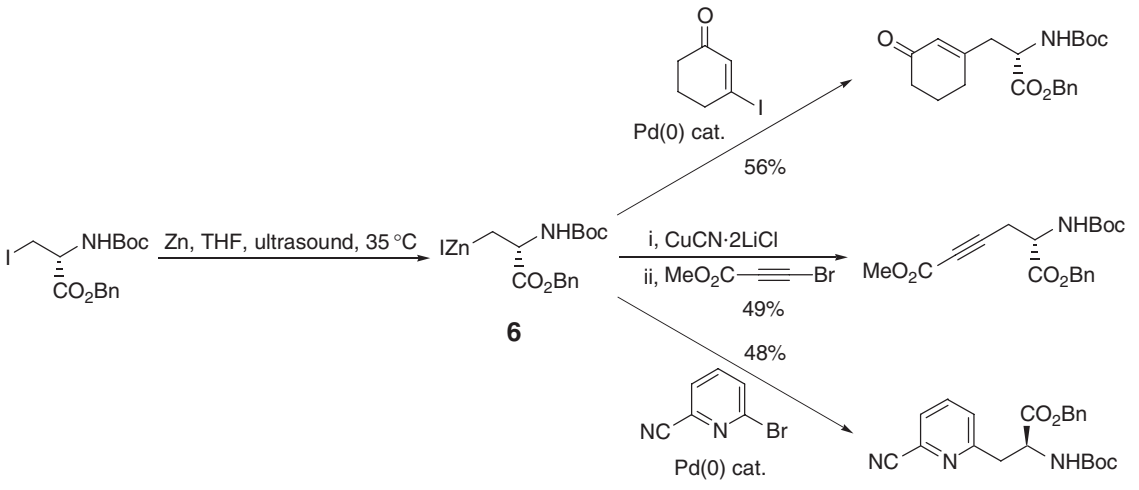
(4)

The formation of arylzinc reagents can also be accomplished by using electrochemical methods. With a sacrificial zinc anode and in the presence of nickel 2,2-bipyridyl, polyfunctional zinc reagents of type **5** can be prepared in excellent yields (Equation (5)).[29,29a–29f] An electrochemical conversion of aryl halides to arylzinc compounds can also be achieved by a cobalt catalysis in DMF/pyridine mixture.[30,30a–30c] The mechanism of this reaction has been carefully studied.[31] This method can also be applied to heterocyclic compounds such as 2- or 3-chloropyridine and 2- or 3-bromothiophenes.[32,32a,29d,29e] Zinc can also be electrochemically activated, and a mixture of zinc metal and small amounts of zinc formed by electroreduction of zinc halides are very reactive toward α-bromoesters and allylic or benzylic bromides.[29e,29f]

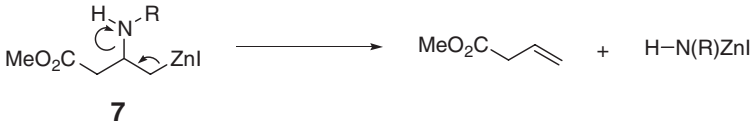


(5)

The preparation of alkylzinc iodides is facilitated if the reaction is performed in THF and NMP mixtures. Such solutions of $MeO_2C(CH_2)_4ZnI$ add to benzaldehyde in the presence of TMSCl (2 equiv.) in 70% yield.[33] The use of ultrasound also promotes the formation of organozinc compounds.[34,34a–34e] This procedure proved to be especially useful for the preparation of Jackson reagent **6** derived from serine. In the presence of a copper(I) or palladium(0) catalyst, this zinc derivative reacts with various electrophiles (Scheme 1).[35,35a–35j] The decomposition of zinc reagent **7** leading to methyl but-3-enoate and the zinc amide has been extensively studied by Jackson and co-workers (Equation (6)).[36] It was found that the zinc species **7a** undergoes the elimination ca. three times faster than the zinc reagent **7b**. This might be surprising since –NHBoc is not as good leaving group as $-NHCOCF_3$. It could be explained by the chelation of the Boc-group with the zinc metallic center, which enhances the ate-character of the metal as well as the electron-density of the C–Zn bond and which favors therefore the elimination. This factor seems to be more important than the leaving group ability of –NHR.[37] Interestingly, a free phenolic function is tolerated in cross-coupling reactions.



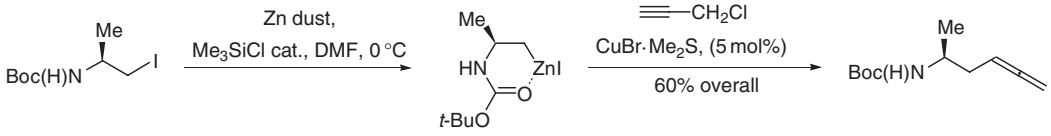
Scheme 1



7 (6)

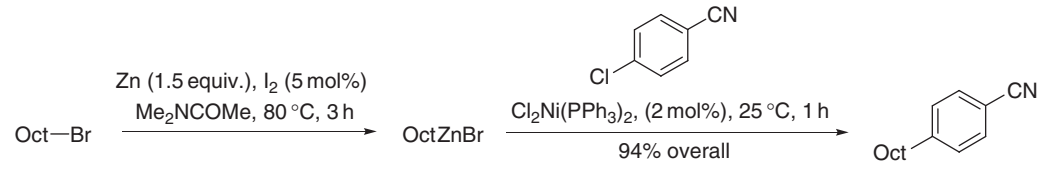
7a 7b

Organozinc reagents bearing a free NH– function in β-position can be readily prepared by the direct insertion of zinc dust previously activated with TMSCl in DMF leading to the corresponding β-iodoamino derivative. Interestingly, best reactivity of this chelate-stabilized zinc species can be obtained by using catalytic amounts of $CuBr{\cdot}Me_2S$ (5 mol%). In the case of the reaction with propargyl chloride, the corresponding allene is obtained in 60% yield via an S_N2'-mechanism (Equation (7)).[38]

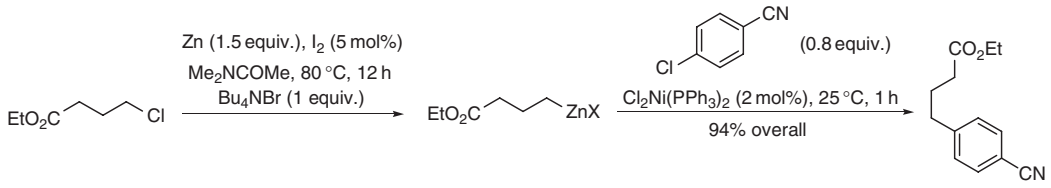


(7)

Alkylzinc bromides bearing various functional groups[39] can be readily prepared by the direct insertion of zinc metal (dust, powder, or shot) to alkyl bromides by performing the reaction in the presence of iodine (1–5 mol%) in a polar solvent like DMAC (Equation (8)). It is also possible to use alkyl chlorides as starting material. In this case, the reaction is best performed in presence of Bu_4NBr (1 equiv.). The resulting zinc reagent undergoes smooth Ni-catalyzed cross-coupling reactions[40,40a,40b] with various aryl chlorides (Equation (9)).

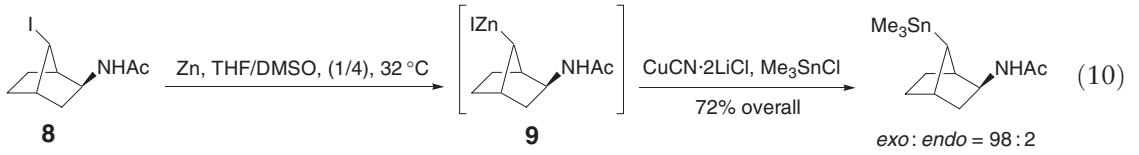


(8)

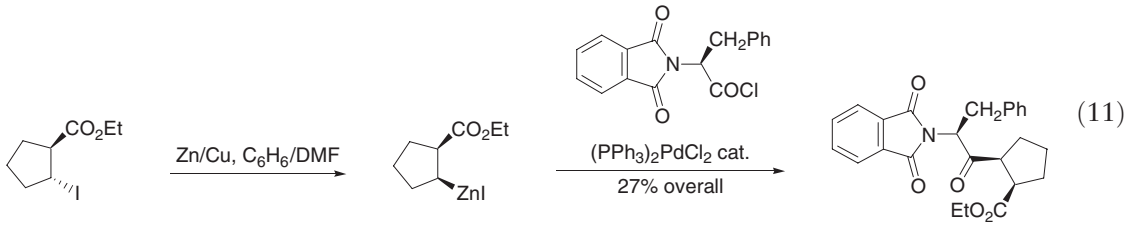


(9)

The preparation of chiral alkylzinc halides by the direct insertion of zinc is complicated due to the radical nature of the zinc insertion. Nevertheless, the strained secondary alkyl iodide **8** is converted to the corresponding chiral secondary organozinc reagent **9** with high retention of configuration leading after stannylation with Me_3SnCl to the tin derivative (Equation (10)).[41] Interestingly, the *trans*-β-iodoester is stereoselectively converted to the *cis*-ester, leading after acylation to the amino ketone (Equation (11)).[42,42a,42b] The chelation with the ester group may be responsible for the *cis*-configuration of the zinc reagent. ^1H NMR-studies[43] confirm that secondary dialkylzincs should display a high configurational stability, although it was noticed that the presence of an excess of zinc(II) salts epimerizes secondary alkylzinc reagents.[43]

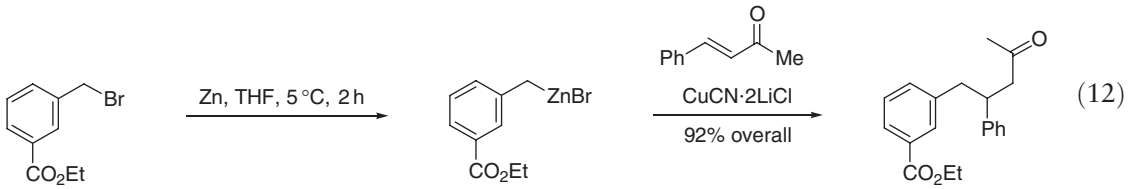


(10)

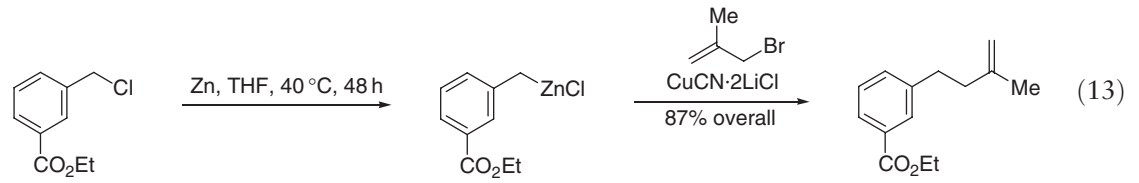


(11)

Interestingly, many electron-deficient heterocyclic and aryl bromides or iodides are sufficiently activated to react with commercially available zinc powder.[22,22a] In the case of benzylic halides, bromides and even chlorides can be used.[44] The benzylic chloride requires a longer reaction time compared to its corresponding bromide derivative (Equations (12) and (13)).

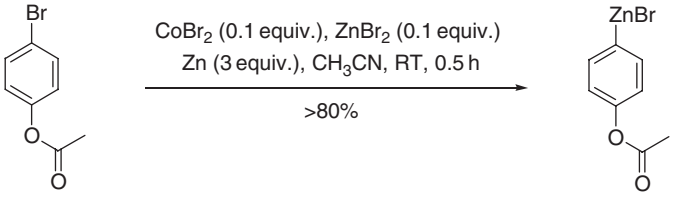


(12)



(13)

Interestingly, low-valent cobalt species obtained by the *in situ* reduction of $CoBr_2$ with zinc catalyze the reaction of aryl bromides with zinc dust. The reaction allows the preparation of a range of functionalized arylzinc halides (Equation (14)).[45,45a–45d]

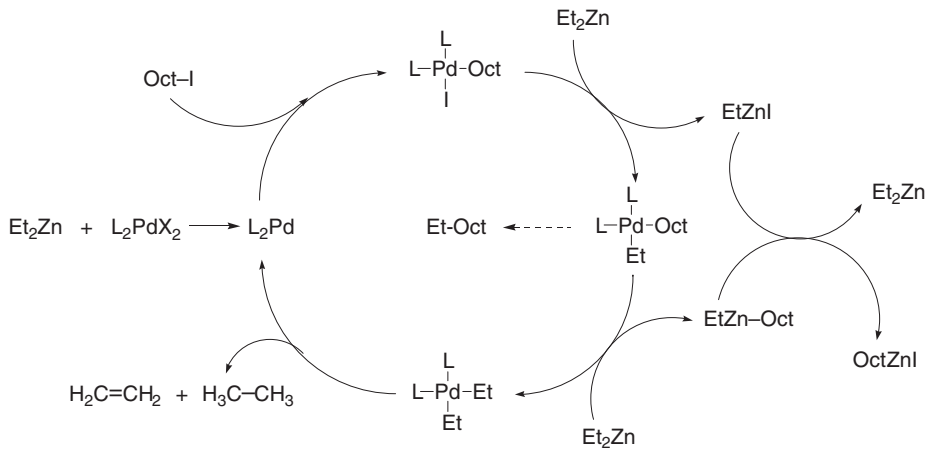


(14)

The direct insertion of zinc dust to organic halides is an excellent method for preparing a broad range of polyfunctional organozinc halides bearing various functional groups like an ester,[46,46a–46g] an ether, an acetate,[47,47a–47c] a ketone, cyano,[48,48a–48d] halide,[49] *N*,*N*-bis(trimethylsilyl)amino,[50] primary and secondary amino, amide phthalimide,[51] sulfide, sulfoxide and sulfone,[52,52a] boronic ester,[53,53a–53c] enone,[54,54a,54b] or a phosphonate.[55] An alternative method is based on halide–zinc exchange reactions.

9.04.1.2.2 The halide–zinc exchange reaction

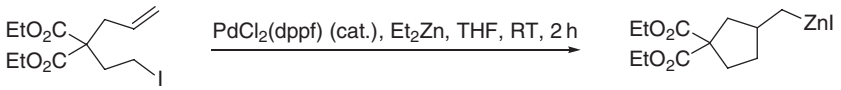
Transition metals may catalyze the zinc insertion reaction. This proves to be the case and the reaction of octyl iodide with Et_2Zn in the presence of $PdCl_2$(dppf) (1.5 mol%) in THF at 25 °C produces OctZnI within 2 h of reaction time in 75–80% yield (Equation (15)).[56,56a,56b] A tentative mechanism is given in Scheme 2.



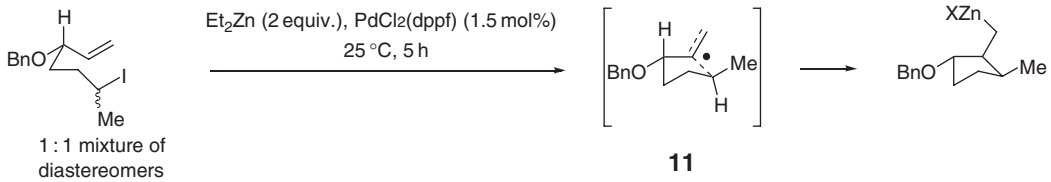
Scheme 2

$$\text{Oct—I} \xrightarrow[75\text{–}80\%]{\text{Et}_2\text{Zn, THF, 25 °C, 5 h}} \text{Oct—ZnI} \qquad (15)$$

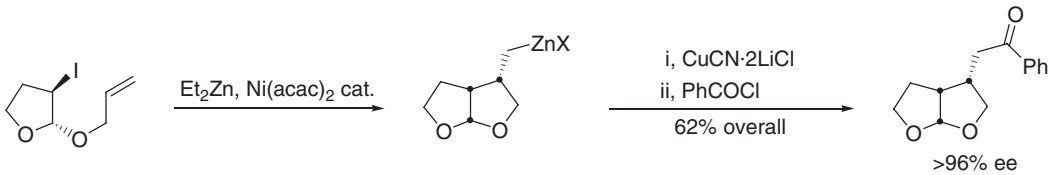
Especially interesting is the palladium(II)- or nickel(II)-catalyzed exchange reaction. In these cases, the product is not a dialkylzinc but rather an alkylzinc iodide.[56,57] The mechanism almost certainly involves radical intermediates (Equation (16)). The palladium-catalyzed cyclization of **10** (1 : 1 mixture of diastereoisomers) provides the cyclopentylmethylzinc derivative in a stereoconvergent way (Equation (17)).[58,58a] The intermediate radical cyclizes via a transition state **11** where all the substituents are in an equatorial position. Interestingly, the analogous reaction using $Ni(acac)_2$ as a catalyst allows the preparation of heterocyclic compounds (Equation (18)). The relative stereochemistry of up to three contiguous centers is set up in this cyclization.[58,58a]



(16)

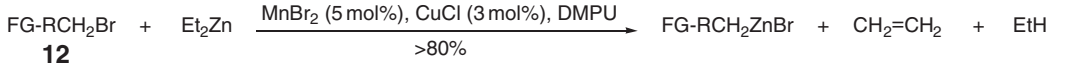


(17)



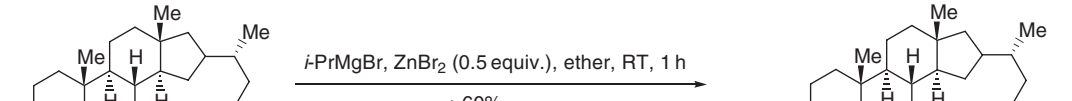
(18)

A range of benzylic halides has been reduced with Et_2Zn in the presence of $Pd(PPh_3)_4$ as a catalyst.[59] Other metallic salts catalyze the I/Zn exchange reaction. Thus, mixed metal catalysis using manganese(II) bromide and copper(I) chloride allows the performance of a Br/Zn exchange with various functionalized alkyl bromides of type **12** (Equation (19)).[60,60a] The reaction proceeds in a polar solvent such as DMPU[45,45a–45d] under very mild conditions. Interestingly, this iodine–zinc exchange can also be initiated by light.[61] Thus, the irradiation (> 280 nm) of an alkyl iodide in CH_2Cl_2 in the presence of Et_2Zn (1 equiv.) provides the desired diorganozinc with excellent yields.

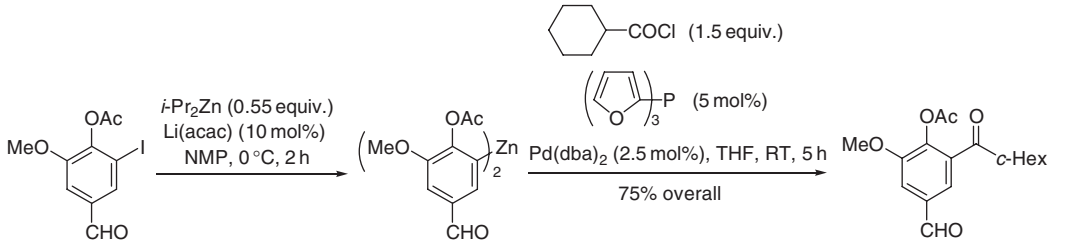


(19)

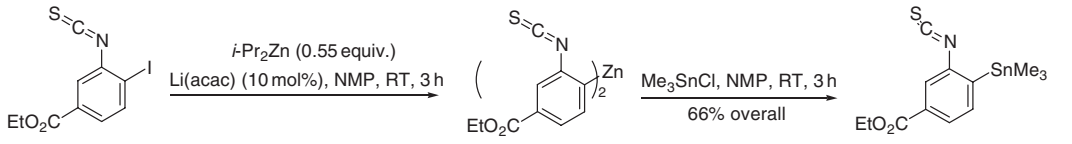
A more reactive exchange reagent (*i*-Pr_2Zn) can be used instead of Et_2Zn. This reagent needs to be salt free if configurationally well-defined reagents are to be prepared.[19,19b–19d,62] However, if the configuration of the zinc organometallics is not relevant, then the *in situ* generation of *i*-Pr_2Zn from *i*-PrMgBr and $ZnBr_2$ (0.5 equiv.) is a convenient method for preparing complex secondary diorganozincs (Equation (20)).[63] Since the isopropyl group is also transferred in the reaction with an electrophile at a comparable rate as the second R group, an excess of electrophile has to be added and tedious separations may be required. A more straightforward approach is possible for diarylzincs. In this case, the I/Zn exchange can be performed under very mild conditions.[64] The intermediate formation of a zincate enhances the nucleophilic reactivity of the substituents attached to the central zinc atom and makes it more prone for undergoing an iodine–zinc exchange reaction. Thus, the addition of catalytic amounts of Li(acac) to an aryl iodide and *i*-Pr_2Zn allows the transfer of the two *i*-Pr groups with the formation of Ar_2Zn and *i*-PrI (2 equiv.). This method allows the preparation of highly functionalized diarylzinc reagents bearing an aldehyde function (Equation (21)) or an isothiocyanate group (Equation (22)). These diarylzinc reagents undergo typical reactions of diorganozincs.



(20)

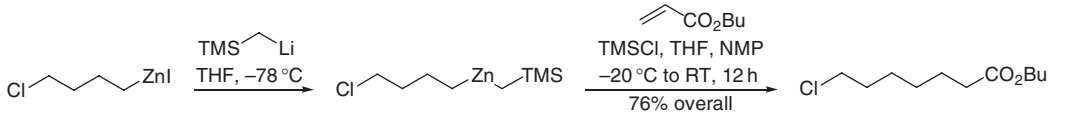


(21)



(22)

Mixed diorganozincs of the type $RZnCH_2SiMe_3$ allow selective transfer to the group R.[65,66] The Me_3SiCH_2 group is too unreactive to be transferred and plays the role of a dummy ligand. These mixed reagents avoid the waste of a precious organic group R in the reaction of diorganozincs with electrophiles (Equation (23)).[66]



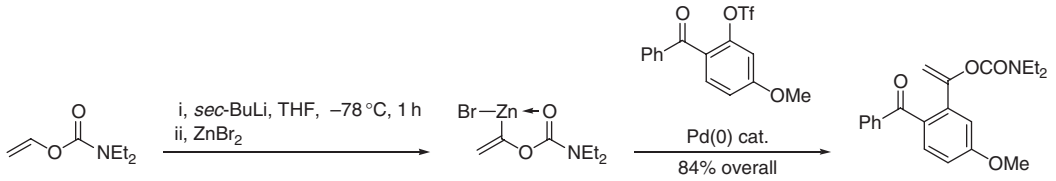
(23)

9.04.1.2.3 Preparation of organozinc halides via transmetallations

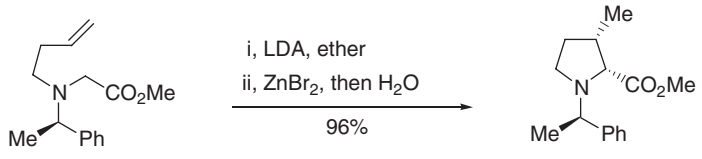
9.04.1.2.3.(i) Lithium–zinc exchange

The lithiation of an *O*-vinyl carbamate with *sec*-BuLi followed by transmetallation with zinc bromide provides the convenient acyl anion derivative, which undergoes smooth Pd(0)-catalyzed cross-coupling reactions (Equation (24)).[67] This reaction sequence has been extended to lithium enolates. The deprotonation of the aminoester with LDA followed by a transmetallation with zinc bromide in ether furnishes a zinc enolate, which readily adds to the double

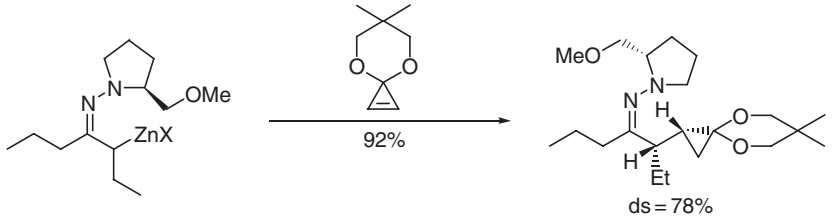
bond providing the proline derivative in high diastereoselectivity (Equation (25)).[68,68a–68h] Similarly, zincated hydrazone derivatives of type **13** undergo an intermolecular carbozincation of strained cyclopropene rings leading to the adduct **14** with 92% yield (Equation (26)).[69,69a–69f] This type of addition can be extended to ethylene.[69b] It proceeds with an excellent stereoselectivity allowing the enantioselective synthesis of α-substituted ketones. Allylic zinc species add as well to cyclopropenone acetals allowing an enantioselective allylzincation to take place.[69e] This reaction provides an entry to quaternary centers with good stereocontrol. Fluorine-substituted alkenes can be readily lithiated by the reaction with a strong base.



(24)



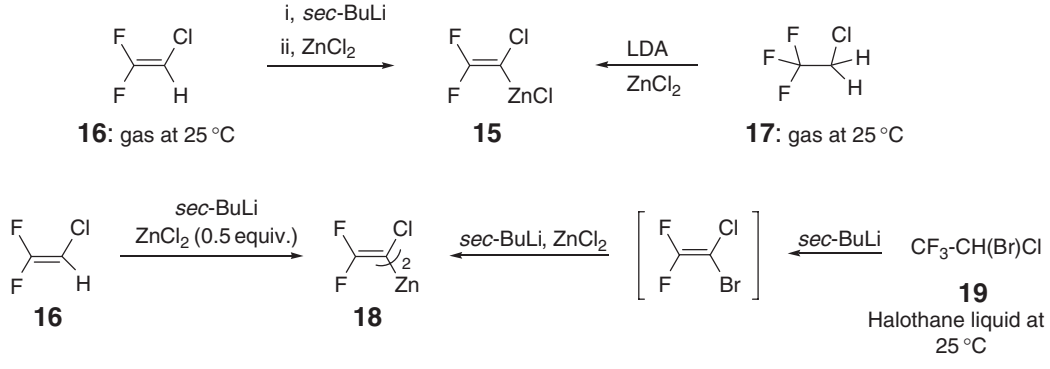
(25)



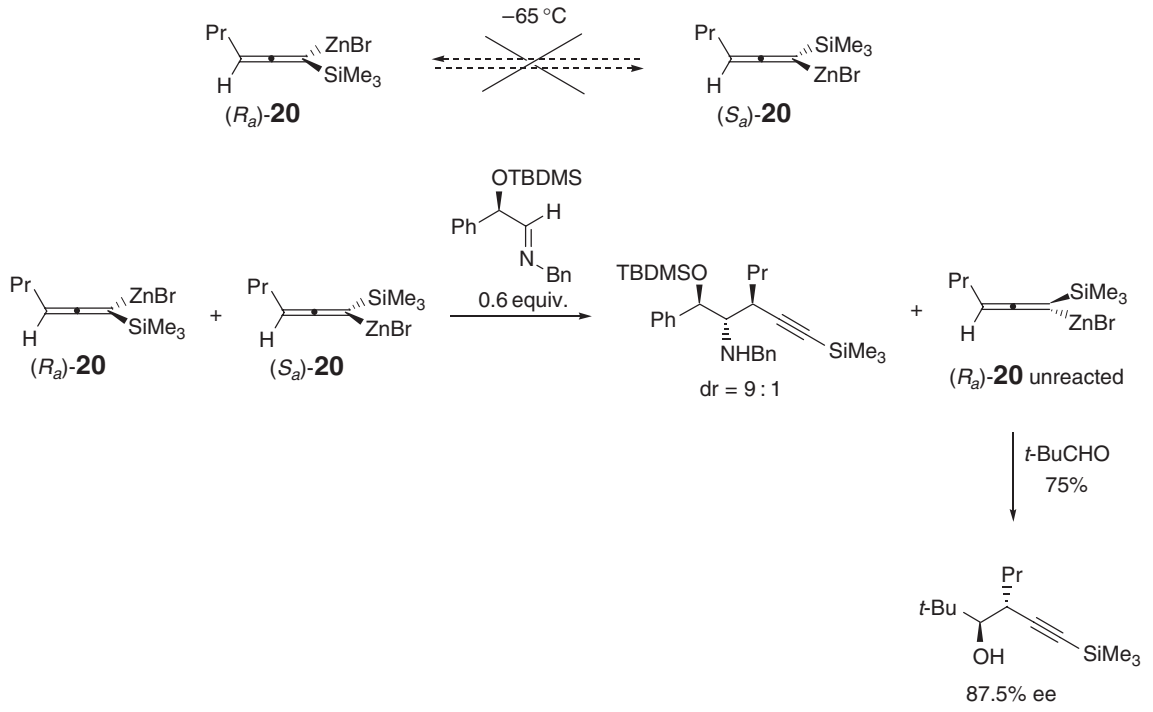
(26)

13 **14**

1-Chloro-2,2-difluorovinylzinc chloride **15** opens the access to a range of fluorine-containing molecules via cross-coupling reactions. Normant and co-workers have prepared this zinc reagent by the deprotonation of 1-chloro-2,2-difluoroethene **16** and transmetallation.[70,70a] Percy and co-workers[71] and Burton and Anilkumar[72] reported that the deprotonation of 1-chloro-2,2,2-trifluoroethane **17** produces after elimination and transmetallation the zinc reagent **15** (Scheme 3). These two steps can be combined in one, and the lithiation of 1-chloro-2,2-difluoroethene **16** with *sec*-BuLi in the presence of $ZnCl_2$ provides the corresponding dialkylzinc **18** as a colorless clear solution.[73,73a] Especially convenient is the deprotonation of liquid halothane **19** with *sec*-BuLi in the presence of $ZnCl_2$. Alkenylzinc reagents such as **20** display configurationally a relatively high stability (little racemization is observed at −65 °C (2 h)). A kinetic resolution with (*R*)-mandelic imine derivate is possible. The reaction is highly preferred with the (S_a)-enantiomer of **20**.



Scheme 3

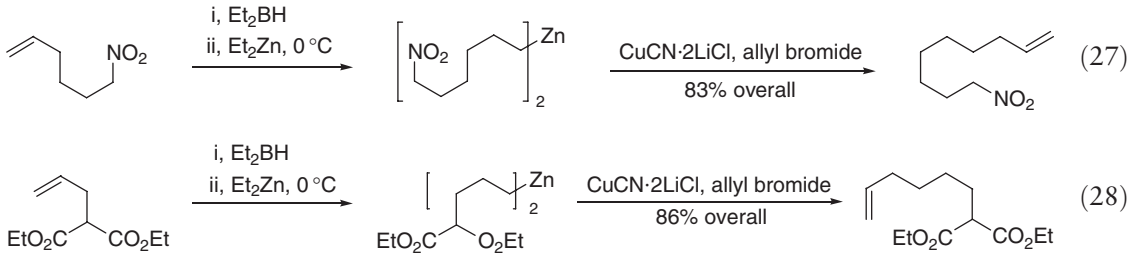


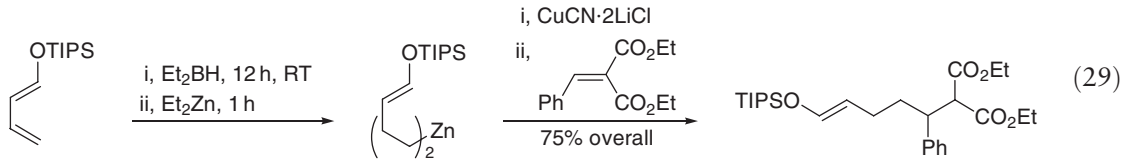
Scheme 4

The remaining unreacted (R_a)-**20** can be trapped with an aldehyde such as pivalaldehyde giving the chiral homopropargylic alcohol in 87.5% ee.[74] This kinetic resolution has been used to prepare *anti*,*anti*-vicinal amino diols in > 95% ee and dr > 40 : 1.[75] In general, diorganozincs are more easily prepared in optically pure form. On another hand, secondary zinc reagents prepared by the direct zinc insertion to secondary alkyl iodides are obtained without stereoselectivity (Scheme 4).[76]

9.04.1.2.3.(ii) Boron–zinc exchange

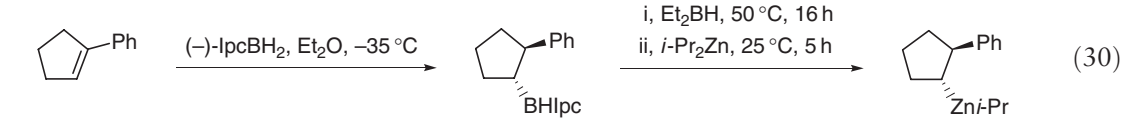
Various organoboranes react with Et_2Zn or *i*-Pr_2Zn providing the corresponding diorganozincs. Pioneered by Zakharin and Okhlobystin[77,77a] and Thiele and co-workers,[78,78a] the method provides a general entry to a broad range of diorganozincs. The exchange reaction proceeds usually under mild conditions and tolerates a wide range of functional groups. It is applicable to the preparation of allylic and benzylic diorganozincs as well as secondary and primary dialkylzincs[79,79a] and dialkenylzincs.[80,80a,80b] Remarkably, functionalized alkenes bearing a nitro group or an alkylidene malonate function are readily hydroborated with Et_2BH[81] prepared *in situ* and converted to diorganozinc reagents as such. After a copper-catalyzed allylation, the expected allylated products are obtained in high yields (Equations (27) and (28)).[79,79a] The hydroboration of dienic silyl enol ethers with Et_2BH leads to organoboranes, which can be converted to new diorganozincs (Equation (29)).[82]



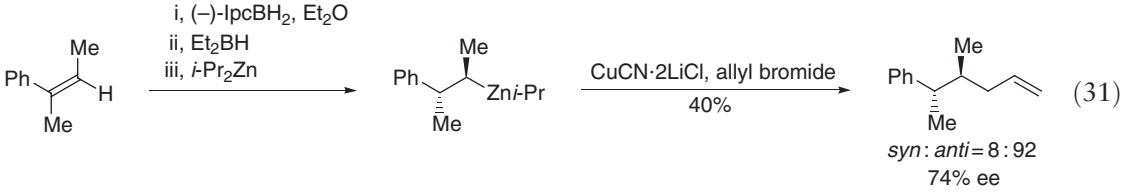


(29)

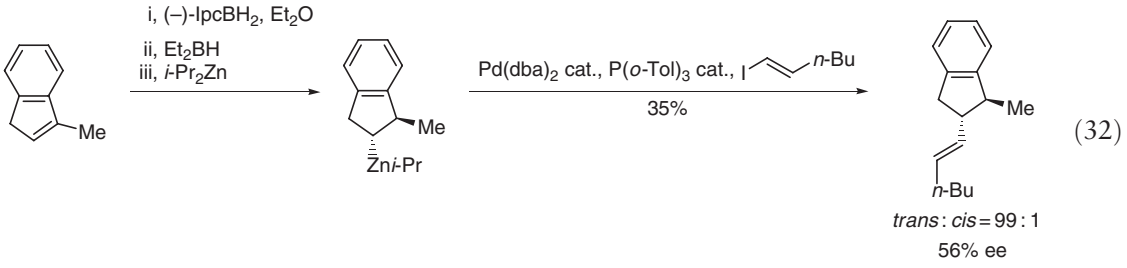
More importantly, this method allows the preparation of chiral secondary alkylzinc reagents. Thus, the hydroboration of 1-phenylcyclopentene with (−)-IpcBH$_2$ (99% ee)[83] produces the chiral organoborane, which reacts with Et$_2$BH (replacing the isopinocampheyl group with an ethyl substituent) and provides after the addition of *i*-Pr$_2$Zn the mixed diorganozinc (Equation (30)).[84,84a] This sequence can be extended to open-chain alkenes (Equation (31)) and to indene derivatives (Equation (32)).[84a]



(30)

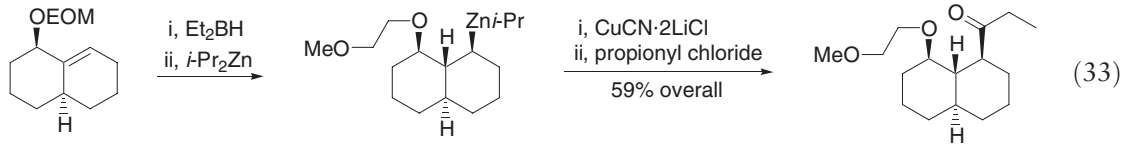


(31)

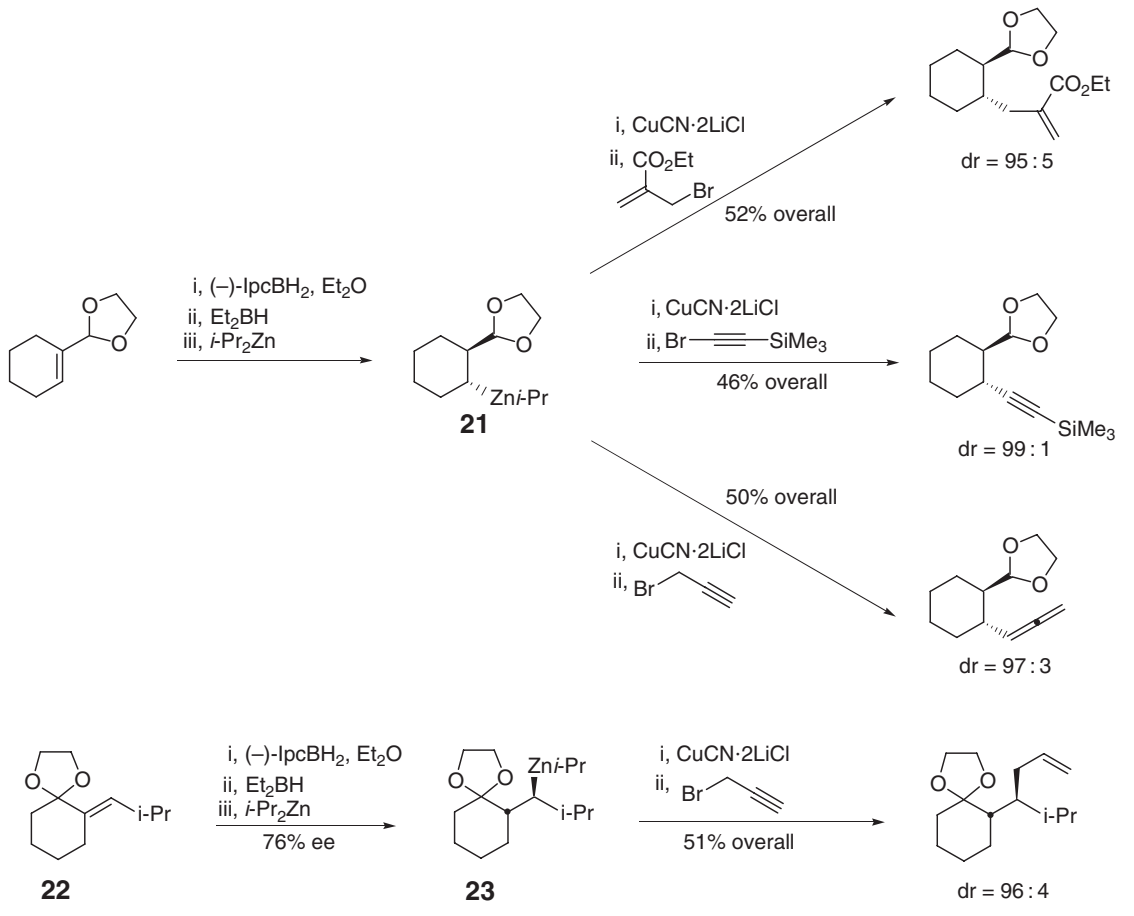


(32)

Several functionalized alkenes have been converted in chiral secondary alkylzinc reagents.[85] Especially interesting are unsaturated acetals, which can be hydroborated with (−)-IpcBH$_2$ with high enantioselectivity (91% ee), providing after B/Zn exchange the mixed zinc reagent **21**. Its trapping with various electrophiles provides chiral products. The *exo*-alkylidene acetal **22** is converted similarly to the zinc reagent **23**, which can be allylated with an excellent diastereoselectivity (dr = 96 : 4) (Scheme 5).[85] A substrate-controlled hydroboration can also be achieved (Equation (33)).[86]

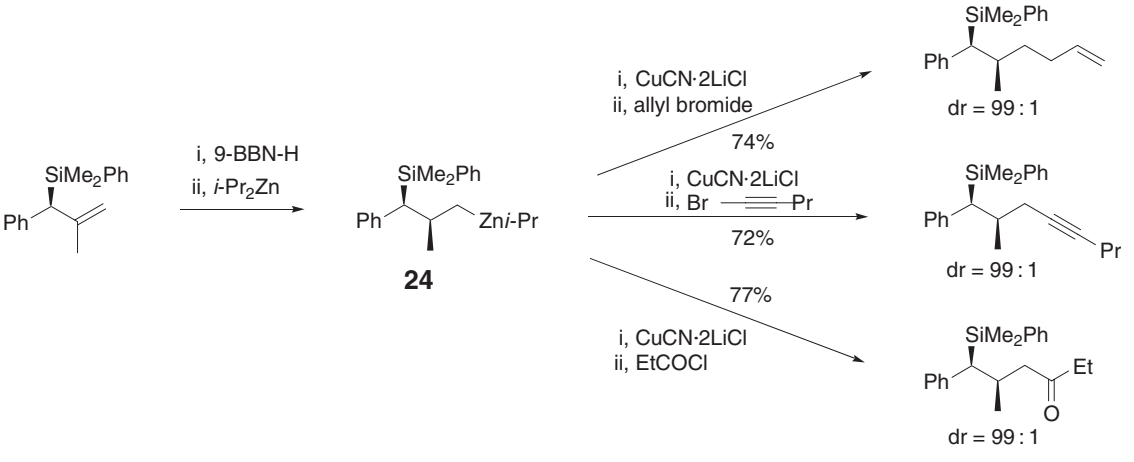


(33)

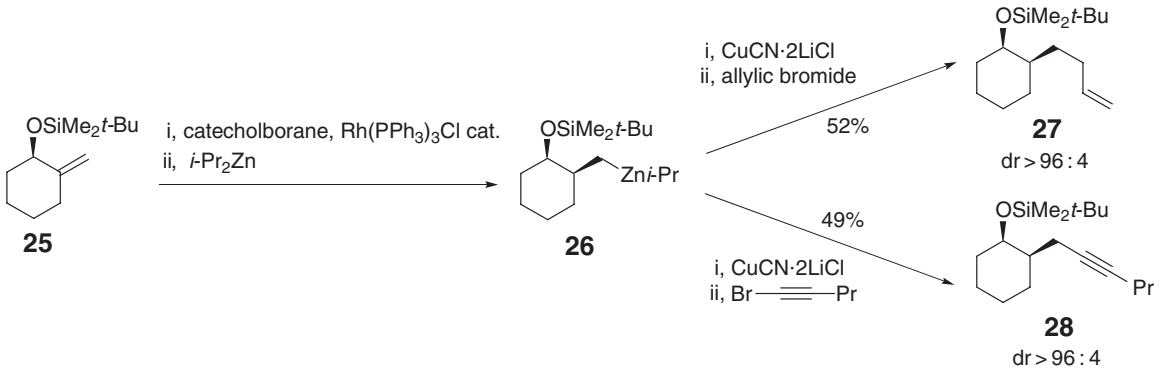


Scheme 5

The hydroboration of allylic silanes proceeds with high diastereoselectivity as demonstrated by Fleming and Lawrence.[87] It is difficult to use the newly formed carbon–boron bond for making new carbon–carbon bonds due to its moderate reactivity. However, the B/Zn exchange converts the unreactive carbon–boron bond to a reactive carbon–zinc bond, as in compound **24**. A further transmetallation with the THF soluble salt CuCN·2LiCl provides copper reagents, which can be allylated, alkynylated, or acylated (Scheme 6).

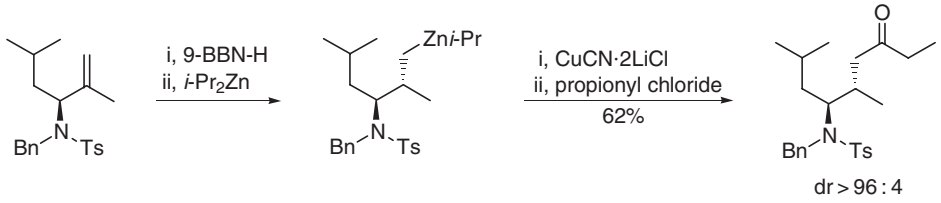


Scheme 6



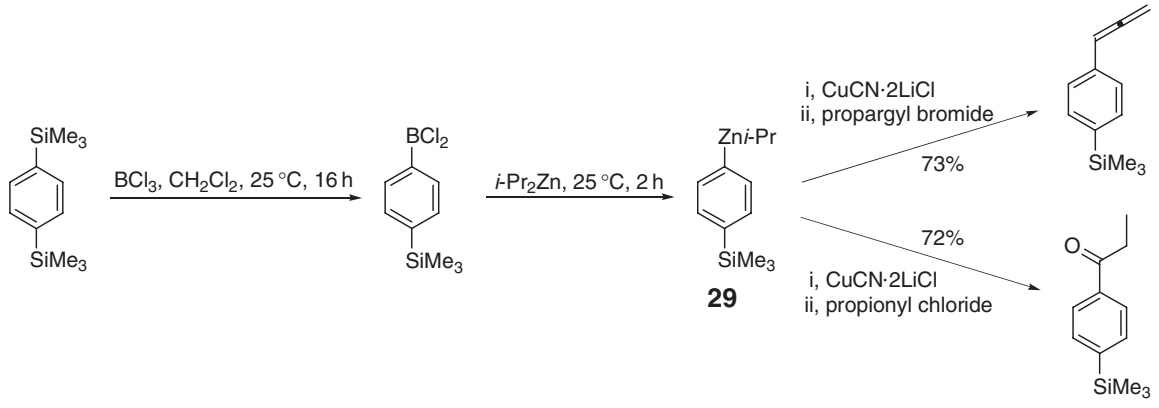
Scheme 7

The hydroboration of allylic amine or alcohol derivatives can be used for the preparation of alkylzinc reagents with excellent diastereoselectivity (Equation (34)).[88,88a,89] Rhodium-catalyzed hydroborations are also compatible with the boron–zinc exchange reaction, and the *exo*-methylene silylated alcohol **25** is readily hydroborated with catecholborane[90,90a] in the presence of $ClRh(PPh_3)_3$,[91,91a] affording after boron–zinc exchange the zinc reagent **26**, which leads after allylation to the *cis*-substituted products **27** and **28** (Scheme 7).[88,88a]



(34)

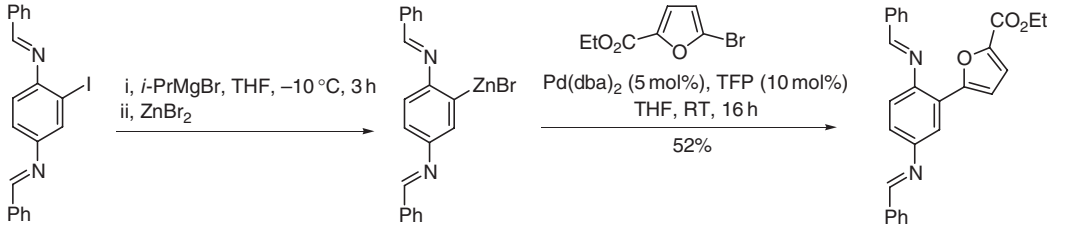
The boron–zinc exchange can be extended to aromatic systems. The required aromatic boron derivatives can be readily prepared from corresponding arylsilanes by using BCl_3.[92] The resulting functionalized arylborane readily undergoes a B/Zn exchange leading to the zinc reagent **29**, which can be trapped by various electrophiles (Scheme 8).[92]



Scheme 8

9.04.1.2.3.(iii) Magnesium–zinc exchange

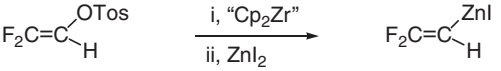
A range of polyfunctional organomagnesium species are available via an iodine– or a bromine–magnesium exchange reaction.[93] Since the carbon–magnesium bond is less polar than a carbon–lithium bond, considerably more functional groups are tolerated in these organometallics and experimentally more convenient reaction conditions can be used. Thus, the reaction of aryl iodide with *i*-PrMgBr provides an intermediate magnesium reagent, which after transmetallation with $ZnBr_2$ furnishes the zinc reagent **30** (Equation (35)). Its palladium-catalyzed cross-coupling with a bromofurane provides the cross-coupling product in 52% yield.[94] This iodine–magnesium exchange can be extended to the preparation of polyfunctional pyridylmagnesium derivatives.[95,96] Also, some alkenyl–iodine bonds undergo a smooth iodine–magnesium exchange leading to polyfunctional alkenylmagnesium compounds with retention of the double-bond configuration.[97]



30 (35)

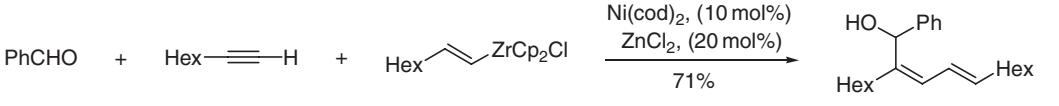
9.04.1.2.3.(iv) Zirconium–zinc exchange

Transmetallations starting from alkenylzirconium species, which are obtained by hydrozirconation using $H(Cl)ZrCp_2$, are readily accomplished.[98,99,99a] Ichikawa, Minami, and co-workers have elegantly shown that diflurovinylzinc iodide is obtained by the addition of "$ZrCp_2$" to the corresponding alkenyl tosylate (Equation (36)).[98] *In situ* transmetallation reactions have also been reported.

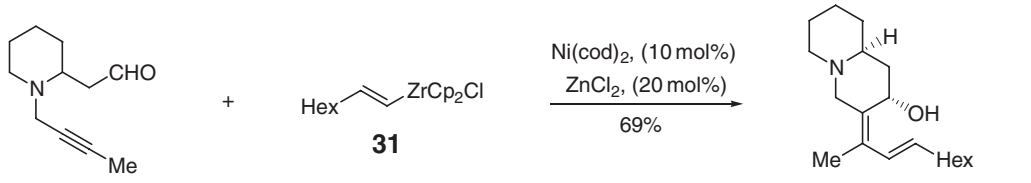


(36)

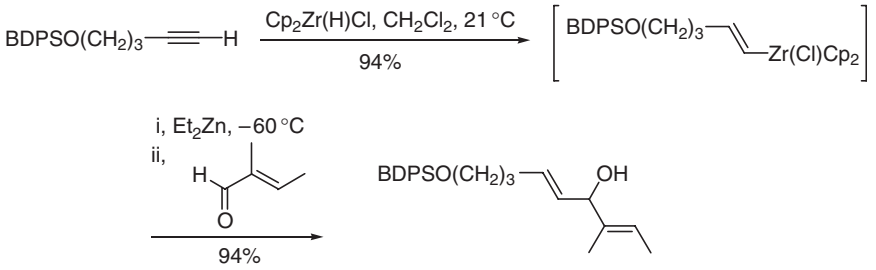
A new three-component reaction[100] has been made possible by treating an alkenylzirconium reagent with an alkyne and an aldehyde in the presence of catalytic amounts of $Ni(cod)_2$ and $ZnCl_2$ (Equation (37)). The transmetallation of the alkenylzirconium species **31** to the corresponding zinc species is essential for the success of the carbometallation reaction.[101] An intramolecular version of the reaction is possible showing the high selectivity of this addition (Equation (38)). The competitive alternative addition to the aldehyde is not observed. The most general application has been reported by Wipf and Xu who have demonstrated that a range of alkenylzirconium species are readily transmetallated to zinc organometallics (Equation (39)).[99,99a]



(37)



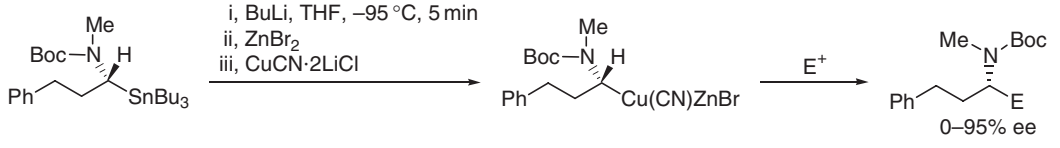
31 (38)



(39)

9.04.1.2.3.(v) Tin–zinc exchange

Organotin compounds have occasionally been converted to zinc and then copper compounds by generating first an organolithium derivative (Equation (40)).[102] α-Aminostannanes undergo a low-temperature Sn/Li exchange reaction with BuLi in THF and lead after a transmetallation to an organozinc species displaying a moderate reactivity. After a further transmetallation with CuCN·2LiCl, a copper–zinc species is obtained. Quenching of this copper–zinc reagent with reactive electrophiles proceeds with retention of configuration with up to 95% ee.

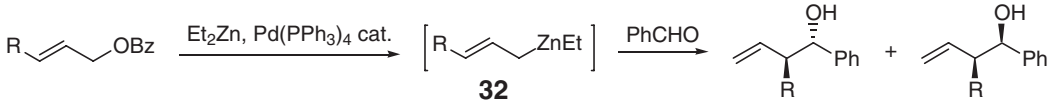


(40)

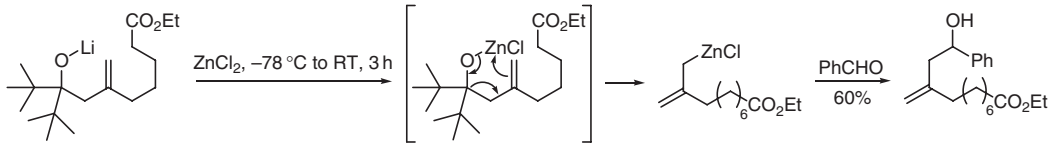
9.04.1.2.4 Other preparation of zinc reagents

9.04.1.2.4.(i) Preparation of allylic zinc compounds by fragmentation

Several methods have been described for preparing allylic zinc derivatives. In contrast to alkylzincs, allylic zinc reagents are much more reactive due to the more ionic nature of the carbon–zinc bond in these organometallics. The chemistry displayed by these reagents is not representative of the usually moderate reactivity of organozinc derivatives. Tamaru and co-workers have converted various allylic benzoates to the corresponding organozinc intermediates in the presence of palladium(0) as catalyst (Equation (41)). The resulting allylic zinc reagent of the tentative structure **32** reacts with aldehydes with high stereoselectivity depending on the substitution pattern.[103–104e] Substituted allylic zinc reagents can be prepared by the fragmentation of sterically hindered homoallylic alcoholates. This method allows the first access to functionalized allylic reagents (Equation (42)).[105,105a–105c]

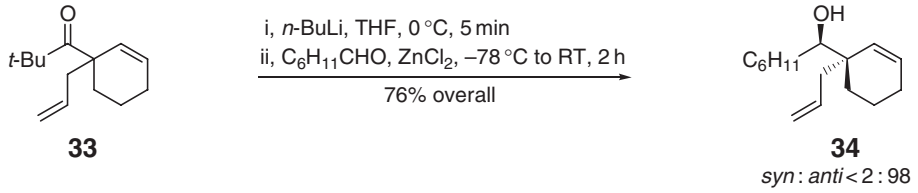


(41)



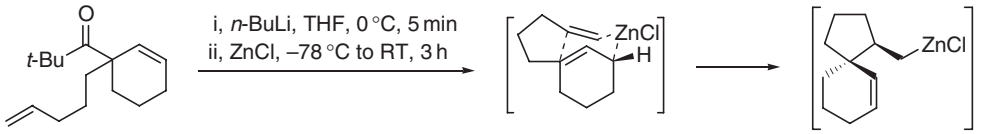
(42)

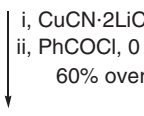
The addition of substituted allylic zinc reagents to aldehydes is usually unselective.[106] Furthermore, the direct zinc insertion to substituted allylic halides is complicated by radical homocoupling reactions. Both of these problems are solved by the fragmentation of homoallylic alcohols. Thus, the ketone **33** reacts with BuLi providing a lithium alcoholate, which after the addition of $ZnCl_2$ and an aldehyde provides the expected addition product **34** with an excellent diastereoselectivity (Equation (43)).[105,105a–105c] Oppolzer and co-workers have shown that the magnesium–ene reaction is a versatile method for adding allylic magnesium reagents to alkenes in an intramolecular fashion.[107] A zinc-ene reaction can be initiated by the addition of BuLi to *tert*-butyl ketone followed by zinc chloride[105d] (Equation (44)).



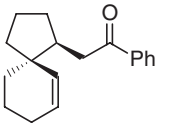
33 **34**

syn : *anti* < 2 : 98 (43)





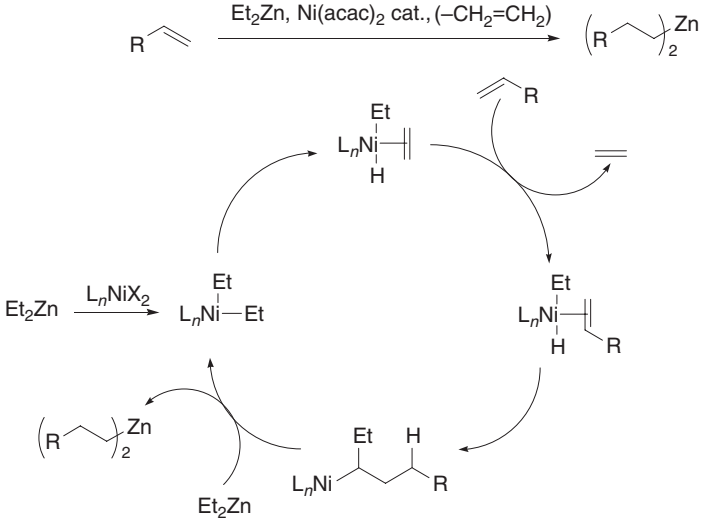
(44)



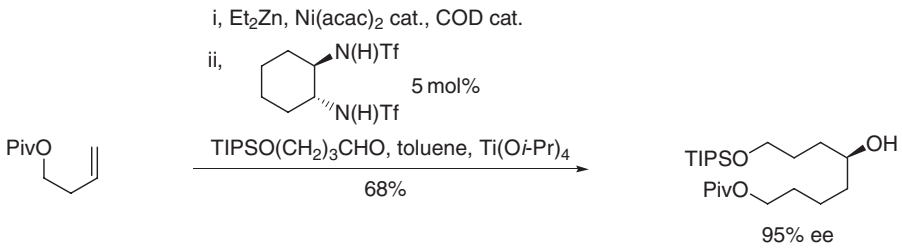
syn : *anti* < 98 : 2

9.04.1.2.4.(ii) Preparation of dialkylzinc compounds by hydrozincation of alkenes

Diorganozincs can also be prepared by a nickel-catalyzed hydrozincation. The reaction of Et_2Zn with $Ni(acac)_2$ may produce a nickel hydride that adds to an alkene leading after transmetallation with Et_2Zn to a diakylzinc (Scheme 9). This reaction proceeds in the absence of solvent and at temperatures of 50–60 °C. A number of functionalized olefins like allylic alcohols or amines can be directly used. This method is especially well suited for the preparation of functionalized diorganozincs for the asymmetric addition to aldehydes (Equation (45)).[108,50]



Scheme 9



(45)

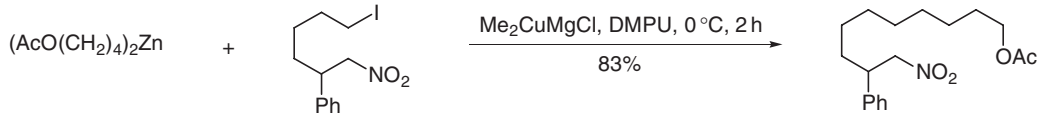
9.04.1.3 Reactivity of Organozinc Compounds

The high covalent degree of the carbon–zinc bond and the small polarity of this bond lead to a moderate reactivity of these organometallics toward many electrophiles. Only powerful electrophiles react in the absence of a catalyst. Thus, bromolysis or iodolysis reactions are high-yield reactions. In general, a direct reaction of organozincs with carbon electrophiles is not efficient, and low yields are obtained. The addition of a catalyst is usually needed. The presence of empty *p*-orbitals at the zinc center facilitates transmetallations, and a number of transition metal organometallics can be prepared in this way. These reagents are usually highly reactive toward organic electrophiles, since the low-lying *d*-orbitals are able to coordinate and activate many electrophilic reagents. Especially useful is the transmetallation of diorganozincs or organozinc halides with the THF-soluble complex of copper(I) cyanide and lithium chloride (CuCN·2LiCl).[109] The simple mixing of organozinc compounds with CuCN·2LiCl produces the corresponding copper species tentatively represented as RCu(CN)ZnX. Many catalytic or stoichiometric transmetallations using zinc organometallics have been developed in recent years.

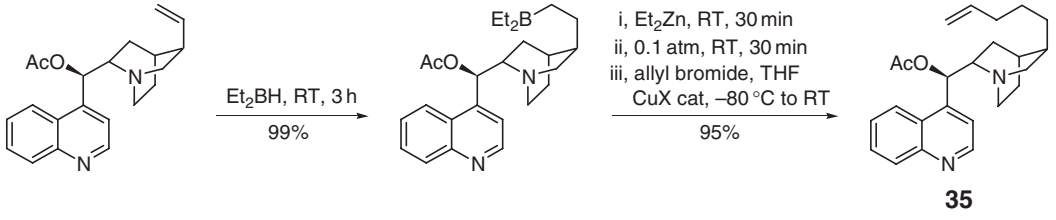
9.04.1.3.1 Substitution reactions

Whereas uncatalyzed substitution reactions of organozinc compounds are limited to very reactive electrophiles, metal-transmetallated organozinc compounds are able to perform substitution reactions on various electrophiles. In the case of conjugated electrophiles, these zinc copper reagents can follow a S_N2 or S_N2' mechanism.

The alkylation of primary alkyl halides and benzylic halides can be readily performed with diorganozincs treated with 1 equiv. of $Me_2CuMgCl$ in DMPU (Equation (46)). This cross-coupling reaction tolerates a range of functionalities (ester, cyanide, halide, and nitro group). The methyl group plays the role of a non-transferable group under our reaction conditions.[110] A quinine alkaloid derivative containing a vinyl group can be transformed to alkaloid derivative such as **35** by performing an hydroboration, a boron–zinc exchange, and copper(I)-catalyzed allylation (Equation (47)).[79,79a] The uncatalyzed reaction of acid chlorides with organozincs is sluggish and inefficient. It is often complicated by side-reactions, and leads usually to low yields of the desired acylation products. In contrast, the CuCN·2LiCl-mediated acylation of various zinc reagents affords ketones in excellent yields (Equations (48) and (49)).[28,28a,111,111a,111b]

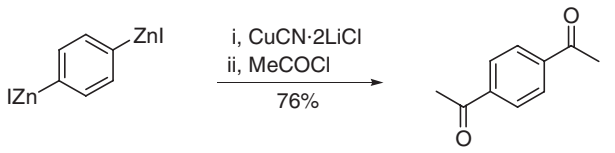


(46)

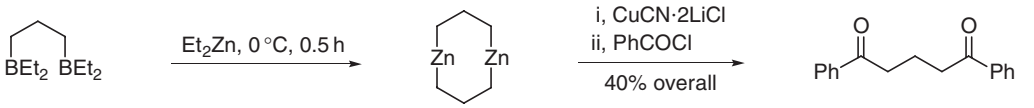


(47)

35

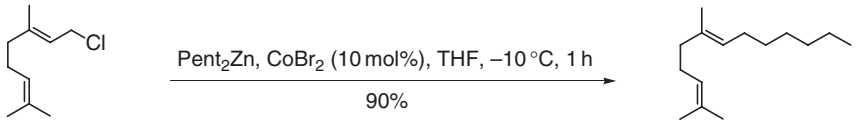


(48)



(49)

A new route to hydrophobic amino acids is possible by using the reaction of the zinc reagent with prenyl chloride in the presence of CuBr·Me_2S (0.1 equiv.). Under these conditions, a mixture of S_N2 and S_N2'-products (55 : 45) is obtained. They can be readily separated by taking advantage of the higher reactivity of trisubstituted alkenes compared with terminal alkenes toward MCPBA (Scheme 10).[112] In many cases, allylic chlorides can react with zinc organometallics in a stereoselective manner. Thus, in presence of catalytic amount of cobalt, geranyl chloride provides the S_N2-substitution product *E* with 90% yield (Equation (50)), and neryl chloride affords the corresponding diene *Z* in 90% yield (Equation (51)).[113] Interestingly, the high S_N2'-selectivity of organozinc–copper derivatives allows the performance of multiple allylic substitutions with excellent results (Equation (52)).[48a,114,114a]



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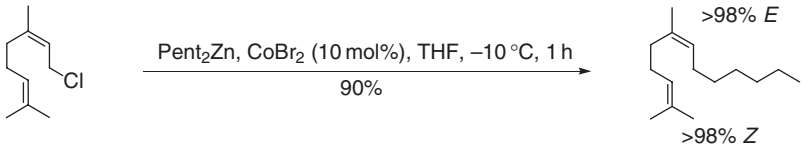
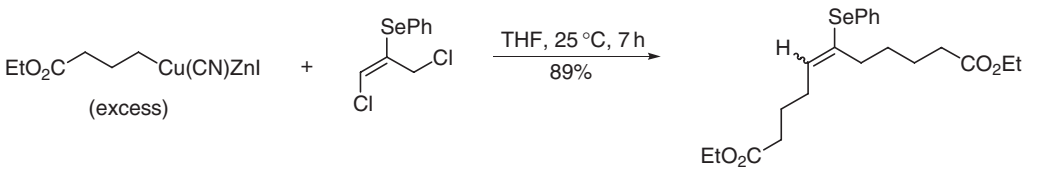
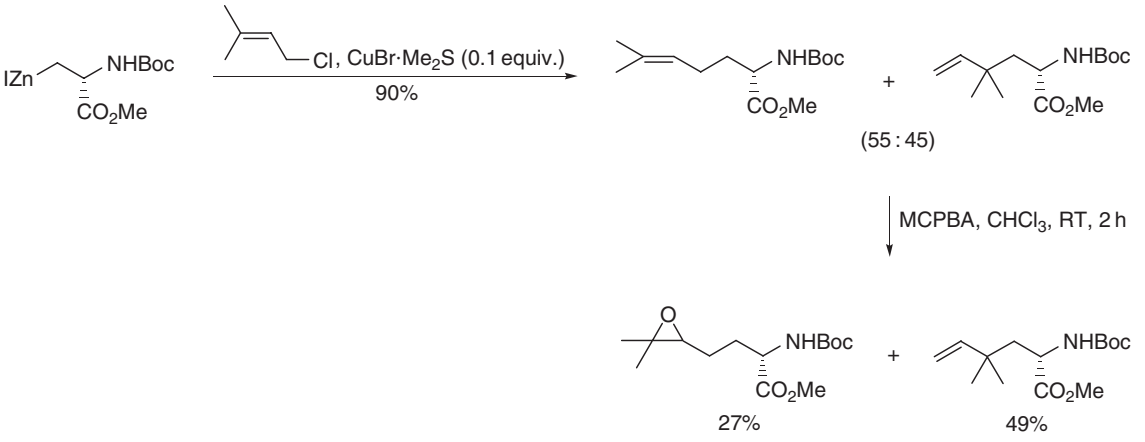


(51)

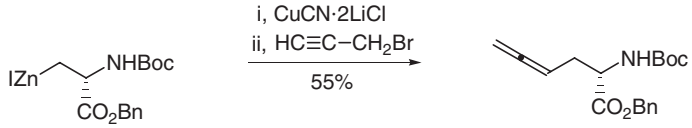


(52)

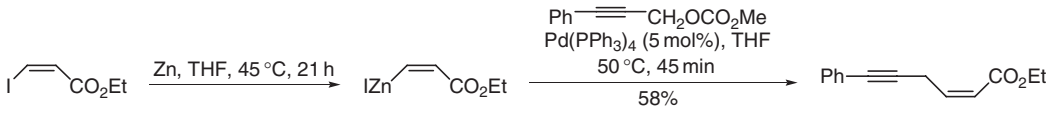


Scheme 10

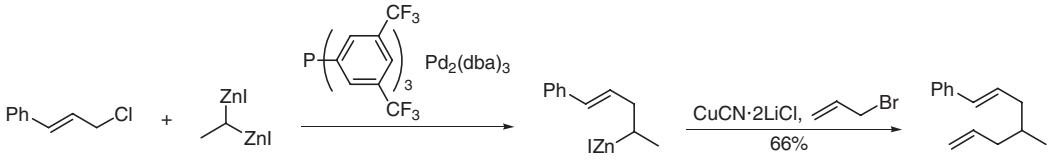
Propargylic halides or sulfonates react with zinc–copper reagents leading to the S_N2'-substitution product (Equation (53)). Interestingly, the regioselectivity is reversed by performing a cross-coupling in the presence of catalytic amounts of palladium(0) (Equation (54)).[115] Bis(iodozinc)ethane undergoes two sequential couplings with electrophiles, with successive palladium catalysis and copper catalysis giving excellent yields (Equation (55)).[116]



(53)

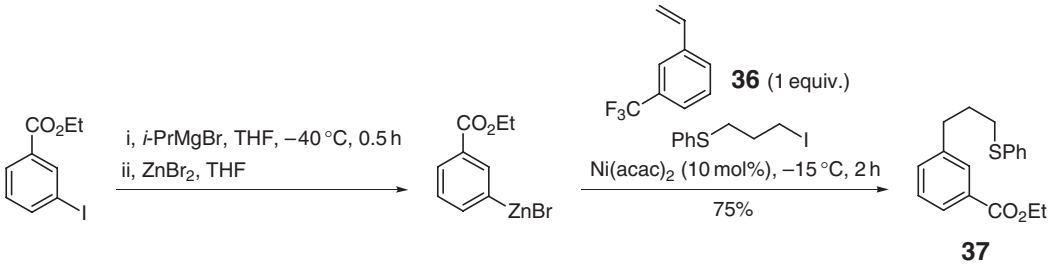


(54)

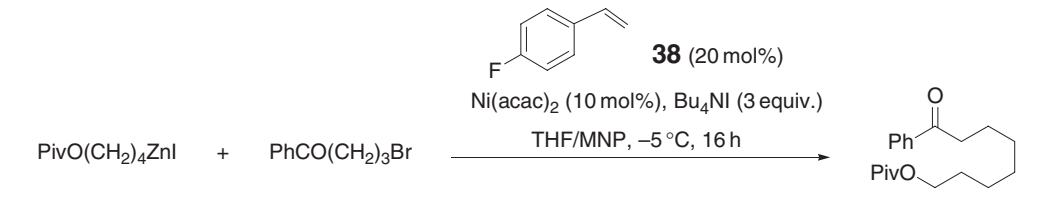


(55)

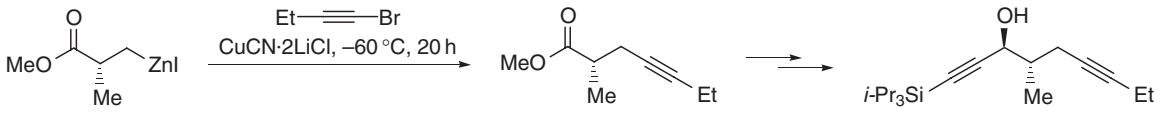
A nickel-catalyzed cross-coupling reaction between an arylzinc reagent and a functionalized alkyl iodide can be successfully achieved using 3-trifluoromethylstyrene **36** as a promoter (Equation (56)). The role of this electron-poor styrene will be to coordinate the nickel(II) intermediate bearing an aryl and an alkyl rest and to promote the reductive elimination leading to the cross-coupling product **37**.[117,117a,117b] Interestingly, this cross-coupling reaction can be readily performed between two C_{sp^3}-centers in presence of 4-fluorostyrene **38**. Thus, the reaction of primary or secondary alkylzinc iodides with various primary alkyl iodides or bromides in the presence of catalytic amount of $Ni(acac)_2$, Bu_4NI, and 4-fluorostyrene provides the corresponding cross-coupling products in satisfactory yields.[118] Polyfunctional products are readily obtained by performing the cross-coupling of functionalized alkylzinc iodides with functionalized alkyl bromides (Equation (57)).[119] More reactive secondary dialkylzincs and the mixed organozinc compounds $RZnCH_2SiMe_3$ undergo the cross-coupling in the absence of Bu_4NI.[119] Thus, the secondary diorganozinc **39** is obtained by the hydroboration of norbornene with Et_2BH, and subsequent boron–zinc exchange undergoes a smooth cross-coupling with iodoketone furnishing stereoselectively the *exo*-ketone in 61% yield (Equation (58)).



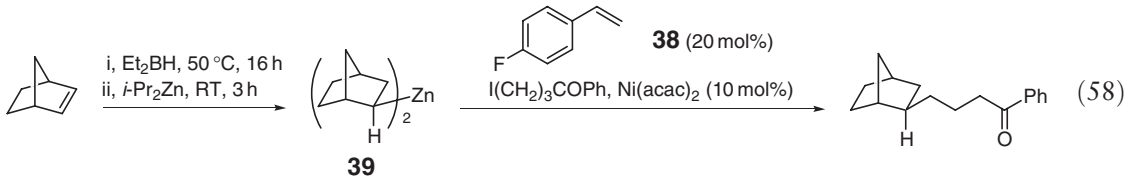
(56)



(57)

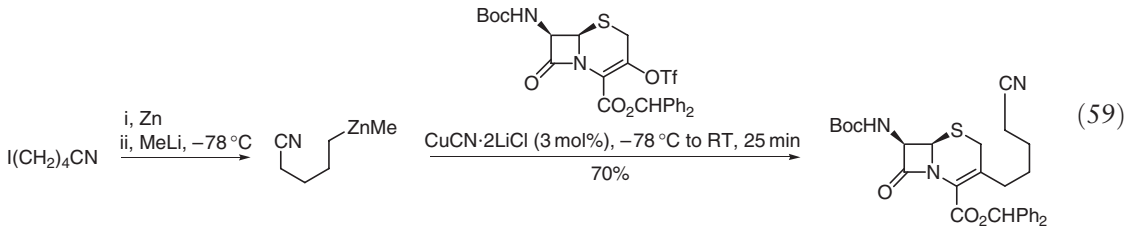


Scheme 11

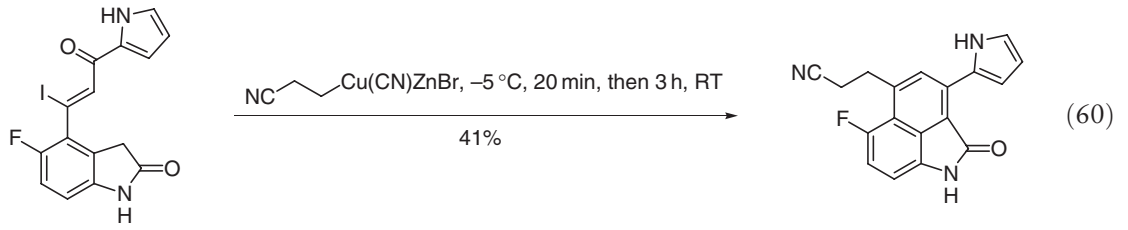


(58)

Alkynyl iodides and bromides smoothly react with various zinc–copper organometallics at −60 °C leading to polyfunctional alkynes.[48c] By this method, a key intermediate of the side chain of Cicaprost™ could be prepared by Corey and Helel (Scheme 11).[120] Substitution at C_{sp^2}-centers can also be accomplished as long as the haloalkene is further conjugated with an electron-withdrawing group at β-position. By using mixed diorganozinc reagents of the type FG–RZnMe,[121] a catalytic addition–elimination can be performed with a wide range of β-keto alkenyl triflates (Equation (59)).[121] Functionalized heterocycles can be prepared in a one-pot synthesis, in which the key-step is the addition–elimination of a functionalized copper–zinc reagent to the unprotected 3-iodoenone producing the annelated heterocycle (Equation (60)).[122]



(59)

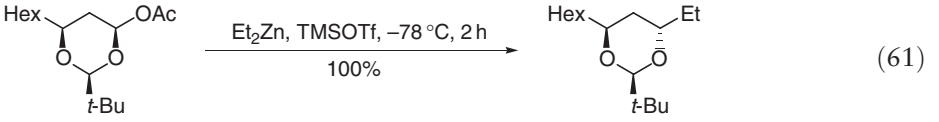


(60)

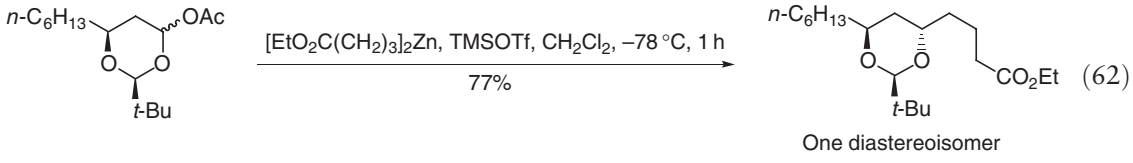
9.04.1.3.2 Asymmetric substitution reactions

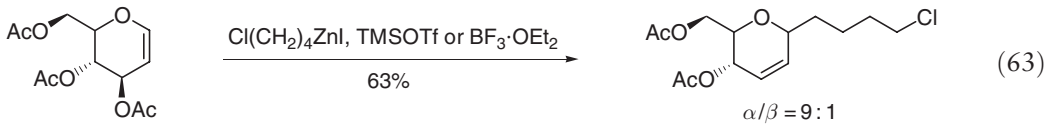
Substitution reactions (in presence or absence of a catalyst) with zinc organometallics can be in some cases asymmetric.

Dialkylzincs undergo formal substitution with 4-acetoxy-6-alkyl-1,3-dioxanes in the presence of trimethylsilyl triflate (TMSOTf) with excellent diastereoselectivity (Equations (61) and (62)).[123,123a–123c] The addition of TMSOTf triggers also the allylic substitution of glycal derivatives, providing the substitution product with excellent regio- and diastereoselectivity (Equation (63)).

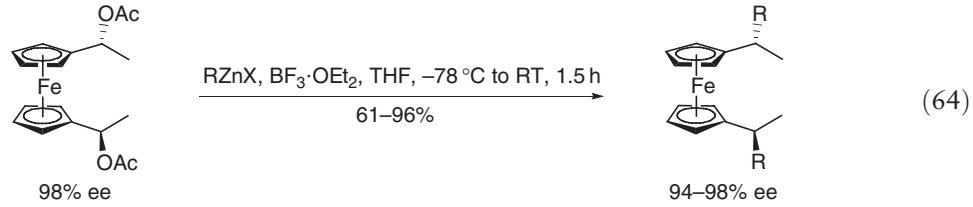


(61)

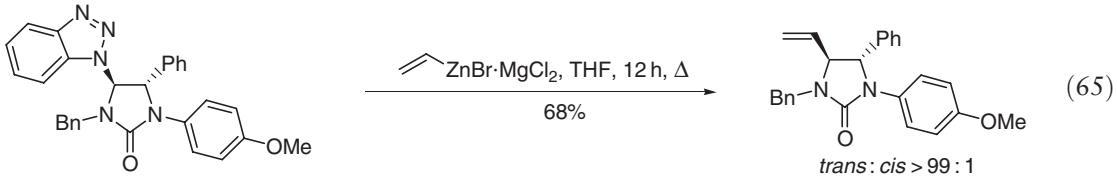


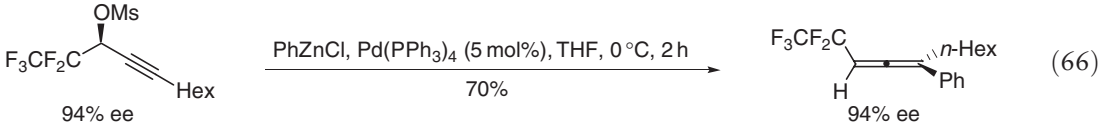


Benzylic acetates are unreactive toward organozinc compounds. However, various ferrocenyl acetates react with alkylzinc halides or allylzinc bromides in the presence of $BF_3{\cdot}OEt_2$ with high retention of configuration, furnishing polyfunctional ferrocenes in optically pure or highly enriched form. These compounds can be readily converted into useful chiral ligands for asymmetric catalysis (Equation (64)).[124,124a,124b]

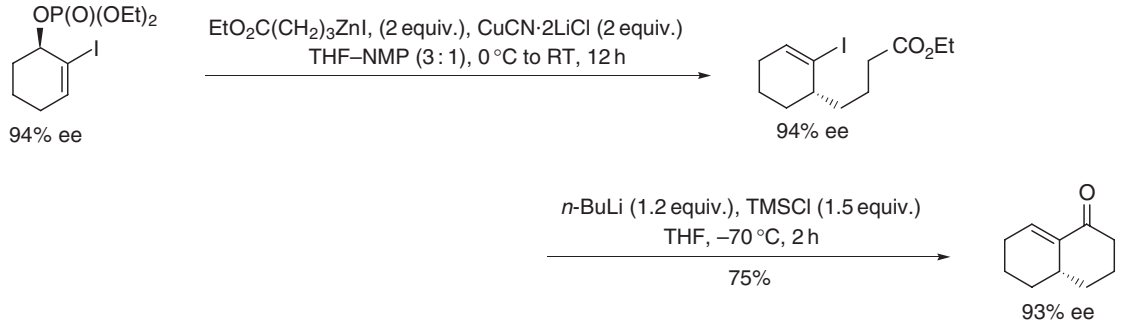


Benzotriazole is an excellent leaving group, and the readily available imidazolidin-2-ones react with aryl-, alkenyl-, or alkylzinc derivates via an elimination–addition mechanism providing the *trans*-products with >99% diastereoselectivity (Equation (65)).[125] Propargylic mesylates such as fluorine-substituted derivatives react with PhZnCl in the presence of $Pd(PPh_3)_4$ (5 mol%) to provide the *anti*-S_N2'-product in excellent yield and complete transfer of the stereochemistry leading to the allene species (Equation (66)).[126]

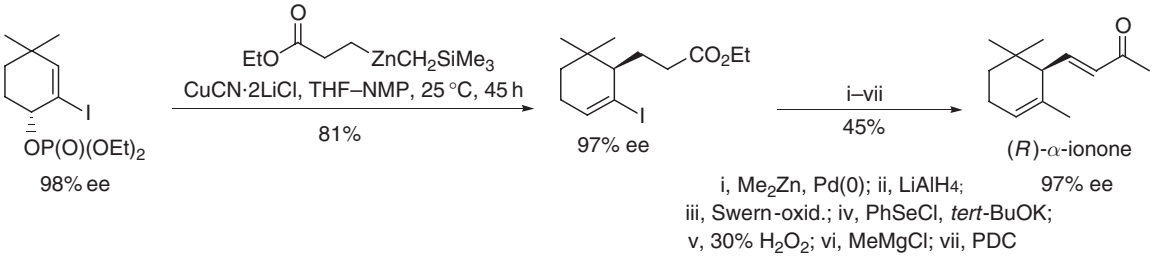




Copper(I)-catalyzed allylic substitutions with functionalized diorganozincs proceed with high S_N2'-selectivity (Scheme 12).[127] Even sterically hindered allylic substrates react with mixed diorganozinc reagents of the type $RZnCH_2SiMe_3$ in the presence of $CuCN{\cdot}2LiCl$, providing only the S_N2'-substitution product regardless of the presence of the two methyl groups adjacent to the allylic center. The reaction with $EtO_2C(CH_2)_2ZnCH_2SiMe_3$ provides *anti*-substitution produt with 97% ee. It is readily converted in (*R*)-α-ionone. The *ortho*-diphenylphosphanyl ligand orients the S_N2'-substitution in a *syn*-manner with high regio- and stereoselectivity to the *cis*-product (Scheme 13).[128,128a,128b]



Scheme 12



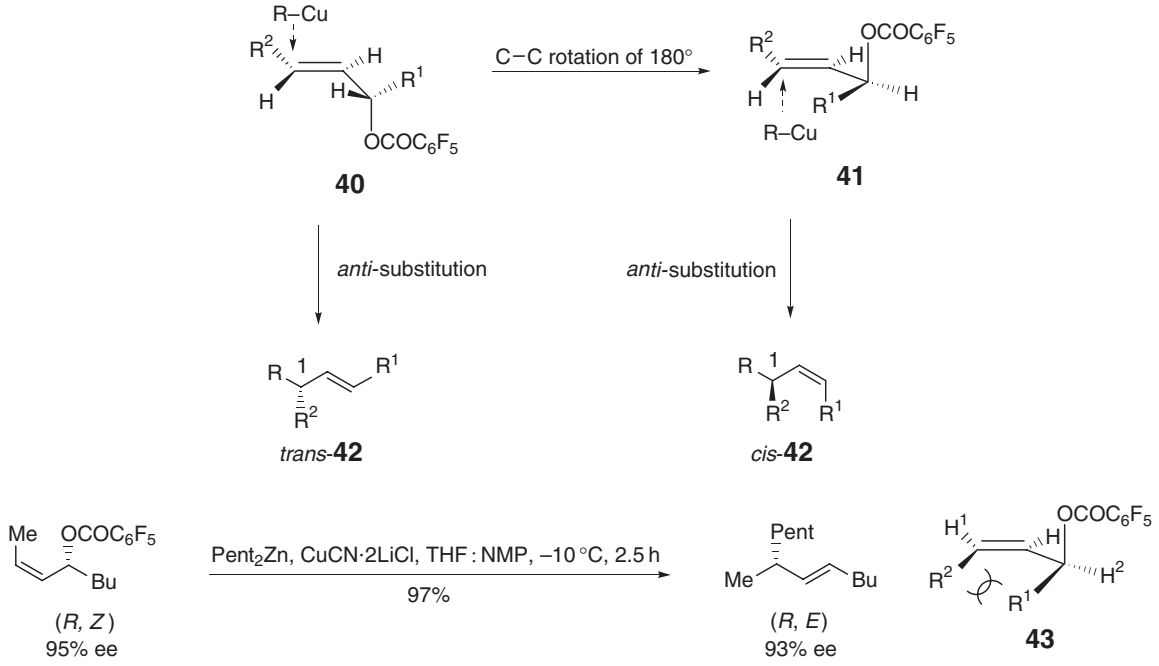
Scheme 13

This reaction can also be extended to open-chain systems. In this case, chiral allylic alcohols have been converted into pentafluorobenzoates which proved to be appropriate leaving groups. Whereas both (*E*)- and (*Z*)-allylic pentafluorobenzoates undergo the S_N2'-substitution, in the case of (*E*)-substrates, two conformations **40** and **41** are available for an *anti*-substitution, providing, besides the major *trans*-product (*trans*-**42**), ca. 10% of the minor product *cis*-**42** also. By using the (*Z*)-allylic pentafluorobenzoates, only *trans*-substitution products are produced, since the conformation **43** leading to a *cis*-product is strongly disfavored due to allylic 1,3-strain.[129] Thus, the *cis*-allylic pentafluorobenzoates reacts with $Pent_2Zn$ furnishing only the *trans*-S_N2'-substitution product with 93% ee (Scheme 14).[130,130a]

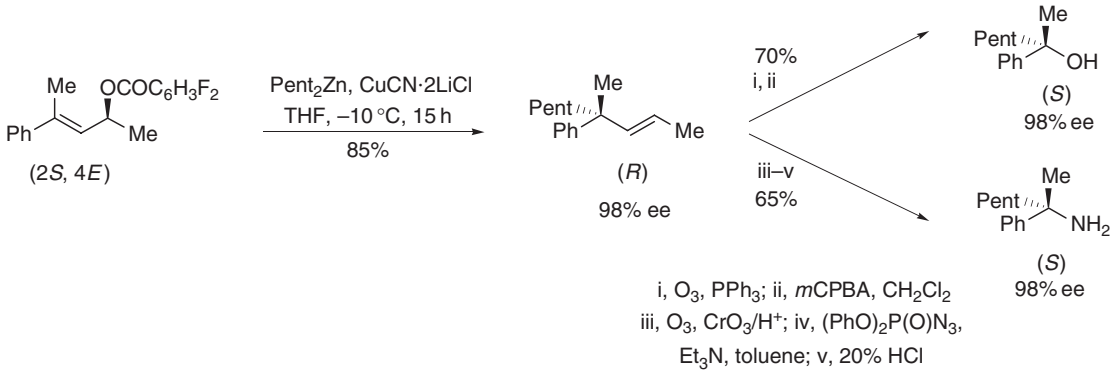
Interestingly, this substitution reaction can be applied to the stereoselective assembly of chiral quaternary centers and has been extended to the preparation of chiral tertiary alcohols via a stereoselective Baeyer–Villiger rearrangement, and chiral tertiary amines via a stereoselective Curtius rearrangement (Scheme 15).[130,130a] Futhermore an enantioselective synthesis of (+)-ibuprofen could be achieved by this methodology (Scheme 16).[130,130a]

Breit and co-workers found that by employing the *ortho*-diphenylphosphanylbenzoate group (*o*-DPPB) as a new reagent-directing leaving group, he could realize a simultaneous control of regio- and stereochemistry of the copper-mediated allylic substitution.[128a,131] Furthermore, it is possible to reverse the stereochemistry through an oxidative on/off switch with regard to this directing group.[132] Thus, allylic substitution of the enolate (−)-**44** with the ethyl Grignard reagent in the presence of $CuBr{\cdot}SMe_2$ gives the product (−)-**45** with excellent chirality transfer. On the other hand, treatment of the allylic *o*-DPPB oxide ester (−)-**46** with diethylzinc reagent in the presence of CuCN·2LiCl furnished the anti S_N2'-substitution product (+)-**45** with perfect regioselectivity and excellent 1,3-anti chirality transfer (Scheme 17).

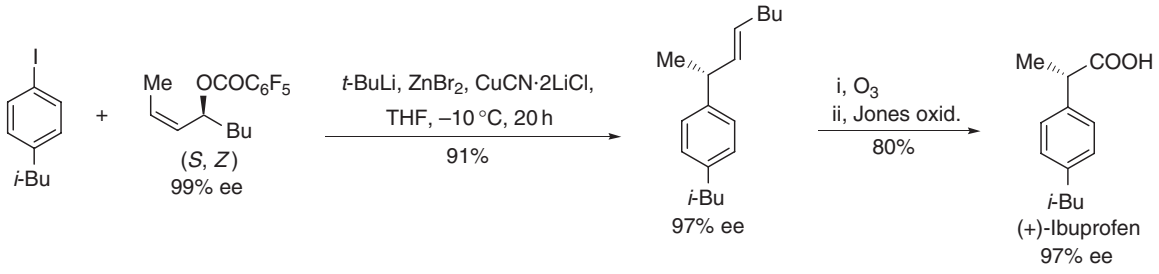
Allylic substitution using organozinc reagents can also be performed using a chiral catalyst.[133,133a–133f] The use of a modular catalyst is an especially versatile strategy and has been applied to the stereoselective preparation of quaternary centers with great success (Equation (67)).[134] Sterically, very hindered diorganozincs like dineopentylzinc react enantioselectively with allylic chlorides in the presence of the chiral ferrocenylamine with up to 98% ee (Equation (68)).[135,135a] In contrast, in the presence of nickel(0) or palladium(0) complexes, the S_N2-substitution product is preferentially obtained.[136,136a]



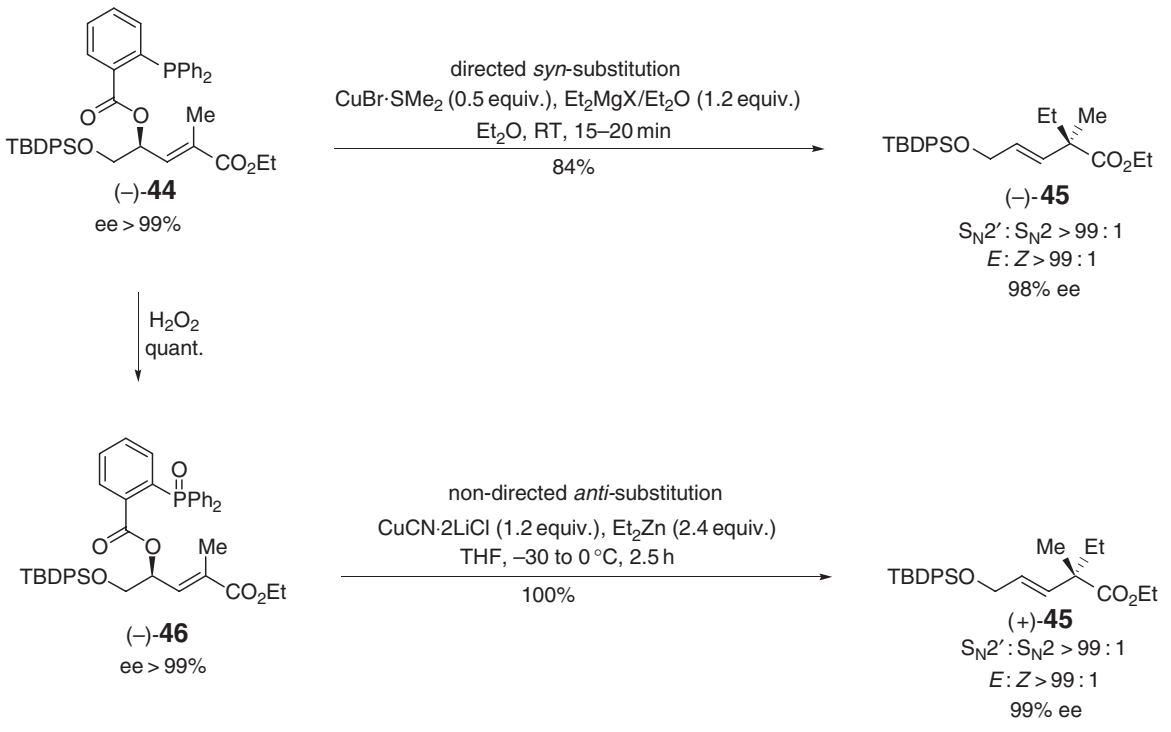
Scheme 14



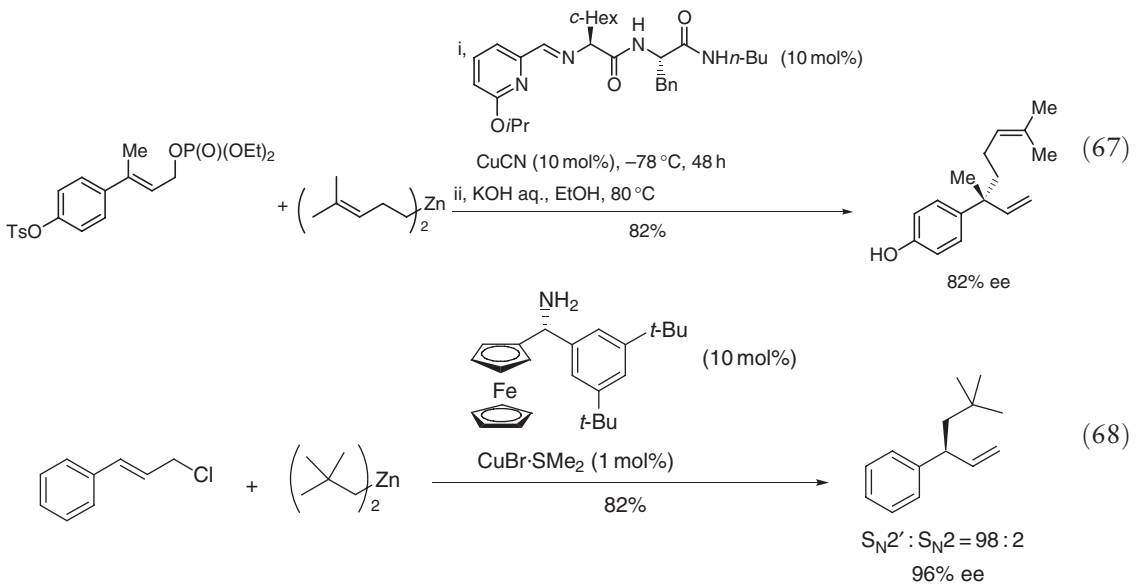
Scheme 15



Scheme 16



Scheme 17

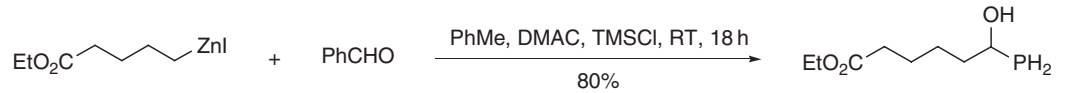


9.04.1.3.3 Addition reactions

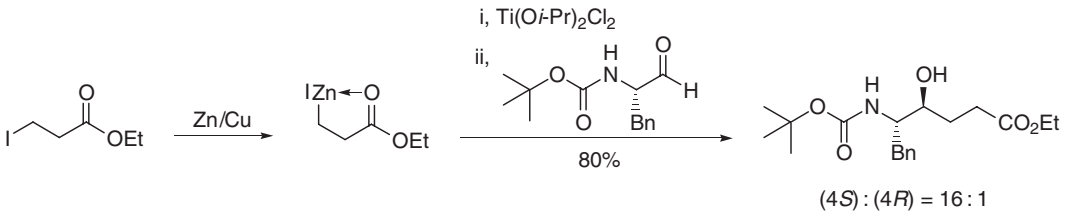
Like substitution reactions, additions of organozinc compounds on electrophiles are very slow and need often activation of the reaction partners.

Alkylzinc halides react only sluggishly with aldehydes or ketones. This reactivity can be improved by activating the carbonyl derivative with a Lewis acid. Excellent results are obtained with titanium alkoxides,[137] Me_3SiCl,[138]

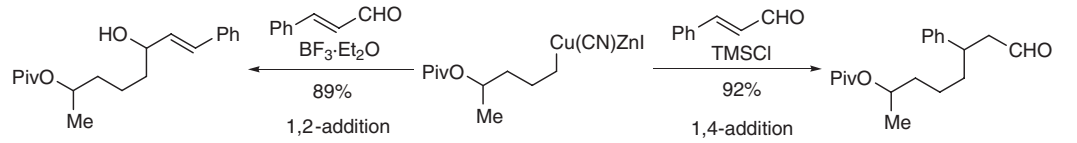
$BF_3{\cdot}OEt_2$,[48b] or $Ti(O\textit{i}\text{-}Pr)_2Cl_2$[139] (Equations (69) and (70)). Depending on the nature of the catalyst, either the 1,2-addition product or the 1,4-addition product is obtained by the addition of the zinc–copper reagent to cinnamaldehyde (Equation (71)).[48b] Polyoxygenated metabolites of unsaturated fatty acids have been prepared by the addition of functionalized zinc–copper reagents to unsaturated aldehydes in the presence of $BF_3{\cdot}OEt_2$, providing allylic alcohols (Equation (72)).[140] *Exo*-methylene ketones add various copper–zinc reagents. This methodology has been applied for the synthesis of various prostaglandins (Equation (73)).[141,141a,141b]



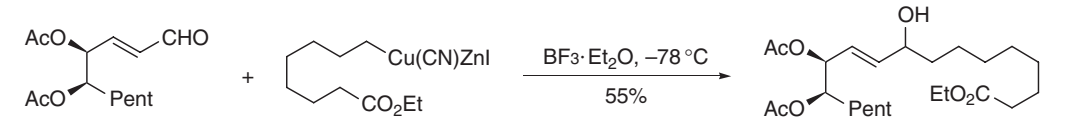
(69)



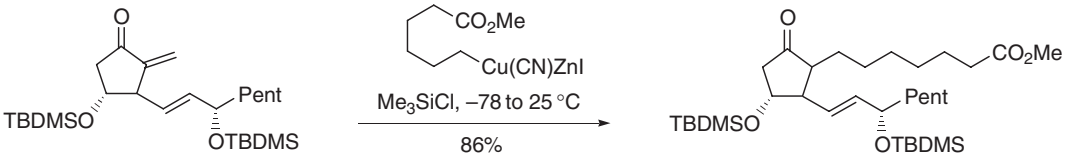
(70)



(71)

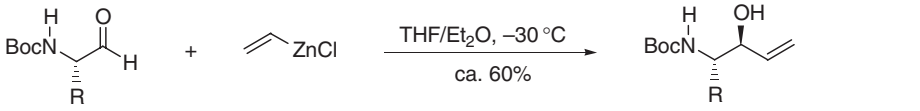


(72)

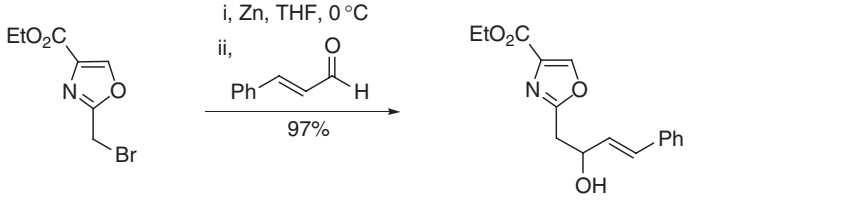


(73)

Although alkylzinc derivatives add only slowly to aldehydes, alkenylzinc derivatives display a higher reactivity (Equation (74)).[142] Reactive benzylic or related zinc reagents smoothly add to aldehydes, providing the allylic alcohol in almost quantitative yield (Equation (75)).[143]

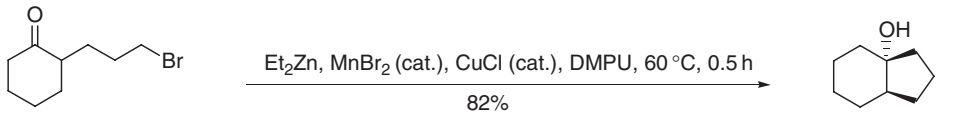


(74)



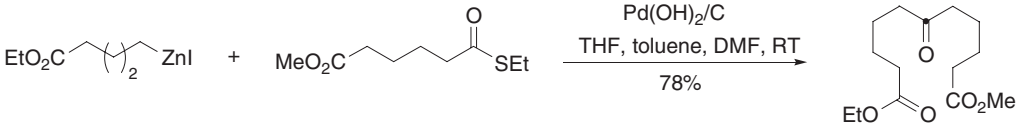
(75)

The reaction of manganese(II) salts with organozinc reagents does not provide the corresponding organomanganese reagents.[144,144a–144g] However, functionalized bromides can be metallated by Et_2Zn in the presence of catalytic amounts of $MnBr_2$,[60,60a] leading to cyclized product (Equation (76)).[145]

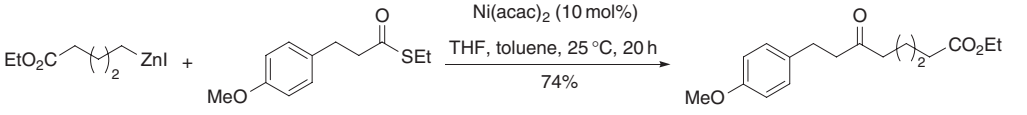


(76)

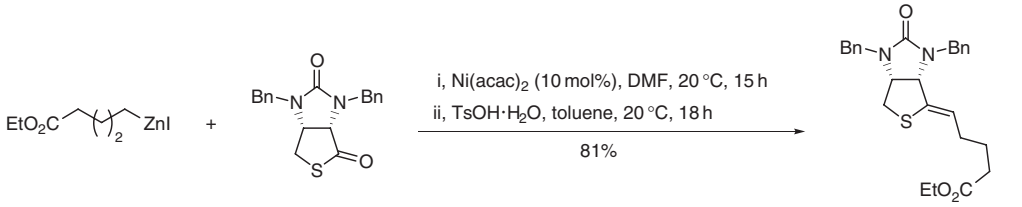
The reaction of thioesters in the presence of non-pyrophoric $Pd(OH)_2/C$ (Pearlman's catalyst) with various functionalized organozinc halides leads to functionalized unsymmetrical ketones in high yield (Fukuyama reaction) (Equation (77)).[146] This catalyst can also be used for Sonogashira and Suzuki reactions.[147] The $Ni(acac)_2$-catalyzed cross-coupling of functionalized zinc reagents with various thioesters provides acylation products under mild conditions (Equation (78)). Interestingly, the addition of the organometallic zinc species to the thiolactone **47** furnishes after acidic treatment the vinylic sulfide **48** in 81% yield. The use of bromine for the activation of zinc dust for the preparation of the zinc reagent was found the be advantageous (Equation (79)).[148,148a]



(77)



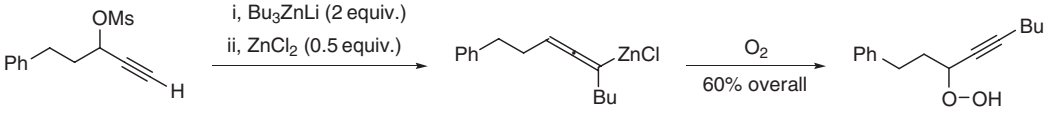
(78)



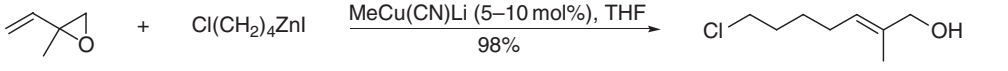
47 **48**

(79)

The direct oxidation of organozincs with oxygen is an excellent method for preparing hydroperoxides.[2] Recently, a new synthesis of propargylic hydroperoxides has been developed by Harada and co-workers using allenylzinc intermediates (Equation (80)).[149,149a] The opening of epoxides with zinc reagents is a difficult reaction. However, reactive α,β-unsaturated epoxides react readily with various functionalized zinc–copper organometallics or functionalized zinc reagents in the presence of a catalytic amount of MeCu(CN)Li (Equation (81)).[150]

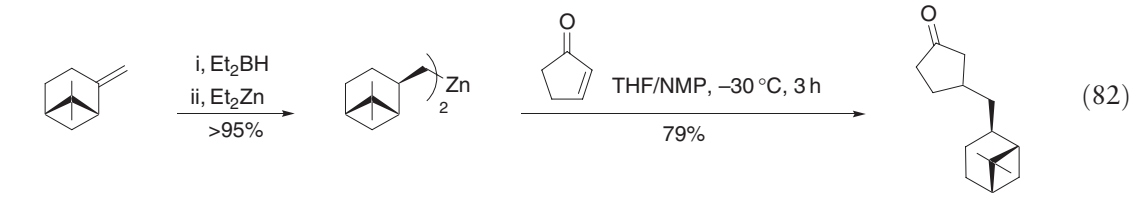


(80)

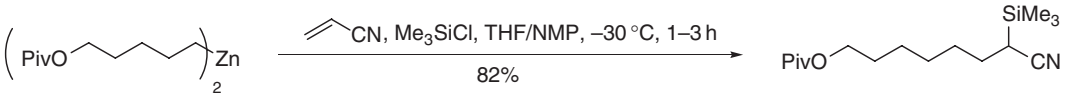


(81)

The reactivity of zinc organometallics can be dramatically increased by adding polar solvents like *N*-methylpyrrolidinone (NMP). Under these conditions, various diorganozincs add to a range of Michael acceptors like α,β-unsaturated ketones, aldehydes, nitriles, or nitro derivatives (Equations (82)–(84)).[151,151a] The preparation of mixed diorganozincs bearing non-transferable Me_3SiCH_2 groups allows a more efficient transfer of the functionalized group to the Michael acceptor (Equations (85)–(87)).[65,66]



(82)



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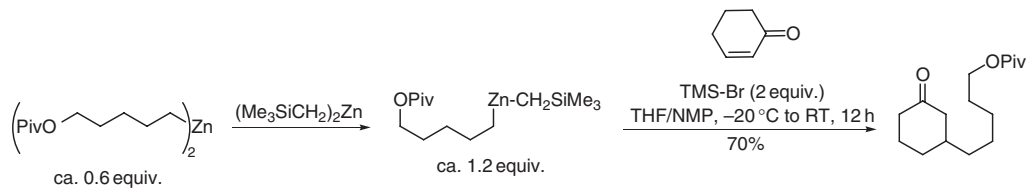

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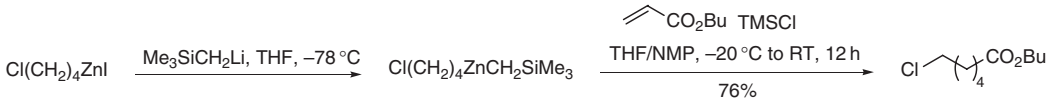

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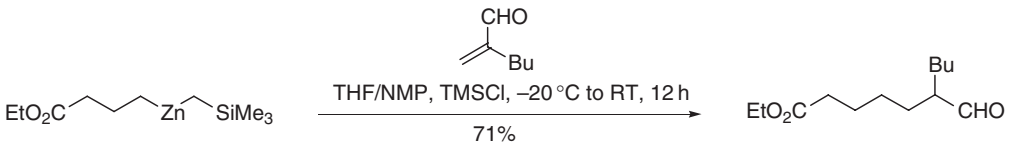
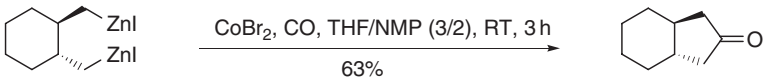


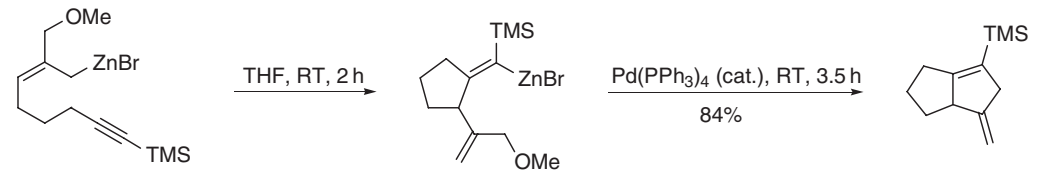
(87)

Reaction of cobalt(II) bromide with dialkylzincs in THF/NMP furnishes blue solutions of organocobalt intermediates that have a half-life of ca. 40 min. at −10 °C. Similarly the reaction of $FeCl_3$ with dipentylzinc produces a gray solution of an organoiron intermediate with a half-life of 2.5 h at −10 °C.[113] Interestingly, these new organocobalt(II) species undergo carbonylations at room temperature under mild conditions affording symmetrical ketones in satisfactory yield (Equation (88)).[152] The stoichiometric preparation of organocobalt species is not necessary, and catalytic amounts of cobalt(II) salts are sufficient to promote the acylation of diorganozincs.[113]

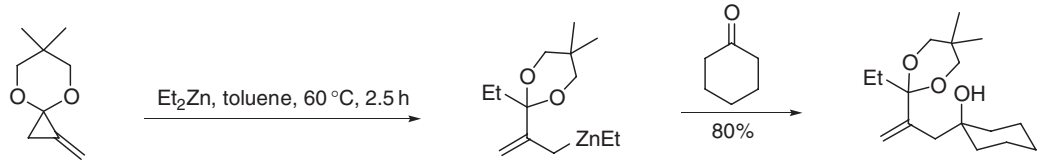


(88)

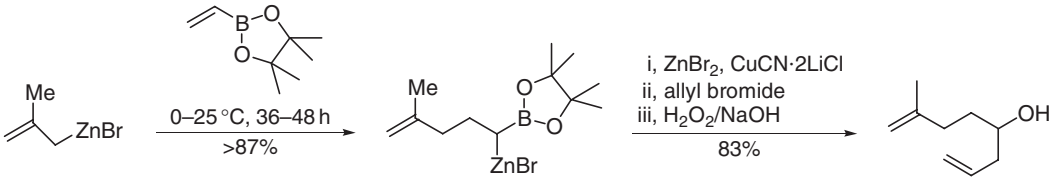
The addition of allylic zinc halides to various alkynes occurs in the absence of copper salts. The related addition to 1-trimethylsilylalkynes,[153,153a] unsaturated acetals,[154] and cyclopropenes[155] occurs readily. The allylzincation of trimethylsilyl acetylenes can be performed intramolecularly providing a functionalized alkenylzinc which cyclizes in the presence of $Pd(PPh_3)_4$ (Equation (89)).[156] Functionalized allylic zinc reagents can be prepared by the carbozincation of a dialkoxymethylenecyclopropane with dialkylzincs (Equation (90)).[69a,69d] Allylic zinc reagents are highly reactive reagents, which are prone to undergo carbozincation of weakly activated alkenes (Equation (91)).[157,157a–157d,158]



(89)

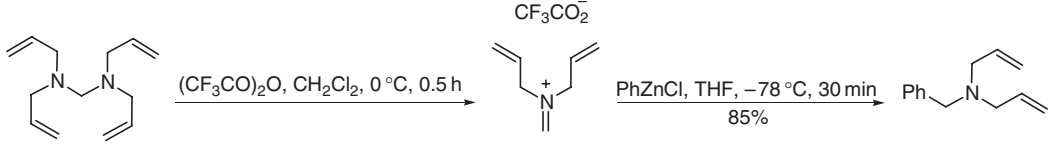


(90)

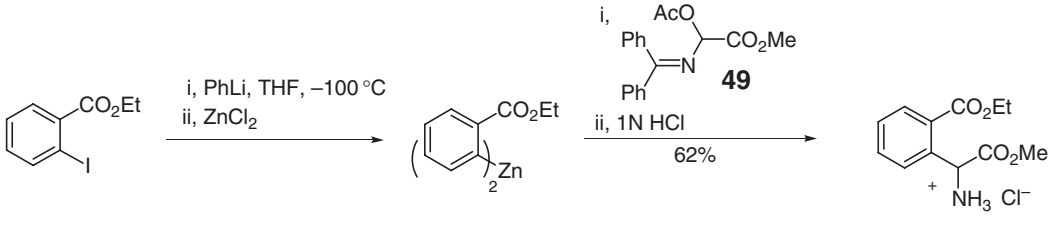


(91)

Reactive organometallic reagents, such as $Cr(CO)_5$·THF, readily add diorganozincs in the presence of CO and $Me_3O^+BF_4^-$ leading to functionalized Fischer carbene complexes.[159,159a] Excellent addition reactions are also obtained with iminium trifluoroacetates (Equation (92)).[160] Interestingly, this approach can be extended to functionalized organomagnesium reagents.[161] Functionalized diarylzincs add to the activated Schiff base **49** leading to an amino acid in 62% yield (Equation (93)).[162]

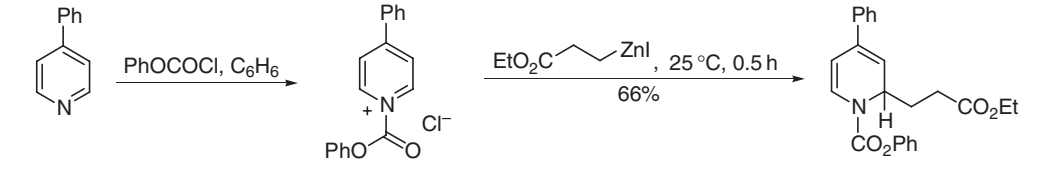


(92)

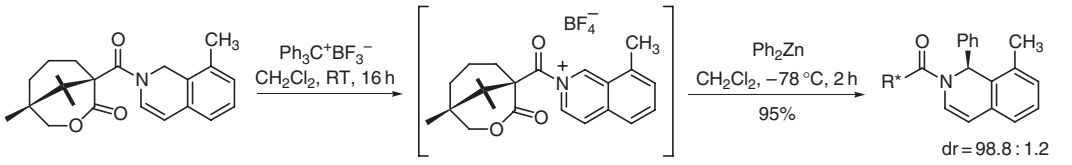


(93)

The formation of activated iminium intermediates derived from nitrogen heterocycles has been reported by Comins and co-workers.[163,163a] The activation of pyridine derivative with phenyl chloroformate provides pyridinium salt, which smoothly reacts with the zinc homoenolate (Equation (94)).[163,163a,164] The reaction of unsaturated amide with $Ph_3C^+BF_4^-$ produces *N*-acyliminium ions, which react with Ph_2Zn in CH_2Cl_2 producing the desired α-substituted amine (Equation (95)).[165]

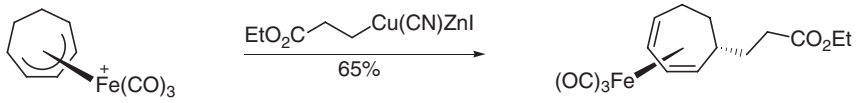


(94)



(95)

The addition of zinc–copper organometallics to unsaturated cationic metal complexes, derived, for example, from pentadienyliron and pentadienylmolybdenum cations, affords the corresponding dienic complexes (Equation (96)).[166] This chemistry has been extensively developed by Yeh and co-workers.[167,167a–167c] The addition of allylic and benzylic zinc reagents to (η^6-arene)-$Mn(CO)_3$ cations provides with excellent stereoselectivity the neutral (η^5-cyclohexadienyl)$Mn(CO)_3$ complexes (Equation (97)). Less reactive functionalized alkylzinc compounds show a more complicated reaction pathway due to an isomerization of the organozinc species (Equation (98)).[168] Rigby and Kirova-Snover[169] have applied these reactions to the synthesis of several natural products. Yeh and Chuang have shown that such addition reactions provide polyfunctional cationic chromium species, which can be converted to highly functionalized bicyclic ring systems, which are difficult to prepare otherwise (Equation (99)).[49]



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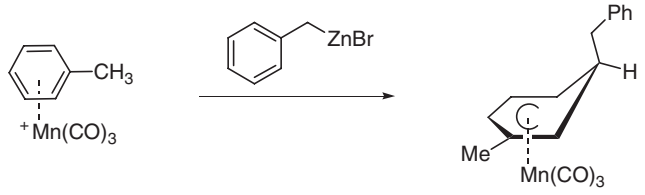
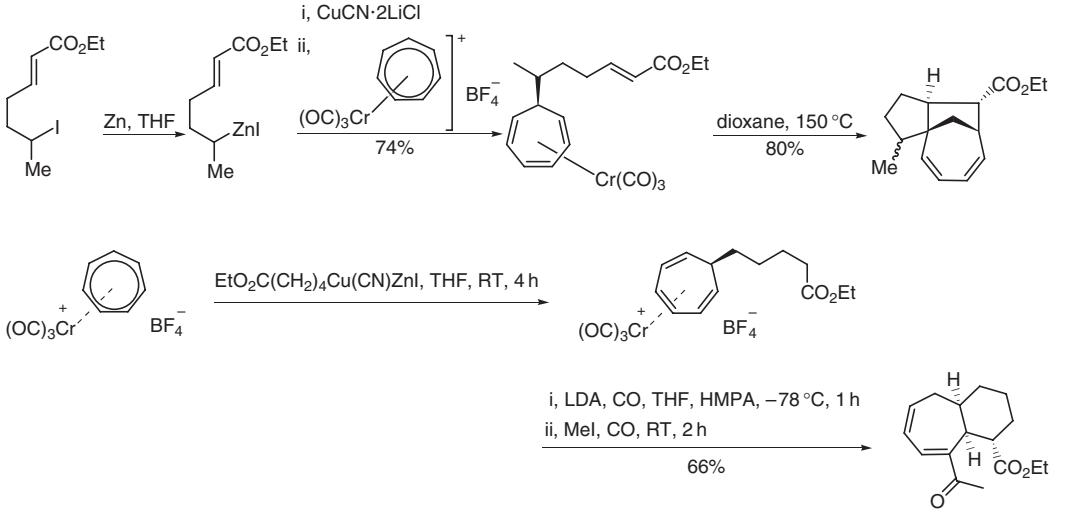


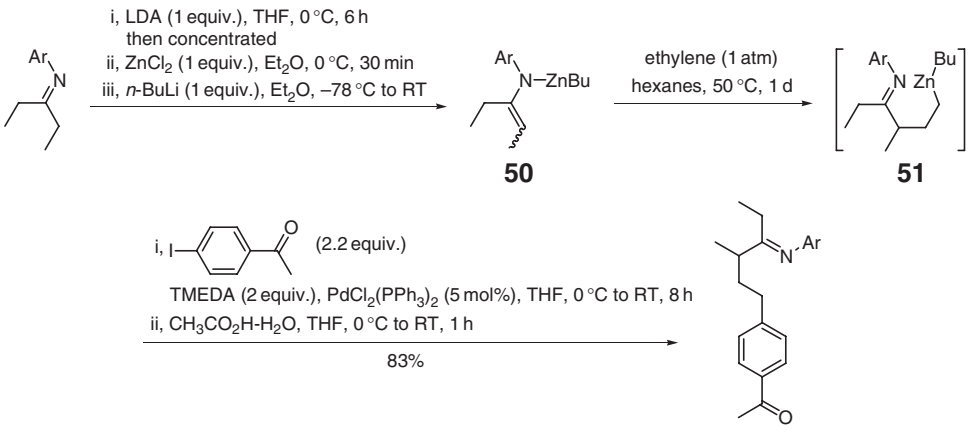
(97)



(98)

(99)

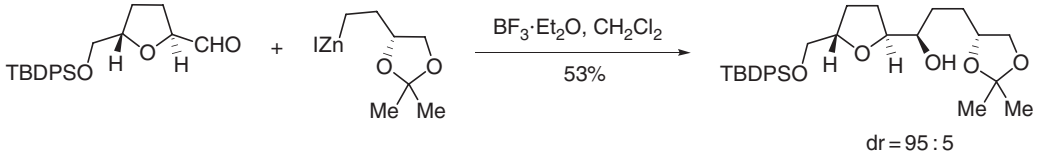
Zinc enamides such as **50** are reactive organozinc species, which can undergo addition to unactivated olefins with good to excellent yields. After trapping of the organozinc intermediate **51** with an electrophile and hydrolysis, a variety of functionalized primary, secondary, and tertiary α-alkylated ketones are isolated (Equation (100)).[170]



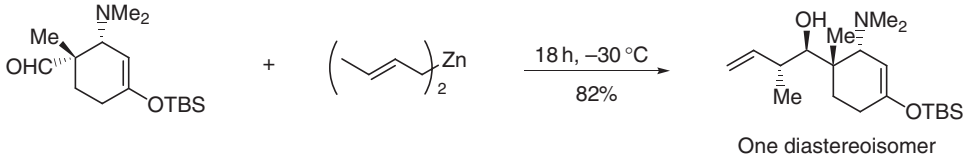
(100)

9.04.1.3.4 Asymmetric addition reactions

Addition of organozincs on aldehydes or ketones can be achieved under appropriate conditions with high enantioselectivities and diastereoselectivities. In a non-complexing solvent, such as dichloromethane, functionalized alkylzinc halides add to α-functionalized aldehydes again with a remarkable diastereoselectivity (Equation (101)).[138,143] Allylic zinc reagents readily add to aldehydes with good stereoselectivity in some cases (Equation (102)). Interestingly, the corresponding Grignard reagent leads to a mixture of diastereoisomers.[171]

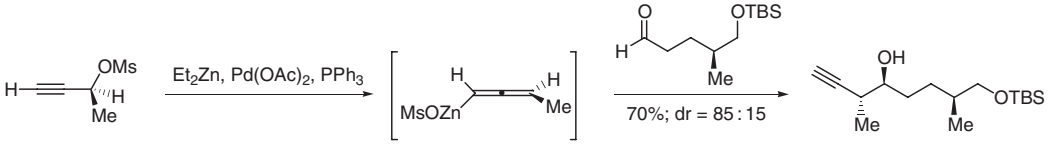


(101)

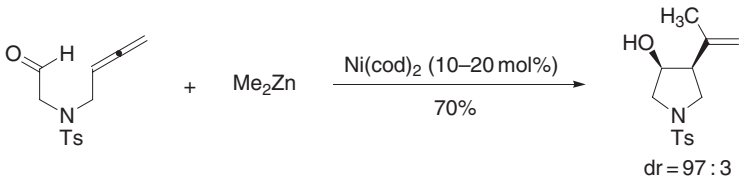


(102)

Propargylic zinc derivatives react with aldehydes or ketones with variable selectivity affording a mixture of allenic and homopropargylic alcohols.[172] Marshall and co-workers have shown that chiral propargylic mesylates are converted to allenylzinc reagents by the treatment with a Pd(0) catalyst. Their addition to an aldehyde provides the *anti*-homopropargylic alcohol as a main diastereoisomer (Equation (103)).[173,173a,173b] Interestingly, 1-trimethylsilyl-propargyl zinc reagents add to aldehydes with high regio- and diastereoselectivity leading to *anti*-homopropargylic alcohols.[174] Functionalized allylic zinc reagents can be generated *in situ*. The direct cyclization of allenyl aldehydes with diorganozincs in the presence of $Ni(cod)_2$ provides cyclic homoallylic alcohols with good diastereoselectivity (Equation (104)).[175,175a]

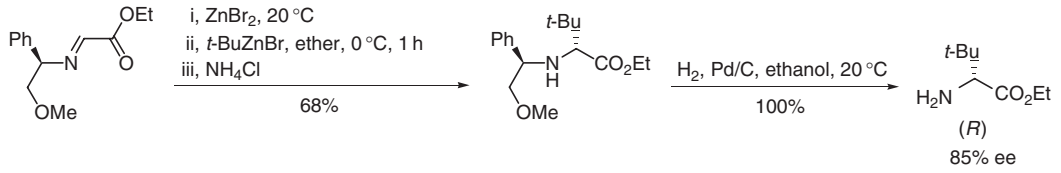


(103)

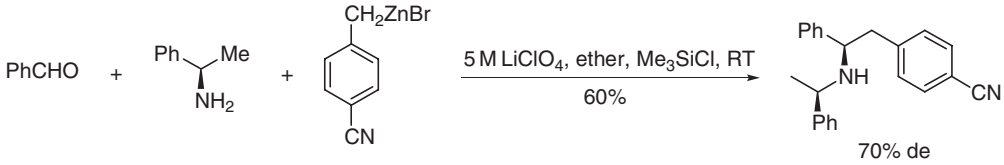


(104)

The addition of copper–zinc organometallics to imines is difficult. However, Mangeney and co-workers have found that alkylzinc reagents add to reactive imine derivatives and have used this property to prepare chiral amino acids (Equation (105)).[176] Benzylic zinc reagents also display an enhanced reactivity, and react directly under well-defined conditions with *in situ* generated imines. A diastereoselective one-pot addition of functionalized zinc organometallics can be realized by performing the reaction in 5 M $LiClO_4$ (in ether) in the presence of TMSCl. By using Reformatsky reagents and a chiral amine like (*R*)-phenylethylamine, diastereoselectivities with up to 95% have been obtained. (Equation (106)).[177]

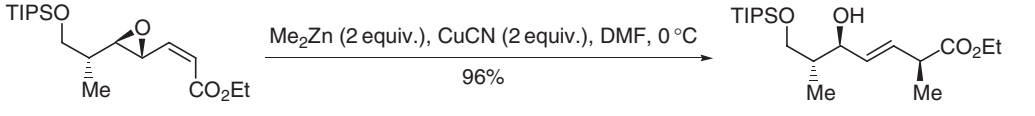


(105)

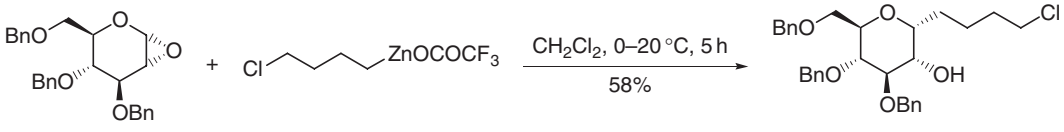


(106)

As mentioned previously, organozinc reagents open only reactive epoxides. This reaction can be achieved in some cases with high regio- and stereoselectivity. Thus the opening of δ-epoxy-α,β-unsaturated esters with $Me_2Zn{\cdot}CuCN$ proceeds with high *anti*-stereoselectivity leading to allylic alcohols (Equation (107)).[178] Activated glycal epoxides react with diorganozincs in the presence of CF_3CO_2H (Equation (108)).[179,179a] Presumably, the reaction of R_2Zn with CF_3CO_2H produces the highly Lewis-acidic species $RZnOCOCF_3$.



(107)

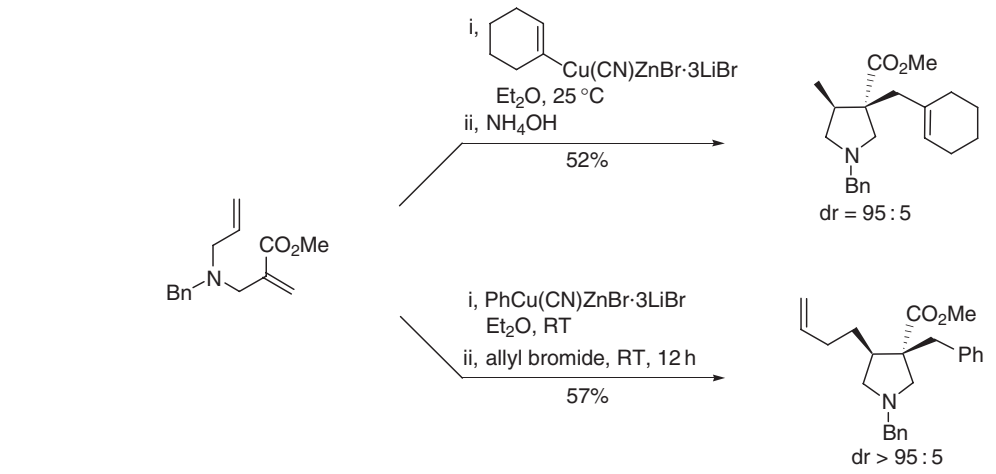


(108)

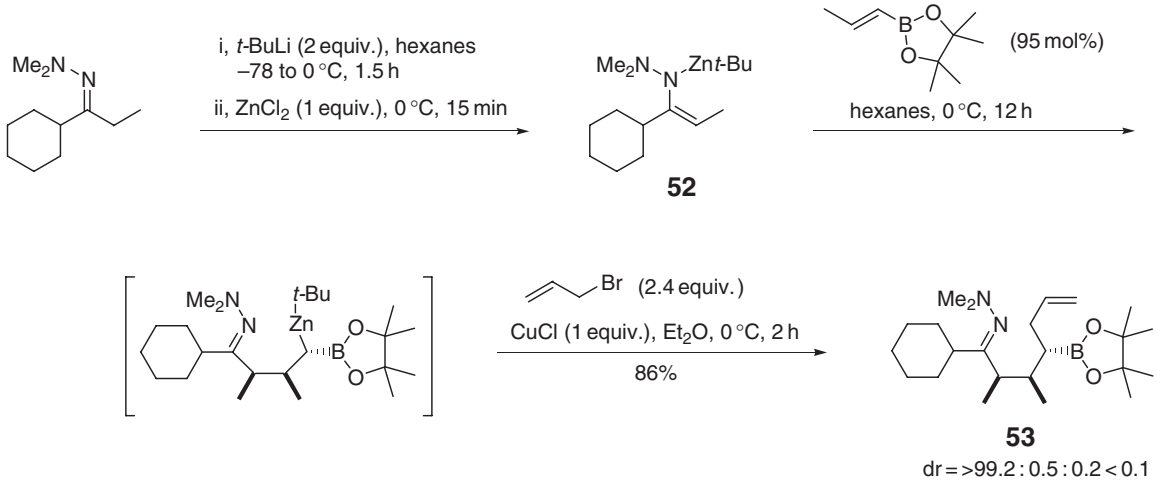
A stereoselective synthesis of substituted pyrrolidines has been achieved by a sequential domino Michael addition and intramolecular carbozincation. The intermediate zinc–copper reagent obtained after cyclization can be trapped with an electrophile such as allyl bromide (Scheme 18).[180] Addition of zincated hydrazones **52** on alkenyl boronates, followed by a trapping with an electrophile, provides adduct of type **53** with good yield and high diastereoselectivity (Scheme 19).[181] By this addition/trapping sequence, several contiguous stereogenic centers are created in one step.

Various asymmetric additions of organozinc compounds are performed by using a chiral ligand.

Hoveyda and Hird have developed a modular ligand synthesis based on various amino acids. The modular ligand **54** has been optimized for the enantioselective addition of Et_2Zn to unsaturated oxazolidinones (Equation (109)).[182] The resulting products can be converted into other carbonyl compounds (ketones, Weinreb amides, carboxylic acids) by standard methods. Enantioselective Michael additions have been pioneered by Feringa and co-workers[183,183a–183e] and Alexakis and co-workers.[184,184a–184e] Remarkably, only a catalytic amount of the chiral ligand **55** (4 mol%) and of

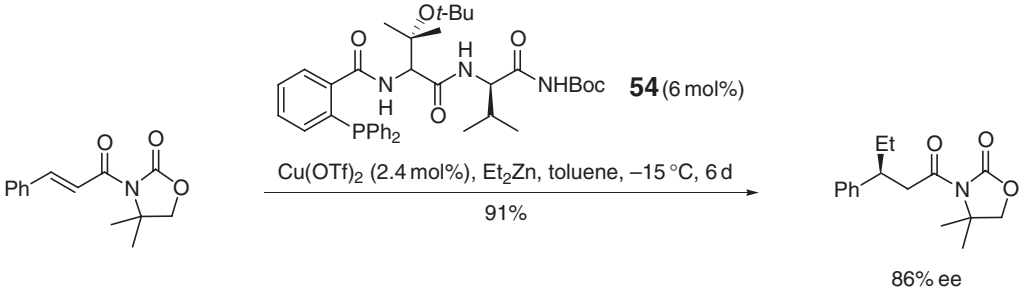


Scheme 18



Scheme 19

$Cu(OTf)_2$ (2 mol%) is required (Equation (110)).[183] The nature of the copper salt strongly influences the enantioselectivity, and copper carboxylates proved to be especially efficient (Equation (111)).[184b] It has been applied for an enantioselective synthesis of prostaglandin E_1 methyl ester (Equation (112)),[185] and can be used for the performance of a highly regiodivergent and catalytic parallel kinetic resolution.[186]



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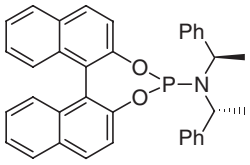

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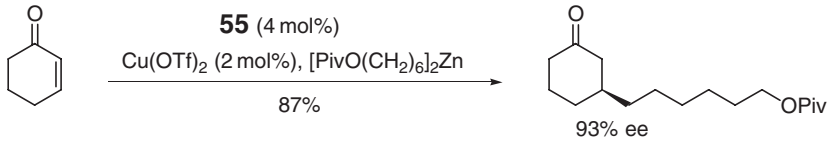

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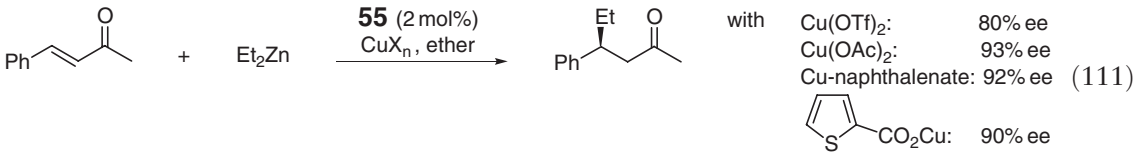
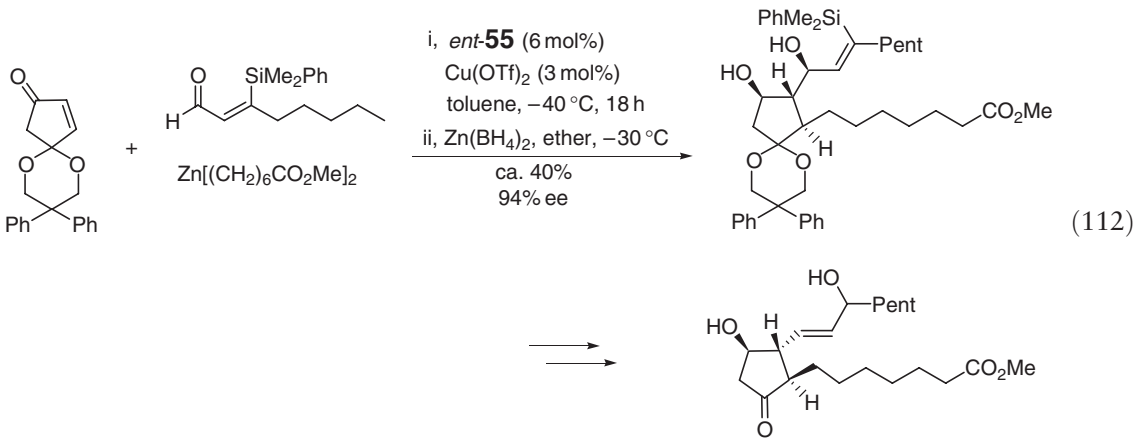
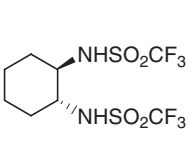


(111)

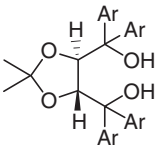


(112)

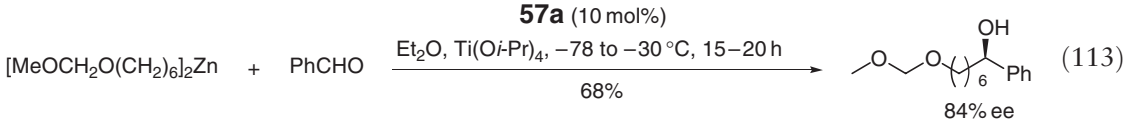
Lewis acids accelerate the addition of zinc organometallics to carbonyl derivatives. Titanium and zirconium(IV) salts are especially efficient catalysts. Oguni and co-workers[187,187a,187b] have shown in pioneering work that various chiral amino alcohols catalyze the addition of diethylzinc to aldehydes.[188,188a,188b] Yoshioka, Ohno, and co-workers have shown that the 1,2-bis-sulfonamide **56** is an excellent ligand for the asymmetric addition of Et_2Zn to various aldehydes.[189,189a,189b] TADDOL ligands such as **57a** and **57b** are remarkable catalysts, which tolerate many functional groups in asymmetric addition of an aldehyde to a diorganozinc. These catalysts introduced by Seebach and co-workers have found numerous applications in asymmetric catalysis.[190,190a] The convenient preparation of diorganozincs starting from alkylmagnesium halides using $ZnCl_2$ in ether as transmetallating reagent followed by the addition of 1,4-dioxane constitutes a practical method for the enantioselective addition of dialkylzincs.[190e] The enantioselective addition of polyfunctional diorganozincs is especially interesting (Equation (113)). The more bulky ligand **57b** allows the addition of diorganozincs to acetylenic aldehydes leading to propargylic alcohols in 96% ee (Equation (114)).[190h]



56



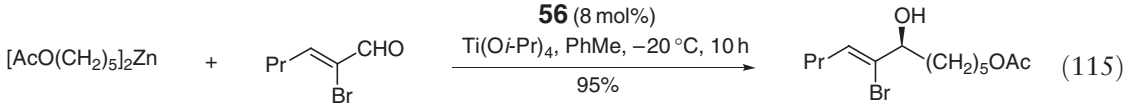
TADDOL: **57a**: Ar = Ph
57b: Ar = 2-naphthyl



(113)

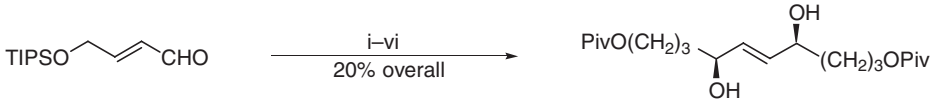
(114)

This approach has been extended to the conjugate addition of primary dialkylzincs to 2-aryl and 2-heteroaryl nitroolefins and allows the preparation of enantio-enriched 2-arylamines.[191] Dendric styryl TADDOLS[192,192a] and polymer-bound Ti-TADDOLates[193] have proved to be very practical chiral catalysts for the enantioselective addition to aldehydes. Likewise, the immobilization of BINOL by cross-linking co-polymerization of styryl derivatives has allowed several enantioselective Ti and Al Lewis acid-mediated additions to aldehydes.[193] Dialkylzincs obtained via an I/Zn exchange or a B/Zn exchange have also been successfully used for the enantioselective additions to a variety of aldehydes.[194,194a] The use of *trans*-(1R,2R)-*bis*(trifluoromethanesulfamido)-cyclohexane **56** is an excellent chiral ligand. The presence of an excess of titanium tetraisopropoxide (2 equiv.) is, however, required (Equation (115)).[194,194a,195] Replacement of Ti(O*i*-Pr)$_4$ with the sterically hindered titanium alkoxide (Ti(O*t*-Bu)$_4$) leads to higher enantioselectivities.[196]



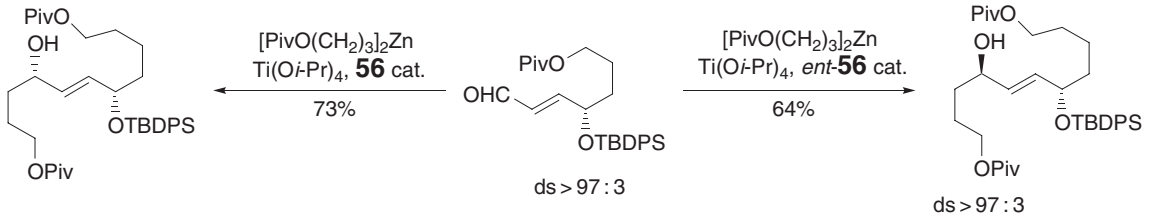
(115)

This enantioselective preparation of allylic alcohols has been applied to the synthesis of the side chain of prostaglandins.[197,197a–197c] The addition to functionalized aldehydes allows the synthesis of C_2-symmetrical 1,4-diols, with excellent diastereoselectivity and enantioselectivity (Equation (116)).[195,198,198a,198b] An extension of this method allows the synthesis of C_3-symmetrical diols.[199] Aldol-type products result from the catalytic enantioselective addition of functionalized dialkylzincs to 3-TIPSO-substituted aldehydes followed by a protection–deprotection and oxidation sequence, affording the addition product in 70% yield and 91% ee (Equation (117)).[200] The addition to α-alkoxyaldehydes provides a general approach to monoprotected 1,2-diols, which can be converted to epoxides in excellent enantioselectivity (Equation (118)).[201] The configuration of the newly chiral center does not depend on the configuration of the ligand **56** (Scheme 20).[198]

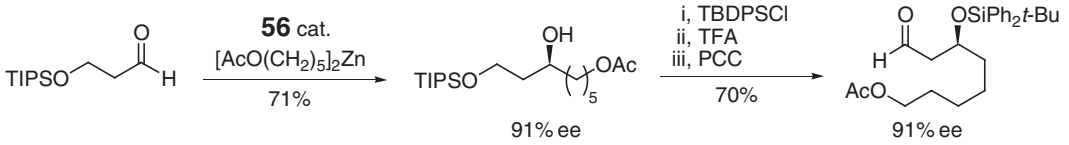


(116)

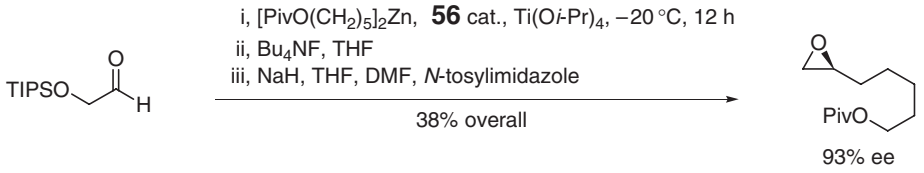
i, $[PivO(CH_2)_3]_2Zn$, **56** cat.; ii,TBDPSCl;
iii, AcOH, H_2O, THF; iv, NMO, Pr_4NRuO_4;
v, $[PivO(CH_2)_3]_2Zn$, **56** cat.; vi, Bu_4NF, 55 °C, 12–21h



Scheme 20

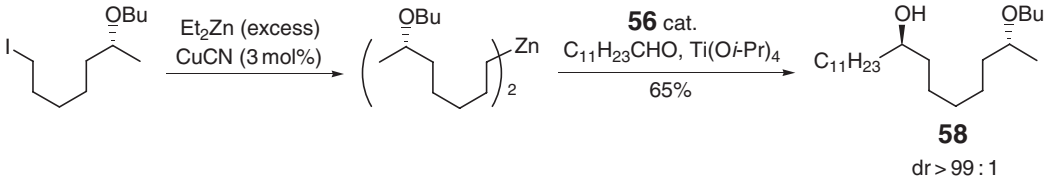


(117)



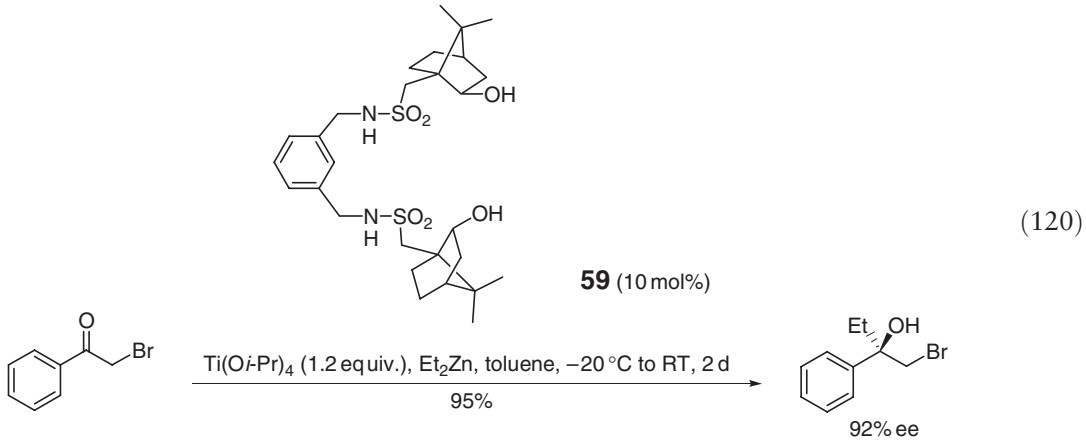
(118)

Further applications to the preparation of chiral polyoxygenated molecules[202] and to the synthesis of the natural product (−)-mucocin[203] have been reported (Equation (119)). The chiral building block **58** was used in the total synthesis of cycloviracin B1, which is of interest for its selective antiviral activity.[204]

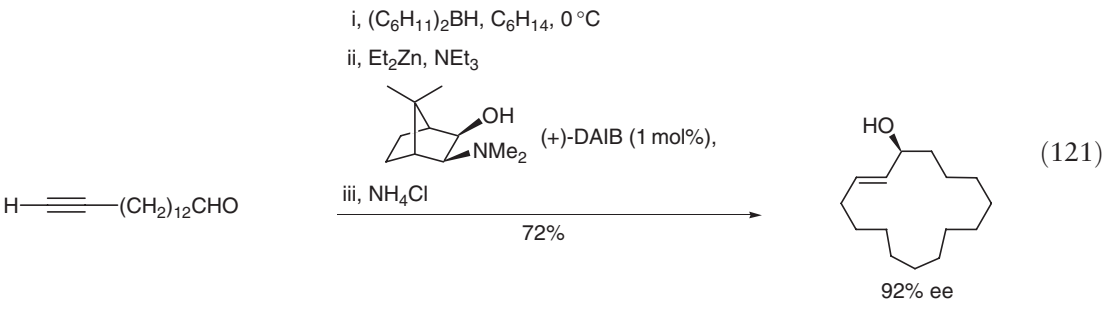


(119)

The enantioselective addition of dialkylzincs to aromatic ketones is especially difficult. Yus and co-workers have developed a new chiral ligand **59**, allowing the addition of dialkylzincs to various aromatic ketones in good yields. The enantioselective addition is promoted by Ti(O*i*-Pr)$_4$, and tolerates the presence of several functional groups (Equation (120)).[205] An elegant synthesis of (*R*)-(−)-muscone has been reported by Oppolzer and co-workers (Equation (121)).[80b,206]

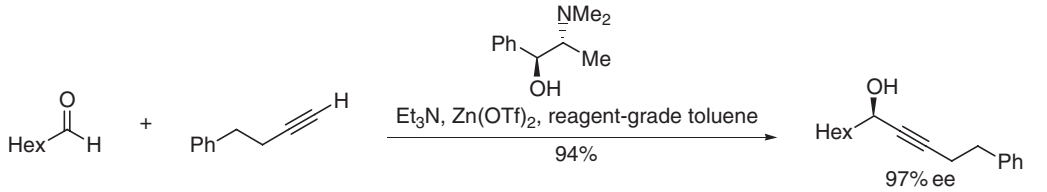


(120)

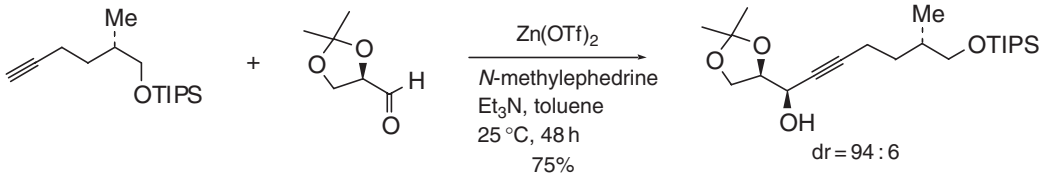


(121)

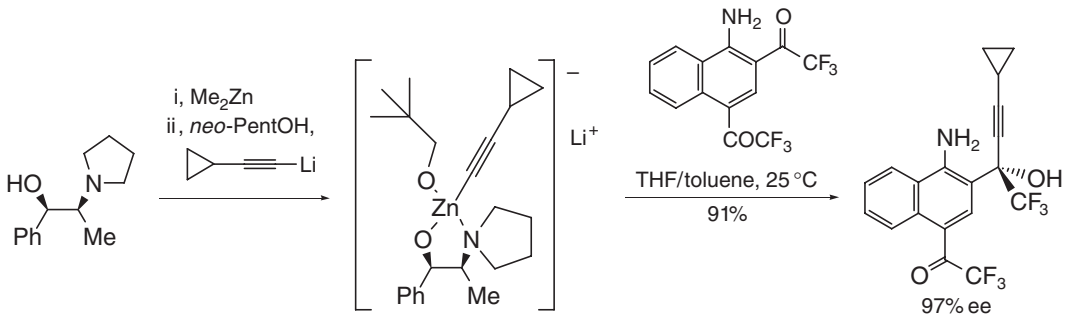
Alkynylzinc species generated *in situ* catalytically add to various aldehydes in very high enantioselectivities using reagent-grade toluene.[207] Chiral propargylic alcohols are obtained in this way (Equation (122)). As an application, a functionalized alkyne has been added to (*R*)-isopropylidene glyceraldehyde in the presence of $Zn(OTf)_2$ and *N*-methylephedrine providing the corresponding propargylic alcohol in Equation (123).[208] The asymmetric addition of alkynylzinc reagents to aldehydes and ketones has recently been reviewed.[209] Especially important has been the stoichiometric addition of alkynylzinc derivatives leading to Efavirenz, a new drug for the treatment of AIDS (Equation (124)).[210] A catalytic version of this reaction has been described by Carreira and Anand.[211]



(122)

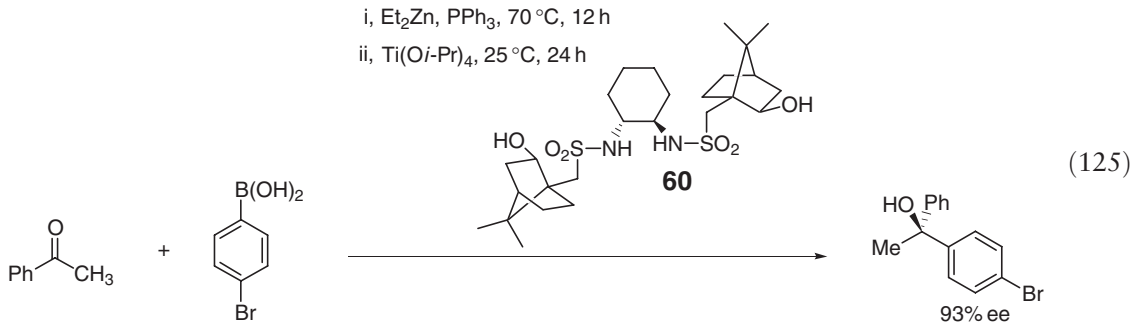


(123)

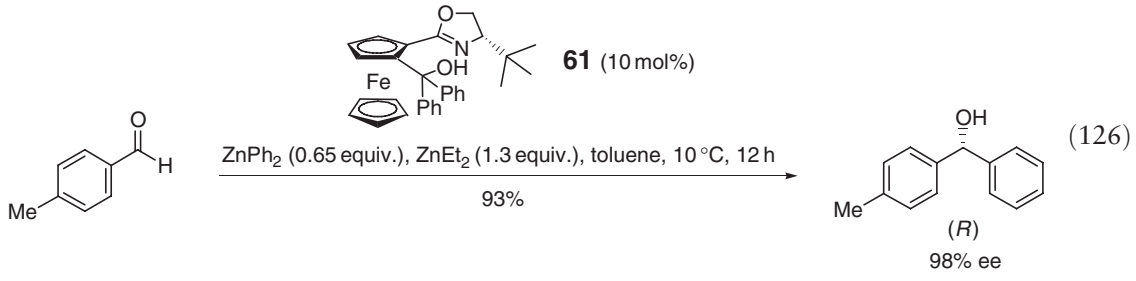


(124)

Interestingly, the chiral diamine **60** catalyzes the enantioselective addition of boronic acids to aromatic ketones like acetophenone. The reaction produces interesting tertiary diarylcarbinols with up to 93% ee (Equation (125)).[212] Bolm and co-workers have shown that this approach can also be used for a simple preparation of chiral diarylcarbinols in the presence of the chiral ferrocenyl ligand **61** (Equation (126)).[213,213a–213f]

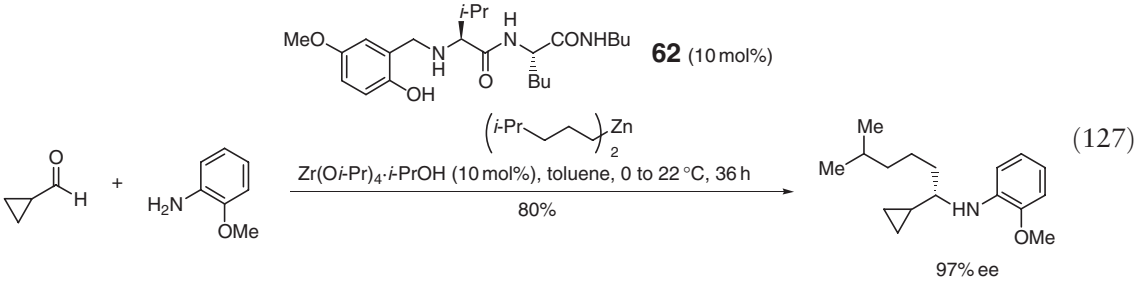


(125)



(126)

The addition of diorganozincs to imines is a difficult reaction. However, Hoveyda, Snapper, and co-workers have found that the *in situ* generation in the presence of $Zr(Oi\text{-}Pr)_4{\cdot}HOi\text{-}Pr$, an excess of a dialkylzinc and a catalytic amount of the amino-acid derivative **62** allows an enantioselective addition leading to various amines with high enantioselectivity (Equation (127)). In the presence of the modular catalyst **63** and $Zr(Oi\text{-}Pr)_4{\cdot}HOi\text{-}Pr$ (11 mol%), the imine reacts with *bis*-alkynylzincs in the presence of $(Me_3SiCH_2)_2Zn$, which is a zinc reagent with non-transferable Me_3SiCH_2 groups.[214] Under these conditions, an efficient addition reaction proceeds affording a propargylic amine in 83% yield and 90% ee (Equation (128)).[215]



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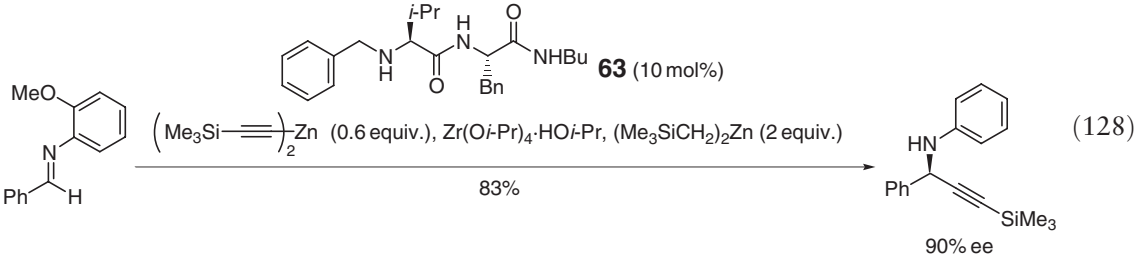
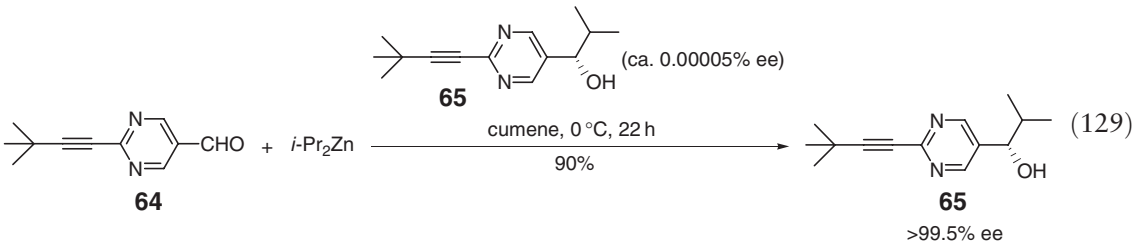


(128)

Soai and co-workers have developed additions of diisopropylzinc to 2-alkynylpyrimidyl-5-carbaldehydes. The resulting alcohol allows a practically perfect asymmetric autocatalysis.[216] Recently, they reported that an efficient amplification by a catalyst with as low as 10^{-5}% ee gives practically enantiomerically pure (> 99.5% ee) product in only three consecutive cycles.[217] The product formed *in situ* with enhanced ee serves as an asymmetric autocatalyst. Thus, addition of diisopropylzinc to the carbaldehyde **64** in presence of 20 mol% of the alkanol (*S*)-**65** with 10^{-5}% ee gives after 1.5 h (*S*)-**65** with 57% ee. A new addition of the mixture diisopropylzinc/carbaldehyde **64** to the reaction

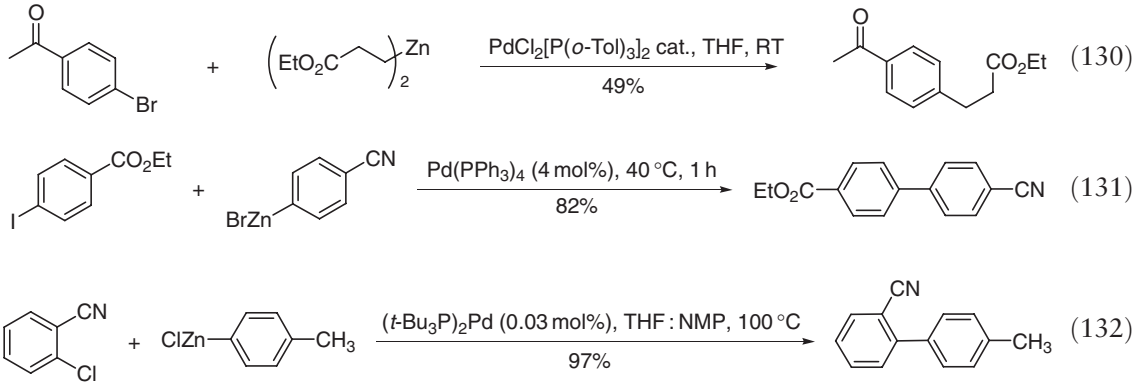
mixture provides (*S*)-**65** with 99% ee. Finally a last addition of diisopropylzinc/carbaldehyde **64** to the reaction mixture furnishes (*S*)-**65** with enantioselectivity up to 99.5% and with 90% yield (Equation (129)).



(129)

9.04.1.3.5 Negishi cross-coupling

Negishi and co-workers discovered 25 years ago that organozinc halides undergo smooth Pd(0)-catalyzed cross-coupling reactions with aryl, heteroaryl, and alkenyl halides, as well as acid chlorides.[14,15] These cross-coupling reactions have a broad scope and have found many applications.[14] They have been performed with a range of polyfunctional organozinc halides.[218,218a–218l] These zinc organometallics may contain a silylated acetylene,[219] an alkenylsilane,[218d] an allylic silane,[220] an alkoxyacetylene,[218e] a polythiophene,[221] polyfunctional aromatics,[218i] heterocyclic rings,[222,222a–222c] an ester,[28,28a,223,223a] a nitrile,[28,28a,224] a ketone,[225] a protected ketone,[222] a protected aminoester,[226] a stannane,[218k] or a boronic ester.[53a] The cross-coupling reaction with homoenolates proceeds especially well with bis-(tris-*o*-tolylphosphine)palladium dichloride,[223] leading to the desired cross-coupling products (Equation (130)). Biphenyls have been often prepared by using $Pd(PPh_3)_4$ as a catalyst (Equation (131)).[28,28a] Recently, Fu and Dai have demonstrated that Negishi cross-coupling reactions can be efficiently performed by using the sterically hindered phosphine $(t\text{-}Bu)_3P$ as a ligand, which results in very active catalytic species $(t\text{-}Bu_3P)Pd$.[40b] In these cases, the cross-coupling can be performed with aryl chlorides and tolerates the presence of some functionalities (Equation (132)).[40b]

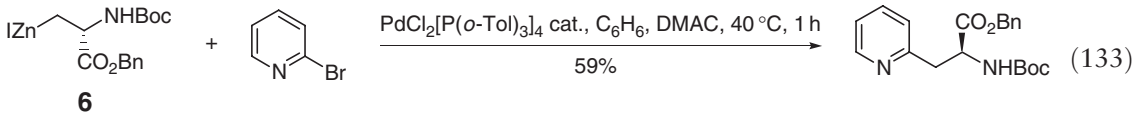


(130)

(131)

(132)

New α-amino acids have been prepared in high optical purity by using the reaction of pyridyl bromide with Jackson reagent **6** (Equation (133)).[35d] Fmoc-protected amino acids are routinely used in automated solid-phase peptide synthesis. The Fmoc-protected zinc reagent **66** is readily prepared from the corresponding alkyl iodide. The Pd-catalyzed cross-coupling with various aryl iodides furnishes the corresponding arylated amino acid derivatives in 25–59% yield.[227] Removal of the *tert*-butyl ester is readily achieved with Et_3SiH and TFA, leading to Fmoc-protected amino acids (Equation (134)).[228]



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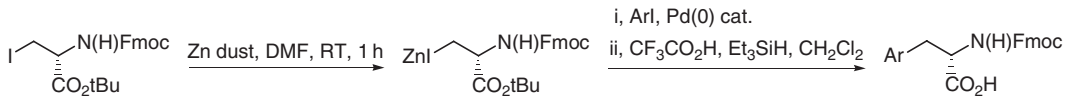
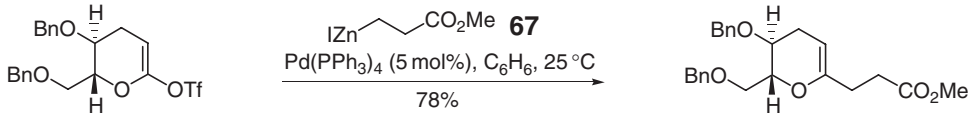


(134)

66

The reaction of the zinc homoenolate **67** with ketene acetal triflates in the presence of a palladium(0) catalyst leads to the corresponding cross-coupling product (Equation (135)). This key sequence has been used for the iterative synthesis of polycyclic ethers.[229,229a,229b] A smooth cross-coupling is observed between (*2E*, *4E*)-5-bromopenta-2,4-dienal and various zinc reagents, leading to dienic aldehydes in good to excellent yields and high stereomeric purity (Equation (136)). Using the isomeric (*2E*, *4Z*)-5-bromopenta-2,4-dienal furnishes the corresponding diene with a partial isomerization of the double bonds.[230] Negishi cross-coupling reaction can be performed with complex alkenyl iodides leading to the steroid derivative in 88% yield (Equation (137)). The palladium(0) catalyst ($Pd(PPh_3)_4$) was generated *in situ* from $Pd(OAc)_2$ (10 mol%) and PPh_3 (40 mol %).[231]



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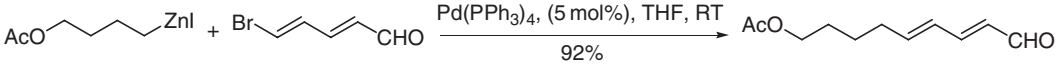

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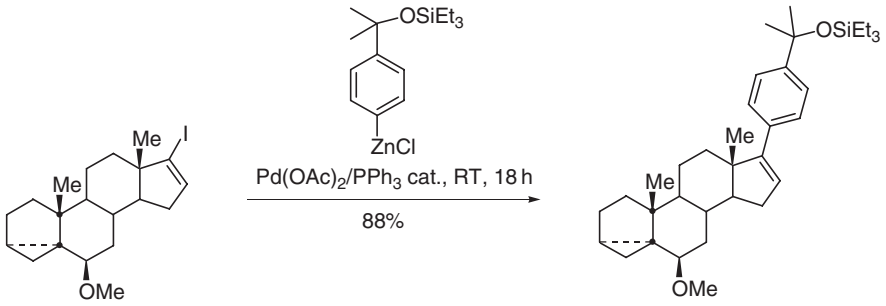
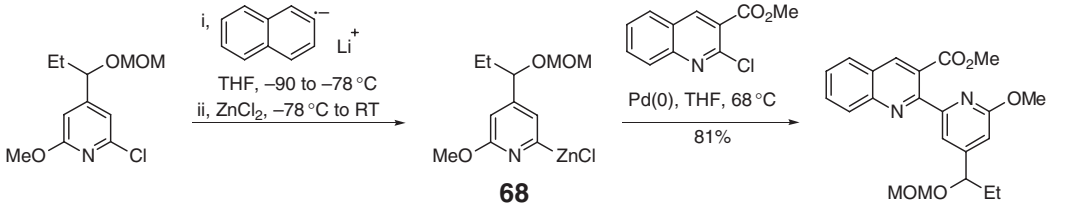


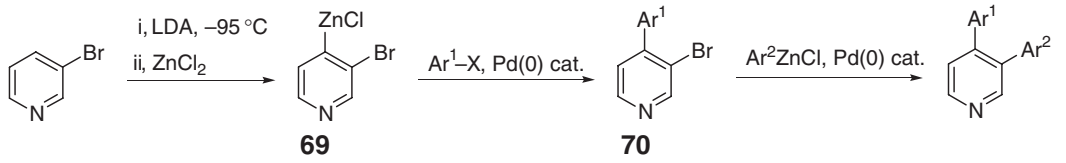
(137)

Functionalized heterocyclic zinc reagents are very useful building blocks for the preparation of polyfunctional heterocycles as shown with the pyridylzinc derivative **68** prepared by reductive lithiation followed by a transmetallation with zinc bromide (Equation (138)).[232] The cross-coupling of the zinc reagent **68** with a quinolyl chloride provides a new heterocyclic compound. The selective functionalization of positions 4 and 3 of pyridines is possible starting from 3-bromopyridine, which is selectively deprotonated in position 4 by the reaction with LDA followed by a transmetallation with $ZnCl_2$ (Equation (139)). The resulting zinc species **69** undergoes a Pd-catalyzed cross-coupling with various aryl halides (Ar^1–X) affording products of type **70**. The cross-coupling of **70** with a zinc reagent Ar^2–X in the presence of a Pd(0) catalyst provides 3,4-diarylpyridines.[233,233a] The functionalized iodoquinoline **71** reacts with *i*-PrMgCl providing an intermediate heteroarylmagnesium species, which after transmetallation to the corresponding zinc derivative undergoes a smooth cross-coupling reaction with ethyl 4-iodobenzoate in the presence of $Pd(dba)_2$ and TFP, providing the desired cross-coupling product in 74% yield (Equation (140)).[234]



(138)

68



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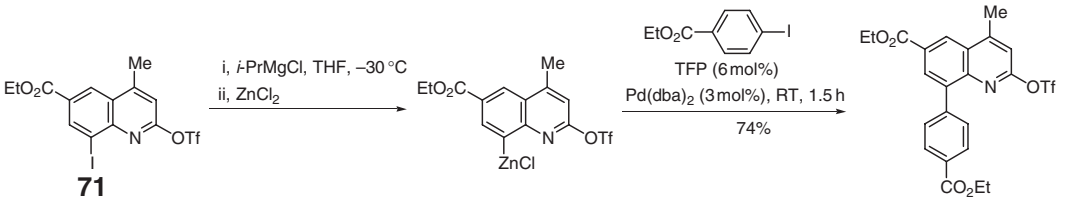
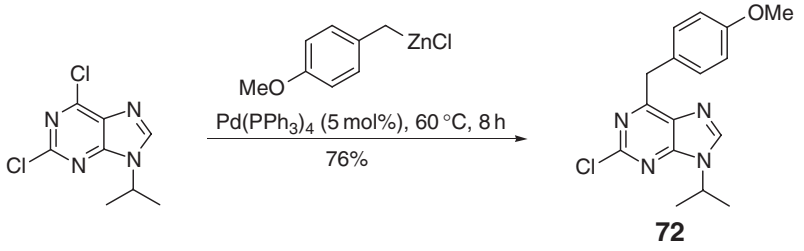
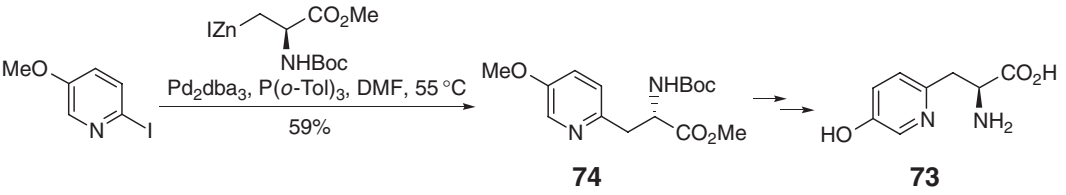


(140)

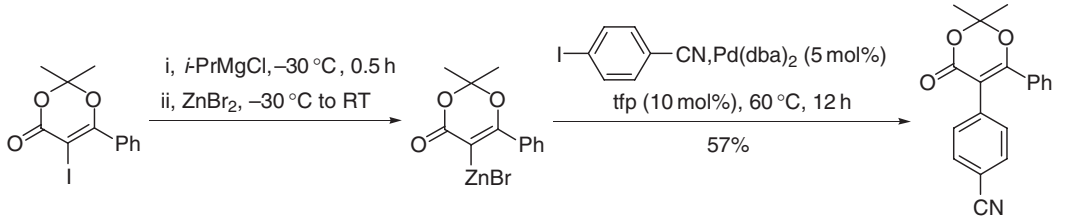
The selective functionalization of heterocycles is an important synthetic goal. Purines display multiple biological activities such as antiviral or cytostatic properties. The synthesis of analogs such as **72** can be achieved by a regioselective cross-coupling of functionalized benzylic zinc reagents with the dichloropurine derivative in the presence of $Pd(PPh_3)_4$ (Equation (141)).[235] L-azatyrosine **73** is an anticancer lead compound, which can be readily prepared using Jackson reagent and a Negishi cross-coupling reaction with 2-iodo-5-methoxypyridine affording the amino ester **74** in 59% yield (Equation (142)). Its deprotection according to a procedure of Burke and Ye[236] produces L-azatyrosine **73**.[237] Functionalized alkenylzinc species can be prepared via an iodine–magnesium exchange followed by a transmetallation with $ZnBr_2$ (Equation (143)). The Pd-catalyzed cross-coupling reaction with 4-iodobenzonitrile proceeds at 60 °C in THF leading to the arylated product in 57% yield.[238]



(141)

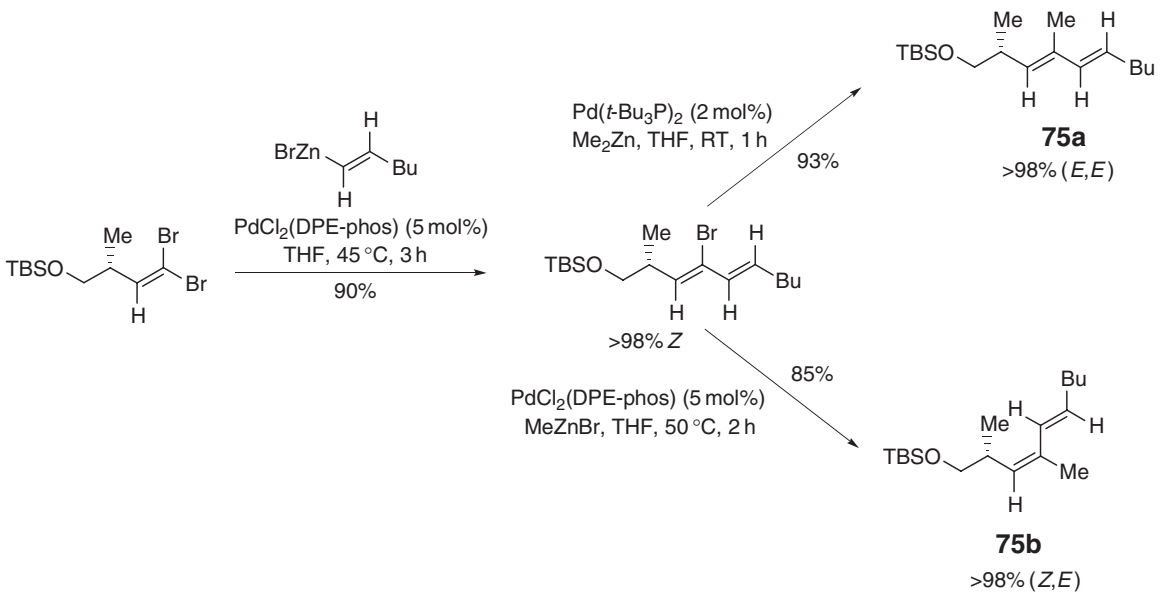


(142)



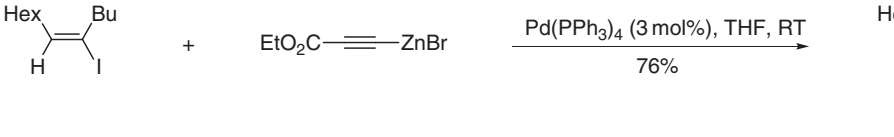
(143)

Negishi and co-workers have developed a high satisfactory Pd-catalyzed alkynylation of various alkenyl halides and triflates with alkynylzincs containing electron-withdrawing groups (Equation (144)).[239] The scope of this cross-coupling appears to be very broad, and the reaction is satisfactory even in those cases where the Sonogashira alkynylation is problematic. 1,1-Dibromo-1-alkenes undergo a highly *trans*-selective Pd-catalyzed cross-coupling with alkylzinc reagents using *bis*-(2-diphenylphosphinophenyl) ether (DPE-phos) as a ligand (Equation (145)). The use of $Pd(t\text{-}Bu_3P)_2$ is crucial for achieving stereospecific methylation with nearly 100% retention of configuration.[240] On the basis of this *trans*-selective cross-coupling, synthesis of 2-methyl-1,3-dienes can be performed. Depending on

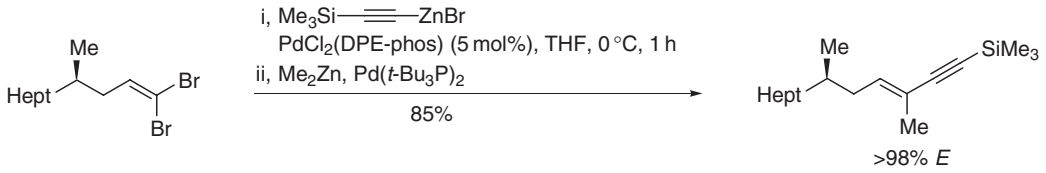


Scheme 21

the used ligand ($Pd(t\text{-}Bu_3P)_2$ or $PdCl_2$(DPE-phos)), either the (1*E*)-2-methyl-1,3-diene **75a** or the (1*Z*)-2-methyl-1,3-diene **75b** can be isolated with stereoselectivity up to 98% (Scheme 21).[241,241a]

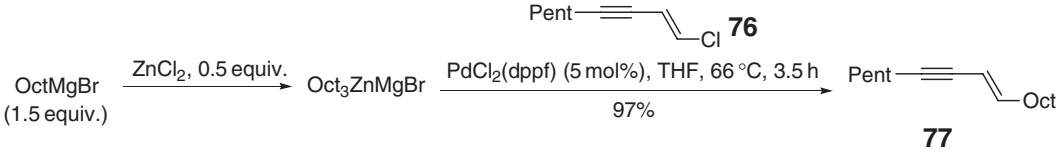


(144)

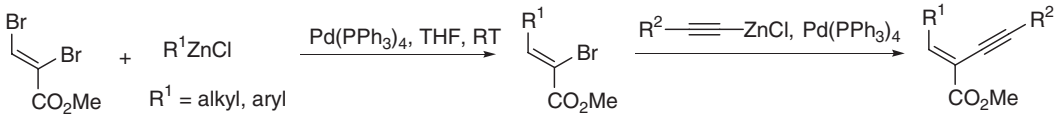


(145)

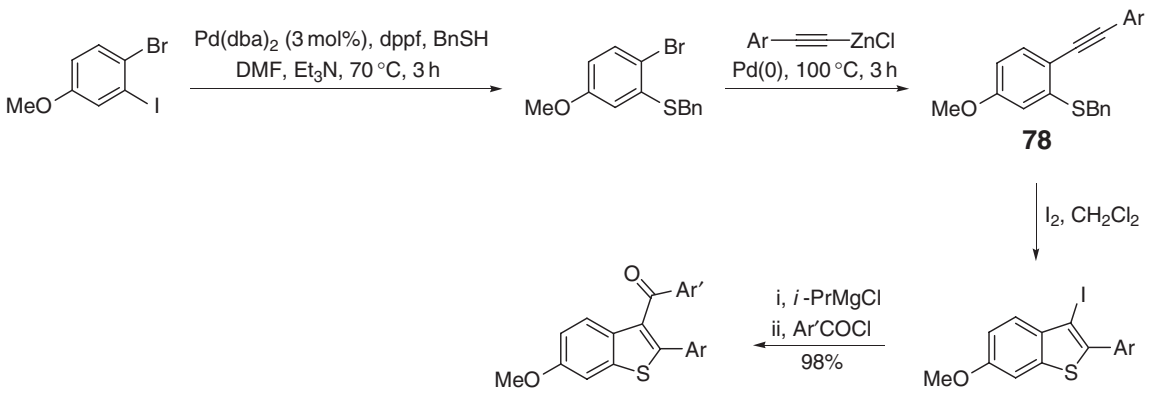
Further applications of Negishi's cross-coupling reactions for the synthesis of new chiral ferrocenyl ligands have been reported.[242,242a–242c] Interestingly, cross-coupling reactions can also be performed using triorganozincates.[243,243a] Chloroenyne **76** reacts with various magnesium zincates generated *in situ* in the presence of $PdCl_2$(dppf), showing that alkenyl chlorides insert readily Pd(0) complexes (Equation (146)). Especially easy is the reaction of conjugated chloroenynes leading to the enyne **77**.[243,243a] A selective cross-coupling reaction of (*Z*)-2,3-dibromopropenoate with organozinc compounds allows the preparation of highly functionalized enoates (Equation (147)).



(146)



(147)

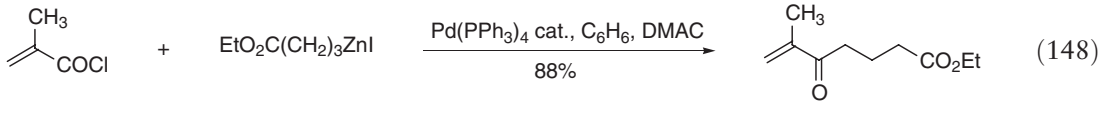


Scheme 22

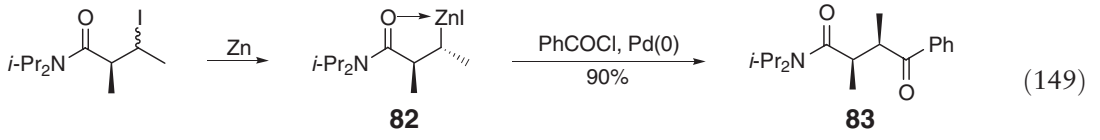
A flexible and convergent access to 2,3-disubstituted benzo[b]thiophenes has been developed (Scheme 22). The most concise approach involves a sequential coupling of an *o*-bromoiodobenzene with benzylthiol and zinc acetylides leading to the adduct **78**. Treatment with iodine followed by an iodine/magnesium exchange and acylation provides the polyfunctional benzofuran derivatives.[244,244a]

Negishi and co-workers have recently developed a linear iterative method for the synthesis of oligoenes and related natural products via Zr-catalyzed carboalumination and Pd-catalyzed cross-coupling of unsaturated zinc reagents.[245,245a,245b] Starting from the terminal amine **79**, a first cross-coupling sequence affords the unsaturated product **80**, which by an iterative reaction sequence and dimerization affords **81**, the precursor of amphotericin with high stereoisomeric purity (Scheme 23).[245a] An interesting asymmetric application is the synthesis of 6,7-dehydrostipiamide, a non-natural multidrug resistance resersal agent.[245b]

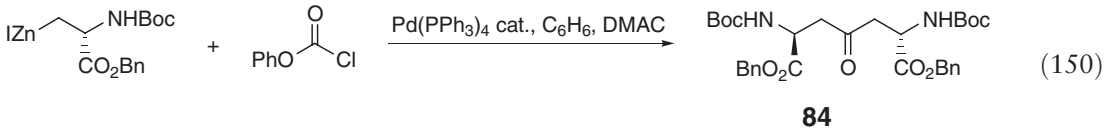
The cross-coupling of 3-carbethoxypropylzinc iodide with methacryl chloride provides an expeditive approach to polyfunctional enones (Equation (148)).[246] The reaction of *syn*- or *anti*-3-iodo-2-methylbutanamide with zinc powder furnishes the zinc reagent **82**, which reacts with benzoyl chloride in the presence of Pd(0) catalyst leading to the *syn*-product **83** (Equation (149)).[247] The acylation of serine or glutamic acid-derived zinc species, as developed by Jackson,[35–37] provides chiral γ-keto-α-amino acids in good yields. The acylation of the Jackson reagent with phenyl chloroformate or the direct reaction of an organozinc reagent with carbon monoxide under sonication in the presence of catalytic amounts of $(PPh_3)_2PdCl_2$ leads to the C_2-symmetrical ketone **84** (Equation (150)).[35j] In a related reaction, organozinc halides are treated with carbon monoxide and an allylic benzoate in the presence of a catalytic amount of palladium(0) complex and provides *S*-keto esters (Equation (151)).[248]



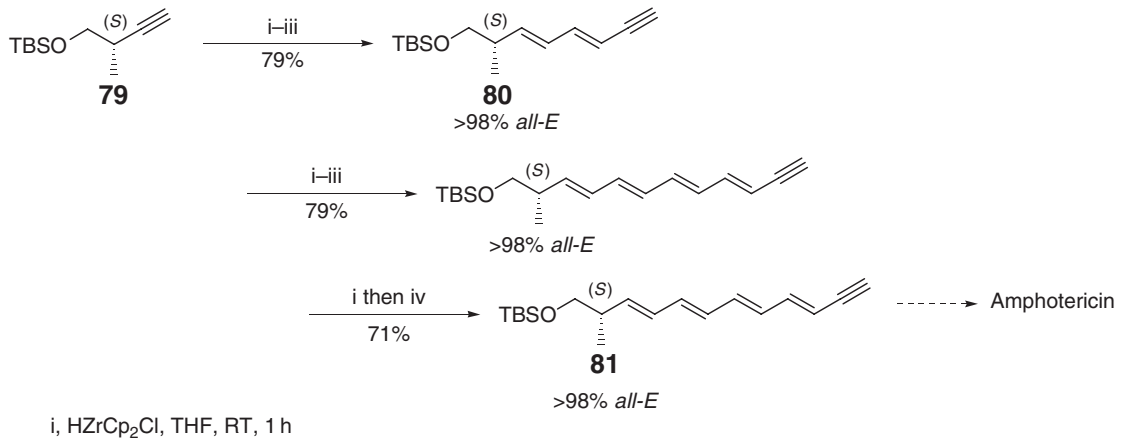
(148)



(149)



(150)



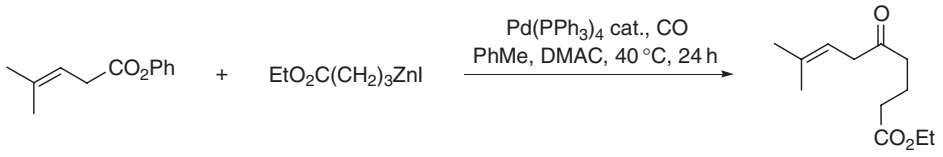
i, $HZrCp_2Cl$, THF, RT, 1 h

ii, Br—≡—$SiMe_3$ (1.05 equiv.), $Cl_2Pd(PPh_3)_2$ + 2DIBAH (5 mol%), $ZnCl_2$ (1 equiv.), THF, RT, 4 h

iii, K_2CO_3 (1.2 equiv.), MeOH

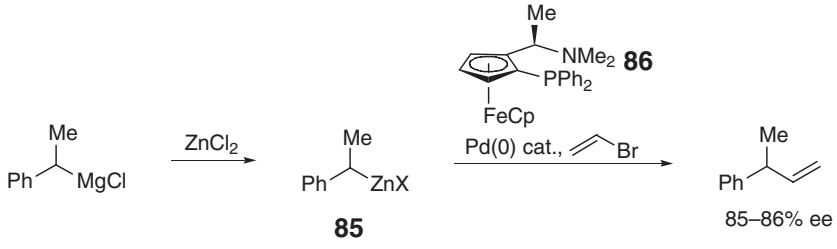
iv, Br—CO_2Et (1.05 equiv.), $Cl_2Pd(PPh_3)_2$ (5 mol%), DIBAH (10 mol%), $ZnCl_2$ (1 equiv.), THF, RT

Scheme 23

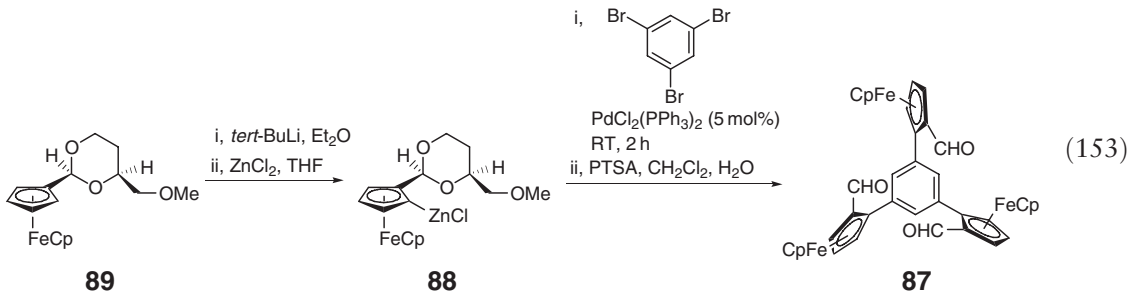


(151)

Substituted ferrocenyl groups are useful asymmetric building groups for stereoselective syntheses. Hayashi and co-workers have discovered a novel class of ferrocenyl catalysts, allowing the kinetic resolution of benzylic zinc derivatives, such as **85**.[249,249a] The racemic mixture of the benzylic zinc reagent **85** obtained by transmetallation from the corresponding Grignard reagent reacts with vinyl bromide in the presence of a Pd catalyst and the ferrocenyl aminophosphine **86**, leading to the asymmetric cross-coupling product with up to 85–86% ee (Equation (152)). Complex ferrocenyl derivatives such as **87**, being of interest as molecular materials with large second-order non-linear optical properties (NLO), have been prepared by the cross-coupling of the ferrocenylzinc reagent **88** with 1,3,5-tribromobenzene (Equation (153)). The starting zinc reagent has been prepared starting from the chiral ferrocenyl derivative **89**. Selective metallation of **89** with *tert*-BuLi followed by a transmetallation with $ZnCl_2$ furnishes the zinc reagent **88**. Negishi cross-coupling was best performed using $PdCl_2(PPh_3)_2$ (5 mol%) as catalyst.[250]



(152)

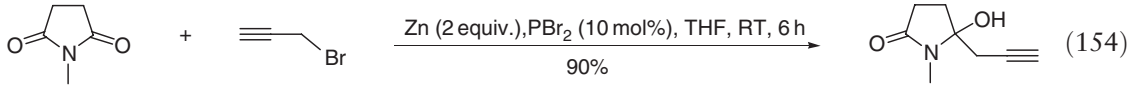


(153)

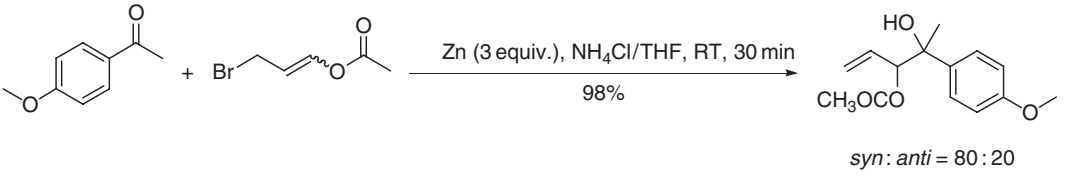
9.04.1.3.6 Barbier reaction

Barbier reactions[251] are performed by mixing an organic halide, an organic electrophile, and zinc dust without the preformation of an organozinc species. These reactions have found increasing applications in organic synthesis. The nature of the reactive intermediate is not always clear.[252] The formation of an alkylzinc halide is unlikely, since many of these reactions are performed in water.[253,253a–253c,254] It seems also not to be a free radical (as Luche and coworkers had proposed[253,253b]), since 5-hexenyl halides do not undergo ring closure under these reaction conditions.[254]

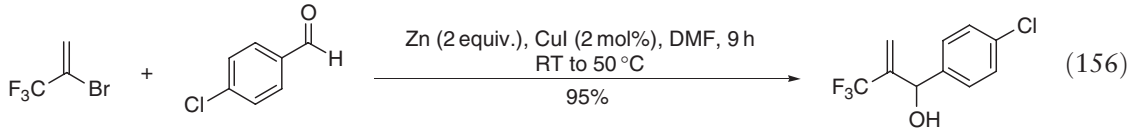
Barbier reactions have been widely developed to add allyl bromide to carbonyl compounds (aldehydes or ketones) in the presence of a metal in order to form homoallylic alcohols.[251,253,253a–253c] But it proved to be also applicable to α,β-unsaturated carbonyl compounds and nitriles,[255] pyrroles and indoles,[256] cyclic imides,[257] imines,[258] iminum ions,[259] and aldimines.[260] Barbier reactions were also carried out with functionalized allylic, propargylic, or benzylic halides such as acetoxyallyl bromide,[261,261a,261b] 2-bromomethyl-1,4-dibromo-2-butene,[262] epoxyalkyl halides,[255] or 1-chloro-3-iodopropene[263] (Equations (154) and (155)). A zinc-promoted Barbier-type reaction of 2-bromo-3,3,3-trifluoropropene with aldehydes was also reported (Equation (156)).[264]



(154)



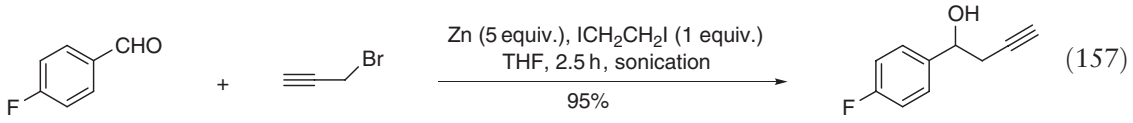
(155)



(156)

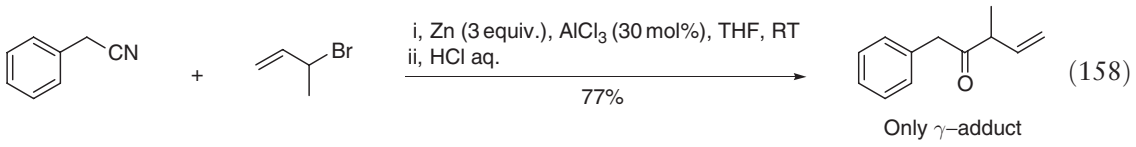
Especially noteworthy in the Barbier reaction is the tolerance of water. Many reactions could be performed in a mixture of an organic solvent and water (THF/NH_4Cl), or in a pure aqueous media (water, aqueous ammonium chloride, mixture of aqueous calcium chloride and ammonium chloride, aqueous $NaBF_4$).[253,253a–253c,263,265,266] Such an aqueous media allows to use water-soluble compounds such as carbohydrates as substrates.[253b,253c,254]

In many cases, activation of the zinc dust is necessary to reach complete conversion or to accelerate the reaction. This activation can be achieved by treatment of zinc dust with an acid chloride[267] but can be achieved also with liquid ammonia[268] or by sonoelectrochemical methods.[259,269,269a] Activation can be achieved by adding metallic salts such as $AlCl_3$, $CeCl_3$, $PbBr_2$, or CuI to the reaction mixture.[253b,257,270] Sonication proved also to enhance the reactivity of Barbier-type reaction in aqueous media (Equation (157)).[253,255,256,270,270a,271]

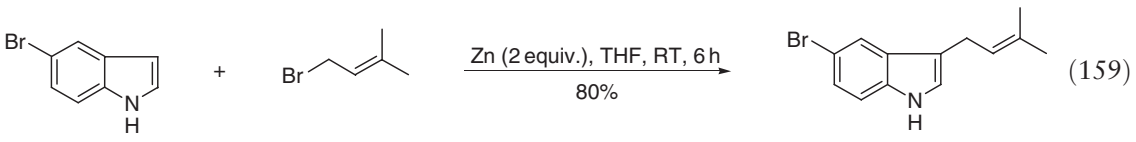


(157)

Barbier reactions can be highly regioselective: depending on the conditions of allylation, they could proceed via S_E2'- or S_E2-pathway.[256,270,272] Good diastereoselectivity can also be obtained by using a chiral electrophile (Equations (158)–(160)).[258,273–275]



(158)



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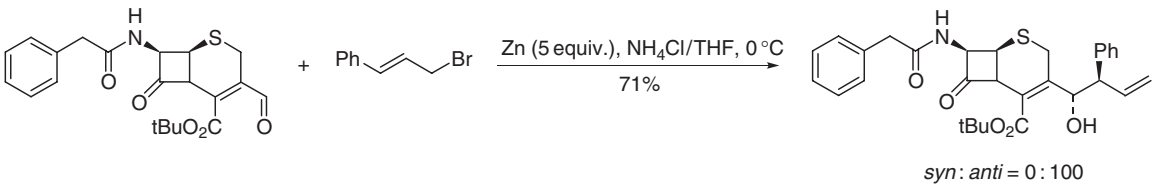


(160)

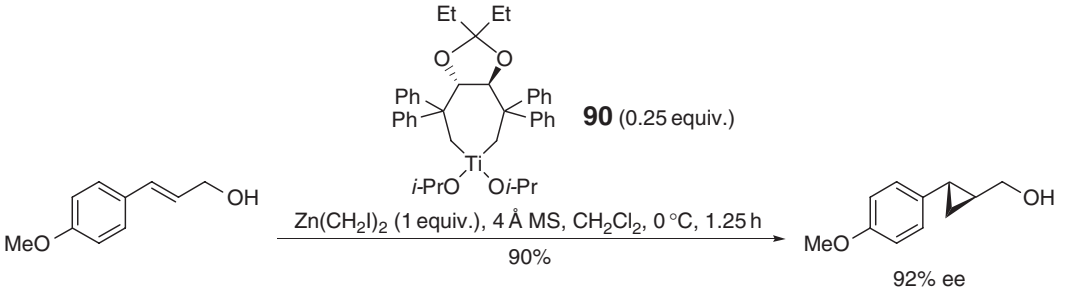
Madsen and Hyldtoft proposed a novel zinc-mediated domino reaction to give functionalized dienes.[267] Using a Barbier reaction, different approaches of interesting compounds have been reported: vitamin D3 analogs,[271] bicyclo[*n*.3.1]alk-1-enes,[276] ipsdienol and ipsenol, (±)-oxerine,[277] and silyl misoprostol.[270]

9.04.1.4 Reactivity of Zinc Carbenoids

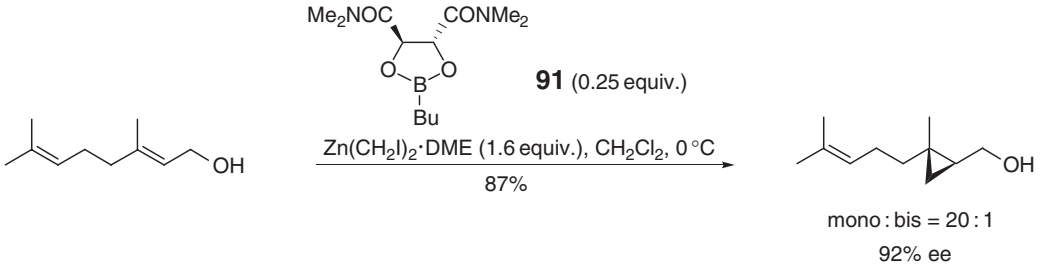
9.04.1.4.1 Cyclopropanations

The Simmons–Smith reaction is a powerful method for preparing cyclopropanes from olefins using zinc carbenoids ($IZnCH_2I$, $EtZnCH_2I$, $Zn(CH_2X)_2$).[7a,278,278a] A variety of versions of this reaction have been developed and new carbenoids species have been made. For recent reviews, see Ref: 279 and 279a.

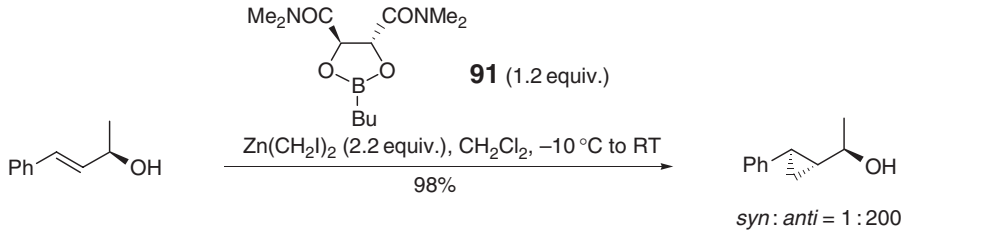
Recently, many efforts have focused on the development of the enantioselective (iodomethyl)zinc-mediated cyclopropanation of allylic alcohols. Kobayashi and co-workers reported that moderate to good enantioselectivities were observed if a C_2-symmetric chiral disulfonamide was added.[280,280a–280e] To reduce the rate of uncatalyzed process responsible for moderate enantioselectivity, Charette and Brochu studied the effect of addition of Lewis acid, and proved that $TiCl_4$ accelerates the reaction.[281] Thus, addition of the chiral titanium catalyst **90** allowed conversion of 3-aryl- and 3-heteroaryl-substituted allylic alcohols to the corresponding cyclopropane derivatives in enantiomeric ratios up to 97 : 3 (Equation (161)).[282] The dioxaborolane ligand **91** is an efficient chiral reagent for the enantioselective cyclopropanation not only of allylic alcohols but also of unconjugated and conjugated polyenes and homoallylic alcohols (Equation (162)).[283,283a,283b] Concerning chiral allylic alcohols, Charette and Lebel have shown that the nature of the zinc carbenoids is very important. Cyclopropanation using $EtZnCH_2I$ (prepared from a 1 : 1 mixture of Et_2Zn and CH_2I_2) proceeds with a high *syn*-selectivity.[284] Interestingly, when the reaction is performed with (iodomethyl)zinc in presence of the dioxaboranolane ligand **91**, *syn*-selectivities with (*Z*)-olefins were obtained when high *anti*-selectivities were observed with (*E*)-olefins (Equation (163)).[285]



(161)

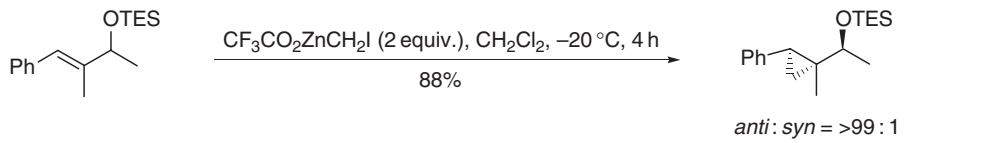


(162)

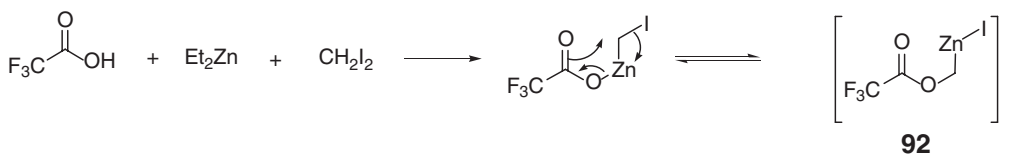


(163)

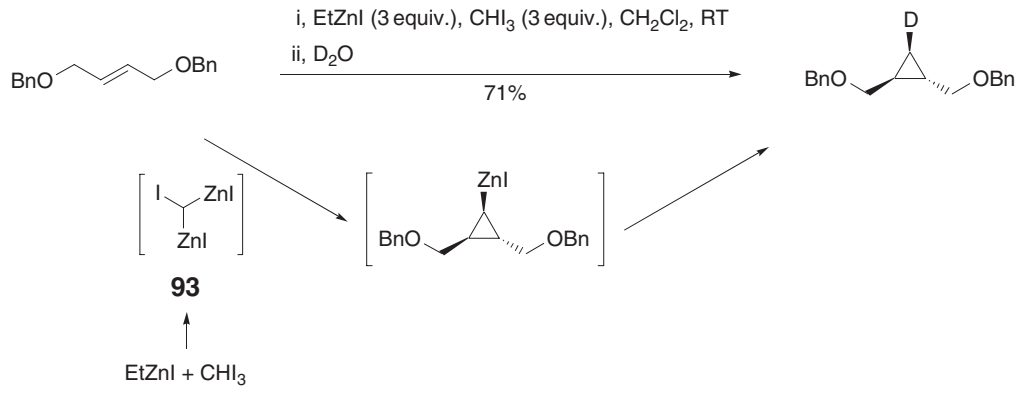
In 1998, Shi and co-workers developed a new efficient organozinc species for cyclopropanation of unfunctionalized olefins, $CF_3CO_2ZnCH_2I$, generated by reacting $Zn(CH_2I)_2$ with CF_3CO_2H.[286] This carbenoid ($CF_3CO_2ZnCH_2I$) allows to prepare *anti*-cyclopropylcarbinyl silyl ethers with good yields and excellent diastereoselectivities (Equation (164)).[287] Charette and co-workers have postulated that the increased reactivity of Shi's carbenoid might be attributed to *in situ* equilibration leading to formation of iodomethylzinc trifluoroacetate **92** under the reaction conditions (Scheme 24). Acyloxymethylzinc derivatives are also promising cyclopropanation reagents (Equation (165)).[288] Shi and co-workers showed that moderate asymmetric cyclopropanations of unfunctionalized olefins are possible by using a chiral (iodomethylzinc)species R^*OZnCH_2I.[289] Recently, a novel *gem*-dizinc carbenoid **93** provided an efficient access to 1,2,3-substituted cyclopropanes with good diastereoselectivity (Scheme 25).[290] In the presence of zinc iodide, this geminal dizinc carbenoid reacts quicker.[291]



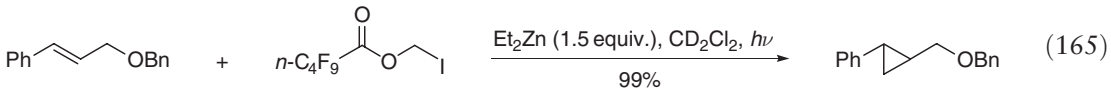
(164)



Scheme 24

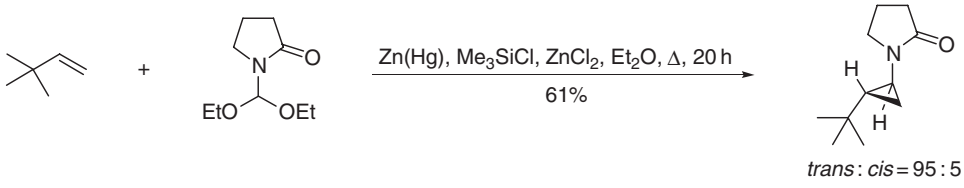


Scheme 25

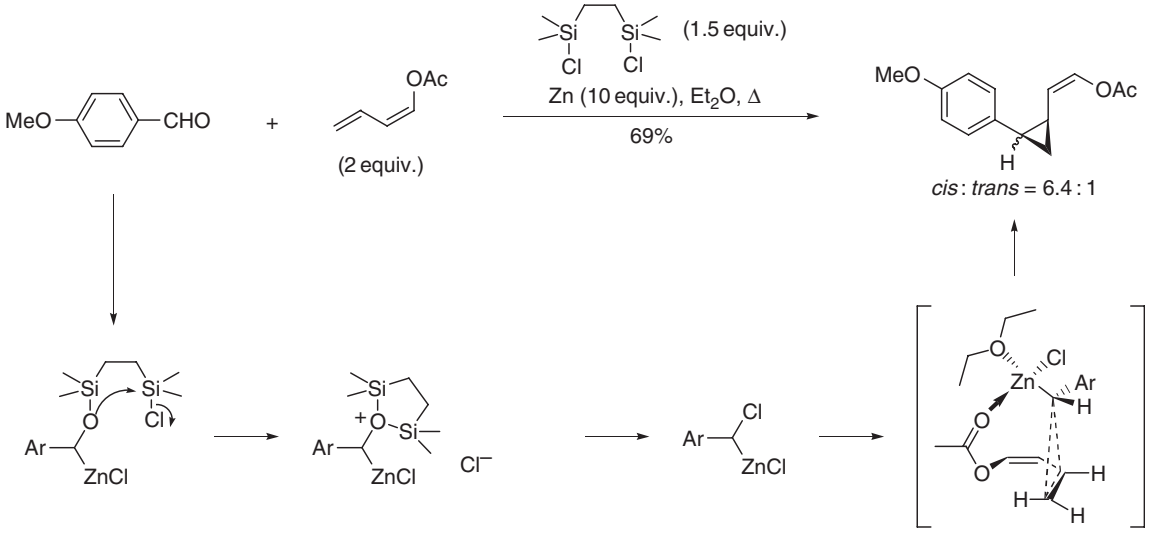


(165)

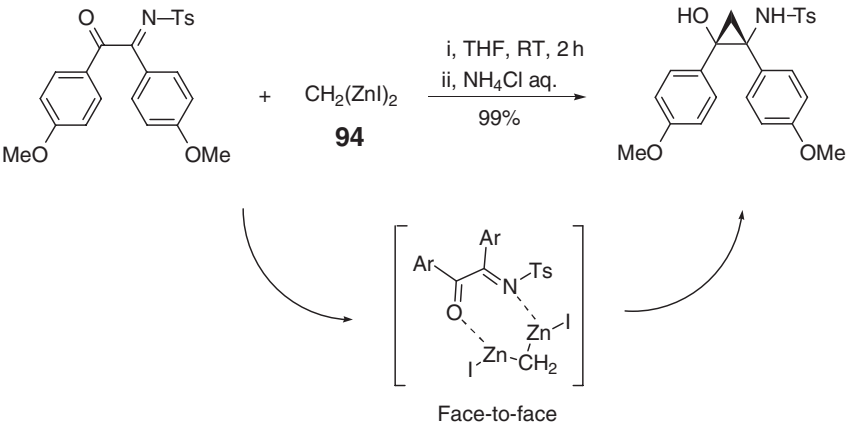
A variety of organozinc carbenoids can be generated by the reaction of carbonyl compounds with metallic zinc in the presence of silicon electrophile. They react with high regiosepecificity with (*Z*)-1-acetoxybutadiene to provide functionalized vinyl and divinyl cyclopropanes. The high *cis*-stereoselectivity can be explained by a coordination of the acetoxy group to the zinc center at the transition state (Scheme 26).[292,292a] Similarly, aryl acetals, orthoformates, and *N*-diethoxymethyl amides provide carbenoid precursors for the formation of aryl cyclopropanes, alkoxy cyclopropanes, and amido cyclopropanes (Equation (166)).[293,293a,293b]



(166)



Scheme 26



Scheme 27

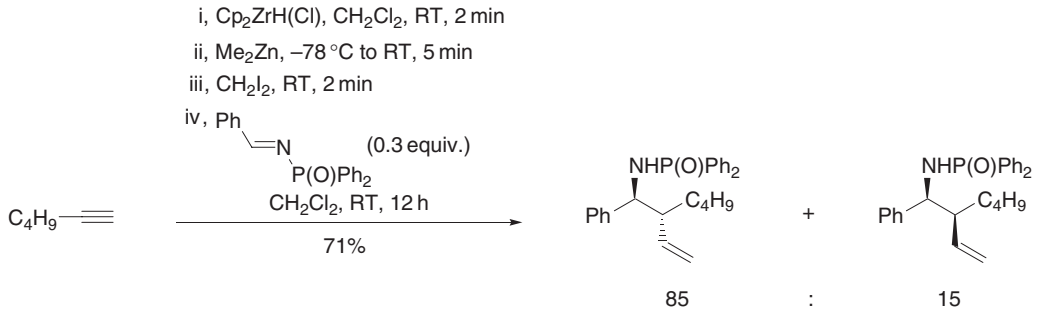
The *gem*-dizinc reagent *bis*(iodozincio)methane **94** undergoes with high diastereoselectivity a [2 + 1] cycloaddition on 1,2-diketones and α-ketoimines to give *cis*-cyclopropan-1,2-diols and *cis*-2-aminocyclopropanols. This reaction proceeds via a sequential nucleophilic attack of **94** on the two sp^2-centers through a face-to-face coordination, responsible for this high diastereoselectivity (Scheme 27).[294,294a]

9.04.1.4.2 Methylene homologation and related reactions

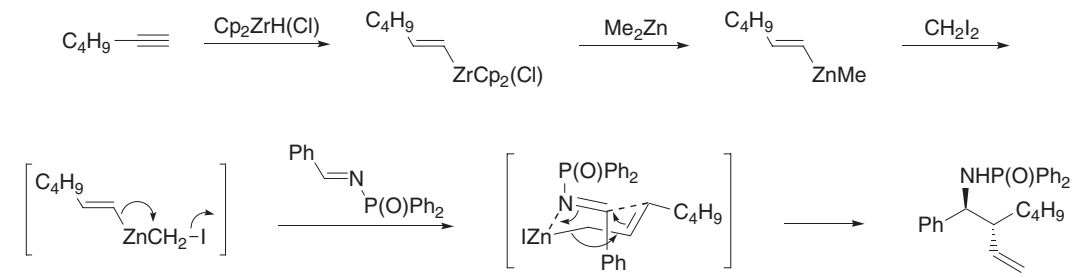
Sp^3-zinc carbenoids such as (iodomethyl)zinc iodide or bis(iodomethyl)zinc have also been used for the selective creation of carbon–carbon bonds through a methylene homologation.[295]

Synthesis of homoallylic amines has been reported by a three-component coupling of aldimines, diiodomethane, and alkenylzirconocenes, in the presence of dimethylzinc (Scheme 28).[296,296a] The formation of homoallylic products is rationalized by the mechanism shown in Scheme 29. The *anti*-relationship of the final product is explained by a cyclic chair-like transition state. This type of homologation was used to form *C,C*-dicyclopropylmethylamines by a double *C,C*-σ-bond insertion into bicyclobutanes (Scheme 30).[297] During the course of this cascade process, 10 *C,C*-bonds are formed, and the final product is isolated in one step with a high diastereoselectivity.

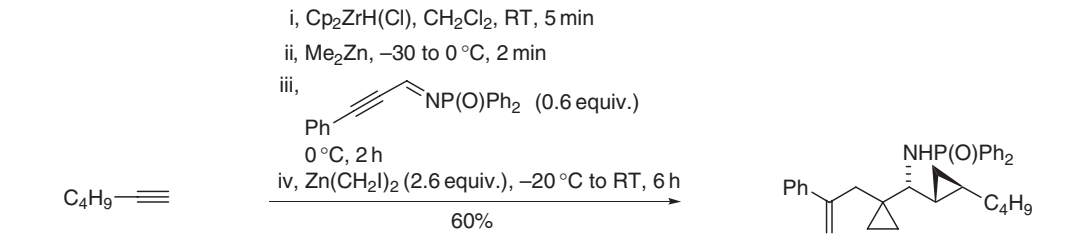
By applying a carbocupration, zinc carbenoid homologation on alkynyl sulfoxides, allylzinc derivatives such as **95** are formed. A *syn*-β-elimination reaction occurs and leads to polysubstitued allenes (Scheme 31).[298] This strategy of homologation–β-elimination allows also the formation of 1,1,3-trisubstituted propadienes, if the homologation reaction is performed with a secondary zinc carbenoid (Scheme 32). As soon as the secondary zinc carbenoid is formed in the reaction mixture, it reacts with the vinylcopper and generates an allylzinc derivative. This reaction sequence allows to prepare also chiral allenes through a thermodynamic equilibration of the secondary organometallic derivative (Scheme 33).[299] An intramolecular chelation between the zinc organometallic compound and the oxygen of the sulfoxide explains the preferential *anti*-relationship between the tolyl and the alkyl group.



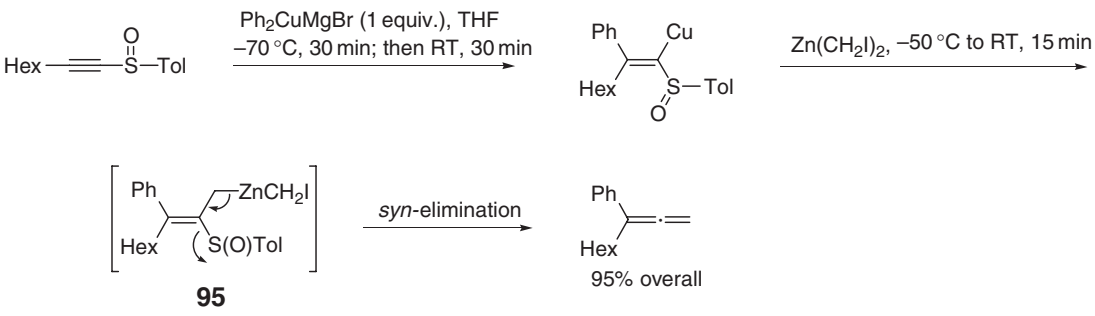
Scheme 28



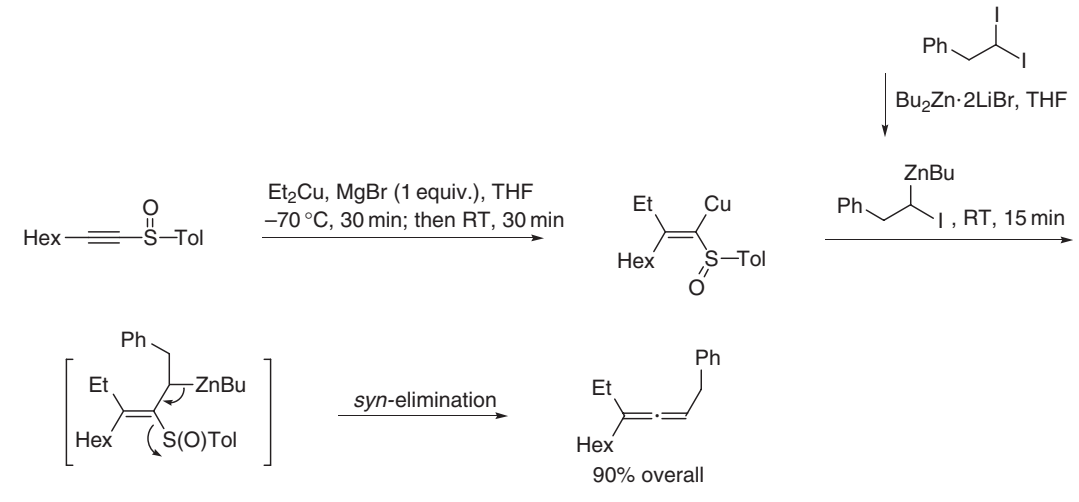
Scheme 29



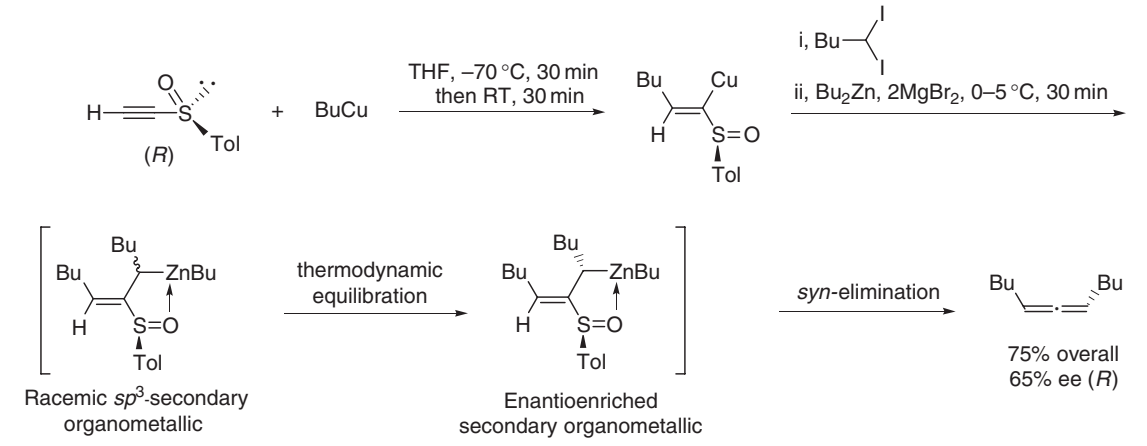
Scheme 30



Scheme 31

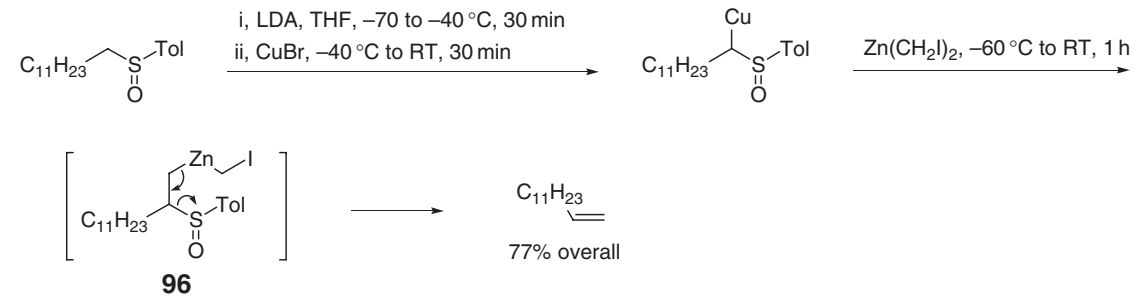


Scheme 32

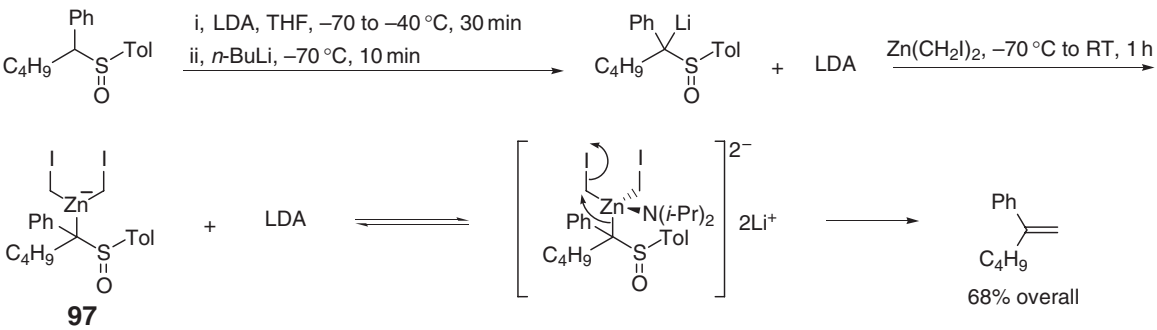


Scheme 33

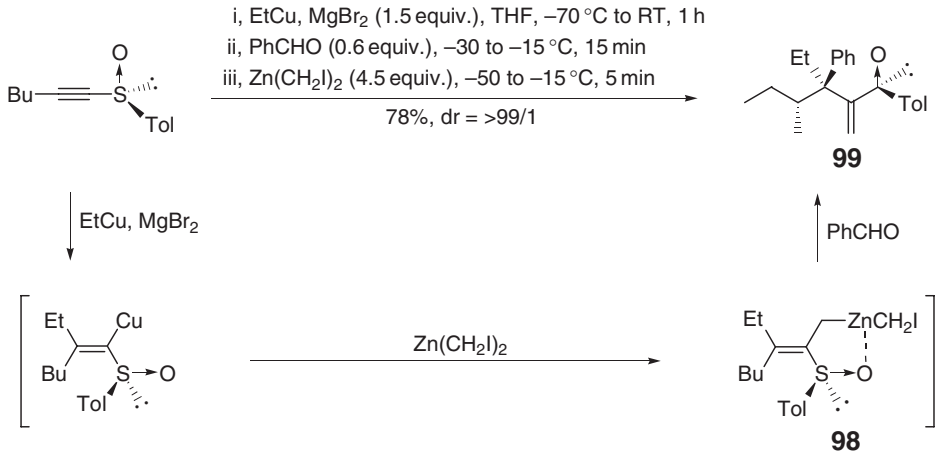
This tandem zinc homologation–β-elimination reaction is a new source of olefins.[300] Transmetallation of secondary α-lithiosulfinyl carbanions with CuBr leads to α-sulfinyl organocopper derivatives, which react intermolecularly in an S_N2-type process with zinc carbenoids to form organozinc compounds **96**. After a β-elimination reaction process, monosubstituted olefins are obtained in good overall yields (Scheme 34). Unfortunately, this olefination reaction from tertiary α-sulfinyl carbanion does not proceed in satisfactory yield. Indeed, the intermediately formed organocopper is thermally unstable and no homologated product is obtained. In this case, it is necessary to form a higher-order zincate **97**, which reacts under an intramolecular 1,2-metallate rearrangement to form α,α-disubstitued olefins in good yields (Scheme 35).



Scheme 34



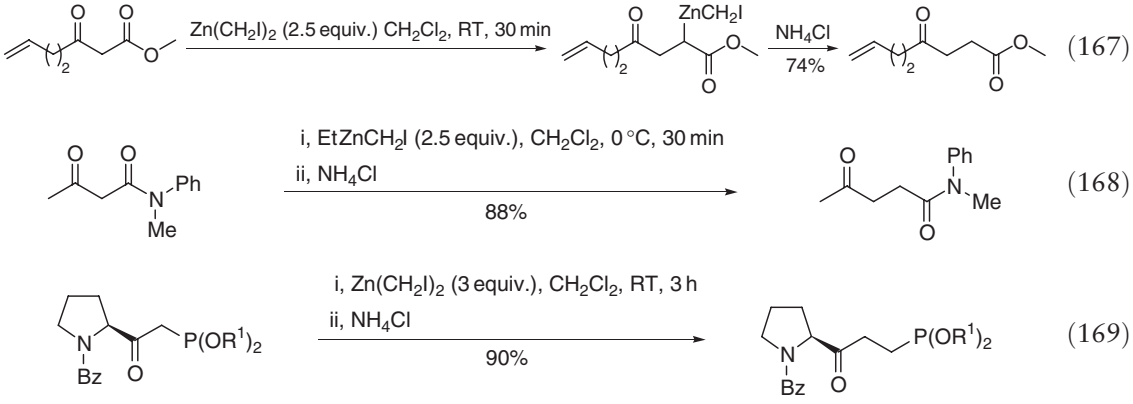
Scheme 35



Scheme 36

Chiral homoallylic alcohols and amines were prepared by using a four-component condensation reaction based on a zinc homologation followed by a trapping with an aldehyde or an imine.[301] A regio- and stereospecific carbocupration reaction on alkynyl sulfoxide provides the corresponding metallated β,β-dialkylated α,β-ethylenic sufoxide **98**. Addition of aldehydes or imines, followed by addition of the bis(iodomethyl)zinc carbenoid, provides adducts **99** in good overall yield and with very high diastereoselectivity (Scheme 36).

Zinc organometallic derivatives bearing a carbonyl function at the β-position (homoenolates) can be obtained by the homologation reaction of lithium enolates with bis(iodomethyl)zinc. This zinc derivative can then be hydrolyzed to provide the corresponding ketones or trapped by an electrophile. This homologation was applied to β-keto esters, phosphonates, and amides, and provides after hydrolysis access to a wide range of γ-keto esters, amides, and phosphonates (Equations (167)–(169)).[302,302a,302b] This reaction is remarkably efficient since either electron-rich or electron-poor keto-olefins undergo selective chain extension of the alkene in preference to cyclopropanation. Similarly, a tandem chain -extension–aldol reaction was developed on β-keto esters for allowing the diastereoselective formation of α-substituted β-keto esters (Scheme 37).[303]

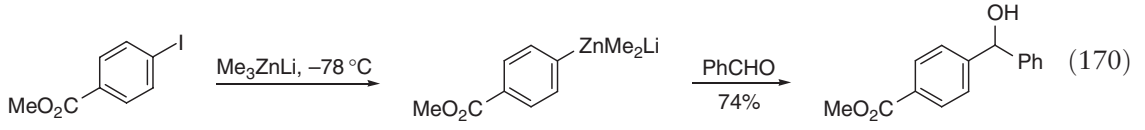


Scheme 37

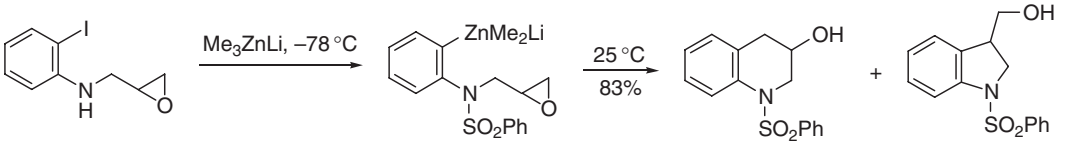
9.04.1.5 Preparation and Reaction of Zincates

Lithium triorganozincates are best prepared by the reaction of an alkyllithium (3 equiv.) with zinc chloride or by the addition of an alkyllithium to a dialkylzinc in an ethereal solvent.[304,304a–304d] Lithium and magnesium trialkylzincates are more reactive compared to dialkylzincs or alkylzinc halides due to the excess of negative charge at the metallic zinc center, which confers a higher nucleophilicity to the organic substituents.

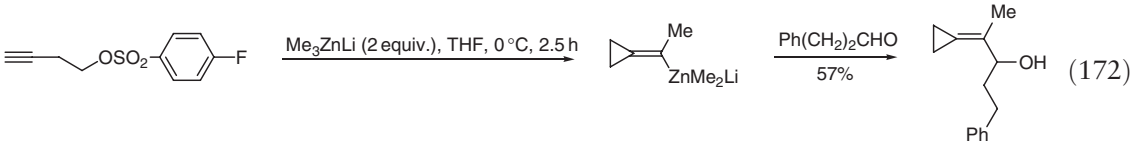
Functionalized lithium triorganozincates can be prepared via an I/Zn exchange reaction. The exchange is highly chemoselective and tolerates sensitive functional groups, such as ester or epoxide. Reaction of aryl iodides with Me_3ZnLi provides functionalized lithium zincates, which may undergo addition to aldehydes (Equation (170)) or addition to epoxides, which can provide ring closure (Equation (171)).[305,305a] Cyclopropylidene alkylzincate can be obtained by the reaction of an alkyne γ-sulfonate with Me_3ZnLi. Its reaction with an aldehyde provides the allylic alcohol (Equation (172)).[304d]



(170)

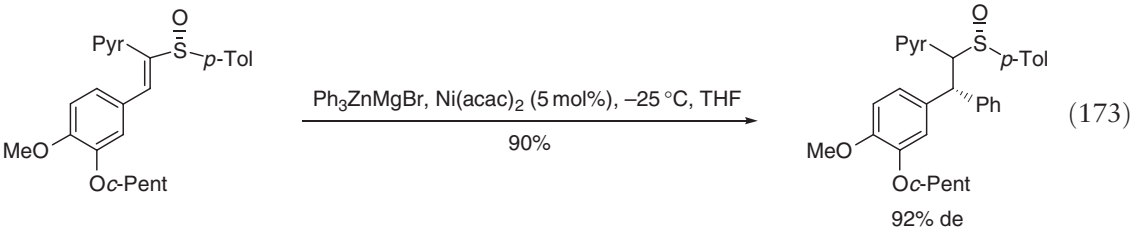


(171)

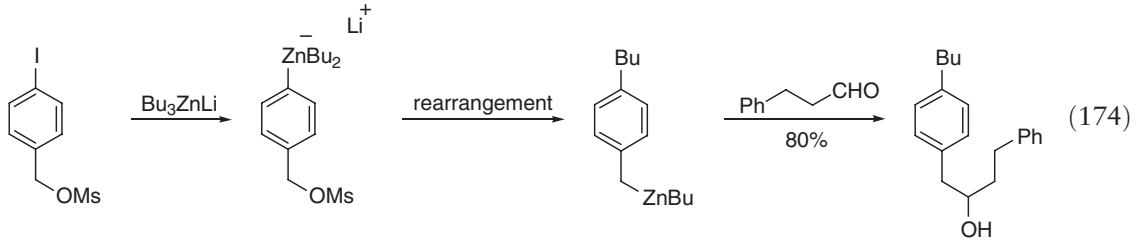


(172)

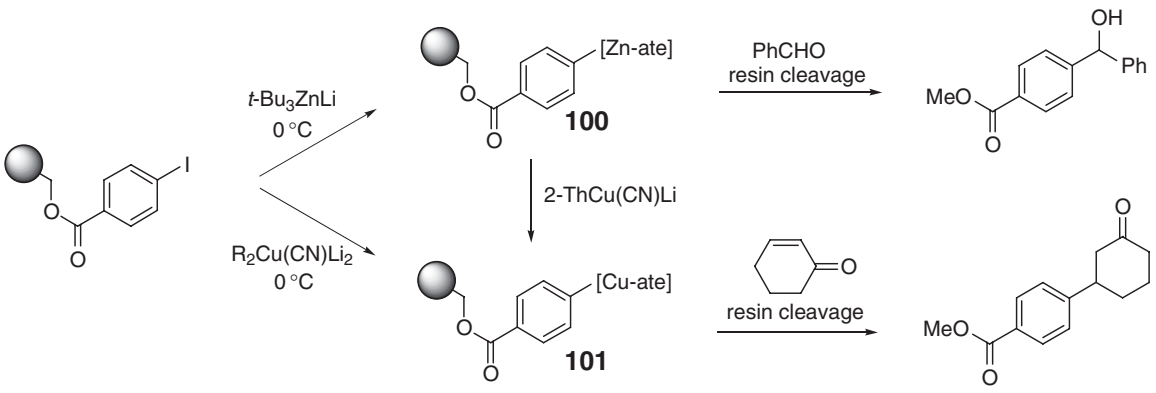
Interestingly, lithium and magnesium triarylzincates add to α,β-unsaturated sulfoxides in the presence of catalytic amounts of $Ni(acac)_2$ with good diastereoselectivity (Equation (173)).[306] Immobilized zincates such as **100** can be prepared by treating serine-bound 4-iodobenzoate with $t\text{-}Bu_3ZnLi$.[307,307a] They react readily with aldehydes. Transmetallation of this zincate species with lithium (2-thienyl)cyanocuprate provides the copper species **101**, which undergoes 1,4-additions (Scheme 38). Lithium trialkylzincates can be used for the preparation of benzylic zinc reagents using the approach of Harada and co-workers (Equation (174)).[308]



(173)



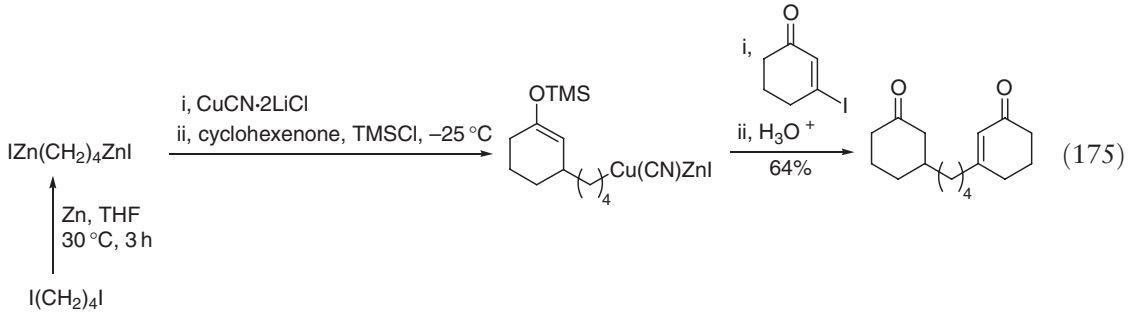
(174)



Scheme 38

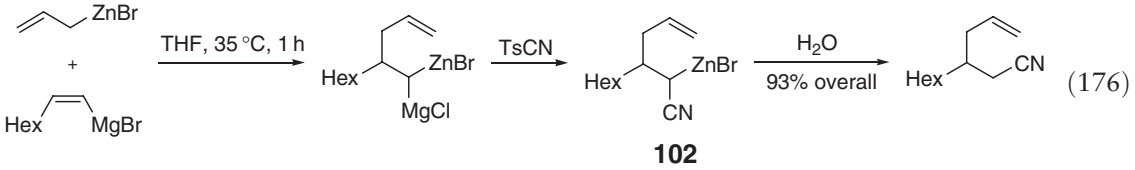
9.04.1.6 Preparation and Reactivity of Bimetallic Reagents of Zinc

The reaction of 1,4-bis-zinc derivatives with CuCN·2LiCl allows the preparation of a range of new polyfunctional zinc–copper reagents.[309] They undergo selectively 1,4-additions on α,β-ethylenic ketones in the presence of TMSCl providing a new zinc–copper reagent, which can react with another electrophile (Equation (175)).[309]



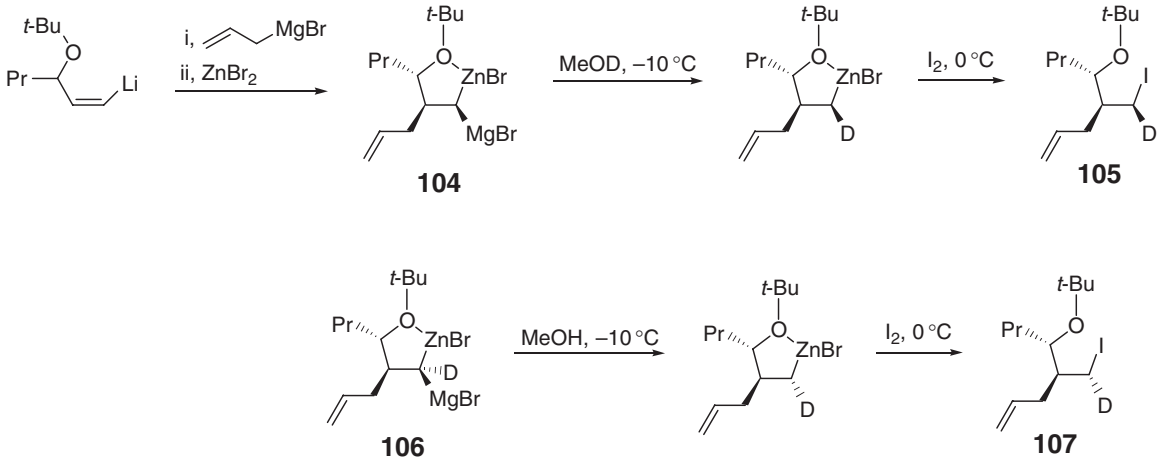
(175)

The allylzincation of alkenylmagnesium reagents is a very convenient synthesis of 1,1-bimetallic reagents of magnesium and zinc.[157,157a,310,310a–310h] The reaction of such a bimetallic species with tosyl cyanide produces the organozinc compound **102**, which after hydrolysis leads to nitrile derivatives (Equation (176)).[157,157a–157d,311] The importance of chelating for the configurational stability of organozinc reagents has recently been demonstrated by Knochel, Normant, and Marek. Thus, the addition of ethoxy-substituted allylic zinc reagents to an alkenylmagnesium reagent provides after addition of Me_3SnCl the α-stannylated alkylzinc species **103** with very good stereoselectivity. This derivative is readily oxidized with O_2 leading to the corresponding aldehyde with an excellent transfer of the stereochemistry (Equation (177)).[312] Starting from 1,1-bimetallic reagents of magnesium and zinc of type **104**, it is possible to perform a selective deuterolysis of the reactive carbon–magnesium bond followed by iodolysis leading to the product **105** as a 60 : 40 mixture of stereoisomers. Starting with α-deuterated bimetallic compound **106** and performing a protonation with MeOH followed by iodolysis furnishes the primary alkyl iodide **107** as a 34 : 66 mixture of diastereoisomers, showing that some open-chain primary organozinc halides can retain their configuration (Scheme 39).[313]

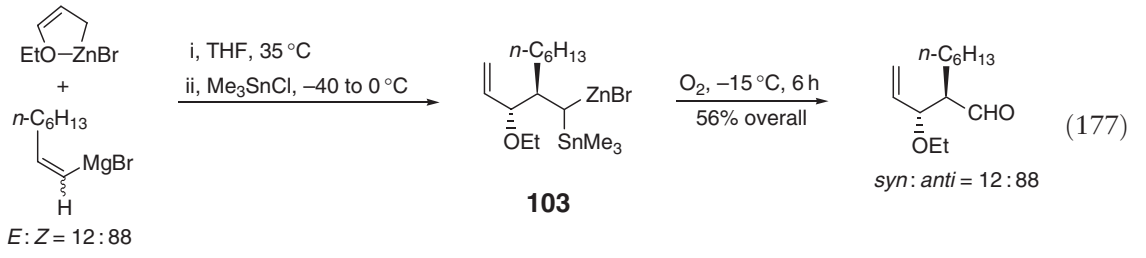


(176)

102



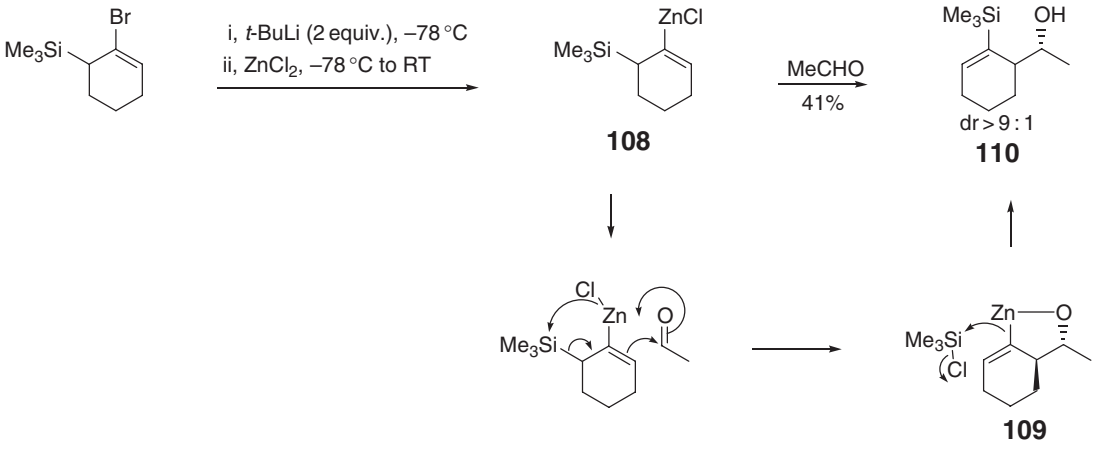
Scheme 39



The mixed 1,2-bimetallic Zn/Si reagent **108** is a versatile species, which reacts with aldehydes in high diastereoselectivity (Scheme 40).[314] It is prepared by a bromine/lithium exchange reaction, followed by a transmetallation with $ZnCl_2$. The reaction with acetaldehyde leads initially to the alkenylzinc species **109**, which reacts with Me_3SiCl providing the alkenylsilane **110** in 41% yield and with a diastereoselectivity >9 : 1.

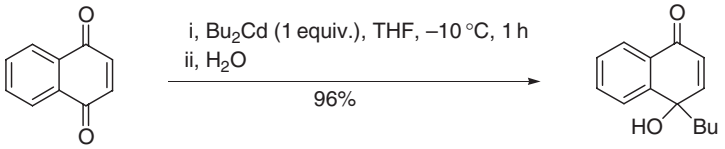
9.04.2 Cadmium Reagents in Organic Synthesis

Alkylation of quinones with organocadmium reagents allows the synthesis of quinol derivatives, without any formation of hydroquinones or bis-addition products (Equation (178)).[315] The regiochemistry of the addition is strongly

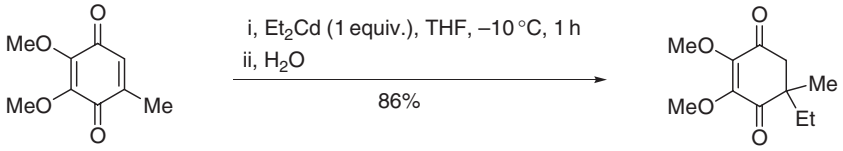


Scheme 40

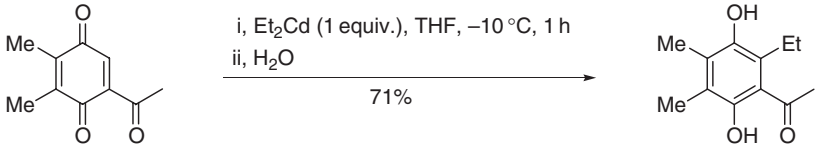
affected by both steric and electronic effects of the substituents. Depending on the quinone, 1,2-addition or 1,4-addition may occur leading to either quinol or hexen-1,4-dione (Equation (179))[316] In the case of acetyl quinones, the selective 1,2-addition of diethylcadmium is explained by the electron-withdrawing effect of the acetyl group at C-5, which increases the electrophilicity of C-6 (Equation (180)).



(178)

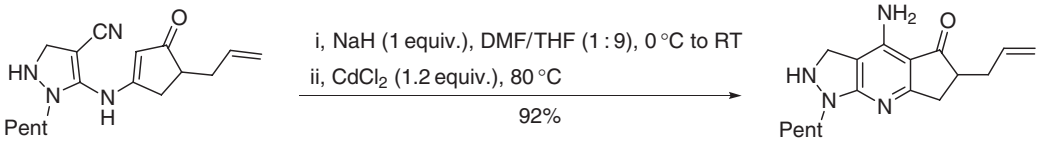


(179)



(180)

Cadmium salts and organocadmium reagents also have found applications in cyclization reaction. Cadmium-mediated cyclization of enaminone occurs under mild conditions, whether in presence of a base and a cadmium(II) salt (60 to 90 °C), or in the presence of dibutylcadmium at room temperature (Equation (181)).[317]



(181)

References

1. Frankland, E. *Liebigs Ann. Chem.* **1849**, *71*, 171.
1a. Frankland, E. *Liebigs Ann. Chem.* **1849**, *71*, 213.
2. Nützel, K. In *Houben-Weyl, Methoden der Organischen Chemie, Metallorganische Verbindungen Be, Mg, Ca, Sr, Ba, Zn, Cd*; Müller, E. Ed.; Georg Thieme Verlag: Stuttgart, 1973; Vol. 13/2a, pp 552.
3. Reformatsky. *Chem. Ber.* **1887**, *20*, 1210.
3a. Reformatsky. *Chem. Ber.* **1887**, *28*, 2842.
4. Fürstner, A. *Synthesis* **1989**, 571.
5. Fürstner, A. *Angew. Chem., Int. Ed.* **1993**, *32*, 164.
6. Shriner, R. L. *Org. React.* **1942**, *1*, 1.
7. Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323.
7a. Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1959**, *81*, 4256.
8. Blanchard, E. P.; Simmons, H. E. *J. Am. Chem. Soc.* **1964**, *86*, 1337.
8a. Blanchard, E. P.; Simmons, H. E. *J. Am. Chem. Soc.* **1964**, *86*, 1347.
9. Simmons, H. E.; Cairns, T. L.; Vladuchick, A.; Hoiness, C. M. *Org. React.* **1972**, *20*, 1.
10. Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron Lett.* **1966**, 3353.
11. Furukawa, J.; Kawabata, N. *Adv. Organomet. Chem.* **1974**, *12*, 83.
12. Sawada, S.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 2669.
13. Negishi, E. *Organometallics in Organic Synthesis*, Wiley: New York; Vol. 1; 1980.
14. Negishi, E.; Valente, L. F.; Kobayashi, M. *J. Am. Chem. Soc.* **1980**, *102*, 3298.
15. Erdik, E. *Tetrahedron* **1992**, *48*, 9577.
16. Kobayashi, M.; Negishi, E. *J. Org. Chem.* **1980**, *45*, 5223.
17. Negishi, E. *Acc. Res.* **1982**, *15*, 340.
18. Negishi, E.; Bagheri, V.; Chatterjee, S.; Luo, F.-T.; Miller, J. A.; Stoll, A. T. *Tetrahedron Lett.* **1983**, *24*, 5181.
19. Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117.
19a. Knochel, P. *Synlett* **1995**, 393.

19b. Knochel, P.; Vettel, S.; Eisenberg, C. *Appl. Organomet. Chem.* **1995**, *9*, 175.
19c. Knochel, P.; Langer, F.; Rottländer, M.; Stüdemann, T. *Chem. Ber.* **1997**, *130*, 387.
19d. Knochel, P.; Almena, J.; Jones, P. *Tetrahedron* **1998**, *54*, 8275.
19e. Knochel, P.; Jones, P. *Organozinc Reagents. A Practical Approach*; Oxford University Press: New York, **1999**.
20. Duddu, R.; Eckhardt, M.; Furlong, M.; Knoess, H. P.; Berger, S.; Knochel, P. *Tetrahedron* **1994**, *50*, 2415.
21. Knochel, P.; Rao, C. J. *Tetrahedron* **1993**, *49*, 29.
22. Stevenson, T. M.; Prasad, B.; Citineni, J. R.; Knochel, P. *Tetrahedron Lett.* **1996**, *37*, 8375.
22a. Prasad, A. S. B.; Stevenson, T. M.; Citineni, J. R.; Nyzam, V.; Knochel, P. *Tetrahedron* **1997**, *53*, 7237.
23. Dow, R. L.; Bechle, B. M. *Synlett* **1994**, 293.
24. Knochel, P.; Millot, N.; Rodriguez, A. L.; Tucker, C. E. *Org. React.* **2001**, *58*, 417.
24a. Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4415.
25. Fürstner, A.; Singer, R.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 1047.
25a. Stadtmüller, H.; Greve, B.; Lennick, K.; Chair, A.; Knochel, P. *Synthesis* **1995**, 69.
26. Rieke, R. D. *Science* **1989**, *246*, 1260.
26a. Rieke, R. D.; Kim, S.-H.; Wu, X. *J. Org. Chem.* **1997**, *62*, 6921.
26b. Zhu, L.; Rieke, R. D. *Tetrahedron Lett.* **1991**, *32*, 2865.
26c. Rieke, R. D.; Sell, M. S.; Xiong, H. *J. Am. Chem. Soc.* **1995**, *117*, 5429.
26d. Rieke, R. D.; Hudnall, P. M.; Uhm, S. T. *J. Chem. Soc., Chem. Commun.* **1973**, 269.
26e. Rieke, R. D.; Li, P. T.-J.; Burns, T. P.; Uhm, S. T. *J. Org. Chem.* **1981**, *46*, 4323.
26f. Rieke, R. D.; Uhm, S. T. *Synthesis* **1975**, 452.
26g. Hanson, M. V.; Brown, J. D.; Rieke, R. D. *Tetrahedron Lett.* **1994**, *35*, 7205.
26h. Hanson, M. V.; Rieke, R. D. *Synth. Commun.* **1995**, *25*, 101.
26i. Rieke, R. D.; Hanson, M. V.; Brown, J. D. *J. Org. Chem.* **1996**, *61*, 2726.
26j. Guijarro, A.; Rieke, R. D. *Angew. Chem., Int. Ed.* **1998**, *37*, 1679.
27. Hanson, M. V.; Rieke, R. D. *J. Am. Chem. Soc.* **1995**, *117*, 10775.
27a. Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, *56*, 1445.
28. Lipshutz, B. H.; Wood, M. R. *J. Am. Chem. Soc.* **1994**, *116*, 11689.
28a. Lipshutz, B. H.; Wood, M. R. *J. Am. Chem. Soc.* **1993**, *115*, 12625.
29. Sibille, S.; Ratovelomanana, V.; Nedelec, J. Y.; Périchon, J. *Synlett* **1993**, *6*, 425.
29a. Chaussard, J.; Folest, J. C.; Nedelec, J. Y.; Périchon, J.; Sibille, S.; Troupel, M. *Synthesis* **1990**, 369.
29b. Durandetti, M.; Devaud, M.; Périchon, J. *New J. Chem.* **1996**, *20*, 659.
29c. Sibille, S.; Ratovelomanana, V.; Nédélec, J.-Y.; Périchon, J. *Synlett* **1993**, 425.
29d. Gosmini, C.; Nédélec, J.-Y.; Périchon, J. *Tetrahedron Lett.* **1997**, *38*, 1941.
29e. Zylber, N.; Zylber, J.; Rollin, Y.; Dunach, E.; Périchon, J. *J. Organomet. Chem.* **1993**, *444*, 1.
29f. Rollin, Y.; Derien, S.; Dunach, E.; Gébéhenne, C.; Périchon, J. *Tetrahedron* **1993**, *49*, 7723.
30. Gomes, P.; Gosmini, C.; Périchon, J. *Synlett* **2002**, 1673.
30a. Gomes, P.; Fillon, H.; Gosmini, C.; Labbé, E.; Périchon, J. *Tetrahedron* **2002**, *58*, 8417.
30b. Fillon, H.; Le Gall, E.; Gosmini, C.; Périchon, J. *Tetrahedron Lett.* **2002**, *43*, 5941.
30c. Gosmini, C.; Rollin, Y.; Nédélec, J.-Y.; Périchon, J. *J. Org. Chem.* **2000**, *65*, 6024.
31. Seka, S.; Buriez, O.; Nédélec, J.-Y.; Périchon, J. *Chem. Eur. J.* **2002**, *8*, 2534.
32. Mellah, M.; Labbé, E.; Nédélec, J.-Y.; Périchon, J. *New. J. Chem.* **2001**, *25*, 318.
32a. Gosmini, C.; Nédélec, J.-Y.; Périchon, J. *Tetrahedron Lett.* **2000**, *41*, 201.
33. Ito, T.; Ishino, Y.; Mizuno, T.; Ishikawa, A.; Kobayashi, J. *Synlett* **2002**, 2116.
34. Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1984**, *25*, 4383.
34a. Peters, D.; Miethchen, R. *J. Prakt. Chem.* **1995**, *337*, 615.
34b. Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186.
34c. Tso, H.; Chou, T.; Lai, Y. *J. Org. Chem.* **1989**, *54*, 4138.
34d. Sestelo, J. P.; Mascarenas, J. L.; Castedo, L.; Mourino, A. *J. Org. Chem.* **1993**, *58*, 118.
34e. Sarandeses, L. A.; Mourino, A.; Luche, J. L. *J. Chem. Soc., Chem. Commun.* **1992**, 798.
35. Dunn, M. J.; Jackson, R. F. W.; Pietruszka, J.; Wishart, N.; Ellis, D.; Wythes, M. J. *Synlett* **1993**, 499.
35a. Jackson, R. F. W.; Wishart, N.; Wythes, M. J. *Synlett* **1993**, 219.
35b. Dunn, M. J.; Jackson, R. F. W.; Pietruszka, J.; Turner, D. *J. Org. Chem.* **1995**, *60*, 2210.
35c. Malan, C.; Morin, C. *Synlett* **1996**, 167.
35d. Jackson, R. F. W.; Wythes, M. J.; Wood, A. *Tetrahedron Lett.* **1989**, *30*, 5941.
35e. Jackson, R. F. W.; Wood, A.; Wythes, M. J. *Synlett* **1990**, 735.
35f. Dunn, M. J.; Jackson, R. F. W. *J. Chem. Soc., Chem. Commun.* **1992**, 319.
35g. Jackson, R. F. W.; Wishart, N.; Wood, A.; James, K.; Wythes, M. J. *J. Org. Chem.* **1992**, *57*, 3397.
35h. Dexter, C. S.; Jackson, R. F. W. *J. Chem. Soc., Chem. Commun.* **1998**, 75.
35i. Fraser, J. L.; Jackson, R. F. W.; Porter, B. *Synlett* **1994**, 379.
35j. Jackson, R. F. W.; Neil, W.; Wythes, M. J. *J. Chem. Soc., Chem. Commun.* **1992**, 1587.
36. Jackson, R. F. W.; Rilatt, I.; Murray, P. J. *Chem. Commun.* **2003**, 1242.
37. Jackson, R. F. W.; Rilatt, I.; Murray, P. J. *Org. Biomol. Chem.* **2004**, *2*, 110.
38. Hunter, C.; Jackson, R. F. W.; Rami, H. K. *J. Chem. Soc., Perkin Trans. 1* **2001**, *1*, 1349.
39. Huo, S. *Org. Lett.* **2003**, *5*, 423.
40. Lipshutz, B. H.; Blomgren, P. A.; Kim, S. K. *Tetrahedron Lett.* **1999**, *40*, 197.
40a. Lipshutz, B. H.; Blomgren, P. A. *J. Am. Chem. Soc.* **1999**, *121*, 5819.
40b. Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719.
41. Duddu, R.; Eckhardt, M.; Furlong, M.; Knoess, H. P.; Berger, S.; Knochel, P. *Tetrahedron* **1994**, *50*, 2415.
42. Sakurai, M.; Hata, T.; Yabe, Y. *Tetrahedron Lett.* **1993**, *34*, 5939.
42a. Sakami, S.; Houkawa, T.; Asaoka, A.; Takei, H. *J. Chem. Soc., Perkin Trans 1* **1995**, 285.

42b. Houkawa, T.; Ueda, T.; Sakami, S.; Asaoka, M.; Takei, H. *Tetrahedron Lett.* **1996**, *37*, 1045.
43. Darcel, C.; Flachsmann, F.; Knochel, P. *Chem. Commun.* **1998**, 205.
44. Berk, S. C.; Yeh, M. C. P.; Jeong, N.; Knochel, P. *Organometallics* **1990**, *9*, 3053.
45. Fillon, H.; Gosmini, C.; Périchon, J. *J. Am. Chem. Soc.* **2003**, *125*, 3867.
45a. Gomes, P.; Gosmini, C.; Périchon, J. *Synthesis* **2003**, 1909.
45b. Kazmierski, I.; Bastienne, M.; Gosmini, C.; Paris, J.-M.; Périchon, J. *J. Org. Chem.* **2004**, *69*, 936.
45c. Kazmierski, I.; Gosmini, C.; Paris, J. M.; Périchon, J. *Tetrahedron Lett.* **2003**, *44*, 6417.
45d. Seka, S.; Buriez, O.; Périchon, J. *Chem. Eur. J.* **2003**, *9*, 3597.
46. Majid, T. N.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 4413.
46a. Prasad, A. S. B.; Knochel, P. *Tetrahedron* **1997**, *53*, 16711.
46b. Berk, S. C.; Knochel, P.; Yeh, M. C. P. *J. Org. Chem.* **1988**, *53*, 5789.
46c. van der Baan, J. J.; Stichter, H.; Out, G. J. J.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron Lett.* **1988**, *29*, 3579.
46d. van der Louw, J.; van der Baan, J. L.; Stichter, H.; Out, G. J. J.; de Kanter, F. J. J.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron* **1992**, *48*, 9877.
46e. van der Louw, J.; van der Baan, J. L.; Out, G. J. J.; de Kanter, F. J. J.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron* **1992**, *48*, 9901.
46f. van der Heide, T. A.; van der Baan, J. L.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron Lett.* **1992**, *33*, 475.
46g. Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1986**, *108*, 4683.
47. Tucker, C. E.; Rao, S. A.; Knochel, P. *J. Org. Chem.* **1990**, *55*, 5446.
47a. Knochel, P.; Chou, T. S.; Chen, H. G.; Yeh, M. C. P.; Rozema, M. J. *J. Org. Chem.* **1989**, *54*, 5202.
47b. Chou, T. S; Knochel, P. *J. Org. Chem.* **1990**, *55*, 4791.
47c. Knochel, P; Chou, T. S.; Jubert, C; Rajagopal, D. *J. Org. Chem.* **1993**, *58*, 588.
48. Yeh, M. C. P.; Knochel, P.; Butler, W. M.; Berk, S. C. *Tetrahedron Lett.* **1988**, *29*, 6693.
48a. Chen, H. G.; Gage, J. L.; Barrett, S. D.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 1829.
48b. Yeh, M. C. P.; Knochel, P.; Santa, L. E. *Tetrahedron Lett.* **1988**, *29*, 3887.
48c. Yeh, M. C. P.; Knochel, P. *Tetrahedron Lett.* **1989**, *30*, 4799.
48d. Retherford, C.; Yeh, M. C. P.; Schipor, I.; Chen, H. G.; Knochel, P. *J. Org. Chem.* **1989**, *54*, 5200.
49. Yeh, M. C. P.; Chuang, C.-N. *J. Chem. Soc., Chem. Commun.* **1994**, 703.
50. Chen, H. G.; Hoechstetter, C.; Knochel, P. *Tetrahedron Lett.* **1989**, *30*, 4795.
51. Yeh, M. C. P.; Chen, H. G.; Knochel, P. *Org. Synth.* **1991**, *70*, 195.
52. Rao, S. A.; Tucker, C. E.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 7575.
52a. Rao, S. A.; Chou, T. S.; Schipor, I.; Knochel, P. *Tetrahedron* **1992**, *48*, 2025.
53. Knochel, P. *J. Am. Chem. Soc.* **1990**, *112*, 7431.
53a. Kanai, G.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1993**, 845.
53b. Watanabe, T.; Miyaura, N.; Suzuki, A. *J. Organomet. Chem.* **1993**, *444*, C1.
53c. Watanabe, T.; Sakai, M.; Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1994**, 467.
54. Rao, C. J.; Knochel, P. *J. Org. Chem.* **1991**, *56*, 4593.
54a. Knochel, P.; Rao, C. J. *Tetrahedron* **1993**, *49*, 29.
54b. Bronk, B. S.; Lippard, S. J.; Danheiser, R. L. *Organometallics* **1993**, *12*, 3340.
55. Retherford, C.; Chou, T. S.; Schelkun, R. M.; Knochel, P. *Tetrahedron Lett.* **1990**, *31*, 1833.
56. Stadtmüller, H.; Lentz, R.; Tucker, C. E.; Stüdemann, T.; Dörner, W.; Knochel, P. *J. Am. Chem. Soc.* **1993**, *115*, 7027.
56a. Stadtmüller, H.; Vaupel, A.; Tucker, C. E.; Stüdemann, T.; Knochel, P. *Chem. Eur. J.* **1996**, *2*, 1204.
56b. Vaupel, A.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 5743.
57. Vettel, S.; Vaupel, A.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 7473.
58. Stadtmüller, H.; Tucker, C. E.; Vaupel, A.; Knochel, P. *Tetrahedron Lett.* **1993**, *34*, 7911.
58a. Vaupel, A.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 8349.
59. Agrios, K. A.; Srebnik, M. *J. Org. Chem.* **1993**, *58*, 6908.
60. Klement, I.; Knochel, P.; Chau, K.; Cahiez, G. *Tetrahedron Lett.* **1994**, *35*, 1177.
60a. Riguet, E.; Klement, I.; Reddy, C. K.; Cahiez, G.; Knochel, P. *Tetrahedron Lett.* **1996**, *37*, 5865.
61. Charette, A. B.; Beauchemin, A.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1998**, *120*, 5114.
62. Hupe, E.; Calaza, M. I.; Knochel, P. *J. Organomet. Chem.* **2003**, *680*, 136.
63. Micouin, L.; Knochel, P. *Synlett* **1997**, 327.
64. Kneisel, F. F.; Dochnahl, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 1017.
65. Berger, S.; Langer, F.; Lutz, C.; Knochel, P.; Mobley, T. A.; Reddy, C. K. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1496.
66. Jones, P.; Reddy, C. K.; Knochel, P. *Tetrahedron* **1998**, *54*, 1471.
67. Superchi, S.; Sotomayor, N.; Miao, G.; Joseph, B.; Snieckus, V. *Tetrahedron Lett.* **1996**, *37*, 6057.
68. Lorthiois, E.; Marek, I.; Normant, J.-F. *Tetrahedron Lett.* **1997**, *38*, 89.
68a. Karoyan, P.; Chassaing, G. *Tetrahedron Lett.* **1997**, *38*, 85.
68b. Karoyan, P.; Quancard, J.; Vaissermann, J.; Chassaing, G. *J. Org. Chem.* **2003**, *68*, 2256.
68c. Karoyan, P.; Chassaing, G. *Tetrahedron: Asymmetry* **1997**, *8*, 2025.
68d. Karoyan, P.; Triolo, A.; Nannicini, R.; Giannotti, D.; Altamura, M.; Chassaing, G.; Perrotta, G. E. *Tetrahedron Lett.* **1999**, *40*, 71.
68e. Karoyan, P.; Chassaing, G. *Tetrahedron Lett.* **2002**, *43*, 253.
68f. Quancard, J.; Magella, H.; Lavielle, S.; Chassaing, G.; Karoyan, P. *Tetrahedron Lett.* **2004**, *45*, 2185.
68g. Lorthiois, E.; Marek, I.; Normant, J. F. *J. Org. Chem.* **1998**, *63*, 566.
68h. Lorthiois, E.; Marek, I.; Normant, J. F. *J. Org. Chem.* **1998**, *63*, 2442.
69. Nakamura, E.; Kubota, K. *J. Org. Chem.* **1997**, *62*, 792.
69a. Kubota, K.; Nakamura, E. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2491.
69b. Nakamura, M.; Hatakeyama, T.; Hara, K.; Nakamura, E. *J. Am. Chem. Soc.* **2003**, *125*, 6362.
69c. Nakamura, M.; Isobe, H.; Nakamura, E. *Chem. Rev.* **2003**, *103*, 1295.
69d. Nakamura, M.; Yoshikai, N.; Nakamura, E. *Chem. Lett.* **2002**, 146.
69e. Nakamura, M.; Inoue, T.; Sato, A.; Nakamura, E. *Org. Lett.* **2000**, *2*, 2193.

69f. Nakamura, E.; Sakata, G.; Kubota, K. *Tetrahedron Lett.* **1998**, *39*, 2157.
70. Gillet, J. P.; Sauvetre, R.; Normant, J.-F. *Synthesis* **1986**, 538.
70a. Normant, J.-F. *J. Organomet. Chem.* **1990**, *400*, 19.
71. Bainbridge, J. M.; Brown, S. J.; Ewing, P. N.; Gibson, R. R.; Percy, J. M. *J. Chem. Soc., Perkin Trans 1* **1998**, 2541.
72. Anilkumar, R.; Burton, D. J. *Tetrahedron Lett.* **2002**, *43*, 6979.
73. Shigeoka, T.; Kuwahara, Y.; Watanabe, K.; Satro, K.; Omote, M.; Ando, A.; Kumadaki, I. *J. Fluorine Chem.* **2000**, *103*, 99.
73a. Shigeoka, T.; Kuwahara, Y.; Watanabe, K.; Satro, K.; Omote, M.; Ando, A.; Kumadaki, I. *Heterocycles* **2000**, *52*, 383.
74. Poisson, J.-F.; Normant, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4639.
75. Poisson, J.-F.; Normant, J. F. *Org. Lett.* **2001**, *3*, 1889.
76. Wilson, I.; Jackson, R. F. W. *J. Chem. Soc., Perkin Trans 1* **2002**, 2845.
77. Zakharin, L. I.; Okhlobystin, O. Y. *Z. Obshch. Chim.* (*Engl. Trans*, P 2109) **1960**, *30*, 2134.
77a. Zakharin, L. I.; Okhlobystin, O. Y. *Z Chem. Abstr.* **1961**, *55*, 9319a.
78. Thiele, K.-H.; Zdunneck, P. *J. Organomet. Chem.* **1965**, *4*, 10.
78a. Thiele, K.-H.; Engelhardt, G.; Köhler, J.; Arnstedt, M. *J. Organomet. Chem.* **1967**, *9*, 385.
79. Langer, F.; Waas, J.; Knochel, P. *Tetrahedron Lett.* **1993**, *34*, 5261.
79a. Langer, F.; Schwink, L.; Devasagayaraj, A.; Chavant, P.-Y.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 8229.
80. Srebnik, M. *Tetrahedron Lett.* **1991**, *32*, 2449.
80a. Oppolzer, W.; Radinov, R. N. *Helv. Chim. Acta* **1992**, *75*, 170.
80b. Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593.
81. Köster, R.; Griasnow, G.; Larbig, W.; Binger, P. *Liebigs Ann. Chem.* **1964**, *672*, 1.
82. Devasagayaraj, A.; Schwink, L.; Knochel, P. *J. Org. Chem.* **1995**, *60*, 3311.
83. Brown, H. C.; Mandal, A. K.; Yoon, N. M.; Singaram, B.; Schwier, J. R.; Jadhav, P. K. *J. Org. Chem.* **1982**, *47*, 5069.
84. Micouin, L.; Oestreich, M.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 245.
84a. Boudier, A.; Flachsmann, F.; Knochel, P. *Synlett* **1998**, 1438.
84b. Hupe, E.; Knochel, P. *Org. Lett.* **2001**, *3*, 127.
85. Hupe, E.; Knochel, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 3022.
86. Boudier, A.; Hupe, E.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 2294.
87. Fleming, I.; Lawrence, N. J. *J. Chem. Soc., Perkin Trans 1* **1992**, 3309.
88. Hupe, E.; Calaza, M. I.; Knochel, P. *Tetrahedron Lett.* **2001**, *42*, 8829.
88a. Hupe, E.; Calaza, M. I.; Knochel, P. *Chem. Eur. J.* **2003**, *9*, 2789.
89. Burgess, K.; Ohlmeyer, M. J. *J. Org. Chem.* **1991**, *56*, 1027.
90. Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179.
90a. Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.
91. Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917.
91a. Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 395.
92. Hupe, E.; Calaza, M. I.; Knochel, P. *Chem. Commun.* **2002**, 1390.
93. Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F. F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 4302.
94. Jensen, A. E.; Knochel, P. *J. Organomet. Chem.* **2002**, *653*, 122.
95. Rottländer, M.; Boymond, L.; Bérillon, L.; Lepêtre, A.; Varchi, G.; Avolio, S.; Laaziri, H.; Quéguiner, G.; Ricci, A.; Cahiez, G.; Knochel, P. *Chem. Eur. J.* **2000**, *6*, 767.
96. Bérillon, L.; Lepêtre, A.; Turck, A.; Plé, N.; Quéguiner, G.; Cahiez, G.; Knochel, P. *Synlett* **1998**, 1359.
97. Rottländer, M.; Boymond, L.; Cahiez, G.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 1080.
98. Ichikawa, J.; Fujiwara, M.; Nawata, H.; Okauchi, T.; Minami, T. *Tetrahedron Lett.* **1996**, *37*, 8799.
99. Wipf, P.; Xu, W. *J. Org. Chem.* **1996**, *61*, 6556.
99a. Wipf, P.; Xu, W. *Tetrahedron Lett.* **1994**, *35*, 5197.
100. Ni, Y.; Amarasinghe, K. K. D.; Montgomery, J. *Org. Lett.* **2002**, *4*, 1743.
101. Negishi, E.; Okukado, N.; King, A. O.; Van Horn, D. E.; Spiegel, B. I. *J. Am. Chem. Soc.* **1978**, *100*, 2254.
102. Dieter, R. K.; Watson, R. T.; Goswami, R. *Org. Lett.* **2004**, *6*, 253.
103. Tamaru, Y.; Tanaka, A.; Yasui, K.; Goto, S.; Tanaka, S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 787.
103a. Shimizu, M.; Kimura, M.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1998**, *39*, 609.
104. Tamaru, Y. *J. Organomet. Chem.* **1999**, *576*, 215.
104a. Kimura, M.; Kiyama, I.; Tomizawa, T.; Horino, Y.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1999**, *40*, 6795.
104b. Kimura, M.; Matsuo, S.; Shibata, K.; Tamaru, Y. *Angew. Chem. Int. Ed.* **1999**, *38*, 3386.
104c. Kimura, M.; Tomizawa, T.; Horino, Y.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **2000**, *41*, 3627.
104d. Shibata, K.; Kimura, M.; Shimizu, M.; Tamaru, Y. *Org. Lett.* **2001**, *3*, 2181.
104e. Kimura, M.; Horino, Y.; Mukai, R.; Tanaka, S.; Tamaru, Y. *J. Am. Chem. Soc.* **2001**, *123*, 10401.
105. Jones, P.; Millot, N.; Knochel, P. *Chem. Commun.* **1998**, 2405.
105a. Jones, P.; Millot, N.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 186.
105b. Jones, P.; Knochel, P. *Chem. Commun.* **1998**, 2407.
105c. Piazza, C.; Millot, N.; Knochel, P. *J. Organomet. Chem.* **2001**, *624*, 88.
105d. Millot, N.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7779.
106. Benn, R.; Hoffmann, E. G.; Lehmkuhl, H.; Nehl, H. *J. Organomet. Chem.* **1978**, *146*, 103.
107. Oppolzer, W.; Bienayme, H.; Genevois-Borella, A. *J. Am. Chem. Soc.* **1991**, *113*, 9660.
108. Vettel, S.; Vaupel, A.; Knochel, P. *Tetrahedron Lett.* **1995**, *36*, 1023.
109. Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.
110. Tucker, C. E.; Knochel, P. *J. Org. Chem.* **1993**, *58*, 4781.
111. Eick, H.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 218.
111a. Bhanu Prasad, A. S.; Eick, H.; Knochel, P. *J. Organomet. Chem.* **1998**, *562*, 133.
111b. Tamaru, Y.; Ochiai, H.; Sanda, F.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 5529.
112. Deboves, H. J. C.; Grabowska, U.; Rizzo, A.; Jackson, R. F. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4284.

113. Reddy, C. K.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1700.
114. Knochel, P.; Seebach, D. *Tetrahedron Lett.* **1982**, *23*, 3897.
114a. Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1984**, *67*, 261.
115. Ma, S.; Zhang, A. *J. Org. Chem.* **2002**, *67*, 2287.
116. Utimo, K.; Toda, N.; Mizuno, T.; Kobata, M.; Matsubara, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2804.
117. Giovannini, R.; Stüdemann, T.; Dussin, G.; Knochel, P. *Angew. Chem., Int. Ed.* **1998**, *37*, 2387.
117a. Devasagayaraj, A.; Stüdemann, T.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2723.
117b. Giovannini, R.; Knochel, P. *J. Am. Chem. Soc.* **1998**, *120*, 11186.
118. Piber, M.; Jensen, A. E.; Rottländer, M.; Knochel, P. *Org. Lett.* **1999**, *1*, 1323.
119. Jensen, A. E.; Knochel, P. *J. Org. Chem.* **2002**, *67*, 79.
120. Corey, E. J.; Helel, C. J. *Tetrahedron Lett.* **1997**, *38*, 7511.
121. Lipshutz, B. H.; Vivian, R. W. *Tetrahedron Lett.* **1999**, *40*, 2871.
122. Liu, J.-J.; Konzelmann, F.; Luk, K.-C. *Tetrahedron Lett.* **2003**, *44*, 3901.
123. Thorn, S. N.; Gallagher, T. *Synlett* **1996**, 185.
123a. Rychnovsky, S. D.; Powell, N. A. *J. Org. Chem.* **1997**, *62*, 6460.
123b. Powell, N. A.; Rychnovsky, S. D. *J. Org. Chem.* **1999**, *64*, 2026.
123c. Rychnovsky, S. D.; Powell, N. A. *J. Org. Chem.* **1997**, *62*, 6460.
124. Almena, P. J. J.; Ireland, T.; Knochel, P. *Tetrahedron Lett.* **1997**, *38*, 5961.
124a. Almena, P. J. J.; Börner, A.; Knochel, P. *Tetrahedron Lett.* **1998**, *39*, 8073.
124b. Lotz, M.; Ireland, T.; Almena, P. J. J.; Knochel, P. *Tetrahedron: Asymmetry* **1999**, *10*, 1839.
125. Katritzky, A. R.; Luo, Z.; Fang, Y.; Steel, P. J. *J. Org. Chem.* **2001**, *66*, 2858.
126. Konno, T.; Tanikawa, M.; Ishihara, T.; Yamanaka, H. *Collect. Czech., Chem. Commun.* **2002**, *67*, 1421.
127. Yanagisawa, A.; Noritake, Y.; Nomura, N.; Yamamoto, H. *Synlett* **1991**, 251.
127a. Calaza, M. I.; Hupe, E.; Knochel, P. *Org. Lett.* **2003**, *5*, 1059.
128. Soorukram, D.; Knochel, P. *Org. Lett.* **2004**, *6*, 2409.
128a. Breit, B.; Demel, P. *Adv. Synth. Catal.* **2001**, *343*, 429.
128b. Breit, B.; Demel, P. *Tetrahedron* **2000**, *56*, 2833.
129. Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.
130. Harrington-Frost, N.; Leuser, H.; Calaza, M. I.; Kneisel, F. F.; Knochel, P. *Org. Lett.* **2003**, *5*, 2111.
130a. Leuser, H.; Perrone, S.; Liron, F.; Kneisel, F. F.; Knochel, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 4627.
131. Breit, B.; Herber, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 2790–3792.
132. Breit, B.; Demel, P.; Studte, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 3786–3789.
133. Karlström, A. S. E.; Huerta, F. F.; Meuzelaar, G. J.; Bäckvall, J. E. *Synlett* **2001**, 923.
133a. Meuzelaar, G. J.; Karlström, A. S. E.; van Klaveren, M.; Persson, E. S. M.; del Villar, A.; van Koten, G.; Bäckvall, J.-E. *Tetrahedron* **2000**, *56*, 2895.
133b. Alexakis, A.; Malan, C.; Lea, L.; Benhaim, C.; Fournioux, X. *Synlett* **2001**, 927.
133c. Alexakis, A.; Croset, K. *Org. Lett.* **2002**, *4*, 4147.
133d. Malda, H.; van Zijl, A. W.; Arnold, L. A.; Feringa, B. L. *Org. Lett.* **2001**, *3*, 1169.
133e. Equey, O.; Vrancken, E.; Alexakis, A. *Eur. J. Org. Chem.* **2004**, 2151.
133f. Tissot-Croset, K.; Polet, D.; Alexakis, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 2426.
134. Luchaco-Cullis, C. A.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 1456.
135. Dübner, F.; Knochel, P. *Tetrahedron Lett.* **2000**, *41*, 9233.
135a. Dübner, F.; Knochel, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 379.
136. Yeh, M. C. P.; Knochel, P. *Tetrahedron Lett.* **1988**, *29*, 2395.
136a. Sekiya, K.; Nakamura, E. *Tetrahedron Lett.* **1988**, *29*, 5155.
137. Ochiai, H.; Nishihara, T.; Tamaru, Y.; Yoshida, Z. *J. Org. Chem.* **1988**, *53*, 1343.
138. Berninger, J.; Koert, U.; Eisenberg-Höhl, C.; Knochel, P. *Chem. Ber.* **1995**, *128*, 1021.
139. Decamp, A. E.; Kawaguchi, A. T.; Volante, R. P.; Shinkai, I. *Tetrahedron Lett.* **1991**, *32*, 1867.
140. Quinton, P.; Le Gall, T. *Tetrahedron Lett.* **1991**, *32*, 4909.
141. Tsujiyama, H.; Ono, N.; Yoshino, T.; Okamoto, S.; Sato, F. *Tetrahedron Lett.* **1990**, *31*, 4481.
141a. Yoshino, T.; Okamoto, S.; Sato, F. *J. Org. Chem.* **1991**, *56*, 3205.
141b. Miyaji, K.; Ohara, Y.; Miyauchi, Y.; Tsuruda, T.; Arai, K. *Tetrahedron Lett.* **1993**, *34*, 5597.
142. Thompson, W. J.; Tucker, T. J.; Schwering, J. E.; Barnes, J. L. *Tetrahedron Lett.* **1990**, *31*, 6819.
143. Koert, U.; Wagner, H.; Pidun, U. *Chem. Ber.* **1994**, *127*, 1447.
144. Cahiez, G. *Actual Chim.* **1984**, 24.
144a. Weidmann, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 31.
144b. Cahiez, G.; Laboue, B. *Tetrahedron Lett.* **1989**, *30*, 3545.
144c. Cahiez, G.; Laboue, B. *Tetrahedron Lett.* **1989**, *30*, 7369.
144d. Cahiez, G.; Alami, M. *Tetrahedron* **1989**, *45*, 4163.
144e. Cahiez, G.; Chavant, P.-Y.; Metais, E. *Tetrahedron Lett.* **1992**, *33*, 5245.
144f. Cahiez, G.; Figadère, B.; Cléry, P. *Tetrahedron Lett.* **1994**, *35*, 3065.
144g. Cahiez, G.; Chau, K.; Cléry, P. *Tetrahedron Lett.* **1994**, *35*, 3069.
145. Stüdemann, T.; Ibrahim-Ouali, M.; Cahiez, G.; Knochel, P. *Synlett* **1998**, 143.
146. Tokuyama, H.; Yokoshima, S.; Yamashita, T.; Fukuyama, T. *Tetrahedron Lett.* **1998**, *39*, 3189.
147. Mori, Y.; Seki, M. *J. Org. Chem.* **2003**, *68*, 1571.
148. Shimizu, T.; Seki, M. *Tetrahedron Lett.* **2002**, *43*, 1039.
148a. Shimizu, T.; Seki, M. *Tetrahedron Lett.* **2001**, *42*, 429.
148b. see also Kimura, M.; Seki, M. *Tetrahedron Lett.* **2004**, *45*, 1635.
149. Harada, T.; Kutsuwa, E. *J. Org. Chem.* **2003**, *68*, 6716.

149a. Harada, T.; Oku, A. In *Organozinc Reagents. A Practical Approach*; Knochel, P., Jones, P., Eds.; Oxford University Press: New York, 1999; Chapter 6.
150. Lipshutz, B. H.; Woo, K.; Gross, T.; Buzard, D. J.; Tirado, R. *Synlett* **1997**, 477.
151. Reddy, C. K.; Devasagayaraj, A.; Knochel, P. *Tetrahedron Lett.* **1996**, *37*, 4495.
151a. Kitamura, M.; Miki, T.; Nakano, K.; Noyori, R. *Tetrahedron Lett.* **1996**, *37*, 5141.
152. Devasagayaraj, A.; Knochel, P. *Tetrahedron Lett.* **1995**, *36*, 8411.
153. Negishi, E.; Miller, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 6761.
153a. Molander, G. A. *J. Org. Chem.* **1983**, *48*, 5409.
154. Yanagisawa, A.; Habane, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1989**, *111*, 366.
155. Kubota, K.; Nakamura, M.; Isaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **1993**, *115*, 5867.
156. van der Louw, J.; Komen, C. M. D.; Knol, A.; de Kanter, F. J. J.; van der Baan, J. L.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron Lett.* **1989**, *30*, 4453.
157. Gaudernar, M. *C. R. Acad. Sci. Paris* **1971**, *273*, 1669.
157a. Knochel, P.; Normant, J.-F. *Tetrahedron Lett.* **1986**, *27*, 1039, 1043 and 4427.
157b. Marek, I.; Normant, J.-F. *Chem. Rev.* **1996**, *96*, 3241.
157c. Marek, I.; Normant, J.-F. *J. Org. Chem.* **1994**, *59*, 4154.
157d. Beruben, D.; Marek, I.; Normant, J.-F.; Platzer, N. *J. Org. Chem.* **1995**, *60*, 2488.
158. Nakamura, M.; Hara, K.; Hatakeyama, T.; Nakamura, E. *Org. Lett.* **2001**, *3*, 3137.
159. Greenfield, S. J.; Agarkov, A.; Gilbertson, S. R. *Org. Lett.* **2003**, *5*, 3069.
159a. Stadtmueller, H.; Knochel, P. *Organometallics* **1995**, *14*, 3163.
160. Millot, N.; Piazza, C.; Avolio, S.; Knochel, P. *Synthesis* **2000**, 941.
161. Gommermann, N.; Koradin, C.; Knochel, P. *Synthesis* **2002**, 2143.
162. Lamaty, F.; Lazaro, R.; Martinez, J. *Tetrahedron Lett.* **1997**, *38*, 3385.
163. Comins, D. L.; O'Connor, S. *Tetrahedron Lett.* **1987**, *28*, 1843.
163a. Comins, D. L.; Foley, M. A. *Tetrahedron Lett.* **1988**, *29*, 6711.
164. Nakamura, E.; Aoki, S.; Sekiya, K.; Oshino, H.; Kuwajima, I. *J. Am. Chem. Soc.* **1987**, *109*, 8056.
165. Ludwig, M.; Polborn, K.; Wanner, K. T. *Heterocycles* **2003**, *61*, 299.
166. Blankenfeldt, W.; Liao, J.-W.; Lo, L.-C.; Yeh, M. C. P. *Tetrahedron Lett.* **1996**, *37*, 7361.
167. Yeh, M. C. P.; Sun, M.-L.; Lin, S.-K. *Tetrahedron Lett.* **1991**, *32*, 113.
167a. Yeh, M. C. P.; Tau, S. J. *J. Chem. Soc., Chem. Commun.* **1992**, 13.
167b. Yeh, M. C. P.; Tsou, C.-J.; Chuang, C.-N.; Lin, H.-C. *J. Chem. Soc., Chem. Commun.* **1992**, 890.
167c. Yeh, M. C. P.; Shen, B.-A.; Fu, H.-W.; Tau, S. I.; Chuang, L. W. *J. Am. Chem. Soc.* **1993**, *115*, 5941.
168. Yeh, M. C. P.; Hwu, C.-C.; Lee, A.-T.; Tsai, M.-S. *Organometallics* **2001**, *20*, 4965.
169. Rigby, J. H.; Kirova-Snover, M. *Tetrahedron Lett.* **1997**, *38*, 8153.
170. Nukamura, M.; Hatakeyama, T.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 11820.
171. Soucy, R. L.; Kozhinov, D.; Behar, V. *J. Org. Chem.* **2002**, *67*, 1947.
172. Yamamoto, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Schreiber, S. L., Eds.; Pergamon: Oxford, 1991; Vol. 2, pp 81.
173. Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163.
173a. Marshall, J. A.; Yanik, M. M. *J. Org. Chem.* **2001**, *66*, 1373.
173b. Gung, B. W.; Xue, X.; Katz, N.; Marshall, J. A. *Organometallics* **2003**, *22*, 3158.
174. Zweifel, G.; Hahn, G. *J. Org. Chem.* **1984**, *49*, 4565.
175. Momtgomery, J.; Song, M. *Org. Lett.* **2002**, *4*, 4009.
175a. Kang, S.-K.; Yoon, S.-K. *Chem. Commun.* **2002**, 2634.
176. Chiev, K. P.; Roland, S.; Mangeney, P. *Tetrahedron: Asymmetry* **2002**, *13*, 2205.
177. Saidi, M. R.; Azizi, N. *Tetrahedron: Asymmetry* **2002**, *13*, 2523.
178. Hirai, A.; Matsui, A.; Komatsu, K.; Tanino, K.; Miyashita, M. *Chem. Commun.* **2002**, 1970.
179. Xue, S.; Han, K.-Z.; He, L.; Guo, Q.-X. *Synlett* **2003**, 870.
179a. Rainier, J. D.; Cox, J. M. *Org. Lett.* **2000**, *2*, 2707.
180. Denes, F.; Chemla, F.; Normant, J. F. *Eur. J. Org. Chem.* **2002**, 3536.
181. Nukamura, M.; Hatakeyama, T.; Hara, K.; Fukudome, H.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 14344.
182. Hird, A. W.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 1276.
183. Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; de Vries, A. H. M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2620.
183a. Keller, E.; Maurer, J.; Naasz, R.; Schader, T.; Meetsma, A.; Feringa, B. L. *Tetrahedron: Asymmetry* **1998**, *9*, 2409.
183b. Naasz, R.; Arnold, L. A.; Pineschi, M.; Keller, E.; Feringa, B. L. *J. Am. Chem. Soc.* **1999**, *121*, 1104.
183c. Imbos, R.; Britman, M. H. G.; Pineschi, M.; Feringa, B. L. *Org. Lett.* **1999**, *1*, 623.
183d. Arnold, L. A.; Imbos, R.; Mandoli, A.; De Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865.
183e. Bertozzi, F.; Crotti, P.; Feringa, B. L.; Macchia, F.; Pineschi, M. *Synthesis* **2001**, 483.
184. Alexakis, A.; Burton, J.; Vastra, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *8*, 3987.
184a. Alexakis, A.; Trevitt, G. P.; Bernadelli, G. *J. Am. Chem. Soc.* **2001**, *123*, 4358.
184b. Alexakis, A.; Benhaim, C.; Rosset, S.; Humann, M. *J. Am. Chem. Soc.* **2002**, *124*, 5262.
184c. Knopff, O.; Alexakis, A. *Org. Lett.* **2002**, *4*, 3835.
184d. Alexakis, A.; Benhaim, C. *Eur. J. Org. Chem.* **2002**, 3221.
184e. Alexakis, A.; March, S. *J. Org. Chem.* **2002**, *67*, 8753.
185. Arnold, L. A.; Naasz, R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2001**, *123*, 5841.
186. Naasz, R.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 927.
187. Oguni, N.; Omi, T.; Yamamoto, Y.; Nakamura, A. *Chem. Lett.* **1983**, 841.
187a. Oguni, N.; Omi, T. *Tetrahedron Lett.* **1984**, *25*, 2823.
187b. Oguni, N.; Matsuda, Y.; Kaneko, T. *J. Am. Chem. Soc.* **1988**, *110*, 7877.
188. Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833.
188a. Evans, D. A. *Science* **1988**, *240*, 420.

188b. Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49.
189. Yoshioka, M.; Kawakita, T.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 1657.
189a. Takahashi, H.; Kawakita, T.; Yoshioka, M.; Kobayashi, S.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 7095.
189b. Takahashi, H.; Kawakita, T.; Ohno, M.; Yoshioka, M.; Kobayashi, S. *Tetrahedron* **1992**, *48*, 5691.
190. Beck, A. K.; Bastani, B.; Plattner, D. A.; Petter, W.; Seebach, D.; Braunschweiger, H.; Gysi, P.; VaVecchia, L. *Chimia* **1991**, *45*, 238.
190a. Schmidt, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 99.
190b. Seebach, D.; Behrendt, L.; Felix, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1008.
190c. Schmidt, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1321.
190d. von dem Bussche-Hünnefeld, J. L.; Seebach, D. *Tetrahedron* **1992**, *48*, 5719.
190e. Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, *75*, 2171.
190f. Seebach, D.; Beck, A. K.; Schmidt, B.; Wang, Y. M. *Tetrahedron* **1994**, *50*, 4363.
191. Schafer, H.; Seebach, D. *Tetrahedron* **1995**, *51*, 2305.
192. Seebach, D.; Beck, A. K.; Hechel, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 92.
192a. Rheiner, B. P.; Sellner, H.; Seebach, D. *Helv. Chim. Acta* **1997**, *80*, 2027.
193. Sellner, H.; Faber, C.; Rheiner, P. B.; Seebach, D. *Chem. Eur. J.* **2000**, *6*, 3692.
194. Schwink, L.; Knochel, P. *Chem. Eur. J.* **1998**, *4*, 950.
194a. Brieden, W.; Ostwald, R.; Knochel, P. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 582.
195. Rozema, M. J.; Eisenberg, C.; Lütjens, H.; Ostwald, R.; Belyk, K.; Knochel, P. *Tetrahedron Lett.* **1993**, *34*, 3115.
196. Nowotny, S.; Vettel, S.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 4539.
197. Noyori, R.; Suzuki, M. *Angew. Chem. Int., Ed. Engl.* **1984**, *23*, 847.
197a. Suzuki, M.; Yanagisawa, A.; Noyori, R. *J. Am. Chem. Soc.* **1990**, *307*, 3348.
197b. Morita, Y.; Suzuki, M.; Noyori, R. *J. Org. Chem.* **1989**, *54*, 1785.
197c. Noyori, R.; Suga, S.; Kawai, K.; Okada, S.; Kitamura, M. *Pure Appl. Chem.* **1988**, *60*, 1597.
198. Vettel, S.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 5849.
198a. Ostwald, R.; Chavant, P.-Y.; Stadtmüller, H.; Knochel, P. *J. Org. Chem.* **1994**, *59*, 4143.
198b. Roush, W. R.; Koyama, K. *Tetrahedron Lett.* **1992**, *33*, 6227.
199. Lütjens, H.; Knochel, P. *Tetrahedron: Asymmetry* **1994**, *5*, 1161.
200. Knochel, P.; Brieden, W.; Rozema, M. J.; Eisenberg, C. *Tetrahedron Lett.* **1993**, *34*, 5881.
201. Eisenberg, C.; Knochel, P. *J. Org. Chem.* **1994**, *59*, 3760.
202. Fürstner, A.; Müller, T. *J. Org. Chem.* **1998**, *63*, 424.
203. Bäurle, S.; Hoppen, S.; Koert, U. *Angew. Chem., Int. Ed.* **1999**, *38*, 1263.
204. Fürstner, A.; Albert, M.; Mlynarski, J.; Matheu, M.; DeClercq, E. *J. Am. Chem. Soc.* **2003**, *125*, 13132.
205. Yus, M.; Ramón, D. J.; Prieto, O. *Tetrahedron: Asymmetry* **2003**, *14*, 1103.
206. Oppolzer, W.; Radinov, R. N.; de Bradander, J. *Tetrahedron Lett.* **1995**, *36*, 2607.
207. Boyalli, D.; Frantz, E.; Carreira, E. M. *Org. Lett.* **2002**, *4*, 2605.
208. Fettes, A.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4098.
209. Pu, L. *Tetrahedron* **2003**, *59*, 9873.
210. Tan, L. S.; Chen, C. Y.; Tillyer, R. D.; Grabowski, E. J. J.; Reider, P. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 711.
211. Anand, N. K.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 9687.
212. Prieto, O.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1955.
213. Rudolph, J.; Rasmussen, T.; Bolm, C.; Norrby, P.-O. *Angew. Chem., Int. Ed.* **2003**, *42*, 3002.
213a. Rudolph, J.; Hermanns, N.; Bolm, C. *J. Org. Chem.* **2004**, *69*, 3997.
213b. Bolm, C.; Mueller, J. *Tetrahedron* **1994**, *50*, 4355.
213c. Bolm, C.; Mueller, J.; Schlingloff, G.; Zehnder, M.; Neuburger, M. *J. Chem. Soc., Chem. Commun.* **1993**, *2*, 182.
213d. Bolm, C.; Schlingloff, G.; Harms, K. *Chem. Ber.* **1992**, *124*, 1191.
213e. Bolm, C.; Hermanns, N.; Classen, A.; Muniz, K. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1795.
213f. Rudolph, J.; Bolm, C.; Norrby, P.-O. *J. Am. Chem. Soc.* **2005**, *127*, 1548.
214. Porter, J. R.; Traverse, J. F.; Hoveyda, A. H.; Snapper, M. L. *J. Am. Chem. Soc.* **2001**, *123*, 10409.
215. Traverse, J. F.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett.* **2003**, *5*, 3273.
216. Shibata, T.; Yonekubo, S.; Soai, K. *Angew. Chem., Int. Ed.* **1999**, *38*, 659.
217. Sato, I.; Urabe, H.; Ishiguro, S.; Shibata, T.; Soai, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 315.
218. Negishi, E.; King, A. O.; Okukado, N. *J. Org. Chem.* **1977**, *42*, 1821.
218a. Rossi, R.; Bellina, F.; Carpita, A.; Gori, R. *Synlett* **1995**, 344.
218b. Negishi, E.; Matsushita, H.; Kobayashi, M.; Rand, C. L. *Tetrahedron Lett.* **1983**, *24*, 3823.
218c. Millar, J. G. *Tetrahedron Lett.* **1989**, *30*, 4913.
218d. Hyuga, S.; Yamashina, N.; Hara, S.; Suzuki, A. *Chem. Lett.* **1988**, 809.
218e. Löffler, A.; Himbert, G. *Synthesis* **1992**, 495.
218f. Borner, R. C.; Jackson, R. F. W. *J. Chem. Soc., Chem. Commun.* **1994**, 845.
218g. Sakamoto, T.; Kondo, Y.; Takazawa, N.; Yamanaka, H. *Tetrahedron Lett.* **1993**, *34*, 5955.
218h. Minato, A.; Suzuki, K.; Tamao, K.; Kumada, M. *Tetrahedron Lett.* **1984**, *25*, 2583.
218i. Quesnelle, C. A.; Familoni, O. B.; Snieckus, V. *Synlett* **1994**, 349.
218j. Sakamoto, T.; Nishimura, S.; Kondo, Y.; Yamanaka, H. *Synthesis* **1988**, 485.
218k. Sato, T.; Kawase, A.; Hirose, T. *Synlett* **1992**, 891.
218l. Negishi, E.; Zeng, X.; Tan, Z.; Qian, M.; Hu, Q.; Huang, Z. In *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; De Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, pp 815–889.
219. Negishi, E.; Matsushita, H.; Kobayashi, M.; Raud, C. L. *Tetrahedron Lett.* **1983**, *24*, 3823.
220. Minota, A.; Suzuki, K.; Tamao, K.; Kumada, M. *Tetrahedron Lett.* **1984**, *25*, 2583.
221. Mignani, G.; Leising, F.; Meyrueix, R.; Samson, H. *Tetrahedron Lett.* **1990**, *31*, 4743.
222. Sakamoto, T.; Kondo, Y.; Murata, N.; Yamanaka, H. *Tetrahedron Lett.* **1992**, *33*, 5373.
222a. Sakamoto, T.; Kondo, Y.; Takazawa, N.; Yamanaka, H. *Heterocycles* **1993**, *36*, 941.

222b. Trauner, D.; Schwartz, J. B.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 3543.
222c. Bell, A. S.; Roberts, D. A.; Ruddock, K. S. *Synthesis* **1987**, 843.
223. Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 83.
223a. Sakamoto, T.; Nishimura, S.; Kondo, Y.; Yamanaka, H. *Synthesis* **1988**, 485.
224. Tucker, C. E.; Majid, T. N.; Knochel, P. *J. Am. Chem. Soc.* **1992**, *114*, 3983.
225. Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Angew. Chem., Int. Ed. Engl.* **1987**, *99*, 1193.
226. Jackson, R. F. W.; Wylhes, M. J.; Wood, A. *J. Chem. Soc., Chem. Commun.* **1989**, 644.
227. Deboves, H. J. C.; Montalbetti, C. A. G. N.; Jackson, R. F. W. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1876.
228. Mehta, A.; Jaouhari, R.; Benson, T. J.; Douglas, K. T. *Tetrahedron Lett.* **1992**, *33*, 5441.
229. Kadota, I.; Takamura, H.; Sato, K.; Yamamoto, Y. *J. Org. Chem.* **2002**, *67*, 3494.
229a. Tamaru, Y.; Ochial, H.; Nakamura, T.; Yoshida, Z. *Tetrahedron Lett.* **1986**, *27*, 955.
229b. Tamaru, Y.; Ochial, H.; Nakamura, T.; Tsubaki, K.; Yoshida, Z. *Tetrahedron Lett.* **1985**, *26*, 5559.
230. Vicart, N.; Saboukoulou, G.-S.; Ramondenc, Y.; Plé, G. *Synth. Commun.* **2003**, *33*, 1509.
231. Przezdziecka, A.; Kurek-Tyrlik, A.; Wicha, J. *Collect. Czech. Chem. Commun.* **2002**, *67*, 1658.
232. Murata, N.; Sugihara, T.; Kondo, Y.; Sakamoto, T. *Synlett* **1997**, 298.
233. Karig, G.; Spencer, J. A.; Gallagher, T. *Org. Lett.* **2001**, *3*, 835.
223a. Sharples, C. G. V.; Karig, G.; Simpson, G. L.; Spencer, J. A.; Wright, E.; Millar, N. S.; Wonnacott, S.; Gallagher, T. *J. Med. Chem.* **2002**, *45*, 3235.
234. Staubitz, A.; Dohle, W.; Knochel, P. *Synthesis* **2003**, 233.
235. Hocek, M.; Votruba, I.; Dvoraka, H. *Tetrahedron* **2003**, *59*, 607.
236. Ye, B.; Burke, T. R., Jr. *J. Org. Chem.* **1995**, *60*, 2640.
237. Seton, A. W.; Stevens, M. F. G.; Westwell, A. D. *J. Chem. Res. (S)* **2001**, 546.
238. Thibonnet, J.; Vu, V. A.; Berillon, L.; Knochel, P. *Tetrahedron* **2002**, *58*, 4787.
239. Negishi, E.; Qian, M.; Zeng, F.; Anastasia, L.; Babinski, D. *Org. Lett.* **2003**, *5*, 1597.
240. Shi, J.-C.; Zeng, X.; Negishi, E. *Org. Lett.* **2003**, *5*, 1825.
241. Zeng, X.; Qian, M.; Negishi, E.-I. *J. Am. Chem. Soc.* **2003**, *125*, 13636.
241a. Zeng, X.; Qian, M.; Hu, Q.; Negishi, E.-I. *Angew. Chem,. Int. Ed.* **2004**, *43*, 2259.
242. Lotz, M.; Kramer, G.; Knochel, P. *Chem. Commun.* **2002**, 2546.
242a. Kloetzing, R. J.; Lotz, M.; Knochel, P. *Tetrahedron: Asymmetry* **2003**, *14*, 255.
242b. Bunlaksananusorn, T.; Polborn, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 3941.
242c. Bunlaksananusorn, T.; Luna, A. P.; Boniu, M.; Micouin, L.; Knochel, P. *Synlett* **2003**, 2240.
243. Peyrat, J.-F.; Thomas, E.; L'Hermite, N.; Alami, M.; Brion, J.-D. *Tetrahedron Lett.* **2003**, *44*, 6703.
243a. Alami, M.; Gueugnot, S.; Doingues, E.; Linstrumelle, G. *Tetrahedron* **1995**, *51*, 1209.
244. Flynn, B. L.; Verdier-Pinard, P.; Hamel, E. *Org. Lett.* **2001**, *3*, 651.
245. Zeng, F.; Negishi, E.-I *Org. Lett.* **2001**, *3*, 719.
245a. Zeng, F.; Negishi, E.-I. *Org. Lett.* **2002**, *4*, 703.
245b. Zeng, X.; Zeng, F.; Negishi, E.-I. *Org. Lett.* **2004**, *6*, 3245.
246. Tamaru, Y.; Ochiai, H.; Nakamura, T.; Yoshida, Z. *Org. Synth.* **1989**, *67*, 98.
247. Asaoka, M.; Tamaka, M.; Houkawa, T.; Ueda, T.; Sakami, S.; Takei, H. *Tetrahedron* **1998**, *54*, 471.
248. Tamaru, Y.; Yasui, K.; Takanabe, H.; Tanaka, S.; Fugami, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 645.
249. Hayashi, T.; Hagihara, T.; Katsuro, Y.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 363.
249a. Hayashi, T. *J. Organomet. Chem.* **2002**, *653*, 41.
250. Mamane, V.; Ledoux-Rak, T.; Deveau, S.; Zyss, J.; Riant, O. *Synthesis* **2003**, 455.
251. Blomberg, C.; Hartog, F. A. *Synthesis* **1977**, 18.
252. Moyano, A.; Petricas, M. A.; Riera, A.; Luche, J.-L. *Tetrahedron Lett.* **1990**, *31*, 7619.
253. Pétrier, C.; Luche, J.-L. *J. Org. Chem.* **1985**, *50*, 910.
253a. Pétrier, C.; Einhorn, J.; Luche, J.-L. *Tetrahedron Lett.* **1985**, *26*, 1449.
253b. Pétrier, C.; Dupuy, C.; Luche, J.-L. *Tetrahedron Lett.* **1986**, *27*, 3149.
253c. Einhorn, C.; Luche, J.-L. *J. Organomet. Chem.* **1987**, *322*, 177.
254. Wilson, S. R.; Guazzaroni, M. E. *J. Org. Chem.* **1989**, *54*, 3087.
255. Sarandeses, L. A.; Mourino, A.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1992**, 798.
256. Yadav, J. S.; Reddy, B. V. S.; Muralikrishna Reddy, P.; Srinivas, C. *Tetrahedron Lett.* **2002**, *43*, 5185.
257. Kim, S. H.; Han, E.-H. *Tetrahedron Lett.* **2000**, 6479.
258. Basile, T.; Bocoum, A.; Savoia, D.; Umani-Romnchi, A. *J. Org. Chem.* **1994**, *59*, 7766.
259. Estevam, I. H. S.; Bieber, L. *Tetrahedron Lett.* **2003**, 677.
260. Legros, J.; Meyer, F.; Coliboeuf, M.; Crousse, B.; Bonnet-Delpon, D.; Bégué, J.-P. *J. Org. Chem.* **2003**, *68*, 6444.
261. Lombardo, M.; Girotti, R.; Morganti, S.; Trombini, C. *Chem. Commun.* **2001**, 2310.
261a. Lombardo, M.; Morganti, S.; Trombini, C. *J. Org. Chem.* **2003**, *68*, 997.
261b. Lombardo, M.; Morganti, S.; d'Ambrosio, F.; Trombini, C. *Tetrahedron Lett.* **2003**, *44*, 2823.
262. Tokuda, M.; Mimura, N.; Yoshioka, K.; Karasawa, T.; Fujita, H.; Suginome, H. *Synthesis* **1993**, 1086.
263. Chan, T.-H.; Li, C.-J. *Organometallics* **1990**, *9*, 2649.
264. Hong, F.; Tang, X.; Hu, C. *J. Chem. Soc., Chem. Commun.* **1994**, 289.
265. Bieber, L. W.; da Silva, M. F.; da Costa, R. C.; Silva, L. O. S. *Tetrahedron Lett.* **1998**, *39*, 3655.
266. Zha, Z.; Xie, Z.; Zhou, C.; Chang, M.; Wang, Z. *New J. Chem.* **2003**, *27*, 1297.
267. Hyldtoft, L.; Madsen, R. *J. Am. Chem. Soc.* **2000**, *122*, 8444.
268. Makosza, M.; Grela, K.; Fabianowski, W. *Tetrahedron* **1996**, *52*, 9575.
269. Durant, A.; Delplancke, J.-L.; Winand, R.; Reisse, J. *Tetrahedron Lett.* **1995**, *36*, 4257.
269a. Durant, A.; Delplancke, J.-L.; Libert, V.; Reisse, J. *Eur. J. Org. Chem.* **1999**, 2845.
270. Lee, A. S.-Y.; Wu, C.-W. *Tetrahedron* **1999**, *55*, 12531.
270a. Lee, A. S.-Y.; Chu, S.-F.; Chang, Y.-T.; Wang, S.-H. *Tetrahedron Lett.* **2004**, *45*, 1551.

271. Pérez-Sestelo, J.; Mascarenas, J. L.; Castedo, L.; Mourino, A. *Tetrahedron Lett.* **1994**, *35*, 275.
272. Lee, A. S.-Y.; Lin, L.-S. *Tetrahedron Lett.* **2000**, *41*, 8803.
273. Keltjuens, R.; Vadivel, S. K.; De Gelder, R.; Klunder, A. J. H.; Zwanenburg, B. *Eur. J. Org. Chem.* **2003**, 1749.
274. Legros, J.; Meyer, F.; Coliboeuf, M.; Crousse, B.; Bonnet-Delpon, D.; Bégué, J.-P. *J. Org. Chem.* **2003**, *68*, 6444.
275. Marquez, F.; Llebaria, A.; Delgado, A. *Tetrahedron Lett.* **2000**, *2*, 547.
276. Mehta, G.; Kumaran, R. S. *Chem. Commun.* **2002**, 1456.
277. Jones, K.; Fiumana, A.; Escudera-Hernandez, M. L. *Tetrahedron* **2000**, *56*, 397.
278. Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53.
278a. Denmark, S. E.; Edwars, J. P. *J. Org. Chem.* **1991**, *56*, 6974.
279. Charette, A. B.; Beauchemin, A. *Org. React.* **2001**, *58*, 1.
279a. Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.
280. Denmark, S. E.; Christenson, B. L.; Coe, D. M.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2215.
280a. Denmark, S. E.; Christenson, B. L.; O'Connor, S. P. *Tetrahedron Lett.* **1995**, *36*, 2219.
280b. Denmark, S. E.; O'Connor, S. P. *J. Org. Lett.* **1997**, *62*, 584.
280c. Kobayashi, S.; Takahashi, H.; Yoshioka, M.; Ohno, M. *Tetrahedron Lett.* **1992**, *33*, 2575.
280d. Kobayashi, S.; Takahashi, H.; Imai, N. *Chem. Lett.* **1994**, 177.
280e. Kobayashi, S.; Takahashi, H.; Imai, N.; Sakamoto, K. *Tetrahedron Lett.* **1994**, *35*, 7045.
281. Charette, A. B.; Brochu, C. *J. Am. Chem. Soc.* **1995**, *117*, 11367.
282. Charette, A. B.; Molinaro, C.; Brochu, C. *J. Am. Chem. Soc.* **2001**, *123*, 12168.
283. Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651.
283a. Charette, A. B.; Juteau, H.; Lebel, H.; Molinaro, C. *J. Am. Chem. Soc.* **1998**, *120*, 11943.
283b. Charette, A. B.; Juteau, H.; Lebel, H.; Deschenes, D. *Tetrahedron Lett.* **1996**, *37*, 7925.
284. Charette, A. B.; Lebel, H. *J. Org. Chem.* **1995**, *60*, 2966.
285. Charette, A. B.; Lebel, H.; Gagnon, A. *Tetrahedron* **1999**, *55*, 8845.
286. Yang, Z.; Lorenz, J. C.; Shi, Y. *Tetrahedron Lett.* **1998**, *39*, 8621.
287. Charette, A. B.; Lacasse, M.-C. *Org. Lett.* **2002**, *4*, 3351.
288. Charette, A. B.; Beauchemin, A.; Francoeur, S. *J. Am. Chem. Soc.* **2001**, *123*, 8139.
289. Lorenz, J. C.; Long, J.; Zhiqiang, Y.; Xue, S.; Xie, Y.; Shi, Y. *J. Org. Chem.* **2004**, *69*, 327.
290. Charette, A. B.; Gagnon, A.; Fournier, J.-F. *J. Am. Chem. Soc.* **2002**, *124*, 386.
291. Fournier, J.-F.; Charette, A. B. *Eur. J. Org. Chem.* **2004**, 1401.
292. Motherwell, W. B. *J. Organomet. Chem.* **2001**, *624*, 41.
292a. Aqil, R.; Motherwell, W. B.; Roberts, L. R.; Russell, C. A. *Tetrahedron Lett.* **2002**, *43*, 9671.
293. Motherwell, W. B.; O'Mahony, D. J. R.; Popkin, M. E. *Tetrahedron Lett.* **1998**, *39*, 5285.
293a. Fletcher, R. J.; Motherwell, W. B.; Popkin, M. E. *Chem. Commun.* **1998**, 2191.
293b. Bégis, G.; Cladingboel, D.; Motherwell, W. B. *Chem. Commun.* **2003**, 2656.
294. Matsubara, S.; Ukai, K.; Fushimi, H.; Yokota, Y.; Yoshino, H.; Oshima, K.; Omoto, K.; Ogawa, A.; Hioki, Y.; Fujimoto, H. *Tetrahedron* **2002**, *58*, 8255.
294a. Nomura, K.; Oshima, K.; Matsubara, S. *Tetrahedron Lett.* **2004**, *45*, 5957.
295. Marek, I. *Tetrahedron* **2002**, 9463.
296. Wipf, P.; Kendall, C. *Org. Lett.* **2001**, *3*, 2773.
296a. Wipf, P.; Kendall, C. *Chem. Eur. J.* **2002**, *8*, 1778.
297. Wipf, P.; Stephenson, C. R. J.; Okumura, K. *J. Am. Chem. Soc.* **2003**, *125*, 14694.
298. Varghese, J. P.; Knochel, P.; Marek, I. *Org. Lett.* **2000**, *2*, 2849.
299. Varghese, J. P.; Zouev, I.; Aufauvre, L.; Knochel, P.; Marek, I. *Eur. J. Org. Chem.* **2002**, 4151.
300. Abramovitch, A.; Varghese, J. P.; Marek, I. *Org. Lett.* **2004**, *6*, 4151.
301. Sklute, G.; Amsallem, D.; Shabli, A.; Varghese, J. P.; Marek, I. *J. Am. Chem. Soc.* **2003**, *125*, 11776.
302. Brogan, J. B.; Zercher, C. K. *J. Org. Chem.* **1997**, *62*, 6444.
302a. Hilgenkamp, R.; Zercher, C. K. *Tetrahedron* **2001**, 8793.
302b. Verbicky, C. A.; Zercher, C. K. *J. Org. Chem.* **2000**, *65*, 5615.
303. Lai, S.; Zercher, C. K.; Jasinski, J. P.; Reid, S. N.; Staples, R. J. *Org. Lett.* **2001**, *3*, 4169.
304. Tückmankel, W.; Oshima, K.; Nozaki, H. *Chem. Ber.* **1986**, *119*, 1581.
304a. Fabicon, R. M.; Parvez, M.; Richey, H. G. *J. Am. Chem. Soc.* **1991**, *113*, 1412.
304b. Fabicon, R. M.; Parvez, M.; Richey, H. G. *J. Am. Chem. Soc.* **1991**, *113*, 6680.
304c. Purdy, A. P.; George, C. F. *Organometallics* **1992**, *11*, 1955.
304d. Toshiro, H.; Wada, H.; Oku, A. *J. Org. Chem.* **1995**, *60*, 5370.
305. Uchiyama, M.; Koike, M.; Kameda, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1996**, *118*, 8733.
305a. Kondo, Y.; Takazawa, N.; Yamazaki, C.; Sakamoto, T. *J. Org. Chem.* **1994**, *59*, 4717.
306. Houpis, I. N.; Molina, A.; Dorziotis, I.; Reamer, R. A.; Volante, R. P.; Reider, P. J. *Tetrahedron Lett.* **1997**, *38*, 7131.
307. Kondo, Y.; Komine, T.; Fujinami, M.; Uchiyama, M.; Sakamoto, T. *J. Comb. Chem.* **1999**, *1*, 123.
307a. Reginato, G.; Taddei, M. *II Farmaco* **2002**, *57*, 373.
308. Harada, T.; Kaneko, T.; Fujiwara, T.; Oku, A. *J. Org. Chem.* **1997**, *62*, 8966.
309. Rao, S. A.; Knochel, P. *J. Org. Chem.* **1991**, *56*, 4591.
310. Frangin, Y.; Gaudemar, M. *C.R. Hebd. Scéances Acad. Sci., Ser. C* **1974**, *278*, 885.
310a. Bellasoued, M.; Frangin, Y.; Gaudemar, M. *Synthesis* **1977**, 205.
310b. Knochel, P.; Normant, J.-F. *Tetrahedron Lett.* **1986**, *27*, 5727.
310c. Beruben, D.; Marek, I.; Labaudinière, L.; Normant, J.-F. *Tetrahedron Lett.* **1993**, *34*, 2303.
310d. Normant, J.-F.; Quirion, J.-C. *Tetrahedron Lett.* **1989**, *30*, 3959.
310e. Marek, I.; Lefrançois, J.-M.; Normant, J.-F. *Synlett* **1992**, 633.
310f. Marek, I.; Lefrançois, J.-M.; Normant, J.-F. *Tetrahedron Lett.* **1992**, *33*, 1747.
310g. Marek, I.; Lefrançois, J.-M.; Normant, J.-F. *Tetrahedron Lett.* **1991**, *32*, 5969.

310h. Marek, I.; Normant, J.-F. *Tetrahedron Lett.* **1991**, *32*, 5973.
311. Klement, I.; Lennick, K.; Tucker, C. E.; Knochel, P. *Tetrahedron Lett.* **1993**, *34*, 4623.
312. Knochel, P.; Xiao, C.; Yeh, M. C. P. *Tetahedron Lett.* **1988**, *29*, 6697.
313. Wang, F.; Tang, J.; Labaudinière, L.; Marek, I.; Normant, J.-F. *Synlett* **1995**, 723.
314. Viseux, E. M. E.; Parsons, P. J.; Pavey, J. B. J. *Synlett* **2003**, 861.
315. Aponick, A.; McKinley, J. D.; Raber, J. C.; Wigal, C. T. *J. Org. Chem.* **1998**, *63*, 2676.
316. Aponick, A.; Buzdygon, R. S.; Tomko, R. J., Jr.; Fazal, A. N.; Shughart, E. L.; McMaster, D. M.; Myers, M. C.; Pitcock, W. H., Jr.; Wigal, C. T. *J. Org. Chem.* **2002**, *67*, 242.
317. Campbell, J. B.; Firor, J. W. *J. Org. Chem.* **1995**, *60*, 5243.

9.05
Boron

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9.05.1 Introduction

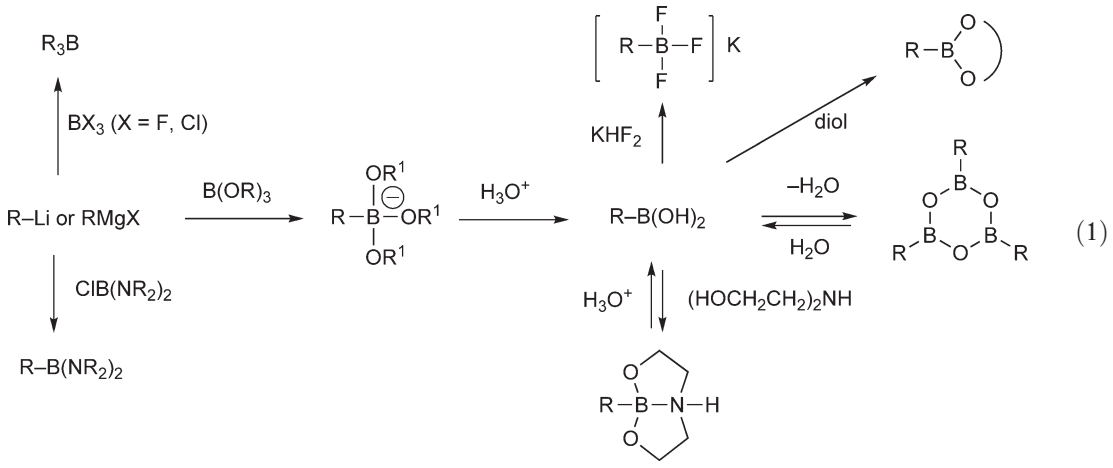
Organoboron compounds have been playing an increasingly important role for organic synthesis, functional molecules, functional polymers, ^{10}B carriers for neutron capture therapy, and biologically active agents. This chapter aims to update the applications of organoboron compounds in organic synthesis covered in COMC (1995). The synthesis of boron compounds by C–B bond-forming reactions or by reactions at sites other than the B–C bond are discussed in Section 9.05.2. The catalytic and stoichiometric use for C–C and C–heteroatom bond-forming reactions and the use of boron compounds as Lewis acid catalysts or reducing reagents are summarized in Section 9.05.3. The references used are mainly those that appeared in 1993–2004, but the reviews cited in each section give the background of each chemistry and additional references related to the topics. There are excellent books covering the synthesis of organoboron compounds and their use in selective organic syntheses.[1–3]

9.05.2 Synthesis of Organoboron Compounds

9.05.2.1 By C–B Bond-forming Reactions

9.05.2.1.1 Transmetallation between organometallic compounds and BX_3

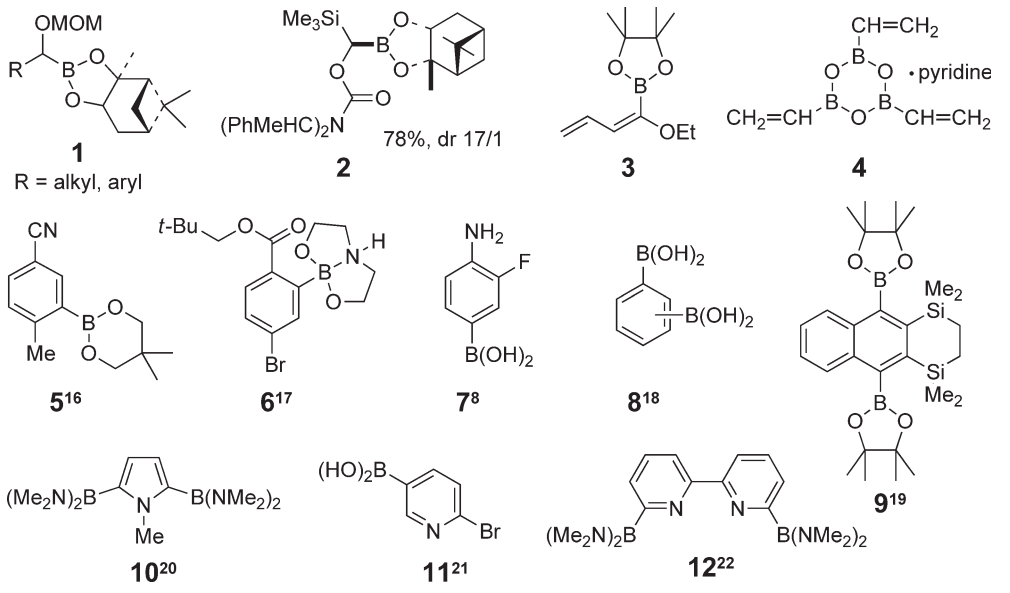
Transmetallation is perhaps the most straightforward method for preparing organoboron compounds if the requisite organometallic reagent is easily available. Organomagnesium or -lithium reagents are the most widely used reagents because of their availability and easy preparation (Equation (1)). Other organometallic derivatives of Al, Zn, Si, Sn, Zr, and Hg also undergo transmetallation to alkoxyboranes or haloboranes.



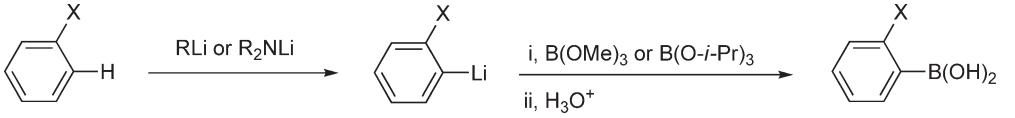
(1)

Selected examples synthesized by transmetallation with organolithium or -magnesium reagents are shown in Scheme 1. Reaction between racemic alkoxyorganolithium or carbamate reagents with chiral boronates provided optically active boronates **1**[4] and **2**[5] with moderate diastereoselectivities. 1,3-Butadienylboronic esters **3**,[6] vinylboroxine stabilized with pyridine **4**,[7] and arylboronic acids or esters, for example **5–12**[8,16–22] and others[8–15] have been synthesized by transmetallation between organolithium or -magnesium reagents with $(MeO)_3B$, $(i\text{-}PrO)_3B$ or $ClB(NR_2)_2$. This method often suffered from compatibility of functional groups or instability of aromatic heterocyclic lithium reagents. *In situ* quenching of the lithium intermediates at low temperature via addition of BuLi to a mixture of ArBr and $B(O^iPr)_3$ allowed the syntheses of pyridine-, quinoline-, 2-chlorophenyl-, and 4-cyanophenylboronic acid.[14]

The *ortho*-lithiation of arenes directed by $CONR_2$,[23] $OCONR_2$,[24] OMe,[25] SO_2NEt_2,[26] $NHCO_2t\text{-}Bu$,[27] CO_2R,[17,28] CN,[28] F or Cl,[15,28] and tetrazole rings[29] is an alternative for regioselective preparation of aryllithiums (Equation (2)), whereby, LDA[15,17] and lithium 2,2,6,6-tetramethylpiperidide (LTMP)[28] have been recognized as the better reagents for selective *ortho*-metallation which has functional groups susceptible to BuLi.



Scheme 1 Synthesis of organoboronic acids, esters, and amides via transmetallation with Li or Mg compounds.

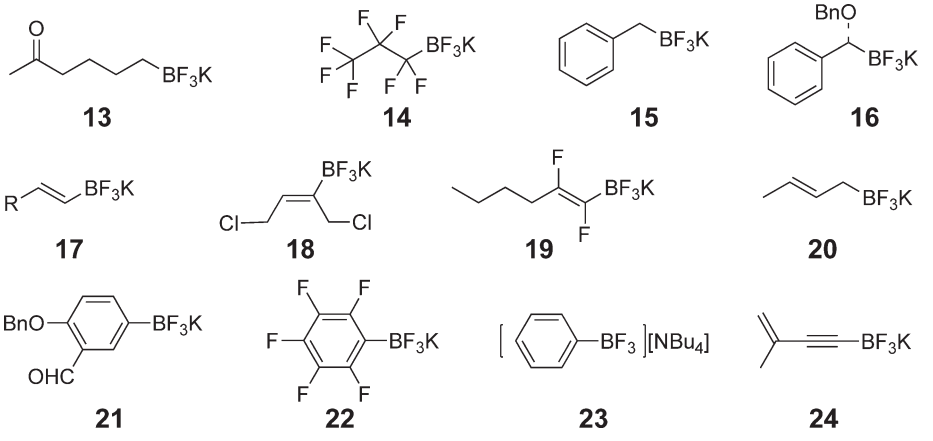


(2)

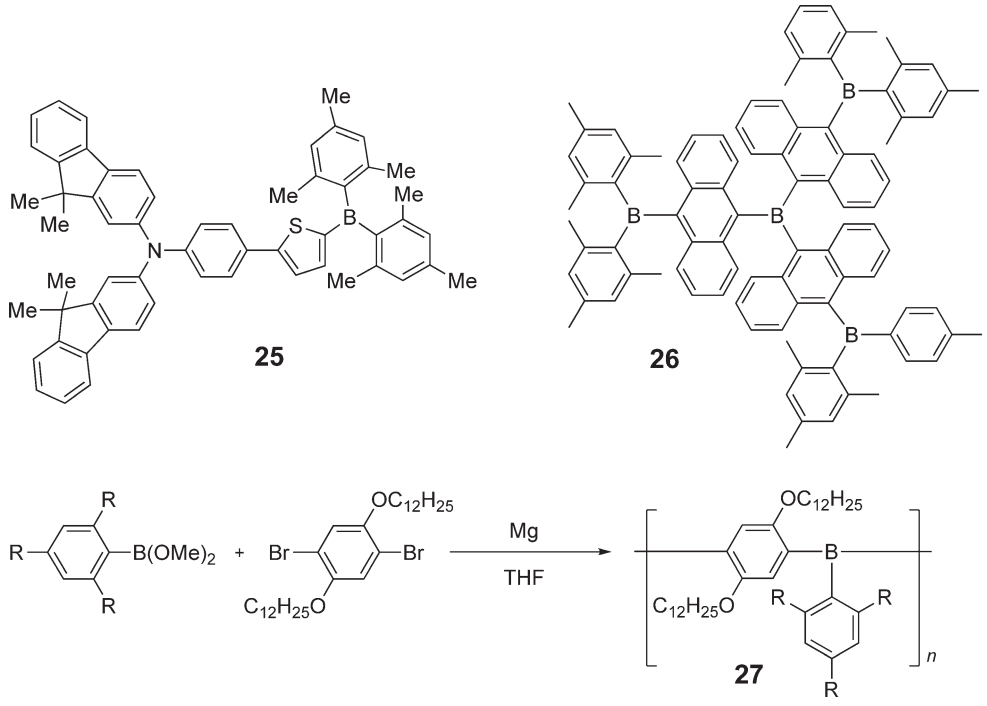
X = OR, SO_2NHR, $CONR_2$, CO_2R, CN, F, Cl, $NHCO_2R$

Synthesis and reactions of $[RBF_3]K$ have been extensively studied because of the simplicity of the preparation of pure and stable crystals compared to the corresponding boronic acids (Scheme 2).[30] Representative boron compounds, including alkyl **13**, **14**,[31,32] benzyl **15**, **16**,[33] 1-alkenyl **17–19**,[34–38] allyl **20**,[39,40] aryl **21–23**,[41–45] and 1-alkynyl **24**[41,46] derivatives, were synthesized. K^+ salts were obtained by treating organoboronic acids with KHF_2.[47,48] Bu_4N^+ salts, which are soluble in polar and nonpolar organic solvents, were prepared by sequential treatment of organoboronic acids with HF and Bu_4NOH.[43]

Arylboranes conjugated with an aromatic chain have been extensively studied due to their unique property as photonic and electronic molecular materials (**25**,[49] **26**[50,51]; Scheme 3). In contrast to small triarylboranes, sterically hindered boranes containing at least two mesityl groups are stable to air and hydrolytic B–C bond cleavage.



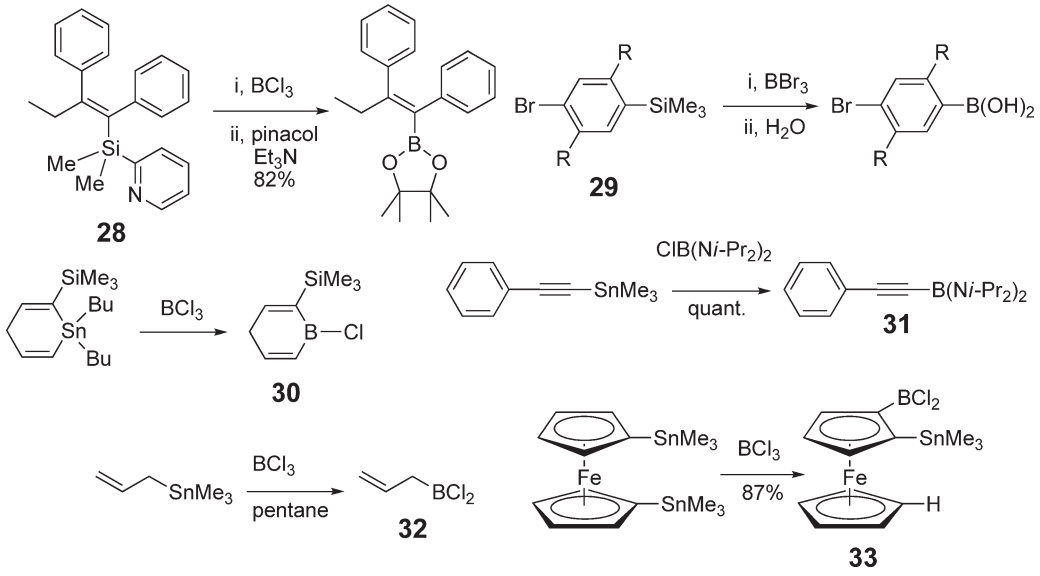
Scheme 2 Synthesis of $[RBF_3]K$ from $ArB(OH)_2$ and KHF_2.



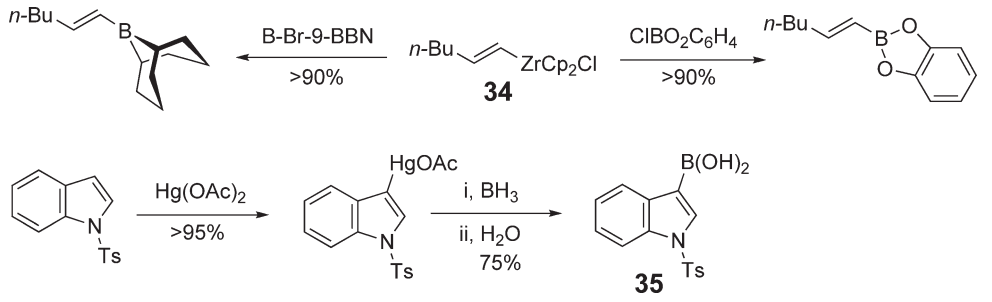
Scheme 3 Synthesis of triorganoboron compounds via transmetallation with Li or Mg compounds.

Poly(phenylene)s expected as a new class of n-type conjugate polymers were synthesized in high yields by the Barbier procedure **27**.[52]

Transmetallation between BX_3 (X = Cl, Br) and organosilicon or -tin compounds is often more advantageous than the lithium or magnesium method (Scheme 4). Although silicon is not as easily displaced as tin derivatives, 1-alkenyl **28**[53,54] and aryl **29**[55–57] compounds reacted with BCl_3. Organotin compounds smoothly reacted with BCl_3 or $ClB(NR_2)_2$ to give boracycles **30**,[58,59] 1-alkynylboranes **31**,[60] allylboranes **32**,[59] and ferrocene-based Lewis acids **33**.[55,56,61]



Scheme 4 Synthesis of organoboron compounds via transmetallation with Si or Sn compounds.



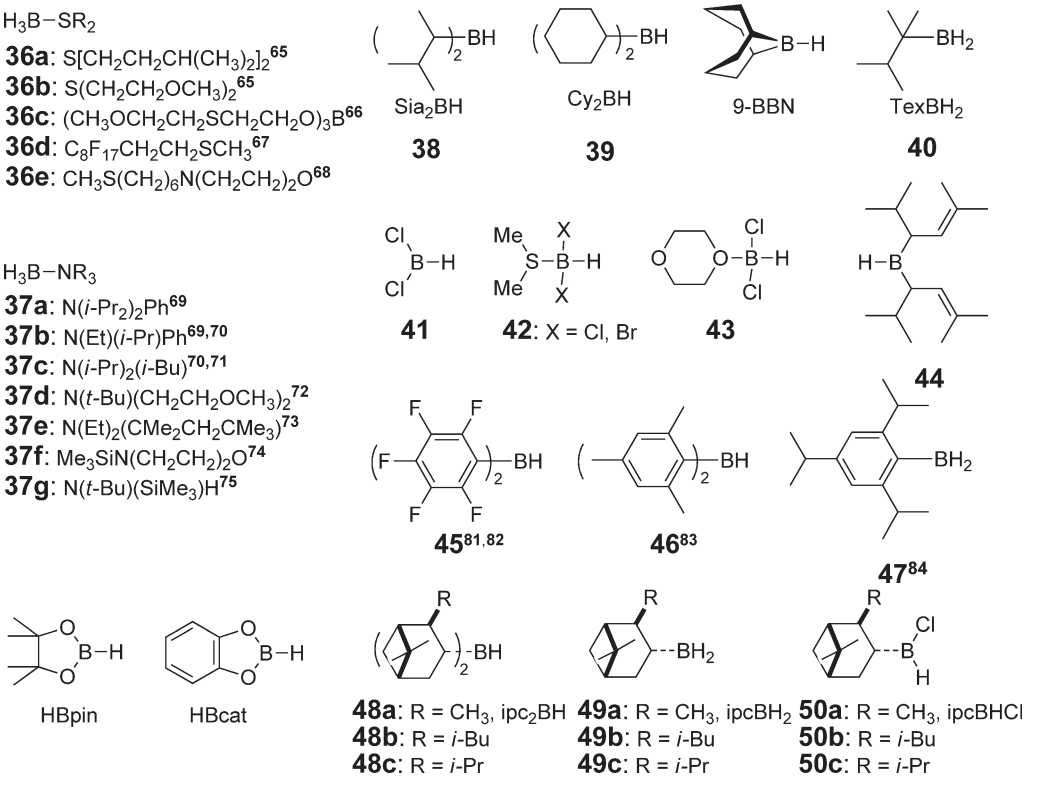
Scheme 5 Synthesis of organoboron compounds via transmetallation with Zr and Hg compounds.

1-Alkenylzirconium compounds **34** obtained by the hydrometallation of alkynes were transformed to 1-alkenylboron compounds via transmetallation with B-halo-9-BBN or B-chlorocatecholborane[62,63] (Scheme 5). Mercuration followed by transmetallation to BH_3 was advantageous over the lithiation route in the synthesis of indole-3-boronic acid **35**.[64]

9.05.2.1.2 Uncatalyzed hydroboration of alkenes and alkynes

Under mild experimental conditions, compounds containing B–H bond add to the alkenes or alkynes to form *anti*-Markovnikov hydroboration products via *syn*-insertion of alkenes. A variety of borane reagents are available for selective hydroboration (Scheme 6).

Odorless borane–sulfide complexes **36a–e**[65–68] and borane–amine complexes **37a–g**[69–75] have been recently prepared because of the growing importance of diborane for the synthesis of pharmaceuticals or other compounds and certain inconveniences of well-established reagents, for example, the low concentration and instability of BH_3·THF and high volatility, flammability, and unpleasant odor of dimethyl sulfide from BH_3·SMe_2. Trialkylsilanes, for example, Me_3SiH, were found to be an efficient reducing reagent for the *in situ* preparation of



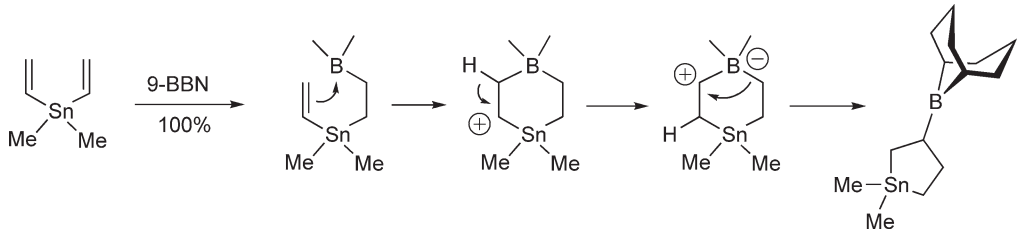
Scheme 6 Hydroboration reagents.

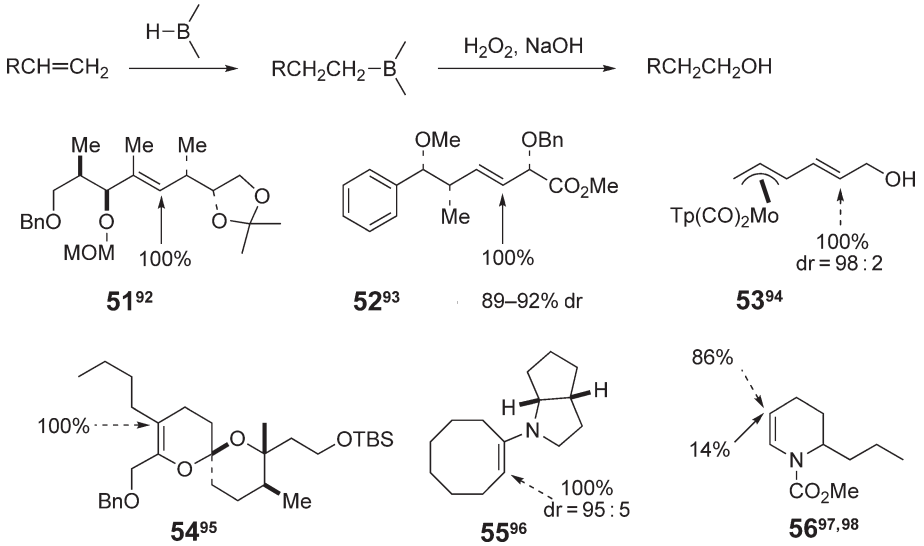
highly reactive ether-free chloroboranes **41** from BCl_3.[76] In addition to the conventional $BHX_2{\cdot}SMe_2$ **42**, analogous Lewis acid–base adducts of dioxane–BH_2Cl[77,78] and dioxane–$BHCl_2$ **43**[79] were synthesized as superior reagents for hydroboration of alkenes and alkynes. Di(isopropylprenyl)borane **44**[80] is a new hydroboration reagent that was generated *in situ* and provides rapid access to alkyl and 1-alkenylboronic acids. A new series of diarylboranes include **45–47**.[81–84] Apoisopinylboranes **48b**,**48c**,[85] **49b**,**49c**,[86–88] **50b**, and **50c**,[89–91] are derivatives of traditional isopinocamphenylboranes **48a**, **49a**, **50a** which have been used for asymmetric hydroboration.

Hydroboration–oxidation is a well-documented protocol for effecting the *syn*- hydration of alkenes. The high regio-, stereo-, or chemoselectivity in the addition of borane reagents has been extensively used in the transformation of alkenes to alcohols (Scheme 7). Internal non-bonded interactions or chelation to ether oxygen resulted in high diastereoface selectivity in the addition of $BH_3{\cdot}THF$ or $BH_3{\cdot}SMe_2$ to alkenes such as **51–56**.[92–98] Other reported examples are the hydroboration of enamines derived from 2-norbornanone,[99] cyclic enamides,[98] and homoallyl alcohols.[100]

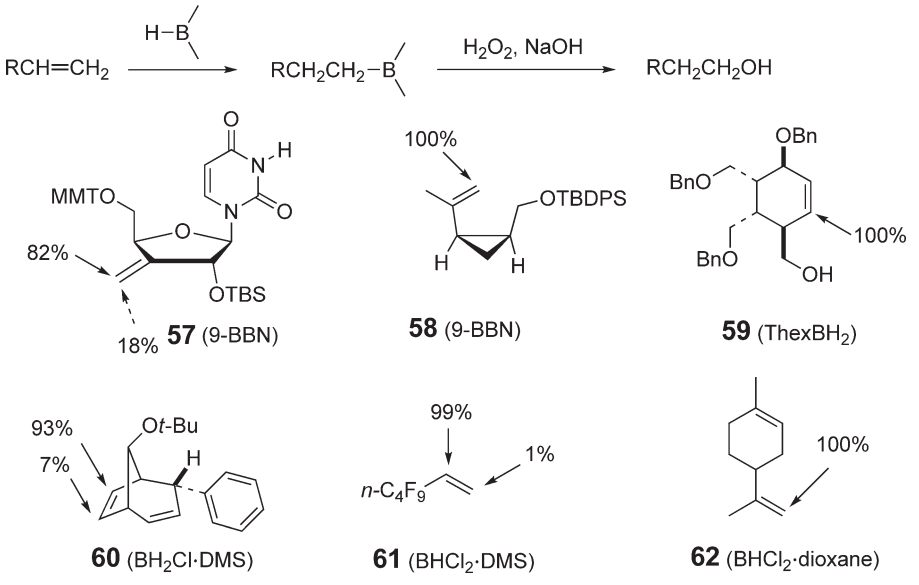
Disiamylborane **38**, dicyclohexylborane **39**, 9-BBN, and other borane reagents having steric bulk are more sensitive to steric hindrance than $BH_3{\cdot}THF$ in the addition to alkenes. The selectivity can also be effected by the electrophilicity of borane reagents (Scheme 8). 9-BBN added from the less hindered face of the double bond of **57**[101] and **58**.[102] The oxy function of homoallylic alcohols **59** played a role in promoting the addition of $ThexBH_2$ from the same face of the hydroxy group via the formation of a borinic ester intermediate.[103,104] The regioselectivity was significantly improved when using the electrophilic reagent $BHCl_2$. The hydroboration of **60** resulted in a 4 : 1 ratio with $BH_3{\cdot}THF$, a 6 : 1 ratio with 9-BBN, and a 16 : 1 ratio with $BHCl_2{\cdot}SMe_2$ by the directive effect of a remote double bond.[105] $BHCl_2$ added to the internal carbon of **61**, whereas $BH_3{\cdot}THF$ give a mixture of internal and terminal adduct in a 85 : 5 ratio.[106,107,108] The dioxane–BH_2Cl complex selectively added to the less-hindered terminal C–C double bond of **62**.[77,78]

Hydroboration of divinyltin with 9-BBN unexpectedly resulted in a previously unknown cyclization (Equation (3)).[109] This unusual behavior contrasts markedly with that of other metalloids (Si, Ge) which undergo normal dihydroboration.



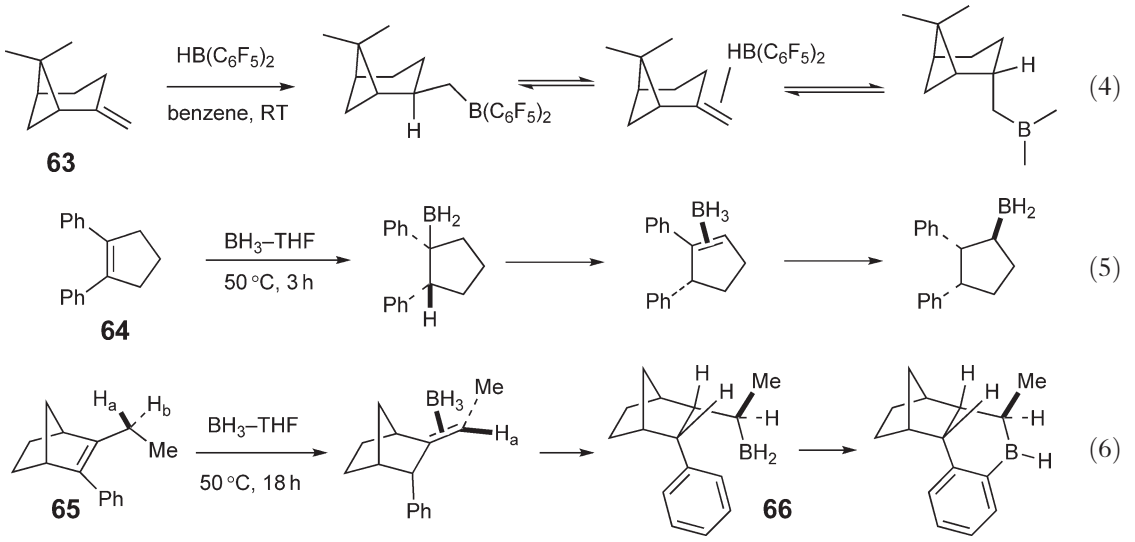


Scheme 7 Regio- and stereoselectivity in hydroboration with $BH_3{\cdot}THF$ or $BH_3{\cdot}BMS$ (solid arrows indicate an attack of boron atom from the front face and dotted arrows from the back face).



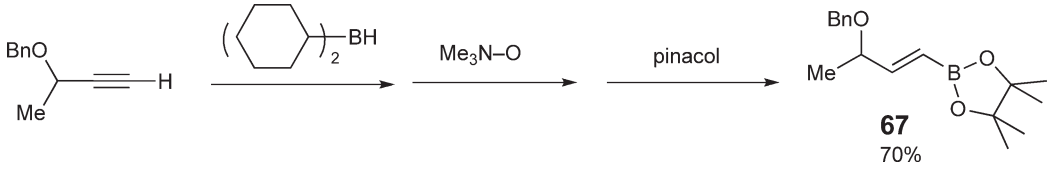
Scheme 8 Regio- and stereoselectvity in hydroboration with 9-BBN, $ThexBH_2$, and $BHCl_2$.

Whereas most organoboranes undergo rearrangements at an elevated temperature via a dehydroboration–hydroboration sequence, it smoothly takes place at room temperature for the sterically hindered products. Hydroboration–oxidation of β-pinene with $HB(C_6F_5)_2$ resulted in the formation of a thermally controlled product, *trans*-myrtanol (Equation (4)).[81,82] Hydroboration of cyclic and acyclic tetrasubstituted alkenes underwent a facile 1,2-thermal rearrangement of the boryl group to release the steric strain in the hydroboration product. The reaction occurred with excellent stereoselectivity, thus allowing the control of up to three stereogenic centers (Equation (5)).[110–112] It was also noted that the resulting BH_2 group undergoes borylation of an adjacent aromatic C–H bond[113] or allylic C–H bond[114,115] under mild conditions (Equation (6)).

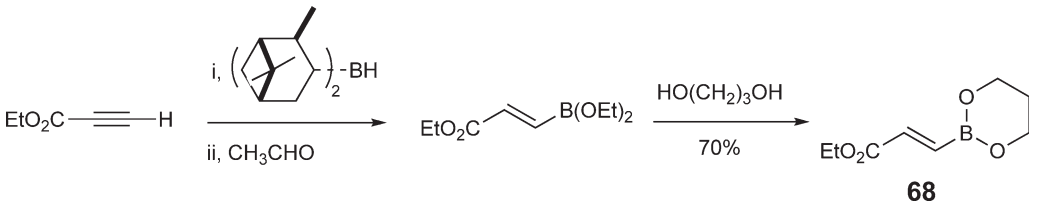


1-Alkenylboronic acids and esters have been prepared by thermal or catalyzed hydroboration of 1-alkynes with catecholborane (HBcat), pinacolborane (HBpin), or dihaloboranes **41–43**, followed by hydrolysis to boronic acids or alcoholysis to boronic esters. A convenient alternative to improve chemo- and regioselectivity is the hydroboration of alkynes with dialkylboranes. For selective removal of dummy groups, the oxidation of two cyclohexyl groups was conduced by treatment of 1-alkenyl(dicyclohexyl)borane intermediates with Me_3N–O (Equation (7)).[116] The

removal of the isopinocampheyl group took place in refluxing acetaldehyde (Equation (8)).[117–119] Hydroboration of terminal alkynes with 9-BBN provides 1-alkenyl-9-BBN together with variable amounts of 1,1-diborylalkanes. A new completely stereoselective route to *trans*-1-alkenyl-9-BBN was found to be the monodeboronation of 1,1-diborylalkenes with PhCHO via an electrocyclic pathway (Equation (9)).[120] Di(isopropylprenyl)borane was newly developed as the most convenient reagent that was generated *in situ* and that provided rapid access to alkyl and 1-alkenylboronic acids via treatment with ROH or aqueous CH_2O at room temperature (Equation (10)).[80]



(7)



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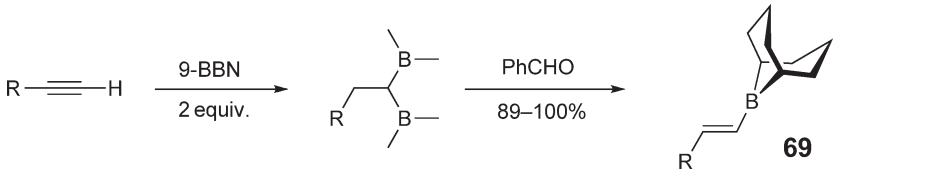
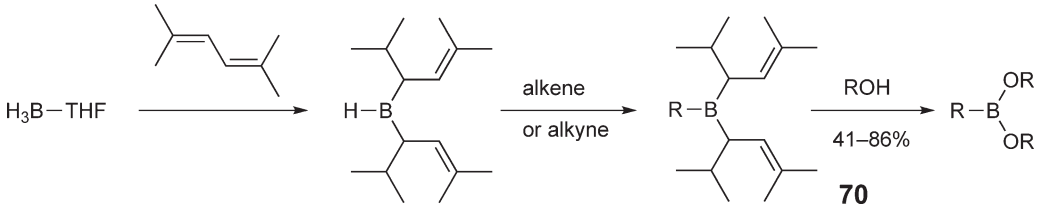


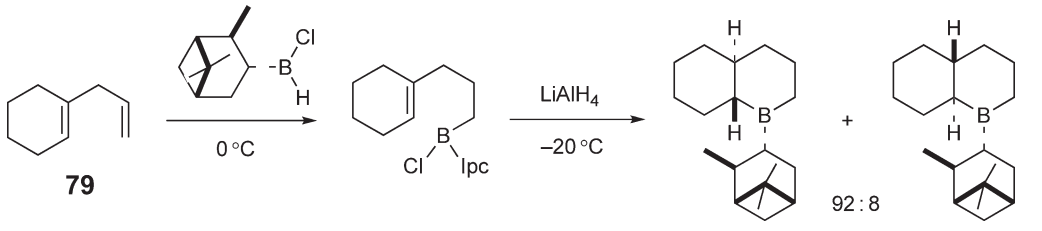
(9)



(10)

Asymmetric hydroboration of prochiral alkenes with isopinocampheylboranes such as Ipc_2BH **48a**, $IpcBH_2$ **49a**, and IpcBHCl **50a** provided optically active organoboranes. Optically pure crystalline Ipc_2BH resulted in excellent enantioselectivity for asymmetric hydroboration of (*Z*)-2-pentene (83% ee), norbornene (83% ee), 2,3-dihydrofurane (99% ee), 2,5-dihydrofurane (99% ee), 2,3-dihydrothiophene (99% ee), and *N*-Bnz-2,3-dihydropyrrole (99% ee).[121] This exceptional ability of Ipc_2BH to hydroborate *cis*-alkenes, cyclic alkenes, and heterocyclic alkenes has been applied to the various synthesis of chiral alcohols via a hydroboration–oxidation sequence (Scheme 9). The reported examples include hydroboration of **71**[122] and **72**[123] with Ipc_2BH, **73** with $IpcBH_2$,[124] and cyclic and acyclic alkenes **74** with IpcBHX (X = Cl, Br) generated *in situ* from $IpcBX_2$ and Me_3SiH.[125,126] Ipc_2BH also worked well for desymmetrization of tropinone derivatives **75**,[127] alkenyl ethers **76**[128] and **77**,[129] and enamines **78**.[130]

The stepwise double hydroboration of dienes with $IpcBHCl{\cdot}OEt_2$ synthesized from $IpcBH_2$ and HCl provided *trans*-fused bicyclic boron compounds with high stereo- and enantioselectivities (Equation (11)).[131] The boron atom of the products were then substituted with a carbonyl group by DCME reaction using Cl_2CHOCH_3 and $LiOCMe_3$ to give chiral bicyclic ketones with up to 99% de and ee.



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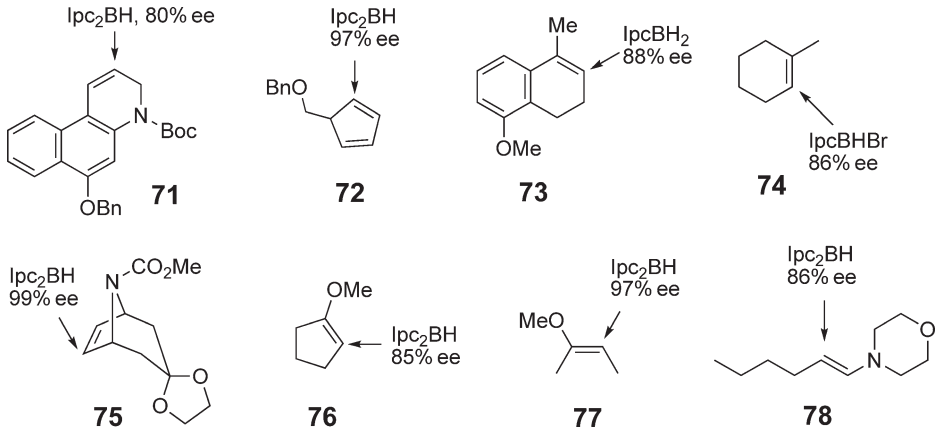


Scheme 9 Asymmetric hydroboration with Ipc_2BH, $IpcBH_2$, and IpcBHX.

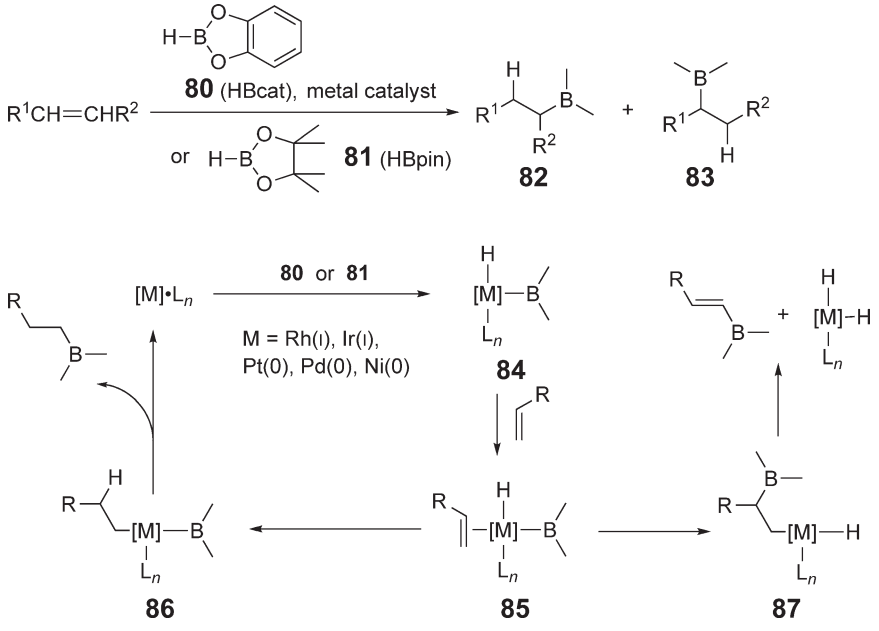
9.05.2.1.3 Catalyzed hydroboration of alkenes and alkynes

The catalyzed hydroboration did not attract much attention until Sneddon in 1980 and Nöth in 1985 reported that rhodium complexes significantly accelerate the addition of B–H bond to alkenes or alkynes. The protocol was proved to be an interesting strategy to realize the different chemo-, regio-, diastereo-, and enantioselectivities, relative to the uncatalyzed reaction. The reaction has been reviewed.[132–135]

9.05.2.1.3.(i) Hydroboration of alkenes and alkynes

Most studies of catalyzed hydroboration have employed HBcat **80** and HBpin **81** (Scheme 10). A catalytic cycle proposed for the metal–phosphine complexes involves the oxidative addition of borane to a low-valent metal yielding a boryl complex **84**; the coordination of alkene leads to the insertion of the double bond into the M–H bond **86** or **87**, and finally the reductive elimination or β-hydride elimination giving a product.

Many metal complexes catalyze the hydroboration. A neutral rhodium–phosphine complex $RhCl(PPh_3)_3$ is the most studied catalyst for the hydroboration of alkenes, but the complex is unfortunately highly sensitive to air. Thus, handling the catalyst under argon or in air resulted in different regioselectivity. The *in situ* preparation of the catalyst



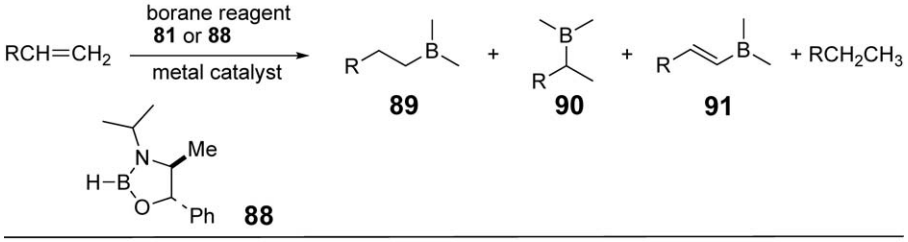
Scheme 10 Catalyzed hydroboration of alkenes.

from $[RhCl(cod)]_2$ and Ph_3P was a convenient alternative giving similarly active catalyst. The internal hydroboration product (**83**; R^1 = aryl; R^2 = H) was selectively given when using $[Rh(cod)_2]BF_4$/2PPh_3[136] and $[Rh(Ph_2Si(CH_2PPh_2)]$-PF_6,[137] which was in contrast to Cp_2TiMe_2,[138,139] $RuCl_2(PPh_3)_4$,[140] $[Ir(cod)Cl]_2$-dppe,[141] SmI_3,[142] $La[N(TMS)_2]_3$[143] to give terminal product **82** for styrene and HBcat or HBpin. Although vinylarenes change the regioselectivity depending on the catalysts and hydroboration reagents, HBpin and HBcat selectively added to the terminal carbon of aliphatic alkenes **82**; R^1 = alkyl, aryl; R^2 = H) when $PhCl(PPh_3)_3$,[144,145] SmI_3,[142] $[RhCl(C_2H_4)_2]_2$/2.5 PPh_3,[146] $[Ir(cod)Cl]_2$/2dppm,[141] Cp_2ZrHCl,[147] and $La[N(TMS)_2]_3$[143] were used for 1-hexene or 1-octene. Aliphatic internal alkenes often resulted in the formation of terminal products. Hydroboration with HBpin catalyzed by cationic rhodium and the iridium complexes was prone to isomerize the boron atom to the terminal carbon.[141]

The dehydrogenative coupling of borane is an attractive method to directly synthesize (*E*)-1-alkenylboronates from alkenes (Scheme 11). The reported procedures recommended a combination of vinylarene, a sterically hindered borane such as HBpin **81** or oxazaborolidine **88**, and a phosphine-free rhodium(I) catalyst for achieving selective coupling (entries 1 and 2,[148,149] entry 3,[150,151] and entry 4).[152] The reaction required 2 equiv. of vinylarene because H_2, generated by β-hydride elimination, hydrogenates a molar amount of vinylarene.

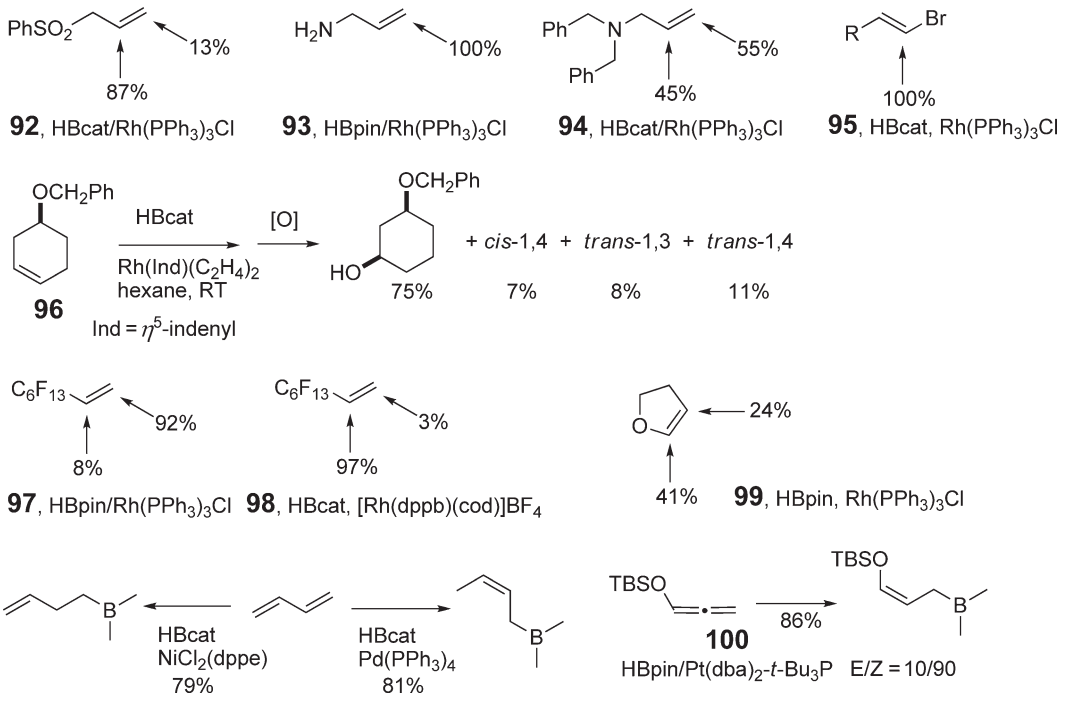
The catalyzed hydroboration of functionalized alkenes resulted in different regio- and stereoselectivities from that of uncatalyzed hydroboration (Scheme 12). Hydroboration of allyl sulfones **92** with 9-BBN gave terminal products (**82**/**83** = 100/0), whereas rhodium-catalyzed reaction of **80**[153] showed internal selectivity, thus suggesting a role of the SO_2 group as a directing group through complexing with rhodium metal. Such directing effect of heteroatom was also reported in the hydroboration of **96**.[154,155] Hydroboration of allylamine **93**[156] with HBpin selectively yielded a terminal product that is in contrast to the hydroboration of protected allylamine **94**[157] resulted in a mixture of two isomers. 1-Bromoalkene **95**[157–159] gave a single isomer. Perfluoroethylenes **97** and **98**[160] were hydroborated in the presence of a rhodium catalyst, whereas the uncatalyzed reaction of 9-BBN or Sia_2BH failed to yield the hydroboration products due to the low nucleophilicity of fluoroalkenes. The reaction afforded one of the two possible isomers with excellent regioselectivity by selecting borane and the catalyst appropriately. The nickel-catalyzed hydroboration of 1,3-butadiene with HBcat provided a homoallylboronate[161] that was in contrast to the palladium-catalyzed reaction giving a *cis*-allylboronate via 1,4-addition of the H–B bond.[162] Cyclic vinyl ethers **99**[157] resulted in a mixture of two isomers, and alkoxyallenes **100**[163] gave a single product via addition of a borane at the terminal double bond.

The catalyzed hydroboration of alkynes with HBcat or HBpin afforded (*E*)-1-alkenylboron compounds at room temperature (Table 1). The $RhCl(PPh_3)_3$-catalyzed reaction of phenylacetylene resulted in a complex mixture of two regioisomers of alkenyl boronates, hydrogenation products, and a trace of a diboration product. Alternatively, $Cp_2Ti(CO)_2$ (entries 1 and 2)[138,139] and nickel-bisphosphine complexes (entries 6 and 7)[164,165] were found to be good catalysts giving a selectivity comparable to that of the uncatalyzed reaction. The rhodium(I)–$^iPr_3P$ complex catalyzed the previously unknown *trans*-hydroboration of terminal alkynes directly yielding *cis*-1-alkenylboron compounds (entries 3–5).[166] A vinylidene complex generated by the oxidative addition of the terminal C–H bond to the catalyst was proposed as a key intermediate of the formal *trans*-hydroboration.



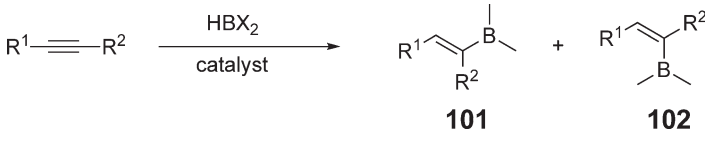
Entry	*Alkene* (*R*=)	*Borane*	*Catalyst*	**89** (%)	**90** (%)	**91** (%)
1	Ph	**81** (HBpin)	$[RhCl(cod)]_2$, RT	3	3	94
2	*n*-Bu	**81** (HBpin)	$[RhCl(cod)]_2$, RT	95	0	5
3	$H_2N(CH_2)_3OCH{=}CH_2$	**81** (HBpin)	$RhCl(PPh_3)_3$, 65 °C			Major
4	4-$MeOC_6H_5$	**88**	$[RhCl(CH_2{=}CH_2)_2]_2$, RT			98

Scheme 11 Dehydrogenative hydroboration giving 1-alkenylboron compounds.



Scheme 12 Catalyzed hydroboration of functionalized alkenes.

Table 1 Catalyzed hydroboration of alkynes

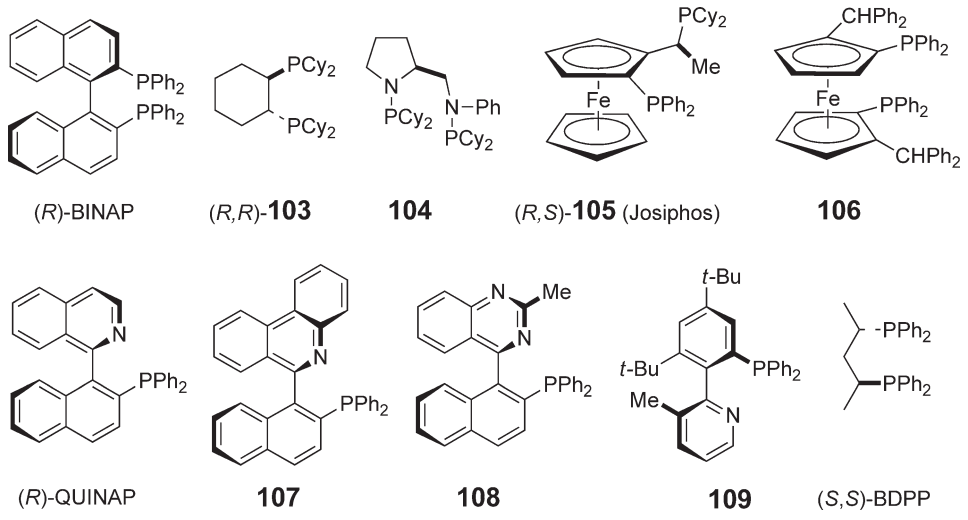


	Alkyne				
Entry	R^1	R^2	HBX_2	*Catalyst/solvent/temp.*	*Yield* (%) **101/102**
1	Ph	H	HBcat	$Cp_2'Ti(CO)_2$, ether, RT	96 (100/0)
2	n-C_4H_9	H	HBcat	$Cp_2'Ti(CO)_2$, ether, RT	97 (100/0)
3	Ph	H	HBcat	$[Rh(cod)Cl]_2$/4i-Pr_3P, Et_3N	60 (1/99)
4	n-C_8H_{17}	H	HBcat	$[Rh(cod)Cl]_2$/4i-Pr_3P, Et_3N	79 (1/99)
5	Me_3Si	H	HBcat	$[Rh(cod)Cl]_2$/4i-Pr_3P, Et_3N	70 (2/98)
6	MeS	Ph	HBcat	$NiCl_2$(dppe), benzene, RT	95 (100/0)
7	PhS	H	HBcat	$NiCl_2$(dppe), benzene, RT	90 (100/0)

9.05.2.1.3.(ii) Asymmetric hydroboration

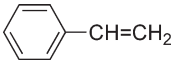
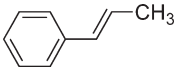
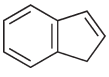
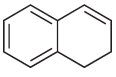
Asymmetric reaction is one of the most exciting features of catalyzed hydroboration since optically active phosphine ligands are the chiral auxiliaries most extensively studied for metal-catalyzed reactions (Scheme 13).[134] The chiral ligands used for asymmetric hydroboration of alkenes include BINAP,[136] **103–106**,[167–170] QUINAP,[171–173] **107–109**,[172,174–176] and BDPP.[177,178]

Various chiral ligands including bisphosphines and aminophosphines succeed in achieving high enantioselectivities exceeding 90% ee for vinylarenes (Table 2). The enantioselectivity is generally dependent on the reaction temperature; at lower temperature, higher selectivity being observed. Thus, the cationic rhodium complexes effective at temperature lower than 0 °C for HBcat were recognized to be the best catalysts. The cationic complexes were also advantageous in attaining high internal selectivity giving benzyl alcohol derivatives (entries **1–7**[136,167,169,170,172,173,176]). Among these



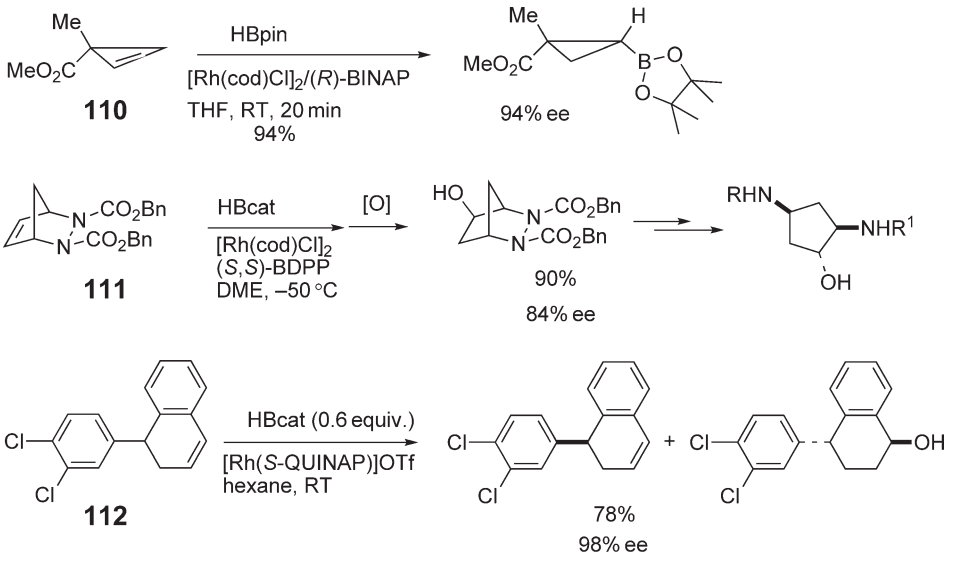
Scheme 13 Selected chiral ligands for asymmetric hydroboration.

Table 2 Asymmetric hydroboration of alkenes with HBcat **80**

Entry	*Alkene*	*Catalyst/temp.*	*Yield (%)*	*% ee*
1		$[Rh(cod)_2]BF_4$/*R*-BINAP, −78 °C	91	96 (R)[136]
2		[Rh(*S*-QUINAP)(cod)]OTf, RT	71	91 (S)[172,173]
3		$[Rh(nbd)_2]BF_4$/*R*,*S*-**105**, −78 °C	65	92 (R)[169]
4		[Rh(*S*,*S*-**106**)(cod)]BF_4, RT	100	85 (R)[170]
5		[Rh(*S*-**108**)(cod)]OTf, RT	88	90 (S)[175]
6		$[Rh(cod)_2]BF_3$/*R*,*R*-**103**, −35 °C	99	92 (S)[167]
7		$[Rh(cod)_2]BF_4$/*R*-**109**, 0 °C	72	90 (R)[176]
8		[Rh(*S*-QUINAP)(cod)]OTf, RT	64	95 (S)
9		[Rh(*R*-**107**)(cod)]OTf, RT	60	91 (S)
10		[Rh(*S*-**108**)(cod)]OTf, RT	86	94 (S)
11		[Rh(*S*-QUINAP)(cod)]OTf, RT	58	91 (S)
12		[Rh(*S*-**108**)(cod)]OTf, RT	99	99 (S)
13		[Rh(*R*-**107**)(cod)]OTf, RT	69	84 (R)
14		[Rh(*S*-**108**)(cod)]OTf, RT	98	89 (S)
15		[Rh(cod)Cl]$_2$/**104**, −78 °C	86	77

chiral ligands, P-N ligands such as QUINAP,[172,173] **107** (entries 9 and 13),[172] and **108** (entries 5, 10, 12, and 14)[175] exceptionally resulted in excellent enantioselectivity for cyclic and acyclic vinylarenes at room temperature. These ligands were not effective for other alkenes, but norbornene showed a moderate enantioselectivity (entry 15).[168]

A catalytic enantioselective hydroboration of cyclopropenes **110** was achieved by HBpin and Rh-BINAP catalyst with high *cis*-selectivity and enantioselectivity[177] (Scheme 14). The ester functionality served as a good directing group, providing virtually a single facial isomer. Enantioselective desymmetrization of *meso*-bicyclic hydrazines **111** provided an asymmetric method for synthesizing polysubstituted amino cyclopentanic cores.[178,179] BDPP was recognized as the best ligand to achieve 84% ee whereas traditional BINAP and QUINAP resulted in 0–24% ee.

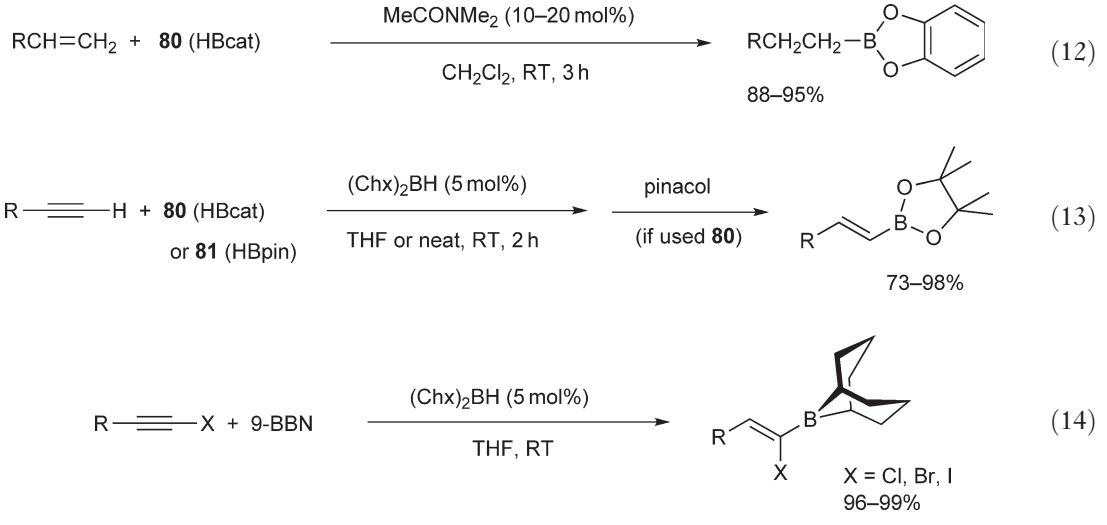


Scheme 14 Asymmetric hydroboration for synthesis.

The kinetic resolution of racemic alkenes **112** was demonstrated in asymmetric hydroboration with Rh-QUINAP catalyst. A 78% yield with 98% ee was achieved when using 0.6 equiv. of HBcat compared to the alkene.[180]

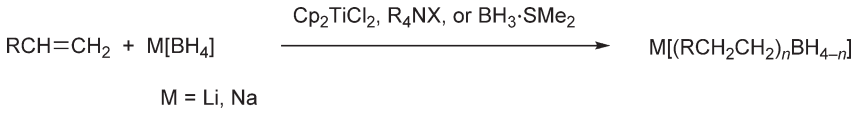
9.05.2.1.3.(iii) Non-metal catalysts

Hydroboration of alkenes with HBcat requires elevate temperatures, typically 70–100 °C. In contrast, the addition of HBcat to mono-, di-, tri-, and tetrasubstituted alkenes smoothly proceeded at room temperature in the presence of 10–20 mol% *N*,*N*-dimethylacetamide (DMA; Equation (12)).[181] Addition of DMA to HBcat generates a small amount of BH_3·DMA via disproportionation of HBcat. Thus, the mechanism involves hydroboration with BH_3·DMA complex giving R_3B, which then undergoes ligand exchange with HBcat. Analogously, hydroboration of alkynes with HBcat or HBpin was catalyzed by dicyclohexylborane (5 mol%)[182] at room temperature (Equation (13)). Dicyclohexylborane was also an effective catalyst for the monohydroboration of haloalkynes with 9-BBN (Equation (14)).[183] The reaction was over within a few hours, whereas the analogous reaction took 30 h in the absence of the catalyst.



9.05.2.1.3.(iv) Hydroboration with $[BH_4]M$ (M = Li, Na)

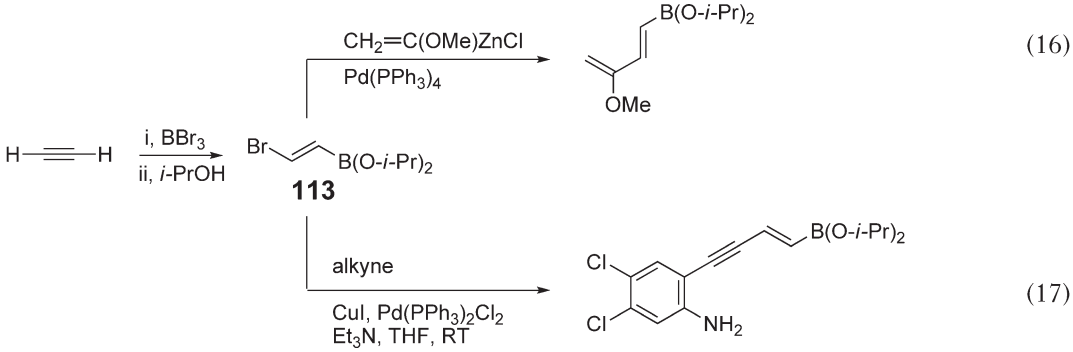
There have been several reports of the catalyzed hydroboration of alkenes with $LiBH_4$ mediated by titanium complexes such as Cp_2TiCl_2 (Equation (15)). This mechanistic work revealed that these reactions involve conventional hydroboration with diborane generated *in situ* by decomposition of the borohydrides with Lewis acids, followed by a titanium-to-boron transfer to give tetraalkyl borates.[184–186] A catalytic amount of $BH_3{\cdot}SMe_2$, $TiCl_4$, or Me_3SiCl provided $LiBH_3R$ in the hydroboration of alkenes with $LiBH_4$ or $NaBH_4$.[187] A PTC catalyst such as methyltricaprylammmonium chloride can be used for the hydroboration of alkenes with $NaBH_4$ when a heterogeneous mixture of a *n*-butyl bromide (2.5 equiv.) solution of alkene and a saturated aqueous solution of $NaBH_4$ (2 equiv.) was stirred at room temperature.[188] The regioselectivity for styrene was internal/terminal alcohol = 78/3 after alkaline hydrogen peroxide oxidation.



(15)

9.05.2.1.4 Haloboration of terminal alkynes

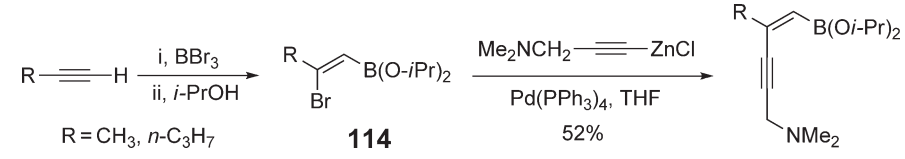
The addition of BX_3 (X = Cl, Br) or 9-X-9-BBN (X = I, Br) to terminal alkynes provided stereodefined β-halo-1-alkenylboron derivatives.[189] The reactivity of haloboranes decreases in the order of B-I-9-BBN, $BBr_3 > BCl_3 >$ B-Br-9-BBN >> B-Cl-9-BBN. The reaction occurred via the Markovnikov *cis*-addition of the halogen–boron bond, but acetylene exceptionally gave the *trans*-addition product **113** via a secondary *cis–trans* isomerization of the double bond. The palladium-catalyzed cross-coupling reaction of **113** with RZnCl[190] (Equation (16)) or terminal alkynes[191] (Equation (17)) gave (*E*)-1-alkenylboronic esters that were not available by the conventional hydroboration protocol.



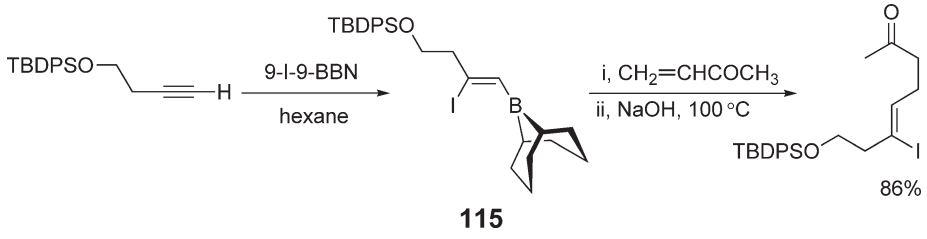
(16)

(17)

Haloboration of terminal alkynes yielded stereodefined (*Z*)-2-halo-1-alkenylboron compounds e.g., **114**, **115** that allowed further functionalization of the resulting C–Br or C–B bond. 2,2-Disubstituted-1-alkenylboronic esters were stereoselectively obtained when the haloboration was followed by cross-coupling with 1-alkynylzinc chlorides (Equation (18)).[192] The iodoboration–conjugate addition sequence gave alkenyl iodides that were used as intermediate for the total synthesis of deoxyepothilone derivatives (Equation (19)).[193–195]

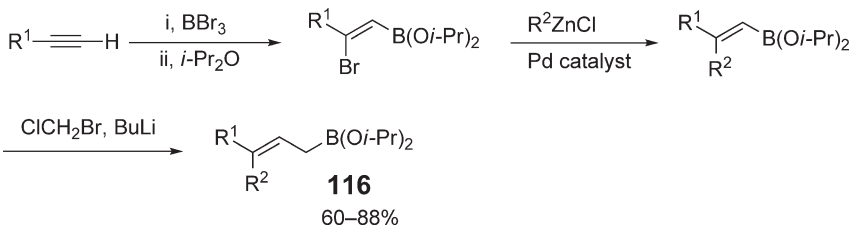


(18)

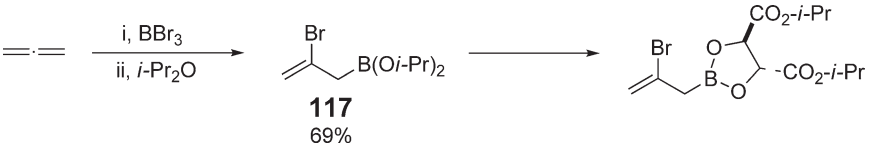


(19)

The haloboration–coupling sequence provided simple access to the stereochemically pure 3,3-disubstituted allylboron compounds **116** via one carbon homologation of the alkenylboron intermediates (Equation (20)).[196] Bromoboration of allene afforded **117** which was converted into a tartrate for asymmetric allylboration (Equation (21)).[197]



(20)



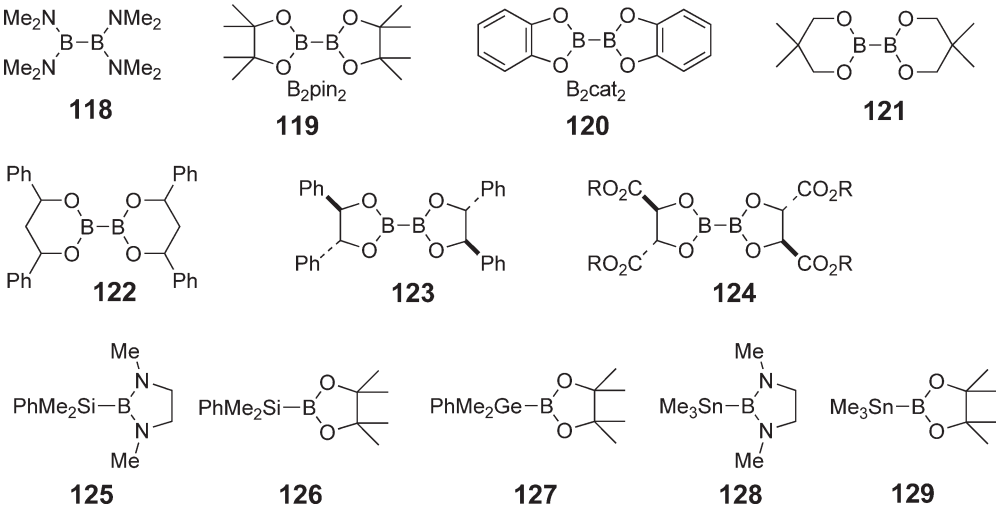
(21)

9.05.2.1.5 Catalyzed addition of B–B, B–Si, B–Sn, B–S, B–CN compounds to alkenes and alkynes

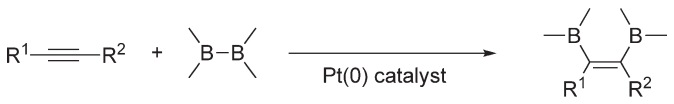
Various B–B, B–Si, and B–Sn compounds are now available for the metal-catalyzed borylation of alkenes and alkynes (Scheme 15). The metal-catalyzed reactions of B–B,[135,198–202] B–Si,[203] and B–Sn[204] compounds have been reviewed.

9.05.2.1.5.(i) Diboration of alkenes and alkynes

The diboration of alkynes was found to be catalyzed by a platinum(0) complex such as $Pt(PPh_3)_4$,[205,206] $Pt(C_2H_4)(PPh_3)_2$,[207,208] or $Pt(nbd)_3/PCy_3$,[209] yielding *cis*-1,2-diborylalkenes in high yields (Equation (22)). A catalytic cycle involves oxidative addition of a B–B bond to Pt(0) giving a B–Pt–B intermediate, which undergoes a *cis*-addition to the alkyne.[206–208] There were no large differences in the yields between internal and terminal alkynes and the reaction tolerated various functional groups. Thus, the first synthesis of tetraborylethylene $(catB)_2C{=}C(Bcat)_2$ was achieved by the addition of B_2cat_2 **120** to catBC≡CBcat in the presence of $Pt(PPh_3)_4$.[210]



Scheme 15 Selected borylation reagents.

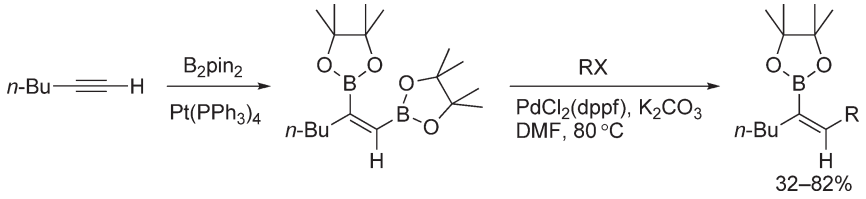


R^1, R^2 = H, alkyl, aryl, 1-alkenyl, 1-alkynyl, R_3Si, Bcat

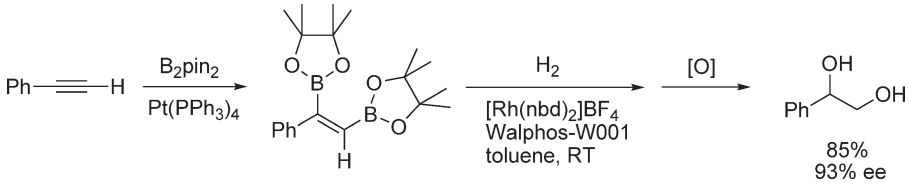
(22)

Reaction conditions
B_2pin_2 **119**, $Pt(PPh_3)_4$, DMF, 80 °C
B_2cat_2 **120**, $Pt(CH_2{=}CH_2)(PPh_3)_2$, toluene, 80 °C
B_2cat_2 **120**, $Pt(nbd)_3/PCy_3$ or $PPh_2(C_6H_4Me\text{-}o)$, toluene, RT

Potential difference in reactivity between two C–B bonds allowed the transformation of 1,2-bis(boryl)-1-alkenes to 1-alkenylboranes via a cross-coupling with the aryl, 1-alkenyl, benzyl, and cinnamyl halides (Equation (23)).[211–213] This tandem procedure synthetically equivalent to a *syn*-carboboration of alkynes was used for synthesizing Tamoxifen derivatives via stepwise double coupling with two of the C–B bonds.[212,213] Hydrogenation of the resulting bisborylalkenes with a chiral rhodium catalyst is synthetically equivalent to an asymmetric diboration of alkenes (Equation (24)).[214]

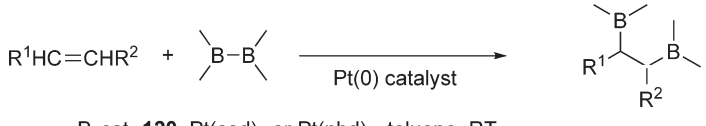


(23)



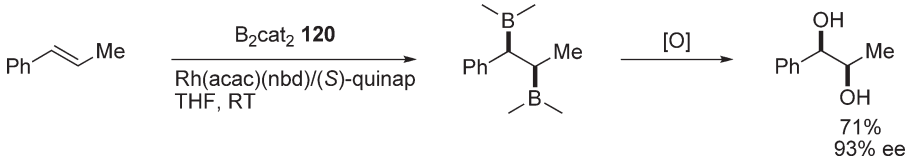
(24)

$Pt(cod)_2$,[215] $Pt(dba)_2$,[216] and Rh(acac)(dpm)[217–219] were found to be excellent catalysts allowing the diboration of terminal alkenes and cyclic alkenes having an internal strain such as norbornene (Equation (25)). In attempts for the asymmetric diboration of alkenes, the reaction between 4-methoxystyrene and chiral diboron $B_2(R,R\text{-}OCHPhCHPhO)_2$ with $Pt(dba)_2$ resulted in 60% de.[220] High enantioselectivities were attained by using chiral phosphine–rhodium(I) catalysts for cyclic and acyclic vinylarenes[221] and terminal alkenes[222] (Equation (26)).



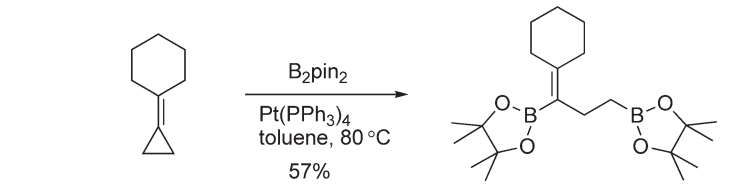
B_2cat_2 **120**, $Pt(cod)_2$ or $Pt(nbd)_2$, toluene, RT
B_2cat_2 **120**, Rh(acac)(dppm), THF, RT
B_2pin_2 **119**, $Pt(dba)_2$, toluene, 50 °C

(25)

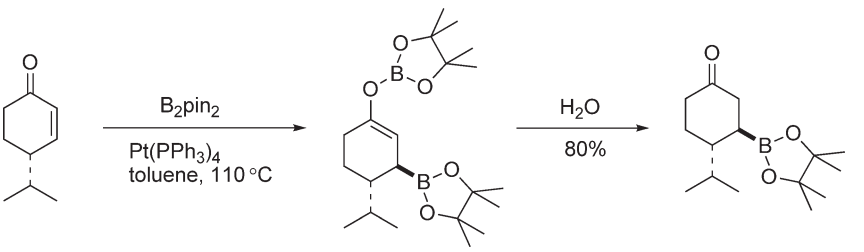


(26)

Methylene cyclopropanes are of interest as the substrate having high reactivity originated from the strained structure. The platinum-catalyzed reaction of diboron proceeded through the proximal bond cleavage of the cyclopropane ring (Equation (27)).[223] Addition of diborons to enones provided 1,4-addition products in the presence of platinum(0)–phosphine catalysts[224–226] (Equation (28)). The reaction was also catalyzed at room temperature by using CuOTf/PBu_3[227] or CuCl/NaOAc[228–231] complexes.

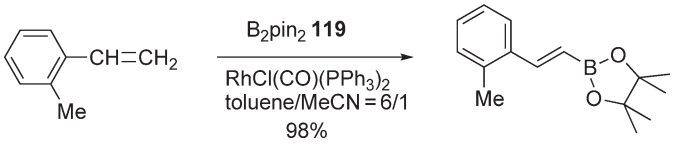


(27)



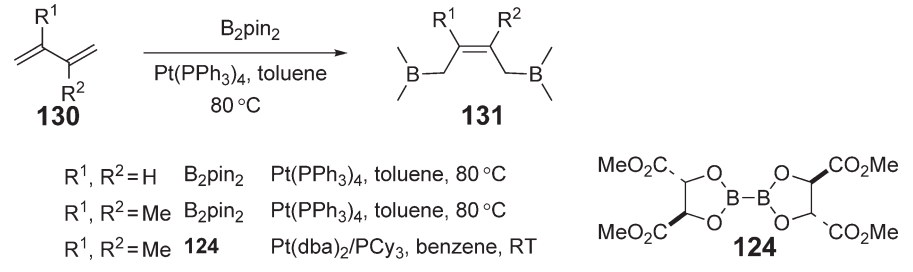
(28)

[Rh(Cl)(CO)(PPh$_3$)$_2$] catalyzed the dehydrogenative monoborylation of vinylarenes and methylene cycloalkanes with B$_2$pin$_2$ via the addition and β-hydride elimination sequence (Equation (29)).[232] Double borylation of two terminal C–H bonds gave 1,1-bisborylalkenes selectively and occurred when 2 equiv. of B$_2$pin$_2$ was used for a vinylarene.

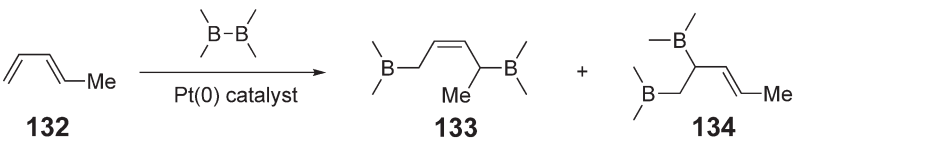


(29)

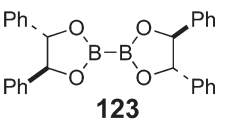
The addition to 1,3-dienes afforded a new class of allylboron compounds. The platinum(0)–phosphine catalysts stereoselectively yielded *cis*-1,4-addition products **131**[233,234] and **133**[216,235] for 2,3-disubstituted butadiene, 1,3-cyclohexadiene, and 1,3-pentadiene by *S-cis*-coordination of a diene to a platinum catalyst (Equations (30) and (31)). In contrast, phosphine-free Pt(dba)$_2$ resulted in the selective formation of a 1,2-addition product **134**[216] for 1,3-pentadiene (Equation (31)). The corresponding chiral allyl boronates were synthesized by diboration of dienes with **123** or **124**.[234,235]



(30)

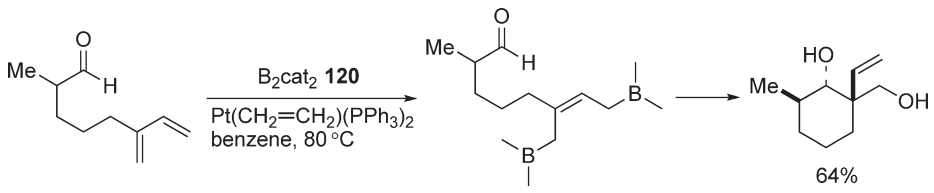


B$_2$pin$_2$	Pt(PPh$_3$)$_4$, toluene, 80 °C	**133**/**134** = 100/0
B$_2$pin$_2$	Pt(dba)$_2$, toluene, RT	**133**/**134** = 0/100
B$_2$cat$_2$	Pt(CH$_2$=CH$_2$)(PPh$_3$)$_2$, toluene, 80 °C	**133**/**134** = 100/0
124	Pt(CH$_2$=CH$_2$)(PPh$_3$)$_2$, toluene, 80 °C	**133**/**134** = 100/0
123	Pt(CH$_2$=CH$_2$)(PPh$_3$)$_2$, toluene, 80 °C	**133**/**134** = 100/0



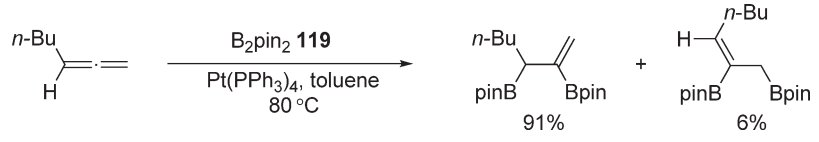
(31)

The reaction tolerated various functional groups, thus allowing the *in situ* preparation of allylboron compounds possessing a carbonyl group (Equation (32)).[236] The tandem diboration–intramolecular allylboration provided a diastereoselective access to the cycloalkanes bearing 1,3-diols.



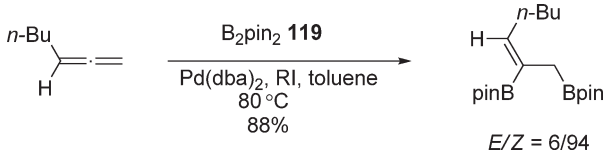
(32)

The diboration of allenes afforded another series of allylboron compounds that each have a boryl group at the vinyl carbon. The addition had a strong tendency to occur at the internal double bond of terminal allenes such as 1,2-heptadiene (Equation (33)).[237] However, steric hindrance in both allenes and phosphine ligands forced the addition toward the terminal double bond of dimethylallene (Equation (34)).[237] On the other hand, addition to the terminal double bond occurred selectively for both monosubstituted and 1,1-disubstituted allenes when $Pd(dba)_2$ was used in the presence of a co-catalyst (RI) such as I_2, ArI, and iodoalkenes (Equation (35)).[238] The role of co-catalyst was attributed to *in situ* formation of I–Bpin intermediate, which undergoes oxidative addition and insertion leading to 2-boryl-π-allylpalladium intermediate.



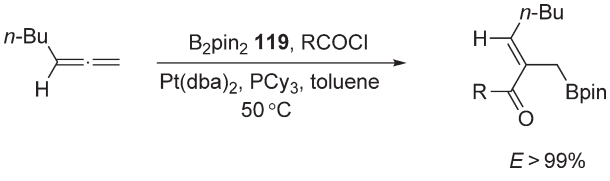
(33)

(34)



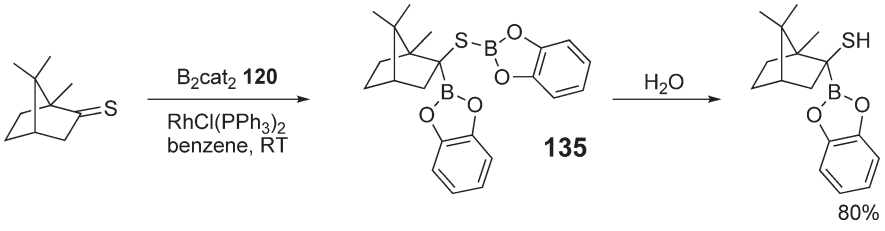
(35)

A new class of 2-acylallylboronates was synthesized via palladium-catalyzed three-component assembling reaction using allenes, acyl chlorides, and B_2pin_2 (Equation (36)).[239,240] The proposed mechanism was an insertion of an allene double bond to the acylpalladium(II) chloride, followed by coupling of the diboron with the resulting π-allylpalladium(II) intermediate.

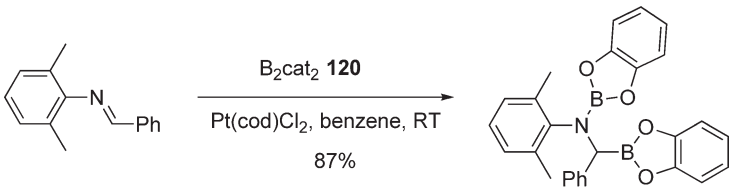


(36)

Two catalyzed reactions have been reported for the addition to the carbon–heteroatom bonds. Rhodium(I) or platinum(II) complexes catalyzed the addition of B_2cat_2 to C–S[241] and C–N[242,243] double bonds (Equations (37) and (38)).



(37)



(38)

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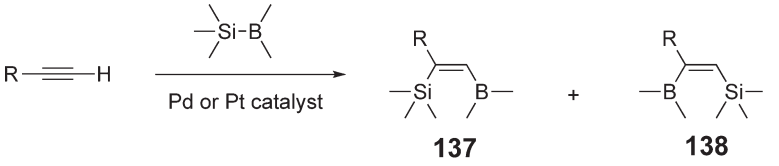
9.05.2.1.5.(ii) Silylboration of alkenes and alkynes

Both amido and pinacol derivatives of B–Si compounds **125** and **126** added to terminal and internal alkynes in the presence of a palladium[244–246] or platinum(0) catalyst[247] by a mechanism involving an oxidative addition–insertion process (Equation (39)).[248] On the other hand, phosphine-free nickel(0) catalyst resulted in the dimerization of alkynes giving a *Z*,*Z*-isomer of 1-silyl-4-borylbutadiene derivatives.[249] Since the palladium-catalyzed cross-coupling at the C–B bond is faster than the C–Si bond of **137**, a silylboration-cross-coupling sequence provided a method for the synthesis of 1-alkenylsilanes.[246]



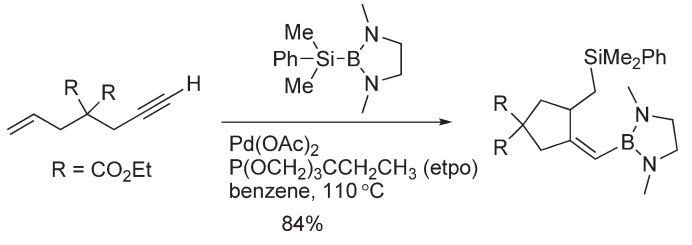
(39)

125 or **126**, $Pd(OAc)_2$, t-$BuCH_2CMe_2NC$, toluene, reflux, **137**/**138** = 99/1

125, $Pd(OAc)_2$, $P(OCH_2)_3CCH_2CH_3$ (etpo), benzene, 110 °C, **137**/**138** = 99/1

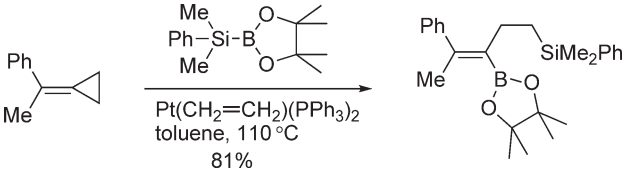
126, $Pt(CH_2{=}CH_2)(PPh_3)_2$, dioxane, reflux, **137**/**138** = 1–16/84–99

The palladium-catalyzed reaction allowed intramolecular five- or six-membered carbocyclization of diynes and enynes (Equation (40)).[245,249] The boryl group was selectively introduced into the more reactive C≡CH bond rather than C=C bond of enynes, and into the terminal C≡CH bond rather than the internal C≡CR bond of diynes.

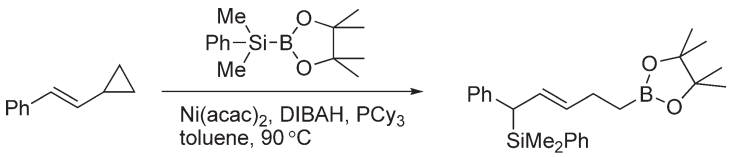


(40)

Silyl(pinacol)borane added to terminal alkenes in the presence of $Pt(CH_2{=}CH_2)(PPh_3)_2$ to give 1-boryl-2-silylalkanes.[247] Platinum-catalyzed silylboration of methylene cyclopropanes provided alkenylboron derivatives via a proximal C–C bond cleavage (Equation (41)).[250] Nickel(0)-catalyzed silylboration of vinyl cyclopropanes and cyclobutanes provided allylsilane derivatives via analogous C–C bond cleavage (Equation (42)).[251]

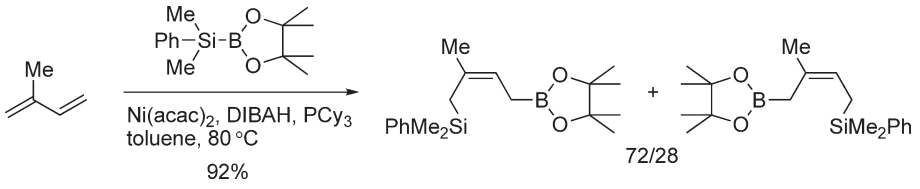


(41)



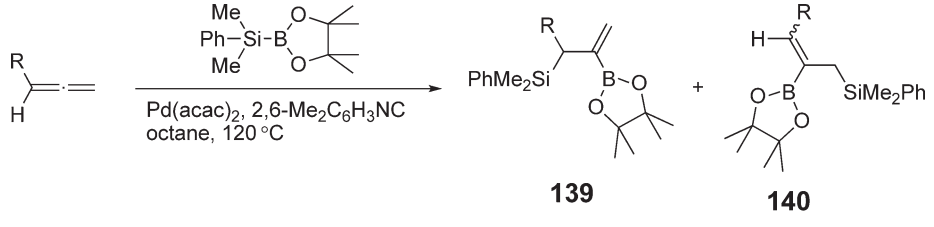
(42)

Addition of silylboranes to 1,3-dienes with a nickel(0)[252,253] or palladium(0) complex[254] afforded 1,4-addition products in high yields as a mixture of two isomers (Equation (43)).[255]



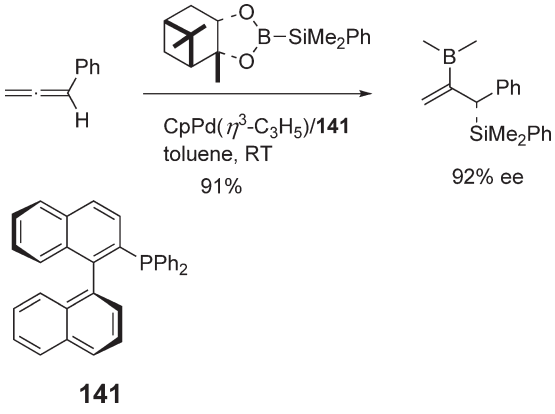
(43)

The palladium-catalyzed silylboration of typical allenes exhibited a strong tendency to occur at the internal double bond giving allylsilanes, which undergo allylation of aldehydes in the presence of a Lewis acid (Equation (44)).[254–257] The selectivity can be varied by changing the substituents, but the boron atom always added to the central carbon. Enantioselective silylboration of terminal monosubstituted allenes was demonstrated by double asymmetric induction using chiral silylboranes and chiral catalysts (Equation (45)).[258]



(44)

R = CH_2CH_2 Ph	99%, **139**/**140** = 100/0
R = MeO	93%, **139**/**140** = 100/0
R = C_6F_{13}	94%, **139**/**140** = 0/100

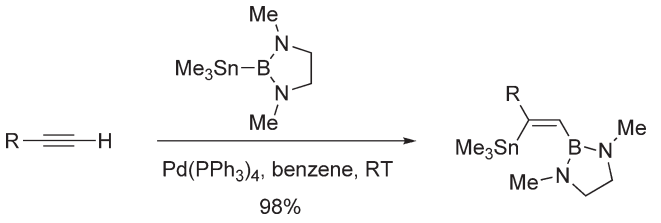


(45)

9.05.2.1.5.(iii) Stannylboration of alkenes and alkynes

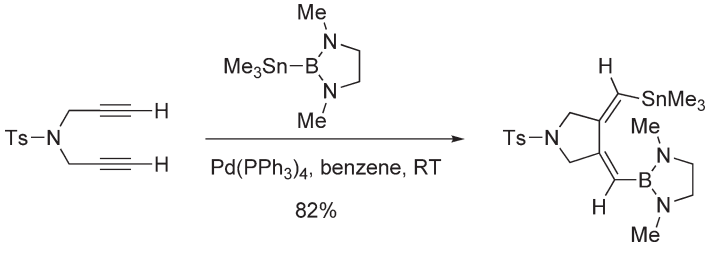
Amido derivatives of B–Sn compounds **128** add to terminal and internal alkynes in the presence of a palladium catalyst (Equation (46)).[259] The reaction takes place even at room temperature because of the very smooth oxidative

addition of the B–Sn bond to the palladium(0) complexes. The reactions stereo- and regioselectively provided *cis*-products via the addition of tin to the internal carbon and boron to the terminal carbon.



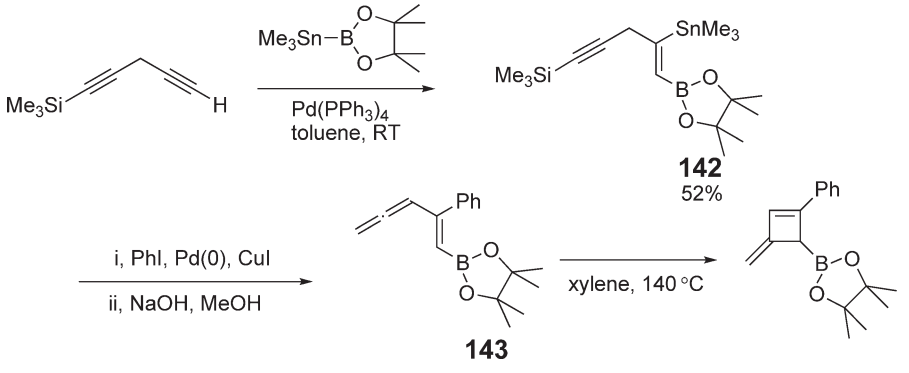
(46)

Carbocyclization of diynes and enynes took place with palladium catalysts and stannylborane **128** at room temperature (Equation (47)).[260] The reaction was feasible for four-, five-, and six-membered cyclization.



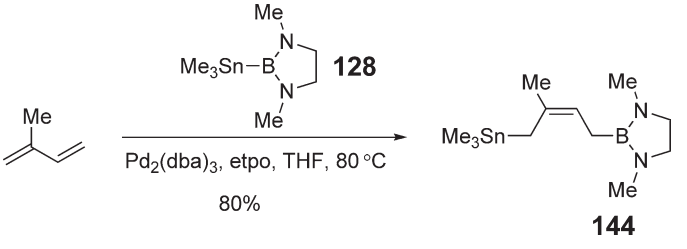
(47)

The stannylboration of alkynes was followed by cross-coupling of the C–Sn bond in the synthesis of stereodefined 1-alkenylboron compounds **143** (Equation (48)).[261] There was a large accelerating effect of boryl substituents on thermal ring closing to the methylene cyclobutenes at 140 °C.



(48)

Addition of stannylborane **128** to 1,3-dienes with palladium(0) catalysts afforded 1,4-addition products in high yields (Equation (49)).[262] The reaction yielded a single product by selective addition of the boryl group to the less-substituted double bond.



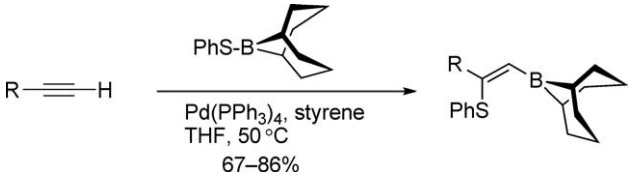
(49)

9.05.2.1.5.(iv) Germylboration

Addition of Ge–B compound to alkynes which is analogous to silylboration was briefly studied.[246]

9.05.2.1.5.(v) Thioboration

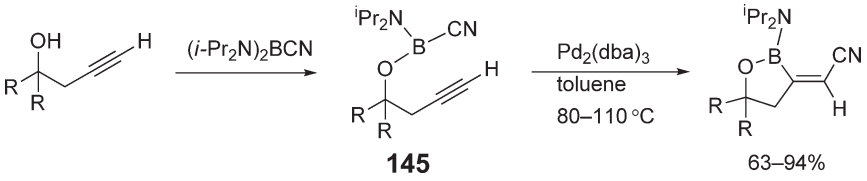
Addition of 9-RS-9-BBN (R = Ph, $PhCH_2$, *n*-Bu) to terminal alkynes was catalyzed by palladium(0) complexes with high regioselectivity to give a terminal boron compound (Equation (50)).[263] The resulting β-alkylthio alkenylboranes smoothly underwent protonolysis with MeOH or palladium-catalyzed coupling reaction with organic halides.



(50)

9.05.2.1.5.(vi) Cyanoboration

A new method for the addition of cyanoboranes to alkynes was developed (Equation (51)).[264] The B–Pd–CN intermediate obtained by oxidative addition was trapped *in situ* by a internal triple bond with high stereo- and regioselectivity for a variety of homopropargyl alcohols.



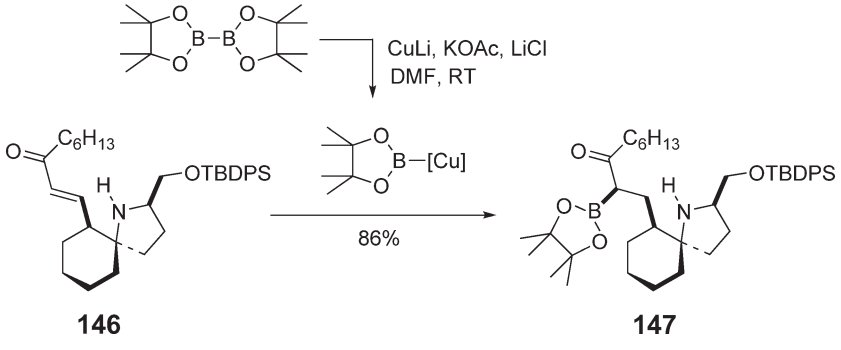
(51)

9.05.2.1.5.(vii) Chloroboration

Oxidative addition of Cl–$B(NR_2)_2$ to Pd(η^3-C_3H_5)(η^5-C_5H_5) and insertion of alkenes to the resulting Cl–Pd–B complex were studied; however, the catalytic reaction has not yet been explored.[265]

9.05.2.1.5.(viii) Addition reactions of a borylcopper(I) reagent generated from diboron

The synthesis of a borylcopper(I) reagent from bis(pinacolato)diboron (B_2pin_2) and CuOAc was developed.[228,229] The reagent used for the 1,4-addition to α,β-unsaturated ketone **146**[230] led to an intermediate for the total synthesis of cylindricine C and 2-epicyclindricine C (Equation (52)).[231]



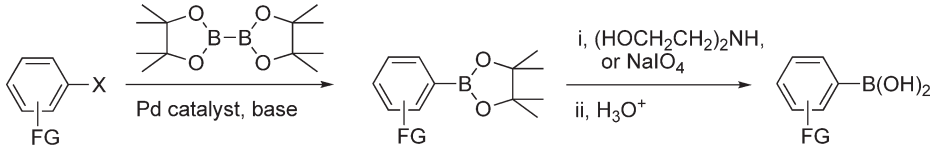
(52)

9.05.2.1.6 Catalyzed borylation of organic halides

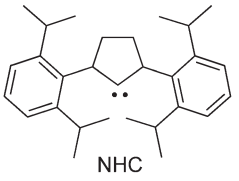
Diborons and HBpin have been found to act as the boron nucleophiles in the presence of a base for the palladium-catalyzed cross-coupling reaction of organic electrophiles. Both reactions provide a simple and direct method for the borylation of organic halides and triflates.[135,266–268]

9.05.2.1.6.(i) Cross-coupling reactions of diborons

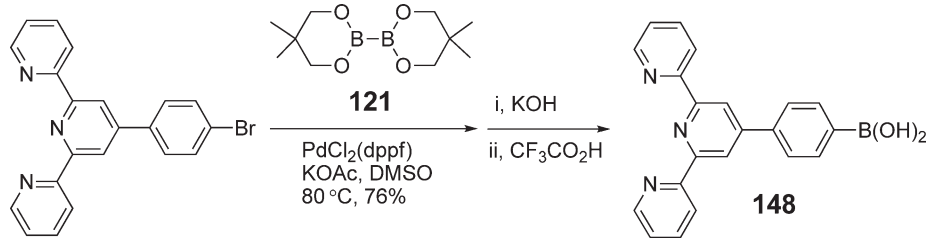
The cross-coupling reaction of diborons with organic halides[269] or triflates[270] provided arylboronic esters in the presence of a palladium catalyst and a base (Equation (53)). KOAc was recognized to be the most suitable base for the borylation of aryl iodides and bromides,[269] chlorides,[271–273] and triflates,[270] whereas the reaction of ArN_2BF_4 took place in the absence of bases.[274,275] For the catalysts, $PdCl_2(dppf)$[269,272,273] was most common, but electron-donating PCy_3[271] and *N*-heterocyclic carbene[276] complex afforded better results for aryl chlorides and electron-rich aryl bromides or triflates due to the rate-determining role of oxidative addition. The reaction was further accelerated in ionic liquids[277] or by irradiation with microwaves.[272,273]



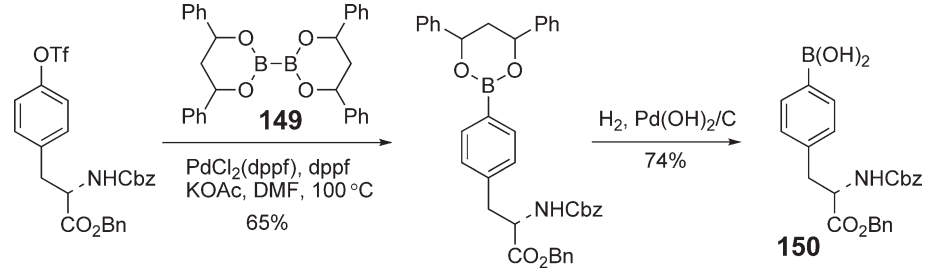
X = I, Br	$PdCl_2(dppf)$, KOAc, DMSO or DMF, 80 °C	(53)
X = Cl, Br	$PdCl_2(dppf)$, KOAc, DOSO or dioxane, microwave	
X = Cl	$Pd(dba)_2$–$2PCy_3$, KOAc, dioxane, 80 °C	
X = Cl	$Pd(OAc)_2$–2NHC, KOAc, THF, reflux	
X = N_2BF_4	$PdCl_2(dppf)$, MeOH, RT	
X = N_2BF_4	$Pd(OAc)_2$–2NHC, THF, RT	



The pinacol boronates thus obtained were especially resistant to hydrolysis under both acidic and basic conditions. Arylboronic acids were obtained when transesterification with diethanolamine was followed by hydrolysis with dilute aqueous acid or oxidative cleavage of the liberated diol using sodium periodate in acetone at neutral pH.[278] Pinacol esters were also cleaved by destruction of the diol with boron tribromide.[279] The coupling reaction of water sensitive **121** was a convenient alternative for the preparation of boronic acids via hydrolysis[280] (Equation (54)). Benzyl diol ester **149** was used for simultaneous deprotection of the three protective groups including a benzyl ester (Bn), a benzyloxycarbonyl (Cbz), and a diphenylpropanediol group on the boron atom by catalyzed hydrogenolysis (Equation (55)).[281]

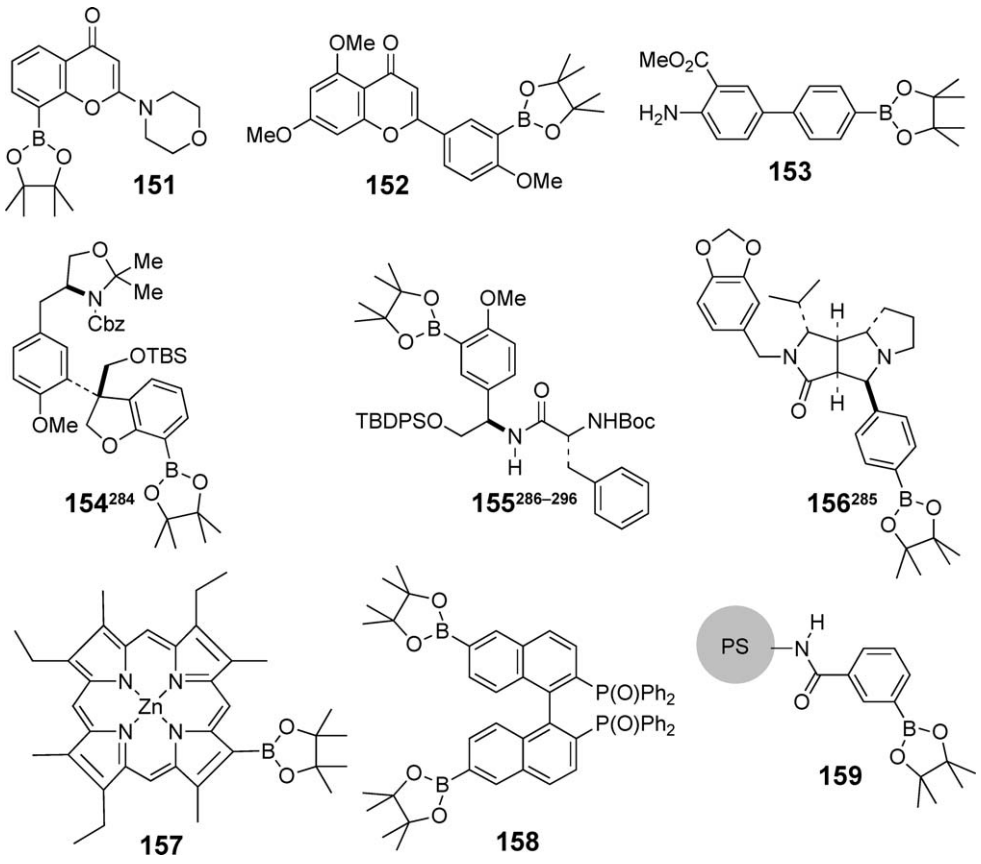


(54)



(55)

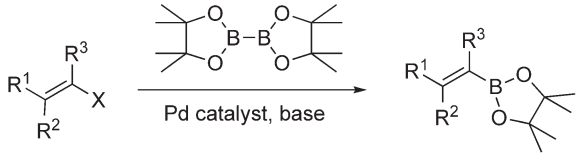
Selected aryl boronates synthesized by Equation (53) are shown in Scheme 16. Since the reaction is tolerant to various functional groups, for example CO_2Me, COMe, NO_2, and CN, the protocol offered a simple method for



Scheme 16 Selected aryl boronates (Equation (53)).

synthesizing functionalized boronic esters. The protocol has been extensively used for the syntheses of natural products, **151**, **152**, **154–156**[282–296] functional materials **153**,[297] **157**,[298] **158**,[299] and polymer-bound boronates **159**.[300,301]

The palladium-catalyzed coupling reaction of diboron and 1-alkenyl halides[302,303] or triflates[304,305] provided 1-alkenylboronic esters and retained the stereochemistry of the electrophiles (Equation (56)). The reaction required a stronger base than that for aryl halides. Fine KOPh suspended in toluene gave the best results for unconjugated bromides or triflates,[302] whereas K_2CO_3 suspended in dioxane was recommended for triflates conjugated to a carbonyl group,[304,305] in the presence of a palladium–triphenylphosphine complex.

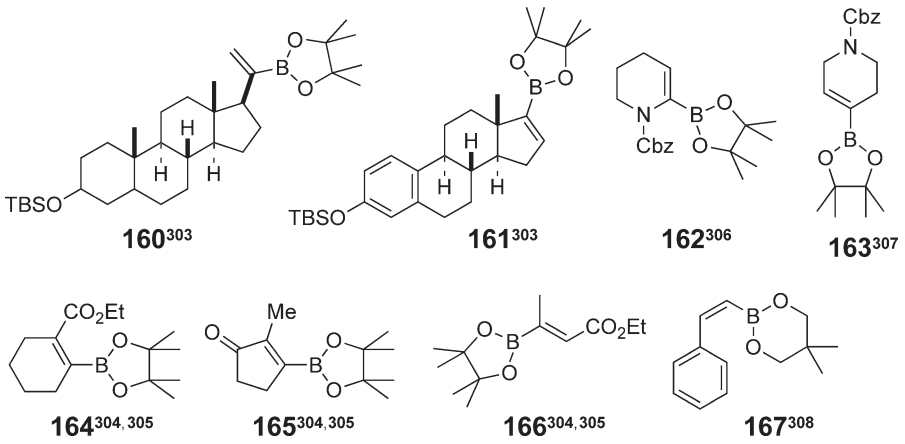


(56)

X = I, Br, OTf; R^1, R^2, R^3 = alkyl — $PdCl_2(PPh_3)_2$–$2PPh_3$, PhOK, toluene or dioxane, 50–80 °C

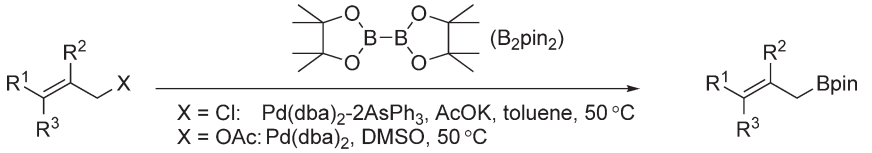
X = OTf; R^1 or R^2 = EW group; R^3 = alkyl — $PdCl_2(PPh_3)_2$–$2PPh_3$, K_2CO_3, dioxane, 80 °C

Selected 1-alkenylboronates synthesized by Equation (56) are shown in Scheme 17. The reaction afforded cyclic and acyclic vinylboronic esters possessing various functional groups, which are not available by conventional hydroboration of alkynes or by a transmetallation method, for example **160–167**.[303–308]



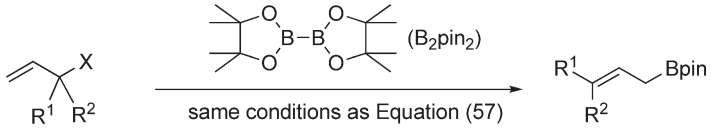
Scheme 17 Synthesis of 1-alkenylboronates (Equation (56)).

The palladium-catalyzed reaction of diboron with allyl acetates or chlorides is a convenient alternative to transmetallation method for the synthesis of functionalized boronates. The reaction of diboron **119** with allyl acetates[309–312] smoothly occurred without the assistance of a base, whereas the presence of AcOK was critical for the coupling with allyl chlorides[313] (Equation (57)). The boron atom coupled with the less-hindered terminal carbon giving the thermally stable (*E*)-allyl boronates. Thus, the (*E*)- and (*Z*)-cinnamyl acetate, chloride (entries 1–4), and their secondary derivatives (entries 7 and 8), all afforded an (*E*)-cinnamyl boronate. The borylation of prenyl acetate was slow (entry 6), but the corresponding chloride (entry 5) and tertiary derivative (entry 9) worked well for the same purpose (Equation (58)).[309,310]



Entry	R^1	R^2	R^3	*X*	*Time* (h)	*Yield* (%)
1	Ph	H	H	Cl	10	70
2	Ph	H	H	OAc	26	73
3	H	Ph	H	Cl	5	71
4	H	Ph	H	OAc	16	89
5	Me	H	Me	Cl	5	78
6	Me	H	Me	OAc	60	24

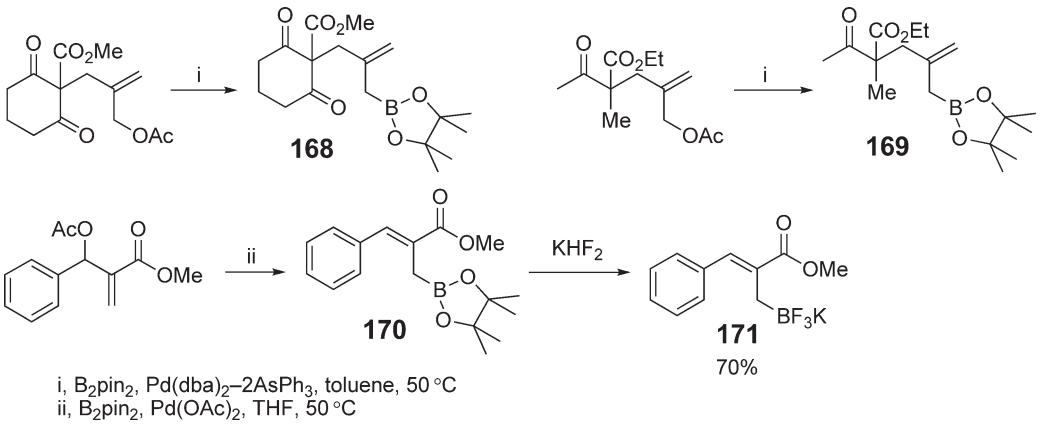
(57)



Entry	R^1	R^2	*X*	*Time* (h)	*Yield* (%)
7	Ph	H	Cl	10	64
8	Ph	H	OAc	16	83
9	Me	Me	OAc	16	83

(58)

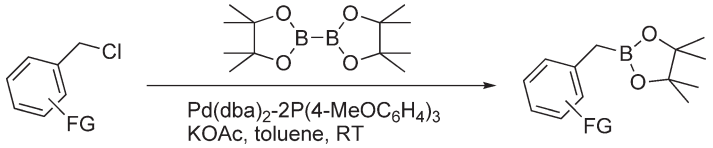
Selected allyl boronates synthesized according to Equation (57) are shown in Scheme 18. The reaction provided a convenient access to allylboranes possessing a carbonyl group **168** and **169**,[310,311] which underwent *in situ* intramolecular allylboration. A variety of 5-5, 6-5, and 7-5 *cis*-fused exomethylene cyclopentanols were synthesized



Scheme 18 Synthesis of allyl boronates (Equations (57) and (58)).

from β-ketoesters via a cross-coupling/intramolecular allylboration sequence. Treatment of the resulting pinacol esters **170** with KHF_2 yielded trifluoroborates **171**,[312] which reacted with aldehydes stereoselectively.

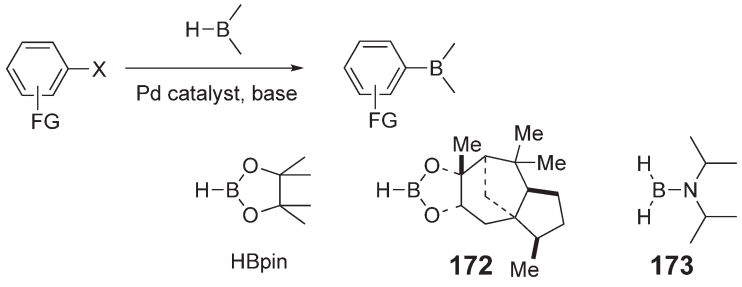
The coupling with benzyl halides was carried out under similar conditions used for allyl chlorides (Equation (59)).[314]



(59)

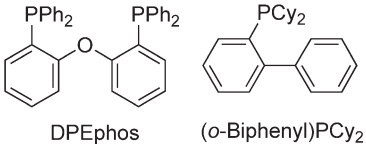
9.05.2.1.6.(ii) Cross-coupling reaction of pinacolborane

HBpin is an economical boron nucleophile for analogous coupling with aryl iodides, bromides, or triflates (Equation (60)).[315–320] The reaction was accelerated in the presence of an electron-donating group while a withdrawing group slowed down the rate of coupling. The borylation with **172**[321] or **173**[322] was also studied.



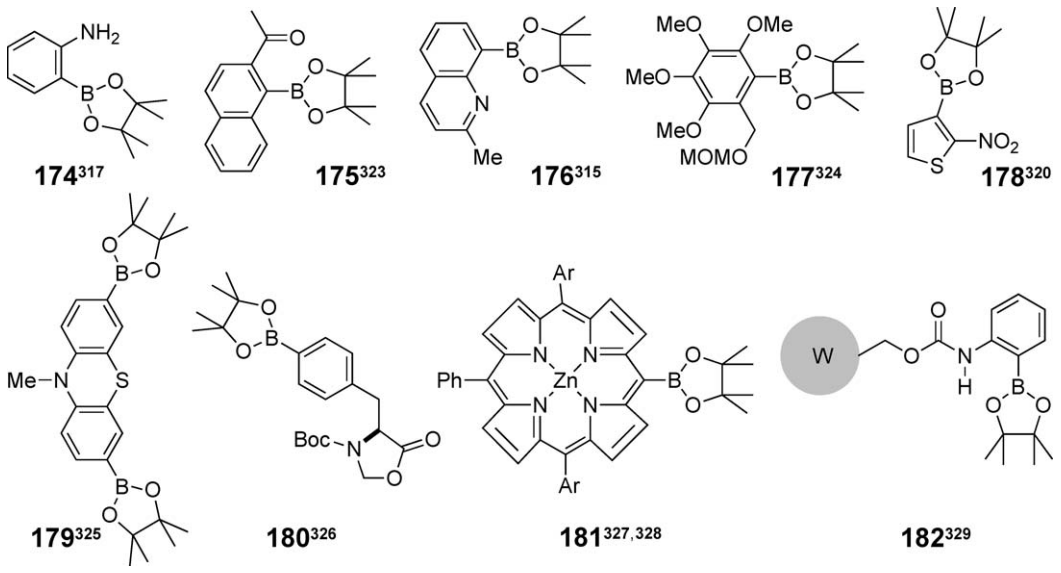
(60)

X = I, Br, OTf	HBpin, $PdCl_2(dppf)$ or $PdCl_2(PPh_3)_2$, Et_3N, dioxane, 80 °C
X = Br	HBpin, $Pd(OAc)_2$, DPEphos, Et_3N, dioxane, 100 °C
X = Br	HBpin, $Pd(OAc)_2$, (*o*-biphenyl)PCy_2, Et_3N, dioxane, 100 °C
X = Br	HBpin, Pd(*t*-$Bu_3P)_2$, THF, 40 °C [F101]
X = I	**172**, $Pd(PPh_3)_4$, CuI, Et_3N, dioxane, 80 °C
X = I, Br	**173**, $PdCl_2(PPh_3)_2$, Et_3N, dioxane, 80 °C



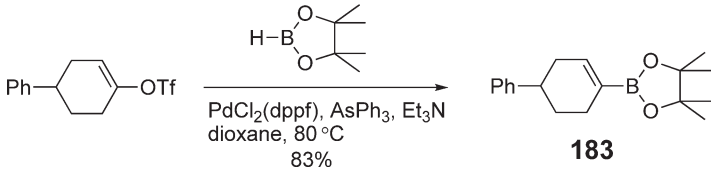
The representative examples synthesized aryl halides and HBpin's, including 174–182[315,317,320,323–329] (Scheme 19). It is interesting that ester, ketone, and nitro groups remain intact during the coupling reaction at 80 °C, though the reaction often competed with the hydrogenation of aryl halides (6–20%).

Borylation of 1-alkenyl iodides and triflates with HBpin was catalyzed by palladium catalyst in the presence of Et_3N (Equation (61)).[330] Platinum(0)–$AsPPh_3$ complexes catalyzed the borylation of allyl chlorides (Equation (62)).[331,332]

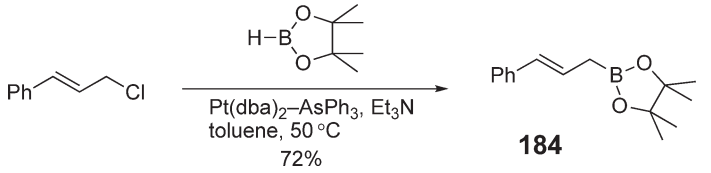


Scheme 19 Synthesis of aryl boronates (Equation (60)).

The coupling occurred at the less-hindered terminal carbon giving thermally stable (*E*)-allyl boronates. Thus, the (*E*)- and (*Z*)-crotyl chloride, and 3-chloro-1-butene, all afforded an (*E*)-crotyl boronate. The reaction with benzyl halides gave benzyl boronates.[333]



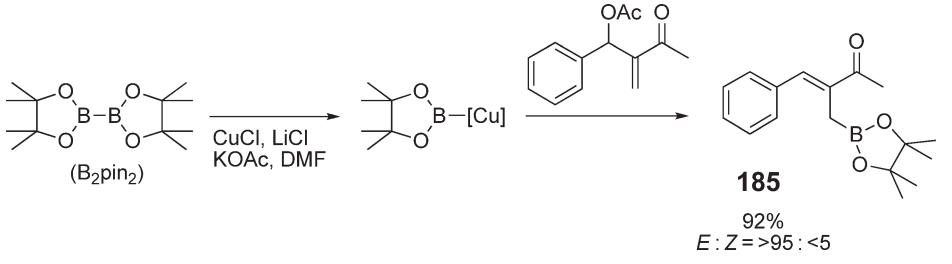
(61)



(62)

9.05.2.1.6.(iii) Coupling reaction of borylcopper reagent

A method for *in situ* preparation of a borylcopper species from diboron and CuOAc was recently developed.[200,201] The reagent coupled with allyl acetate to give allyl boronates **185** (Equation (63)).[334]



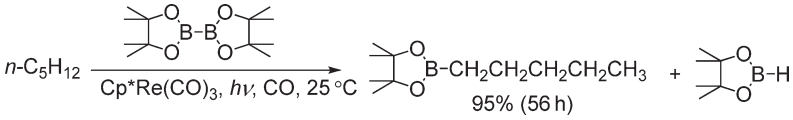
(63)

9.05.2.1.7 Catalyzed borylation of aliphatic and aromatic C–H bonds

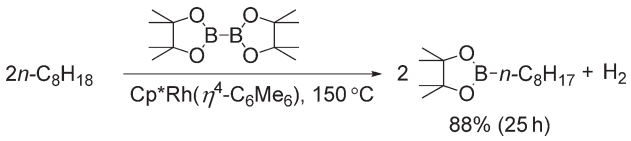
The catalytic C–H borylation of hydrocarbons with B_2pin_2 or HBpin has been reviewed.[2,201,335]

9.05.2.1.7.(i) Aliphatic C–H borylation

A catalyzed C–H borylation of alkanes was first demonstrated by the photochemical activation of $Cp^*Re(CO)_3$ (Equation (64)).[336,337] Rh complexes catalyzed the reaction under thermal conditions, thus allowing the borylation of non-activated alkanes at 150 °C (Equation (65)).[338,339] Among the catalysts screened, $Cp^*Rh(\eta^4\text{-}C_6Me_6)$ exhibited greater long-term activity with a low catalyst loading. The alkanes regiospecifically reacted at the terminal carbon with pin_2B_2. The reaction of 1 equiv. of pin_2B_2 afforded almost 2 equiv. of 1-borylalkanes, thus indicating the participation of pinBH in the catalytic cycle.

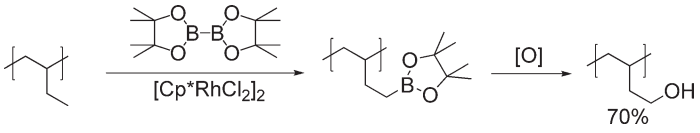


(64)



(65)

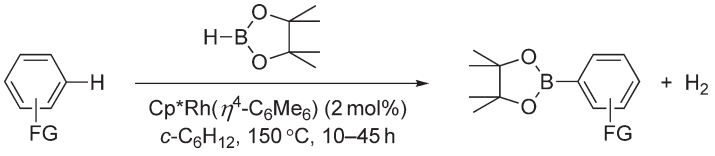
Rhodium-catalyzed borylation with B_2pin_2 at 150 °C provides functionalized polyolefins[340] (Equation (66)). One methyl group per main chain is hydroxylated by borylation–oxidation sequence.



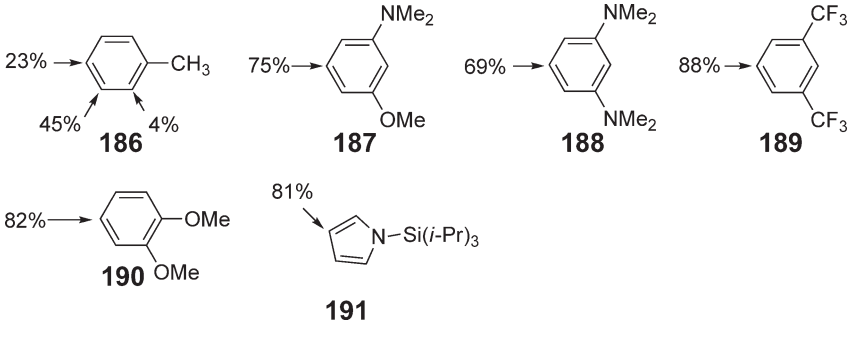
(66)

9.05.2.1.7.(ii) Aromatic C–H borylation

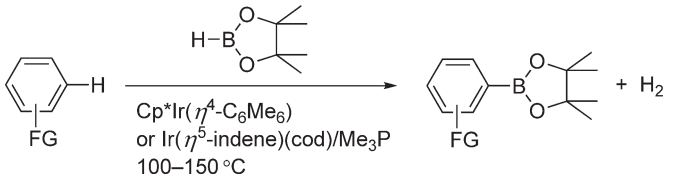
Under irradiation of light, $Cp^*Re(O)_3$ catalyzed the borylation of benzene with B_2pin_2.[337] $Cp^*Rh(\eta^4\text{-}C_6Me_6)$, which generates a coordinatively unsaturated Cp^*Rh active for oxidative addition, was found to be the best catalyst, giving a 92% yield after 2.5 h with 5 mol% catalyst loading and an 82% yield (328 TON; TON = turnover number) with 0.5 mol% loading at 150 °C (Equation (67)).[338,341–345] The coupling reaction occurred at the less-hindered C–H bond for avoiding steric hindrance of the substituents. In cyclohexane as solvent at 150 °C in a sealed ampule, 1,3-disubstituted arenes were selectively borylated at the 5-position and 1,2-disubstituted arenes were borylated at the 4-position, whereas monosubstituted arenes resulted in a mixture of *para*- and *meta*-coupling products **186–191**. The reaction took place at the α-carbon for pyrrole, but the steric hindrance of *N*-triisopropylsilyl group changed the coupling position to the β-carbon.



(67)

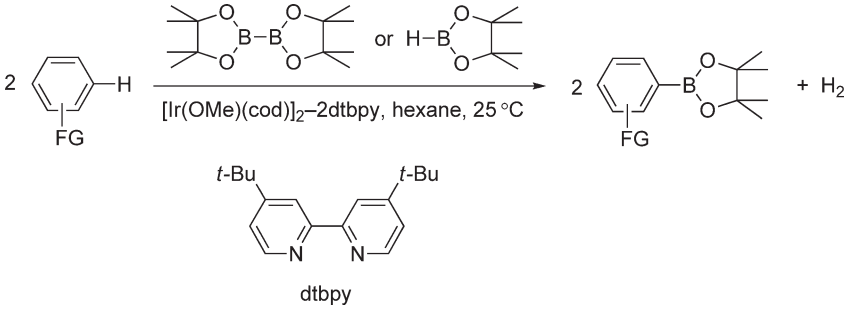


Iridium complexes such as $Cp^*Ir(\eta^4\text{-}C_6Me_6)$ and $Ir(\eta^5\text{-indene})(cod)$ themselves were inefficient, but addition of the small electron-donating phosphines such as PMe_3 or the chelating 1,2-bis(dimethylphosphino)ethane (dmpe) substantially increased the catalyst activity and TON (Equation (68)).[344,346] The maximum TON achieved for benzene with HBpin at 150 °C was 4,500 TON.



(68)

A class of iridium(I) complexes possessing 2,2′-bipyridine (bpy) or 4,4′-di-*tert*-butyl-2,2′-bipyridine (dtbpy) ligands exhibited excellent activity and selectivity for aromatic C–H borylation with B_2pin_2[347–349] or HBpin.[350,351] The reaction was first demonstrated at 80–100 °C using an Ir–Cl complex, but it was found to proceed even at room temperature when the catalyst was prepared from 1/2[Ir(OMe)(COD)]$_2$ and dtbpy (Equation (69)).[352,353] The dtbpy complex showed a high efficiency for most arenes, including heteroaromatic compounds. The catalytic cycle involving oxidative addition of an arene to a tris(boryl)Ir(III) intermediate giving an Ir(V) species has been proposed by theoretical studies.[354,355]



(69)

The borylation of arenes with B_2pin_2[347–349,352,353] or HBpin[350] smoothly proceeded at room temperature in the presence of [Ir(OMe)(cod)]$_2$–2dtbpy, and various functional groups were tolerated (Table 3). The reaction was suitable for arenes possessing OMe, I, Br, Cl, CO_2Me, CN, and CF_3 substituents or benzylic C–H bonds. Both 1, 2- and 1,4-disubstituted arenes bearing identical substituents yielded the corresponding borylarenes as single isomers **192**. The borylation of 1,3-disubstituted arenes **193**–**195** occurred at the common *meta*-position; therefore,

Table 3 Aromatic C–H borylation with B_2pin_2 and [Ir(OMe)(COD)]$_2$–2dtbpy at room temperature

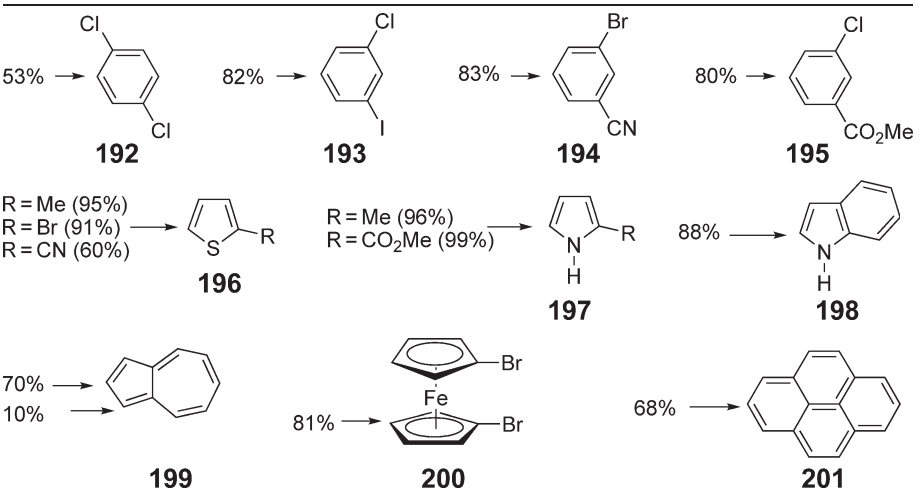
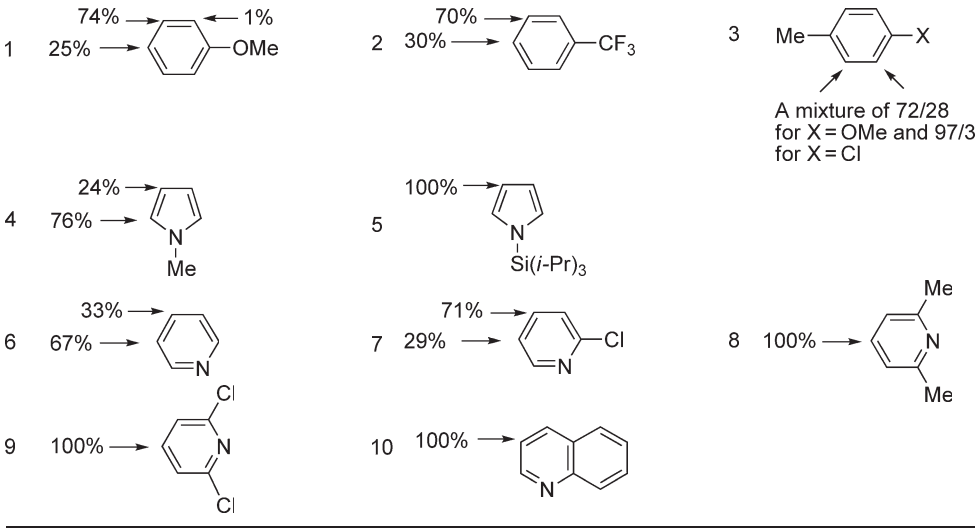


Table 4 Orientation of aromatic C–H borylation with [Ir(OMe)(COD)]$_2$–2dtbpy catalyst

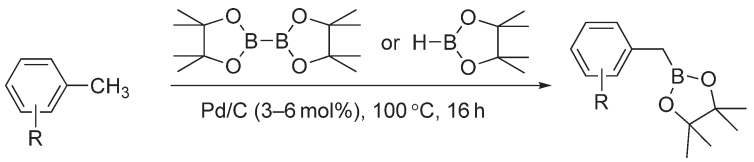


isomerically pure products were obtained even with arenes containing two distinct substituents. Five-membered heteroarenes such as thiophene **196**, pyrrole **197**, indole **198**, furan, and their derivatives were selectively borylated at the α-carbon of a heteroatom.[348,350,351,353] Borylation of azulene **199**,[356] ferrocenes **200**,[357] perylene **201**,[358] and porphyrins[359] has also been studied.

The orientation of other substrates is shown in Table 4.[347,350,352,353] The proportion of coupling products at the *ortho*-carbon is negligible and the reaction rather resulted in a mixture of *meta*- and *para*-products in statistical ratios (ca. 2 : 1) for monosubstituted arenes (entries 1 and 2). The orientation can be controlled by varying the steric hindrance of substituents. For example, the orientation changed from a selective borylation at the 2-position of pyrrole to a selective 3-borylation of *N*-triisopropylsilylpyrrole (entries 4 and 5). Unsubstituted pyridine has an exceptionally strong coordination ability for Lewis acids; thus, the reaction only took place at 100 °C to give a mixture of two isomers (entry 6). In contrast, monosubstitution at an α-carbon effectively blocked the coordination of pyridines to allow the smooth reaction at room temperature. 2-Chloropyridine yielded a mixture of 4- and 5-borylpyridines (entry 7), but 2,6-disubstituted derivatives gave 4-borylpyridines (entries 8 and 9).

9.05.2.1.7.(iii) Benzylic C–H borylation

The reaction of HBpin in toluene in the presence of RhCl{P(*i*-Pr)$_3$}$_2$(N$_2$) (1 mol%) at 140 °C resulted in a mixture of (borylmethyl)benzene (69%) and {bis(boryl)methyl}benzene (7%), along with several products arising from aromatic C–H borylation (ca. 15%).[345] Rhodium–bpy complexes catalyzed the borylation at the benzylic C–H bond.[351] Pd/C was found to be a unique catalyst for selective benzylic C–H borylation of alkylbenzenes by B_2pin_2 or HBpin (Equation (70)).[360] Toluene, xylenes, and mesitylene were all viable substrates; however, the reaction can be strongly retarded by the presence of heteroatom functionalities such as MeO and F. Ethylbenzene resulted in a 3 : 1 mixture of pinacol 1-phenylethylboron and 2-phenylethylboron derivatives.



(70)

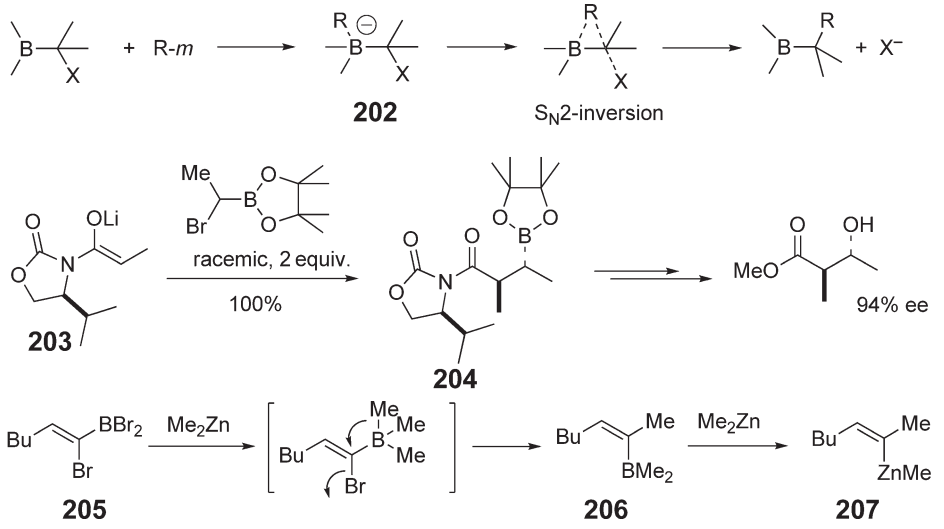
R = H (74%), 2-Me (77%), 4-Me (72%), 3,4-Me$_2$ (64%), 4-MeO (13%), 4-F (26%)

9.05.2.1.8 Homologation of B–C bond via insertion of nucleophiles possessing a leaving group

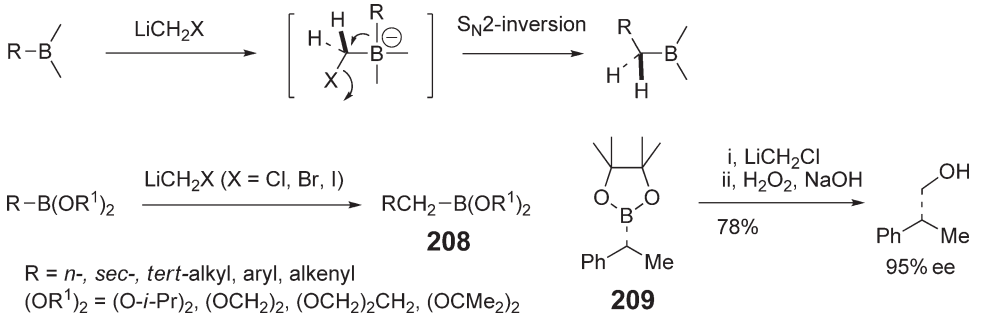
Organoboranes undergo ligand migrations from boron to adjacent carbon that are the major utility in functionalization via homologation of C–B bond.[1–3] These reactions involve the initial formation of a tetracoordinated ate complex **202**, which rearranges with migration of a ligand R from boron to carbon via intramolecular S_N2-mechanism. Assembly of **202** can be accomplished by the addition of a nucleophile (R-*m*) to α-haloboranes or by addition of a nucleophile possessing a leaving group such as diazo compounds, carbenoids, and ylides. A lithium enolate of chiral oxazolidinone selectively reacted with one enantiomer of excess racemic (1-boromomethyl)boronic ester to form a single isolable *threo*-product.[361] Such an α-rearrangement also took place at the sp^2-carbon with inversion of the stereochemistry.[362,363] The reaction provided a method for synthesizing stereodefined alkenylzinc reagents (**207**; Scheme 20).[364]

In situ generation and capture of nucleophiles possessing a leaving group with triorganoboranes or organoboronic esters is another process for the homologation of the C–B bond. (Chloromethyl)lithium generated from $ClCH_2X$ (X = Cl, Br, I) and BuLi at −78 °C in the presence of an organoborane is a typical example (Scheme 21).[365] Instantaneous capture of such a highly reactive carbenoid by organoboranes gives rise to the intermediate ate complex, which then undergoes α-rearrangement with stereoinversion of C–X bond and retention at the migrating carbon center, as was demonstrated in the one-carbon homologation of the optically active **209**.[366,367]

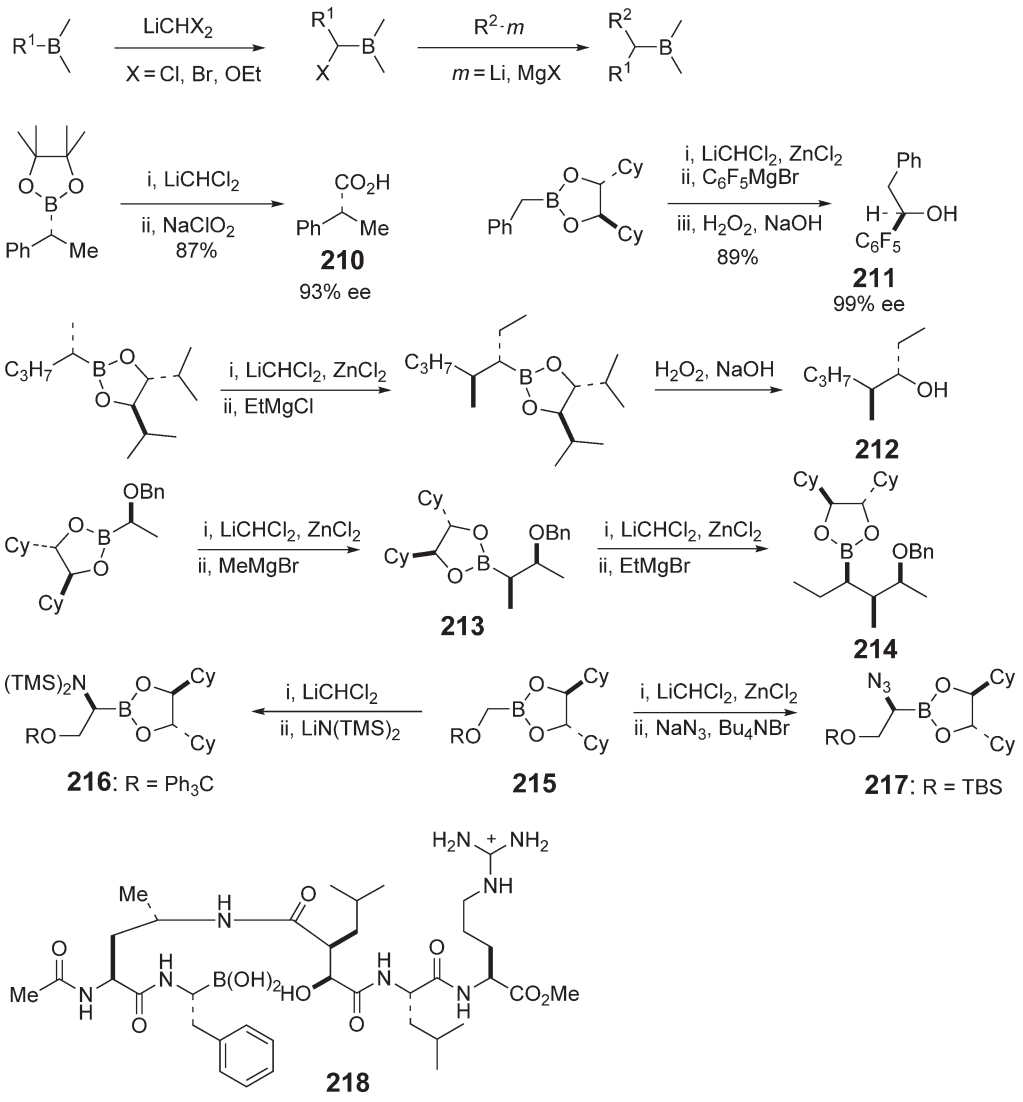
The reaction of $LiCHCl_2$ with organoboronic esters of chiral diols provided chiral (α-chloroalkyl)boronic esters with diastereoselection often ~100 : 1 in the presence of $ZnCl_2$. This reaction can be followed by treatment with nucleophiles (R^2–*m*) for asymmetric homologation of boronic esters (Scheme 22). Carboxylic acids **210**[366] were obtained with retention of configuration when the reaction with $LiCHCl_2$ was followed by oxidation. Optically active alcohols **211**[368] and **212**[369] were produced when asymmetric homologation was followed by oxidation. Organoboronic esters containing several adjacent stereogenic centers were synthesized by repetition of this process



Scheme 20 Insertion of nucleophiles to α-haloalkylboronic esters.



Scheme 21 Insertion of $LiCH_2X$ into C–B bond.

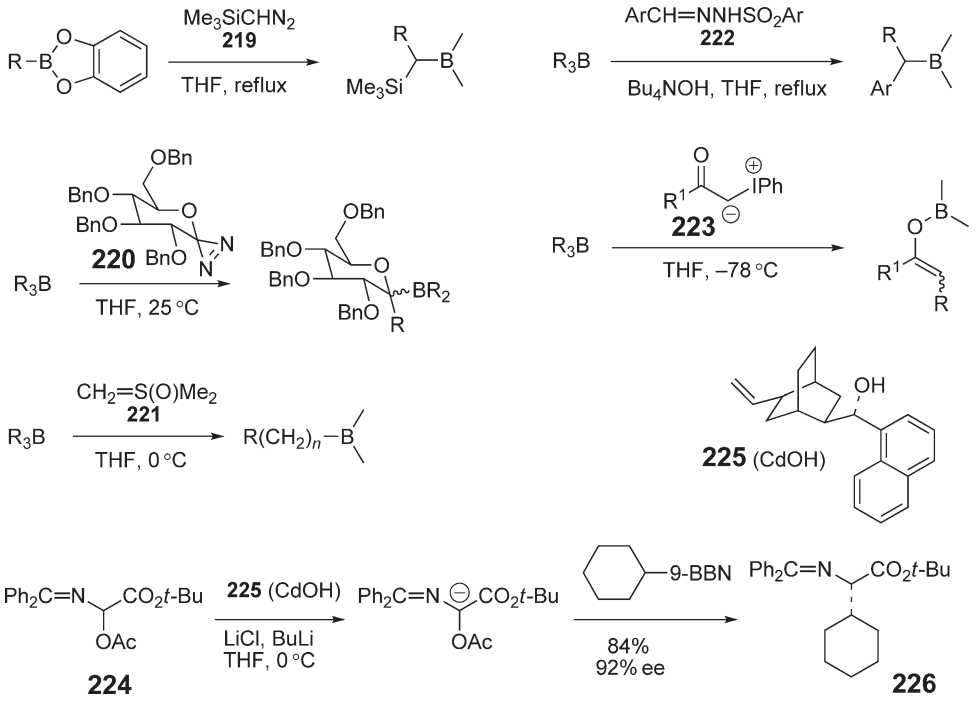


Scheme 22 Insertion of $LiCHX_2$ (X = Cl, Br, OR) and chiral boronates.

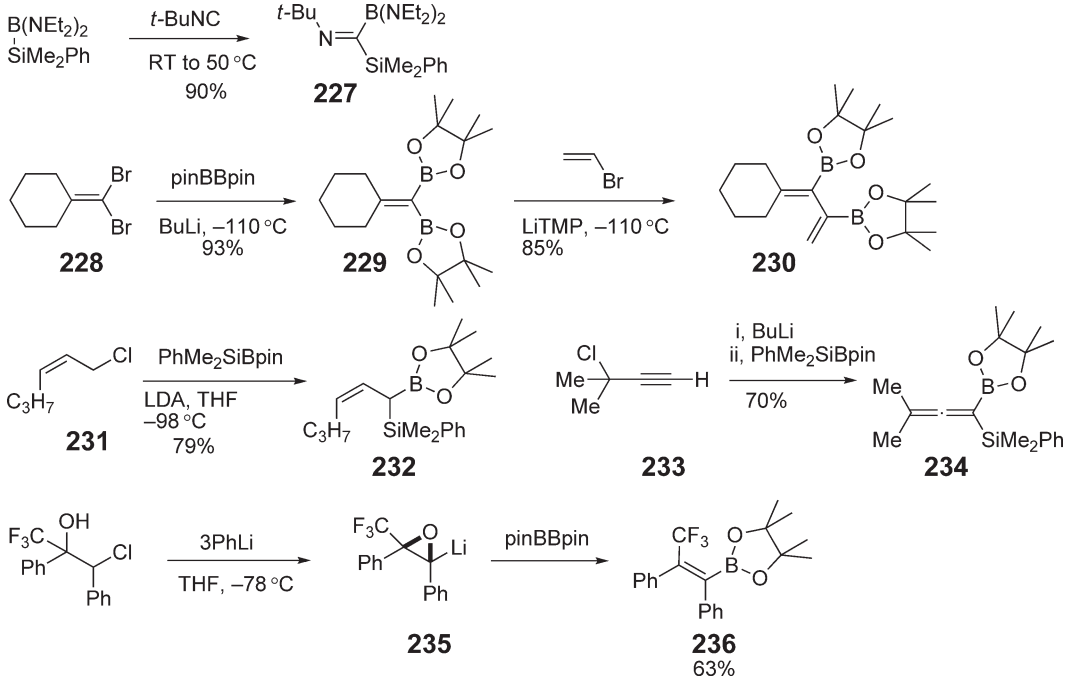
214.[370,371] Chiral α-aminoboronic esters were obtained via amination of the intermediate with $LiN(SiMe_3)_2$ **216**[361,372] or NaN_3 **217**.[373] These boronic esters of bulky diols are strongly resistant to hydrolytic cleavage with water. They were converted to the corresponding boronic acids by treatment with $SOCl_2$–pyridine[374] or $(HOCH_2)_3CNH(CH_2)_3SO_3Na$[370] and to $[RBF_3]K$ with KHF_2.[374] The reaction was used to synthesize [(1R)-amino-2-phenylethyl]boronic acid, which was a key component of boron-containing peptide **218**, the most potent inhibitor of serine proteases.[375]

Reactions of organoboranes with other nucleophiles including carbenes, carbenoids, ylides, and related compounds are summarized in Scheme 23. Me_3SiCHN_2 **219**[376] and diazirine **220**[377] provided monohomologation products, whereas dimethylsulfoxonium methylide **221**[378–380] underwent multiple insertion for living polymerization of trialkylboranes. Trialkylboranes alkylated aldehyde (arenesulfonyl)hydrazones **222**[381] and keto iodonium ylides **223**.[382] The enantioselective synthesis of α-amino acids has been realized with up to 95% ee via the alkylation of benzophenone imines of glycine esters **224**.[383–385] Other nucleophiles reported in this category are $LiCH(OEt)_2$ generated from $(EtO)_2CHSnBu_3$ and BuLi at −100 °C[386] and $LiCCl_2OMe$ generated from Cl_2CHOMe and $LiOCEt_3$.[387]

Insertion of isonitriles and carbenoids into the B–B and B–Si bonds have recently been developed as a method for synthesizing geminal bis(boryl) and boryl–silyl compounds (Scheme 24). The insertion of alkyl and aryl isonitriles into the B–Si bond proceeded at room temperature to provide monomeric (boryl)(silyl)imines **227**.[388,389] Alkylidene



Scheme 23 Other nucleophiles posessing a leaving group for insertion into the C–B bond.



Scheme 24 Insertion of carbenoids and isonitriles into B–B and B–Si bonds.

carbenoids *in situ* generated from 1,1-dihaloalkenes **228** reacted with B_2pin_2 or $PhMe_2SiBpin$ to give **229**.[390–392] Treatment of allylic chlorides with LDA generated α-chloroallyllithiums, which underwent an insertion into the B–Si bond **232**.[393,394] The compound **232** underwent allylboration of aldehydes at 100 °C and allylsilylation of aldehydes at −78 °C in the presence of catalytic Me_3SiOTf or $TiCl_4$.[393] Geminal silylboration of 3-acyloxy- or

3-chloroalkynyllithiums provided novel 1-boryl-1-silylallenes **234**.[393,395] CF_3-substituted lithio-oxiranes generated from chlorohydrins and aryllithiums reacted with B_2pin_2 to stereoselectively give **236**.[396]

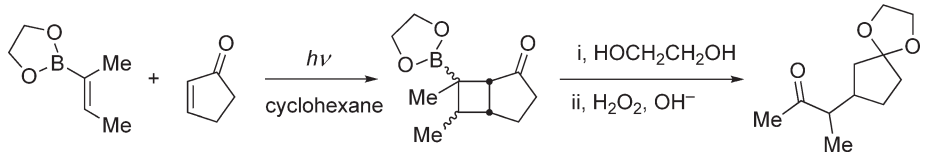
9.05.2.2 Reactions at Sites other than the B–C Bond

9.05.2.2.1 Cycloaddition reactions of alkenyl- and alkynylboron compounds

Due to their great versatility, boron-substituted dienophiles and dienes have emerged as attractive building blocks in cycloaddition reactions. The early works in the field have been reviewed.[1]

9.05.2.2.1.(i) [2+2]-Addition

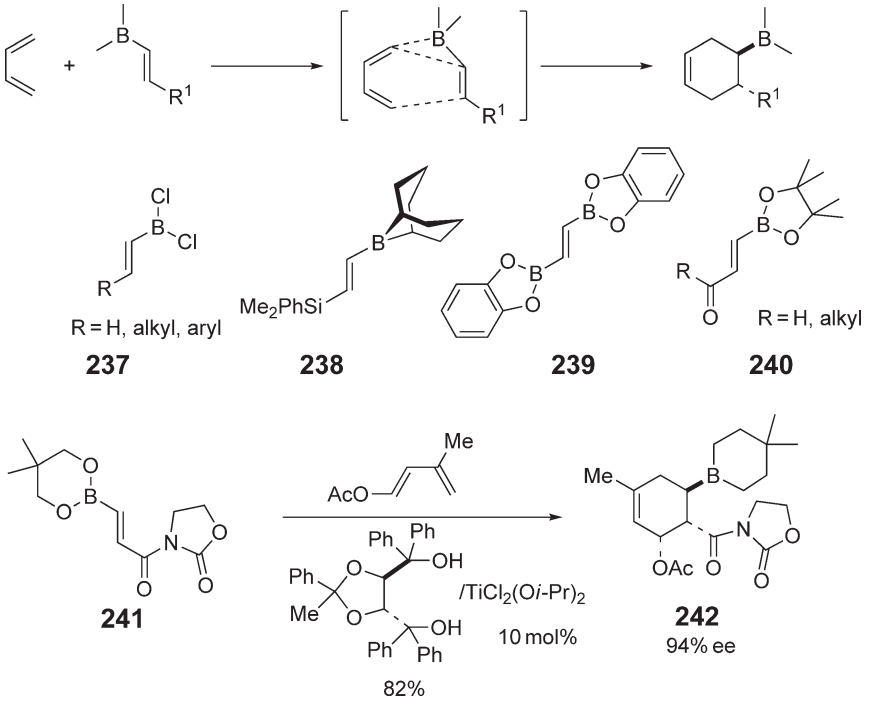
The photocycloaddition of 1-alkenylboranes in cyclohexane provided *cis*-fused head-to-head adducts for 2-cyclopentenone and a mixture of *cis*- and *trans*-isomer for 2-cyclohexenone (Equation (71)).[397]



(71)

9.05.2.2.1.(ii) [2+4]-cycloaddition (Diels–Alder reaction)

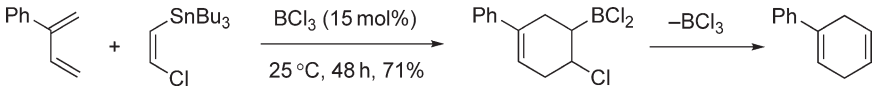
Cycloaddition reaction of vinylboron compounds was first demonstrated by dibutyl vinylboronate, but 1-alkenylboranes lacking backbonding from the ligands to the vacant *p*-orbital of boron are much more reactive than boronic esters. *Ab initio* calculation of Diels–Alder reaction of vinylboranes with butadiene suggested a [4+3]-*endo*-transition state, whereby the boron atom bonds significantly to the terminal carbon of the diene[398] (Scheme 25). Vinyl(dichloro)borane **237** reacted with common dienes at −78 °C to room temperature, giving a 1 : 1 mixture of *endo*- and *exo*-adducts for cyclopentadiene and a 3 : 2 mixture of 1,4- and 1,3-disubstituted adducts for isoprene.[399,400] 9-Vinyl-9-BBN **238** reacted with 1,3-butadiene 200 times faster than methyl acrylate.[401] The replacement of the



Scheme 25 Boron dienophiles for [4+2]-cycloaddition.

vinylic hydrogen β to the boryl group by an electron-withdrawing group provided reactive alkenylboronates **240**, which reacted with cyclopentadiene at temperatures lower than −10 °C.[402] Analogously, 1,2-bis-borylethenes **239** and 2-silylvinylboranes were reactive dienophiles, which provided diol derivatives via a cycloaddition–oxidation sequence.[401] Asymmetric Diels–Alder reaction of **241** catalyzed by a chiral titanium complex afforded a key intermediate **242** for the synthesis of (+)-paniculide A.[403]

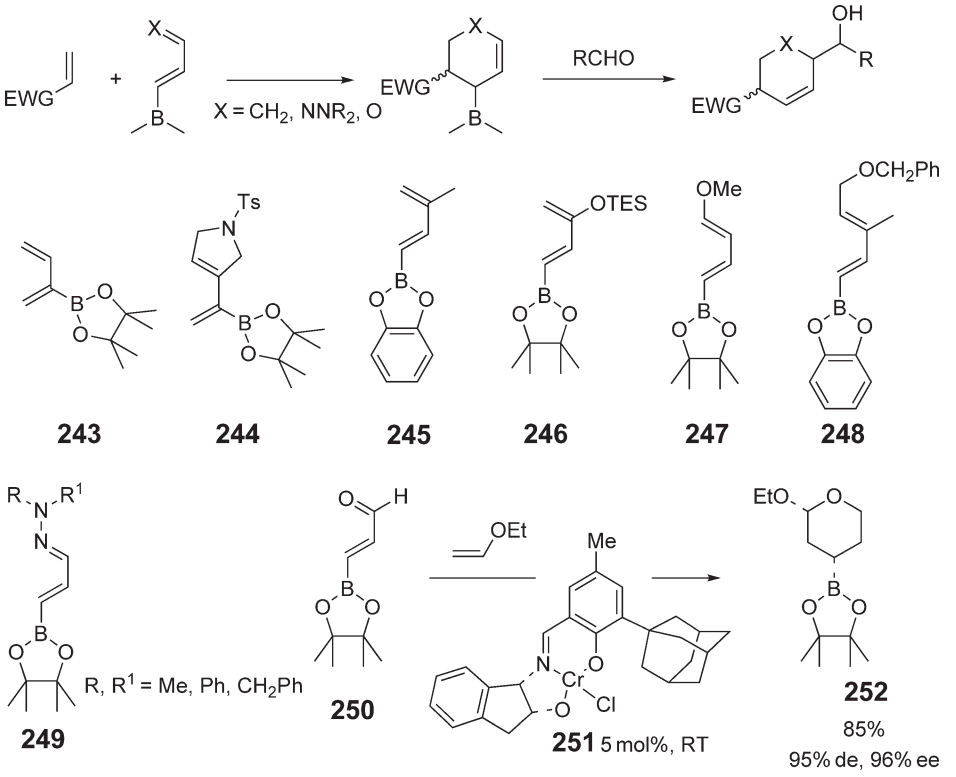
Cycloaddition reaction of *cis*-chlorotributylstannane was catalyzed by BCl_3 or 9-Br-9-BBN at 25 °C (Equation (72)).[404] A catalytic cycle involved [2+4]-reaction of 1-alkenylborane, generated *in situ* by Si–B transmetallation.



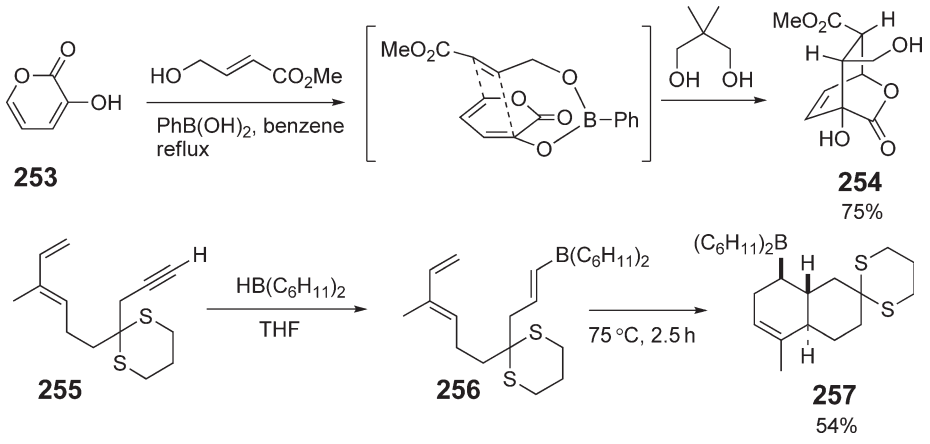
(72)

Butadienylboronic esters react as typical dienes in Diels–Alder reactions with activated alkenes (Scheme 26). A 1,3-butadienyl-2-boronic ester **243** was prepared via hydroboration of 1,4-dichloro-2-butyne followed by dechlorination with zinc.[405] Cyclic 1,3-dienylboronic esters **244**.[406] were synthesized by the ruthenium-catalyzed enyne metathesis of alkynyl boronates. Hydroboration of terminal enynes provided 1,3-butadienyl-1-boronic esters **245–248**. Reactions of these boronates with alkenes gave cyclic allylboron compounds which underwent allylboration of aldehydes to furnish several stereogenic centers diastereoselectively.[407–410] It was also found that the reaction of **245** was greatly accelerated by quaternarization of boron atom with CsF[407] or activation of dienophiles with $EtAlCl_2$.[408] 1-Aza-4-borono-1,3-butadiene **249** was synthesized for the tandem aza [4+2]-cycloaddition–allylboration, giving piperidine derivatives.[411–413] The cycloaddition of 3-borylacrolein **250** with vinyl ethers was catalyzed by a Lewis acid such as $Yb(fod)_3$[414] and chiral chromium(III) complex **251**.[413] Accelerating effect of an internal dialkoxyboryl group that chelates to the carbonyl group of dienophile was also studied.[415]

The reactivity and selectivity of cycloaddition can be considerably increased in intramolecular versions. The protocol was first demonstrated in the Diels–Alder reaction between anthrone **253**[416,417] and 4-hydroxy-2-butenoate mediated by phenylboronic acid (Equation (73)).[418,419] Another method developed for the intramolecular cycloaddition is the synthesis of trienylboranes **256** by hydroboration of terminal alkynes (Equation (74)).[419–422]



Scheme 26 Boryl dienes for intramolecular [4+2]-cycloaddition.

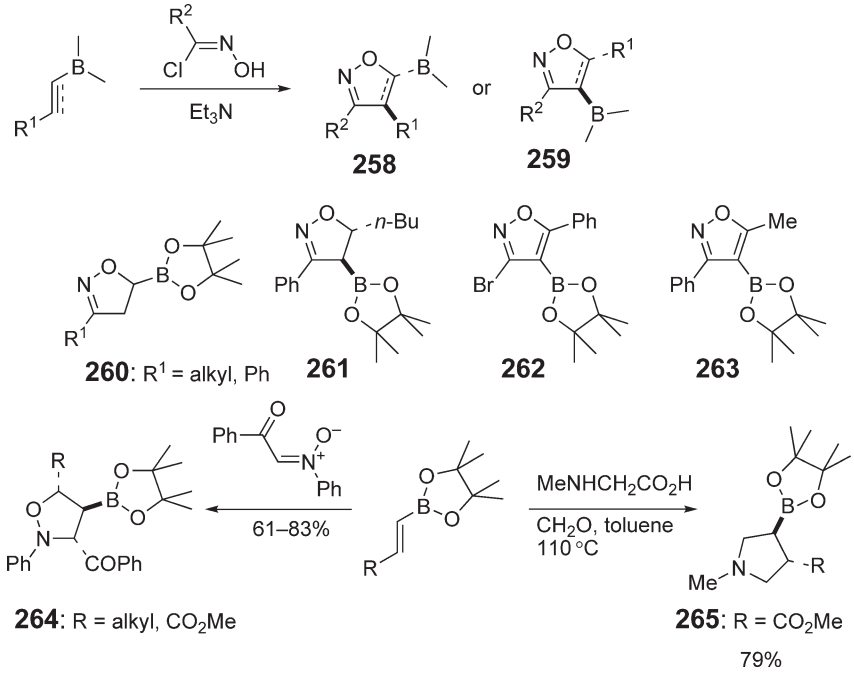


9.05.2.2.1.(iii) [3+4]-1,3-Dipolar cycloaddition

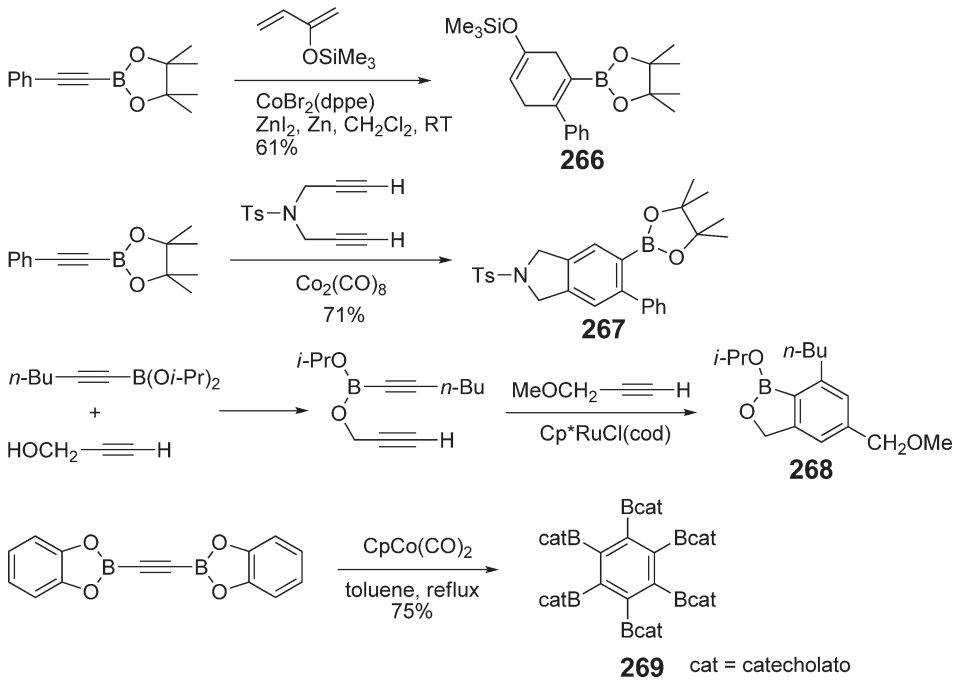
Alkenyl- and alkynylboronic esters have been shown to be good dienophiles in a range of 1,3-dipolar addition, thus giving access to the boron-functionalized heterocycles **258** or **259**; (Scheme 27). Nitrile oxides generated *in situ* from nitroalkanes/PhNCO/Et_3N or hydroxamic acid chloride/Et_3N smoothly reacted with (*E*)-1-alkenylboronic esters **260** and **261**.[423–426] The reaction with 1-alkynylboronic esters gave isoxazoleboronic esters **262** and **263**[427,428] with good levels of regioselectivities. Other reactions in this category were cycloaddition of nitrones and azomethyne ylides giving **264**[429] or **265**.[430]

9.05.2.2.1.(iv) Metal-catalyzed cycloaddition

In contrast to the thermal reactions of 1-alkynylboronic esters, the cycloaddition smoothly takes place under very mild conditions in the presence of metal catalysts (Scheme 28). A cobalt(I) complex catalyzed the [4+2]-cycloaddition of alkynyl boronates with 1,3-dienes to give cycloalkenyl boronates **266**[431] and with α,ω-diynes giving arylboronates



Scheme 27 1,3-Dipolar cycloaddition to 1-alenyl- or 1-alkynylboron compounds.



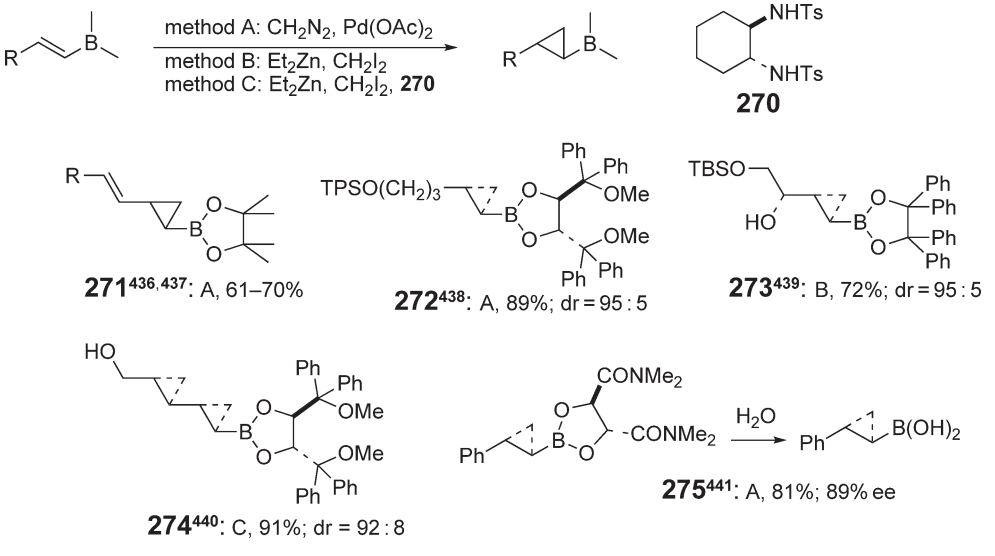
Scheme 28 Metal-mediated cycloadditions.

267.[432] The intramolecular version was studied to control the selectivity of the insertion **268**.[433] Cyclotrimerization of bis(boryl) acetylene provided a novel hexa(boryl)benzene **269** (cat represents catecholato group).[434,435]

9.05.2.2.2 Addition reactions to alkenyl- and alkynylboron compounds

9.05.2.2.2.(i) Cyclopropanation

The methods for stereocontrolled synthesis of cyclopropylboronic esters have been studied (Scheme 29). The palladium-catalyzed reaction of diazoalkanes (method A), Simmons–Smith reaction (method B), or asymmetric Simmons–Smith reaction using chiral diamines such as **270** (method C) for chiral or achiral 1-alkenylboronic esters

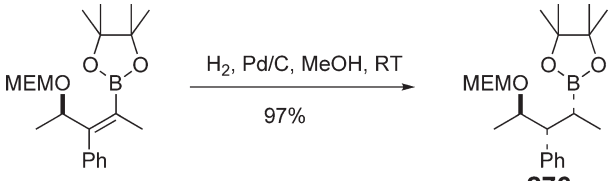


Scheme 29 Cyclopropanation of 1-alkenylboronic esters.

afforded **271**–**275**[436–441] and their derivatives in high yields with high diastereoselectivities. Two chiral diols **272** and **274** were recently synthesized as efficient chiral auxiliaries or as stable protecting groups of the boronic acids for chromatography over silica gel.[438–445]

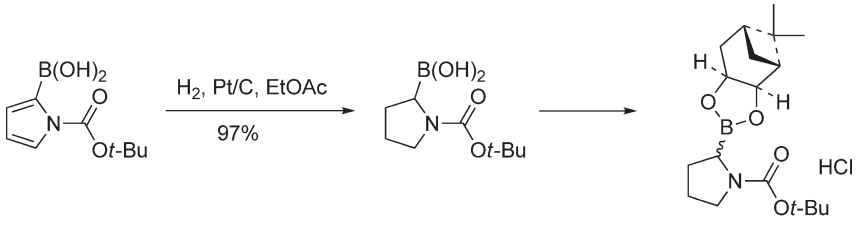
9.05.2.2.2.(ii) Hydrogenation and epoxidation

The catalyzed hydrogenation of alkenylboronic esters was used for the diastereoselective synthesis of alkylboronic esters **276**[446] (Equation (75)). The hydrogenation of a pyrrolboronic acid provided a prolineboronic acid, which was then resolved by HPLC to give an optically active boronic ester **277**[447] (Equation (76)).



276
>93% dr

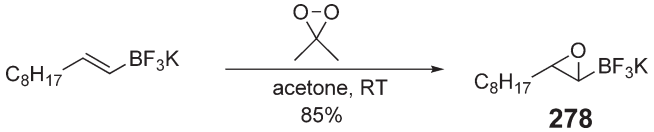
(75)



277

(76)

Potassium 1-alkenyltrifluoroborates permitted alkene epoxidation with oxone or *m*-CPBA with excellent conversions without cleavage of the C–B bond (Equation (77)).[448]

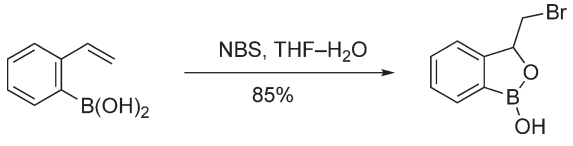


278

(77)

9.05.2.2.2.(iii) Haloetherification

Arylboronic acids possessing an *ortho*-1-alkenyl or 2-alkenyl group underwent preferential bromoetherification with NBS in aqueous THF, whereas the B–C bond cleavage predominated under basic pH's (Equation (78)).[449]



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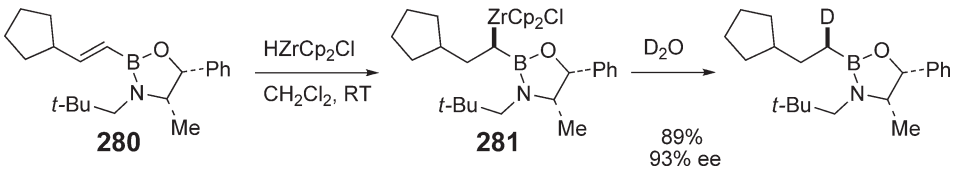
(78)

9.05.2.2.2.(iv) Addition of metallic reagents

Diastereoselective hydrozirconation of optically active 1-alkenylboronic esters **280**[450] provided chiral boronates up to 93% dr (Equation (79)). The reaction can be followed by halogenolysis of the C–Zr bond with NCS, NBS, or NIS in the synthesis of α-haloboronates.[451] 1-Alkenyl and 1-alkynylboron compounds worked as acceptors for nucleophilic addition of organometallic reagents due to their ability to stabilize the resulting carbanions. Dimesitylboryl group **282** was found to be an excellent activator of double bonds and triple bonds, suppressing the ate complex formation (Equation (80)).[452] Pinacol 1-alkenylboronic esters were used as an acceptor of zincated hydrazones **285**,[453] allylic zinc reagents **286**,[454] and the functionalization of resulting C–Zr and C–B bond (Equation (81)).



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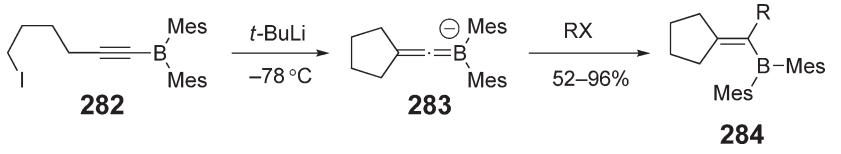
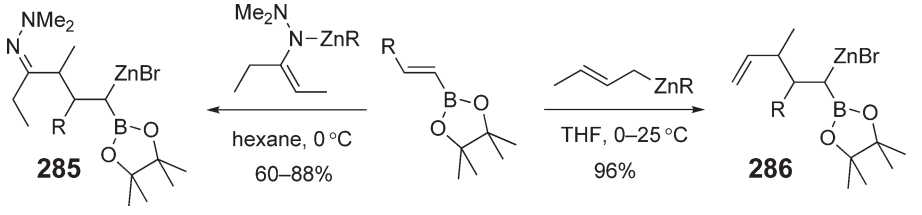


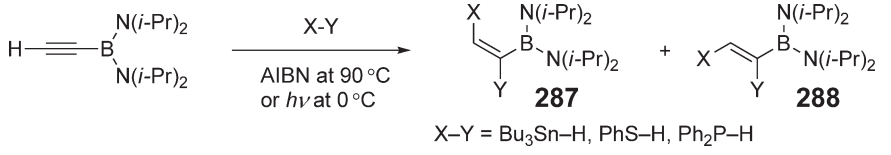
(80)



(81)

9.05.2.2.2.(v) Radical addition reactions

The radical addition to 1-alkenyl or 1-alkynylboronic esters or amides took place extremely smoothly because the boron atom stabilizes the resulting α-radical intermediates. Bu_3SnH and PhSH predominated the *trans*-addition products **287** in the addition to 1-alkynylboronic amides at 90 °C, whereas Bu_3SnH and Ph_2PH produced the *cis*-addition products **288** at 0 °C (>98%; Equation (82)).[455] Intramolecular addition to 1-alkenylboronic esters has been demonstrated in boron-tethered radical cyclization that provided 1,3- or 1,4-alkanediols **290** via oxidative workup (Equation (83)).[456] Inter- and intramolecular additions of alkyl radical[457] and sulfonyl radical[458] have also been studied.



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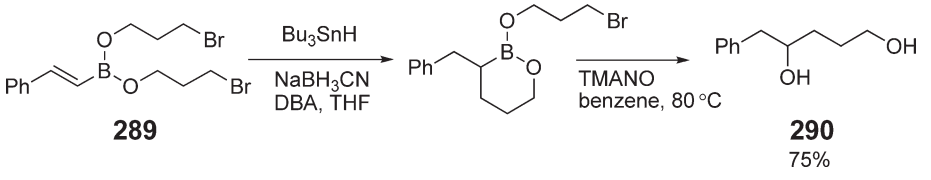
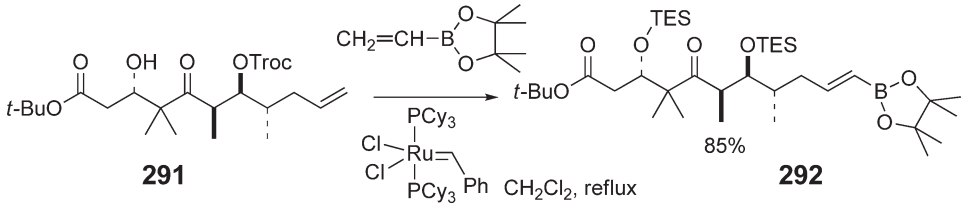


(83)

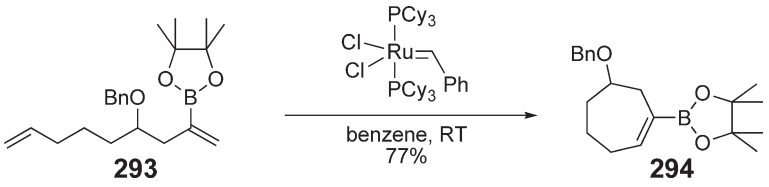
9.05.2.2.3 Metal-catalyzed reactions of alkenyl- and alkynylboron compounds

Ruthenium-catalyzed olefin cross-metathesis (ring-closing metathesis, RCM) between terminal alkenes and vinylboronic acid or esters has recently been developed for the synthesis of (*E*)-1-alkenylboron compounds from alkenes.[459,460] The efficiency of protocol was proved in the synthesis of a key intermediate of epothilone 490 **292**;[461] (Equation (84)). The vinyl boronate was given almost exclusively the *trans*-adduct.



(84)

An intramolecular version of olefin cross-metathesis has been demonstrated in cyclization of α,ω-alkadienes **293**[462] (Equation (85)), cyclization of enyne to provide 1,3-dienylboronic esters **297**[406] (Equation (86)), and in cyclization of boron-tethered enynes obtained from 1-alkynylboronates and allylic alcohols (**298**;[463] (Equation (87)) or allyl boronates and propargyl alcohols.[464]



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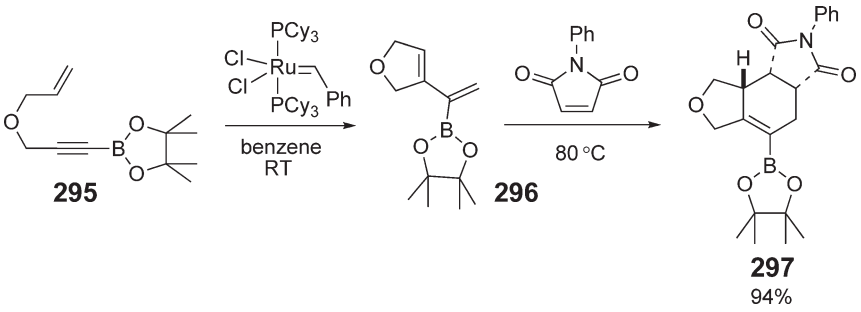
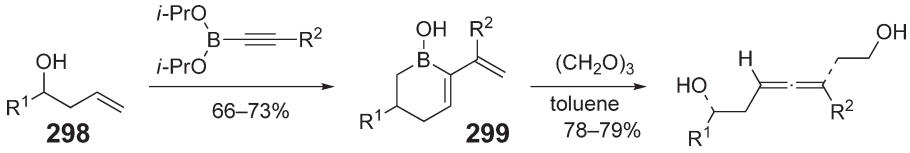
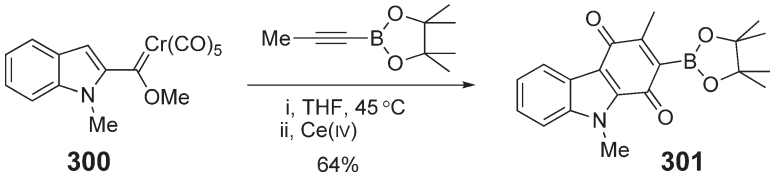


(86)



(87)

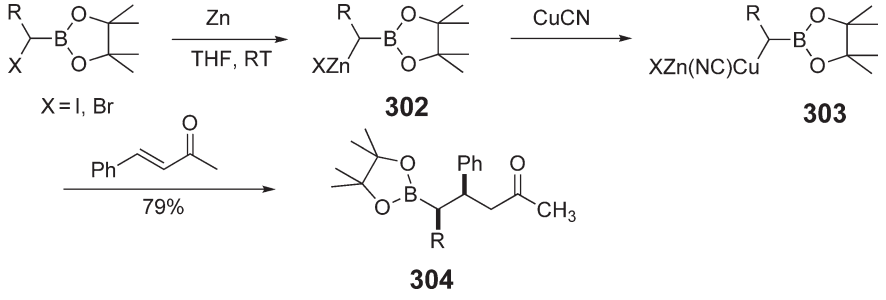
A novel class of quinone boronic esters **301**[465] was synthesized by utilizing a highly regioselective benzannulation of Fischer carbene complexes **300** with 1-alkynylboronates (Equation (88)).



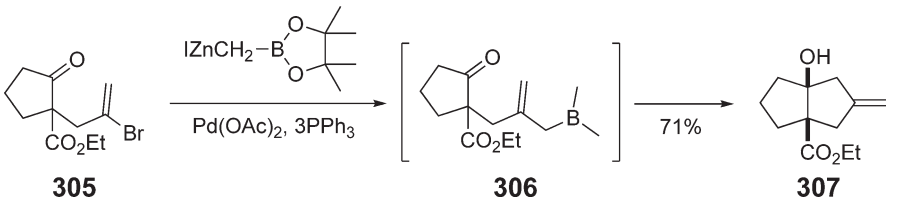
(88)

9.05.2.2.4 Addition and coupling reactions of boron-substituted carbanions

Boron-stabilized carbanions are versatile reagents that have found numerous synthetic applications. They have been prepared via deprotonation of sterically hindered boranes, a boron–lithium exchange of 1,1-diborylalkanes, and nucleophilic addition of organometallic reagents to 1-alkenylboranes (see Section 9.05.2.2.3, Equations (79)–(81)). An α-borylalkylcopper reagent **303** has newly synthesized from **302** that undergo coupling reaction with alkyl halides and 1,4-addition reaction to unsaturated carbonyl compounds (Equation (89)).[466] The reagents were used for the synthesis of allylic **306**[467] and benzylic[468] boron compounds via palladium-catalyzed cross-coupling (Equation (90)).

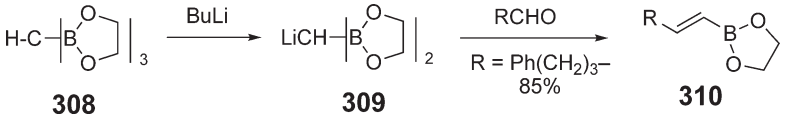


(89)



(90)

The boron-Wittig reaction has been carried out by bis(boryl)methyllithium **309** generated *in situ* from tris(boryl)-methane **308** (Equation (91)).[469] The geminal dichromium reagent **312**[470] was found to be an excellent alternative yielding 1-alkenylboronic esters **313**[470–472] with high *trans*-selectivity (Equation (92)).



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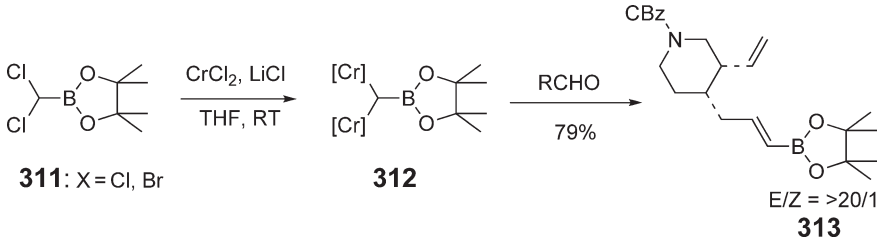

(92)

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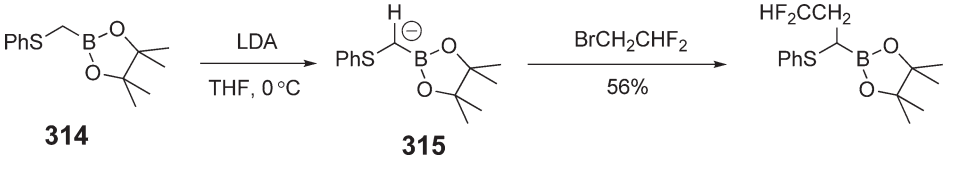
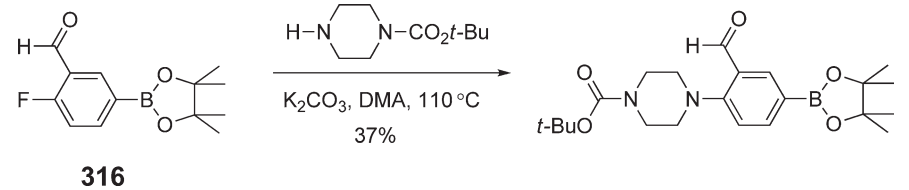
A treatment of **314** with LDA yielded a carbanion stabilized by boron and sulfur atom, which undergoes alkylation with organic halides and with methyl acrylate (Equation (93)).[473]



(93)

9.05.2.2.5 Other methods for functionalization of remote sites

The covalent C–B bonds of organoboronic acids and esters are very inert to ionic and radical reactions, thus allowing functionalization of remote sites other than the B–C bond (Equations (94)–(97)). Bulky diols such as pinacol have been used as the protecting group of $B(OH)_2$ because of their high stability to nucleophiles and water and silica gel in amination of **316**,[474] hydroboration–amination of **317**,[475] Wittig reaction of **318**,[476] and oxidation-alkylation of **319**.[477]



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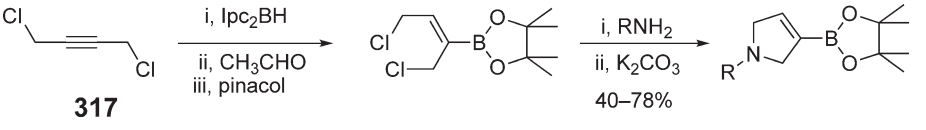

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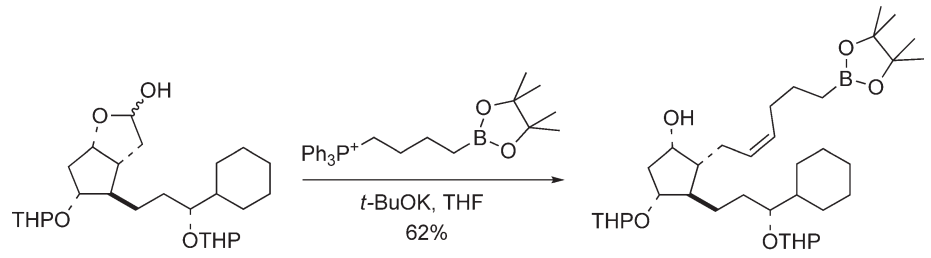
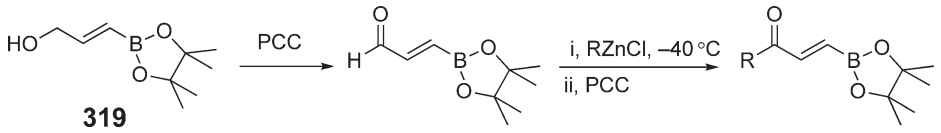
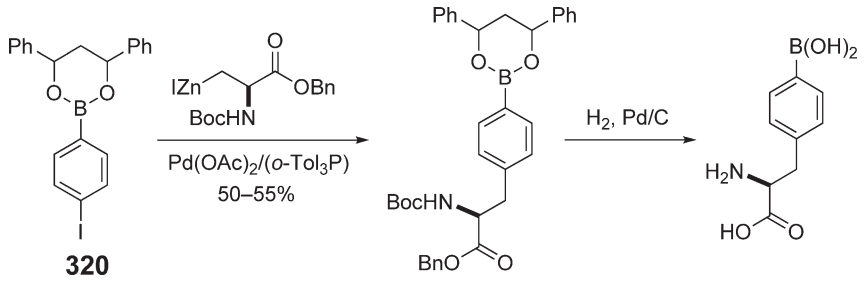


(96)



(97)

The C–B bond of boronic esters is inert for functionalization of remote sites other than the B–C bond by metal-catalyzed reactions (Equations (98)–(100)). Cross-coupling reactions of **320**[478] and **321**,[479] and titanium-Wittig reaction on polymer resin **323**[480] have been studied.



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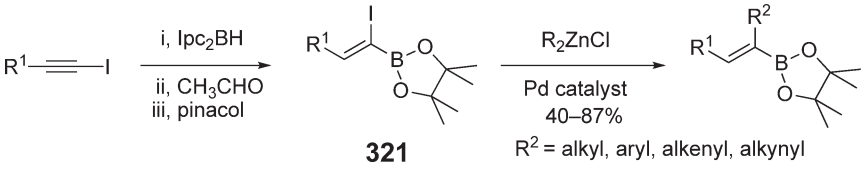
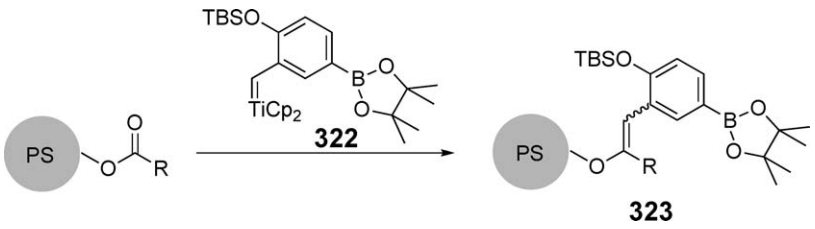


(99)



(100)

9.05.3 Organic Synthesis Using Organoboron Compounds

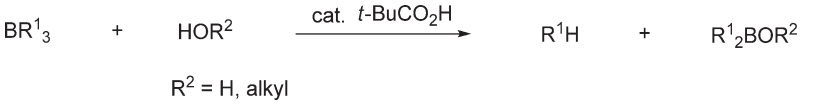
9.05.3.1 Protodeboronation, Oxidation, Halodeboronation, Amination

The empty *p*-orbital on the boron atom of organoboranes makes them electrophilic and highly susceptible to attack by nucleophiles. The tetrahedral species thus formed are known as organoborates. If the nucleophile bears a leaving group, then migration of an organic group on the boron atom occurs very easily.

9.05.3.1.1 Protodeboronation

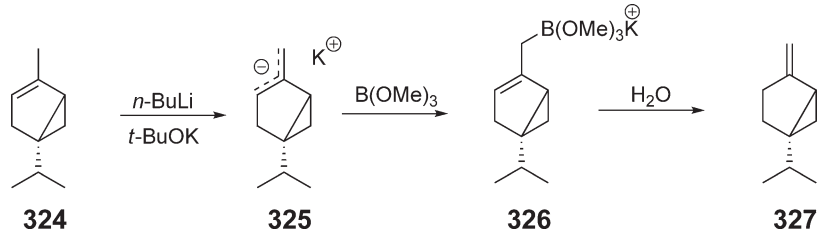
Typical trialkylboranes are relatively stable toward protonolysis by treatment with alcohols, water, aqueous bases, and mineral acids,[481–485] with the exception of anhydrous hydrogen fluoride.[486] In contrast, carboxylic acids react with

trialkylboranes removing the first alkyl group very rapidly. The use of pivalic acid as catalyst allowed selective protonolysis of one of the three alkyl groups with water or alcohols (Equation (101)).[487]

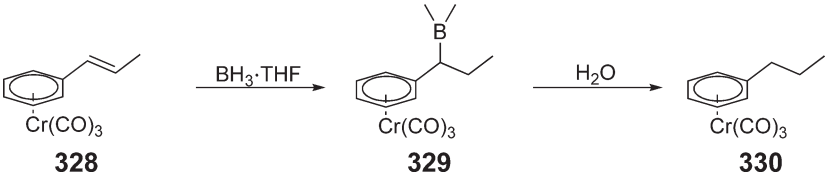


(101)

The B–C bond of allyl-, alkynyl-, aryl-, and benzylboranes is more easily cleaved than that of alkylboranes. The C–B bond of aromatic boronic acids is stable to water, but polyfluorinated phenylboronic acids are exceptionally sensitive to MeOH–H_2O–KOH and MeOH–H_2O–pyridine.[488] Allylic organoboranes were hydrolyzed with water at room temperature with complete allylic rearrangement (Equation (102)).[489,490] Addition of water resulted in the rapid hydrolysis of benzylic C–B bond of **329** due to the electron-withdrawing effect of $Cr(CO)_3$ group (Equation (103)).[491]



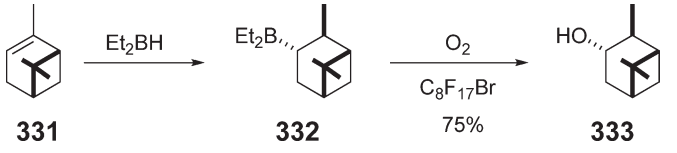
(102)



(103)

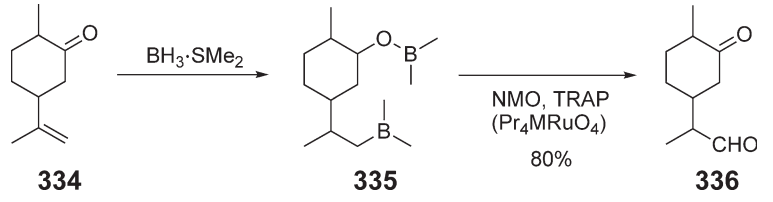
9.05.3.1.2 Oxidation

The standard oxidation procedure employs 30% hydrogen peroxide and 3 M sodium hydroxide. However, functionalities sensitive to strong alkali require milder conditions. In such cases, buffering, simultaneous addition of base and peroxide,[492] or oxidation with Oxone®,[493] triethylamine *N*-oxide,[494–498] peracids,[499,500] or sodium hypochlorite[501] were recommended. Oxygen has been rarely used for such purpose,[502] but trialkylboranes in bromoperfluorooctane were cleanly reacted with oxygen with the retention of configuration of the secondary alkylboranes (Equation (104)).[503]



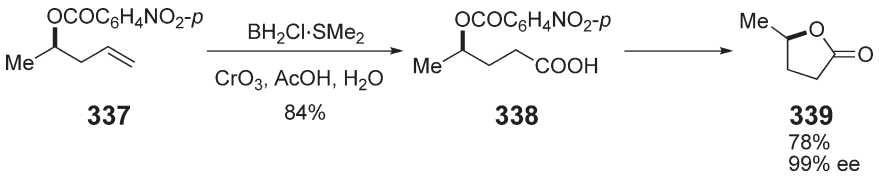
(104)

The oxidation of primary and secondary trialkylboranes with pyridinium chlorochromate (PCC) provided aldehydes or ketones.[504–507] An oxidative conversion of alkenes into a carbonyl compound was conducted by tandem hydroboration and oxidation with excess *N*-methylmorpholine-*N*-oxide (NMO) in the presence of Pr_4NRuO_4 (TPAP) (Equation (105)).[508]



(105)

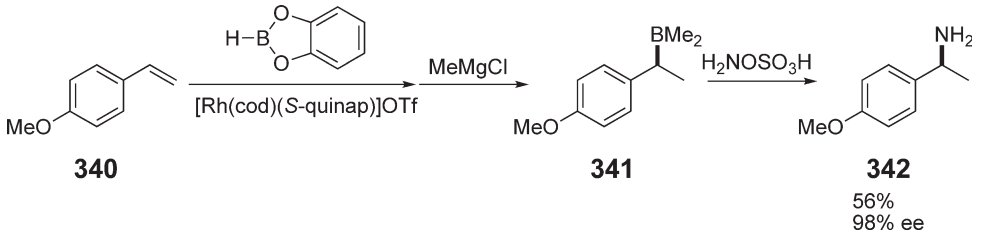
Primary trialkylboranes were directly converted into carboxylic acids by the oxidation with pyridinium dichromate in dimethylformamide, sodium dichromate in aqueous sulfuric acid, or chromium trioxide in 90% aqueous acetic acid (Equation (106)).[509]



(106)

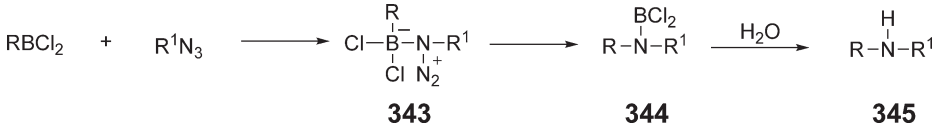
9.05.3.1.3 Amination

Trialkylboranes and dialkylborinic acid or esters react with monosubstituted ammonia derivatives possessing a good leaving group to give primary amines. Amination with chloramine-T, *N*-tosyl-phenyliodinane, *N*-chloro-*N*-sodium carbamates, or lithium and potassium tert-butyl-*N*-tosylcarbamate provided *N*-protected amines,[510] *N*-toluenesulfonamide,[511] *N*-alkylcarbamates,[512] and *N*-tert-butoxycarbonyl derivatives,[513] respectively. Hydrazoic acid is a new reagent which also provided an easy access to the primary amines.[514,515] Hydroxylamine-*O*-sulfonic acid and mesitylsulfonylhydroxylamine were reported to be preferred reagents as against chloramine-T for amination of chiral benzylboranes (Equation (107)).[516–518]

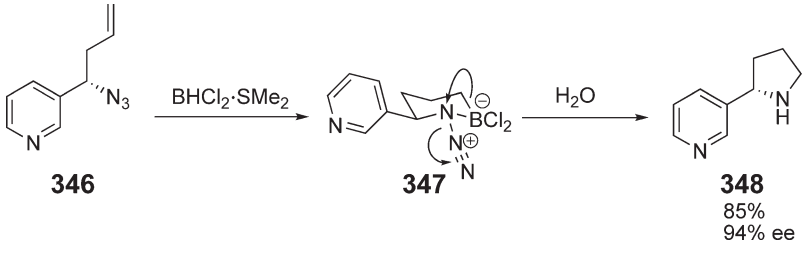


(107)

The reaction of trialkylboranes with *N*-chloro- or *N*-(benzoyloxy)alkylamines afforded secondary amines *via* an anisotropic 1,2-shift of the alkyl group from boron atom to nitrogen in the B–N complex intermediate.[519–521] Alkylation of *N*-chlorodimethylamine with primary trialkylboranes to give *N*,*N*-dimethylalkylamines was conducted in the presence of galvinoxyl to avoid the formation of alkyl chlorides via free radical process.[522,523] A convenient approach to mixed secondary amines is alkylation of alkyl azides with relatively unhindered trialkylboranes in refluxing xylene followed by hydrolysis with water. The reaction smoothly took place at low temperature when trialkylboranes were replaced by alkyl(dichloro)boranes (Equation (108)).[524] Intramolecular amination furnished cyclic amines (Equation (109)).[400,525–528]



(108)



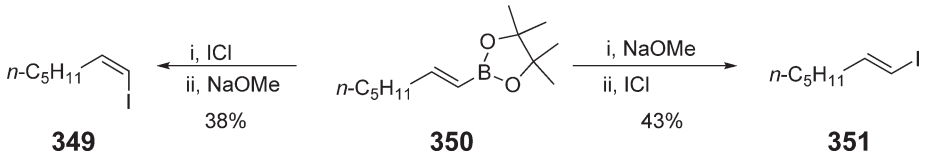
(109)

9.05.3.1.4 Halogenolysis

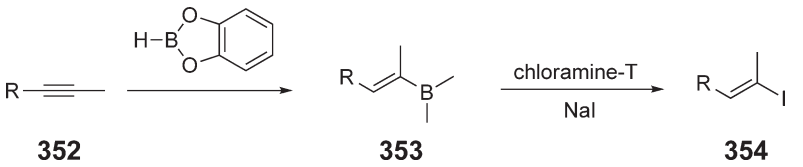
The reaction of trialkylboranes with halogens is sluggish, but the B–C bond can be converted into a C–halogen bond under appropriate reaction conditions.[529,530] Nitrogen trichloride,[531] Cl_2/BCl_3,[532] $CuCl_2$,[533] $FeCl_2$,[534] and dichloramine-T[535,536] have been used for the chlorination of trialkylboranes. The reaction of bromine with trialkylboranes

can be greatly accelerated by the presence of NaOMe.[537] The reaction also took place under neutral conditions in carbon tetrachloride or cyclohexane via a tandem process involving the free-radical bromination of α-CH bond and a cleavage of resulting α-bromoalkylboranes with hydrogen bromide.[538] The reaction between trialkylboranes and iodine was accelerated by bases such as sodium methoxide,[539] but milder reaction conditions employing iodine monochloride–sodium acetate,[540] or sodium iodide in the presence of chloramine-T or *N*-chlorosuccinimide,[541,542] were also suitable for the synthesis of functionalized iodides.

The addition of bromine or iodine to (*E*)-alkenylboronic acids or esters afforded intermediates, which were converted by base into (*Z*)-1-halo-1-alkenes.[543] On the other hand, (*E*)-iodo-1-alkenes of high stereochemical purity were prepared by treatment of (*E*)-1-alkenylboronic acids or esters with sodium hydroxide followed by 1 molar equiv. of iodine.[544] Iodine monochloride was used in place of iodine for such a base-induced iodination with retention or inversion of the stereochemistry (Equation (110)).[545] Chloramine-T/NaI (Equation (111)),[546,547] CuX_2 (X = Cl, Br) (Equation (112)),[548] and *N*-halosuccinimides (Equation (113))[549] halogenated the C–B bond with retention of stereochemistry.



(110)



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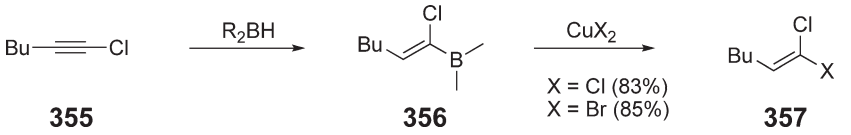
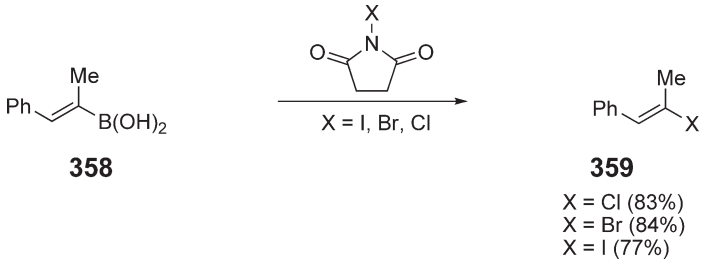


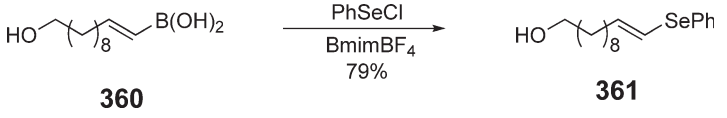
(112)



(113)

9.05.3.1.5 Other transformations

Trialkylboranes were converted into alkyl phenyl selenides and alkyl phenyl tellurides by reactions with PhSeSePh and PhTeTePh in the presence of stoichiometric amounts of air.[550] Vinyl selenides and tellurides were synthesized by treating vinylboronic acids or esters with phenylselenyl chloride in ionic liquids (Equation (114))[551] or by palladium-catalyzed coupling reaction of diorgano ditellurides (Equation (115)).[552]



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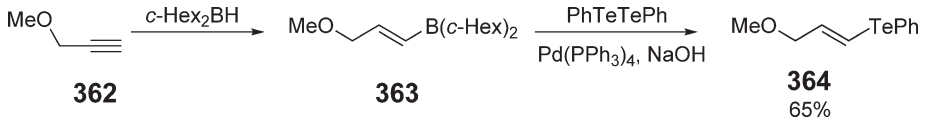
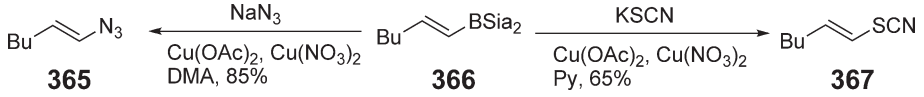


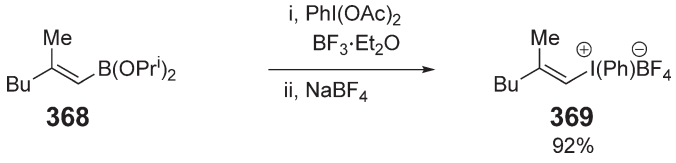
(115)

Iron(II) salts mediated the coupling of trialkylboranes with KSCN to give RSCN via a radical process.[553,554] Stereochemically pure (*E*)-1-thiocyanato-alkenes or (*E*)-1-azide-alkenes were obtained from alkynes when hydroboration with disiamylborane was followed by reaction with potassium thiocyanate or sodium azide in the presence of copper(II) nitrate, copper(II) acetate, and small amount of water in polar aprotic solvent (Equation (116)).[555]

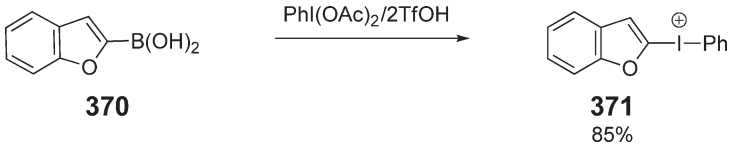


(116)

A boron–iodine exchange between vinyl- and arylboronic acids or esters and hypervalent phenyliodanes gave vinyl- (Equation (117)) and aryl(phenyl)iodonium salts (Equation (118)) with complete retention of configuration.[556,557]



(117)



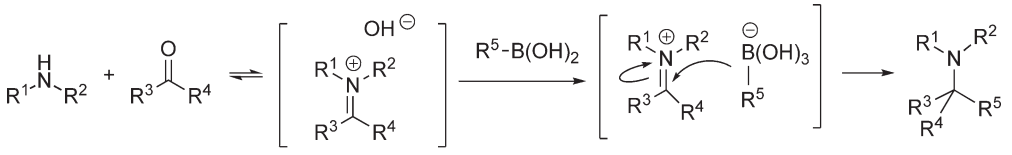
(118)

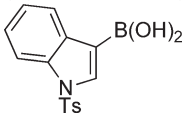
9.05.3.2 Nucleophilic Alkylation of Iminium Ions and other Electrophiles

9.05.3.2.1 Boron-Mannich reactions

Multi-component procedures based upon the Mannich reaction and boron reagents were reported in 1993 as a reaction between vinylboronic acids and the adducts of secondary amines and paraformaldehyde (Table 5, entries 1 and 2).[558]

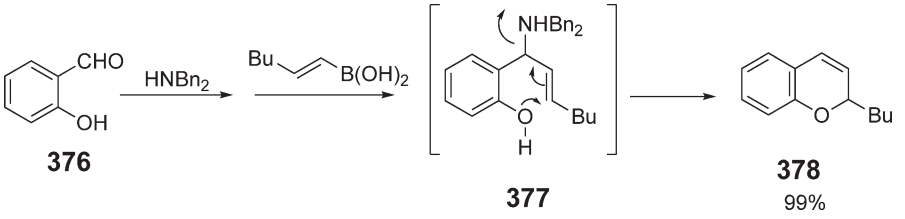
Table 5 Boron-Mannich reactions



Entry	R^1	R^2	R^3	R^4	$R^5B(OH)_2$	*Yield* (%)
1	Bn	Me	H	H	(*E*)-C_5H_{11}CH=CH-B(OH)$_2$	84
2	–$(CH_2)_2O(CH_2)_2$–		H	H	(*E*)-PhCH=CH-B(OH)$_2$	89
3	$(CH_2)_2OH$	H	H	CO_2H	(*E*)-PhCH=CH-B(OH)$_2$	82
4	$CHPh_2$	H	H	CO_2H	(*E*)-BrCH=CH-B(OH)$_2$	80
5	$CHPh_2$	H	Me	CO_2H	(*E*)-*p*-MeC_6H_4-CH=CH-B(OH)$_2$	76
6	Bn	Bn	H	$CH(OH)CH_3$	*p*-$MeOC_6H_4$-B(OH)$_2$	63
7	Bn	Me	H	*o*-HOC_6H_4	(*E*)-PhCH=CH-B(OH)$_2$	81
8	CHMePh	H	H	CO_2H		77
9	$NHCO_2{}^tBu$	CH_2Cy	H	CO_2H	*p*-$MeOC_6H_4$-B(OH)$_2$	99
10	$S(O)^tBu$	H	H	CO_2H	3,4-$(MeO)_2C_6H_3$-B(OH)$_2$	73
11	Me	OMe	H	CO_2H	Ph-B(OH)$_2$	96
12	Bn	Bn	H	*o*-HOC_6H_4	*n*-Bu—≡—BF_3K	81

The reaction has been extensively used for the synthesis of α-amino acids (entries 3–5),[559] *anti*-β-amino alcohols (entry 6),[560] aminophenol (entry 7),[561] optically active *N*-substituted glycines (entries 7 and 8),[562] α-hydrazinocarboxylic acids (entry 9),[563] *N*-sulfinyl and *N*-alkoxy-α-amino acids (entries 10 and 11),[564] and propargyl amines (entry 12).[565]

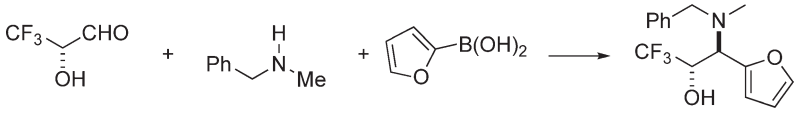
The boron-Mannich condensation was assisted by a hydroxy group adjacent to the aldehyde moiety. The products derived from salicylaldehydes and vinylboronic acids underwent cyclization to 2H-chromene derivatives with elimination of the amine upon heating (Equation (119)).[566]



376 **377** **378** 99%

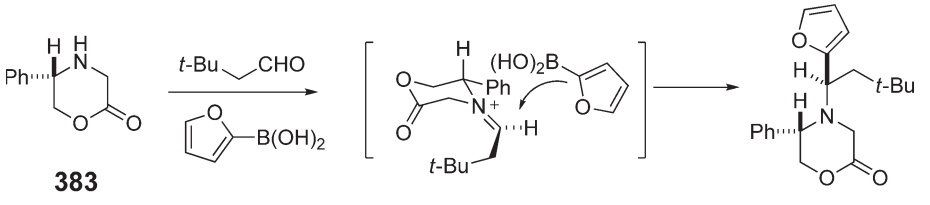
(119)

The synthesis of optically active *anti*-α-(trifluoromethyl)-β-amino alcohols[567] and *anti*-α-(difluoromethyl)-β-amino alcohols[568] was accomplished with high diastereoselectivity starting from the chiral aldehydes (Equation (120)). The use of chiral amines such as (*S*)-5-phenylmorpholine-2-one (Equation (121))[569,570] and (*S*)-2-phenylglycinol (Equation (122))[559] also achieved high diastereoselectivity by nucleophilic attack of an organoboronic acid from the less-hindered face of a chiral (*E*)-iminium ion intermediate.[569]



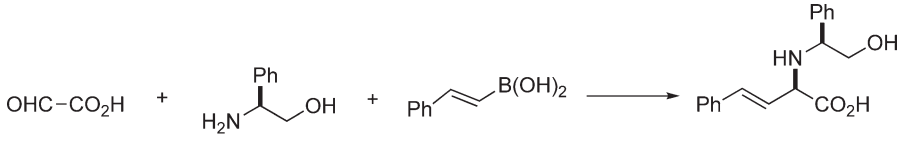
379 **380** **381** **382** 85% 99% de

(120)



383 **384** 75% 92% de

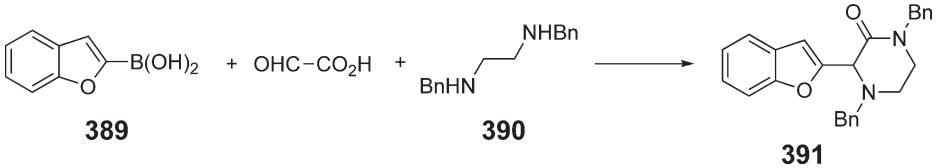
(121)



385 **386** **387** **388** 78% >99% de

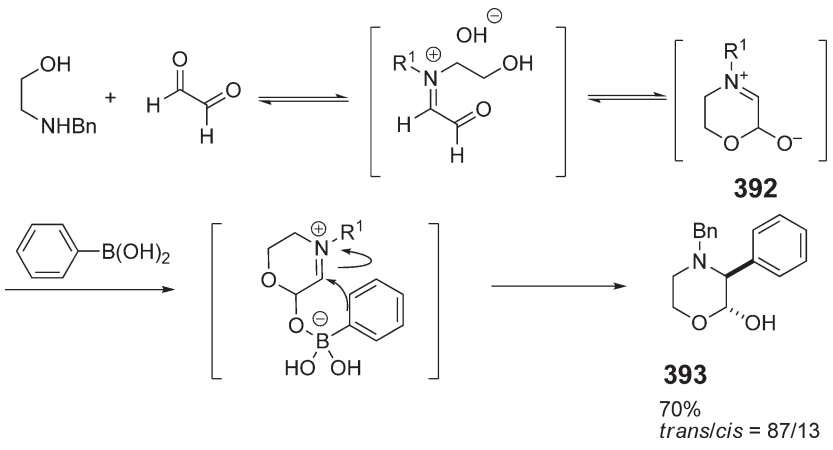
(122)

Alkenyl, aryl, and heteroaryl boronic acids reacted with 1,2-diamines and glyoxylic acid giving directly piperazinones (Equation (123)).[571] 2-Hydroxymorpholines were synthesized from glyoxal, 2-aminoethanols, and aryl- or 1-alkenylboronic acids (Equation (124)).[572]



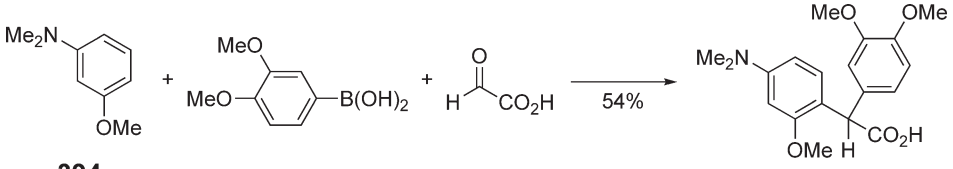
389 **390** **391** 85%

(123)

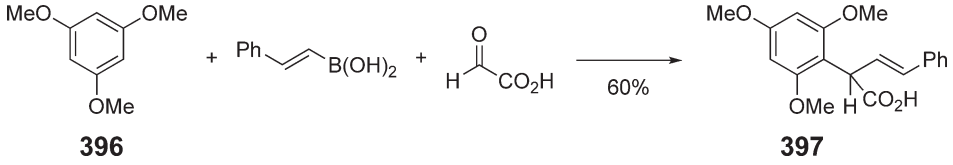


(124)

Tertiary amines can serve as amine substrates for the boron-Mannich reaction, providing aromatic alkylation products of N,N-dialkyl-3-alkoxyanilines (Equation (125))[573] and 1,3,5-alkoxy- or hydroxybenzenes (Equation (126)).[574] The use of chiral diol esters of (*E*)-2-phenylethenylboronic acid for enantioselective alkylation resulted in 6–15% ee.[575]



(125)

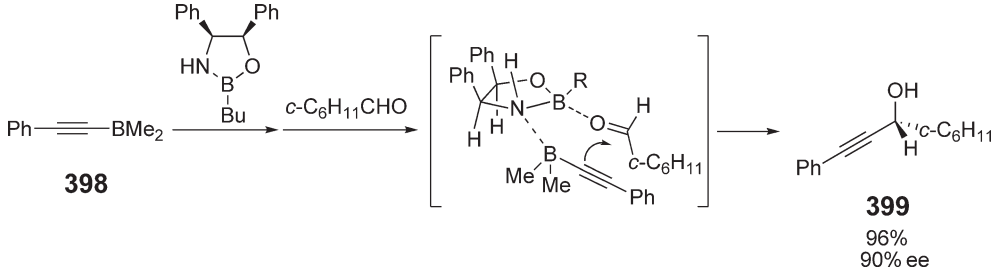


(126)

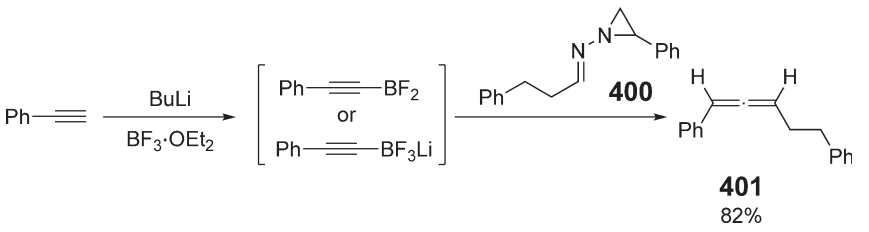
Other reports for the boron-Mannich reaction include the synthesis of aminophenol derivatives,[561] α-arylglycines,[576] a growth hormone secretagogue NN703,[577] a polyhydroxyindolizine alkaloid uniflorine A,[578] and cyclic α-amino acids.[579] The reaction has been applied to solution-phase reactions[580] and the solid-phase reaction[581–585] for the synthesis of libraries of peptides, α-amino acids, and bicyclic diketopiperazines. The reactions were accelerated by the irradiation of microwave.[586]

9.05.3.2.2 Nucleophilic alkylation of C═O, C═N, and enones

The use of chiral oxazaborolidines as catalysts for the enantioselective addition of alkynylboranes to aldehydes took place in a manner analogous to the asymmetric reduction of ketones with boranes mediated by proline-derived oxazaborolidines (Equation (127)).[587] Addition of alkynylboranes to *N*-aziridinylimines provided a convenient method to prepare allenes from carbonyl compounds (Equation (128)).[588]

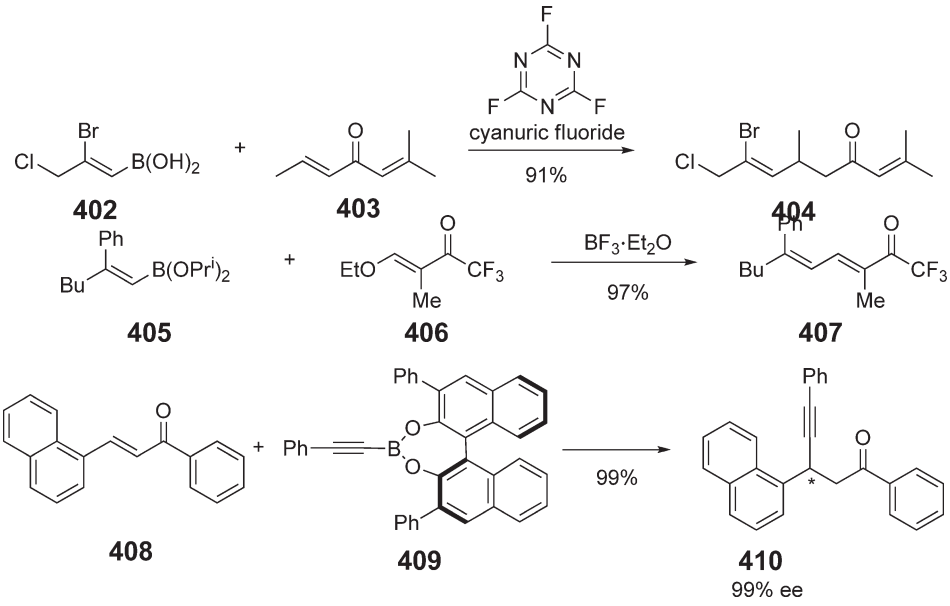


(127)



(128)

Alkenylboronic acids and esters underwent conjugated addition to α,β-unsaturated ketones in the presence of trifluoroborane etherate[589] or cyanuric fluoride (Equation (129)).[590,591] Alkadienyl trifluoromethyl ketones were stereoselectively prepared from (2-alkoxyvinyl) trifluoromethyl ketones (Equation (130)).[592] Alkynyl boronates can transfer the alkynyl groups regioselectively and enantioselectively to enones (Equation (131)).[593]

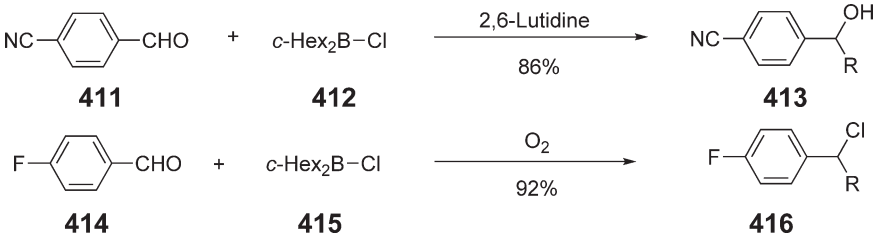


(129)

(130)

(131)

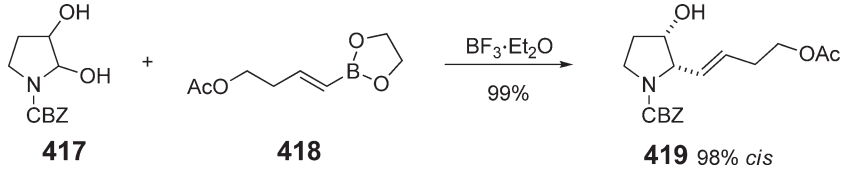
Organoboranes do not normally react with carbonyl compounds in Grignard-like fashion with the exception of allylboranes. Aromatic aldehydes reacted with dialkylboron chloride derivatives in the presence of base to generate arylalkylmethanols in good yields (Equation (132)).[594] On the other hand, reactions of aromatic aldehydes with dialkylboron chlorides in the presence of oxygen resulted in chlorination (Equation (133)).[595]



(132)

(133)

Activated *N*-acyliminium ion precursors were alkylated with 1-alkenyl or aryl boronates in the presence of a Lewis acid catalyst, presumably by an analogous process to that of the boron-Mannich reaction (Equations (134) and (135)).[596,597]



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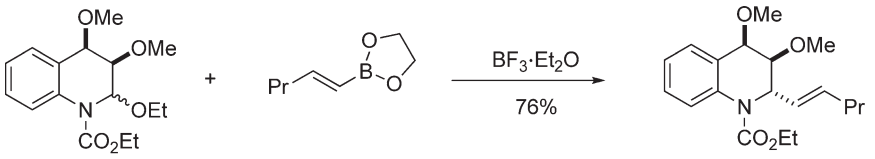
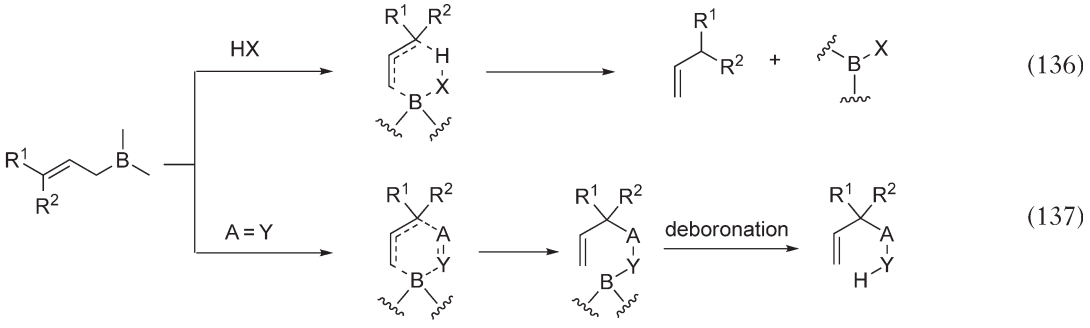


(135)

9.05.3.3 Allylboration, Allenylboration, and Propargylboration

9.05.3.3.1 Synthesis and reactions of allylboron compounds

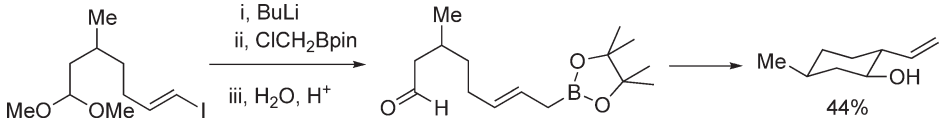
The following reactions proceed with the participation of the allylic boron system: (i) allylboration and protolytic cleavage of organic compounds with multiple bonds, (ii) allylboron–alkyne condensation,[598,599] (iii) reductive mono- and *trans*-α,α'-diallylation of nitrogen aromatic compounds, (iv) disproportionation processes between tribut-2-enylborane and BX_3 (X = Cl, Br, OR, SR). Allylboration of carbonyl compounds, thioketones, imines, or nitriles leads to the homoallylic alcohols, thiols, or amines (Equations (136) and (137). It is most important that 1,2-addition to aldehydes and imines proceeds with high diastereoselectivity so that (*E*)-allylic boranes and boronates give the *anti*-products, while *syn*-products are formed preferentially from (*Z*)-isomers.



(136)

(137)

Several methods for the synthesis of allylboronic esters possessing an ω-carbonyl group were newly developed for intramolecular allylboration. The reported procedures include the reaction between 1-alkenyllithiums and chloromethylboronic pinacol ester ($ClCH_2Bpin$) (Equation (138)),[600,601] the palladium-catalyzed coupling reaction of (*E*)- or (*Z*)-alkenyl halides with $IZnCH_2Bpin$,[600,602,603] and the catalyzed borylation of allyl acetates with bis(pinacolato)diboron (B_2pin_2) (Equation (139)).[309,310] For the synthesis of γ-alkoxyallylboron compounds and for intramolecular allylboration, the iridium-catalyzed isomerization of 3-alkoxy-1-propenylboronic esters (Equation (140))[604,605] and a method for generation of a formyl group via rhodium-catalyzed hydroformylation (Equation (141))[606, 607] were recently developed.



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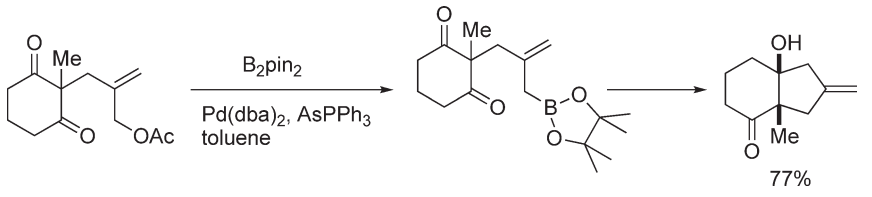

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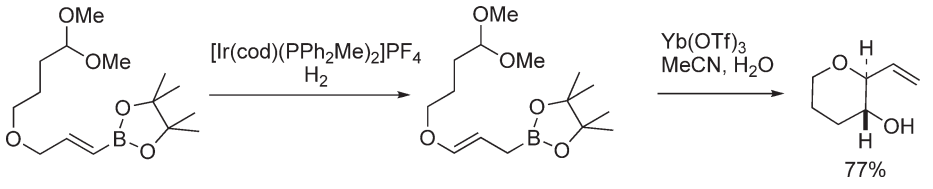
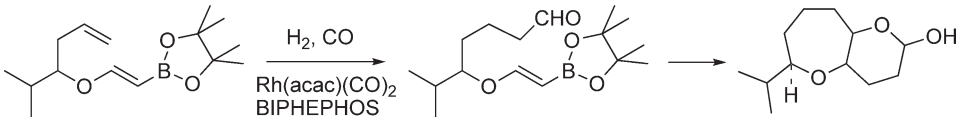
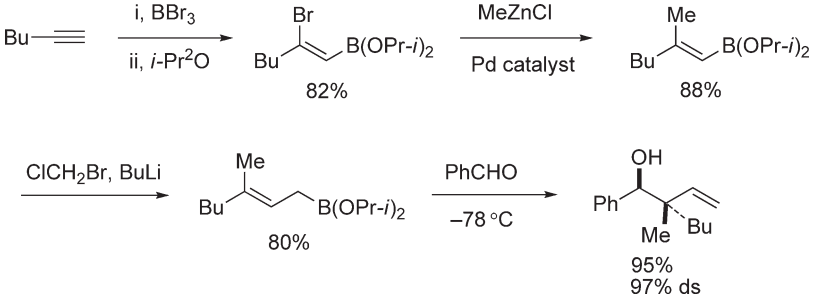


(140)

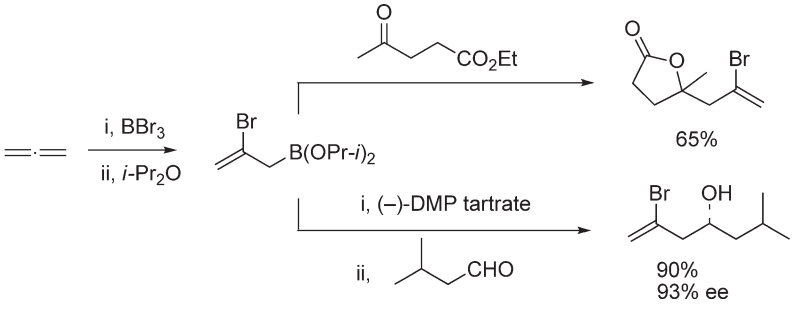


(141)

New classes of allylboron compounds were synthesized based on haloboration. 3,3-Disubstituted allylborane derivatives were stereoselectively synthesized by a sequence of haloboration, Negishi coupling, and Matteson homologation reaction. They afforded homoallylic alcohols having a quaternary carbon with high diastereoselectivities (Equation (142)).[196] An asymmetric version using the tartrate ester derivatives resulted in 40–85% ee.[608] Bromoboration of allene with BBr_3 provided 2-bromoallylboronic esters, which undergo allylboration of carbonyl compounds (Equations (143)[197] and (144)[609]).



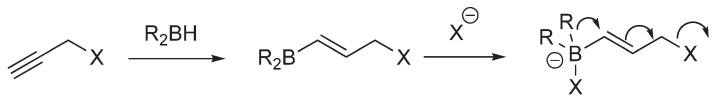
(142)

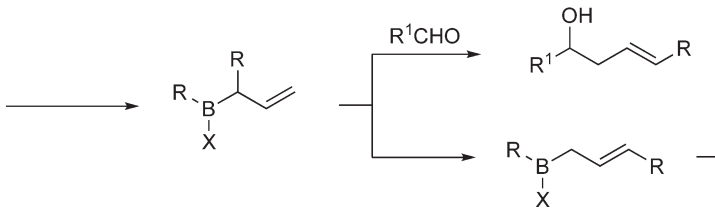


(143)

(144)

(3-Haloalken-1-yl)dialkylboranes, obtained by hydroboration of propargyl halides with dialkylboranes, smoothly rearranged to (*E*)-allyboranes, which can be trapped with aldehydes. This one-pot three-component sequence provided linear homoallyl alcohols (Equation (145)) or *anti*-homoallyl alcohols (Equation (146)).[610–612]

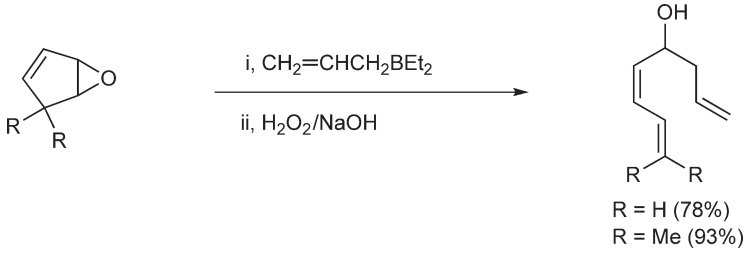




(145)

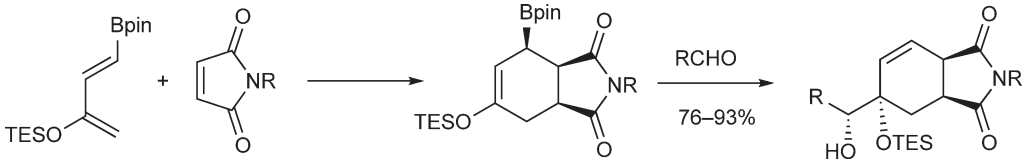
(146)

Allylboration of representative vinylic epoxides with allylboranes afforded a mixture of 1,2- and 1,4-addition products with epoxide ring opening. In contrast, 3,4-epoxycyclopentenes (R = H, Me) unexpectedly resulted in opening the five-membered ring (Equation (147)).[613]



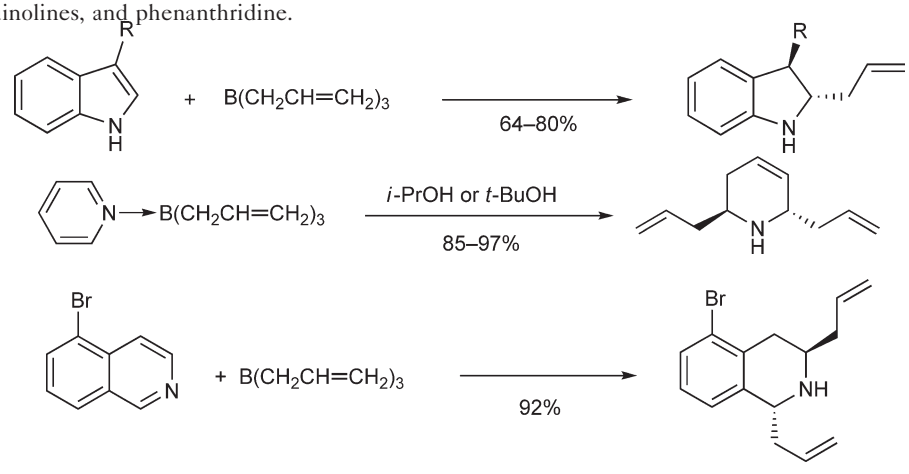
(147)

3-Alkoxy-1-boronobutadiene reacted with maleimides, acrylates, and acrylamides to provide cyclic allyl boronates which undergo allylboration with aldehydes (Equation (148)).[409] Analogous syntheses of cyclic allylboron compounds via [2+4]-cycloaddition is discussed in Section 9.05.2.2.1.



(148)

Indoles underwent the reductive α-allylation upon treatment with allylboranes (Equation (149)).[614] Analogously, allylboranes added to pyridines (Equation (150))[615] and isoquinolines (Equation (151))[616] as well as 4,4-dipyridyl, pyrroles, quinolines, and phenanthridine.

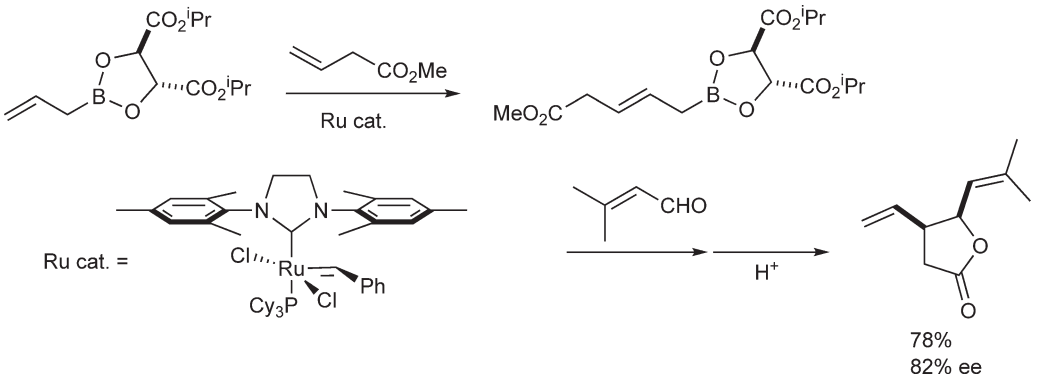


(149)

(150)

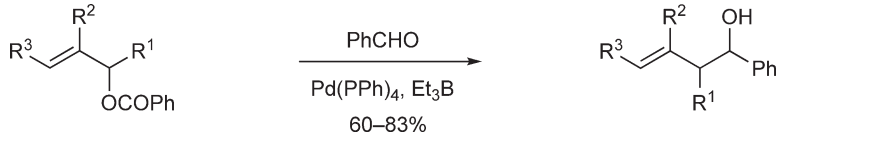
(151)

The ruthenium-catalyzed olefin cross-metathesis to the preparation of functionalized allyl boronates has resulted in a one-pot three-component coupling procedure for the synthesis of functionalized homoallylic alcohols.[617,618] The utility of the protocol was demonstrated in asymmetric allylboration using a tartrate ester (Equation (152)).[617]



(152)

Various metal catalysts accelerate the allylation of carbonyl and imine substrates. Triethylborane induced the addition of allylbenzoates, -phenyl ethers, and -benzyl ethers in the presence of $Pd(PPh_3)_4$ (Equation (153)).[619] Lewis acids and Bu_4NI catalyzed allylboration with potassium allyl- and crotyltrifluoroborates (Equation (154)).[30,40,620,621] The reaction of pinacol ester derivatives was very slow even at room temperature, but $Sc(OTf)_3$ smoothly catalyzed the addition at −78 °C with high diastereoselectivity (Equation (155)[622] and (156)[623,624]). A palladium pincer complex catalyzed the addition of trifluoroborate to tosylimines (Equation (157)).[625]



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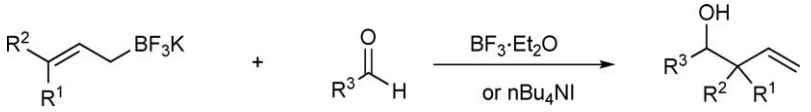
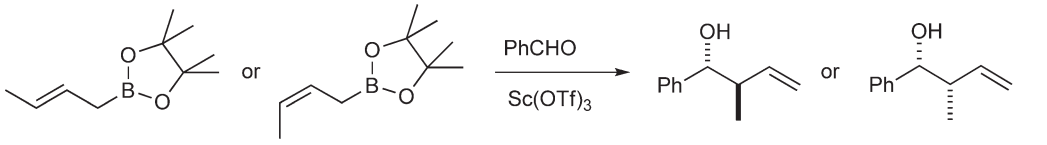


(154)



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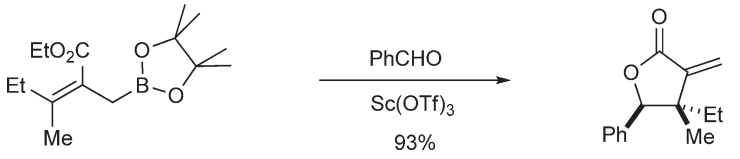
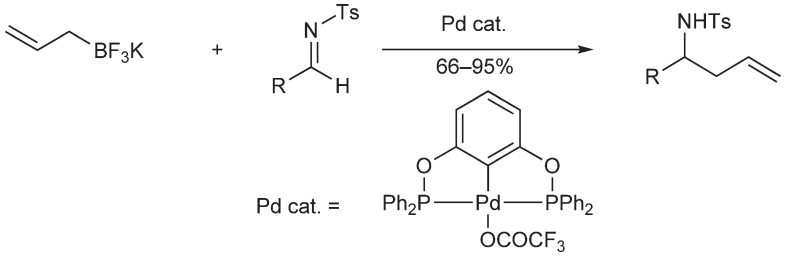


(156)



(157)

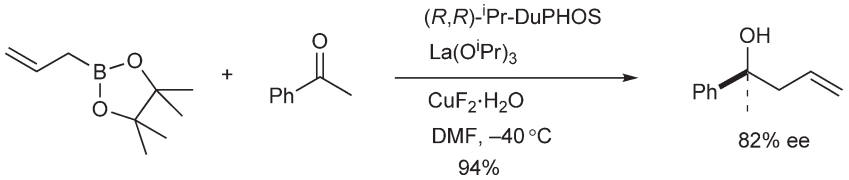
9.05.3.3.2 Asymmetric allylboration

For the purpose of asymmetric allylborations, chiral diols have been used as excellent directing groups. Chiral *B*-allyldiisopinocampheylboranes (allylB(Ipc)$_2$) were found to be excellent alternatives. There are useful reviews of

stereoselective allylmetal chemistry, including a comprehensive summary of the reactions of allylic boron compounds.[1,3,624,626,627]

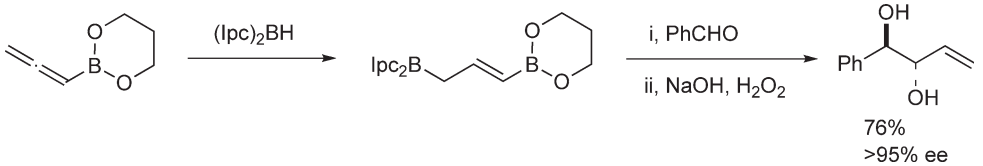
The metal-catalyzed allylboration is efficient to control both diastereoselectivity and enantioselectivity. The $Sc(OTf)_3$-catalyzed reaction of chiral allyl boronates resulted in 90–98% ee for representative aldehydes (Equation (158)).[624,628,629] The first catalytic enantioselective allylboration and crotylboration was achieved by a chiral lanthanide catalyst (Equation (159)).[630]

(158)



(159)

B-Allyldiisopinocampheylboranes introduced by Brown are particularly useful for asymmetric allylboration.[627] The reagents can be prepared by monohydroboration of terminal allenes or from either Ipc_2BCl or Ipc_2BOMe and allylmagnesium or -lithium reagents. Hydroboration of allenes with Ipc_2BH was followed by *in situ* allylboration of aldehydes for various synthesis of chiral homoallyl alcohols. γ-Borylallylborane obtained by hydroboration of boryl allene reacted with aldehydes at −78 °C. After oxidative work-up, *anti*-diols were afforded with high enantioselectivity (Equation (160)).[631] Analogously, optically active alcohols were synthesized starting from acyclic allenes (Equation (161))[632–635] and cyclic dienes (Equation (162)).[636]



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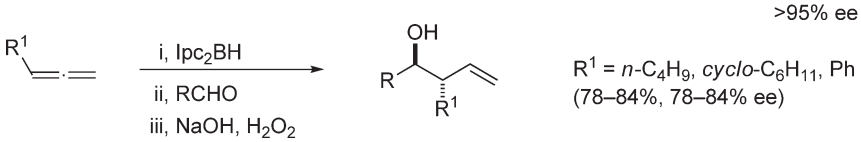
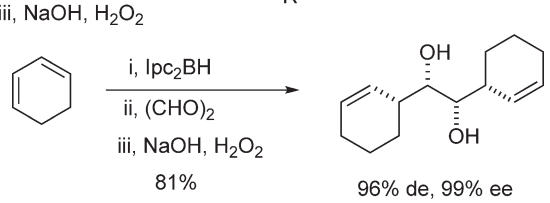
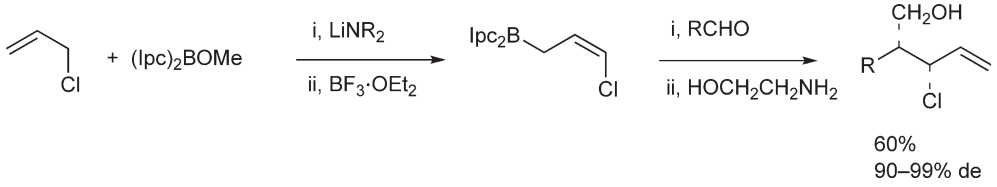


(161)

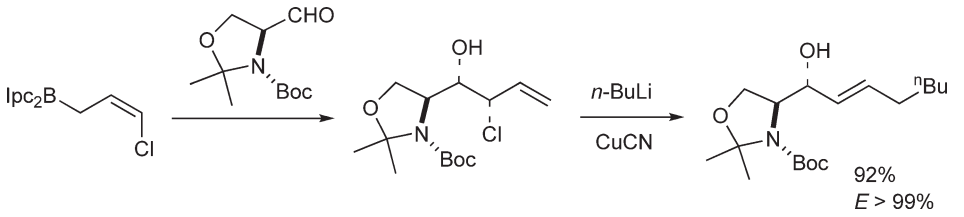


(162)

The (*Z*)-γ-chloroallyl derivatives of (+)- or (−)-diisocampheylborane were prepared via the sequential treatment of a mixture of allyl chloride and $(Ipc)_2BOMe$ with $LiN(c\text{-Hex})_2$ and $BF_3{\cdot}OEt_2$ which was directly reacted with aldehydes to give chiral *syn*-chlorohydrins (Equation (163)).[637] The chlorohydrines thus obtained were converted into optically active epoxides for the synthesis of (+)-disparlure[638] and D- and L-*erythro*-sphingosine and its analogs via treatment with organocopper reagents (Equation (164)).[639]

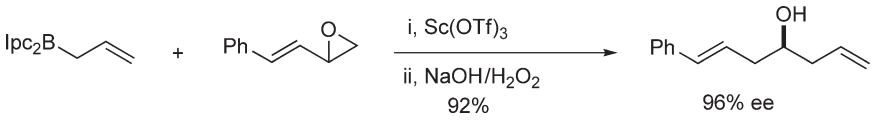


(163)



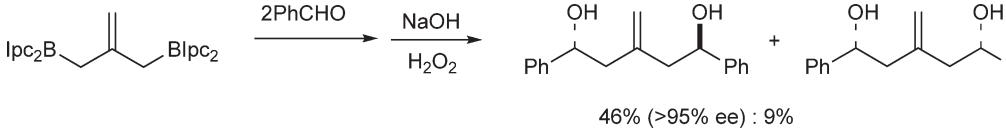
(164)

2-Vinyloxiranes have been found to be excellent surrogates to β,γ-unsaturated aldehydes in the preparation of bis(homoallylic) alcohols. $Sc(OTf)_3$ catalyzed the reaction at −78 °C (Equation (165)).[640]

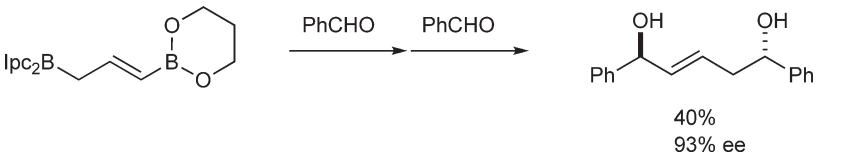


(165)

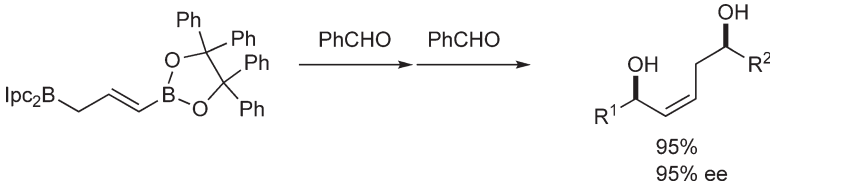
The double allylboration of aldehydes using 1,3-bisboryl-2-methylenepropane provided C_2-symmetric 1,5-diols with excellent ee (Equation (166)).[641,642] (*E*)-1,5-diols (Equation (167))[643] or (*Z*)-1,5-diols (Equation (168))[643] were diastereoselectively synthesized via double allylboration of aromatic or aliphatic aldehydes with γ-borylallylboranes.



(166)

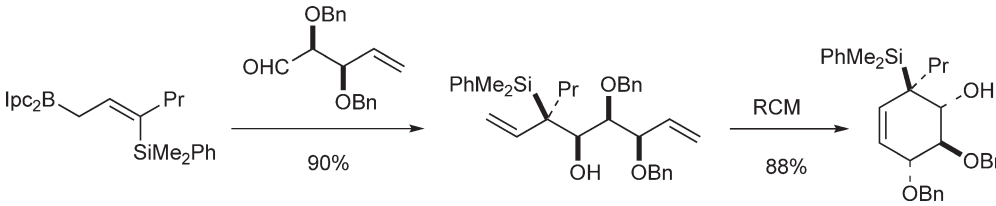


(167)



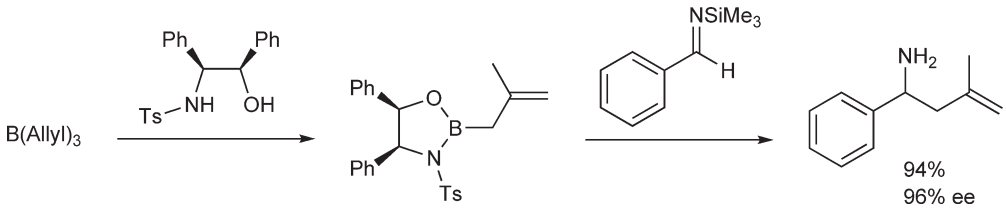
(168)

Hydroboration of silylallenes with Ipc_2BH, followed by addition to aldehydes, produced *syn*-homoallylalcohols, which were converted into optically active cyclic allylsilanes via RCM (Equation (169)).[644,645]

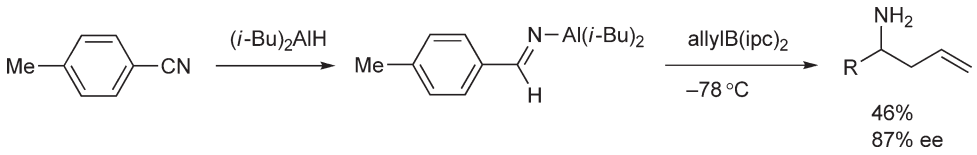


(169)

Optically active *N*-sulfonylamino alcohols derived from D-camphor or norephedrine were found to be efficient chiral ligands for the enantioselective allylboration of *N*-silylimines (Equation (170)).[646–648] B-Allyl(diisopinocampheyl)borane allylated *N*-diisobutylaluminum imines with 87% ee (Equation (171)).[649,650]

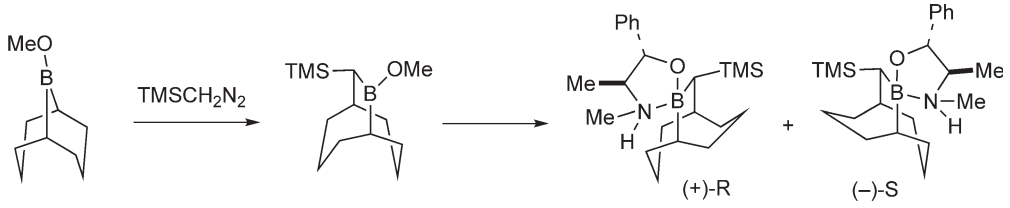


(170)

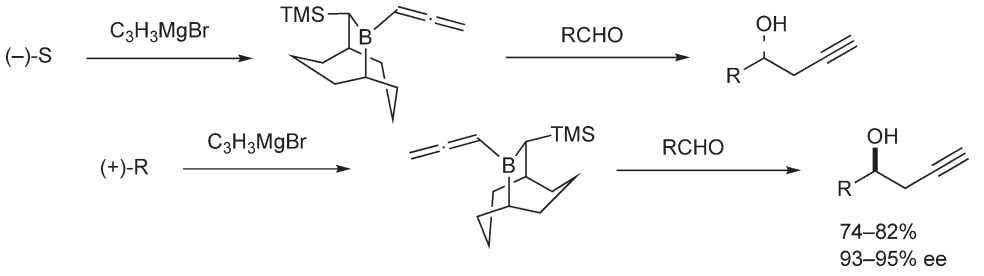


(171)

B-allyl-[651] and *B*-allenyl-10-TMS-9-borabicyclo[3,3,2]decane[652] were newly synthesized for allylboration and allenylboration of carbonyl compounds. They were easily and efficiently prepared in either enantiomeric form and gave homoallyl alcohols and homopropargylic alcohols with high enantioselectivity (Equations (172) and (173)).[652]



(172)



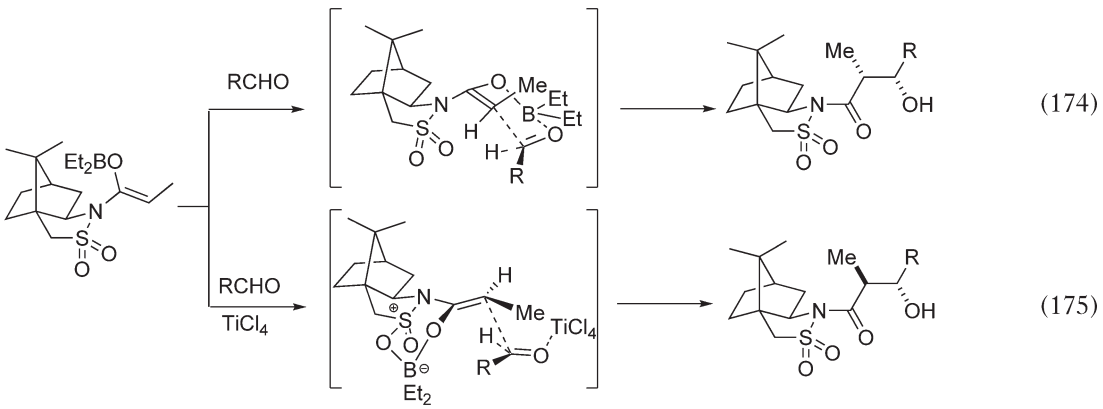
(173)

Asymmetric allylboration using tartrate- and pinane-derived reagents have been successfully exploited in the synthesis of various natural products.[653–673]

9.05.3.4 Aldol Reaction of Boron Enolates

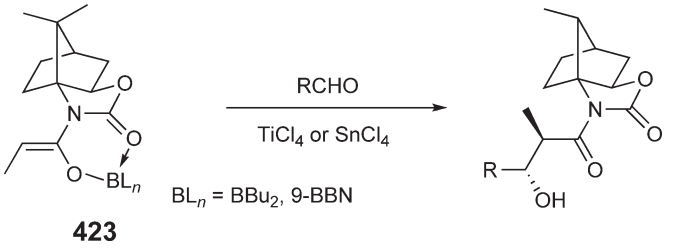
Boron enolates are important intermediates for the aldol reaction, since the transition states of their addition reactions to aldehydes and ketones appear tightly organized, transmitting well the spatial arrangement to the aldol product. The reaction has been reviewed.[674,675]

Boryl enolates prepared from *N*-propionylsultam reacted with aliphatic, aromatic and α,β-unsaturated aldehydes to provide diastereomerically pure *syn*-aldols (Equation (174), whereas the presence of $TiCl_4$ caused complete reversal of the diastereoface selectivity giving *anti*-aldols (Equation (175)).[676–678] Camphor-derived chiral boryl enolates **423** were highly reactive and highly anti-selective enolate synthon system in aldol addition reactions promoted by $TiCl_4$ or $SnCl_4$ co-catalyst (Equation (176)).[679]



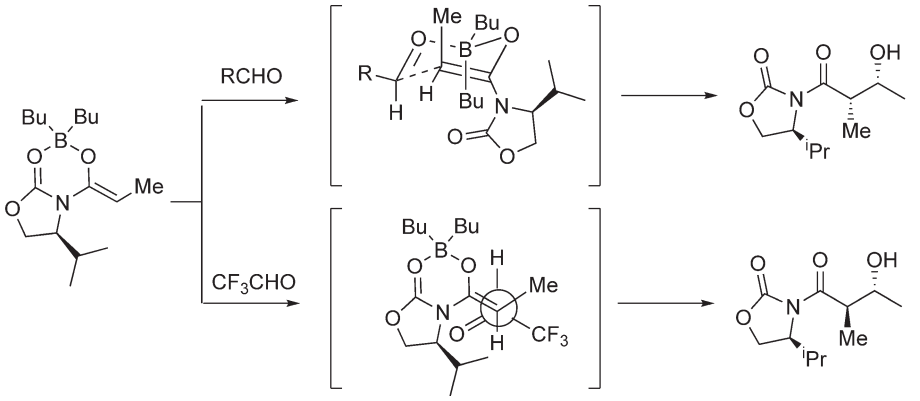
(174)

(175)



(176)

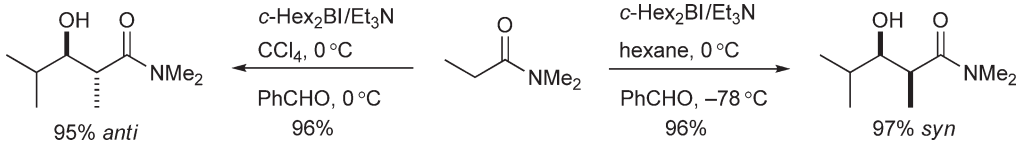
The Evans-aldol method using a boron enolate derived from chiral *N*-acyloxazolidinone reacted with aldehydes to give *syn*-aldols via attack exclusively on the *re* face of the double bond of the enolate (Equation (177)). Unexpected and unusual *si* face attack was resulted in the reaction with fluorine-containing carbonyl compounds such as trifluoro acetaldehyde (Equation (178)).[680,681]



(177)

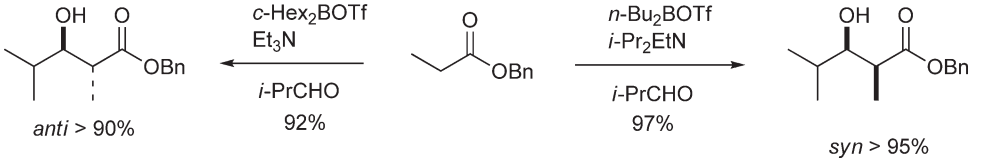
(178)

Both the nature of solvent and the temperature influenced the stereochemistry of boron enolates, with the solvent effect being greater than that of the temperature. Aliphatic and alicyclic hydrocarbon solvent favored the formation of *syn*-aldols at −78 °C, whereas aromatic and chlorinated aliphatic solvents favored the formation of *anti*-aldols at 0–25 °C (Equation (179)).[682,683]

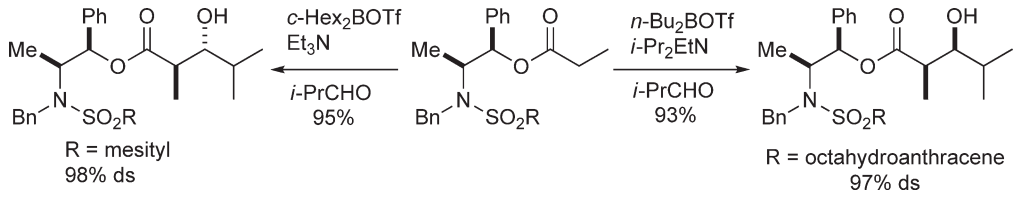


(179)

The stereochemical course of the aldol reaction can be controlled by the judicious selection of the enolization reagents. Treatment of propionate esters with *c*-Hex_2BOTf and triethylamine produced *anti*-aldol products, and that of with Bu_2BOTf and diisopropylethylamine selectively gave *syn*-aldol products after reaction with aldehydes (Equation (180)).[684,685] Complementary *anti*- and *syn*-selective asymmetric aldol reactions were also demonstrated in structurally related chiral norephedrine-derived propionate esters (Equation (181)).[686]

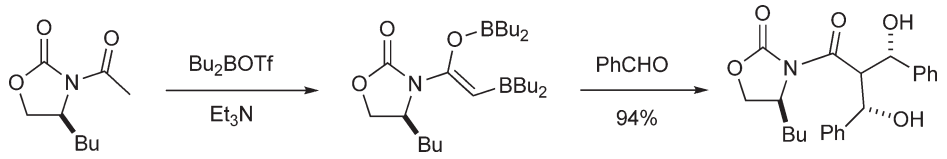


(180)



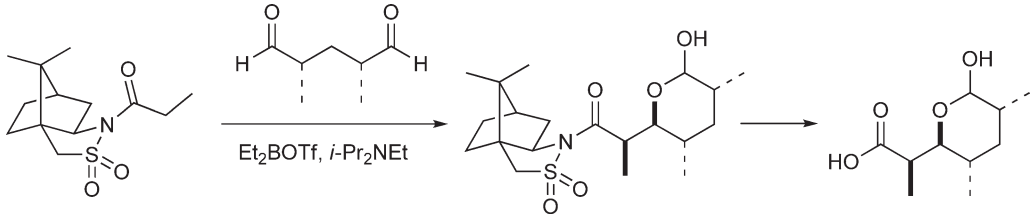
(181)

Treatment of chiral oxazolidinone with Bu_2BOTf and Et_3N quantitatively produced a novel doubly borylated enolate, which afforded the double aldol products with high diastereoselectivity in the reaction with aldehydes (Equation (182)).[687,688]



(182)

The group-selective aldolization/desymmetrization of *meso*-dialdehyde with a boron enolate of *N*-propionylsultam yielded lactols with simultaneous generation of four stereogenic centers. Oxidation followed by saponification of the sultam moiety provided the Prelog–Djerassi lactonic acid in 61–71% overall yields (Equation (183)).[689]



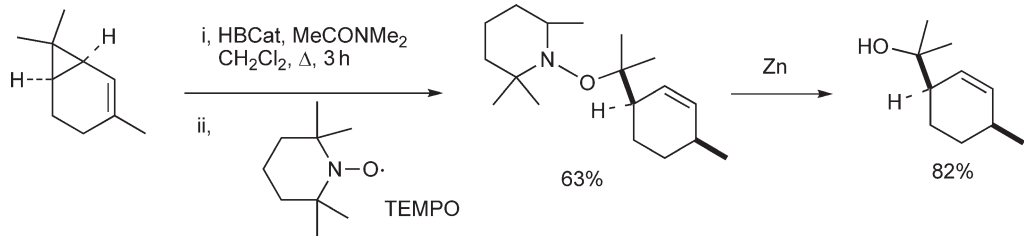
(183)

9.05.3.5 Radical Addition and Coupling Reactions

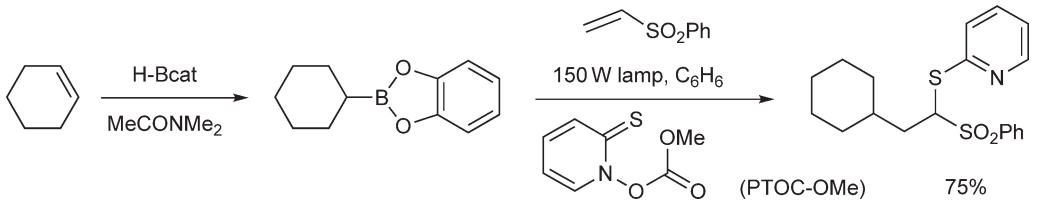
The ability of organoboranes to participate in free-radical reactions has been identified since the earliest investigations of their chemistry. For instance, the autoxidation of organoboranes has been proved to involve radical intermediates (Equation (184)). The reaction has led recently to the use of triethylborane as a universal radical initiator, functioning under a very wide range of reaction conditions.[690–697]

(184)

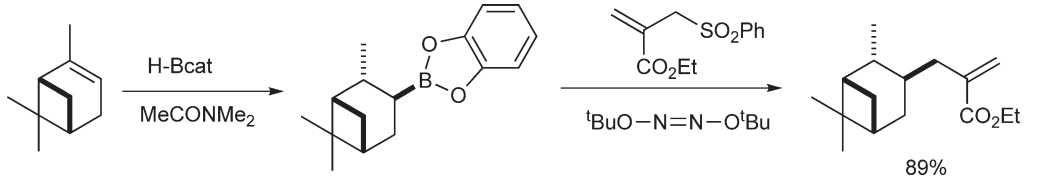
Although typical boronic esters are inert to oxygen, B-alkylcatecholboranes are sensitive toward oxygen and alkoxyl radicals such as TEMPO. The hydroboration of 2-carene with HBcat, followed by treatment with TEMPO, resulted in the ring opening of 2-carene (Equation (185)).[698,699] *B*-alkylcatecholboranes were used as radical precursors in the presence of oxygen for conjugate addition to α,β-unsaturated aldehydes and ketones.[700] Other radical traps such as unsaturated esters, amides, and sulfones failed to react under these conditions. PTOC-OMe was found to be an initiator under irradiation with 150 W tungsten lamp (Equation (186)).[701–704] The reaction of allylsulfones with primary, secondary, and tertiary alkyl radicals afforded coupling products (Equation (187)).[705] Both the hydroboration and the radical reaction occurred from the less-hindered face on the alkene and of the radical intermediate.



(185)

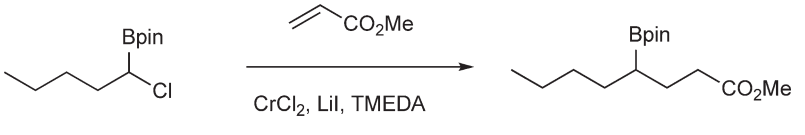


(186)

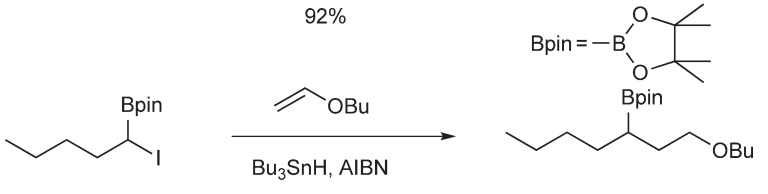


(187)

Alkyl radicals stabilized with boron atom are easily generated and undergo addition and coupling reactions. Such α-boryl radicals were generated *in situ* by treatment of α-chloroalkylboronic esters with $CrCl_2$ (Equation (188))[706] or with radical initiators such as AIBN (Equation (189)).[707]

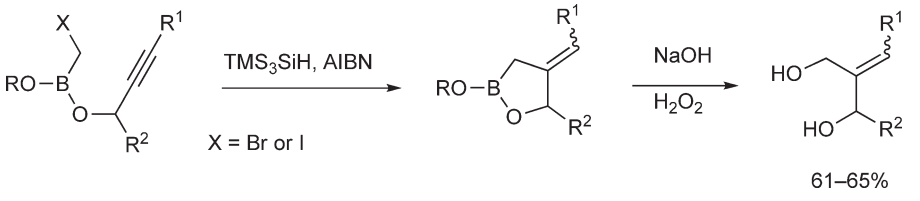


(188)



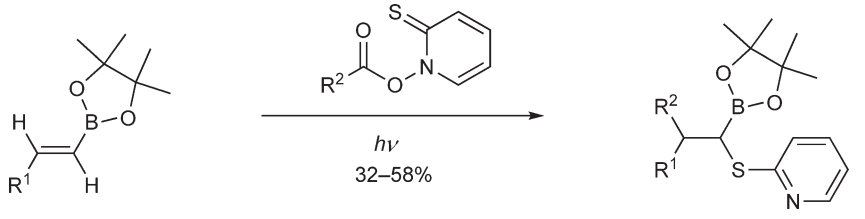
(189)

α-Boryl alkyl radicals underwent cyclization onto alkenyl and alkynyl traps tethered by a C–B–O linkage (Equation (190)).[708]

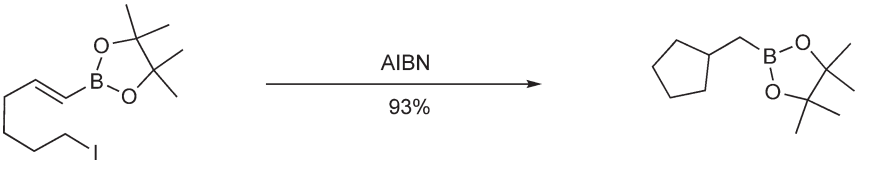


(190)

1-Alkenylboranes were proved to be useful traps for nucleophilic alkyl radicals, thus opening attractive routes to diversely substituted alkyl- and alkenylboronic esters (Equations (191) and (192)).[457]



(191)

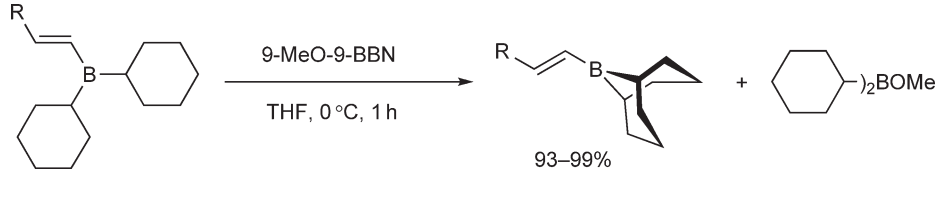


(192)

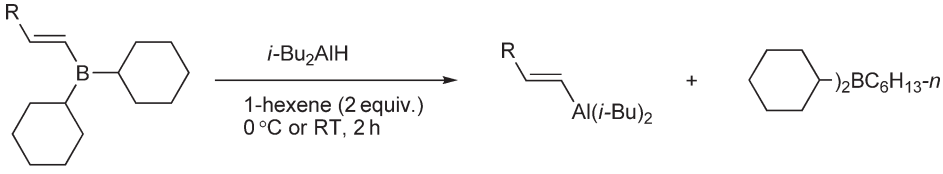
9.05.3.6 Transmetallation to other Metals for Addition and Coupling Reactions

The covalent B–C bond of organoboron compounds shows little reactivity toward representative electrophiles, but the presence of an empty low-lying orbital facilitates transmetallation to other metals. The transmetallation to zinc[709] and other metal reagents has been extensively studied for carbon–carbon bond formation via addition and coupling reactions of trialkylboranes and alkylboronic acids.

The synthesis of 9-alkenyl-9-BBN via hydroboration of terminal alkynes with 9-BBN suffered from the formation of 1,1-diborylalkanes via dihydroboration along with desired monohydroboration products. Alternatively, selective monohydroboration of terminal alkynes with dicyclohexylborane was followed by transmetallation with 9-MeO-9-BBN (Equation (193)).[710] Treatment of the hydroboration intermediates with DIBAL-H in the presence of a borane-trapping reagent such as 1-hexene gave 1-alkenylaluminum compounds with complete retention of the (E)-stereochemistry (Equation (194)).[711]



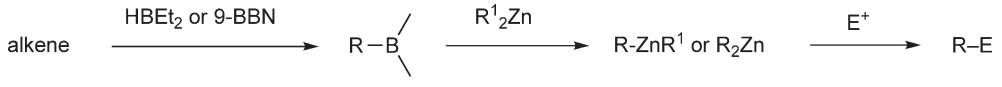
(193)



(194)

R = *n*-C_8H_{17}, *t*-C_4H_9, Ph, *cyclo*-C_6H_{11} (72–87%)

Organoboranes in nonpolar solvents transmetallate to dialkylzinc compounds under mild conditions (Equation (195)). The driving force of the reaction is the formation of stable dialkylzinc compounds or the formation of volatile organoboranes such as BMe_3 when Me_2Zn was used. Transmetallations with Me_2Zn or Et_2Zn were used for the preparation of primary dialkylzinc, dibenzylzinc, and 1-alkenylzinc compounds. On the other hand, *i*-Pr_2Zn gave the better results for preparation of the secondary dialkylzinc compounds.

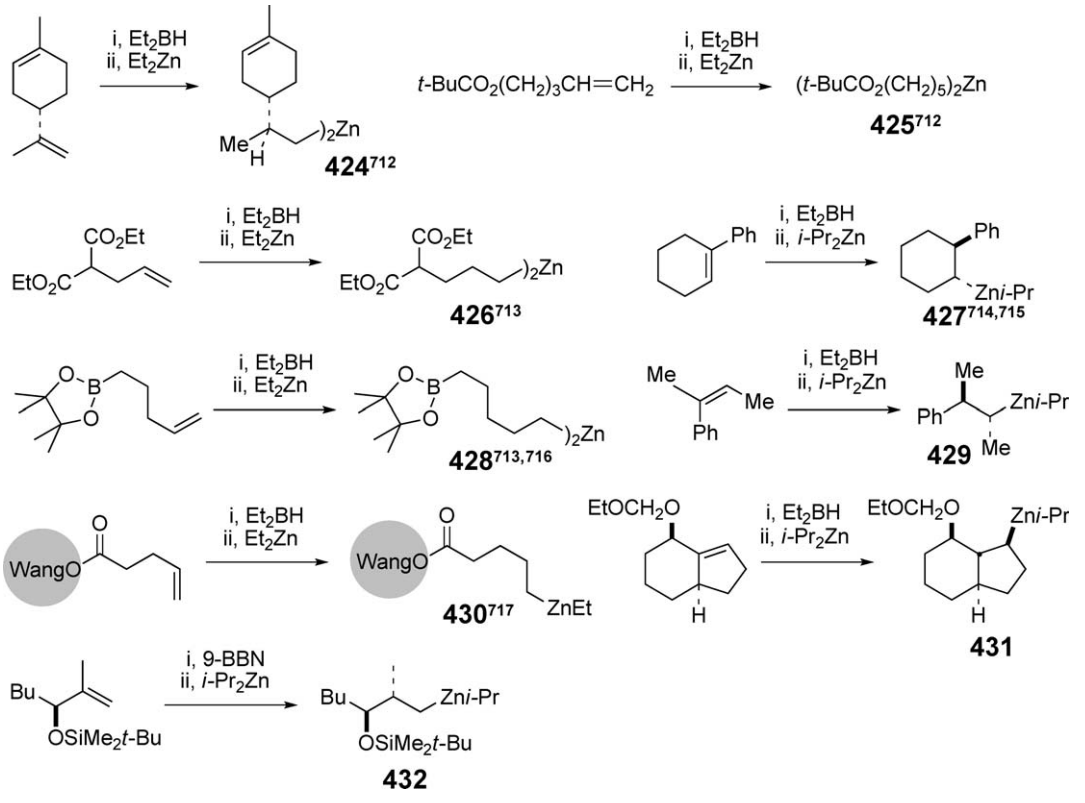


(195)

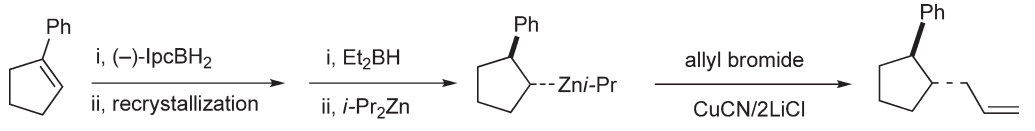
R^1 = Me or Et for primary and benzyl R
R^1 = *i*-Pr for secondary R

Selected examples reported in the boron–zinc transmetallation are summarized in Scheme 30. In most cases, chemoselective hydroboration of alkenes with Et_2BH was directly followed by transmetallation to diorganozinc reagents to prepare functionalized zinc compounds which are not available by conventional synthesis from organic halides and zinc metal. A number of sensitive functional groups such as ester, nitro, diethyl malonate, boryl, and enol ether are tolerated as shown in the syntheses of **424–428**[712–716] and **430**.[717] A sequence of diastereoselective hydroboration and transmetallation to *i*-Pr_2Zn provided a convenient method for synthesizing stereodefined organozinc reagents **429**,[714] **431**,[718] and **432**.[719,720] The organozinc intermediates thus obtained smoothly undergo addition reactions to Michael acceptors or aldehydes, and coupling reactions with organic halides in the presence of a copper(I) catalyst.

As a result of the covalent character of the carbon–zinc bond, secondary alkylzinc derivatives are configurationally stable. Thus, asymmetric hydroboration of alkenes with $IpcBH_2$ (94% ee) was followed by transmetallation to *i*-Pr_2Zn and allylation in the presence of CuCN·2LiCl with retention of configuration (*trans*/*cis* = 2/98, 94% ee).[721,722] *i*-Pr_2Zn was recognized to be the best reagent since the transmetallation to Et_2Zn resulted in partial racemization (Equation (196)).

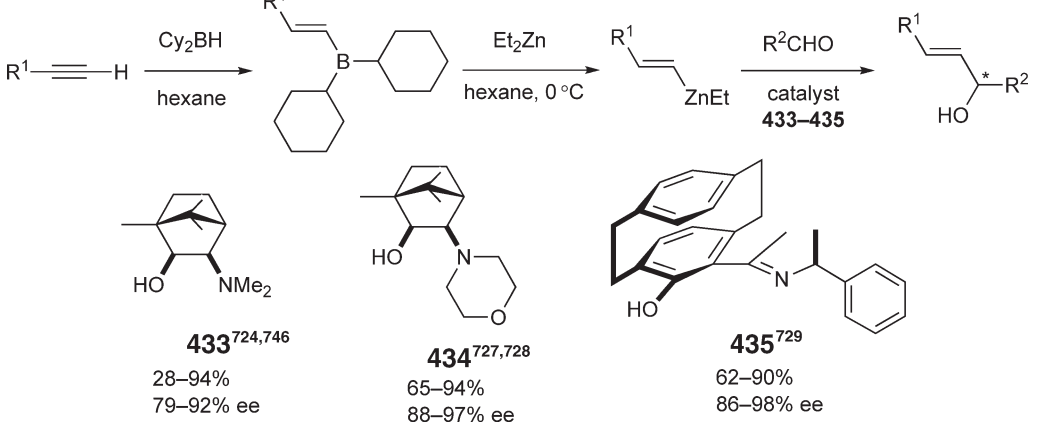


Scheme 30 Synthesis of alkylzinc reagents via hydroboration–transmetallation (Equation (195)).

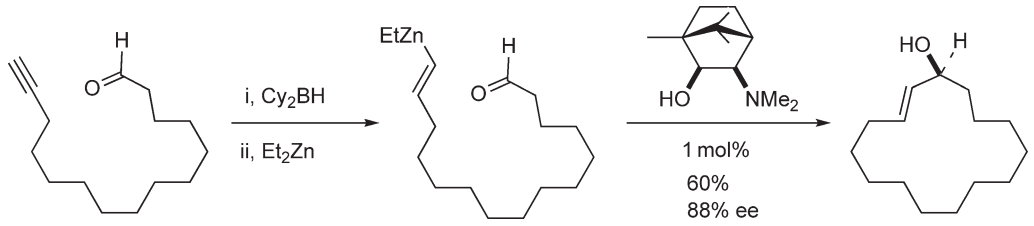


(196)

A transmetallation sequence from the products of hydrometallation of alkynes provides access to stereodefined alkenylzinc compounds. A rapid equilibrium was established in hexane with preferential formation of $(alkenyl)_2Zn$ when the 2 : 3 ratio of $(alkenyl)_3B$ and R_2Zn was used, while the mixed (alkenyl)(R)Zn species dominated in the 1 : 3 ratio.[723] The protocol provided a new access to the enantioselective synthesis of secondary allyl alcohols via addition to aldehydes catalyzed by chiral amino alcohols such as **433–435**[724–746] (Equation (197)). The intramolecular version gave a key intermediate for the synthesis of (*R*)-muscone with 75% yield and 92% ee (Equation (198)).[725,726]

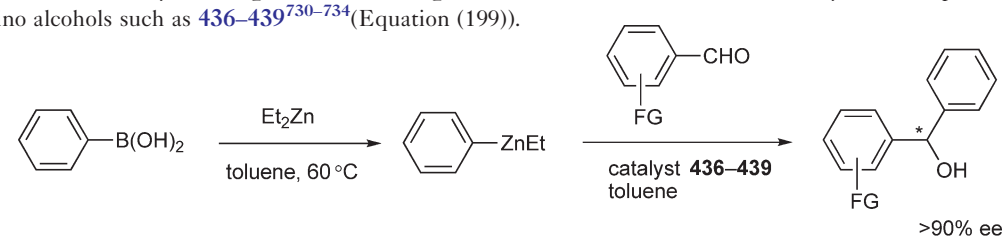


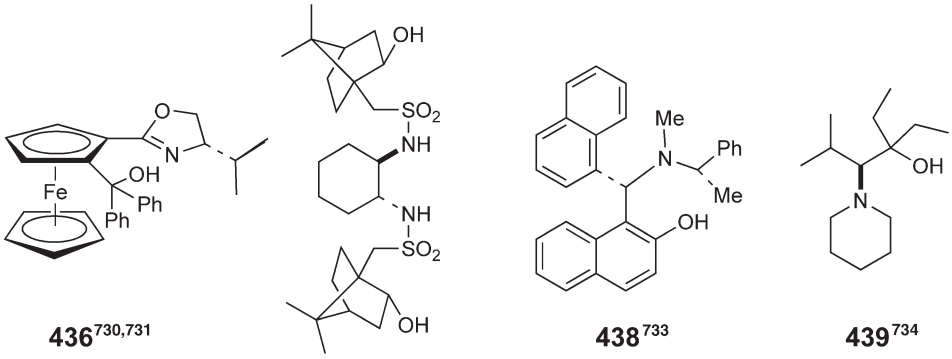
(197)



(198)

Diarylzincs can be conveniently prepared from lithium or Grignard reagents by transmetallation; however, the preparation is tedious since salt-free reagents are required for achieving high enantioselectivities in asymmetric addition to aldehydes. The reaction between arylboronic acids and Et_2Zn (3 equiv.) in toluene at 60 °C for 12 h afforded salt-free arylzinc reagents which undergo enantioselective addition to the aldehydes in the presence of chiral amino alcohols such as **436–439**[730–734](Equation (199)).





436[730,731]
33–95%
90–95% ee

437[732]
25–79%
6–93% ee

438[733]
87–95%
92–99% ee

439[734]
87–98%
81–97% ee

(199)

Transmetallation to other elements includes BF_3-mediated arylation of Ar_3BiF_2 with arylboronic acids giving $[Ar_3Ar'Bi][BF_4]$,[735] BF_3-mediated alkenylation or arylation of $PhI(OAc)_2$ providing $[R(Ph)I][BF_4]$ (R = aryl, alkenyl),[736] and arylation of $Pb(OAc)_4$ with arylboronic acids to give $ArPb(OAc)_3$.[737]

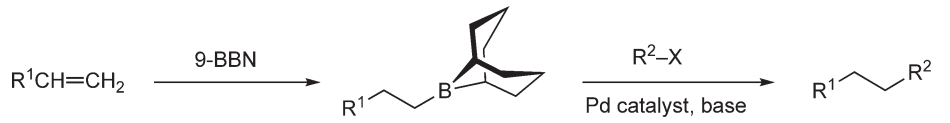
9.05.3.7 Metal-catalyzed Addition and Coupling Reactions

9.05.3.7.1 Cross-coupling reactions

Many organometallic reagents are now used for cross-coupling reactions, but much attention has recently been focused on the use of organoboronic acids in laboratories and industries since they are convenient reagents, generally thermally stable, and inert to water and oxygen, thus allowing handling without special precautions. The reactions have been extensively reviewed.[135,199,267,738–749]

9.05.3.7.1.(i) Reactions of *B*-alkylboron compounds

Trialkylboranes, including 9-alkyl-9-BBN, underwent cross-coupling with 1-alkenyl or aryl halides or triflates.[750,751] The reaction was limitedly used for primary alkylboranes; thus, hydroboration of terminal alkenes with 9-BBN was the most convenient to furnish the desired boron reagents in the presence of a base and $PdCl_2(dppf)$[750,751] or $PdCl_2(dppf)/2Ph_3As$ (Equation (200)).[752]

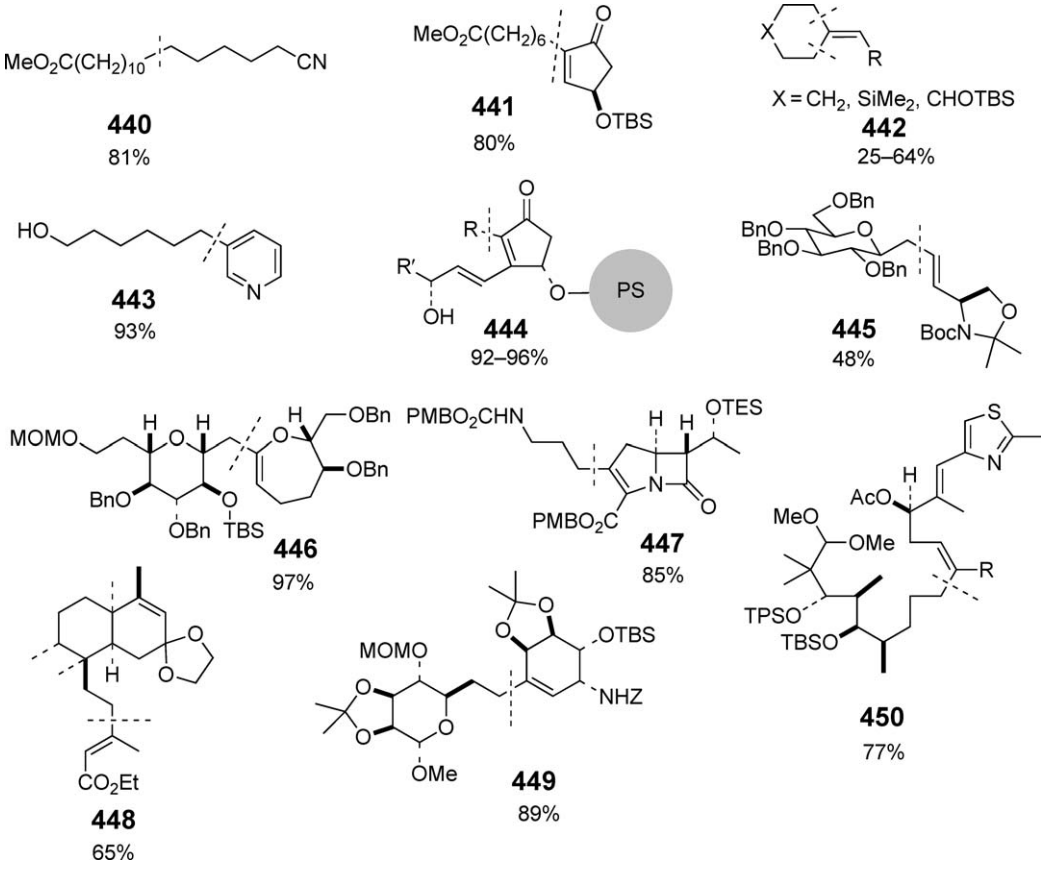


(200)

R^2 = alkyl, aryl, 1-alkenyl halides and triflates

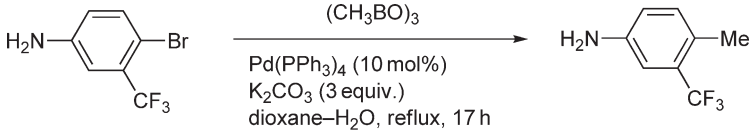
The sp^3–sp^3 bond formation between alkyl derivatives has been much less successful among the possible combinations of different type nucleophiles and electrophiles. However, a complex prepared from $Pd(OAc)_2$ or $Pd_2(dba)_3$ and PCy_3 was found to be highly efficient for the coupling of primary-alkyl bromides and chlorides with primary alkyl-9-BBN obtained by hydroboration of terminal alkenes **440**.[753,754] A hydroboration–cross-coupling strategy has been extensively used in the synthesis of biologically active compounds, including synthetic intermediates of PGE1 **441**,[755] exocyclic alkenes via double coupling of 1,1-dibromoalkenes **442**,[756] 3-alkylpyridines **443**,[757] ciguatoxin **446**,[758–763] 2-alkylcarbapenems **447**,[764] clerodane diterpenic acid **448**,[765] aza-*C*-disaccharides **449**,[766] and epothilone A and B **450**[767–770] (Scheme 31). The B-alkyl coupling reaction readily proceeds on polymer resins, as has been demonstrated in the preparation of members of several structurally distinct PG classes **444**.[771]

Other examples reported in the hydroboration-coupling strategy are a novel class of glycomimetic compounds, sphingofungin F which acts as a serinepalmitoyl transferase inhibitor,[772,773] a rare family of C_{15} lupine alkaloid, aloperine,[774] 5-alkylresorcinols with DNA-cleaving properties,[775] a fungal metabolite, caloporoside,[776] salicylihalamide,[777] (+)-aspicilin,[778] an inhibitor of VCAN-1, (+)-halichlorine,[779] a cytotoxic polyketide marine natural product, callystatin A,[780] a macrolide antibiotic, 5,6-dihydrocineromycin B,[781] natural and unnatural pinnanic acids which mediate anti-inflammatory properties,[782] a chemically and metabolically stable prostaglandin analog, carbacyclin,[783] and enantiomerically pure α-amino acids.[784–790]

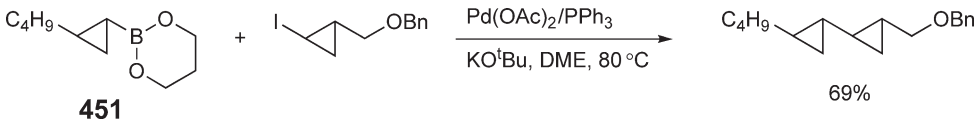


Scheme 31 Cross-coupling of alkyl (sp^3-C) boranes via hydroboration–coupling sequence. The left parts come from terminal alkenes and the right parts from halides or triflates (Equation (200)).

The coupling reaction of alkylboronic acids and esters is slower than that of trialkylboranes, but it has been found that they also participate in the catalytic cycle of palladium-catalyzed cross-coupling. Methylboroxine $(MeBO)_3$ or methylboronic acid alkylated bromoarenes with a common palladium/triphenylphosphine catalyst (Equation (201)).[791,792] The reactions of aryl iodides, bromides, or triflates with alkylboronic acids possessing β-hydrogen are catalyzed by $PdCl_2$(dppf),[33,793,794] $Pd(dba)_2$–Qphos,[795] or $Pd(OAc)_2$–*N*-cyclic carbene complex.[796] These reactions are only used for primary alkylboronic acids; however, cyclopropylboronic acids exceptionally alkylated various electrophiles, including iodocyclopropanes (Equation (202)),[797,798] aryl and 1-alkenyl halides or triflates,[799–803] and acyl chlorides.[804]



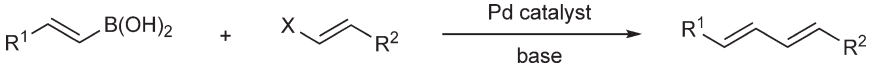
(201)



(202)

9.05.3.7.1.(ii) Reactions of *B*-alkenylboron compounds

Alkenyl–alkenyl cross-coupling afforded stereodefined dienes, trienes, and further conjugated polyenes (Equation (203)).



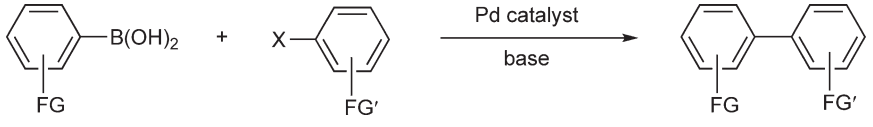
(203)

The protocol has been successfully used for a number of syntheses of natural products, including (−)-bafilomycin A **452**,[805,806] the (*Z*,*Z*,*E*)-triene structure in (+)-fostriecin **453**,[807] orevactaene,[808] DiHETE **454**,[809] polyunsaturated butenolides such as peridinin **456**,[810] vitamin A **457**,[811] (*E*)-enyne **458**, which was then converted into a sex pheromone of the melon worm,[812] hexaalkenylbenzene **459** via sixfold alkenylation of hexabromobenzene,[813] PGE_1 derivatives **460** obtained by alkenyl–allyl cross-coupling,[814] and alkenylcyclopropanes via coupling with iodocyclopropanes **461**.[797] Alkenyl–alkenyl coupling for the synthesis of vitamin D_3 derivatives proceeded on resins **455** in high yields[815] (Scheme 32).

Since a variety of 1-alkenylboron compounds, including (*E*)- and (*Z*)-isomers, are available, the alkenyl–alkenyl coupling reaction has been used for the synthesis of various biologically active natural products, including a macrolide antibiotic, rutamycin B,[816] (5*Z*,8*Z*,10*E*,12*R*,14*Z*)-12-hydroxy-5,8,10,14-icosatetraenoic acid [(12R)-HETE],[817,818] an anti-proliferative agent, (+)-curacin A,[653] an aglycon of chlorothricin, (−)-chlorothricolide,[819,820] a small family of C_{15} lupinine alkaloids, (+)-aloperine,[821] restrictinols that exhibit antifungal activity,[822] marine alkaloids, (−)-lepadins A, B, and C,[823] a highly unsaturated 20-membered macrocyclic system having four carbohydrate units, apoptolidin[824] and cytotoxic substance FR 182877, and clinic acid.[825] Syntheses of polyene natural products via metal-catalyzed protocol have recently been reviewed.[826]

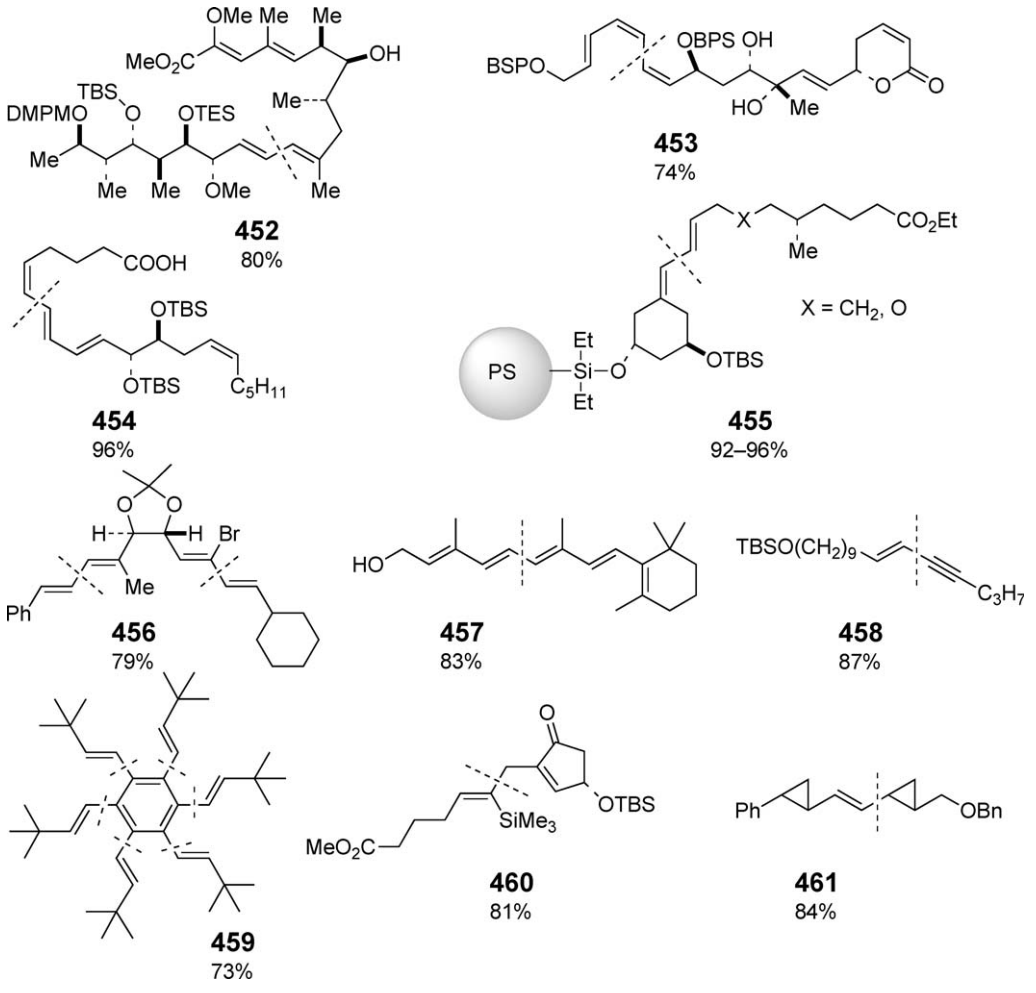
9.05.3.7.1.(iii) Reactions of *B*-arylboron compounds

After the discovery of a cross-coupling reaction of arylboronic acids with aryl halides or triflates, numerous syntheses of natural and unnatural biaryls have been explored (Equation (204)).



(204)

The biaryl coupling of arylboronic acid furnished a one-pot, two-step procedure for the synthesis of the angiotensin II receptor antagonist losartan **462**, which played a critical role in the regulation of blood pressure,[827] the AB biaryl ring of vancomycin aglycon **464**, S/R = 1/1.3),[828] bisporphyrin-based synthetic receptors **463** via a sequential double

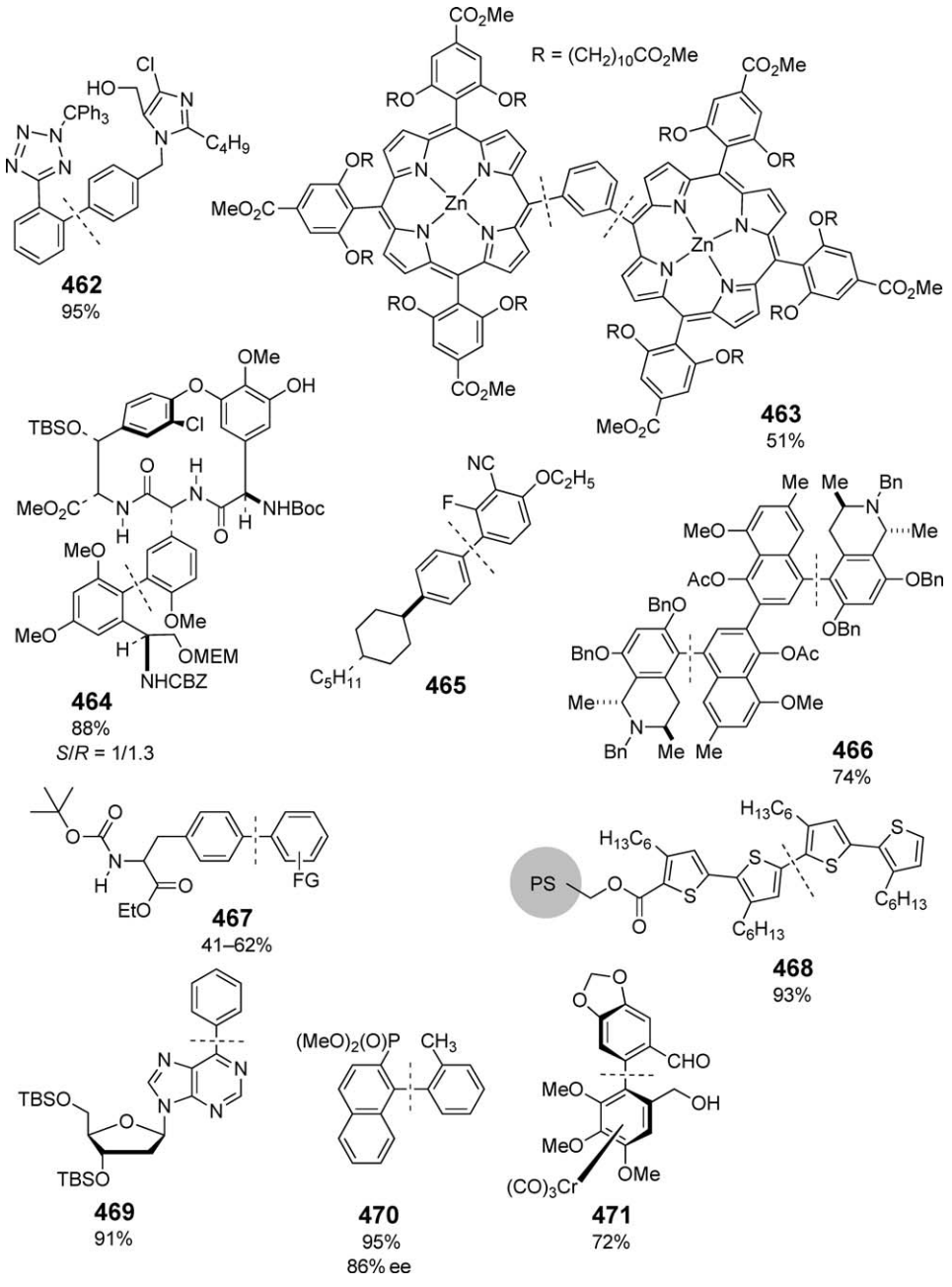


Scheme 32 Cross-coupling 1-alkenylboron compounds. The left parts come from vinylboron compounds and the right parts from halides or triflates (Equation (203)).

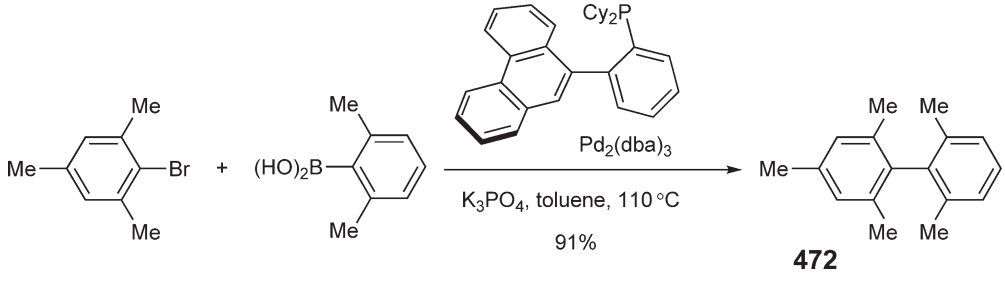
cross-coupling reaction with 1,3-diiodobenzene,[829] log, lath-like liquid crystals **465**,[830–837] anti-HIV alkaloids, michellamines A and B **466**,[838,839] 4-aryl phenylalanine derivatives **467**,[840] C(6)–aryl nucleoside derivatives **469**,[841,842] oligo(thiophene)s via a solid-phase coupling of two thiophene units **468**,[843,844] axially chiral biaryls via asymmetric cross-coupling reaction using a chiral catalyst **470**,[845,846] and optically active biaryl–$Cr(CO)_3$ complexes **471** via coupling with chiral bromoarene–chromium complexes (Scheme 33).[847,848]

Biaryls are useful in designing functional molecules and materials. The semirigid structure due to restricted rotation allows rational design of various molecular recognition compounds, including drug substances. Coupling reactions of arylboronic acids have provided porphyrin derivatives,[849–851] molecular-scale motors that rotate by chemical power or light,[852,853] photoswitchable electron-transfer aromatic compounds for the design of molecular photonic devices,[854,855] single-layer 2,5-diarylsilole electroluminescent devices,[856] chiral sensory materials based on 1,1′-binaphthyl oligomers,[857,858] stable thioaminyl radicals,[859,860] dendrimers,[861,862] polycyclic aromatic materials,[863–867] and a promising lead for synthesis of a reversible proteasome inhibitor, TMC-95A.[868,869] The mild reaction conditions, broad tolerance for functional groups, and high reaction conversions on a polymer surface were suitable for creating combinatorial libraries of various pharmaceutically or materially interesting lead structures.[844,870–877] The synthesis of poly(phenylene)s based on arylboronic acids has recently been reviewed.[878]

A general method for biaryl coupling has been limitedly used for tri-*ortho*-substituted biaryls. A phenanthrene-based ligand exceptionally allowed the synthesis of sterically hindered biaryls where each reactant possesses two *ortho*-substituents (Equation (205)).[879]

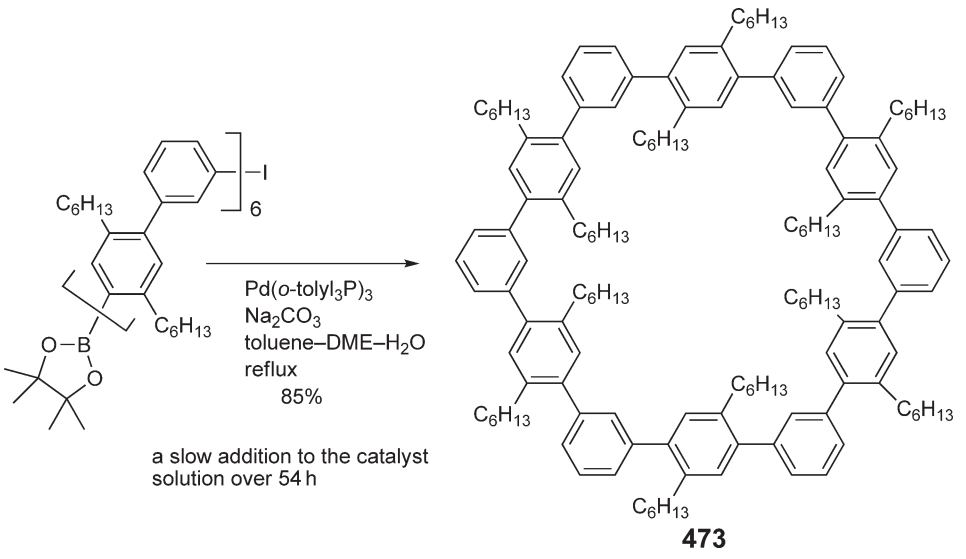


Scheme 33 Cross-coupling of arylboronic acids or esters for synthesis of biaryls.



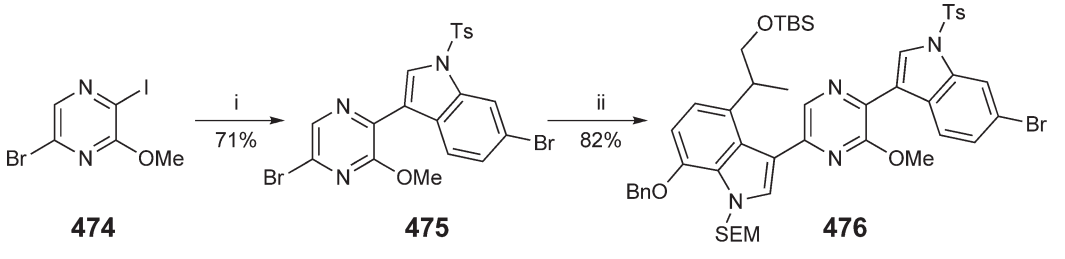
(205)

An intramolecular reaction for the synthesis of biaryl-bridged macrocycles[880] or polyaryls[881] has newly developed. A difficulty arising from competition between the intramolecular and intermolecular coupling was solved by the high-dilution method in which (ω-iodododecaphenyl)borate was added to the catalyst solution using a syringe pump (Equation (206)).[881]



(206)

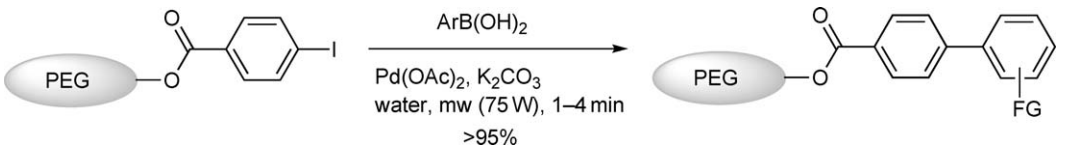
Stepwise double coupling of two different arylboronic acids with a dihaloarene afforded one-pot, two-step method for synthesizing unsymmetrical teraryls, quateraryls, and other higher order polyaryls.[882] The first total synthesis of dragmacidin D involved a sequential double coupling of two different pinacol 3-indoleboronic esters (ArBpin; Equation (207)).[882]



(207)

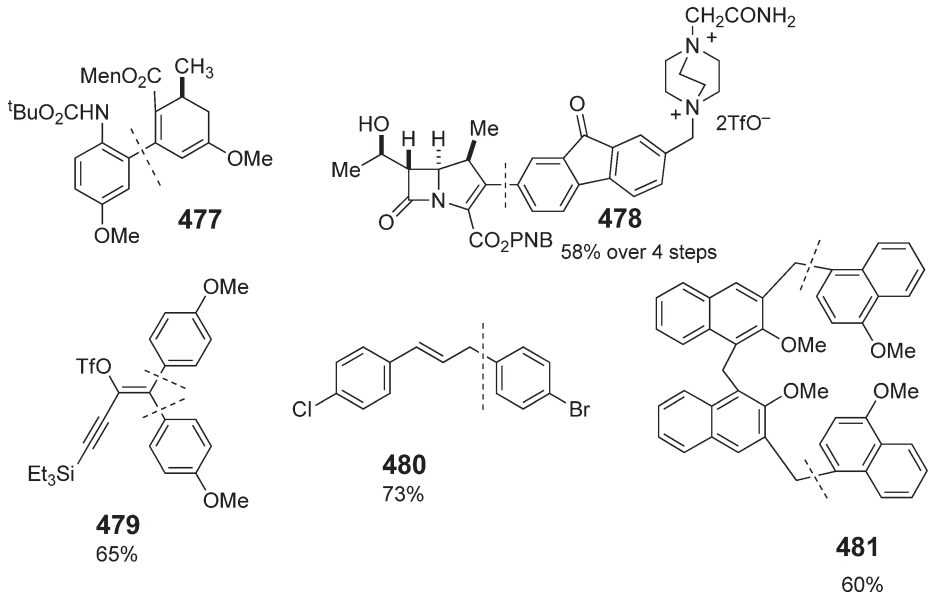
i, ArBpin, Na_2CO_3, PhH–MeOH–H_2O, 23 °C, 72 h;
ii, ArBpin, Na_2CO_3, PhH–MeOH–H_2O, 50 °C, 72 h

The use of microwaves was first reported in 1996 for both homogeneous[883] and solid-phase coupling reactions of arylboronic acids (Equation (208)).[884] Microwave irradiation significantly increases the efficiency of ligandless palladium acetate,[885] solid-phase coupling for combinatorial synthesis,[886] solid-phase coupling using KF-γ-alumina, and a palladium catalyst without the use of any solvents.[887,888]



(208)

Among the representative organoboronic acids, arylboronic acids are exceptionally reactive reagents that allow a wide range of cross-coupling reactions for representative organic electrophiles. Arylation of 1-alkenyl allyl and benzyl halides or triflate occurred under conditions similar to those used for aryl–aryl coupling (Scheme 34). The aryl–alkenyl coupling allowed a short-step synthesis of the ABC rings of (+)-dynemicin A,[27] the introduction of aryl moieties at the 2-position of carbapenum **478**,[889] and double arylation of 1,1-dibromoalkenes **479**.[890] 1,3-Diarylpropenes are obtained by coupling of cinnamyl bromides with arylboronic acids **480** in the presence of

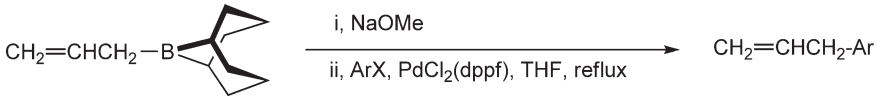


Scheme 34 Cross-coupling of arylboronic acids with 1-alkenyl, allyl, and benzyl halides or triflates.

ligandless $Pd(dba)_2$.[891] The aryl–benzyl coupling reaction provides a simple method for the synthesis of mixed calix[4]arenes **481**.[892] Arylation of α-bromoacetates or amides[893–896] and 1-alkynyl sulfides giving arylalkynes[897] also have been studied.

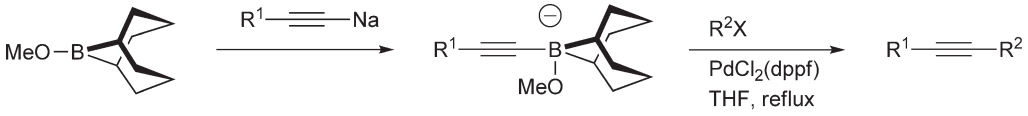
9.05.3.7.1.(iv) Reactions of *B*-allyl- and alkynylboron compounds

Less is known about the reactions of allylboron compounds; however, an ate complex between B-allyl-9-BBN and NaOMe afforded allylarenes in high yields within 0.5–1 h (Equation (209)).[898]

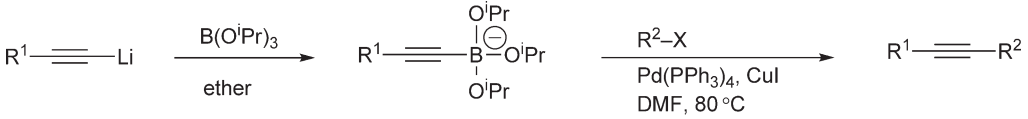


(209)

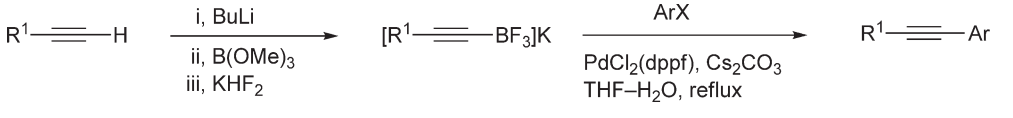
Alkynyl(methoxy)borates prepared *in situ* from an alkynyllithium or sodium and 9-methoxy-9-BBN coupled with 1-alkenyl and aryl halides (Equation (210)).[899–902] Addition of triisopropylborate to lithium acetylide yielded an air stable and isolable ate complex that couples with aryl and alkenyl halides (Equation (211)).[903,904] Air and moisture stable alkynyltrifluoroborates were probably the most convenient reagents that allow handling in air and coupling reactions in basic aqueous media (Equation (212)).[46]



(210)



(211)



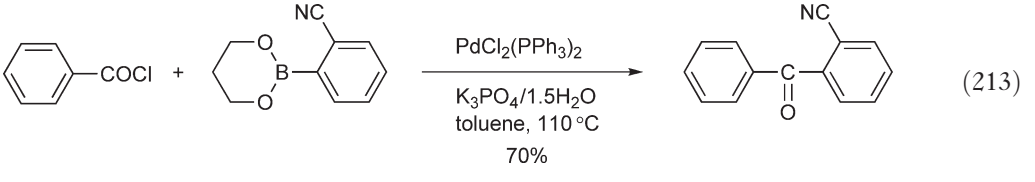
(212)

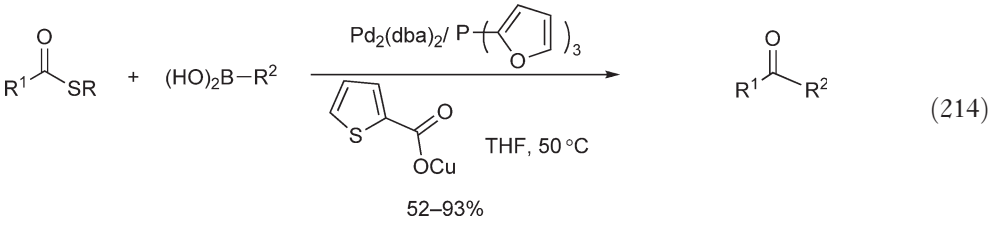
9.05.3.7.1.(v) Reactions of $[RBF_3]K$

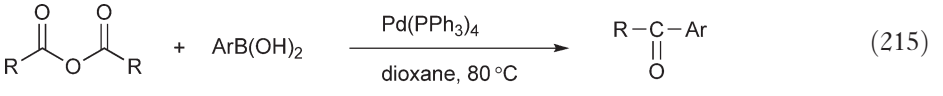
Coupling reactions of organotrifluoroborates $[RBF_3]K$ have been extensively studied because of the simplicity of the preparation of pure and stable crystals compared to the preparation of the corresponding boronic acids (Scheme 35). Representative boron reagents, including aryl- **482–484**,[44,905–908] 1-alkenyl- **485**,[35,909] **486**,[908] 1-alkynyl- **487**,[46] and alkylboron derivatives **488**,[33] were easily synthesized and successfully used for cross-coupling reactions with organic halides in the presence of bases. $[RBF_3]K$ is obtained by treatment of boronic acids with KHF_2[47,48] and Bu_4N^+ salts, which are soluble in a wide range of polar and nonpolar organic solvents, prepared by sequential treatment of organoboronic acids with HF and Bu_4NOH.[906,910]

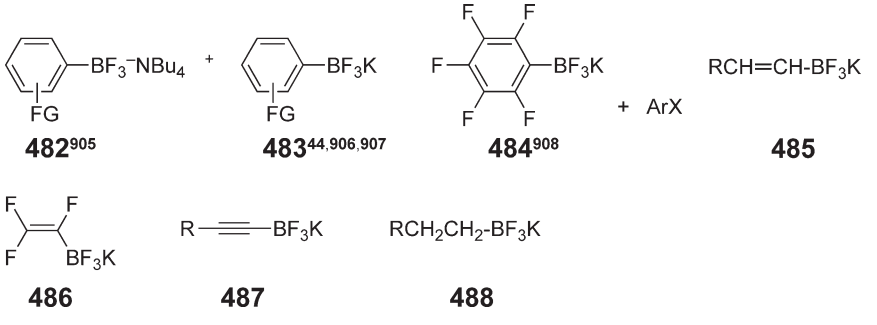
9.05.3.7.1.(vi) Reactions leading to ketones (acylation reactions)

Cross-coupling reactions of acyl chlorides, thiol esters, or carboxylic anhydrides give ketones. The reaction of acid chlorides in aqueous bases suffered from competitive hydrolysis,[911,912] but such decomposition was minimized when arylboronic esters and $K_3PO_4 \cdot nH_2O$ ($n = 1.5$, 1.5 equiv.) were used in toluene at 110 °C, so that aromatic or aliphatic acyl chlorides provide aromatic ketones in yields of 68–95% (Equation (213)).[913] The cross-coupling reaction of thiol esters with organoboronic acids gave ketones under strictly non-basic reaction conditions when aqueous copper(I) thiophene-2-carboxylate was used as the base (Equation (214)).[914–918] Palladium-catalyzed reaction of phenyl trifluoroacetate[919] or carboxylic anhydrides[920–922] afforded the corresponding ketones in the absence of bases (Equation (215)). Carbonylative cross-coupling is an alternative approach for the preparation of unsymmetrical ketones. The protocol allowed various combinations of halides and organoboron compounds possessing alkyl, 1-alkenyl, or aryl groups in either of the coupling partners (Equation (216)).[923–930]

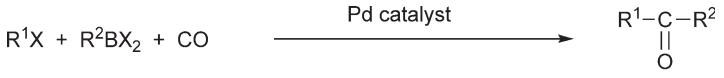








Scheme 35 Organotrifluoroborates for cross-coupling reagents.



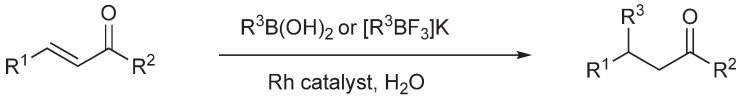
(216)

R^1 = aryl, 1-alkenyl; R^2 = alkyl, 1-alkenyl, alkyl

9.05.3.7.2 Addition to unsaturated bonds

9.05.3.7.2.(i) Conjugate addition to electron-deficient alkenes

Addition reactions of organoboronic acids to electron-deficient alkenes were found to be catalyzed by rhodium(I)[931] or dicationic palladium(II) complexes.[932,933] The reaction proceeding through the transmetallation to a transition metal has been proved to be a general technique for a wide range of selective carbon–carbon bond formation via 1,4-addition to α,β-unsaturated ketones, aldehydes, esters, and amides, and the 1,2-addition to aldehydes and imines (Equation (217)).[934]

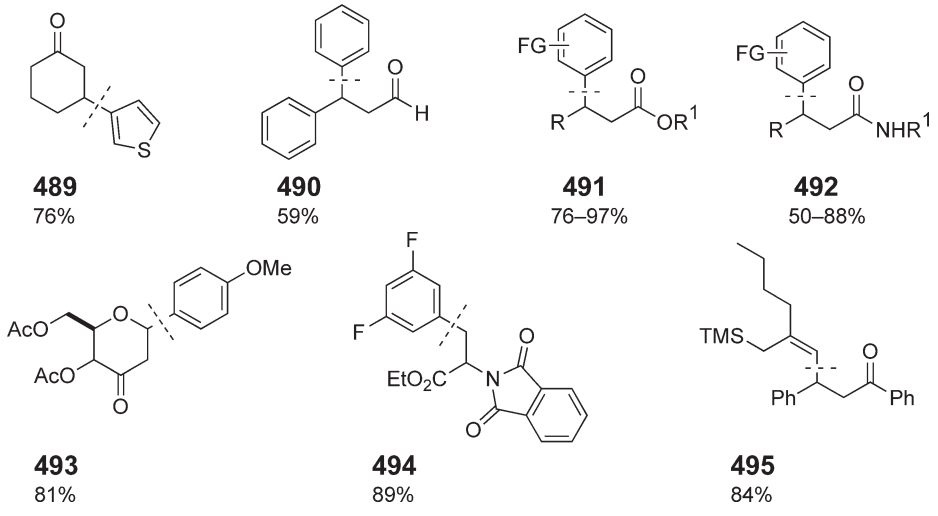


(217)

R^2 = alkyl, aryl, OR, NHR; R^3 = aryl, 1-alkenyl

Various rhodium(I) complexes catalyze the addition reaction of aryl- and 1-alkenylboronic acids to α,β-unsaturated ketones **489**,[935,936] **493**,[941] and **495**,[937] aldehydes **490**,[938] esters **491**,[939] and **493**,[940] lactones **494**,[941] and amides **492**[942] in an aqueous solvent (Scheme 36).

The reaction which is accelerated by the presence of water can be carried out in water when a 2β-cyclodextrin-$[Rh(OH)(cod)]_2$,[943,944] $[Rh(cod)Cl]_2$/TPPTS,[945] or amphiphilic resin-supported rhodium(I) complex was used.[946] It was also reported that potassium alkenyl and aryltrifluoroborates $[RBF_3]K$ undergo similar addition to enones in the presence of an Rh(I) catalyst.[935,947,948] The cationic rhodium(I) complexes such as $[Rh(cod)]BF_4$, $[Rh(cod)(CH_3CN)_2]BF_4$, or its combination with a diphosphine ligand (dppp or dppb) efficiently catalyzed the reaction. The neutral complexes, generated *in situ* from $Rh(acac)(CH_2{=}CH_2)_2$, or $Rh(acac)(coe)_2$, and dppp or dppb, were also effective. The effects of catalysts, solvents, and bases,[949] and the mechanism of catalytic cycle[950] have been studied in detail.



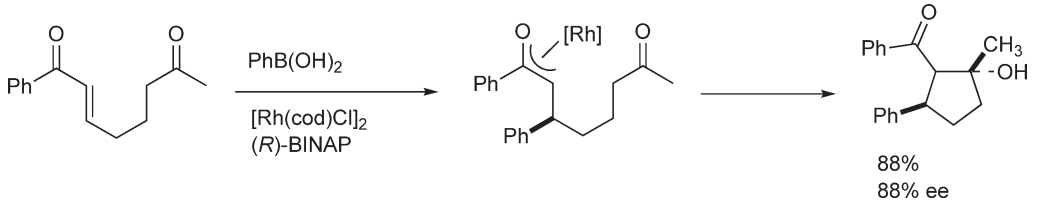
Scheme 36 Conjugate addition to α,β-unsaturated ketones, esters, and amides.

9.05.3.7.2.(ii) Asymmetric additions

Chiral phosphine ligands are the chiral auxiliaries extensively studied for transition metal-catalyzed asymmetric reactions. Most of the ligands were originally designed for asymmetric hydrogenation, but they also worked well in the conjugate addition of organoboronic acids to electron-deficient alkenes.[951,952] The rhodium(I) complexes of **496–503**[953–966] have been successfully utilized for these asymmetric reactions (Scheme 37).

High enantioselectivities exceeding 95% ee were easily achieved for cyclic five- to six-membered enones **505**[953–957,964,966–968] and **506**,[953] lactones **510**,[956,969] and **514**,[966] lactams **513**,[970] and nitroalkenes **512**[971] (Scheme 38). It was more difficult to achieve high enantioselectivities for acyclic substrates, but over 90% ee's were reported for some unsaturated ketones **504**[953,967,968] and **509**,[966] esters **507**,[939,965,969,972] amides **508**,[942,960] phosphates **100**,[973] and sulfoxides **515**.[958] Most reactions were conducted at 100 °C using rhodium complexes generated *in situ* from $Rh(acac)(CH_2{=}CH_2)_2$ and bidentate phosphine ligands, but $[Rh(OH)(binap)]_2$,[967] $[Rh(binap)(nbd)]BF_4/Et_3N$,[949] $[RhCl(C_2H_4)_2]_2$/**501**/KOH,[959] $[RhCl(C_2H_4)_2]_2$/**503**/KOH,[966] and $[RhCl(C_2H_4)_2]_2$/**502**/KOH[964] were found to be effective for carrying out the reactions at 25–50 °C.

A catalytic tandem conjugate addition–aldol cyclization[950] allowed the formation of five- and six-membered ring products from aromatic and aliphatic ketone precursors (Equation (218)).[974]

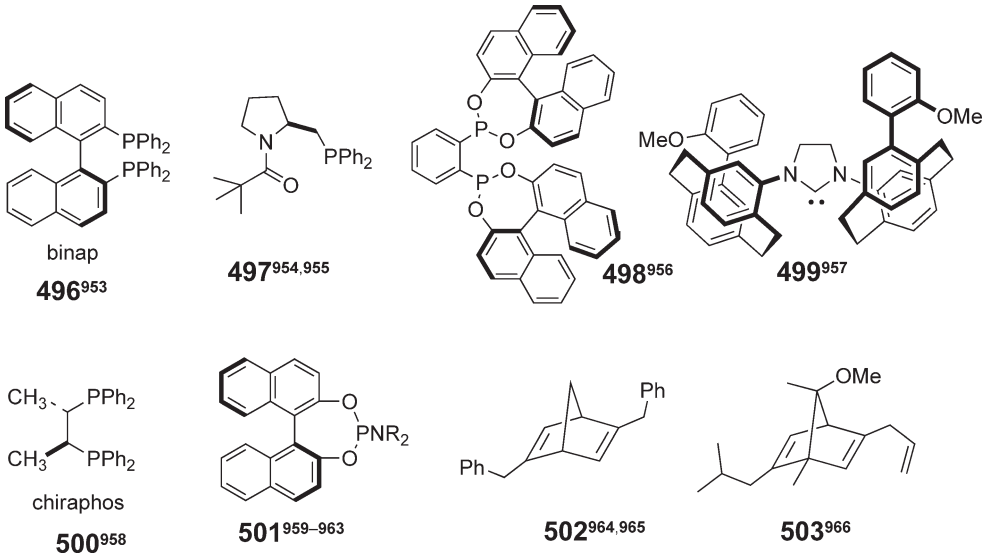


(218)

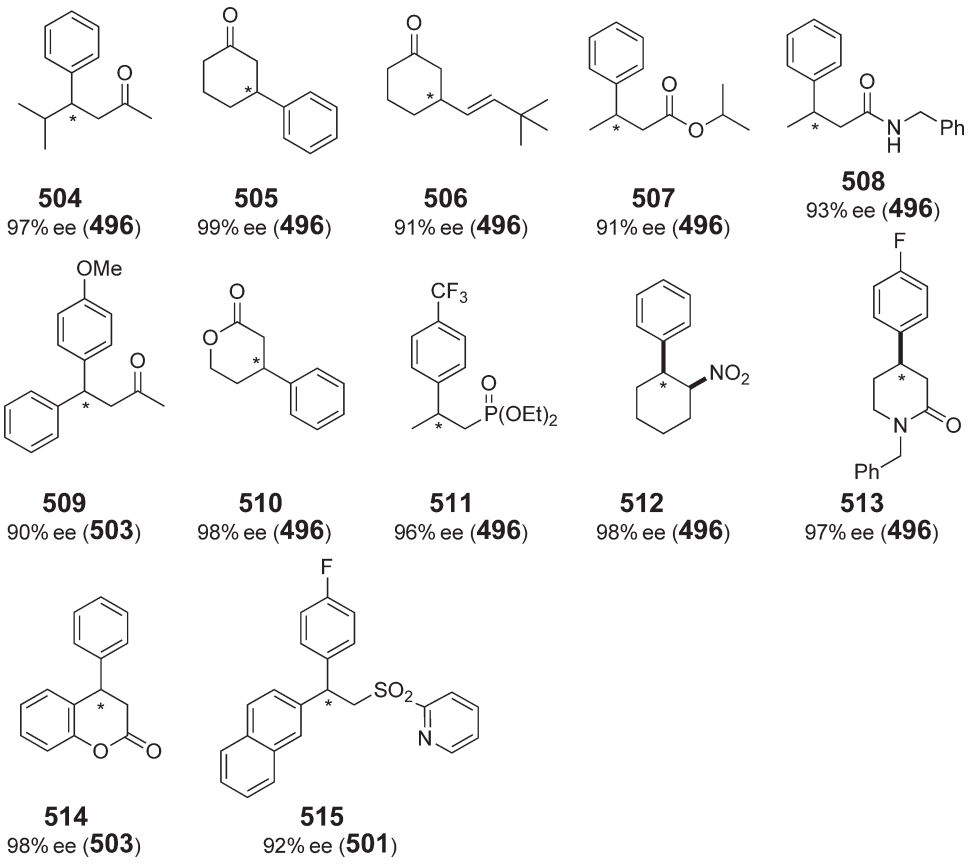
9.05.3.7.2.(iii) Addition to alkenes and alkynes

Arylboronic acids added to alkynes[975–977] and activated alkenes such as norbornene[978–981] or 2-vinylpyridines[982] in the presence of a rhodium(I) catalyst. Addition of arylboronic acids to allenes was reported to be catalyzed by $Pd(PPh_3)_4$ in the presence of AcOH.[983]

Aryl boronates possessing a Michael acceptor at the *ortho*-carbon underwent tandem cyclization with strained alkenes such as norbornene[981,984] and alkynes[977] (Equation (219)). The addition of phenylboronic acid to norbornene

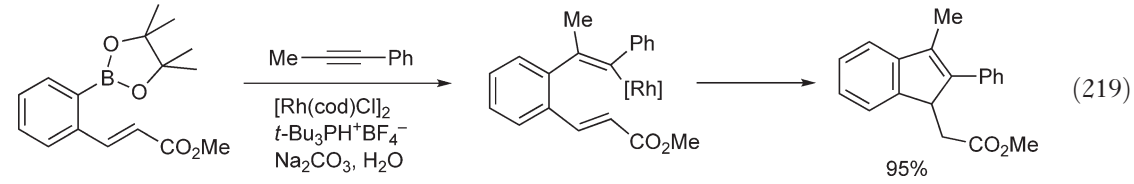


Scheme 37 Chiral ligands for asymmetric additions.

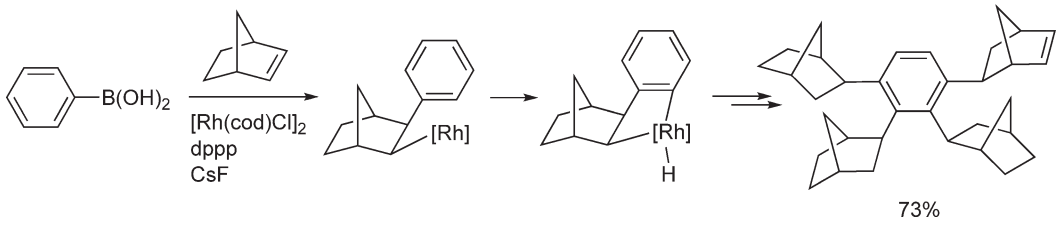


Scheme 38 Asymmetric addition to electron-deficient alkenes.

with $[Rh(cod)Cl]_2$/dppp gave 1 : 2, 1 : 3, or 1 : 4 coupling products via repetition of insertion of the double bond of norbornene (Equation (220)).[978]

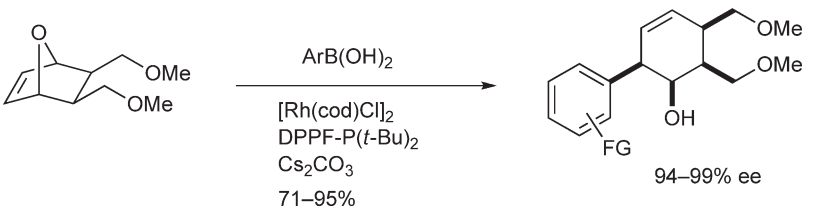


(219)



(220)

The addition of arylboronic acids to oxabicyclic alkenes yielded ring-opening products via insertion–elimination process.[979,980] Chiral DPPF-P(*t*-Bu)$_2$ was identified as the ligand giving the best reactivity and enantioselectivity (Equation (221)).



(221)

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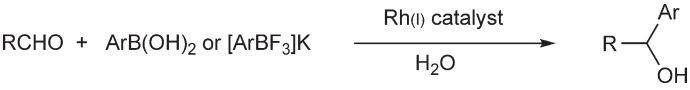
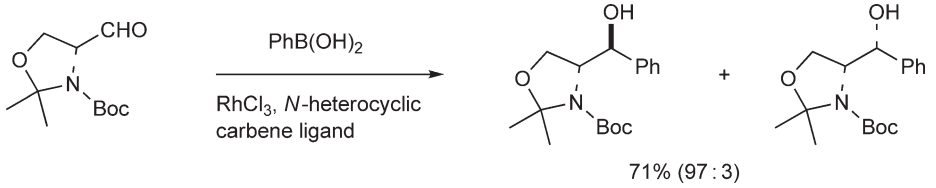
9.05.3.7.2.(iv) Addition to C═O and C═N bonds

The addition of aryl- or 1-alkenylboronic acids to aldehydes was found to be catalyzed by rhodium(I) complexes via insertion of C═O bond into the C–Rh intermediate generated by transmetallation (Equation (222)).[985,986] The rhodium(I)-tri(*t*-butyl)phosphine complexes catalyzed the addition to aromatic aldehydes at room temperature.[986] Rhodium(I) complexes of *N*-heterocyclic carbene have been studied extensively as an analogous electron-donating ligand.[987–989]



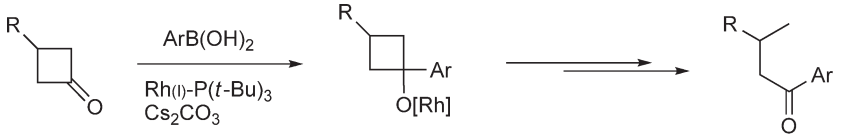
(222)

The addition of phenylboronic acid to Garner aldehyde showed a high anti-selectivity, thus suggesting no chelation between the oxygen atom and rhodium metal center during the addition (Equation (223)).[987] Asymmetric addition using chiral phosphine ligands was studied; however, there have not yet been any practical procedures.[985,990]



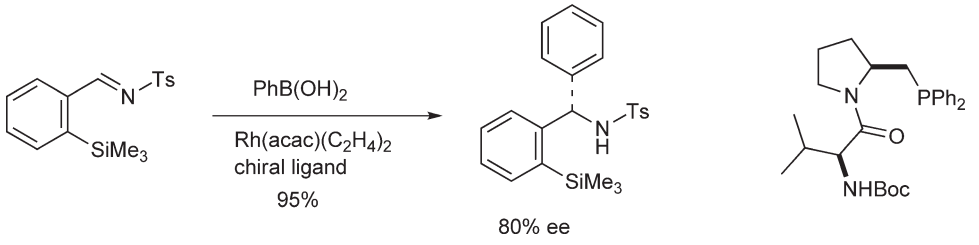
(223)

Cyclobutanones reacted with arylboronic acids in the presence of a rhodium(I) complex to afford butyrophenone derivatives via addition-ring-opening process (Equation (224)).[991] On the other hand, the addition-β-hydride-elimination process provided a direct method for synthesizing ketones from aldehydes and arylboronic acids.[992]



(224)

The cationic rhodium complexes such as $[Rh(cod)(MeCN)_2]BF_4$/dppb were the most efficient catalysts for addition of arylboronic acids or Ph_4BNa to both aromatic and aliphatic *N*-sulfonyl imines.[993,994] The asymmetric version giving optically active amines was achieved by amidomonophosphine catalysts (Equation (225)).[995]



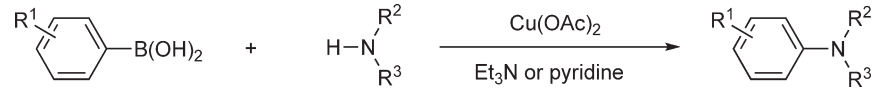
(225)

9.05.3.8 Arylation of N–H, O–H, and S–H Mediated by CuX_2

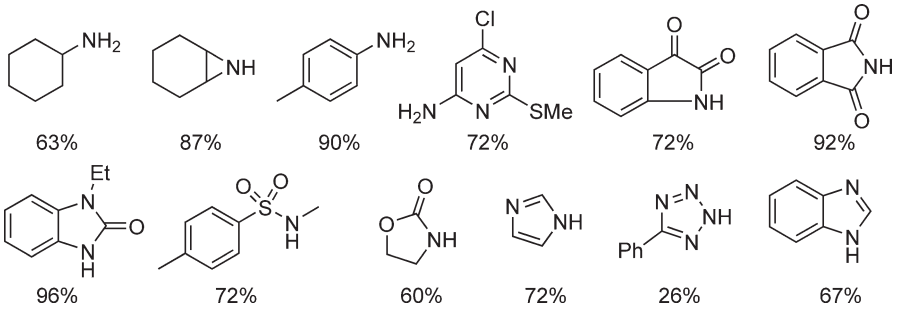
Copper-promoted C–heteroatom bond-coupling reactions of N–H, O–H, and S–H containing substrates with arylboronic acids were found to proceed at room temperature in the presence of $Cu(OAc)_2$ and an amine base.[996–998] The reactions have been reviewed.[3,999]

9.05.3.8.1 Copper-mediated C–N bond formation

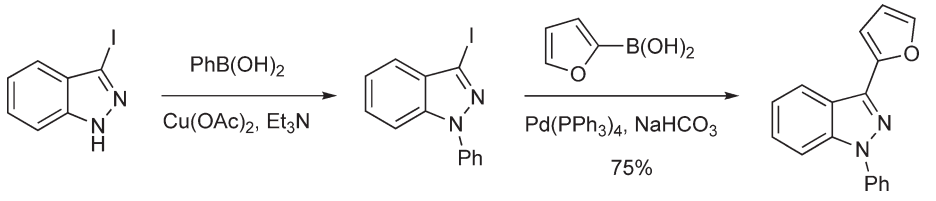
An impressive range of nucleophiles was successful for arylboronic acids in the presence of $Cu(OAc)_2$ and base, which included amine, anilines, amides, imines, ureas, carbamates, sulfonamides, and aromatic heterocycles (e.g., imidazoles, pyrazoles, triazoles, tetrazoles, benzimidazoles, and indazoles) (Equation (226)).[996,997,1000–1011] For all the reactions investigated with *N*-nucleophiles, the use of Et_3N resulted in yields superior to those obtained with pyridine, but pyridine was the base of choice for the preparation of imidazole derivatives from heteroarenes. For the tetrazole, NMO and DBU were studied as alternative bases. There are mechanistic studies.[999,1002–1013]



(226)

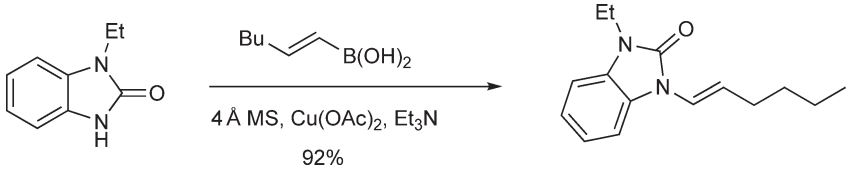


A one-pot two-step process using two different arylboronic acids for 3-iodoindazole furnished 1,3-diaryl indazoles (Equation (227)).[1014]

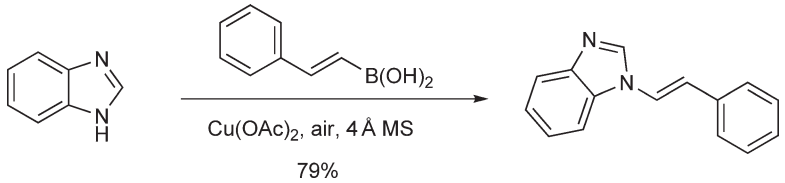


(227)

It was shown that the partner could be extended with a vinyl group (Equations (228) and (229)).[1015,1016] The best yields of the desired coupling products were obtained in the presence of stoichiometric amounts of $Cu(OAc)_2$ exposed to air.

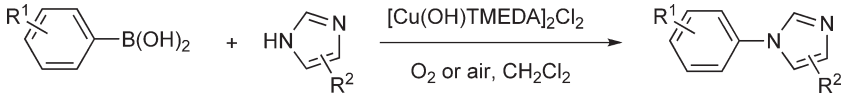


(228)

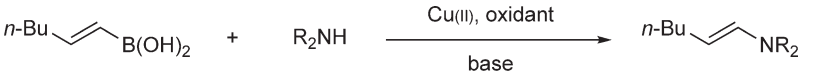


(229)

The reaction was made catalytic when a suitable oxidant of Cu(I) species was used. In the presence of catalytic amount of copper salt, aryl- (Equation (230)) and alkenylboronic acids (Equation (231)) smoothly reacted with *N*-nucleophiles, such as imidazoles, at room temperature.[1012,1013,1015,1017,1018] TEMPO, pyridine *N*-oxide, oxygen were effective reoxidants to recycle the copper catalyst.



(230)



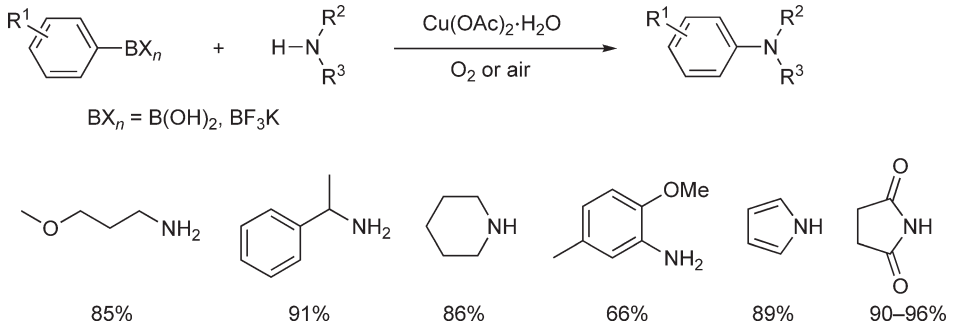
(231)

C(II) : $Cu(OAc)_2$, $[Cu(OH)TMEDA]_2Cl_2$

Oxidant: O_2, air, TEMPO in air, pyridine *N*-oxide

Base: Et_3N, pyridine

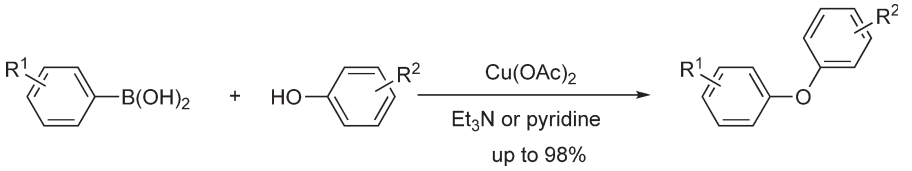
A ligandless and base-free Cu-catalyzed protocol for the coupling of arylboronic acids and potassium aryltrifluoroborates with primary and secondary aliphatic amines and anilines was developed. The process utilized catalytic copper(II) acetate monohydrate or $CuCl_2$ and 4 Å MS in dichloromethane at slightly elevated temperatures under an atmosphere of oxygen (Equation (232)).[1019–1021]



(232)

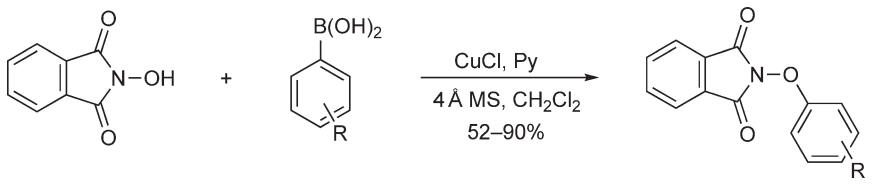
9.05.3.8.2 Copper-mediated C–O bond formation

A mixture of the phenol, arylboronic acid, anhydrous $Cu(OAc)_2$, and Et_3N in dichloromethane was stirred in air for 1–2 days for arylation of the O–H bond. $Cu(OAc)_2$ was recognized to be the best copper source. $Cu(OPiv)_2$, $Cu(NO_3)_2$, $Cu(acac)_2$, and $Cu(OCOCF_3)_2$ did not lead to the products of an arylation reaction and $CuSO_4$, $CuCl_2$, $Cu(ClO_4)_2$, and $Cu(OTf)_2$ resulted in significant C–C bond formation. The use of molecular sieves resulted in significant yield enhancement (Equation (233)).[998,1022] For catalytic reaction, the best yields were obtained with oxygen as oxidant, but it was possible to use TEMPO/air, pyridinium *N*-oxide/air, or $[\{Cu(\mu\text{-}OH)(tmeda)\}_2]Cl_2$/oxygen in the presence of $Cu(OAc)_2$ as the Cu(II) source.[1015,1016]



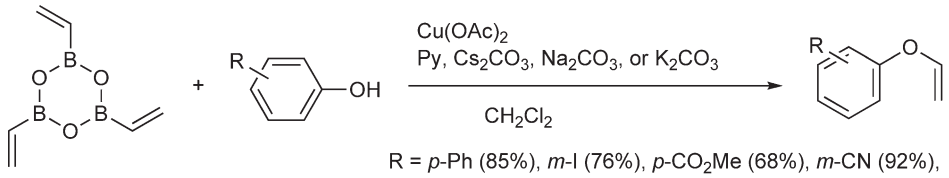
(233)

The coupling of *N*-hydroxyimides proceeded under slightly modified conditions. All copper sources such as $Cu(OAc)_2$, $Cu(OTf)_2$, CuCl, and $CuBr{\cdot}SMe_2$ afforded the desired coupling products in the presence of pyridine (Equation (234)).[1023]



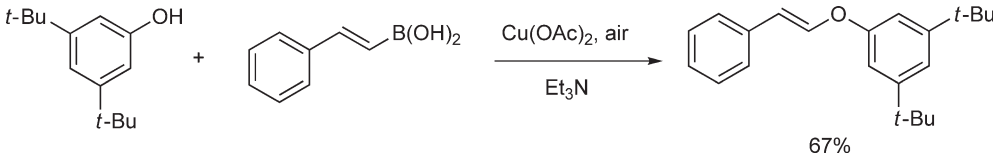
(234)

In an extension to the method, it was shown that vinylboroxine and 1-alkenylboronic acids could function well in the coupling reaction although a catalytic system was not successful (Equations (235) and (236)).[1015,1016,1024]



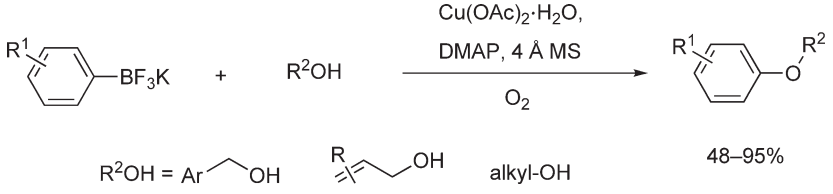
(235)

R = *p*-Ph (85%), *m*-I (76%), *p*-CO_2Me (68%), *m*-CN (92%), *p*-CHO (84%), *o*-OMe (70%), *m*-NMe_2 (88%), o-NHCOMe (80%)



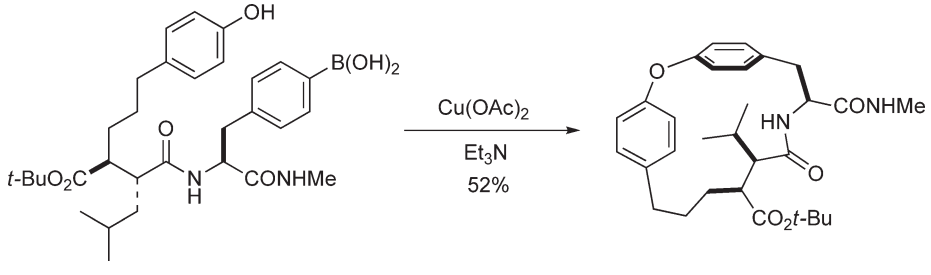
(236)

The formation of an aryl–O bond by the reaction of a phenol with air and moisture stable potassium alkenyl and aryltrifluoroborates was mediated by a copper species. The reaction procedure involved catalytic amounts of $Cu(OAc)_2$ with DMAP as a ligand in the presence of oxygen and molecular sieves. A variety of aliphatic primary and secondary alcohols as well as phenols were suitable reaction partners, thus displaying a broad functional group tolerance (Equation (237)).[1025]



(237)

The copper acetate-mediated inter- and intramolecular *O*-arylation of phenols with phenylboronic acid was the key step in the preparation of natural or macrocyclic biphenyl ethers. The intramolecular macrocyclization was mild and tolerant of chemical functionality (Equation (238)).[289,1026] The protocol has been used for the synthesis of (−)-tejedine,[1027] tecoplanin aglycon,[1028] L,L-cycloisodityrosine,[295,1029] and anti-HIV agent chloropepten I.[1030]

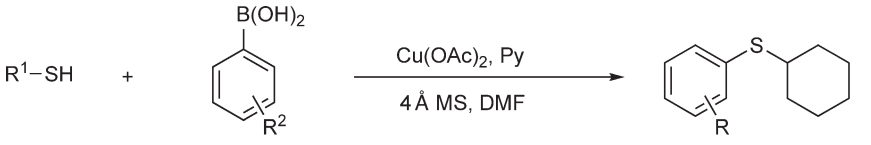


(238)

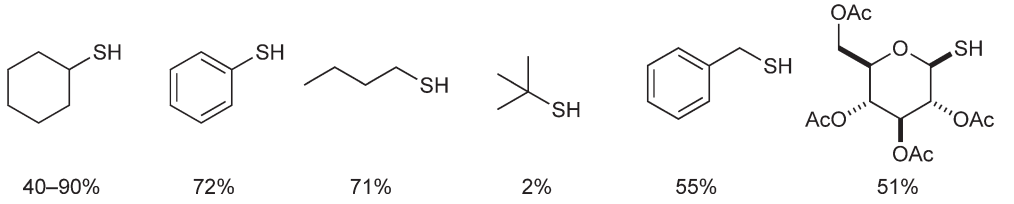
9.05.3.8.3 Copper-mediated C–S bond formation

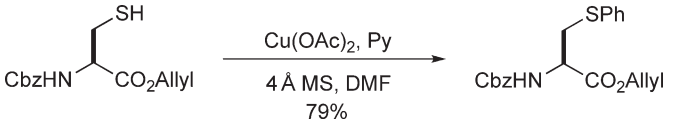
Under standard conditions for *N*- and *O*-arylation, the reactions were too slow because of significant disulfide formation as a result of competitive oxidation. However, the reaction of a wide range of thiolate substrates with arylboronic acids proceeded well when heated to 155 °C in DMF (Equations (239)) and (240)).[1031] Liebeskind *et al.*

reported a mild copper-mediated strategy for the synthesis of thioethers.[295,1032] A range of boronic acids smoothly reacted with *N*-thioimides in the presence of [CuMeSal] in THF at 50 °C (Equation (241)).

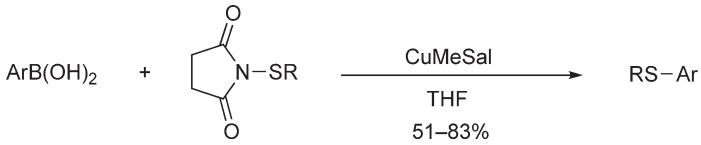


(239)





(240)



(241)

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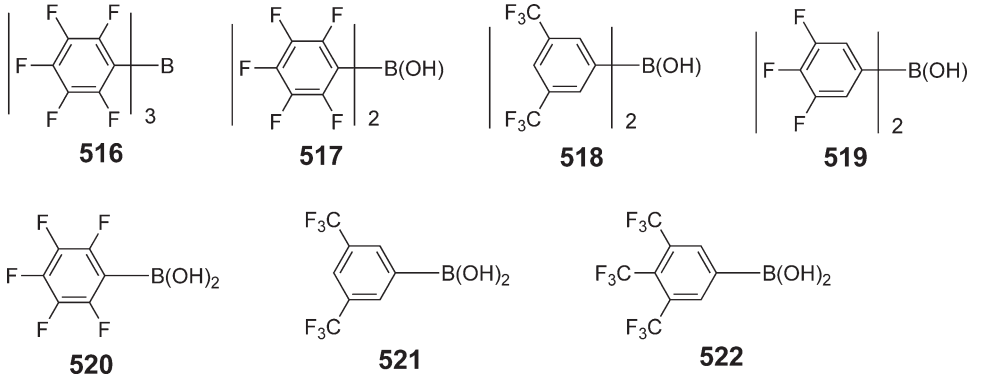
9.05.3.9 Boron as Lewis Acid Catalysts

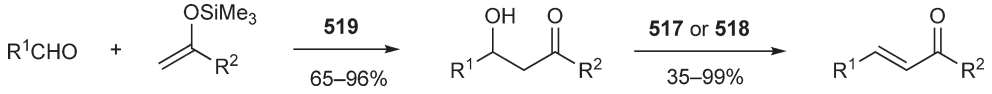
Aryl boron compounds, $Ar_nB(OH)_{3-n}$ ($n = 1$–3), bearing electron-withdrawing aromatic groups such as triarylboranes, diarylborinic acids, and arylboronic acids, represent a new class of air stable and water-tolerant Lewis acid or Brønsted acid catalyst in organic synthesis. In particular, tris(pentafluorophenyl)borane, primarily used as a co-catalyst in metallocene-mediated olefin polymerization, has the potential as a Lewis acid catalyst for various organic transformations. Diarylborinic acids and arylboronic acids have shown themselves to be powerful tools in the design of chiral boron catalysts. The reactions using boron Lewis acids have been reviewed (Scheme 39).[1033]

Aldol reactions of various silyl enol ethers or ketone silyl acetals with aldehydes and imines proceed smoothly in the presence of catalytic amount of **516** or **519** (Equations (242) and (243)).[1034–1037] $B(C_6F_5)_3$ **516** catalyzed the

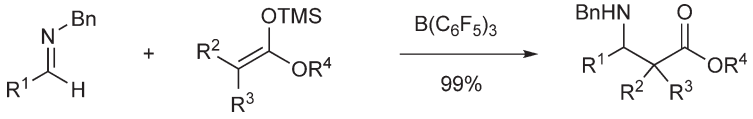


Scheme 39 Boron Lewis acids.

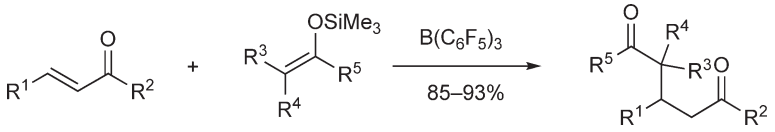
conjugate addition of silyl enol ethers to α,β-unsaturated ketones (Equation (244)), allylation reaction of benzaldehyde with allyltrimethylsilane, and Diels–Alder reaction of cyclopentadiene with 2-methyl-2-propanal.[1036] The arylboronic acids bearing electron-withdrawing aromatic groups such as **3** and **4** acted as highly efficient catalysts in the amidation of carboxylic acids (Equation (245)).[1038] The synthesis of verbacine has been accomplished by addition of cinnamoyl chloride and **521** (Equation (246)).[1039,1040]



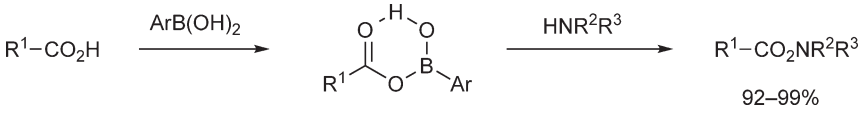
(242)



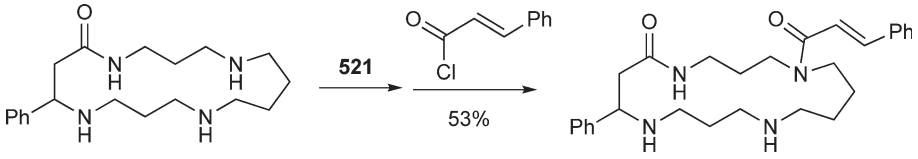
(243)



(244)

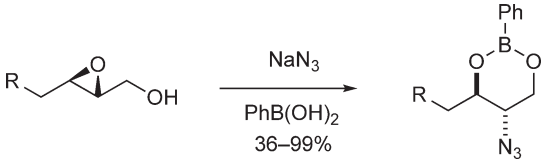


(245)



(246)

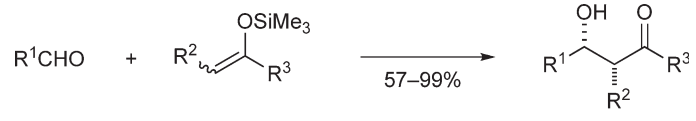
The ring-opening reaction of *trans*-2,3-epoxy alcohols with NaN_3 was mediated with $PhB(OH)_2$ (Equation (247)).[1041]



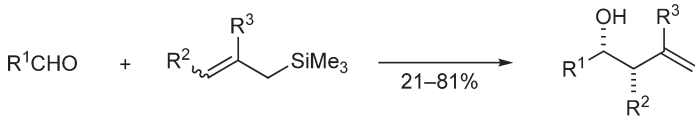
(247)

For asymmetric acid-catalyzed reactions, various chiral boron compounds were developed that include **523–531**,[1042–1051] (Scheme 40).

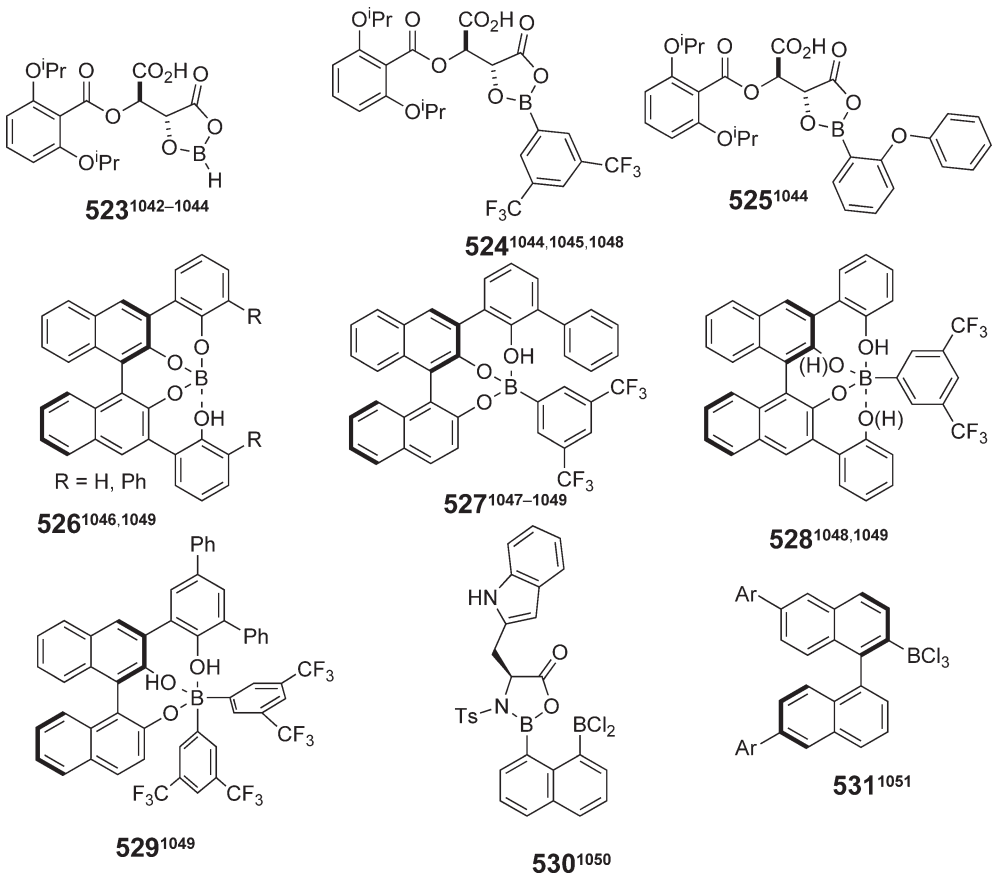
Chiral(acyloxy)boranes **523–525** were reported to be excellent catalysts for the enantioselective Mukaiyama condensation (Equation (248)) and allylation reaction of aldehydes leading to homoallylic alcohols (Equation (249)).[1042–1045]



(248)

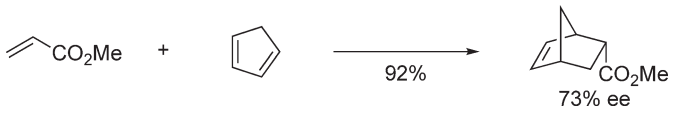


(249)



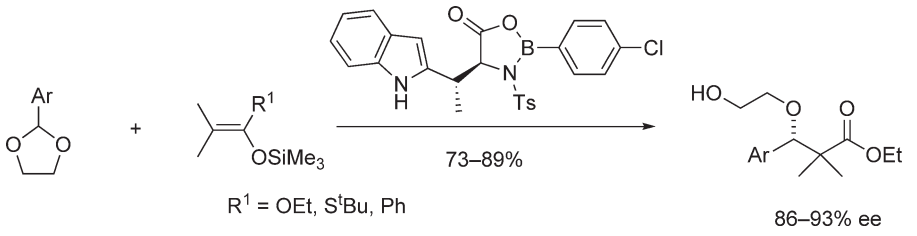
Scheme 40 Chiral boron catalysts.

Chiral alkyldihaloboranes are among the most powerful of chiral Lewis acids. The Diels–Alder reaction of cyclopentadiene with methyl acrylate proceeded smoothly at −78 °C in the presence of **530** or **531** to give the *endo*-adduct with >99% ee (Equation (250)).[1046–1052]



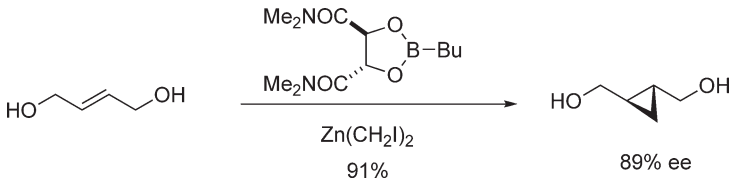
(250)

N-tosyl-(α*S*,β*R*)-β-methyltryptophan and dibromo(*p*-chlorophenyl)borane served as excellent catalysts for enantioselective ring cleavage of 1,3-dioxolanes with enol silyl ethers (Equation (251)).[1053–1055]



(251)

The alkylboronic ester of chiral diol was used as the most efficient chiral ligand for the enantioselective Simmons–Smith cyclopropanation of substituted allylic alcohols (Equation (252)).[1056–1059]

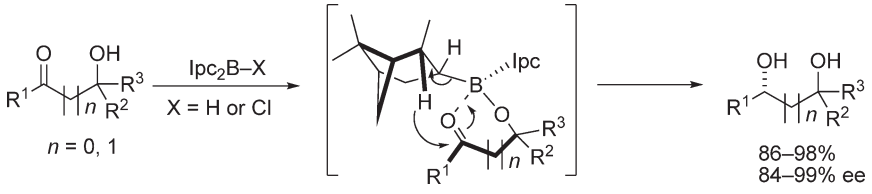


(252)

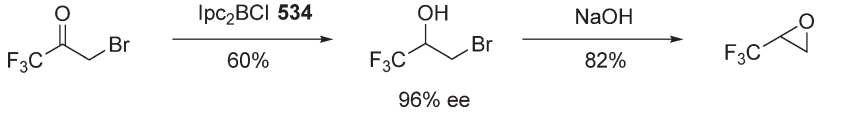
9.05.3.10 Boranes as Reducing Reagents

Potentially useful asymmetric reduction using boron-based reducing agents involves stoichiometric and catalytic processes.[1060,1061] Of the stoichiometric reagents reported, those that are the most promising for the highly enantioselective reduction of various functionalized ketones are **532**,[1062] **533**,[1062] **48a**,[1063–1065] **534**,[1063,1066–1071] and **535** (Scheme 41).[1061]

The stoichiometric, asymmetric reduction of α- and β-hydroxy ketones with **48a** or **534** (Equation (253)),[1063] and reduction of α-, β-, and γ-keto acids with **48a**[1064,1069,1070] proceeded with excellent ee via an intramolecular shift of a β-hydrogen of isopinocampheyl group. Ipc_2BCl **534** was employed for the reduction of 1-bromo-3,3,3-trifluoropropanone (Equation (254)),[1066] perfluorinated ketones, and 1,4-diphenyl-1,4-butanedione.[1067,1068] 2-Amino acetophenones[1062,1065] and α-keto phosphonates[1071] were reduced by **532**, **533**, or **48a** to β-amino alcohols or α-hydroxy phosphonates.

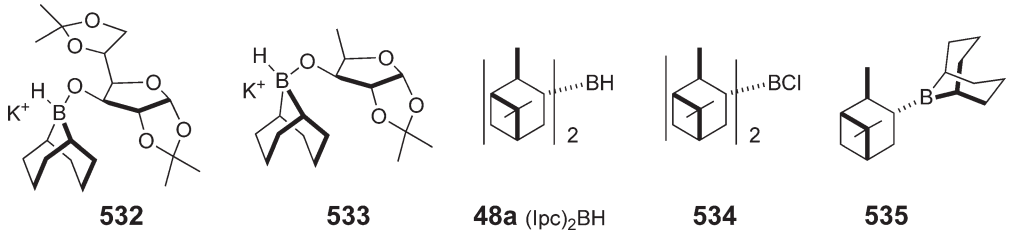


(253)



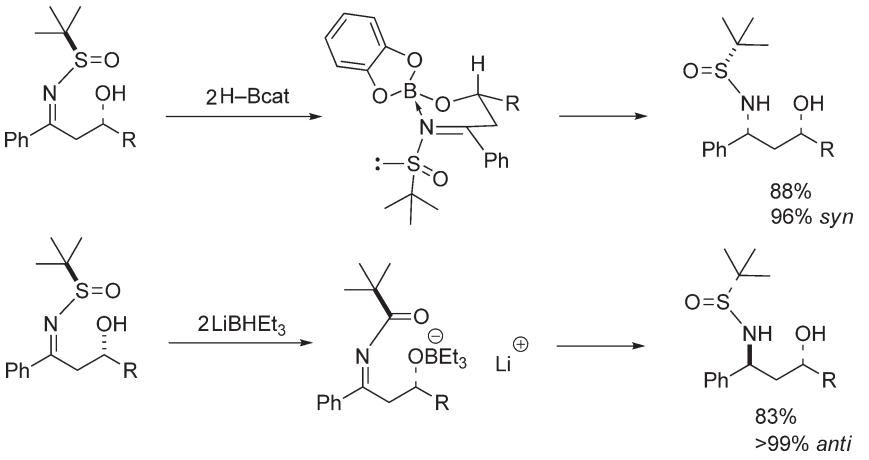
(254)

The reduction of the chiral β-hydroxy sulfinyl imines with HBcat or $LiBHEt_3$ provided *syn*- and *anti*-1,3-amino alcohols, respectively, with very high diastereomeric ratios (Equations (255) and (256)).[1072]



532 **533** **48a** $(Ipc)_2BH$ **534** **535**

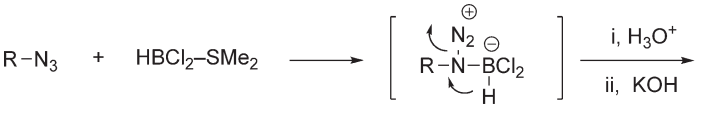
Scheme 41 Boron-based reducing reagents.



(255)

(256)

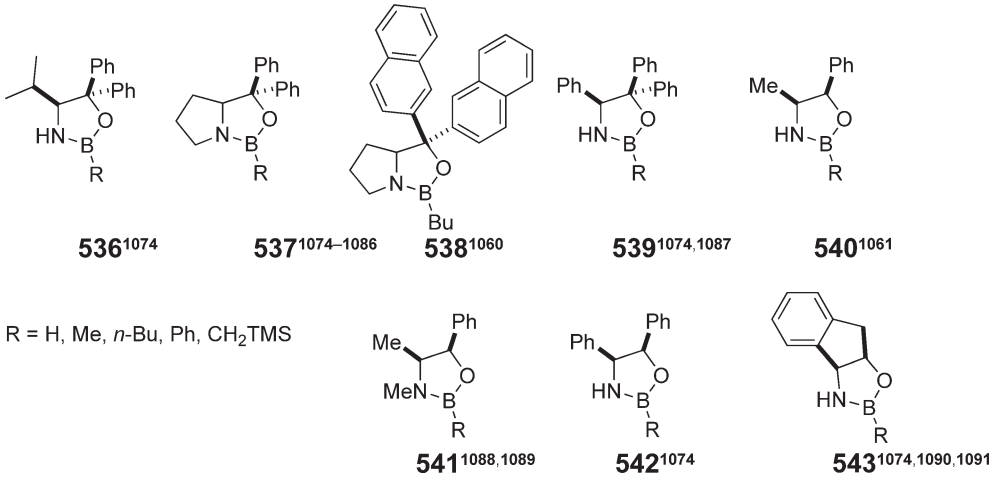
The high chemoselectivity of $BHCl_2{\cdot}SMe_2$ was demonstrated in the selective reduction of azide group in the presence of an ester, halide, nitrile, and nitro group (Equation (257)).[1073] The reduction of azides with $BHCl_2{\cdot}SMe_2$ was faster than the hydroboration of alkenes.



(257)

The catalyzed reactions are advantageous in terms of efficiency and selectivity. The catalyzed reduction using oxazaborolidines and boranes has been extensively studied for the large-scale preparation of optically active alcohols and amines. Various oxazaborolidine derivatives including **536–543**[1060,1061,1074–1091] were recently synthesized as enantioselective catalysts (Scheme 42). Borane–THF, borane methyl sulfide (BMS), and HBcat have so far been the most commonly used borane carriers for the catalytic reduction. These carriers have certain disadvantages such as high air and moisture sensitivity, low concentration and stability of borane–THF, and high volatility, flammability, and unpleasant odor of BMS. Using *N*-ethyl-*N*-isopropyl aniline–borane complex and *N*,*N*-diethyl-aniline–borane complex overcame these drawbacks.

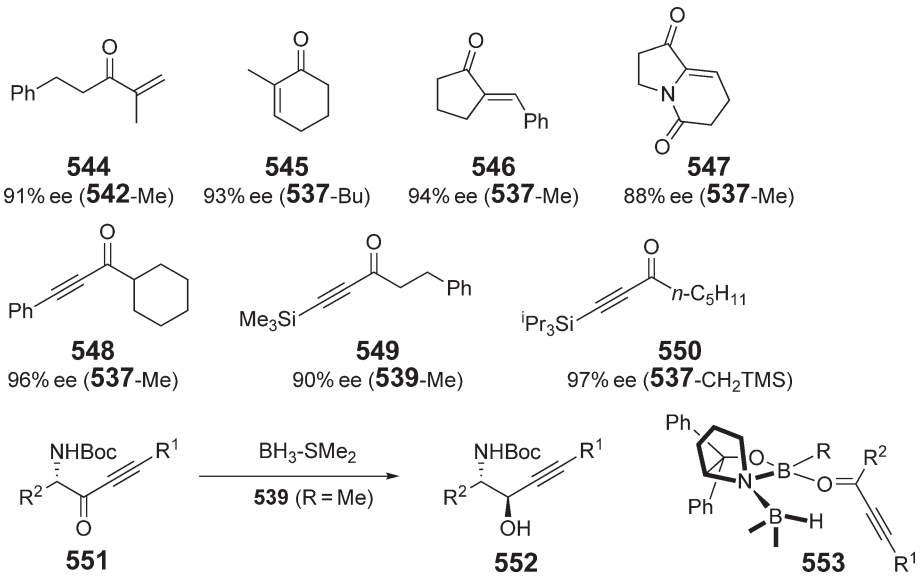
The catalyzed reduction has a wide scope for various ketones with excellent enantioselectivity (Table 6). The protocol was successfully applied to the reduction of α-siloxy and tetahydropyranyloxy ketones (entry 1),[1074] α-bromo and α-chloroacetophenne (entry 2),[1091–1094] trihalomethyl ketones (entry 3),[1095–1099] α-sulfonyl ketones (entry 4),[1100]



Scheme 42 Oxazaborolidine catalysts for asymmetric reduction.

Table 6 Catalyzed reduction of ketones (R^1COR^2)

Entry	R^1	R^2	*Catalyst*	*Borane*	*Yield* (%)	*ee* (%)
1	Ph	CH_2OTIPS	**537**-H	BH_3–THF	95	99
2	Ph	CH_2Cl	**543**-Me	BH_3–THF	95	96
3	$PhCH_2CH_2$	CCl_3	**537**-Bu	HBcat	96	95
4	*p*-MeC_6H_4	$CH_2OSO_2C_6H_4CH_3$-*p*	**537**-Me	PhN(*i*-Pr)Et·BH_3	95	97
5	Naph	$CH(OMe)_2$	**537**-Me	$PhEt_2·BH_3$	97	99
6	Ph	CH_2N_3	**537**-H	$BH_3·SMe_2$	92	100
7	*o*-ClC_6H_4	$P(O)(O^iPr)_2$	**537**-Bu	HBcat	96	97
8	*cyclo*-C_6H_{11}	$CH_2SO_2C_6H_4CH_3$-*p*	**537**-Me	PhN(*i*-Pr)Et·BH_3	99	99
9	*p*-FC_6H_4	CH_2S(*p*-tolyl)	**537**-Me	PhN(*i*-Pr)Et·BH_3	98	99

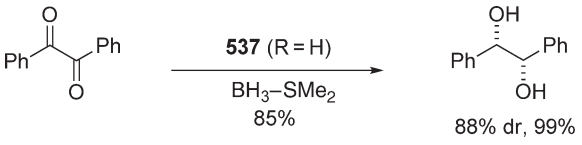


Scheme 43 Catalyzed reduction of enones and ynones.

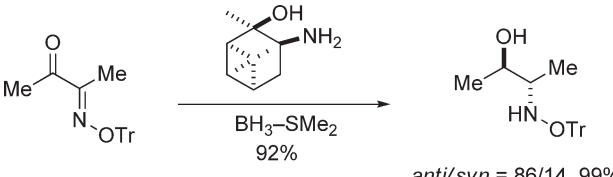
aliphatic and aromatic α-keto acetals, acyclic and cyclic α-keto thioketals (entry 5),[1101] α-azidomethyl aryl ketone, α-*N*,*N*-diakylamino ketones and α-imino ketones (entry 7),[1102] α-,β-, and γ-ketophosphonates (entry 7),[1103,1104] β-keto sulfones (entry 8),[1105] and β-keto *p*-tolylsulfide (entry 9).[1106]

The catalyzed reduction was effective for selective reduction of carbonyl groups of enones and ynones without affecting the C–C unsaturated bond (Scheme 43). Acyclic enones **544**,[1107] endocyclic enones **545**,[1108,1109] exocyclic enones **546** and **547**,[1110,1111] and ynones **548**–**551**[1112–1115] were enantioselectively reduced under catalytic conditions. The reductions of ynones, for example, **551**, to give *anti*-product **552** via a cyclic chelate **553** were sensitive to the steric size of the distal group of alkyne and to the nature of substituents on the carbonyl carbon.

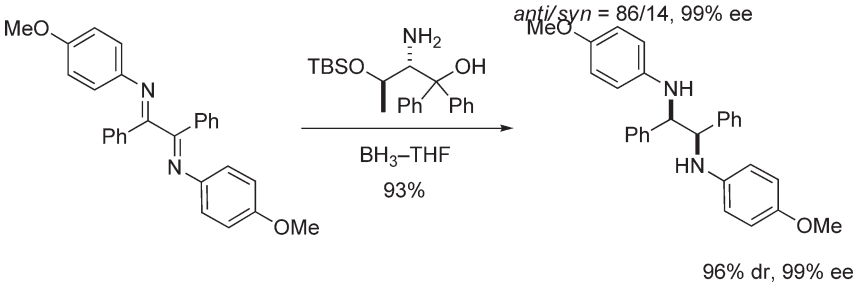
The oxazaborolidine-catalyzed reduction of 1,2-diketones (Equation (258)),[1116–1120] 1,2-keto-imines (Equation (259)),[1121–1123] and 1,2-diimines (Equation (260))[1124] provided optically active 1,2-diols, amino alcohols, and 1,2-diamines with both high enantiomeric and diastereomeric excess. The method can be also effective for β- and γ-analogs.



(258)

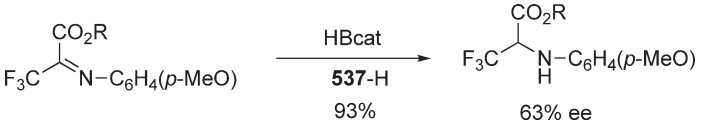


(259)

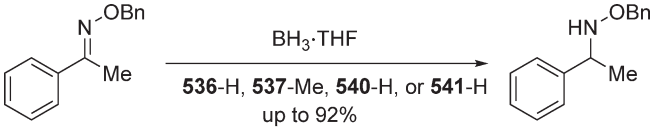


(260)

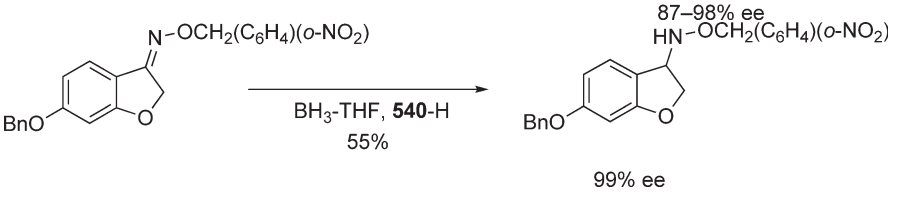
Only limited success has been reported in the reduction of ketimines due to the low electrophilicity of the imine carbon and the rapid equilibration between the (E)- and (Z)-isomers. However, high enantioselectivity was achieved in catalytic reduction of imines of keto esters (Equation (261))[1125] and oximes of acetophenone (Equation (262))[1089, 1125–1131] cyclic ketones (Equation (263)),[1127] and a ketone possessing a boryl group (Equation (264)).[1128]



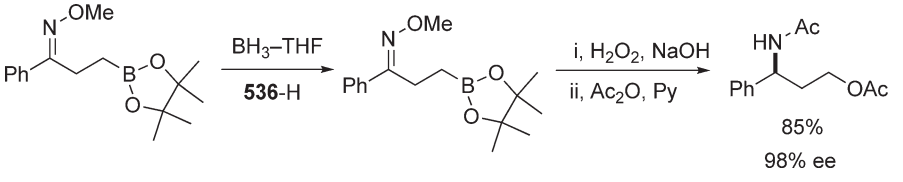
(261)



(262)

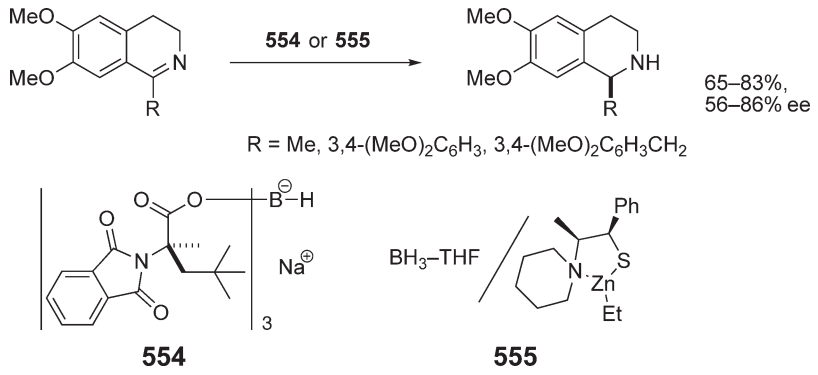


(263)



(264)

Chiral sodium acyloxy borohydride **554** prepared from $NaBH_4$ and *N*,*N*-phthaloyl amino acid reduced cyclic imines in good enantioselectivity. Thiazazincolidine complex **555** was shown to be an excellent catalyst for the catalytic reduction of dihydroisoquinolines with BH_3–THF (Equation (265)).[1132–1134]



(265)

554 **555**

References

1. Matteson, D. S. *Stereodirected Synthesis with Organoboranes*; Springer: Berlin, 1995.
2. Hall, D. G. *Boronic acids*; Wiley-VCH Verlag GmbH: Weinheim, 2005.
3. Kaufmann, D. E., Matteson, D. S., Eds.; *Science of Syntheses, Houben-Wey Methods of Molecular Transformation*; Georg Thieme Verlag: Stuttgart, 2005; Vol. 6.
4. Carmès, L.; Carreaux, F.; Carboni, B.; Mortier, J. *Tetrahedron Lett.* **1998**, *39*, 555.
5. Simov, B. P.; Rohn, A.; Brecker, L.; Giester, G.; Hammerschmidt, F. *Synthesis* **2004**, 2704.
6. Tivola, P. B.; Deagostino, A.; Prandi, C.; Venturello, P. *Org. Lett.* **2002**, *4*, 1275.
7. Kerins, F.; O'Shea, D. F. *J. Org. Chem.* **2002**, *67*, 4968.
8. Das, S.; Alexeev, V. L.; Sharma, A. C.; Geib, S. J.; Asher, S. A. *Tetrahedron Lett.* **2003**, *44*, 7719.
9. Morrison, D. J.; Piers, W. E.; Parvez, M. *Synlett* **2004**, 2429.
10. Manickam, G.; Schlüter, A. D. *Synthesis* **2000**, 442.
11. Roschangar, F.; Brown, J. C.; Cooley, B. E., Jr.; Sharp, M. J.; Matsuoka, R. T. *Tetrahedron* **2002**, *58*, 1657.
12. Liess, P.; Hensel, V.; Schlüter, A.-D. *Liebigs Annalen* **1996**, 1037.
13. Wong, K. T.; Chien, Y. Y.; Liao, Y. L.; Lin, C. C.; Chou, M. Y.; Leung, M. *J. Org. Chem.* **2002**, *67*, 1041.
14. Li, W.; Nelson, D. P.; Jensen, M. S.; Hoerrner, R. S.; Cai, D.; Larsen, R. D.; Reider, P. J. *J. Org. Chem.* **2002**, *67*, 5394.
15. Parry, P. R.; Wang, C.; Batsanov, A. S.; Bryce, M. R.; Tarbit, B. *J. Org. Chem.* **2002**, *67*, 7541.
16. Zhong, Z.; Anslyn, E. V. *J. Am. Chem. Soc.* **2002**, *124*, 9014.
17. Caron, S.; Hawkins, J. M. *J. Org. Chem.* **1998**, *63*, 2054.
18. Todd, M. H.; Balasubramanian, S.; Abell, C. *Tetrahedron Lett.* **1997**, *38*, 6781.
19. Yamaguchi, S.; Miyasato, M.; Tamao, K. *Chem. Lett.* **2003**, *32*, 1104.
20. Faderl, J.; Deobald, B.; Guilard, R.; Pritzkow, H.; Siebert, W. *Eur. J. Inorg. Chem.* **1999**, 399.
21. Bouillon, A.; Lancelot, J. C.; Collot, V.; Bovy, P. R.; Rault, S. *Tetrahedron* **2002**, *58*, 2885.
22. Weis, N.; Pritzkow, H.; Siebert, W. *Eur. J. Inorg. Chem.* **1999**, 393.
23. Sattelkau, T.; Qandil, A. M.; Nichols, D. E. *Synthesis* **2001**, 262.
24. Godard, A.; Rocca, P.; Pomel, V.; Thomas-dit-Dumont, L.; Rovera, J. C.; Thaburet, J. F.; Marsais, F.; Quéguiner, G. *J. Organomet. Chem.* **1996**, *517*, 25.
25. Wipf, P.; Jung, J. K. *J. Org. Chem.* **2000**, *65*, 6319.
26. MacNeil, S. L.; Familoni, O. B.; Snieckus, V. *J. Org. Chem.* **2001**, *66*, 3662.
27. Myers, A. G.; Tom, N. J.; Fraley, M. E.; Cohen, S. B.; Madar, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 6072.
28. Kristensen, J.; Lysén, M.; Vedsø, P.; Begtrup, M. *Org. Lett.* **2001**, *3*, 1435.
29. Larsen, R. D.; King, A. O.; Chen, C. Y.; Corley, E. G.; Foster, B. S.; Roberts, F. E.; Yang, C.; Lieberman, D. R.; Reamer, R. A.; Tschaen, D. M., *et al. J. Org. Chem.* **1994**, *59*, 6391.
30. Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2003**, 4313.
31. Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153.
32. Frohn, H.-J.; Bardin, V. V. *Z. Anorg. Allg. Chem.* **2001**, *627*, 15.
33. Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393.
34. Darses, S.; Michaud, G.; Genêt, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5045.
35. Molander, G. A.; Rivero, M. R. *Org. Lett.* **2002**, *4*, 107.
36. Petasis, N. A.; Yudin, A. K.; Zavialov, I. A.; Prakash, G. K. S.; Olah, G. A. *Synlett* **1997**, 606.
37. Bardin, V. V.; Frohn, H.-J. *Z. Anorg. Allg. Chem.* **2002**, *628*, 721.
38. Frohn, H.-J.; Bardin, V. V. *Z. Anorg. Allg. Chem.* **2001**, *627*, 2499.
39. Batey, R. A.; Thadani, A. N.; Smil, D. V. *Tetrahedron Lett.* **1999**, *40*, 4289.
40. Batey, R. A.; Thadani, A. N.; Smil, D. V.; Lough, A. J. *Synthesis* **2000**, 990.
41. Darses, S.; Michaud, G.; Genêt, J.-P. *Eur. J. Org. Chem.* **1999**, 1875.
42. Frohn, H.-J.; Franke, H.; Fritzen, P.; Bardin, V. V. *J. Organomet. Chem.* **2000**, *598*, 127.
43. Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099.
44. Molander, G. A.; Biolatto, B. *Org. Lett.* **2002**, *4*, 1867.
45. Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.
46. Molander, G. A.; Katona, B. W.; Machrouhi, F. *J. Org. Chem.* **2002**, *67*, 8416.

47. Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020.
48. Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460.
49. Shirota, Y.; Kinoshita, M.; Noda, T.; Okumoto, K.; Ohata, T. *J. Am. Chem. Soc.* **2000**, *122*, 11021.
50. Yamaguchi, S.; Shirasaka, T.; Tamao, K. *Org. Lett.* **2000**, *2*, 4129.
51. Yamaguchi, S.; Akiyama, S.; Tamao, K. *J. Am. Chem. Soc.* **2000**, *122*, 6335.
52. Matsumi, N.; Naka, K.; Chujo, Y. *J. Am. Chem. Soc.* **1998**, *120*, 10776.
53. Itami, K.; Kamei, T.; Yoshida, J.-I. *J. Am. Chem. Soc.* **2003**, *125*, 14670.
54. Babudri, F.; Farinola, G. M.; Flandanese, V.; Mazzone, L.; Naso, F. *Tetrahedron* **1998**, *54*, 1085.
55. Jäkle, F.; Lough, A. J.; Manners, I. *Chem. Commun.* **1999**, 453.
56. Wong, M. K.; Leung, C. Y.; Wong, H. N. C. *Tetrahedron* **1997**, *53*, 3497.
57. Ye, X. S.; Wong, H. N. C. *J. Org. Chem.* **1997**, *62*, 1940.
58. Nöth, H.; Schmidt, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 292.
59. Ashe, A. J., III; Fang, X. *Org. Lett.* **2000**, *2*, 2089.
60. Goswami, A.; Maier, C. J.; Pritzkow, H.; Siebert, W. *Eur. J. Inorg. Chem.* **2004**, 2635.
61. Gamboa, J. A.; Sundararaman, A.; Kakalis, L.; Lough, A. J.; Jäkle, F. *Organometallics* **2002**, *21*, 4169.
62. Cole, T. E.; Quintanilla, R.; Rodewald, S. *Organometallics* **1991**, *10*, 3777.
63. Lee, B. Y.; Bazan, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 8577.
64. Zheng, Q.; Yang, Y.; Martin, A. R. *Tetrahedron Lett.* **1993**, *34*, 2235.
65. Zaidlewicz, M.; Kanth, J. V. B.; Brown, H. C. *J. Org. Chem.* **2000**, *65*, 6697.
66. Brown, H. C.; Zaidlewicz, M.; Dalvi, P. V.; Biswas, G. K. *J. Org. Chem.* **2001**, *66*, 4795.
67. Crich, D.; Neelamkavil, S. *Org. Lett.* **2002**, *4*, 4175.
68. Patra, P. K.; Nishide, K.; Fuji, K.; Node, M. *Synthesis* **2004**, 1003.
69. Brown, H. C.; Zaidlewicz, M.; Dalvi, P. V. *Organometallics* **1998**, *17*, 4202.
70. Brown, H. C.; Kanth, J. V. B.; Zaidlewicz, M. *Tetrahedron* **1999**, *55*, 5991.
71. Brown, H. C.; Zaidlewicz, M.; Dalvi, P. V.; Narasimhan, S.; Mukhopadhyay, A. *Organometallics* **1999**, *18*, 1305.
72. Brown, H. C.; Kanth, J. V. B.; Dalvi, P. V.; Zaidlewicz, M. *J. Org. Chem.* **1999**, *64*, 6263.
73. Brown, H. C.; Kanth, J. V. B.; Dalvi, P. V.; Zaidlewicz, M. *J. Org. Chem.* **2000**, *65*, 4655.
74. Soderquist, J. A.; Medina, J. R.; Huertas, R. *Tetrahedron Lett.* **1998**, *39*, 6119.
75. Soderquist, J. A.; Huertas, R.; Medina, J. R. *Tetrahedron Lett.* **1998**, *39*, 6123.
76. Soundararajan, R.; Matteson, D. S. *Organometallics* **1995**, *14*, 4157.
77. Kanth, J. V. B.; Brown, H. C. *J. Org. Chem.* **2001**, *66*, 5359.
78. Kanth, J. V. B.; Brown, H. C. *Org. Lett.* **1999**, *1*, 315.
79. Josyula, K. V. B.; Gao, P.; Hewitt, C. *Tetrahedron Lett.* **2003**, *44*, 7789.
80. Kalinin, A. V.; Scherer, S.; Snieckus, V. *Angew. Chem., Int. Ed.* **2003**, *42*, 3399.
81. Parks, D. J.; Spance, R. E. von, H.; Piers, W. E. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 809.
82. Parks, D. J.; Piers, W. E.; Yap, G. P. A. *Organometallics* **1998**, *17*, 5492.
83. Entwistle, C. D.; Batsanov, A. S.; Howard, J. A. K.; Fox, M. A.; Marder, T. B. *Chem. Commun.* **2004**, 702.
84. Smith, K.; Pelter, A.; Jin, Z. *J. Chem. Soc., Perkin Trans* **1993**, *1*, 395.
85. Brown, H. C.; Dhokte, U. P. *J. Org. Chem.* **1994**, *59*, 2025.
86. Brown, H. C.; Dhokte, U. P. *J. Org. Chem.* **1994**, *59*, 2365.
87. Dhokte, U. P.; Brown, H. C. *Tetrahedron Lett.* **1994**, *35*, 4715.
88. Brown, H. C.; Dhokte, U. P. *J. Org. Chem.* **1994**, *59*, 5479.
89. Dhokte, U. P.; Brown, H. C. *Organometallics* **1998**, *17*, 2891.
90. Dhokte, U. P.; Brown, H. C. *Organometallics* **1996**, *15*, 3504.
91. Dhokte, U. P.; Soundararajan, R.; Ramachandran, P. V.; Brown, H. C. *Tetrahedron Lett.* **1996**, *37*, 8345.
92. Coutts, L. D.; Cywin, C. L.; Kallmerten, J. *Synlett* **1993**, 696.
93. Panek, J. S.; Xu, F.; Rondón, A. C. *J. Am. Chem. Soc.* **1998**, *120*, 4113.
94. Pearson, A. J.; Mesaros, E. F. *Org. Lett.* **2001**, *3*, 2665.
95. Sous, M. E.; Rizzacasa, M. A. *Tetrahedron Lett.* **2000**, *41*, 8591.
96. Pennemann, H.; Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **2000**, *11*, 2133.
97. Plehiers, M.; Hootelé, C. *Tetrahedron Lett.* **1993**, *34*, 7569.
98. Oppolzer, W.; Bochet, C. G. *Tetrahedron Lett.* **1995**, *36*, 2959.
99. Goralski, C. T.; Hasha, D. L.; Nicholson, L. W.; Singaram, B. *Tetrahedron Lett.* **1994**, *35*, 5165.
100. Nguyen, T.; Sherman, D.; Ball, D.; Solow, M.; Singaram, B. *Tetrahedron: Asymmetry* **1993**, *4*, 189.
101. Winqvist, A; Strömberg, R. *Eur. J. Org. Chem.* **2001**, 4305.
102. Cossy, J.; Blanchard, N.; Meyer, C. *Synthesis* **1999**, 1063.
103. Yadav, J. S.; Sasmal, P. K. *Tetrahedron Lett.* **1997**, *38*, 8769.
104. Sugimura, T.; Nishida, F.; Tei, T.; Morisawa, A.; Tai, A.; Okuyama, T. *Chem. Commun.* **2001**, 2180.
105. Ng, F.; Chiu, P.; Danishefsky, S. J. *Tetrahedron Lett.* **1998**, *39*, 767.
106. Brown, H. C.; Chen, G. M.; Jennings, M. P.; Ramachandran, P. V. *Angew. Chem., Int. Ed.* **1999**, *38*, 2052.
107. Ramachandran, P. V.; Jennings, M. P. *Org. Lett.* **2001**, *3*, 3789.
108. Ramachandran, P. V.; Jennings, M. P. *Chem. Commun.* **2002**, 386.
109. Soderquist, J. A.; León, G. *Tetrahedron Lett.* **1998**, *39*, 2511.
110. Lhermitte, F.; Knochel, P. *Angew. Chem., Int. Ed.* **1998**, *37*, 2460.
111. Laaziri, H.; Bromm, L. O.; Lhermitte, F.; Gschwind, R. M.; Knochel, P. *J. Am. Chem. Soc.* **1999**, *121*, 6940.
112. Bromm, L. O.; Laaziri, H.; Lhermitte, F.; Harms, K.; Knochel, P. *J. Am. Chem. Soc.* **2000**, *122*, 10218.
113. Varela, J. A.; Peña, D.; Goldfuss, B.; Polborn, K.; Knochel, P. *Org. Lett.* **2001**, *3*, 2395.
114. Hupe, E.; Denisenko, D.; Knochel, P. *Tetrahedron* **2003**, *59*, 9187.
115. Varela, J. A.; Peña, D.; Goldfuss, B.; Denisenko, D.; Kulhanek, J.; Polborn, K.; Knochel, P. *Chem. Eur. J.* **2004**, *10*, 4252.
116. Hoffmann, R. W.; Dresely, S. *Synthesis* **1988**, 103.

117. Kamabuchi, A.; Moriya, T.; Miyaura, N.; Suzuki, A. *Synth. Commun.* **1993**, *23*, 2851.
118. Collet, S.; Carreaux, F.; Boucher, J. L.; Pethe, S.; Lepoivre, M.; Danion-Bougot, R.; Danion, D. *Chem. Soc., Perkin Trans.* **2000**, *1*, 177.
119. Denniel, V.; Bauchat, P.; Danion, D.; Danion-Bougot, R. *Tetrahedron Lett.* **1996**, *37*, 5111.
120. Colberg, J. C.; Rane, A.; Vaquer, J.; Soderquist, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 6065.
121. Brown, H. C.; Ramachandran, P. V. *J. Organomet. Chem.* **1995**, *500*, 1.
122. Boger, D. L.; McKie, J. A.; Boyce, C. W. *Synlett* **1997**, 515.
123. Ludek, O. R.; Meier, C. *Synthesis* **2003**, 2101.
124. Reddy, N. L.; Francesconi, I.; Bellott, E. M. *Tetrahedron: Asymmetry* **1999**, *10*, 3281.
125. Dhokte, U. P.; Brown, H. C. *Tetrahedron Lett.* **1996**, *37*, 9021.
126. Dhokte, U. P.; Kulkarni, S. V.; Brown, H. C. *J. Org. Chem.* **1996**, *61*, 5140.
127. Cramer, N.; Laschat, S.; Baro, A.; Frey, W. *Synlett* **2003**, 2175.
128. Brown, H. C.; Murali, D.; Singaram, B. *J. Organomet. Chem.* **1999**, *581*, 116.
129. Fisher, G. B.; Goralski, C. T.; Nicholson, L. W.; Hasha, D. L.; Zakett, D.; Singaram, B. *J. Org. Chem.* **1995**, *60*, 2026.
130. Fisher, G. B.; Goralski, C. T.; Nicholson, L. W.; Singaram, B. *Tetrahedron Lett.* **1993**, *34*, 7693.
131. Dhokte, U. P.; Pathare, P. M.; Mahindroo, V. K.; Brown, H. C. *J. Org. Chem.* **1998**, *63*, 8276.
132. Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179.
133. Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957.
134. Hayashi, T. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 1, p 351.
135. Miyaura, N. In *Catalytic Heterofunctionalization*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH: Chichester, 2001; Chapter 1.
136. Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 3426.
137. Betley, T. A.; Peters, J. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 2385.
138. He, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 1696.
139. Hartwig, J. F.; Muhoro, C. N. *Organometallics* **2000**, *19*, 30.
140. Burgess, K.; Jaspars, M. *Organometallics* **1993**, *12*, 4197.
141. Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. *Tetrahedron* **2004**, *60*, 10695.
142. Evans, D. A.; Muci, A. R.; Stürmer, R. *J. Org. Chem.* **1993**, *58*, 5307.
143. Horino, Y.; Livinghouse, T.; Stan, M. *Synlett* **2004**, 2639.
144. Grasa, G. A.; Moore, Z.; Martin, K. L.; Stevens, E. D.; Nolan, S. P.; Paquet, V.; Lebel, H. *J. Organomet. Chem.* **2002**, *658*, 126.
145. Evans, D. A.; Fu, G. C.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1992**, *114*, 6671.
146. Edwards, D. R.; Crudden, C. M.; Yam, K. *Adv. Synth. Catal.* **2005**, *347*, 50.
147. Pereira, S.; Srebnik, M. *J. Am. Chem. Soc.* **1996**, *118*, 909.
148. Murata, M.; Watanabe, S.; Masuda, Y. *Tetrahedron Lett.* **1999**, *40*, 2585.
149. Murata, M.; Kawakita, K.; Asana, T.; Watanabe, S.; Masuda, Y. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 825.
150. Westcott, S. A.; Marder, T. B.; Baker, R. T. *Organometallics* **1993**, *12*, 975.
151. Vogels, C. M.; Hayes, P. G.; Shaver, M. P.; Westcott, S. A. *Chem. Commun.* **2000**, 51.
152. Brown, J. M.; Lloyd-Jones, G. C. *J. Am. Chem. Soc.* **1994**, *116*, 866.
153. Hou, X. L.; Hong, D. G.; Rong, G. B.; Guo, Y. L.; Dai, L. X. *Tetrahedron Lett.* **1993**, *34*, 8513.
154. Garrett, C. E.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 1370.
155. Brinkman, J. A.; Nguyen, T. T.; Sowa, J. R., Jr. *Org. Lett.* **2000**, *2*, 981.
156. Vogels, C. M.; O'Connor, P. E.; Phillips, T. E.; Watson, K. J.; Shaver, M. P.; Hayes, P. G.; Westcott, S. A. *Can. J. Chem.* **2001**, *79*, 1898.
157. Colin, S.; Vaysse-Ludot, L.; Lecouvé, J. P.; Maddaluno, J. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 4505.
158. Elgendy, S.; Patel, G.; Kakkar, V. V.; Claeson, G.; Green, D.; Skordalakes, E.; Baban, J. A.; Deadman, J. *Tetrahedron Lett.* **1994**, *35*, 2435.
159. Elgendy, S.; Claeson, G.; Kakkar, V. V.; Green, D.; Patel, G.; Goodwin, C. A.; Baban, J. A.; Scully, M. F.; Deadman, J. *Tetrahedron* **1994**, *50*, 3803.
160. Ramachandran, P. V.; Jennings, M. P.; Brown, H. C. *Org. Lett.* **1999**, *1*, 1399.
161. Zaidlewicz, M.; Meller, J. *Tetrahedron Lett.* **1997**, *38*, 7279.
162. Sato, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1989**, *30*, 3789.
163. Yamamoto, Y.; Fujikawa, R.; Yamada, A.; Miyaura, N. *Chem. Lett.* **1999**, 1069.
164. Gridnev, I. D.; Miyaura, N.; Suzuki, A. *J. Org. Chem.* **1993**, *58*, 5351.
165. Gridnev, I. D.; Miyaura, N.; Suzuki, A. *Organometallics* **1993**, *12*, 589.
166. Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990.
167. Demay, S.; Volant, F.; Knochel, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1235.
168. Brunel, J. M.; Buono, G. *Tetrahedron Lett.* **1999**, *40*, 3561.
169. Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062.
170. Kang, J.; Lee, J. H.; Kim, J. B.; Kim, G. I. *Chirality* **2000**, *12*, 378.
171. Doucet, H.; Fernandez, E.; Layzell, T. P.; Brown, J. M. *Chem. Eur. J.* **1999**, *5*, 1320.
172. Valk, J. M.; Whitlock, G. A.; Layzell, T. P.; Brown, J. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2593.
173. Brown, J. M.; Hulmes, D. I.; Layzell, T. P. *J. Chem. Soc., Chem. Commun.* **1993**, 1673.
174. McCarthy, M.; Hooper, M. W.; Guiry, P. J. *Chem. Commun.* **2000**, 1333.
175. Connolly, D. J.; Lacey, P. M.; McCarthy, M.; Saunders, C. P.; Carroll, A. M.; Goddard, R.; Guiry, P. J. *J. Org. Chem.* **2004**, *69*, 6572.
176. Kwong, F. Y.; Yang, Q.; Mak, T. C. W.; Chan, A. S. C.; Chan, K. S. *J. Org. Chem.* **2002**, *67*, 2769.
177. Rubina, M.; Rubin, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2003**, *125*, 7198.
178. Pérez Luna, A.; Ceschi, M.-A.; Bonin, M.; Micouin, L.; Husson, H.-P. *J. Org. Chem.* **2002**, *67*, 3522.
179. Pérez Luna, A.; Bonin, M.; Micouin, L.; Husson, H. P. *J. Am. Chem. Soc.* **2002**, *124*, 12098.
180. Maeda, K.; Brown, J. M. *Chem. Commun.* **2002**, 310.
181. Garrett, C. E.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 3224.
182. Shirakawa, K.; Arase, A.; Hoshi, M. *Synthesis* **2004**, *11*, 1814.
183. Hoshi, M.; Arase, A. *Synth. Commun.* **1997**, *27*, 567.
184. Burgess, K.; van der Donk, W. A. *Organometallics* **1994**, *13*, 3616.
185. Burgess, K.; van der Donk, W. A. *Tetrahedron Lett.* **1993**, *34*, 6817.

186. Burgess, K.; van der Donk, W. A. *J. Am. Chem. Soc.* **1994**, *116*, 6561.
187. Villiers, C.; Ephritikhine, M. *Tetrahedron Lett.* **2003**, *44*, 8077.
188. Albanese, D.; Landini, D.; Maia, A.; Penso, M. *Synlett* **2000**, 997.
189. Suzuki, A. *Rev. Heteroatom Chem.* **1997**, *17*, 271.
190. Smith, A. B., III; Friestad, G. K.; Barbosa, J.; Bertounesque, E.; Duan, J. J.-W.; Hull, K. G.; Iwashima, M.; Qiu, Y.; Spoors, P. G.; Salvatore, B. A. *J. Am. Chem. Soc.* **1999**, *121*, 10478.
191. Yu, M. S.; De Leon, L. L.; McGuire, M. A.; Botha, G. *Tetrahedron Lett.* **1998**, *39*, 9347.
192. Tarli, A.; Wang, K. K. *J. Org. Chem.* **1997**, *62*, 8841.
193. Lee, C. B.; Wu, Z.; Zhang, F.; Chappell, M. D.; Stachel, S. J.; Chou, T. C.; Guan, Y.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2001**, *123*, 5249.
194. Chappell, M. D.; Harris, C. R.; Kuduk, S. D.; Balog, A.; Wu, Z.; Zhang, F.; Lee, C. B.; Stachel, S. J.; Danishefsky, S. J.; Chou, T. C., *et al. J. Org. Chem.* **2002**, *67*, 7730.
195. Chappell, M. D.; Stachel, S. J.; Lee, C. B.; Danishefsky, S. J. *Org. Lett.* **2000**, *2*, 1633.
196. Sato, M.; Yamamoto, Y.; Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1993**, *34*, 7071.
197. Hara, S.; Suzuki, A. *Org. Synth.* **1998**, *75*, 129.
198. Marder, T. B.; Norman, N. C. *Top. Catal.* **1998**, *5*, 63.
199. Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392.
200. Beletskaya, I.; Moberg, C. *Chem. Rev.* **1999**, *99*, 3435.
201. Ishiyama, T.; Miyaura, N. *Chem. Rec.* **2004**, *3*, 271–280.
202. Irvine, G. J.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R.; Robins, E. G.; Roper, W. R.; Whittell, G. R.; Wright, L. J. *Chem. Rev.* **1998**, *98*, 2685.
203. Suginome, M.; Ito, Y. *Chem. Rev.* **2000**, *100*, 3221.
204. Han, L.-B.; Tanaka, M. *Chem. Commun.* **1999**, 395.
205. Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 11018.
206. Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. *Organometallics* **1996**, *15*, 713.
207. Iverson, C. N.; Smith, M. R., III. *Organometallics* **1996**, *15*, 5155.
208. Lesley, G.; Nguyen, P.; Taylor, N. J.; Marder, T. B.; Scott, A. J.; Clegg, W.; Norman, N. C. *Organometallics* **1996**, *15*, 5137.
209. Thomas, R. L.; Souza, F. E. S.; Marder, T. B. *J. Chem. Soc., Dalton Trans.* **2001**, 1650.
210. Maderna, A.; Pritzkow, H.; Siebert, W. *Angew. Chem., Int. Ed.* **1996**, *35*, 1501.
211. Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Lett.* **1996**, 1117.
212. Brown, S. D.; Armstrong, R. W. *J. Am. Chem. Soc.* **1996**, *118*, 6331.
213. Wenckens, M.; Jakobsen, P.; Vedsø, P.; Huusfeldt, P. O.; Gissel, B.; Barfoed, M.; Brockdorff, B. L.; Lykkesfeldt, A. E.; Begtrup, M. *Bioorg. Med. Chem.* **2003**, *11*, 1883.
214. Morgan, J. B.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 15338.
215. Iverson, C. N.; Smith, M. R., III. *Organometallics* **1997**, *16*, 2757.
216. Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1997**, 689.
217. Dai, C.; Robins, E. G.; Scott, A. J.; Clegg, W.; Yufit, D. S.; Howard, J. A. K.; Marder, T. B. *Chem. Commun.* **1998**, 1.
218. Baker, R. T.; Nguyen, P.; Marder, T. B.; Westcott, S. A. *Angew. Chem., Int. Ed.* **1995**, *34*, 1336.
219. Nguyen, P.; Coapes, R. B.; Woodward, A. D.; Taylor, N. J.; Burke, J. M.; Howard, J. A. K.; Marder, T. B. *J. Organomet. Chem.* **2002**, *652*, 77.
220. Marder, T. B.; Norman, N. C.; Rice, C. R. *Tetrahedron Lett.* **1998**, *39*, 155.
221. Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702.
222. Miller, S. P.; Morgan, J. B.; Nepveux, F. J. V; Morken, J. P. *Org. Lett.* **2004**, *6*, 131.
223. Ishiyama, T.; Momota, S.; Miyaura, N. *Synlett* **1999**, 1790.
224. Lawson, Y. G.; Lesley, M. J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R. *Chem. Commun.* **1997**, 2051.
225. Ali, H. A.; Goldberg, I.; Srebnik, M. *Organometallics* **2001**, *20*, 3962.
226. Kabalka, G. W.; Das, B. C.; Das, S. *Tetrahedron Lett.* **2002**, *43*, 2323.
227. Ito, H.; Yamanaka, H.; Tateiwa, J.-I.; Hosomi, A. *Tetrahedron Lett.* **2000**, *41*, 6821.
228. Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2001**, *625*, 47.
229. Takahashi, K.; Ishiyama, T.; Miyaura, N. *Chem. Lett.* **2000**, 982.
230. Kabalka, G. W.; Das, B. C.; Das, S. *Tetrahedron Lett.* **2001**, *42*, 7145.
231. Canesi, S.; Bouchu, D.; Ciufolin, M. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 4336.
232. Coapes, R. B.; Souza, F. E. S.; Thomas, R. L.; Hall, J. J.; Marder, T. B. *Chem. Commun.* **2003**, 614.
233. Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1996**, 2073.
234. Morgan, J. B.; Morken, J. P. *Org. Lett.* **2003**, *5*, 2573.
235. Clegg, W.; Johann, T. R. F.; Marder, T. B.; Norman, N. C.; Orpen, A. G.; Peakman, T. M.; Quayle, M. J.; Rice, C. R.; Scott, A. J. *J. Chem. Soc., Dalton Trans.* **1998**, 1431.
236. Ballard, C. E.; Morken, J. P. *Synthesis* **2004**, 1321.
237. Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357.
238. Yang, F. Y.; Cheng, C. H. *J. Am. Chem. Soc.* **2001**, *123*, 761.
239. Yang, F. Y.; Wu, M. Y.; Cheng, C. H. *J. Am. Chem. Soc.* **2000**, *122*, 7122.
240. Yang, F. Y.; Shanmugasundaram, M.; Chuang, S. Y.; Ku, P. J.; Wu, M. Y.; Cheng, C. H. *J. Am. Chem. Soc.* **2003**, *125*, 12576.
241. Carter, C. A. G.; Vogels, C. M.; Harrison, D. J.; Gagnon, M. K. J.; Norman, D. W.; Langler, R. F.; Baker, R. T.; Westcott, S. A. *Organometallics* **2001**, *20*, 2130.
242. Cameron, T. M.; Baker, R. T.; Westcott, S. A. *Chem. Commun.* **1998**, 2395.
243. Mann, G.; John, K. D.; Baker, R. T. *Org. Lett.* **2000**, *2*, 2105.
244. Suginome, M.; Nakamura, H.; Ito, Y. *Chem. Commun.* **1996**, 2777.
245. Onozawa, S.-Y.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1997**, 1229.
246. Suginome, M.; Matsuda, T.; Nakamura, H.; Ito, Y. *Tetrahedron* **1999**, *55*, 8787.
247. Suginome, M.; Nakamua, H.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2516.
248. Sagawa, T.; Asano, Y.; Ozawa, F. *Organometallics* **2002**, *21*, 5879.
249. Suginome, M.; Matsuda, T.; Ito, Y. *Organometallics* **1998**, *17*, 5233.

250. Suginome, M.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **2000**, *122*, 11015.
251. Suginome, M.; Matsuda, T.; Yoshimoto, T.; Ito, Y. *Organometallics* **2002**, *21*, 1537.
252. Suginome, M.; Nakamura, H.; Matsuda, T.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4248.
253. Suginome, M.; Matsuda, T.; Yoshimoto, T.; Ito, Y. *Org. Lett.* **1999**, *1*, 1567.
254. Suginome, M.; Ohmori, Y.; Ito, Y. *J. Organomet. Chem.* **2000**, *611*, 403.
255. Suginome, M.; Ito, Y. *J. Organomet. Chem.* **2003**, *680*, 43.
256. Onozawa, S.-Y.; Hatanaka, Y.; Tanaka, M. *Chem. Commun.* **1999**, 1863.
257. Suginome, M.; Ohmori, Y.; Ito, Y. *J. Am. Chem. Soc.* **2001**, *123*, 4601.
258. Suginome, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 11174.
259. Onozawa, S.-Y.; Hatanaka, Y.; Sakakura, T.; Shimada, S.; Tanaka, M. *Organometallics* **1996**, *15*, 5450.
260. Onozawa, S.-Y.; Hatanaka, Y.; Choi, N.; Tanaka, M. *Organometallics* **1997**, *16*, 5389.
261. Murakami, M.; Ashida, S.; Matsuda, T. *J. Am. Chem. Soc.* **2004**, *126*, 10838.
262. Onozawa, S.-Y.; Hatanaka, Y.; Tanaka, M. *Tetrahedron Lett.* **1998**, *39*, 9043.
263. Ishiyama, T.; Nishijima, K. i.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 7219.
264. Suginome, M.; Yamamoto, A.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 6358.
265. Onozawa, S.-Y.; Tanaka, M. *Organometallics* **2001**, *20*, 2956.
266. Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392.
267. Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11.
268. Miyaura, N. In *Metal-catalyzed Cross-coupling reactions*, 2nd ed.; Meijere, A., Diederich, F., Eds.; Wiley-VCH, 2004; Vol. 1, pp 41–124.
269. Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508.
270. Ishiyama, T.; Itoh, Y.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1997**, *38*, 3447.
271. Ishiyama, T.; Ishida, K.; Miyaura, N. *Tetrahedron* **2001**, *57*, 9813.
272. Han, J. W.; Castro, J. C.; Burgess, K. *Tetrahedron Lett.* **2003**, *44*, 9359.
273. Appukkuttan, P.; Van der Eycken, E.; Dehaen, W. *Synlett* **2003**, 1204.
274. Willis, D. M.; Strongin, R. M. *Tetrahedron Lett.* **2000**, *41*, 8683.
275. Ma, Y.; Song, C.; Jiang, W.; Xue, G.; Cannon, J. F.; Wang, X.; Andrus, M. B. *Org. Lett.* **2003**, *5*, 4635.
276. Furstner, A.; Seidel, G. *Org. Lett.* **2002**, *4*, 541.
277. Zaidlewicz, M.; Wolan, A. *J. Organomet. Chem.* **2002**, *657*, 129.
278. Becht, J. M.; Meyer, O.; Helmchen, G. *Synthesis* **2003**, 2805.
279. Malan, C.; Morin, C. *J. Org. Chem.* **1998**, *63*, 8019.
280. Aspley, C. J.; Williams, J. A. G. *New J. Chem.* **2001**, *25*, 1136.
281. Nakamura, H. Fujiwara, M.; Yamamoto, Y. *J. Org. Chem.* **1998**, *63*, 7529.
282. Abbott, B.; Thompson, P. *Aust. J. Chem.* **2003**, *56*, 1099.
283. Zembower, D. E.; Zhang, H. *J. Org. Chem.* **1998**, *63*, 9300.
284. Nicolaou, K. C.; Snyder, S. A.; Giuseppone, N.; Huang, X.; Bella, M.; Reddy, M. V.; Rao, P. B.; Koumbis, A. E.; Giannakakou, P.; O'Brate, A. *J. Am. Chem. Soc.* **2004**, *126*, 10174.
285. Obst, U.; Betschman, P.; Lerner, C.; Seiler, P.; Diederich, F.; Gramlich, V.; Weber, L.; Banner, D. W.; Schönholzer, P. *Helv. Chim. Acta* **2000**, *83*, 855.
286. Firooznia, F.; Gude, C.; Chan, K.; Marcopulos, N.; Satoh, Y. *Tetrahedron Lett.* **1999**, *40*, 213.
287. Elder, A. M.; Rich, D. H. *Org. Lett.* **1999**, *1*, 1443.
288. Lin, S.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1967.
289. Decicco, C. P.; Song, Y.; Evans, D. A. *Org. Lett.* **2001**, *3*, 1029.
290. Lin, S.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 512.
291. Kaiser, M.; Groll, M.; Renner, C.; Huber, R.; Moroder, L. *Angew. Chem., Int. Ed.* **2002**, *41*, 780.
292. Albrecht, B. K.; Williams, R. M. *Org. Lett.* **2003**, *5*, 197.
293. Inoue, M.; Sakazaki, H.; Furuyama, H.; Hirama, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 2654.
294. Hutton, C. A.; Skaff, O. *Tetrahedron Lett.* **2003**, *44*, 4895.
295. Hitotsuyanagi, Y.; Ishikawa, H.; Naito, S.; Takeya, K. *Tetrahedron Lett.* **2003**, *44*, 5901.
296. Hunter, L.; Hutton, C. A. *Aust. J. Chem.* **2003**, *56*, 1095.
297. Read, M. W.; Escobedo, J. O.; Willis, D. M.; Beck, P. A.; Strongin, R. M. *Org. Lett.* **2000**, *2*, 3201.
298. Deng, Y.; Chang, C. K.; Nocera, D. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 1066.
299. Yu, H. B.; Hu, Q. S.; Pu, L. *J. Am. Chem. Soc.* **2000**, *122*, 6500.
300. Piettre, S. R.; Baltzer, S. *Tetrahedron Lett.* **1997**, *38*, 1197.
301. Kim, T. H.; Hangauer, D. G. *Bull. Kor. Chem. Soc.* **2000**, *21*, 753.
302. Takahashi, K.; Takagi, J.; Ishiyama, T.; Miyaura, N. *Chem. Lett.* **2000**, 126.
303. Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001.
304. Takagi, J.; Kamon, A.; Ishiyama, T.; Miyaura, N. *Synlett* **2002**, 1880.
305. Ishiyama, T.; Takagi, J.; Kamon, A.; Miyaura, N. *J. Organomet. Chem.* **2003**, *687*, 284.
306. Ferrali, A.; Guarna, A.; Lo Galbo, F.; Occhiato, E. G. *Tetrahedron Lett.* **2004**, *45*, 5271.
307. Eastwood, P. R. *Tetrahedron Lett.* **2000**, *41*, 3705.
308. Kabalka, G. W.; Akula, M. R.; Zhang, J. *Nucl. Med. Biol.* **2003**, *30*, 369.
309. Ishiyama, T.; Ahiko, T.-A.; Miyaura, N. *Tetrahedron Lett.* **1996**, *37*, 6889.
310. Ahiko, T.-A.; Ishiyama, T.; Miyaura, N. *Chem. Lett.* **1997**, 811.
311. Sebelius, S.; Wallner, O. A.; Szabó, K. J. *Org. Lett.* **2003**, *5*, 3065.
312. Kabalka, G. W.; Venkataiah, B.; Dong, G. *J. Org. Chem.* **2004**, *69*, 5807.
313. Ishiyama, T. unpublished observations.
314. Ishiyama, T.; Oohashi, Z.; Ahiko, T.-A.; Miyaura, N. *Chem. Lett.* **2002**, 780.
315. Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **2000**, *65*, 164.
316. Broutin, P. E.; Cerna, I.; Campaniello, M.; Leroux, F.; Colobert, F. *Org. Lett.* **2004**, *6*, 4419.
317. Baudoin, O.; Guénard, D.; Guéritte, F. *J. Org. Chem.* **2000**, *65*, 9268.

318. Ferreira, I. C. F. R.; Queiroz, M. J. P. R.; Kirsch, G. *Tetrahedron Lett.* **2003**, *44*, 4327.
319. Abreu, A. S.; Silva, N. O.; Ferreira, P. M. T.; Queiroz, M. J. R. P. *Tetrahedron Lett.* **2003**, *44*, 6007.
320. Christophersen, C.; Begtrup, M.; Ebdrup, S.; Petersen, H.; Vedsø, P. *J. Org. Chem.* **2003**, *68*, 9513.
321. Song, Y. L.; Morin, C. *Synlett* **2001**, 266.
322. Euzenat, L.; Horhant, D.; Ribourdouille, Y.; Duriez, C.; Alcaraz, G.; Vaultier, M. *Chem. Commun.* **2003**, 2280.
323. Penhoat, M.; Levacher, V.; Dupas, G. *J. Org. Chem.* **2003**, *68*, 9517.
324. Baudoin, O.; Décor, A.; Cesario, M.; Guéritte, F. *Synlett* **2003**, 2009.
325. Krämer, C. S.; Zimmermann, T. J.; Sailer, M.; Müller, T. J. J. *Synthesis* **2002**, 1163.
326. Nakamura, H.; Fujiwara, M.; Yamamoto, Y. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 231.
327. Yamane, O.; Sugiura, K.-I.; Miyasaka, H.; Nakamura, K.; Fujimoto, T.; Nakamura, K.; Kaneda, T.; Sakata, Y.; Yamashita, M. *Chem. Lett.* **2004**, *33*, 40.
328. Iovine, P. M.; Kellett, M. A.; Redmore, N. P.; Therien, M. J. *J. Am. Chem. Soc.* **2000**, *122*, 8717.
329. Baudoin, O.; Cesario, M.; Guénard, D.; Guéritte, F. *J. Org. Chem.* **2002**, *67*, 1199.
330. Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *Synthesis* **2000**, 778.
331. Murata, M.; Watanabe, S.; Masuda, Y. *Tetrahedron Lett.* **2000**, *41*, 5877.
332. Murata, M.; Watanabe, S.; Masuda, Y. *J. Chem. Res.-S* **2002**, 142.
333. Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *Synth. Commun.* **2002**, *32*, 2513.
334. Ramachandran, P. V.; Pratihar, D.; Biswas, D.; Srivastava, A.; Reddy, M. V. R. *Org. Lett.* **2004**, *6*, 481.
335. Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2003**, *680*, 3.
336. Chen, H. Y.; Hartwig, J. F. *Angew Chem., Int. Ed.* **1999**, *38*, 3391.
337. Wan, X. H.; Wang, X. J.; Luo, Y.; Takami, S.; Kubo, M.; Miyamoto, A. *Organometallics* **2002**, *21*, 3703.
338. Chen, H. Y.; Schlecht, S.; Semple, T. C.; Hartwig, J. F. *Science* **2000**, *287*, 1995–1997.
339. Lawrence, J. D.; Takahashi, M.; Bae, C.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 15334.
340. Kondo, Y.; Carcfa-Cuadrado, D.; Hartwig, J. F.; Boaen, N. K.; Wanger, N. L.; Hillmyer, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 1164.
341. Iverson, C. N.; Smith, M. R., III. *J. Am. Chem. Soc.* **1999**, *121*, 7696–7697.
342. Cho, J.-Y.; Iverson, C. N.; Smith, M. R., III. *J. Am. Chem. Soc.* **2000**, *122*, 12868.
343. Tse, M. K.; Cho, J.-Y.; Smith, M. R., III. *Org. Lett.* **2001**, *3*, 2831.
344. Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr.; Smith, M. R., III. *Science* **2002**, *295*, 305.
345. Shimada, S.; Batsanov, A. S.; Howard, K. J. A.; Marder, T. B. *Angew Chem., Int. Ed.* **2001**, *40*, 2168.
346. Maleczka, R. E.; Shi, F.; Holmes, D.; Smith, M. R. *J. Am. Chem. Soc.* **2003**, *125*, 7792.
347. Ishiyama, T.; Takagi, J.; Ishida, K.; Miyaura, N.; Anastasi, N. R.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 390.
348. Takagi, J.; Sato, K.; Hartwig, J. F.; Ishiyama, T.; Miyaura, N. *Tetrahedron Lett.* **2002**, *43*, 5649.
349. Tagata, T.; Nishida, M. *Adv. Synth. Catal.* **2004**, *346*, 1655.
350. Ishiyama, T.; Nobuta, Y.; Hartwig, J. F.; Miyaura, N. *Chem. Commun.* **2003**, 2924.
351. Mertins, K.; Zapf, A.; Beller, M. *J. Mol. Cat.* **2004**, *207*, 21.
352. Ishiyama, T.; Takagi, J.; Hartwig, J. F.; Miyaura, N. *Angew Chem., Int. Ed.* **2002**, *41*, 3056.
353. Ishiyama, T.; Takagi, J.; Yonekawa, Y.; Hartwig, J. F.; Miyaura, N. *Adv. Synth. Catal.* **2003**, *345*, 1103–1106.
354. Tamura, H.; Yamazaki, H.; Sato, H.; Sakaki, S. *J. Am. Chem. Soc.* **2003**, *125*, 16114.
355. Han, W.; Lin, Z. *Organometallics* **2003**, *22*, 473.
356. Kurotobi, K.; Miyauchi, M.; Takakura, K.; Murafuji, T.; Sugihara, Y. *Eur. J. Org. Chem.* **2003**, 3663.
357. Datta, A.; Kollhofer, A.; Plenio, H. *Chem. Commun.* **2004**, 1508.
358. Coventry, D. N.; Batsanov, A. S.; Goeta, A. E.; Howard, J. A. K.; Marder, T. B.; Perutz, R. N. *Chem. Commun.* **2005**, 2172.
359. Hata, H.; Shinokubo, H.; Osuka, A. *J. Am. Chem. Soc.* **2005**, *127*, 8264.
360. Ishiyama, T.; Ishida, K.; Takagi, J.; Miyaura, N. *Chem. Lett.* **2001**, 1082.
361. Matteson, D. S.; Man, H. W. *J. Org. Chem.* **1994**, *59*, 5734.
362. Shoup, T. M.; Zweifel, G. *Synth. Commun.* **1993**, *23*, 2937.
363. Bhat, N. G.; Martinez, C.; De Los Santos, J. *Tetrahedron Lett.* **2000**, *41*, 6541.
364. Chen, Y. K.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 3702.
365. Soundararajan, R.; Li, G.; Brown, H. C. *Tetrahedron Lett.* **1994**, *35*, 8957.
366. Chen, A.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704.
367. Ren, L.; Crudden, C. M. *Chem. Commun.* **2000**, 721.
368. Singh, R. P.; Twamley, B.; Fabry-Asztalos, L.; Mattesn, D. S.; Shreeve, J. M. *J. Org. Chem.* **2000**, *65*, 8123.
369. Tripathy, P. B.; Matteson, D. S. *Synthesis* **1990**, 200.
370. Matteson, D. S.; Man, H. W. *J. Org. Chem.* **1996**, *61*, 6047.
371. Matteson, D. S.; Singh, R. P.; Lu, J.; Yang, J.; Pharazyn, P. S. *Polyhedron* **2000**, *19*, 587.
372. Matteson, D. S.; Singh, R. P.; Sutton, C. H.; Verheyden, J. D.; Lu, J. *Heteroat. Chem.* **1997**, *8*, 487.
373. Singh, R. P.; Matteson, D. S. *J. Org. Chem.* **2000**, *65*, 6650.
374. Matteson, D. S. *Pure Appl. Chem.* **2003**, *75*, 1249.
375. Tian, Z. Q.; Brown, B. B.; Mack, D. P.; Hutton, C. A.; Bartlett, P. A. *J. Org. Chem.* **1997**, *62*, 514.
376. Goddard, J. P.; Le Gall, T.; Mioskowski, C. *Org. Lett.* **2000**, *2*, 1455.
377. Vasella, A.; Wenger, W.; Rajamannar, T. *Chem. Commun.* **1999**, 2215.
378. Shea, K. J.; Walker, J. W.; Zhu, H.; Paz, M.; Greaves, J. *J. Am. Chem. Soc.* **1997**, *119*, 9049.
379. Shea, K. J.; Staiger, C. L.; Lee, S. Y. *Macromolecules* **1999**, *32*, 3157.
380. Wagner, C. E.; Shea, K. J. *Org. Lett.* **2001**, *3*, 3063.
381. Kabalka, G. W.; Maddox, J. T.; Bogas, E.; Kelley, S. W. *J. Org. Chem.* **1997**, *62*, 3688.
382. Ochiai, M.; Tuchimoto, Y.; Higashiura, N. *Org. Lett.* **2004**, *6*, 1505.
383. O'Donnell, M. J.; Delgado, F.; Drew, M. D.; Pottorf, R. S.; Zhou, C.; Scott, W. L. *Tetrahedron Lett.* **1999**, *40*, 5831.
384. O'Donnell, M. J.; Drew, M. D.; Cooper, J. T.; Delgado, F.; Zhou, C. *J. Am. Chem. Soc.* **2002**, *124*, 9348.
385. O'Donnell, M. J.; Cooper, J. T.; Mader, M. M. *J. Am. Chem. Soc.* **2003**, *125*, 2370.
386. Carmès, L.; Carreaux, F.; Carboni, B. *J. Org. Chem.* **2000**, *65*, 5403.
387. Brown, H. C.; Mahindroo, V. K. *Tetrahedron: Asymmetry* **1993**, *4*, 59.

388. Suginome, M.; Fukuda, T.; Nakamura, H.; Ito, Y. *Organometallics* **2000**, *19*, 719.
389. Suginome, M.; Fukuda, T.; Ito, Y. *J. Organomet. Chem.* **2002**, *643–644*, 508.
390. Hata, T.; Kitagawa, H.; Masai, H.; Kurahashi, T.; Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 790.
391. Shimizu, M.; Kurahashi, T.; Hiyama, T. *Synlett* **2001**, *SI*, 1006.
392. Kurahashi, T.; Hata, T.; Masai, H.; Kitagawa, H.; Shimizu, M.; Hiyama, T. *Tetrahedron* **2002**, *58*, 6381.
393. Shimizu, M.; Kurahashi, T.; Hiyama, T. *J. Synth. Org. Chem. Jpn.* **2001**, *59*, 1062.
394. Shimizu, M.; Kitagawa, H.; Kurahashi, T.; Hiyama, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 4283.
395. Shimizu, M.; Kurahashi, T.; Kitagawa, H.; Hiyama, T. *Org. Lett.* **2003**, *5*, 225.
396. Liu, X.; Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 879.
397. Hollis, W. G., Jr.; Lappenbusch, W. C.; Everberg, K. A.; Woleben, C. M. *Tetrahedron Lett.* **1993**, *34*, 7517.
398. Singleton, D. A. *J. Am. Chem. Soc.* **1992**, *114*, 6563.
399. Noiret, N.; Youssofi, A.; Carboni, B.; Vaultier, M. *J. Chem. Soc., Chem. Commun.* **1992**, 1105.
400. Jego, J. M.; Carboni, B.; Youssofi, A.; Vaultier, M. *Synlett* **1993**, 595.
401. Singleton, D. A.; Redman, A. M. *Tetrahedron Lett.* **1994**, *35*, 509.
402. Rasset-Deloge, C.; Vaultier, M. *Bull. Soc. Chim. Fr.* **1994**, *131*, 919.
403. Yamamoto, I.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 3327.
404. Singleton, D. A.; Leung, S. W.; Martinez, J. P.; Lee, Y. K. *Tetrahedron Lett.* **1997**, *38*, 3163.
405. Kamabuchi, A.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1993**, *34*, 4827.
406. Renaud, J.; Graf, C. D.; Oberer, L. *Angew. Chem., Int. Ed.* **2000**, *39*, 3101.
407. Garnier, L.; Plunian, B.; Mortier, J.; Vaultier, M. *Tetrahedron Lett.* **1996**, *37*, 6699.
408. Renald, P. Y.; Six, Y.; Lallemand, J. Y. *Tetrahedron Lett.* **1997**, *38*, 6589.
409. Gao, X.; Hall, D. G. *Tetrahedron Lett.* **2003**, *44*, 2231.
410. Lallemand, J. Y.; Six, Y.; Ricard, L. *Eur. J. Org. Chem.* **2002**, 503.
411. Tailor, J.; Hall, D. G. *Org. Lett.* **2000**, *2*, 3715.
412. Touré, B. B.; Hoveyda, H. R.; Tailor, J.; Ulaczyk-Lesanko, A.; Hall, D. G. *Chem. Eur. J.* **2003**, *9*, 466.
413. Touré, B. B.; Hall, D. G. *Angew. Chem.* **2004**, *116*, 2035.
414. Deligny, M.; Carreaux, F.; Toupet, L.; Carboni, B. *Adv. Synth. Catal.* **2003**, *345*, 1215.
415. Deligny, M.; Carreaux, F.; Carboni, B.; Toupet, L.; Dujardin, G. *Chem. Commun.* **2003**, 276.
416. Narasaka, K.; Shimada, S.; Osoda, K.; Iwasawa, N. *Synthesis* **1991**, 1171.
417. Kennedy, J. W. J.; Hall, D. G. *Synlett* **2002**, 477.
418. Batey, R. A.; Thadani, A. N.; Lough, A. J. *Chem. Commun.* **1999**, 475.
419. Batey, R. A.; Thadani, A. N.; Lough, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 450.
420. Singleton, D. A.; Lee, Y. K. *Tetrahedron Lett.* **1995**, *36*, 3473.
421. Lorvelec, G.; Vaultier, M. *Tetrahedron Lett.* **1998**, *39*, 5185.
422. Batey, R. A.; Lin, D.; Wong, A.; Hayhoe, C. L. S. *Tetrahedron Lett.* **1997**, *38*, 3699.
423. Wallace, R. H.; Zong, K. K. *Tetrahedron Lett.* **1992**, *33*, 6941.
424. Wallace, R. H.; Liu, J. *Tetrahedron Lett.* **1994**, *35*, 7493.
425. Jazouli, M.; Baba, S.; Carboni, B.; Carrié, R.; Soufiaoui, M. *J. Organomet. Chem.* **1995**, *498*, 229.
426. Davies, C. D.; Marsden, S. P.; Stokes, E. S. E. *Tetrahedron Lett.* **2000**, *41*, 4229.
427. Moore, J. E.; Goodenough, K. M.; Spinks, D.; Harrity, J. P. A. *Synlett* **2002**, 2071.
428. Davies, M. W.; Wybrow, R. A. J.; Johnson, C. N.; Harrity, J. P. A. *Chem. Commun.* **2001**, 1558.
429. Carboni, B.; Ollivault, M.; Le Bouguenec, F.; Carrié, R.; Jazouli, M. *Tetrahedron Lett.* **1997**, *38*, 6665.
430. Belfaitah, A.; Isly, M.; Carboni, B. *Tetrahedron Lett.* **2004**, *45*, 1969.
431. Hilt, G.; Smolko, K. I. *Angew. Chem., Int. Ed.* **2003**, *42*, 2795.
432. Gandon, V.; Leca, D.; Aechtner, T.; Vollhardt, K. P. C.; Malacria, M.; Aubert, C. *Org. Lett.* **2004**, *6*, 3405.
433. Yamamoto, Y.; Ishii, J.-I.; Nishiyama, H.; Itoh, K. *J. Am. Chem. Soc.* **2004**, *126*, 3712.
434. Ester, C.; Maderna, A.; Pritzkow, H.; Siebert, W. *Eur. J. Inorg. Chem.* **2000**, 1177.
435. Gu, Y.; Pritzkow, H.; Siebert, W. *Eur. J. Inorg. Chem.* **2001**, 373.
436. Markó, I. E.; Kumamoto, T.; Giard, T. *Adv. Synth. Catal.* **2002**, *344*, 1063.
437. Markó, I. E.; Giard, T.; Sumida, S.; Gies, A. E. *Tetrahedron Lett.* **2002**, *43*, 2317.
438. Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **1999**, *64*, 8287.
439. Pietruszka, J.; Witt, A. *Synlett* **2003**, 91.
440. Luithle, J. E. A.; Pietruszka, J. *J. Org. Chem.* **2000**, *65*, 9194.
441. Zhou, S. M.; Deng, M. Z.; Xia, L. J.; Tang, M. H. *Angew. Chem.* **1998**, *110*, 3061.
442. Luithle, J. E. A.; Pietruszka, J. *Eur. J. Org. Chem.* **2000**, 2557.
443. Pietruszka, J.; Witt, A. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 4293.
444. Pietruszka, J.; Witt, A.; Frey, W. *Eur. J. Org. Chem.* **2003**, 3219.
445. Luithle, J. E. A.; Pietruszka, J.; Witt, A. *Chem. Commun.* **1998**, 2651.
446. Hupe, E.; Marek, I.; Knochel, P. *Org. Lett.* **2002**, *4*, 2861.
447. Kelly, T. A.; Fuchs, V. U.; Perry, C. W.; Snow, R. J. *Tetrahedron* **1993**, *49*, 1009.
448. Molander, G. A.; Ribagorda, M. *J. Am. Chem. Soc.* **2003**, *125*, 11148.
449. Falck, J. R.; Bondlela, M.; Venkataraman, S. K.; Srinivas, D. *J. Org. Chem.* **2001**, *66*, 7148.
450. Zheng, B.; Srebnik, M. *Tetrahedron Lett.* **1994**, *35*, 6247.
451. Zheng, B.; Srebnik, M. *Tetrahedron Lett.* **1994**, *35*, 1145.
452. Cooke, M. P., Jr. *J. Org. Chem.* **1994**, *59*, 2930.
453. Nakamura, M.; Hatakeyama, T.; Hara, K.; Fukudome, H.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 14344.
454. Nakamura, M.; Hara, K.; Hatakeyama, T.; Nakamura, E. *Org. Lett.* **2001**, *3*, 3137.
455. Lhermitte, F.; Carboni, B. *Synlett* **1996**, 377.
456. Batey, R. A.; Smil, D. V. *Angew. Chem., Int. Ed.* **1999**, *38*, 1798.
457. Guennouni, N.; Lhermitte, F.; Cochard, S.; Carboni, B. *Tetrahedron* **1995**, *51*, 6999.

458. Guennouni, N.; Rasset-Deloge, C.; Carboni, B.; Vaultier, M. *Synlett* **1992**, 581.
459. Morrill, C.; Grubbs, R. H. *J. Org. Chem.* **2003**, *68*, 6031.
460. Chatterjee, A. K.; Grubbs, R. H. *Angew. Chem.* **2002**, *114*, 3304.
461. Njardarson, J. T.; Biswas, K.; Danishefsky, S. J. *Chem. Commun.* **2002**, 2759.
462. Renaud, J.; Ouellet, S. G. *J. Am. Chem. Soc.* **1998**, *120*, 7995.
463. Micalizio, G. C.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 3272.
464. Micalizio, G. C.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2002**, *41*, 152.
465. Davies, M. W.; Johnson, C. N.; Harrity, J. P. A. *J. Org. Chem.* **2001**, *66*, 3525.
466. Knochel, P. *J. Am. Chem. Soc.* **1990**, *112*, 7431.
467. Watanabe, T.; Sakai, M.; Miyaura, N.; Suzuki, A. *Chem. Commun.* **1994**, 467.
468. Kanai, G.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1993**, 845.
469. Schummer, D.; Höfle, G. *Tetrahedron* **1995**, *51*, 11219.
470. Takai, K.; Shinomiya, N.; Kaihara, H.; Yoshida, N.; Moriwake, T.; Utimoto, K. *Synlett* **1995**, 963.
471. Matsubara, S.; Otake, Y.; Hashimoto, Y.; Utimoto, K. *Chem. Lett.* **1999**, 747.
472. Raheem, I. T.; Goodman, S. N.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 706.
473. Jagannathan, S.; Forsyth, T. P.; Kettner, C. A. *J. Org. Chem.* **2001**, *66*, 6375.
474. Holland, R.; Spencer, J.; Deadman, J. J. *Synthesis* **2002**, 2379.
475. Hetcouet, A.; Neu, A.; Peyronel, J. F.; Carboni, B. *Synlett* **2002**, 829.
476. Feng, Z.; Hellberg, M. *Tetrahedron Lett.* **2000**, *40*, 5813.
477. Jehanno, E.; Vaultier, M. *Tetrahedron Lett.* **1995**, *36*, 4439.
478. Malan, C.; Morin, C. *Synlett* **1996**, 167.
479. Moriya, T.; Miyaura, N.; Suzuki, A. *Chem. Lett.* **1993**, 1429.
480. McKierman, G. J.; Hartley, R. C. *Org. Lett.* **2003**, *5*, 4389.
481. Brown, H. C. *Organic Syntheses via Boranes*; Wiley: New York, 1975; p 81.
482. Brown, H. C.; Zaidlewicz, M. *Organic Syntheses via Boranes*; Aldrich Chemical Co.: Milwaukee, **2001**; Vol. 2, p 115.
483. Köster, R. *Methoden der Organischen Chemie* **1982**, *13/3c*, 229.
484. Brown, H. C.; Murray, K. J. *Tetrahedron* **1986**, *42*, 5497.
485. Smith, K.; Pelter, A. In *Comprehensive Organic Synthesis*; Fleming, I., Ed.; Pergamon: Oxford, 1991; Vol. 8, p 724.
486. Olah, G. A.; Westerman, P. W.; Mo, Y. K.; Klopman, G. *J. Am. Chem. Soc.* **1972**, *94*, 7859.
487. Köster, R.; Bellut, H.; Fenzl, W. *Liebigs Ann. Chem.* **1974**, 54.
488. Frohn, H.-J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *Z. Anorg. Allg. Chem.* **2002**, *628*, 2834.
489. Zaidlewicz, M.; Panda, C. S. *Synthesis* **1987**, 645.
490. Zaidlewicz, M.; Gimiñska, M. *Tetrahedron: Asymmetry* **1997**, *8*, 3847.
491. Caro, B.; Sénéchal-Tocquer, M.-C.; Sénéchal, D; Guen, F. R.-L. *J. Organomet. Chem.* **1996**, *525*, 283.
492. Brown, H. C.; Keblys, K. A. *J. Am. Chem. Soc.* **1964**, *86*, 1791.
493. Ripin, D. H. B; Cai, W.; Brenek, S. J. *Tetrahedron Lett.* **2000**, *41*, 5817.
494. Pearson, A. J. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: New York, 1995; Vol. 7, p 5197.
495. Kabalka, G. W.; Hedgecock, H. C., Jr. *J. Org. Chem.* **1975**, *40*, 1776.
496. Köster, R.; Morita, Y. *Justus Liebigs Ann. Chem.* **1967**, *704*, 70.
497. Köster, R.; Arora, S.; Binger, P. *Angew. Chem., Int. Ed.* **1969**, *8*, 205.
498. Soderquist, J. A.; Najafi, M. R. *J. Org. Chem.* **1986**, *51*, 1330.
499. Masamune, S.; Lu, L. D.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982**, *104*, 5523.
500. Pelter, A.; Rowlands, M. *Tetrahedron Lett.* **1987**, *28*, 1203.
501. Brown, H. C. U.S. Patent 3439046, 1969.
502. Brown, H. C.; Midland, M. M. *Tetrahedron* **1986**, *42*, 5523.
503. Klement, I.; Knochel, P. *Synlett* **1996**, 1004.
504. Pappo, R. *J. Am. Chem. Soc.* **1959**, *81*, 1010.
505. Brown, H. C.; Grag, C. P. *J. Am. Chem. Soc.* **1961**, *83*, 2951.
506. Ware, J. C.; Traylor, T. G. *J. Am. Chem. Soc.* **1963**, *85*, 3026.
507. Brown, H. C.; Rao, C.; Kulkarni, S. *J. Organomet. Chem.* **1979**, *172*, C20.
508. Yates, M. H. *Tetrahedron Lett.* **1997**, *38*, 2813.
509. Brown, H. C.; Kulkarni, S. V.; Racherla, U. S. *J. Org. Chem.* **1994**, *59*, 365.
510. Jigajinni, V. B.; Pelter, A.; Smith, K. *Tetrahedron Lett.* **1978**, *19*, 181.
511. Genêt, J.-P.; Hajicek, J.; Bischoff, L.; Greck, C. *Tetrahedron Lett.* **1992**, *33*, 2677.
512. Wachter-Jurcsak, N.; Scully, F. E., Jr. *Tetrahedron Lett.* **1990**, *31*, 5261.
513. Yang, R.-Y.; Dai, L.-K. *Synthesis* **1993**, 481.
514. Kabalka, G. W.; Henderson, D. A.; Varma, R. S. *Organometallics* **1987**, *6*, 1369.
515. Kabalka, G. W.; Goudgaon, N. M.; Liang, Y. *Synth. Commun.* **1988**, *18*, 1363.
516. Brown, H. C.; Malhotra, S. V.; Ramachandran, P. V. *Tetrahedron: Asymmetry* **1996**, *7*, 3527.
517. Fernandez, E.; Hooper, M. W.; Knight, F. I.; Brown, J. M. *Chem. Commun.* **1997**, 173.
518. Fernandez, E.; Maeda, K.; Hooper, M. W.; Brown, J. M. *Chem. Eur. J.* **2000**, *6*, 1840.
519. Kabalka, G. W.; Wang, Z. *Synth. Commun.* **1990**, *20*, 231.
520. Kabalka, G. W.; Wang, Z. *Organometallics* **1989**, *8*, 1093.
521. Phanstiel, O., IV; Wang, Q. X.; Powell, D. H.; Ospina, M. P.; Leeson, B. A. *J. Org. Chem.* **1999**, *64*, 803.
522. Bartlett, P. D.; Funahashi, T. *J. Am. Chem. Soc.* **1962**; *84*, 2596.
523. Davies, A. G; Hook, S. C. W.; Roberts, B. P. *J. Organomet. Chem.* **1970**, *23*, C11.
524. Brown, H. C.; Midland, M. M.; Levy, A. B.; Suzuki, A.; Sono, S.; Itoh, M. *Tetrahedron* **1987**, *43*, 4079.
525. Brown, H. C.; Salunkhe, A. M. *Tetrahedron Lett.* **1993**, *34*, 1265.
526. Carboni, B.; Benalil, A.; Vaultier, M. *J. Org. Chem.* **1993**, *58*, 3736.
527. Salmon, A.; Carboni, B. *J. Organomet. Chem.* **1998**, *567*, 31.

528. Felpin, F.-X.; Girard, S.; Vo-Thanh, G.; Robins, R. J.; Villiéras, J.; Lebreton, J. *J. Org. Chem.* **2001**, *66*, 6305.
529. Brown, H. C. *Hydroboration*; Benjamin: New York, 1962; p 604.
530. Vaultier, M.; Carboni, B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11, p 218.
531. Brown, H. C.; De Lue, N. R. *Tetrahedron* **1988**, *44*, 2785.
532. Morrill, T. C.; Lu, Q.; Brister, A.; O'Shaughnessy, B.; Belfield, K. *Synthesis* **1993**, 973.
533. Masuda, Y.; Hoshi, M.; Arase, A. *J. Chem. Soc., Perkin Trans.* **1992**, *1*, 2725.
534. Arase, A.; Masuda, Y.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2511.
535. Jigajinni, V. B.; Paget, W. E.; Smith, K. *J. Chem. Res., Synop.* **1981**, 376.
536. Nelson, D. J.; Soundararajan, R. *J. Org. Chem.* **1988**, *53*, 5664.
537. Brown, H. C.; Lane, C. F. *Tetrahedron* **1988**, *44*, 2763.
538. Brown, H. C.; Lane, C. F.; De Lue, N. R. *Tetrahedron* **1988**, *44*, 2773.
539. Brown, H. C.; Rathke, M. W.; Rogic, M. M.; De Lue, N. R. *Tetrahedron* **1988**, *44*, 2751.
540. Kabalka, G. W.; Gooch, E. E. *J. Org. Chem.* **1980**, *45*, 3578.
541. Kabalka, G. W.; Gooch, E. E. *J. Org. Chem.* **1981**, *46*, 2582.
542. Kabalka, G. W. *Acc. Chem. Res.* **1984**, *17*, 215.
543. Brown, H. C.; Subrahmanyam, C.; Hamaoka, T.; Ravindran, N.; Bowman, D. H.; Misumi, S.; Unni, M. K.; Somayaji, V.; Bhat, N. *J. Org. Chem.* **1989**, *54*, 6068.
544. Brown, H. C.; Hamaoka, T.; Ravindran, N.; Subrahmanyam, C.; Somayaji, V.; Bhat, N. G. *J. Org. Chem.* **1989**, *54*, 6075.
545. Stewart, S. K.; Whiting, A. *Tetrahedron Lett.* **1995**, *36*, 3929.
546. Kabalka, G. W.; Sastry, K. A.; Somyaji, V. *Heterocycles* **1982**, *18*, 157.
547. Paterson, I.; Perkins, M. V. *J. Am. Chem. Soc.* **1993**, *115*, 1608.
548. Masuda, Y.; Suyama, T.; Murata, M.; Watanabe, S. *J. Chem. Soc., Perkin Trans.* **1995**, *1*, 2955.
549. Petasis, N. A.; Zavialov, I. A. *Tetrahedron Lett.* **1996**, *37*, 567.
550. Abe, T.; Aso, Y.; Otsubo, T.; Ogura, F. *Chem. Lett.* **1990**, 1671.
551. Kabalka, G. W.; Venkataiah, B. *Tetrahedron Lett.* **2002**, *43*, 3703.
552. Huang, X.; Liang, C.-G. *J. Chem. Soc., Perkin Trans.* **1999**, *1*, 2625.
553. Arase, A.; Masuda, Y. *Chem. Lett.* **1976**, 785.
554. Arase, A.; Masuda, Y. *Chem. Lett.* **1976**, 1115.
555. Masuda, Y.; Murata, M.; Ikeda, M.; Watanabe, S. *J. Chem. Soc., Perkin Trans.* **1998**, *1*, 1013.
556. Ochiai, M.; Takema, T.; Chen, D.-W.; Kida, M. *Tetrahedron Lett.* **1997**, *38*, 6709.
557. Carroll, M. A.; Pike, V. W.; Widdowson, D. A. *Tetrahedron Lett.* **2000**, *41*, 5393.
558. Petasis, N. A.; Akrtopoulou, I. *Tetrahedron Lett.* **1993**, *34*, 583.
559. Petasis, N. A.; Zavialov, I. *J. Am. Chem. Soc.* **1997**, *119*, 445.
560. Petasis, N. A.; Zavialov, I. *J. Am. Chem. Soc.* **1998**, *120*, 11798.
561. Petasis, N. A.; Boral, S. *Tetrahedron Lett.* **2001**, *42*, 539.
562. Jiang, B.; Yang, C.-G.; Gu, X.-H. *Tetrahedron Lett.* **2001**, *42*, 2545.
563. Portlock, D. E.; Naskar, D.; West, L.; Li, M. *Tetrahedron Lett.* **2002**, *43*, 6845.
564. Naskar, D.; Roy, A.; Seibel, W. L.; Portlock, D. E. *Tetrahedron Lett.* **2003**, *44*, 8865.
565. Kabalka, G. W.; Venkataiah, B.; Dong, G. *Tetrahedron Lett.* **2004**, *45*, 729.
566. Wang, Q.; Finn, M. G. *Org. Lett.* **2000**, *2*, 4063.
567. Surya, G. K.; Mandal, M.; Schweizer, S.; Petasis, N. A.; Olah, G. A. *Org. Lett.* **2000**, *2*, 3173.
568. Surya, G. K.; Mandal, M.; Schweizer, S.; Petasis, N. A.; Olah, G. A. *J. Org. Chem.* **2002**, *67*, 3718.
569. Harwood, L. M.; Currie, G. S.; Drew, M. G. B.; Luke, R. W. A. *Chem. Commun.* **1996**, 1953.
570. Currie, G. S.; Drew, M. G. B.; Harwood, L. M.; Hughes, D. J.; Luke, R. W. A.; Vickers, R. J. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 2982.
571. Petasis, N. A.; Patel, Z. D. *Tetrahedron Lett.* **2000**, *41*, 9607.
572. Berrée, F.; Debache, A.; Marsac, Y.; Carboni, B. *Tetrahedron Lett.* **2001**, *42*, 3591.
573. Naskar, D.; Roy, A.; Seibel, W. L.; Portlock, D. E. *Tetrahedron Lett.* **2003**, *44*, 5819.
574. Naskar, D.; Roy, A.; Seibel, W. L. *Tetrahedron Lett.* **2003**, *44*, 8861.
575. Koolmeister, T.; Södergren, M.; Scobie, M. *Tetrahedron Lett.* **2002**, *43*, 5965.
576. Petasis, N. A.; Goodman, A.; Zavialov, I. A. *Tetrahedron* **1997**, *53*, 16463.
577. Hansen, T. K.; Schlienger, N.; Hansen, B. S.; Andersen, P. H.; Bryce, M. R. *Tetrahedron Lett.* **1999**, *40*, 3651.
578. Portlock, D. E.; Ostaszewski, R.; Naskar, D.; West, L. *Tetrahedron Lett.* **2003**, *44*, 603.
579. Davis, A. S.; Pyne, S. G.; Skelton, B. W.; White, A. H. *J. Org. Chem.* **2004**, *69*, 3139.
580. Grigg, R.; Sridharan, V.; Thayaparan, A. *Tetrahedron Lett.* **2003**, *44*, 9017.
581. Thompson, K. A.; Hall, D. G. *Chem. Commun.* **2000**, 2379.
582. Klopfenstein, S. R.; Chen, J. J.; Golebiowski, A.; Li, M.; Peng, S. X.; Shao, X. *Tetrahedron Lett.* **2000**, *41*, 4835.
583. Golebiowski, A.; Klopfenstein, S. R.; Chen, J. J.; Shao, X. *Tetrahedron Lett.* **2000**, *41*, 4841.
584. Schlienger, N.; Bryce, M. R.; Hansen, T. K. *Tetrahedron* **2000**, *56*, 10023.
585. Koolmeister, T.; Södergren, M.; Scobie, M. *Tetrahedron Lett.* **2002**, *43*, 5969.
586. McLean, N. J.; Tye, H.; Whittaker, M. *Tetrahedron Lett.* **2004**, *45*, 993.
587. Corey, E. J.; Cimprich, K. A. *J. Am. Chem. Soc.* **1994**, *116*, 3151.
588. Kim, S.; Cho, C. M.; Yoon, J.-Y. *J. Org. Chem.* **1996**, *61*, 6018.
589. Takada, E.-I.; Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1993**, *34*, 7067.
590. Hara, S.; Ishimura, S.; Suzuki, A. *Synlett* **1996**, 993.
591. Hara, S.; Shudoh, H.; Ishimura, S.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2403.
592. Hara, S.; Kato, N.; Takada, E.-I.; Suzuki, A. *Synlett* **1994**, 961.
593. Chong, J. M.; Shen, L.; Taylor, N. J. *J. Am. Chem. Soc.* **2000**, *122*, 1822.
594. Kabalka, G. W.; Wu, Z.; Trotman, S. E.; Gao, X. *Org. Lett.* **2000**, *2*, 255.
595. Kabalka, G. W.; Wu, Z.; Ju, Y. *Tetrahedron Lett.* **2001**, *42*, 6239.

596. Batey, R. A.; MacKay, D. B.; Santhakumar, V. *J. Am. Chem. Soc.* **1999**, *121*, 5075.
597. Batey, R. A.; MacKay, D. B. *Tetrahedron Lett.* **2000**, *41*, 9935.
598. Wrackmeyer, B.; Tok, O. L.; Bubnov, Y. N. *Angew. Chem., Int. Ed.* **1999**, *38*, 124.
599. Wrackmeyer, B.; Tok, O. L.; Klimkina, E.; Bubnov, Y. N. *Inorg. Chim. Acta* **2000**, *300–302*, 169.
600. Hoffmann, R. W.; Sander, T.; Hense, A. *Liebigs Ann. Chem.* **1993**, 771.
601. Hoffmann, R. W.; Sander, T. *Liebigs Ann. Chem.* **1993**, 1185.
602. Watanabe, T.; Miyaura, N.; Suzuki, A. *J. Organomet. Chem.* **1993**, *444*, C1.
603. Watanabe, T.; Sakai, M.; Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1994**, 467.
604. Yamamoto, Y.; Miyairi, T.; Ohmura, T.; Miyaura, N. *J. Org. Chem.* **1999**, *64*, 296.
605. Yamamoto, Y.; Kurihara, K.; Yamada, A.; Takahashi, M.; Takahashi, Y.; Miyaura, N. *Tetrahedron Lett.* **2003**, *59*, 537.
606. Hoffmann, R. W.; Krüger, J.; Brückner, D. *New J. Chem.* **2001**, *25*, 102.
607. Hoffmann, R. W.; Bruckner, D.; Gerusz, V. J. *Heterocycles* **2000**, *52*, 121.
608. Yamamoto, Y.; Hara, S.; Suzuki, A. *Synlett* **1996**, 883.
609. Hara, S.; Yamamoto, Y.; Fujita, A.; Suzuki, A. *Synlett* **1994**, 639.
610. Gaddoni, L.; Lombardo, M.; Trombini, C. *Tetrahedron Lett.* **1998**, *39*, 7571.
611. Lombardo, M.; Morganti, S.; Trombini, C. *Synlett* **2001**, 601.
612. Lombardo, M.; Morganti, S.; Tozzi, M.; Trombini, C. *Eur. J. Org. Chem.* **2002**, 2823.
613. Zaidlewicz, M.; Krzemiński, M. P. *Org. Lett.* **2000**, *2*, 3897.
614. Bubnov, Y. N.; Zhun', I. V.; Klimkina, E. V.; Ignatenko, A. V.; Starikova, Z. A. *Eur. J. Org. Chem.* **2000**, 3323.
615. Bubnov, Y. N. *Pure Appl. Chem.* **1994**, *66*, 235.
616. Pastukhov, F. V.; Yampolsky, I. V.; Bubnov, Y. N. *J. Organomet. Chem.* **2002**, *657*, 123.
617. Yamamoto, Y.; Takahashi, M.; Miyaura, N. *Synlett* **2002**, 128.
618. Goldberg, S. D.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 807.
619. Kimura, M.; Kiyama, I.; Tomizawa, T.; Horino, Y.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **1999**, *40*, 6795.
620. Hunter, R.; Michael, J. P.; Tomlinson, G. D. *Tetrahedron* **1994**, *50*, 871.
621. Thadani, A. N.; Batey, R. A. *Org. Lett.* **2002**, *4*, 3827.
622. Ishiyama, T.; Ahiko, T.-A.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 12414.
623. Kennedy, J. W.; Hall, D. G. *J. Am. Chem. Soc.* **2002**, *124*, 11586.
624. Kennedy, J. W.; Hall, D. G. *Angew. Chem., Int. Ed.* **2003**, *42*, 4732.
625. Solin, N.; Wallner, O. A.; Szabó, K. J. *Org. Lett.* **2005**, *7*, 689.
626. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.
627. Ramachandran, P. V. *Aldrichim. Acta* **2002**, *35*, 23.
628. Lachance, H.; Lu, X.; Gravel, M.; Hall, D. G. *J. Am. Chem. Soc.* **2003**, *125*, 10160.
629. Rauniyar, V.; Hall, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 4518.
630. Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910.
631. Brown, H. C.; Narla, G. *J. Org. Chem.* **1995**, *60*, 4686.
632. Narla, G.; Brown, H. C. *Tetrahedron Lett.* **1997**, *38*, 219.
633. Ramachandran, P. V.; Krzeminski, M.; Reddy, M. V. R.; Brown, H. C. *Tetrahedron: Asymmetry* **1999**, *10*, 11.
634. Kumar, D. J. S.; Madhavan, S.; Ramachandran, V. R.; Brown, H. C. *Tetrahedron: Asymmetry* **2000**, *11*, 4629.
635. Ramachandran, P. V.; Padiya, K. J.; Rauniyar, V.; Reddy, M. V. R.; Brown, H. C. *Tetrahedron Lett.* **2004**, *45*, 1015.
636. Chen, G.-M.; Ramachandran, P. V. *Tetrahedron: Asymmetry* **1997**, *8*, 3935.
637. Hu, S.; Jayaraman, S.; Oehlschlager, A. C. *Tetrahedron Lett.* **1998**, *39*, 8059.
638. Hu, S.; Jayaraman, S.; Oehlschlager, A. C. *J. Org. Chem.* **1999**, *64*, 3719.
639. Hertweck, C.; Boland, W. *J. Org. Chem.* **1999**, *64*, 4426.
640. Lautens, M.; Maddess, M. L.; Sauer, E. L. O.; Ouellet, S. G. *Org. Lett.* **2002**, *4*, 83.
641. Barrett, A. G. M.; Braddock, D. C.; de Koning, P. D. *Chem. Commun.* **1999**, 495.
642. Barrett, A. G. M.; Braddock, D. C.; de Koning, P. D.; White, A. J. P.; Williams, D. *J. Org. Chem.* **2000**, *65*, 375.
643. Flamme, E. M.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 13644.
644. Gu, Y. G.; Wang, K. K. *Tetrahedron Lett.* **1991**, *32*, 3029.
645. Heo, J.-N.; Micalizio, G. C.; Roush, W. *Org. Lett.* **2003**, *5*, 1693.
646. Chen, G.-M.; Ramachandran, P. V.; Brown, H. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 825.
647. Itsuno, S.; Watanabe, K.; Ito, K.; El-Shehawy, A. A.; Sarhan, A. A. *Angew. Chem., Int. Ed.* **1997**, *36*, 109.
648. Itsuno, S.; Watanabe, K.; Matsumoto, T.; Kuroda, S.; Yokoi, A.; El-Shehawy, A. A. *J. Chem. Soc., Perkin Trans.* **1999**, *1*, 2011.
649. Itsuno, S.; Yokoi, A.; Kuroda, S. *Synlett* **1999**, 1987.
650. Watanabe, K.; Kuroda, S.; Yokoi, A.; Ito, K.; Itsuno, S. *J. Organomet. Chem.* **1999**, *581*, 103.
651. Burgos, C. H.; Canales, E.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 8044.
652. Lai, C.; Soderquist, J. A. *Org. Lett.* **2005**, *7*, 799.
653. White, J. D.; Kim, T.-S.; Nambu, M. *J. Am. Chem. Soc.* **1997**, *119*, 103.
654. Felpin, F.-X.; Vo-Thanh, G.; Villiéras, J.; Lebreton, J. *Tetrahedron: Asymmetry* **2001**, *12*, 1121.
655. Girard, S.; Robins, R. J.; Villiéras, J.; Lebreton, J. *Tetrahedron Lett.* **2000**, *41*, 9245.
656. Ghosh, A. K.; Wang, Y. *Tetrahedron Lett.* **2000**, *41*, 2319.
657. Greer, P. B.; Donaldson, W. A. *Tetrahedron Lett.* **2000**, *41*, 3801.
658. Wu, Y.; Esser, L.; De Brabander, J. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 4308.
659. Yu, W.; Zhang, Y.; Jin, Z. *Org. Lett.* **2001**, *3*, 1447.
660. Kadota, I.; Oguro, N.; Yamamoto, Y. *Tetrahedron Lett.* **2001**, *42*, 3645.
661. Kadota, I.; Park, C.-H.; Sato, K.; Yamamoto, Y. *Tetrahedron Lett.* **2001**, *42*, 6195.
662. Reddy, M. V. R.; Brown, H. C.; Ramachandran, P. V. *J. Organomet. Chem.* **2001**, *624*, 239.
663. Anderson, O. P.; Barrett, A. G. M.; Edmunds, J. J.; Hachiya, S.-I.; Hedrix, J. A.; Horita, K.; Malecha, J. W.; Parkinson, C. J.; VanSickle, A. *Can. J. Chem.* **2001**, *79*, 1562.

664. Archibald, S. C.; Barden, D. J.; Bazin, J. F. Y.; Fleming, I.; Foster, C.; Mandal, A. K.; Mandal, A. K.; Parker, D.; Takaki, K.; Ware, A. C., *et al. Org. Biomol. Chem.* **2004**, *2*, 1051.
665. Esumi, T.; Okamoto, N.; Hatakeyama, S. *Chem. Commun.* **2002**, 3042.
666. Nicolaou, K. C.; Kim, D. W.; Baati, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 3701.
667. Greer, P. B.; Donaldson, W. A. *Tetrahedron* **2002**, *58*, 6009.
668. Pitts, M. R.; Mulzer, J. *Tetrahedron Lett.* **2002**, *43*, 8471.
669. Falomir, E.; Murga, J.; Carda, M.; Marco, A. *Tetrahedron Lett.* **2003**, *44*, 539.
670. Kang, S. H.; Kang, S. Y.; Kim, C. M.; Choi, H.-W.; Jun, H.-S.; Lee, B. M.; Park, C. M.; Jeong, J. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 4779.
671. Ramachandran, P. V.; Prabhudas, B.; Pratihar, D.; Chandra, J. S.; Reddy, M. V. R. *Tetrahedron Lett.* **2003**, *44*, 3745.
672. Vidya, R.; Eggen, M.; Georg, G. I.; Himes, R. H. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 757.
673. Ghosh, A. K.; Kim, J.-H. *Tetrahedron Lett.* **2003**, *44*, 7659.
674. Cowden, C. J.; Paterson, I. *Org. React.* **1997**, *51*, 1.
675. Abiko, A. *Acc. Chem. Res.* **2004**, *37*, 387.
676. Oppolzer, W.; Lienard, P. *Tetrahedron Lett.* **1993**, *34*, 4321.
677. Iseki, K.; Oishi, S.; Kobayashi, Y. *Chem. Pharm. Bull.* **1996**, *44*, 2003.
678. Yan, T.-H.; Hung, A.-W.; Lee, H.-C.; Chang, C.-S.; Liu, W.-H. *J. Org. Chem.* **1995**, *60*, 3301.
679. Wang, Y.-C.; Hung, A.-W.; Chang, C.-S; Yan, T.-H. *J. Org. Chem.* **1996**, *61*, 2038.
680. Iseki, K.; Oishi, S.; Taguchi, T.; Kobayashi, Y. *Tetrahedron Lett.* **1993**, *34*, 8147.
681. Iseki, K.; Oishi, S.; Kobayashi, Y. *Tetrahedron* **1996**, *52*, 71.
682. Ganesan, K.; Brown, H. C. *J. Org. Chem.* **1994**, *59*, 2336.
683. Ganesan, K.; Brown, H. C. *J. Org. Chem.* **1994**, *59*, 7346.
684. Abiko, A.; Liu, J.-F.; Masamune, S. *J. Org. Chem.* **1996**, *61*, 2590.
685. Abiko, A.; Liu, J.-F.; Masamune, S. *J. Am. Chem. Soc.* **1997**, *119*, 2586.
686. Abiko, A.; Inoue, T.; Fruno, H.; Schwalbe, H.; Fieres, C.; Masamune, S. *J. Am. Chem. Soc.* **2001**, *123*, 4605.
687. Furuno, H.; Inoue, T.; Abiko, A. *Tetrahedron Lett.* **2002**, *43*, 8297.
688. Abiko, A.; Inoue, T.; Masamune, S. *J. Am. Chem. Soc.* **2002**, *124*, 10759.
689. Oppolzer, W.; Walther, E.; Balado, C. P.; Brabander, J. D. *Tetrahedron Lett.* **1997**, *38*, 809.
690. Ueda, M.; Miyabe, H.; Teramachi, M.; Miyata, O.; Naito, T. *Chem. Commun.* **2003**, 426.
691. Sibi, M. P.; Ji, J.; Sausker, J. B.; Jasperse, C. P. *J. Am. Chem. Soc.* **1999**, *121*, 7517.
692. Iserloh, U.; Curran, D. P.; Kanemasa, S. *Tetrahedron: Asymmetry* **1999**, *10*, 2417.
693. Sibi, M. P.; Zimmerman, J.; Rheault, T. *Angew. Chem., Int. Ed.* **2003**, *42*, 4521.
694. Friestad, G. K.; Shen, Y.; Ruggles, E. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 5061.
695. Alves, M. J.; Fortes, G.; Guimarães, E.; Lemos, A. *Synlett* **2003**, 1403.
696. Kondo, J.; Shinokubo, H.; Ohsima, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 825.
697. Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *J. Org. Chem.* **2001**, *66*, 7776.
698. Schaffner, A.-P.; Renaud, P. *Eur. J. Org. Chem.* **2004**, 2291.
699. Cadot, C.; Dalko, P. I.; Cossy, J.; Ollivier, C.; Chuar, R.; Renaud, P. *J. Org. Chem.* **2002**, *67*, 7193.
700. Ollivier, C.; Renaud, P. *Chem. Eur. J.* **1999**, *5*, 1468.
701. Ollivier, C.; Renaud, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 925.
702. Renaud, P.; Ollivier, C.; Weber, V. *J. Org. Chem.* **2003**, *68*, 5769.
703. Becattini, B.; Ollivier, C.; Renaud, P. *Synlett* **2003**, 1485.
704. Schaffner, A.-P.; Becattini, B.; Ollivier, C.; Weber, V. *Synthesis* **2003**, 2740.
705. Schaffner, A.-P.; Renaud, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 2658.
706. Takai, K.; Shinomiya, N.; Ohta, M. *Synlett* **1998**, 253.
707. Batey, R. A.; Pedram, B.; Yong, K.; Baquer, G. *Tetrahedron Lett.* **1996**, *37*, 6847.
708. Batey, R.; Smil, D. V. *Tetrahedron Lett.* **1999**, *40*, 9183.
709. Boudier, A.; Bromm, L. O.; Lotz, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 4414.
710. Hoshi, M.; Shirakawa, K.; Arase, A. *Chem. Commun.* **1998**, 1225.
711. Hoshi, M.; Shirakawa, K. *Chem. Commun.* **2002**, 2146.
712. Langer, F.; Waas, J.; Knochel, P. *Tetrahedron Lett.* **1993**, *34*, 5261.
713. Langer, F.; Devasagayaraj, A.; Chavant, P.-Y.; Knochel, P. *Synlett* **1994**, 410.
714. Micouin, L.; Oestreich, M.; Knochel, P. *Angew. Chem., Int. Ed.* **1997**, *36*, 245.
715. Hupe, E.; Knochel, P. *Org. Lett.* **2001**, *3*, 127.
716. Langer, F.; Schwink, L.; Devasagayaraj, A.; Chavant, P.-Y.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 8229.
717. Boudier, A.; Hupe, E.; Knochel, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 2294.
718. Jackson, R. F. W.; Oates, L. J.; Block, M. H. *Chem. Commun.* **2000**, 1401.
719. Hupe, E.; Calaza, M. I.; Knochel, P. *Tetrahedron Lett.* **2001**, *42*, 8829.
720. Hupe, E.; Calaza, M. I.; Knochel, P. *Chem. Eur. J.* **2003**, *9*, 2789.
721. Boudier, A.; Flachsmann, F.; Knochel, P. *Synlett* **1998**, 1438.
722. Boudier, A.; Darcel, C.; Flachsmann, F.; Micouin, L.; Oestreich, M.; Knochel, P. *Chem. Eur. J.* **2000**, *6*, 2748.
723. Srebnik, M. *Tetrahedron Lett.* **1991**, *32*, 2449.
724. Oppolzer, W.; Radinov, R. N. *Helv. Chem. Acta* **1992**, *75*, 170.
725. Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593.
726. Oppolzer, W.; Radinov, R. N.; El-Sayed, E. *J. Org. Chem.* **2001**, *66*, 4766.
727. Chen, Y. K.; Lurain, A. E.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 12225.
728. García, C.; Libra, E. R.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc.* **2003**, *125*, 3210.
729. Dahmen, S.; Bräse, S. *Org. Lett.* **2001**, *3*, 4119.
730. Bolm, C.; Rudolph, J. *J. Am. Chem. Soc.* **2002**, *124*, 14850.
731. Rudolph, J.; Schmidt, F.; Bolm, C. *Synthesis* **2005**, 840.
732. Prieto, O.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1955.

733. Ji, J. X.; Wu, J.; Au-Yeung, T. T.-L.; Yip, C. W.; Haynes, R. K.; Chan, A. S. C. *J. Org. Chem.* **2005**, *70*, 1093.
734. Braga, A. L.; Lüdtke, D. S.; Vargas, F.; Paixão, M. W. *Chem. Commun.* **2005**, 2512.
735. Matano, Y.; Begum, S. A.; Miyamatsu, T.; Suzuki, H. *Organometallics* **1999**, *18*, 5668.
736. Ochiai, M.; Toyonari, M.; Nagaoka, T.; Chen, D. W.; Kida, M. *Tetrahedron Lett.* **1997**, *38*, 6709.
737. Morgan, J.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans.* **1990**, *1*, 715.
738. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
739. Suzuki, A.; Brown, H. C. *Organic Syntheses via Boranes Vol. 3*; Aldrich Chemical Co.: Milwaukee, 2003.
740. Suzuki, A. *J. Organomet. Chem.* **1998**, *576*, 147.
741. Suzuki, A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VHC: Weinheim, 1998; p 49.
742. Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron Lett.* **2002**, *58*, 9633.
743. Hassan, J.; Sévingnon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359.
744. Buchwald, S. L.; Fox, J. M. *Strem Chemiker* **2000**, *18*(1).
745. Miyaura, N. In *Advances in Metal Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Stanford, 1998; Vol. 6, p 187.
746. Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263.
747. Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176.
748. Chemler, S. R.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4544.
749. Irvine, G. J.; Lesley, J. G.; Marder, T. B.; Norman, N. C.; Rice, C. R.; Robins, E. G.; Roper, W. R.; Whittel, G. R.; Wright, L. J. *Chem. Rev.* **1998**, *98*, 2685.
750. Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314.
751. Ishiyama, T.; Miyaura, N.; Suzuki, A. *Org. Synth.* **1992**, *71*, 89.
752. Johnson, C. R.; Braun, M. P. *J. Am. Chem. Soc.* **1993**, *115*, 11014.
753. Netherton, M. R.; Dai, C.; Neuschütz, K.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 10099.
754. Kirchhoff, J. H.; Dai, C.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 1945.
755. Johnson, C. R.; Braun, M. P. *J. Am. Chem. Soc.* **1993**, *115*, 11014.
756. Soderquist, J. A.; Leon, G.; Colberg, J. C.; Martinez, L. *Tetrahedron Lett.* **1995**, *36*, 3119.
757. Alvarez, R.; Herrero, M.; López, S.; de Lera, A. R. *Tetrahedron* **1998**, *54*, 6793.
758. Sasaki, M.; Fuwa, H.; Inoue, M.; Tachibana, K. *Tetrahedron Lett.* **1998**, *39*, 9027.
759. Sasaki, M.; Fuwa, H.; Ishikawa, M.; Tachibana, K. *Org Lett.* **1999**, *1*, 1075.
760. Sasaki, M.; Tsukano, C.; Tachibana, K. *Org. Lett.* **2002**, *4*, 1747.
761. Fuwa, H.; Sasaki, M.; Tachibana, K. *Org. Lett.* **2001**, *3*, 3549.
762. Takakura, H.; Noguchi, K.; Sasaki, M.; Tachibana, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 1090.
763. Sasaki, M.; Ishikawa, M.; Fuwa, H.; Tachibana, K. *Tetrahedron* **2002**, *58*, 1889.
764. Narukawa, Y.; Nishi, K.; Onoue, H. *Tetrahedron* **1997**, *53*, 539.
765. Lee, T.-H.; Liao, C.-C. *Tetrahedron Lett.* **1996**, *37*, 6869.
766. Johns, B. A.; Pan, Y. T.; Elbein, A. D.; Johson, C. R. *J. Am. Chem. Soc.* **1997**, *119*, 4856.
767. Meng, D.; Bertinato, P.; Balog, A.; Su, D.-S.; Kamenecka, T.; Sorensen, E. J.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 10073.
768. Stachel, S. J.; Chappell, M. D.; Lee, C. B.; Danishefsky, S. J.; Chou, T.-C.; He, L.; Horwitz, S. B. *Org. Lett.* **2000**, *2*, 1637.
769. Harris, C. R.; Kuduk, S. D.; Balog, A.; Savin, K.; Glunz, P. W.; Danishefsky, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 7050.
770. Balog, A.; Meng, D.; Kamenecka, T.; Bertinato, P.; Su, D.-S.; Sorensen, E. J.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **1996**, *35*, 2801.
771. Thompson, L. A.; Moore, F. L.; Moon, Y.-C.; Ellman, J. A. *J. Org. Chem.* **1998**, *63*, 2066.
772. Trost, B. M.; Lee, C. *J. Am. Chem. Soc.* **2001**, *123*, 12191.
773. Trost, B. M.; Lee, C. B. *J. Am. Chem. Soc.* **1998**, *120*, 6818.
774. Brosius, A. D.; Overman, L. E. *J. Org. Chem.* **1997**, *62*, 440.
775. Fürstner, A.; Seidel, G. *J. Org. Chem.* **1997**, *62*, 2332.
776. Fürstner, A.; Konetzki, I. *J. Org. Chem.* **1998**, *63*, 3072.
777. Bauer, M.; Maier, M. E. *Org. Lett.* **2002**, *4*, 2205.
778. Kobayashi, Y.; Nakano, M.; Kumar, G. B.; Kishihara, K. *J. Org. Chem.* **1998**, *63*, 7505.
779. Trauner, D.; Schwarz, J. B.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **1999**, *38*, 3542.
780. Marshall, J. A.; Bourbeau, M. P. *J. Org. Chem.* **2002**, *67*, 2751.
781. Tietze, L. F.; Völkel, L. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 901.
782. Carson, M. W.; Kim, G.; Hentemann, M. F.; Trauner, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 4450.
783. Okamoto, S.; Subburaj, K.; Sato, F. *J. Am. Chem. Soc.* **2000**, *122*, 11244.
784. Collier, P. N.; Campbell, A. D.; Patel, I.; Taylor, R. J. K. *Tetrahedron Lett.* **2000**, *41*, 7115.
785. Kamatani, A.; Overman, L. E. *J. Org. Chem.* **1999**, *64*, 8743.
786. Kim, G.; Jung, S.-D.; Kim, W.-J. *Org. Lett.* **2001**, *3*, 2985.
787. Lapinsky, D. J.; Bergmeier, S. C. *Tetrahedron Lett.* **2001**, *42*, 8583.
788. Campbell, A. D.; Raynham, T. M.; Taylor, R. J. K. *Tetrahedron Lett.* **1999**, *40*, 5263.
789. Collier, P. N.; Campbell, A. D.; Patel, I.; Raynham, T. M.; Taylor, R. J. K. *J. Org. Chem* **2002**, *67*, 1802.
790. Collier, P. N.; Patel, I.; Taylor, R. J. K. *Tetrahedron Lett.* **2001**, *42*, 5953.
791. Gray, M.; Andrews, I. P.; Hook, D. F.; Kitteringham, J.; Voyle, M. *Tetrahedron Lett.* **2000**, *41*, 6237.
792. Niu, C.; Li, J.; Doyle, T. W.; Chen, S.-H. *Tetrahedron* **1998**, *54*, 6311.
793. Zou, G.; Reddy, Y. K.; Falck, J. R. *Tetrahedron Lett.* **2001**, *42*, 7213.
794. Molandrer, G. A.; Yun, C.-S. *Tetrahedron* **2002**, *58*, 1465.
795. Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553.
796. Selvakumar, K.; Zapf, A.; Spannenberg, A.; Beller, M. *Chem. Eur. J.* **2002**, *8*, 3901.
797. Charette, A. B.; Giroux, A. *J. Org. Chem.* **1996**, *61*, 8718.
798. Charette, A. B.; Freitas-Gil, R. P. D. *Tetrahedron Lett. 38*, 2809.
799. Yao, M. L.; Deng, M.-Z. *J. Org. Chem.* **2000**, *65*, 5034.
800. Wallace, D. J.; Chen, C.-Y. *Tetrahedron Lett.* **2002**, *43*, 6987.
801. Yao, M.-L.; Deng, M.-Z. *Synlett.* **2000**, 1095.

802. Zhou, S.-M.; Deng, M.-Z.; Xia, L.-J.; Tang, M.-H. *Angew. Chem., Int. Ed.* **1998**, *37*, 2845.
803. Zhou, S.-M.; Yan, Y.-L.; Deng, M.-Z. *Synlett* **1998**, 198.
804. Chen, H.; Deng, M.-Z. *Org Lett.* **2000**, *2*, 1649.
805. Scheidt, K. A.; Tasaka, A.; Bannister, T. D.; Wendet, M. D.; Roush, W. R. *Angew. Chem., Int. Ed.* **1999**, *38*, 1652.
806. Scheidt, K. A.; Bannister, T. D.; Tasaka, A.; Wendt, M. D.; Savall, B. M.; Fegley, G. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 6981.
807. Reddy, Y. K.; Falck, J. R. *Org. Lett.* **2002**, *4*, 969.
808. Organ, M. G.; Bilokin, Y. V.; Bratovanov, S. *J. Org. Chem.* **2002**, *67*, 5176.
809. Kobayashi, Y.; Shimizu, K.; Sato, F. *Chem. Commun.* **1997**, 493.
810. Hanisch, I.; Brückner, R. *Synlett* **2000**, 374.
811. Torrado, A.; Iglesias, B.; Lopez, S.; de Lera, A. A. *Tetrahedron* **1995**, *51*, 2435.
812. Cabezas, J. A.; Oehlschlager, A. C. *Synlett* **1999**, 107.
813. Prinz, P.; Lansky, A.; Haumann, T.; Boese, R.; Noltemeyer, M.; Knieriem, B.; Meijere, A. *Angew. Chem., Int. Ed.* **1997**, *36*, 1289.
814. Kawanaka, Y.; Ono, N.; Yoshida, Y.; Okamoto, S.; Sato, F. *J. Chem. Soc., Perkin Trans.* **1996**, *1*, 715.
815. Hanazawa, T.; Wada, T.; Masuda, T.; Okamoto, S.; Sato, F. *Org. Lett.* **2001**, *3*, 3975.
816. Evans, D. A.; Ng, H. P.; Rieger, D. L. *J. Am. Chem. Soc.* **1993**, *115*, 11446.
817. Nicolaou, K. C.; Ramphal, J. Y.; Palazon, J. M.; Spanevello, R. A. *Angew. Chem., Int. Ed.* **1989**, *28*, 587.
818. Nicolaou, K. C. *Angew. Chem., Int. Ed.* **1991**, *30*, 1100.
819. Roush, W. R.; Riva, R. *J. Org. Chem.* **1998**, *53*, 710.
820. Roush, W. R.; Sciotti, R. J. *J. Am. Chem. Soc.* **1994**, *116*, 6457.
821. Brosius, A. D.; Overman, L. E.; Schwink, L. *J. Am. Chem. Soc.* **1999**, *121*, 700.
822. Barrett, A. G. M.; Bennett, A. J.; Menzer, S.; Smith, M. L.; White, A. J. P.; Williams, D. J. *J. Org. Chem.* **1999**, *64*, 162.
823. Ozawa, T.; Aoyagi, S.; Kibayashi, C. *J. Org. Chem.* **2001**, *66*, 3338.
824. Nicolaou, K. C.; Li, Y.; Fylaktakidou, K. C.; Mitchell, H. J.; Wei, H.-X.; Weyershausen, B. *Angew. Chem., Int. Ed.* **2001**, *40*, 3849.
825. Evans, D. A.; Starr, J. T. *Angew. Chem., Int. Ed.* **2002**, *41*, 1787.
826. Thirsk, C.; Whiting, A. *J. Chem. Soc., Perkin Trans.* **2002**, *1*, 999.
827. Larson, R. D.; King, A. O.; Chen, C. Y.; Corley, E. G.; Foster, B. S.; Roberts, F. E.; Yang, C. Y.; Lieberman, D. R.; Reamer, R. A.; Tschaen, D. M., *et al. J. Org. Chem.* **1994**, *59*, 6391.
828. Boger, D. L.; Miyazaki, S.; Kim, S. H.; Wu, J. H.; Castle, S. L.; Loiseleur, O.; Jin, Q. *J. Am. Chem. Soc.* **1999**, *121*, 10004.
829. Mizutani, T.; Wada, K.; Kitagawa, S. *J. Am. Chem. Soc.* **2001**, *123*, 6459.
830. Marck, G.; Villiger, A.; Buchecker, R. *Tetrahedron Lett.* **1994**, *35*, 3277.
831. Hird, M.; Gray, G. W.; Toyne, K. *J. Mol. Cryst. Liq. Cryst.* **1991**, *206*, 187.
832. Trollsas, M.; Ihre, H.; Geddle, U. W.; Hult, A. *Macromol. Chem. Phys.* **1996**, *197*, 767.
833. Wulff, G.; Schmidt, H.; Witt, H.; Zental, R. *Angew. Chem., Int. Ed.* **1994**, *33*, 188.
834. Hird, M.; Lewis, R. A.; Toyne, K. J.; West, J. J.; Wilson, M. K. *J. Chem. Soc., Perkin Trans.* **1998**, *1*, 3479.
835. Improved preparation of cross-coupling products, Poetsch, E.; Meyer, V. DE4241747, 1992.
836. Improved process for coupling arylboronic acids with aryl halides, Poetsch, E.; Meyer, V.; Kompter, H. M.; Krause, J. DE4340490A1, 1992.
837. Process and catalysts for the preparation of bisaryl compounds by the coupling of arylmagnesium chlorides with aryl chlorides in the presence of phosphine ligands, Poetsch, E.; Meyer, V. DE4326169A1, 1993.
838. Bringmann, G.; Götz, R.; Keller, P. A.; Walter, R.; Boyd, M. R.; Lang, F.; Garcia, A.; Walsh, J. J.; Tellitu, I.; Bhaskar, K. V., *et al. J. Org. Chem.* **1998**, *63*, 1090.
839. Hobbs, P. D.; Upender, V.; Dawson, M. I. *Synlett* **1997**, 965.
840. Firooznia, F.; Gude, C.; Chan, K.; Satoh, Y. *Tetrahedron Lett.* **1998**, *39*, 3985.
841. Lakshman, M. K.; Hilmer, J. H.; Martin, J. Q.; Keeler, J. C.; Dinh, Y. Q. V.; Ngassa, F. N.; Russon, L. M. *J. Am. Chem. Soc.* **2001**, *123*, 7779.
842. Lakshman, M. K.; Thomson, P. F.; Nuqui, M. A.; Hilmer, J.; Sevova, N.; Boggess, B. *Org. Lett.* **2002**, *4*, 1479.
843. Kirschbaum, T.; Briehn, C. A.; Bäuerle, P. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 1211.
844. Bäuerle, P. *J. Organomet. Chem.* **2002**, *653*, 200.
845. Cammidge, A. N.; Crépy, K. V. L. *Chem. Commun.* **2000**, 1723.
846. Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051.
847. Monovich, L. G.; Huérou, Y. L.; Rönn, M.; Molander, G. A. *J. Am. Chem. Soc.* **2000**, *122*, 52.
848. Kamikawa, K.; Watanabe, T.; Uemura, M. *J. Org. Chem.* **1996**, *61*, 1375.
849. Shi, B.; Boyle, R. W. *J. Chem. Soc., Perkin Trans.* **2002**, *1*, 1397.
850. Zhou, X.; Chan, K. S. *J. Org. Chem.* **1998**, *63*, 99.
851. Shultz, D.; Gwaltney, K. P.; Lee, H. *J. Org. Chem.* **1998**, *63*, 769.
852. Kelly, T. R.; Silva, R. A.; Silva, H. D.; Jasmin, S.; Zhao, Y. *J. Am. Chem. Soc.* **2000**, *122*, 6935.
853. Schoevaars, A. M.; Kruizinga, W.; Zijlstra, R. W. J.; Veldman, N.; Spek, A. L.; Feringa, B. L. *J. Org. Chem.* **1997**, *62*, 4943.
854. Endtner, J. M.; Effenberger, F.; Hartschuh, A.; Port, H. *J. Am. Chem. Soc.* **2000**, *122*, 3037.
855. Takeshita, M.; Irie, M. *J. Org. Chem.* **1998**, *63*, 6643.
856. Yamaguchi, S.; Endo, T.; Uchida, M.; Izumizawa, T.; Furukawa, K.; Tamao, K. *Chem. Lett.* **2001**, 98.
857. Ma, L.; White, P. S.; Lin, W. *J. Org. Chem.* **2002**, *67*, 7577.
858. Chow, H.-F.; Wan, C.-W. *J. Org. Chem.* **2001**, *66*, 5042.
859. Teki, Y.; Miyamoto, S.; Nakatsuji, M.; Miura, Y. *J. Am. Chem. Soc.* **2001**, *123*, 294.
860. Miura, Y.; Momoki, M.; Nakatsuji, M. *J. Org. Chem.* **1998**, *63*, 1555.
861. Deng, X.; Mayeux, A.; Cai, C. *J. Org. Chem.* **2002**, *67*, 5279.
862. Bharathi, P.; Zhao, H.; Thayumanavan, S. *Org. Lett.* **2001**, *3*, 1961.
863. Brownstein, S. K.; Ding, J.; Robertson, G.; Roovers, J. *J. Org. Chem.* **2002**, *67*, 663.
864. Gong, L.-Z.; Hu, Q.-S.; Pu, L. *J. Org. Chem.* **2001**, *66*, 2358.
865. Zhang, F.-J.; Cortez, C.; Harvey, R. G. *J. Org. Chem.* **2000**, *65*, 3952.
866. Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Org. Chem.* **1998**, *63*, 1676.
867. Goldfinger, M. B.; Crawford, K. B.; Swager, T. M. *J. Am. Chem. Soc.* **1997**, *119*, 4578.
868. Lin, S.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 1967.

869. Kaiser, M.; Groll, M.; Renner, C.; Huber, R.; Moroder, L. *Angew. Chem., Int. Ed.* **2002**, *41*, 780.
870. Gravel, M.; Thompson, K. A.; Zak, M.; Bérubé, C.; Hall, D. G. *J. Org. Chem.* **2002**, *67*, 3.
871. Lutz, C.; Bleicher, K. H. *Tetrahedron Lett.* **2002**, *43*, 2211.
872. Chhabra, S. R.; Mahajan, A.; Chan, W. C. *J. Org. Chem.* **2002**, *67*, 4017.
873. Revell, J. D.; Ganesan, A. *Org. Lett.* **2002**, *4*, 3071.
874. Barrett, A. G. M.; Procopiou, P. A.; Voigtmann, U. *Org. Lett.* **2001**, *3*, 3165.
875. Brill, W. K.-D.; Riva-Toniolo, C.; Müller, S. *Synlett* **2001**, 1097.
876. Atkinson, G. E.; Fischer, P. M.; Chan, W. C. *J. Org. Chem.* **2000**, *65*, 5048.
877. Sammelson, R. E.; Kurth, M. J. *Chem. Rev.* **2001**, *101*, 137.
878. Schlüter, A. D. *J. Polym. Sci., Part A: Polym. Chem.* **2001**, *39*, 1533.
879. Yin, J.; Rainka, M. P.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162.
880. Carbonnelle, A.-C.; Zhu, J. *Org. Lett.* **2000**, *2*, 3477.
881. Hensel, V.; Lützow, K.; Jacob, J.; Gessler, K.; Saenger, W.; Schlüter, A. D. *Angew. Chem., Int. Ed.* **1997**, *36*, 2654.
882. Garg, N. K.; Sarpong, R.; Stoltz, B. M. *J. Am. Chem. Soc.* **2002**, *124*, 13179.
883. Hallberg, A.; Larhed, M. *J. Org. Chem.* **1996**, *61*, 9582.
884. Hallberg, A.; Lindeberg, G.; Larhed, M. *Tetrahedron Lett.* **1996**, *37*, 8219.
885. Leadbeater, N. E.; Marco, M. *Org. Lett.* **2002**, *4*, 2973.
886. Blettner, C. G.; Kong, W. A.; Stenzel, W.; Schötten, T. *J. Org. Chem.* **1999**, *64*, 3885.
887. Kabalka, G. W.; Pagni, R. M.; Hair, C. M. *Org. Lett.* **1999**, *1*, 1423.
888. Melucci, M.; Barbarella, G.; Sotgiu, G. *J. Org. Chem.* **2002**, *67*, 8877.
889. Yasuda, N.; Huffman, M. A.; Ho, G.-J.; Xavier, L. C.; Yang, C.; Emerson, K. M.; Tsay, F.-R.; Li, Y.; Kress, M. H.; Rieger, D. L., *et al. J. Org. Chem.* **1998**, *63*, 5438.
890. Rankin, T.; Tykwinski, R. R. *Org. Lett.* **2003**, *5*, 213.
891. Moreno-Manas, M.; Pajuelo, F.; Pleixats, R. *J. Org. Chem.* **1995**, *60*, 2396.
892. Chowdhury, S.; Georghiou, P. E. *Tetrahedron Lett.* **1999**, *40*, 7599.
893. Gooβen, L. J. *Chem. Commun.* **2001**, 669.
894. Liu, X.-X.; Deng, M.-Z. *Chem. Commun.* **2002**, 622.
895. Lei, A.; Zhang, X. *Tetrahedron Lett.* **2002**, *43*, 2525.
896. Lei, A.; Zhang, X. *Org. Lett.* **2002**, *4*, 2285.
897. Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2001**, *3*, 91.
898. Fürstner, A.; Seidel, G. *Synlett* **1998**, 161.
899. Wang, D.; Schlegel, J. M.; Galoppini, E. *Tetrahedron* **2002**, *58*, 6027.
900. Fürstner, A.; Nikolakis, K. *Liebigs Annalen* **1996**, 2107.
901. Soderquist, J. A.; Matos, K.; Rane, A.; Ramos, J. *Tetrahedron Lett.* **1995**, *36*, 2401.
902. Fürstner, A.; Seidel, G. *Tetrahedron* **1995**, *51*, 11165.
903. Castanet, A.-S.; Colobert, F.; Schlama, T. *Org. Lett.* **2000**, *2*, 3559.
904. Oh, C. H.; Jung, S. H. *Tetrahedron Lett.* **2000**, *41*, 8513.
905. Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099.
906. Darses, S.; Michaud, G.; Genêt, J.-P. *Eur. J. Org. Chem.* **1999**, 1875.
907. Darses, S; Genêt, J.-P.; Brayer, J.-L.; Demoute, J.-P. *Tetrahedron Lett.* **1997**, *38*, 4393.
908. Frohn, H.-J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *Tetrahedron Lett.* **2002**, *43*, 8111.
909. Molander, G. A.; Bernardi, C. R. *J. Org. Chem.* **2002**, *67*, 8424.
910. Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095.
911. Haddach, M.; McCarthy, J. R. *Tetrahedron Lett.* **1999**, *40*, 3109.
912. Bumagin, N. A.; Korolev, D. N. *Tetrahedron Lett.* **1999**, *40*, 3057.
913. Urawa, Y.; Ogura, K. *Tetrahedron Lett.* **2003**, *44*, 271.
914. Liebeskind, L. S.; Srogl, J. *Org. Lett.* **2002**, *4*, 979.
915. Kusturin, C. L.; Liebeskind, L. S.; Neumann, W. L. *Org. Lett.* **2002**, *4*, 983.
916. Alphonse, F. A.; Suzenet, F.; Keromnes, A.; Lebret, B.; Guillaumet, G. *Synlett* **2002**, 447.
917. Lengar, A.; Kappe, C. O. *Org. Lett.* **2004**, *6*, 771.
918. Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2000**, *2*, 3229.
919. Kakino, R.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 371.
920. Kakino, R.; Yasumi, S.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 137.
921. Kakino, R.; Narahashi, H.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1333.
922. Yamamoto, A.; Kakino, R.; Shimizu, I. *Hev. Chim. Acta* **2001**, *84*, 2996.
923. Ishiyama, T.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1991**, *32*, 6923.
924. Ishiyama, T.; Murata, M.; Suzuki, A.; Miyaura, N. *Chem. Commun.* **1995**, 295.
925. Ishiyama, T.; Miyaura, N.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1999.
926. Wakita, Y.; Yasunaga, T.; Akita, M.; Kojima, M. *J. Organomet. Chem.* **1986**, *301*, C17.
927. Ishiyam, T.; Kizaki, H.; Hayashi, T.; Suzuki, A.; Miyaura, N. *J. Org. Chem.* **1998**, *63*, 4726.
928. Ishiyama, T.; Kizaki, H.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1993**, *34*, 7595.
929. Couve-Bonnaire, S.; Carpentier, J.-F.; Mortreux, A.; Castanet, Y. *Tetrahedron Lett.* **2001**, *42*, 3689.
930. Andrus, M. B.; Ma, Y.; Zang, Y.; Song, C. *Tetrahedron Lett.* **2002**, *43*, 9137.
931. Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229.
932. Nishikata, T.; Yamamoto, Y.; Miyaura, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 2768.
933. Nishikata, T.; Yamamoto, Y.; Miyaura, N. *Organometallics* **2004**, *23*, 4317.
934. Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169.
935. Batey, R. A.; Thadani, A. N.; Smil, D. V. *Org. Lett.* **1999**, *1*, 1683.
936. Ogasawara, M.; Yoshida, K.; Hayashi, T. *Organometallics* **2000**, *19*, 1567.
937. Yamamoto, Y.; Fujita, M.; Miyaura, N. *Synlett* **2002**, 767.

938. Wang, Z.; Zou, G.; Tang, J. *Chem. Commun.* **2004**, 1192.
939. Sakuma, S.; Sakai, M.; Itooka, R.; Miyaura, N. *J. Org. Chem.* **2000**, *65*, 5951.
940. Chapman, C. J.; Frost, C. G. *Adv. Synth. Catal.* **2003**, *345*, 353.
941. Ramnauth, J.; Poulin, O.; Bratovanov, S. S.; Rakhit, S.; Maddaford, S. P. *Org. Lett.* **2001**, *3*, 2571.
942. Sakuma, S.; Miyaura, N. *J. Org. Chem.* **2001**, *66*, 8944.
943. Itooka, R.; Iguchi, Y.; Miyaura, N. *Chem. Lett.* **2001**, 722.
944. Harada, A.; Yamamoto, S.; Takahashi, S. *Organometallics* **1989**, *8*, 2560.
945. Amengual, R.; Michelet, V.; Genêt, J.-P. *Tetrahedron Lett.* **2002**, *43*, 5905.
946. Uozumi, Y.; Nakazono, M. *Adv. Synth. Catal.* **2002**, *344*, 274.
947. Pucheault, M.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2002**, *43*, 6155.
948. Batey, R. A.; Quach, T. D.; Shen, M.; Thadani, A. N.; Smil, D. V.; Li, S. W.; MacKay, D. B. *Pure Appl. Chem.* **2002**, *74*, 43.
949. Itooka, R.; Iguchi, Y.; Miyaura, N. *J. Org. Chem.* **2003**, *68*, 6000.
950. Yoshida, K.; Ogasawara, M.; Hayashi, T. *J. Am. Chem. Soc.* **2002**, *124*, 10984.
951. Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829.
952. Hayashi, T. *Synlett* **2001**, 879.
953. Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. *J. Am. Chem. Soc.* **1998**, *120*, 5579.
954. Kuriyama, M.; Tomioka, K. *Tetrahedron Lett.* **2001**, *42*, 921.
955. Kuriyama, M.; Nagai, K.; Yamada, K.-i.; Miwa, Y.; Taga, T.; Tomioka, K. *J. Am. Chem. Soc.* **2002**, *124*, 8932.
956. Reetz, M. T.; Moulin, D.; Gosberg, A. *Org. Lett.* **2001**, *3*, 4083.
957. Ma, Y.; Song, C.; Ma, C.; Sun, Z.; Chai, Q.; Andrus, M. B. *Angew. Chem., Int. Ed.* **2003**, *42*, 5871.
958. Mauleón, P.; Carretero, J. C. *Org. Lett.* **2004**, *6*, 3195.
959. Iguchi, Y.; Itooka, R.; Miyaura, N. *Synlett* **2003**, 1040.
960. Boiteau, J. G.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2003**, *68*, 9481.
961. Duursma, A.; Hoen, R.; Schuppan, J.; Hulst, R.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2003**, *5*, 3111.
962. Boiteau, J. G.; Imbos, R.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2003**, *5*, 681.
963. Duursma, A.; Boiteau, J. G.; Lefort, L.; Boogers, J. A. F.; de Vries, A. H. M.; de Vries, J. G.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2004**, *69*, 8045.
964. Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. *J. Am. Chem. Soc.* **2003**, *125*, 11508.
965. Shintani, R.; Ueyama, K.; Yamada, I.; Hayashi, T. *Org. Lett.* **2004**, *6*, 3425.
966. Defieber, C.; Paquin, J. F.; Serna, S.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 3873.
967. Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **2002**, *124*, 5052.
968. Takaya, Y.; Ogasawara, M.; Hayashi, T. *Tetrahedron Lett.* **1999**, *40*, 6957.
969. Takaya, Y.; Senda, T.; Kurushima, H.; Ogasawara, M.; Hayashi, T. *Tetrahedron: Asymmetry* **1999**, *10*, 4047.
970. Senda, T.; Ogasawara, M.; Hayashi, T. *J. Org. Chem.* **2001**, *66*, 6852.
971. Hayashi, T.; Senda, T.; Ogasawara, M. *J. Am. Chem. Soc.* **2000**, *122*, 10716.
972. Navarre, L.; Pucheault, M.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2005**, *46*, 4247.
973. Hayashi, T.; Senda, T.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **1999**, *121*, 11591.
974. Cauble, D. F.; Gipson, J. D.; Krische, M. J. *J. Am. Chem. Soc.* **2003**, *125*, 1110.
975. Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918.
976. Lautens, M.; Yoshida, M. *Org. Lett.* **2002**, *4*, 123.
977. Lautens, M.; Marquardt, T. *J. Org. Chem.* **2004**, *69*, 4607.
978. Oguma, K.; Miura, M.; Satoh, T.; Nomura, M. *J. Am. Chem. Soc.* **2000**, *122*, 10464.
979. Murakami, M.; Igawa, H. *Chem. Commun.* **2002**, 390.
980. Lautens, M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett.* **2002**, *4*, 1311.
981. Lautens, M.; Mancuso, J. *Org. Lett.* **2002**, *4*, 2105.
982. Lautens, M.; Roy, A.; Fukuoka, K.; Fagnou, K.; Martín-Matute, B. *J. Am. Chem. Soc.* **2001**, *123*, 5358.
983. Ma, S.; Jiao, N.; Ye, L. *Chem. Eur. J.* **2003**, *9*, 6049.
984. Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004**, *69*, 3478.
985. Sakai, M.; Ueda, M.; Miyaura, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 3279.
986. Ueda, M.; Miyaura, N. *J. Org. Chem.* **2000**, *65*, 4450.
987. Fürstner, A.; Krause, H. *Adv. Synth. Catal.* **2001**, 343.
988. Moreau, C.; Hague, C.; Weller, A. S.; Frost, C. G. *Tetrahedron Lett.* **2001**, *42*, 6957.
989. Imlinger, N.; Mayr, M.; Wang, D.; Wurst, K.; Buchmeiser, M. R. *Adv. Synth. Catal.* **2004**, *346*, 1836.
990. Focken, T.; Rudolph, J.; Bolm, C. *Synthesis* **2005**, 429.
991. Matsuda, T.; Makino, M.; Murakami, M. *Org. Lett.* **2004**, *6*, 1257.
992. Pucheault, M.; Darses, S.; Genêt, J.-P. *J. Am. Chem. Soc.* **2004**, *126*, 15356.
993. Ueda, M.; Miyaura, N. *J. Organomet. Chem.* **2000**, *595*, 31.
994. Ueda, M.; Saito, A.; Miyaura, N. *Synlett* **2000**, 1637.
995. Kuriyama, M.; Soeta, T.; Hao, X.; Chen, Q.; Tomioka, K. *J. Am. Chem. Soc.* **2004**, *126*, 8128.
996. Chan, D. M. T.; Monaco, K. L.; Wang, R.-P.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933.
997. Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941.
998. Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937.
999. Ley, S. T.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400.
1000. Cundy, D. J.; Forsyth, S. A. *Tetrahedron Lett.* **1998**, *39*, 7979.
1001. Mederski, W. W. K. R.; Lefort, M.; Germann, M.; Kux, D. *Tetrahedron* **1999**, *55*, 12757.
1002. Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Averill, K. M.; Chan, D. M. T.; Combs, A. *Synlett* **2000**, 674.
1003. Simon, J.; Ssalzbrunn, S.; Prakash, G. K. S.; Petasis, N. A.; Olah, G. A. *J. Org. Chem.* **2001**, *66*, 633.
1004. Ding, S.; Gray, N. S.; Ding, Q.; Schulz, P. G. *Tetrahedron Lett.* **2001**, *42*, 8751.
1005. Yu, S.; Saenz, J.; Srirangam, J. K. *J. Org. Chem.* **2002**, *67*, 1699.
1006. Lam, P. Y. S.; Bonne, D.; Vincent, G.; Clark, C. G.; Combs, A. P. *Tetrahedron Lett.* **2003**, *44*, 1691.

1007. Sasaki, M.; Dalili, S.; Yudin, A. K. *J. Org. Chem.* **2003**, *68*, 2045.
1008. Bakkestuen, A. K.; Gundersen, L.-L. *Tetrahedron Lett.* **2003**, *44*, 3359.
1009. Chan, D. M. T.; Monaco, K. L.; Li, R.; Bonne, D.; Clark, C. G.; Lam, P. Y. S. *Tetrahedron Lett.* **2003**, *44*, 3863.
1010. Shimi, K.; Boyer, G.; Finet, J.-P.; Galy, J.-P. *Lett. Org. Chem.* **2004**, *1*, 34.
1011. Joshi, R. A.; Patil, P. S.; Muthukrishnan, M.; Ramana, C. V.; Gurjar, M. K. *Tetrahedron Lett.* **2004**, *45*, 195.
1012. Collman, J. P.; Zhong, M. *Org. Lett.* **2000**, *2*, 1233.
1013. Collman, J. P.; Zhong, M.; Zhang, C.; Costanzo, S. *J. Org. Chem.* **2001**, *66*, 7892.
1014. Collot, V.; Bovy, P. R.; Rault, S. *Tetrahedron Lett.* **2000**, *41*, 9053.
1015. Lam, P. Y. S.; Vincent, G.; Clark, C. G.; Deudon, S.; Jadhav, P. K. *Tetrahedron Lett.* **2001**, *42*, 3415.
1016. Lam, P. Y. S.; Vincent, G.; Bonne, D.; Clark, C. G. *Tetrahedron Lett.* **2003**, *44*, 4927.
1017. Collman, J. P.; Zhong, M.; Zeng, L.; Costanzo, S. *J. Org. Chem.* **2001**, *66*, 1528.
1018. Antilla, J. C.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 2077.
1019. Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 4397.
1020. Lan, J.-B.; Chen, L.; Yu, X.-Q.; You, J.-S.; Xie, R.-G. *Chem. Commun.* **2004**, 188.
1021. Lan, J.-B.; Zhang, G.-L.; Yu, X.-Q.; You, J.-S.; Chen, L.; Yan, M.; Xie, R.-G. *Synlett* **2004**, 1095.
1022. Sagar, A. D.; Tale, R. H.; Adude, R. N. *Tetrahedron Lett.* **2003**, *44*, 7061.
1023. Petrassi, H. M.; Sharpless, K. B.; Kelly, J. W. *Org. Lett.* **2001**, *3*, 139.
1024. McKinley, N. F.; O'Shea, D. F. *J. Org. Chem.* **2004**, *69*, 5087.
1025. Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 1381.
1026. Jung, M. E.; Lazarova, T. I. *J. Org. Chem.* **1999**, *64*, 2976.
1027. Wang, Y.-C.; Georghiou, P. E. *Org. Lett.* **2002**, *4*, 2675.
1028. Evans, D. A.; Katz, J. L.; Peterson, G. S.; Hintermann, T. *J. Am. Chem. Soc.* **2001**, *123*, 12411.
1029. Krenisky, P. J.; Boger, D. L. *Tetrahedron Lett.* **2002**, *43*, 407.
1030. Deng, H.; Jung, J.-K.; Liu, T.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 9032.
1031. Herradura, P. S.; Pendola, K. A.; Guy, R. K. *Org. Lett.* **2000**, *2*, 2019.
1032. Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2002**, *4*, 4309.
1033. Ishihara, K.; Yamamoto, H. *Eur. J. Org. Chem.* **1999**, 527.
1034. Ishihara, K.; Hanaki, N.; Yamamoto, H. *Synlett* **1993**, 577.
1035. Ishihara, K.; Funahashi, M.; Hanaki, N.; Miyata, M.; Yamamoto, H. *Synlett* **1994**, 963.
1036. Ishihara, K.; Hanaki, N.; Funahashi, M.; Miyata, M.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1721.
1037. Ishihara, K.; Kurihara, H.; Yamamoto, H. *Synlett* **1997**, 597.
1038. Ishihara, K.; Ohara, S.; Yamamoto, H. *J. Org. Chem.* **1996**, *61*, 4196.
1039. Ishihara, K.; Kuroki, Y.; Hanaki, N.; Ohara, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 1569.
1040. Kuroki, Y.; Ishihara, K.; Hanaki, N.; Ohara, S.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1221.
1041. Hayakawa, H.; Okada, N.; Miyazawa, M.; Miyashita, M. *Tetrahedron Lett.* **1999**, *40*, 4589.
1042. Furuta, K.; Maruyama, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1991**, *113*, 1041.
1043. Furuta, K.; Mouri, M.; Yamamoto, H. *Synlett* **1991**, 561.
1044. Ishihara, K.; Maruyama, T.; Mouri, M.; Gao, Q.; Furuta, K.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3483.
1045. Ishihara, K.; Mouri, M.; Gao, Q.; Maruyama, T.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 11490.
1046. Ishihara, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 1561.
1047. Ishihara, K.; Kurihara, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 3049.
1048. Ishihara, K.; Kondo, S.; Kurihara, H.; Yamamoto, H. *J. Org. Chem.* **1997**, *62*, 3026.
1049. Ishihara, K.; Kurihara, H.; Matsumoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1998**, *120*, 6920.
1050. Reilly, M.; Oh, T. *Tetrahedron Lett.* **1995**, *36*, 221.
1051. Ishihara, K.; Inanaga, K.; Kondo, S.; Funahashi, M.; Yamamoto, H. *Synlett* **1998**, 1053.
1052. Thormeier, S.; Carboni, B.; Kaufmmann, D. E. *J. Organomet. Chem.* **2002**, *657*, 136.
1053. Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651.
1054. Kinugasa, M.; Harada, T.; Egusa, T.; Fujita, K.; Oku, A. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 3639.
1055. Kinugasa, M.; Harada, T.; Oku, A. *J. Org. Chem.* **1996**, *61*, 6772.
1056. Kinugasa, M.; Harada, T.; Fujita, K.; Oku, A. *Synlett* **1996**, 43.
1057. Charette, A. B.; Prescott, S.; Brochu, C. *J. Org. Chem.* **1995**, *60*, 1081.
1058. Barrett, A. G. M.; Hamprecht, D.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1997**, *119*, 8608.
1059. Charette, A. B.; Lebel, H. *Org. Synth.* **1998**, *76*, 86.
1060. Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1986.
1061. Cho, B. T. *Aldrichim. Acta* **2002**, *35*, 3.
1062. Cho, B. T.; Chun, Y. S. *Tetrahedron: Asymmetry* **1992**, *3*, 341.
1063. Ramachandran, P. V.; Lu, Z.-H.; Brown, H. C. *Tetrahedron Lett.* **1997**, *38*, 761.
1064. Ramachandran, P. V.; Brown, H. C.; Pitre, S. *Org. Lett.* **2001**, *3*, 17.
1065. Beardsley, D. A.; Fisher, G. B.; Goralski, C. T.; Nicholson, L. W.; Singaram, B. *Tetrahedron Lett.* **1994**, *35*, 1511.
1066. Ramachandran, P. V.; Gong, B.; Brown, H. C. *J. Org. Chem.* **1995**, *60*, 41.
1067. Ramachandran, P. V.; Teodrović, A. V.; Brown, H. C. *Tetrahedron* **1993**, *49*, 1725.
1068. Chong, J. M.; Clarke, I. S.; Koch, I.; Olbach, P. C.; Taylor, N. J. *Tetrahedron: Asymmetry* **1995**, *6*, 409.
1069. Wang, Z.; La, B.; Fortunak, J. M. *Tetrahedron Lett.* **1998**, *39*, 5501.
1070. Wang, Z.; Zhao, C.; Pierce, M. E.; Fortunak, J. M. *Tetrahedron: Asymmetry* **1999**, *10*, 225.
1071. Meler, C.; Laux, W. H. G. *Tetrahedron: Asymmetry* **1996**, *7*, 89.
1072. Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 6518.
1073. Salunkhe, A. M.; Ramachandran, P. V.; Brown, H. C. *Tetrahedron* **2002**, *58*, 10059.
1074. Cho, B. T.; Chun, Y. S. *J. Org. Chem.* **1998**, *63*, 5280.
1075. Quallich, G. J.; Woodall, T. M. *Tetrahedron Lett.* **1993**, *34*, 785.
1076. Burgess, K.; Prote, A. M. *Angew. Chem., Int. Ed.* **1994**, *33*, 1182.

1077. Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1995**, *36*, 9153.
1078. Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1996**, *37*, 5675.
1079. Masui, M.; Shioiri, T. *Synlett* **1997**, 273.
1080. Salunkhe, A. M.; Burkhardt, E. R. *Tetrahedron Lett.* **1997**, *38*, 1523.
1081. Torrens, A.; Castrillo, J. A.; Claparols, A.; Redondo, J. *Synlett* **1999**, 765.
1082. Xu, J.; Su, X.; Zhang, Q. *Tetrahedron: Asymmetry* **2003**, *14*, 1781.
1083. Huertas, R. E.; Corella, J. A.; Soderquist, J. A. *Tetrahedron Lett.* **2003**, *44*, 4435.
1084. Bringmann, G.; Hinrichs, J. *Tetrahedron: Asymmetry* **1997**, *8*, 4121.
1085. Bringmann, G.; Hinrichs, J.; Kraus, J.; Wuzik, A.; Schulz, T. *J. Org. Chem.* **2000**, *65*, 2517.
1086. Ostendorf, M.; Romagnoli, R.; Pereiro, I. C.; Roos, E. C.; Moolenaar, M. J.; Speckamp, W. N.; Hiemstra, H. *Tetrahedron: Asymmetry* **1997**, *8*, 1773.
1087. Berenguer, R.; Garcia, J.; Vilarrasa, J. *Tetrahedron: Asymmetry* **1994**, *5*, 165.
1088. Cho, B. T.; Chun, Y. S. *Tetrahedron: Asymmetry* **1992**, *3*, 1539.
1089. Cho, B. T.; Ryu, M. H. *Bull. Kor. Chem. Soc.* **1994**, *15*, 191.
1090. Dixon, R. A.; Jones, S. *Tetrahedron: Asymmetry* **2002**, *13*, 1115.
1091. Hong, Y.; Gao, Y.; Nie, X.; Zepp, C. M. *Tetrahedron Lett.* **1994**, *35*, 6631.
1092. Hett, R.; Stare, R.; Helquist, P. *Tetrahedron Lett.* **1994**, *35*, 9375.
1093. Hett, R.; Fang, Q. K.; Gao, Y.; Hong, Y.; Butler, T.; Nie, X.; Wald, S. A. *Tetrahedron Lett.* **1997**, *38*, 1125.
1094. Hett, R.; Senanayake, H.; Wald, S. A. *Tetrahedron Lett.* **1998**, *39*, 1705.
1095. Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *31*, 611.
1096. Corey, E. J.; Link, J. O. *Tetrahedron Lett.* **1992**, *33*, 3431.
1097. Corey, E. J.; Link, J. O.; Bakshi, R. K. *Tetrahedron Lett.* **1992**, *33*, 7107.
1098. Corey, E. J.; Link, J. O. *J. Am. Chem. Soc.* **1992**, *114*, 1906.
1099. Mellin-Morlière, C.; Aitken, D. J.; Bull, S. D.; Davies, S. G.; Husson, H.-P. *Tetrahedron: Asymmetry* **2001**, *12*, 149.
1100. Cho, B. T.; Yang, W. K.; Choi, O. K. *J. Chem. Soc., Perkin Trans.* **2001**, *1*, 1204.
1101. Cho, B. T.; Chun, Y. S. *J. Chem. Soc., Perkin Trans.* **1999**, *1*, 2095.
1102. Yadav, J. S.; Reddy, T.; Hashim, S. R. *Synlett* **2000**, 1049.
1103. Meier, C.; Laux, W. H. G. *Tetrahedron: Asymmetry* **1995**, *6*, 1089.
1104. Meier, C.; Laux, W. H. G. *Tetrahedron* **1996**, *52*, 589.
1105. Cho, B. T.; Kim, D. J. *Tetrahedron: Asymmetry* **2001**, *12*, 2043.
1106. Cho, B. T.; Choi, K. O.; Kim, D. J. *Tetrahedron: Asymmetry* **2002**, *13*, 697.
1107. Bach, J.; Berenguer, R.; Farràs, J.; Garcia, J.; Meseguer, J.; Vilarrasa, J. *Tetrahedron: Asymmetry* **1995**, *6*, 2683.
1108. Kurosu, M.; Kishi, Y. *J. Org. Chem.* **1998**, *63*, 6100.
1109. McMorris, T. C.; Staake, M. D. *J. Org. Chem.* **2002**, *67*, 7902.
1110. Simpson, A. F.; Szeto, P.; Lathbury, D. C.; Gallagher, T. *Tetrahedron: Asymmetry* **1997**, *8*, 673.
1111. Simpson, A. F.; Bodkin, C. D.; Butts, C. P.; Armitage, M. A.; Gallagher, T. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 3047.
1112. Parker, K. A.; Ledeboer, M. W. *J. Org. Chem.* **1996**, *61*, 3214.
1113. Bach, J.; Berenguer, R.; Garcia, J.; Loscertales, T.; Vilarrasa, J. *J. Org. Chem.* **1996**, *61*, 9021.
1114. Helal, C. J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 10938.
1115. Alemany, C.; Bach, J.; Farràs, J.; Garcia, J. *Org. Lett.* **1999**, *1*, 1831.
1116. Quallich, G. J.; Keavey, K. N.; Woodall, T. M. *Tetrahedron Lett.* **1995**, *36*, 4729.
1117. Prasad, K. R. K.; Joshi, N. N. *J. Org. Chem.* **1996**, *61*, 3888.
1118. Aldous, D. J.; Dutton, W. M.; Steel, P. G. *Tetrahedron: Asymmetry* **2000**, *11*, 2455.
1119. Shimizu, M.; Yamada, S.; Fujita, Y.; Kobayashi, F. *Tetrahedron: Asymmetry* **2000**, *11*, 3883.
1120. Lin, C.-W.; Lin, C.-C.; Li, Y.-M.; Chan, A. S. C. *Tetrahedron Lett.* **2000**, *41*, 4425.
1121. Tillyer, R. D.; Boudreau, C.; Tschaen, D.; Dolling, U.-H.; Reider, P. J. *Tetrahedron Lett.* **1995**, *36*, 4337.
1122. Masui, M.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 5195.
1123. Shimizu, M.; Tsukamoto, K.; Matsutani, T.; Fujisawa, T. *Tetrahedron* **1998**, *54*, 10265.
1124. Shimizu, M.; Kamei, M.; Fujisawa, T. *Tetrahedron Lett.* **1995**, *36*, 8607.
1125. Sakai, T.; Yan, F.; Kashino, S.; Uneyama, K. *Tetrahedron* **1996**, *52*, 233.
1126. Cho, B. T.; Ryu, M. H.; Chun, Y. S.; Dauelsberg, C.; Wallbaum, S.; Martens, J. *Bull. Kor. Chem. Soc.* **1994**, *15*, 53.
1127. Dougherty, J. T.; Flisak, J. R.; Hayes, J.; Lantos, I.; Liu, L.; Tucker, L. *Tetrahedron: Asymmetry* **1997**, *8*, 497.
1128. Sailes, H. E.; Watts, J. P.; Whiting, A. *J. Chem. Soc., Perkin Trans.* **2000**, *1*, 3362.
1129. Fontaine, E.; Namane, C.; Meneyrol, J.; Gealin, M.; Serva, L.; Roussey, E.; Tissandié, S.; Maftouh, M.; Roger, P. *Tetrahedron: Asymmetry* **2001**, *12*, 2185.
1130. Krzemiński, M. P.; Zaidlewicz, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1463.
1131. Kirton, E. H.; Tughan, G.; Morris, R. E.; Field, R. A. *Tetrahedron Lett.* **2004**, *45*, 853.
1132. Ling, I.; Podányi, B.; Hámori, T.; Sólyom, S. *J. Chem. Soc., Perkin Trans.* **1995**, *1*, 1423.
1133. Kang, J.; Kim, J. B.; Cho, K. H.; Cho, B. T. *Tetrahedron: Asymmetry* **1997**, *8*, 657.
1134. Hajipour, A. R.; Hantehzadeh, M. *J. Org. Chem.* **1999**, *64*, 8475.

9.06 Aluminum

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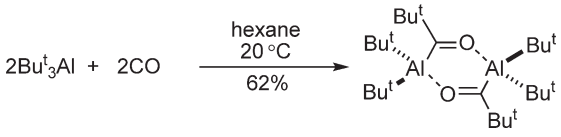
9.06.1 Introduction

Modern aluminum organometallic chemistry began in earnest with the pioneering work of Ziegler in the 1950s.[1] He was the first to synthesize alkylaluminum reagents directly from aluminum metal, olefins, and hydrogen. With only modest changes, this reaction is still used industrially to manufacture detergents. Ziegler also discovered that the "ate complex" lithium tetraethylaluminate ($Et_3Al + EtLi$) was an active catalyst for the oligomerization of ethylene, and shortly thereafter he realized that titanium dramatically accelerated the reaction and produced polyethylene. The astonishing discoveries that the ate complex showed potential reactivity, and especially, that alkylaluminums could activate transition metals for the polymerization of olefins, revolutionized polymer chemistry and made researchers around the world suddenly aware of the utility and potential importance of organoaluminums. In fact, subsequent studies disclosed that aluminum alkyls are highly reactive with a variety of simple molecules including oxygen, water, carbon dioxide, hydrogen, and alkenes.[2–5] Very recently, it was shown that even carbon monoxide inserted into Bu^t–Al bonds at 20 °C[6] (Equation (1)) on the basis of the earlier observation that increased Me_3Al monomer concentration resulted in increased formation of the $Me_3Al\cdots(O{=}C)$ complex at 15–35 K.[7] Investigation of the fundamental reactivity has led to the development of commercially important aluminum alkyl catalysts and co-catalysts for polymerization of higher olefins,[8,9] dienes,[10] epoxides,[11,12] as well as for the production of linear terminal alkenes and alcohols.[2–5,13]



(1)

In view of the established technology base concerning aluminum alkyls and the state-of-the-art of aluminum reagents in organic and polymerization processes, organoaluminum compounds have undoubtedly been among the most thoroughly investigated organometallics, in turn expanding their scope in catalytic applications and even in material science[14–19] over only a few decades. A recent SciFinder search of "organoaluminum" since 1993 produced more than 6500 citations of new publications. This number includes more than 4500 patents issued since then and 1800 scientific publications from academia and this result clearly forecasts organoaluminum significance in industry due to commercial availability as bulk chemicals. Alkylaluminum reagents are readily prepared from oil byproducts and are generally inexpensive, serving as polymerization catalysts, ceramic precursors, and specialty chemicals in electronic device fabrication. By 1967, organoaluminum compounds were available in 100 000 lb lots at a cost of $1 per pound. It is therefore not surprising that both general and specialized interests in organoaluminums will continue to experience growth in the next half century in both industry and academia, as well as much further research to establish the fundamentals regarding their chemical and physical properties. The major advances made in organoaluminum chemistry until ~2000 have been well summarized in several reviews and monographs. Some cover the more synthetic aspects of utilizing aluminum reagents in organic synthesis,[20–27] and an extremely broad range of the structural and coordinative properties of aluminum species has been accumulated.[28–32] In particular, Professor Eisch's contributions made in the previous COMC (1982) and COMC (1995)[3–5] are deserving of appreciation. It is strongly recommended that readers refer back to those clear-cut outlines which cover the historical, more fundamental, and even advanced aspects of organoaluminum chemistry under scrutiny from the 1950s to 1993.

A number of scientific and industrial works have been dealing with the research and development (R & D) of polymerization technology and material applications in the field of aluminum chemistry, the details of which are excluded as much as possible unless otherwise notable features are found. These came out during the period 1993–2004, encompassing more than 3000 patents and papers. Recent developments in this area, especially during this period, constitute the main focus of this chapter. Over 300 scientific papers are surveyed, chosen carefully from more than 1800 scientific papers, which the author considered to be deserving of particular mention due to their presentation of the most valuable issues. Emphasis is placed more on applied aspects, rather than fundamentals. These include the specialized topics that are notable for novelty and significance in: the bonding and structural features of the aluminum atom in relation to its catalytic activity, the mechanism of formation and reaction of organoaluminum species, and those properties applied in organic and polymer synthesis.

It is highly likely that the three broad areas of improved aluminum chemistry, that is, novel catalysis, functional materials, and biological studies, will see substantial activity in the future. This will be the result of a further understanding of organoaluminum chemistry, not only from an advanced synthesis perspective in conjunction with elucidation of reactivity, structural, and physical features, but also against the environmentally and biologically important practice of the scattering of inorganic aluminum wastes, which has been receiving significant attention of late.[29]

9.06.2 Basic Bond Properties of Organoaluminum Compounds

9.06.2.1 Aluminum–Carbon Covalent and Non-covalent Bonds

9.06.2.1.1 Aluminum(III)–carbon interactions

Progress in the theoretical and experimental chemistry of organoaluminum compounds requires knowledge of their physiochemical properties, which is based either on reliable experimental data or on empirical relationships. The characteristic features of aluminum(III) reagents are generally derived from the high Lewis acidity of organoaluminum monomers, which feasibly leads to the dimeric, trimeric, and even higher oligomeric structures. Heteroatom-containing solvents such as Et_2O and THF coordinate to an aluminum atom, allowing preferential formation of the monomeric tetracoordinate aluminum complex. The formation of higher coordinates (penta-, hexa-, and even higher coordinates) also results in special cases. In contrast, in hydrocarbon solvents, coordination of solvent is minimal and self-association of the organoaluminums is more significant.

The temperature- and solvent-dependent reactivity of organoaluminum compounds has been described in detail,[33] where the association behavior of Me_3Al in toluene at variable temperatures was illustrated. At −55 °C, the ratio between bridged methyl and terminal methyl was found to be 1 : 2, that is, most of the Me_3Al has the dimeric structure. With an increase in temperature, the methyl groups start rapidly exchanging and the NMR signals randomize, while the two distinct resonance peaks of the methyl groups are maintained. At −35 °C, the set of signals coalesced into a single broad peak and were no longer distinguishable at higher temperatures. Even at room temperature (RT), the vacant *p*-orbital of an aluminum atom may be occupied and relatively unavailable for reaction. Unlike most aluminum alkyls for which dimerization is strongly favored, *t*-Bu_3Al is a monomer even at RT (Figure 1).[34] Recent ebullioscopic studies of Me_3Al and Et_3Al clearly showed that these compounds are associated even in vapor. Up to 60% of Me_3Al is associated at 413 K, and 12% of Et_3Al, at 423 K.[35] Another study showed that upon heating of dimeric Me_3Al at 573 K, a 200 : 1 ratio of monomer to dimer resulted in the deposited matrix.[7] The stability of the dimer Al_2Me_6 was even measured in the gas phase, with an enthalpy of approximately 20 kcal mol^{-1} in favor of the dimeric form.[2] The degree of association of trialkylaluminums in vapor sharply decreases with increasing alkyl chain length. At low pressure and high temperature, the monomeric form predominates.[2] Additional thermodynamic and thermochemistry investigations thoroughly checked the accuracy and reliability of previous data on the vaporization of organoaluminum compounds, and estimated the dissociation energies of Al–R covalent bonds (E_g = 288.6 (Al–Me); 272.5 (Al–Et); 273.1 (Al–Pr); 280.3 (Al–Bu) kJ mol^{-1}).[36]

Analogous to Al–Me–Al bonding, Al–Me–M-type bonding (M = Sm,[37] Zr,[38] Y[39]) is commonly seen in a number of the XRD structures of the corresponding heterobimetallic compounds (Figure 2). The Al–Me–Ti bond in Cp_2TiCl_2–Me_3Al (μ-chlorobis(cyclopentadienyl)(dimethylaluminum)-μ-methylenetitanium)[40,41] is well known to easily decompose into an Al–(CH_2)–Ti species, and further into the CH_2=$TiCp_2$ formation (Figure 3). Those reactivity properties have been well featured in the synthetic application of the Tebbe reagent, which was originally devised for the

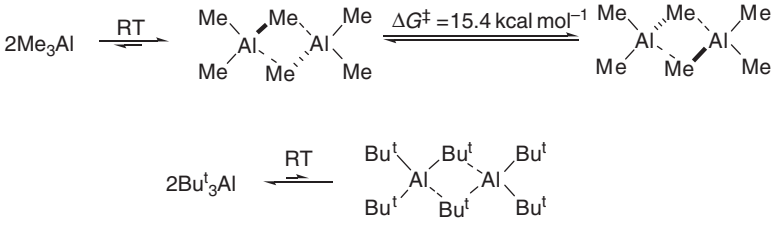


Figure 1 Equilibrium between trialkylaluminum monomer and dimer.

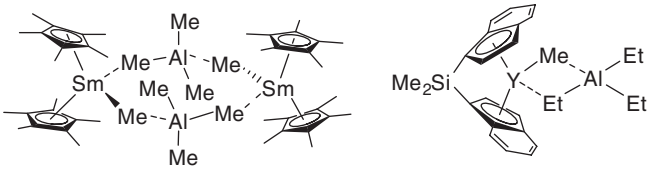


Figure 2 Al–Me–M (M = Sm, Y) bonds.

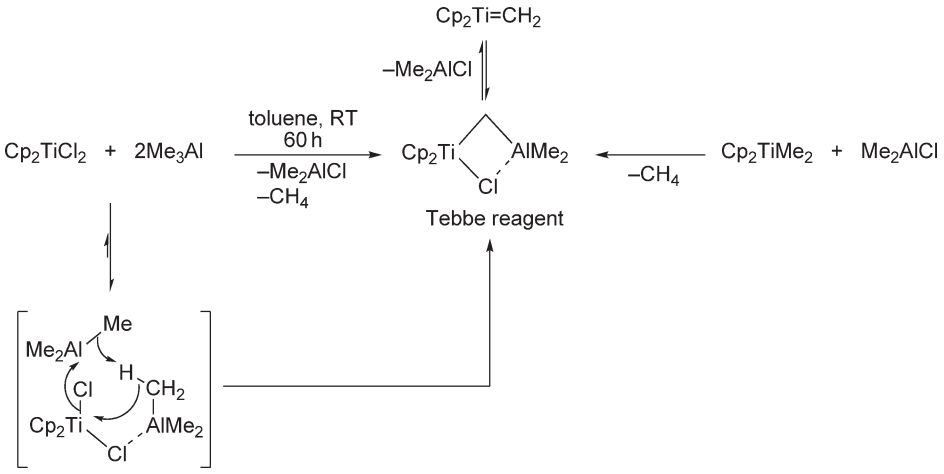


Figure 3 Synthesis of the Tebbe reagent.

metathesis of terminal olefins and the olefination of carbonyl (C═O) groups, and which recently found expanded scope in the metathesis of P═O, S═O, and Se═O groups (Figure 4).[42] Hence the Tebbe reagent is often represented as a "protected" alkylidene complex, that is, a weak complex between $ClAlMe_2$ and $Cp_2Ti{=}CH_2$, such as in **1** (Figure 5). However, ^1H NMR results are more suggestive of a cyclic structure **2**. A structural model for the Tebbe reagent, $ClAlH_2/H_2Ti{=}CH_2$, has been calculated theoretically and shows the Lewis acid $ClAlH_2$ to be strongly bound to the titanium alkylidene, rather than, as often represented, only weakly associated.[43] A similar cyclic structure was found in a related compound consisting of a methylalumoxane (MAO) and *ansa*-titanocene complex (Figure 6).[44]

Although carbenes and their transition metal complexes, as well as their bonding properties, have attracted considerable attention recently,[45] there are few reports of 13-group adducts of carbenes involving characteristic

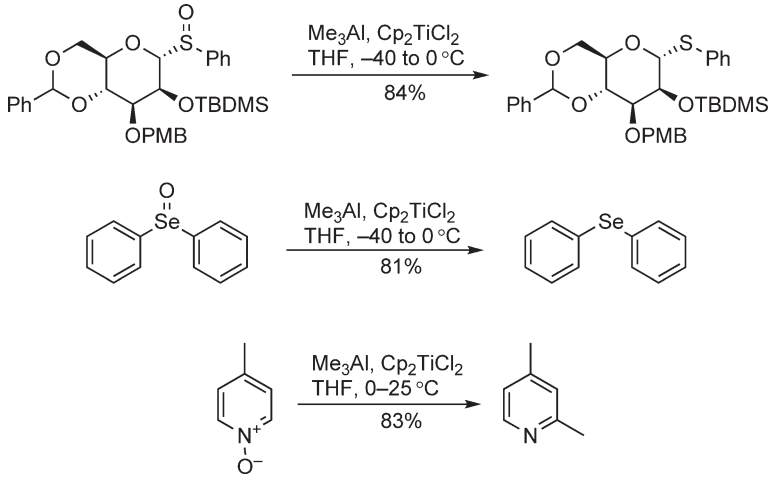


Figure 4 Tebbe reagent in deoxygenation reactions.

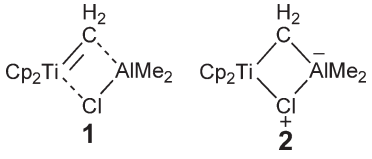


Figure 5 Two different candidates for the structures of the Tebbe reagent.

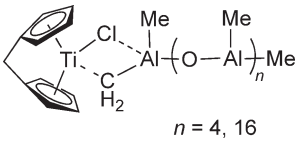


Figure 6 MAO–*ansa*-titanocene complex.

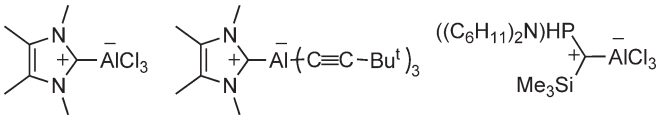
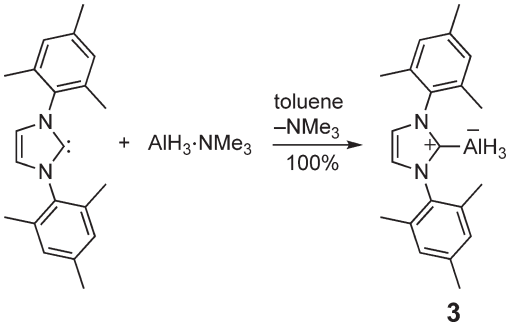


Figure 7 Aluminum–carbene complexes.

Al–C bonds. A preliminary high-yield synthesis and characterization of a stable *N*-heterocyclic carbene bound to an aluminum atom was accomplished in 1992.[46] The aluminum carbene adduct 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene–AlH_3 **3** was obtained by treatment of 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene with $Me_3N{\cdot}AlH_3$ in toluene (Equation (2)). Thus, carbene adduct **3** is more stable than the corresponding Me_3N adduct. The ^{13}C NMR signal for the C_2 of **3** appears at δ 175.3, substantially upfield from the free carbene (δ 219.7 ppm). The ^{27}Al NMR resonance of δ 107 for **3** is typical of four-coordinate aluminum species. These resonances suggest an electronic structure for the imidazole fragment, which is intermediate between the free carbene and the fully delocalized imidazolium ion. The C(carbene)–Al distance is 2.034(3) Å, which is slightly longer than the Al–C(terminal) distance of 1.958 Å observed for $AlPh_3$. Roesky[47,48] and Bertrand[49] recently reported the carbene adducts of $AlCl_3$ and $Al(C{\equiv}CBu^t)_3$ (Figure 7). The former has an Al–C(carbene) distance of 2.009(5) Å, which is slightly shorter than the 2.051(2) Å of the latter.



(2)

Roesky studied in depth the properties of Al–alkynyl covalent bonds using the XRD structures of several alkynylaluminum compounds.[48] In the IR spectra of all alkynylaluminum compounds, a sharp absorption band was observed around 2100 cm^{-1}, which can be ascribed to the $\nu(C{\equiv}C)$ stretching frequency. Of particular interest is the fact that the geometry of the aluminum atom varies from tetrahedral to trigonal bipyramidal by simply changing one of the three alkynyl substituents on aluminum to a more electron-withdrawing bromo group (Figure 8). In contrast with the previously reported π-complex dimer[50] or oligomer[51] of the alkynylaluminum complex (Figure 8),

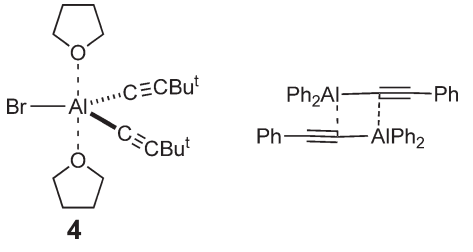


Figure 8 Aluminum–alkyne σ and π bonds.

noncovalent interaction of THF, dioxane, or Me_3N with an aluminum atom allowed isolation of monomeric structures such as **4**. Al–alkenyl bonds have been synthesized extensively through carboalumination and hydroalumination processes and ^{13}C NMR data of the corresponding alkenylaluminum compounds have accumulated in the recent literature.[52]

9.06.2.1.2 Al(0)– or Al(I)–carbon interactions

The absorption of unsaturated organic molecules such as benzene or olefins on Al metal surface has become the subject of intense scrutiny because of the growing technological importance of a microscopic understanding of the interactions and bonding mechanisms in organic substrate–metal interfaces. In addition, fundamental investigations of the relatively weak interaction between Al^+ and hydrocarbons could predict the potential reactivity of the more positive aluminum species, and could provide insight into how they could be utilized in the activation of organic molecules, which definitely provides a new avenue to organic synthesis.

The structure and bond-dissociation energies (BDEs) for Al(methane)$^+$, Al(acetylene)$^+$, Al(ethene)$^+$, and Al(ethane)$^+$ have been determined using both the *ab initio* calculations using post-HF methods MP2, MP4, and QCISD(T) with polarization and diffuse functions and Fourier-transform ion cyclotron resonance (FTICR) mass spectrometry.[53] The *ab initio* results indicate the following 300 K data: BDE(Al^+–methane) = 5.2, BDE(Al^+–acetylene) = 13.2, BDE(Al^+–ethene) = 13.6, BDE(Al^+–ethane) = 8.4 (end-on), and BDE(Al^+–ethane) = 8.5 kcal mol^{-1} (side-on). According to the results of the FTICR experiments, the Al^+–ligand BDE values increase in the following order: $Al^+–CH_4 < Al^+–C_2H_6 < Al^+–C_2H_4 < Al^+–C_2H_2$. Compared to the literature data of several transition metal ion (e.g., $M^+ = Co^+$, Fe^+, Zr^+, Nb^+) complexes (ca. 15–22 kcal mol^{-1} for $M^+–CH_4$; ca. 57–59 kcal mol^{-1} for $M^+–C_2H_2$; 15–28 kcal mol^{-1} for $M^+–C_2H_6$), the BDE values for the aluminum ions are lower in general. Two effects are considered to be responsible for the difference between these absolute BDE data. One is that the classical π-MO backdonation from Al^+ to the empty antibonding (σ^*-) orbitals of each hydrocarbon ligand does not exist due to the unoccupied π-orbital of Al^+. The second effect results from the Pauli repulsion due to the filled Al^+ *s*-orbital, resulting in an increased Al^+–hydrocarbon distance and a less efficient overlap of bonding orbitals. Although the slight discrepancy of the BDE ordering with regard to Al^+–ethane and Al^+–acetylene was also obtained in other theoretical studies,[54] the experimental results are, in general, comparable to the theoretical. The bonding, structure, and vibrational properties of the Al–C_2H_4 complex (Al(C_2H_4)) have also been investigated theoretically by Bouteiller using a DFT approach.[55] It has been found that this complex is π-bonded in its ground state, with $^2B_2$ electronic symmetry and C_{2v}-structure, in which the ethane geometry is largely altered. From topological charge density studies, it was proposed, on the one hand, that the bonding between Al and C_2H_4 belongs to the unshared electron interaction and therefore corresponds to a mostly electrostatic interaction and, on the other hand, that the electron density in the valence shell of the aluminum region is pushed away from C_2H_4. As for Al(C_2H_4), several bonding schemes are suggested by Kasai (Figures 9(a)–9(d)),[56] Manceron (9(b), 9(c), and 9(e)),[57] and Bouteiller.[55] The difference in bonding properties between Al(C_2H_4) and Al(C_2H_4)$^+$ was reinvestigated more recently.[58] The binding in Al(C_2H_4)$^+$ is due to a σ-bond between the ethylene π-bond and an empty 3*p*-orbital on aluminum (Figure 9(f)). In Al(C_2H_4), the dominant interaction is due to the same σ-bond with an additional contribution from a singly occupied π-bond formed between the occupied aluminum 3*p*-orbital and the ethane π^*-orbital (Figure 9(g)). The weakness of the bonding interaction of the Al–unsaturated hydrocarbon, compared to the bonding with transition metals, was similarly demonstrated by another experiment along with theoretical studies, in which the adsorption behavior of benzene

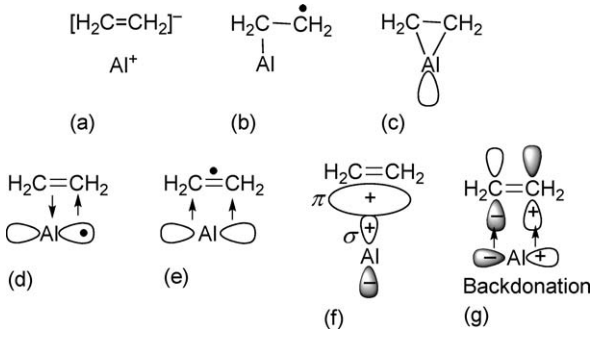


Figure 9 Possible variation in Al(0)– and Al(I)–ethylene interactions.

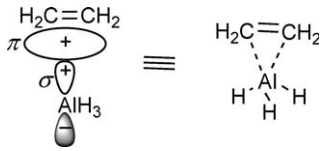


Figure 10 Al(III)–ethylene interaction.

on an Al(111) surface was evaluated using angle-resolved ultraviolet photoelectron, high resolution electron energy loss, thermal desorption spectroscopies, and work function measurements, as well as DFT calculations.[59] The experimental observation that only small changes in electronic and vibrational structure of benzene occur on adsorption was supported by DFT calculations. It was also strongly suggested that the aromatic ring is oriented parallel to the Al surface, but the main bonding mechanism is the mutual polarization of adsorbate and substrate. The adsorption of isolated C_2H_4 molecules onto Al(100) was calculated in a different way, but no chemical binding was observed although physisorption was predicted. The addition of an aluminum atom (Al(0)) to an ethene[60] or an allene compound[61] was investigated using ESR and EPR techniques. In addition to the theoretical studies on the interactions of Al(0) or Al(I) species with olefins, *ab initio* calculations were used to characterize the validity of π-complexes formed between trivalent aluminum (Al(III)) species and alkenes[62,63] (Figure 10) or alkynes.[64] Features of the interactions of Al(III) in the formation of π-allylaluminum hydrides were substantiated using EPR studies.[65]

9.06.2.2 Aluminum–Halogen Covalent and Non-covalent Bonds

Al–halogen covalent bond energy decreases in the order Al–F > Al–Cl > Al–Br > Al–I.[66] Of the halides, the bonding properties of weak non-covalent interactions in organoaluminum chloride dimers have been the most widely investigated. Alkylaluminum chlorides are dimeric in vapor and in liquid. Al–Et–Al bridging bonds in Et_3Al are weaker than similar bonds in alkylaluminum chlorides: E_g(Al–Et–Al) (33.1 kJ mol^{-1}) < E_g (Al–Cl–Al) (58.6 kJ mol^{-1}) (the latter value was taken as being equal to the dissociation energy of the $AlCl_3$ dimer (117.2 kJ mol^{-1})).[67] In addition, the bonding and structural features of organoaluminum(halide) complexes were investigated by experimental far-infrared spectroscopy, combined with quantum simulations.[68] The experimental and calculated far-infrared spectra agree very well, holding promise for the far-infrared/quantum simulation approach employed to reveal more detail on the catalytically active site in Ziegler–Natta catalysis. Hartree–Fock calculations support the previous conclusions that the dimer of $Me_{n-3}AlCl_n$ ($n = 1-3$) is consistently more stable than the corresponding monomers by 18.6 kcal mol^{-1} (78 kJ mol^{-1}) for $MeAlCl_2$, 19.2 kcal mol^{-1} for Me_2AlCl, and 18.3 kcal mol^{-1} for $AlCl_3$. Participation of two chloro groups in the bridging events significantly stabilizes the dimeric structure, while bridging by a methyl group reduces the stability (Figure 11). If both methyl groups take part in the self-bridging of $2MeAlCl_2$, destabilization by 1.2 kcal mol^{-1} occurs as compared to the separated monomers.

The Al–F covalent and dative bonds were thoroughly investigated by Roesky through their synthesis, and their versatile bonding features were highlighted in his excellent review.[69,70] Recent theoretical methods revealed that peroxo compounds of aluminum, such as $F_2Al(\mu\text{-}\eta^2\text{:}\eta^2\text{-}O_2)AlF_2$, are stabilized by covalent Al–F bonds (Figure 12).[71] Organoaluminum complexes comprising Al–F—Zr^+ dative bonds are particularly intriguing subjects for the study of the molecular basis of polymerization catalysis (Equation (3)).[72] Tertiary alkyl fluorides are likely to be activated

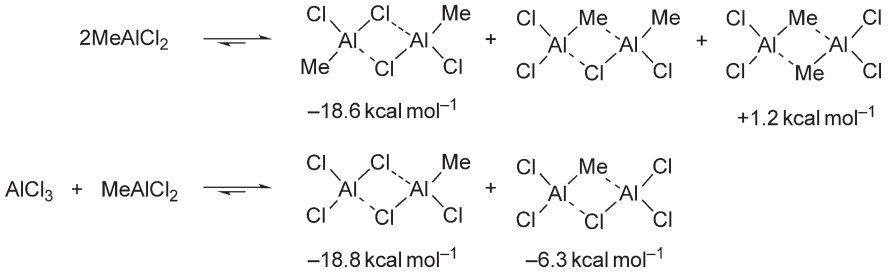


Figure 11 Al–Cl bonds in alkylaluminum chlorides.

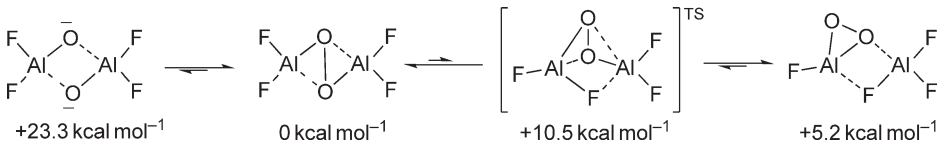
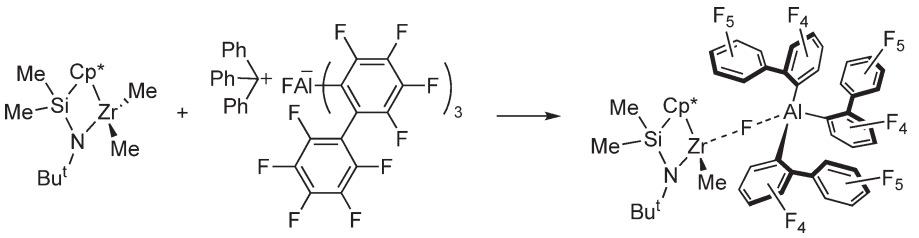


Figure 12 Peroxoaluminum compounds stabilized by Al–F bonds.

upon coordination of both stoichiometric and catalytic amounts of alkylaluminum compounds, as evidenced by the substitution reaction with several nucleophiles (Equation (4)).[73]



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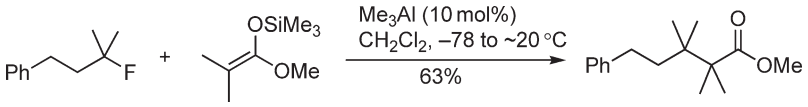


(4)

9.06.2.3 Aluminum(III)–Oxygen Covalent and Non-covalent Bonds

It has been well recognized that a combination of Al–O covalent and non-covalent interactions leads to extremely complex molecular aggregates of aluminum alkoxide species.[74–79] These aggregates provide structural diversity and disproportionation dynamics, in which it is difficult to identify and predict the most stable structure. Raman spectroscopy was used to determine the dominant structure of a sequential family of organo(alkoxy)aluminum compounds.[80] A series of samples varying in ligand composition and location, prepared via a redistribution reaction between different ratios of tri-*t*-butoxyaluminum and Me_3Al, was surveyed (Figure 13). An average structure of the general formula $Al_2(OBu^t)_nMe_{6-n}$ ($n = 1-5$) was correlated with the typical signals (904 cm^{-1} peak from the stretching of terminal Bu^tO groups; 921 cm^{-1} peak from the stretching of bridging OBu^t groups, etc.)

Although this type of complex aggregates fulfills the vacant *p*-orbital of aluminum, thereby significantly reducing its Lewis-acidic character, intramolecularly oxygen-stabilized organoaluminum is monomeric, frequently adopting pentacoordinate structure with respect to the aluminum atom (Figure 14),[81,82] and thus it could be a strong catalyst candidate. In conjunction with the development of efficient co-catalysts for Ziegler–Natta olefin polymerization, a series of this class of organoaluminum compounds was synthesized and applied in $TiCl_4$-catalyzed ethylene polymerization.[82] The incorporation of coordinating oxygen functionalities into the ligand systems of the organoaluminum complexes

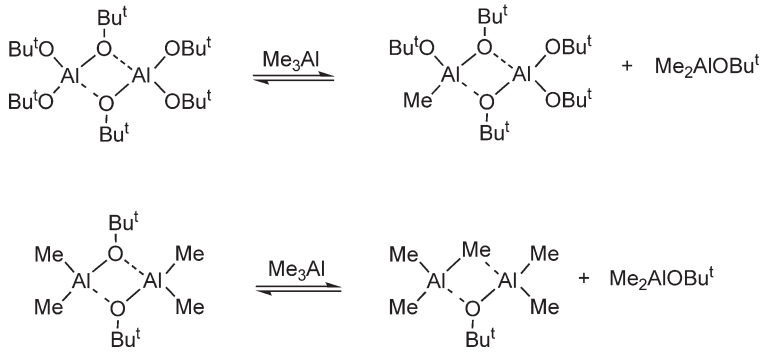


Figure 13 Al–O covalent and dative bonds in alkoxyaluminum dimers.

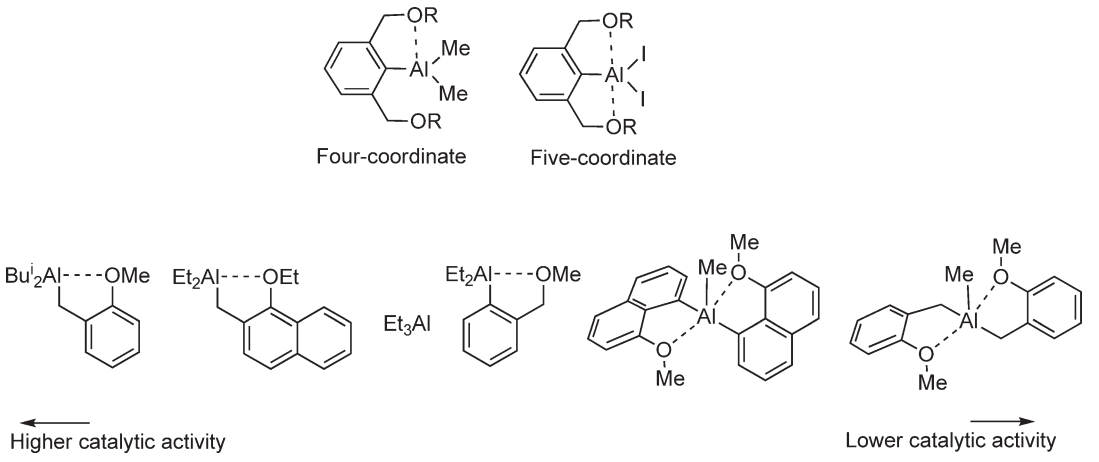
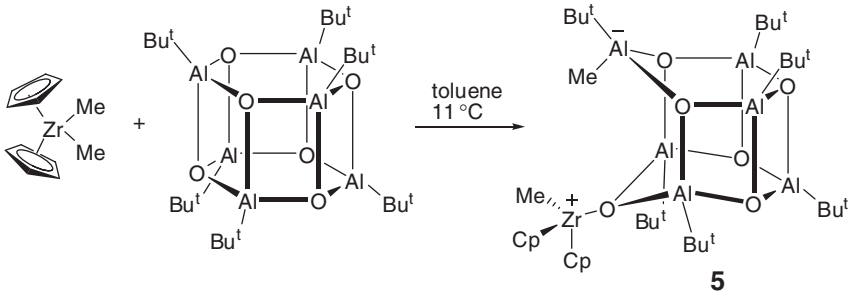


Figure 14 Intramolecular Al–O dative bonds and their influence on the order of catalytic activity.

causes a significant increase in co-catalytic activity (Figure 14). Some of these, in which the oxygen atom is directly bound to an aromatic ring system, showed an activity even higher than that of Et_3Al. Modifications of the donor groups yield an expected trend: the oxygen atom of aryl ethers provides weaker binding than alkyl ethers in Al···O dative bonds. It is thus reasonable to ascribe the highest reactivity to the electronic environment of aluminum, where the oxygen atom is most weakly bound to the aluminum atom. This might allow for an alternative route to either tetra- or pentacoordinate complex. In the case of propene polymerization using the $MgCl_2/TiCl_4$ catalyst system, the most active co-catalyst (Figure 14) showed results comparable to those obtained by Et_3Al.[83]

Alternating covalent and non-covalent bonds as seen in the Al–O···Al unit constitute the basic components of methylalumoxane (MAO) and other alkylalumoxane derivatives. The general scope of their preparation, as well as the basic aspects and the rich variety of dynamic behavior of Al–O···Al linkages, have been well summarized in COMC (1995). Despite the great importance of MAO as co-catalyst for olefin polymerization, its structure is essentially elusive.[84,85] Although the identification of a structural and reactivity relationship between MAO and much simpler alkylalumoxane derivatives[86] has been a concern for over 30 years, many unsolved problems still remain. Recent results from Barron's group published in 1995[87] (preliminarily in 1993[88] and 1994[89]) on the structure of oligomers of tetra-*t*-butyldialumoxane and *t*-butylalumoxanes are probably best viewed in this light. Using ^{1}H NMR measurements, structure **5** was proposed to be formed when $[(Bu^t)Al(\mu_3\text{-}O)]_6$ and Cp_2ZrMe_2 were mixed in a 1 : 1 ratio (Equation (5)). Unlike $[(Bu^t)_2Al\{\mu\text{-}OAl(Bu^t)_2\}]_2$, $[(Bu^t)Al(\mu_3\text{-}O)]_7$ **6** and $[(Bu^t)Al(\mu_3\text{-}O)]_9$ **7** are also active co-catalysts for the polymerization of ethylene (Figure 15). In this view, the terminal unit of the alumoxane, and even that of MAO, might be responsible for the co-catalytic activity. However, except for the $[(Bu^t)Al(\mu_3\text{-}O)]_6$ species forming **5**, it was impossible to characterize any compounds, formed from the interaction with Cp_2ZrMe_2. The formation of an alumoxane cage structure is highly dependent upon reaction conditions: when trioxane structure **8** is heated in boiling hexane on a small scale (1.5 g), it yields three compounds **6, 7,** and **9**. The latent catalytic activity underlying the compound diversity is obvious, but what the electronic basis would be for the actual catalytic unit in those alkylalumoxanes remains totally unclear. Structure **10** was proposed to be most responsible for the substantial reactivity of MAO.[90,90a] The alumoxane hydroxides **11** represent the first structural characterization of an alkylalumoxane, in which all the aluminum centers adopt a distorted five-coordinate geometry.[91]



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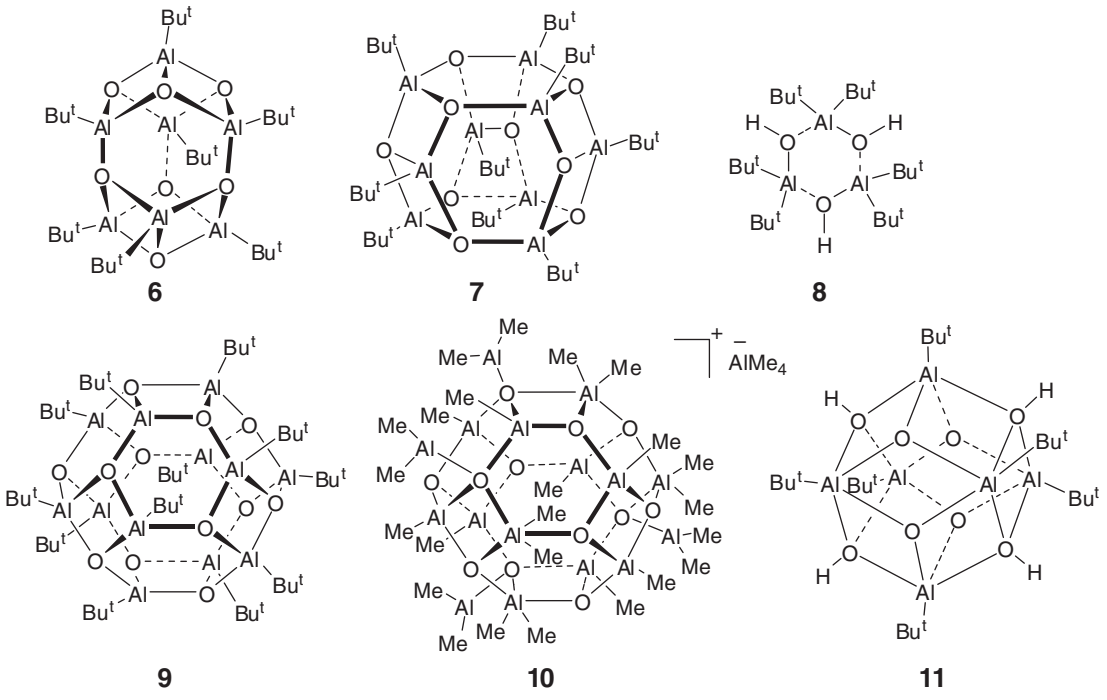
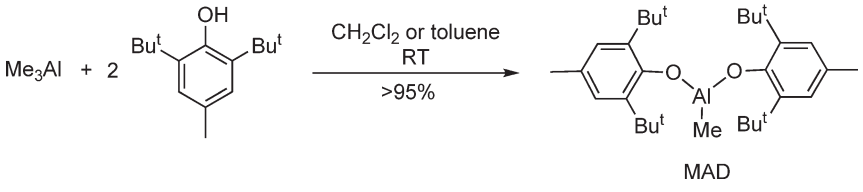


Figure 15 Various structures of MAO.

Unlike the unpredictable structural diversity in complex aggregates of alumoxanes and relatively small organoaluminum alkoxides, bulky aluminum aryloxides tend to form monomeric structures even in solution and in the solid state. For example, monomeric methylaluminum bis(2,6-di-*t*-butyl-4-methylphenoxide) (MAD)[92] (Equation (6)) and aluminum tris(2,6-diphenylphenoxide) (ATPH)[93] (Equation (7)) were isolated as pale yellow solids from hydrocarbon solvents. These reagents are readily prepared by treatment of Me_3Al with 2 and 3 equiv. of the corresponding phenol, respectively. In contrast, the steric requirement of methylaluminum bis(2,6-diphenylphenoxide) (MAPH)[94] does not allow for persistence of the monomeric structure, so that this organoaluminum compound is in equilibrium with the dimethylaluminum phenoxide species and ATPH. This disproportionation process, which has been well investigated by Barron,[75] is ascribed to self-association occurring between two or multiple MAPH molecules. The extremely bulky aluminum tris(2,6-di-*t*-butyl-4-methylphenoxide)[95] was also synthesized but through a separate pathway, involving the stepwise reactions of two distinct aluminum hydrides (Equation (8)).



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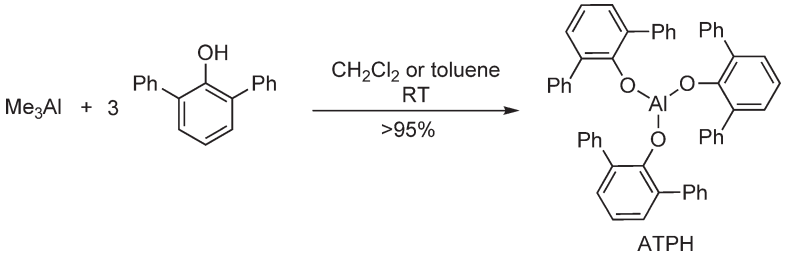

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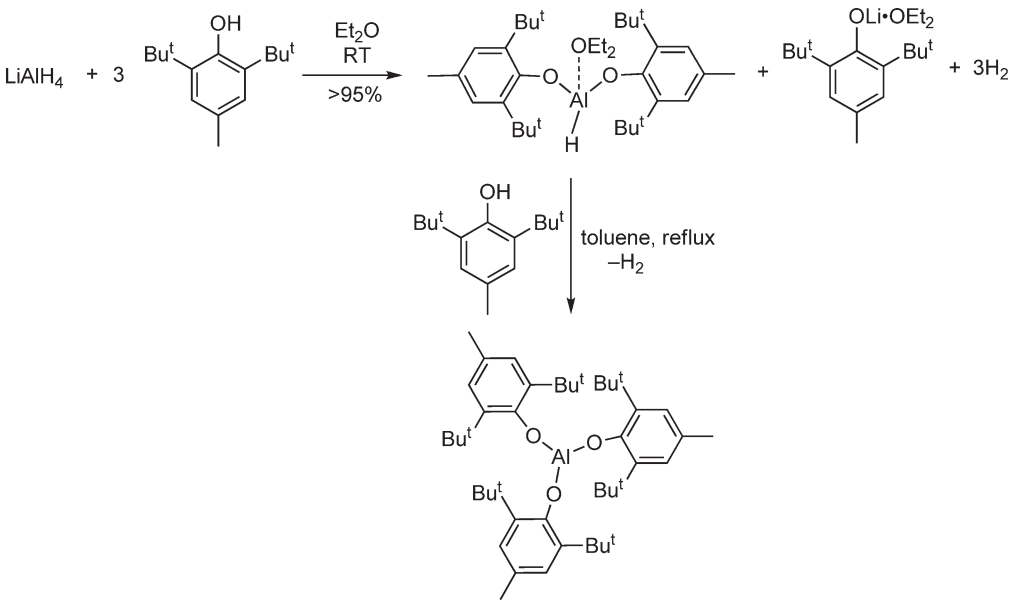
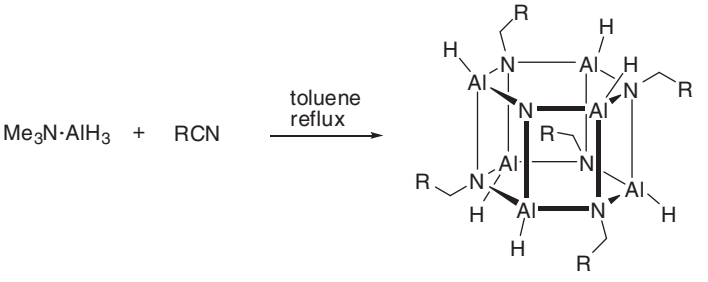


(8)

The use of these monomeric species is advantageous for organic synthesis because the vacant *p*-orbital is not occupied with any undesirable base components and barely exposed prior to the activation of heteroatom-containing reactants. The Lewis acidity of these reagents might decrease with covalent Al–O bond formation, especially in cases where the π-bonding between the aryloxy lone pairs and the empty $3p$ of Al is involved.[96,97] However, this π-bonding seems unlikely in most cases, as discussed by Eisch in COMC (1995). In addition, loosening of the aggregation can compensate for the assumed decrease in reactivity, and thus high oxophilicity is preserved. In fact, the MAD complexes of carbonyl compounds such as benzophenone,[96] acetophenone,[97] a camphor derivative,[98] and ethyl and methyl benzoates[75] were relatively stable and have structures determined by XRD. The ATPH complexes of DMF,[99] benzaldehyde,[100] benzoyl chloride,[100] α,β-unsaturated aldehydes,[101] ketones,[101] and esters[101] were also verified. ATPH has found broad utility in obtaining unprecedented reactivity and selectivity in organic synthesis: for example, conjugate addition to α,β-unsaturated aldehydes[99] and ketones,[102] vinylogous aldol reaction,[103–105] alkylation at the more substituted α-site of unsymmetrical ketones,[106] and dearomatic functionalization of aromatic carbonyl compounds (Figure 16).[100] The exceptional reaction behavior can be ascribed mainly to the steric influence of these aluminum reagents.

9.06.2.4 Aluminum(III)–Nitrogen Covalent and Non-covalent Bonds

Both Al–N covalent and non-covalent bonds are the basic components of the well-organized aggregates of aluminum amides or imides, yielding aluminazene,[107] a cubane-like tetramer, or hexagonal cage hexamer (Equation (9)).[108] Al–N covalent bonds are frequently so labile that this nature has been successfully applied in organic synthesis including the carbon–nitrogen bond formation via novel alumino-nitrogenation of terminal alkynes (Equation (10)),[109] as well as deprotonation of carbonyl[20] and imino[110] compounds that generates the aluminum enolate equivalents in the Fischer indole synthesis (Equation (11)).[110]



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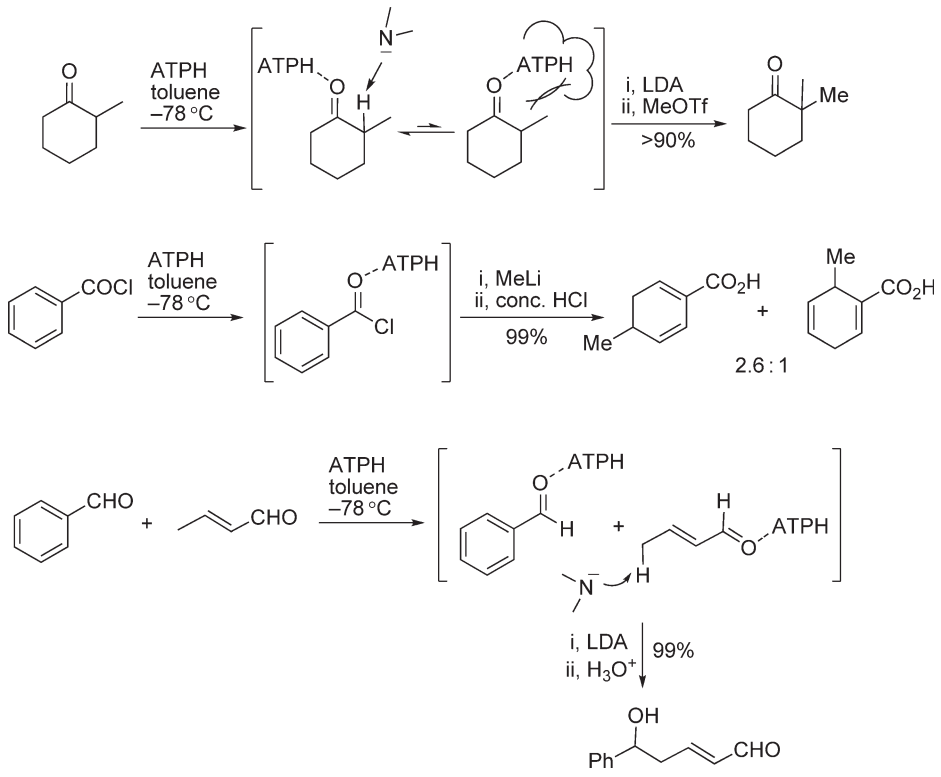
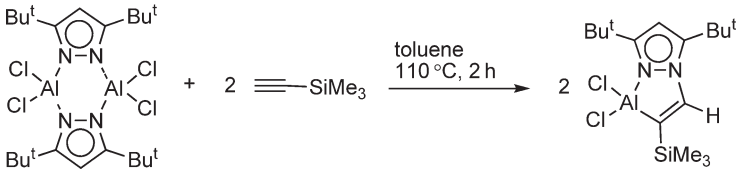


Figure 16 ATPH in organic synthesis.



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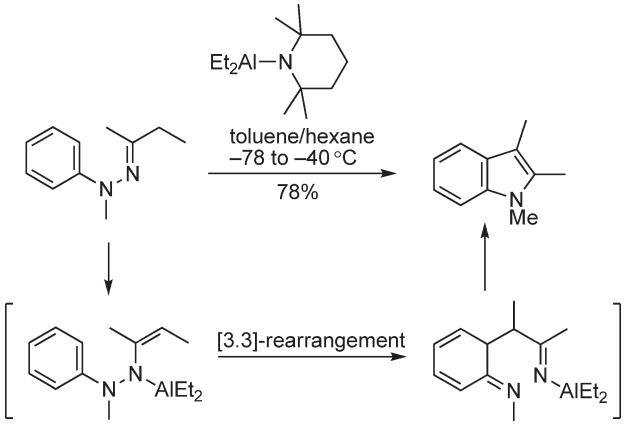


(11)

In contrast to the oligomers formed by intermolecularly connected Al···N dative bonds, a series of monomeric metallacycles was synthesized and their XRD structures were determined (Figure 17).[111–119] Several five-membered structures are comprised of one Al–C covalent and one Al···N dative bond provided by the bidentate ligand conformation. Their potential ability as candidates for co-catalysts in $MgCl_2/TiCl_4$-mediated polymerization was also demonstrated (Figure 17).[83] For the propene polymerization, all co-catalysts reach activities in the range of Et_3Al

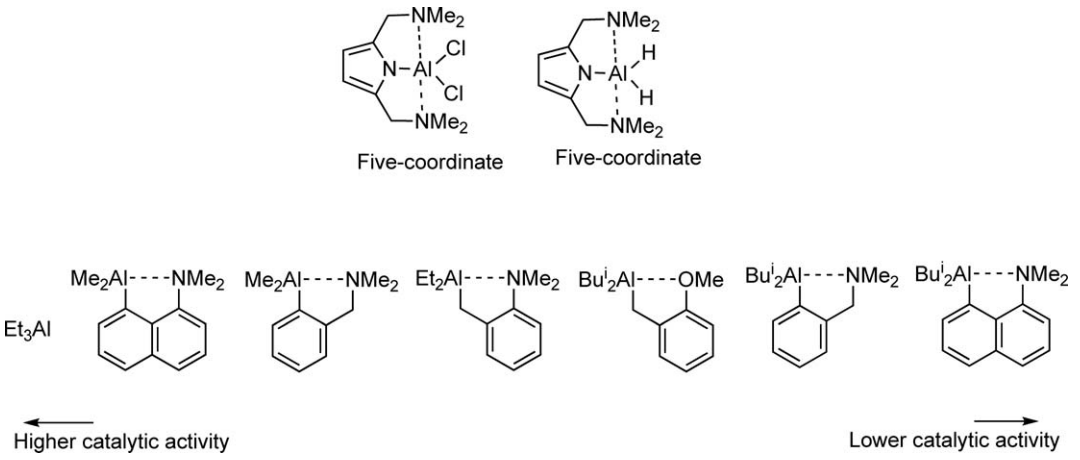


Figure 17 Intramolecular Al–N dative bonds and their influence on the order of catalytic activity.

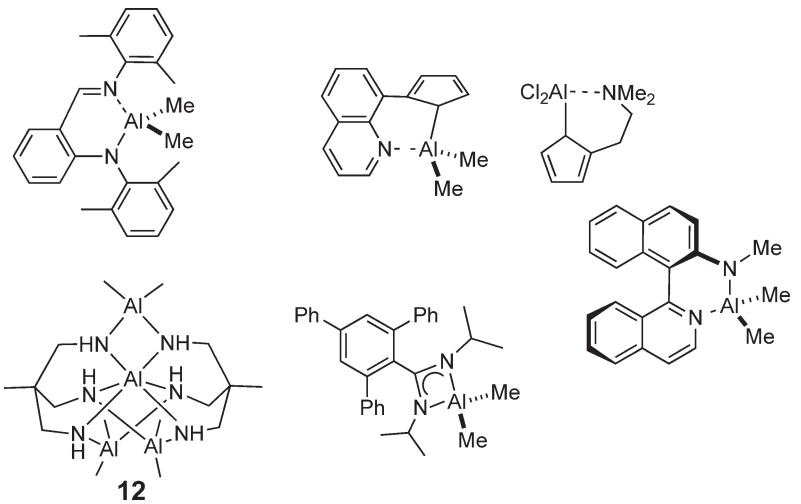


Figure 18 Structure diversity imposed by Al–N bonds.

and some of those exceed the results of Et_3Al in ethylene–propene co-polymerization. Intriguing and complicated chelation structures involving aluminum amide or imide compounds are frequently found in the literature (Figure 18).[111–119] Both four- and six-coordinated Al atoms were observed with a tripodal ligand, in which three NH groups serve as both chelating and bridging units to give **12**. Some of these are strong candidates for aluminum cations, as shown later in the chapter.

9.06.2.5 Aluminum(III)–Sulfur–Selenium and –Tellurium Covalent and Non-covalent Bonds

Similarly, small organoaluminum thiolates tend to make the dimer, trimer, or highly oligomeric structure (Figure 19).[120] A series of intramolecularly sulfur-stabilized monomeric organoaluminum compounds has also been reported (Figure 20).[121] Unusual structural geometry, where a dinuclear aluminum compound adopts a five- and four-coordinate geometry at once, has been verified in the structure of organoaluminum complexes in N_2S and N═S coordination environments (Figure 20).[122] Cubic clusters, the composite elements of which are Al and Se, or Al and Te, have been prepared by treatment of **13** with an excess of elemental selenium or tellurium (Equation (12)).[123] The reaction proceeded smoothly at elevated temperature to give iterative units of aluminum selenide or aluminum

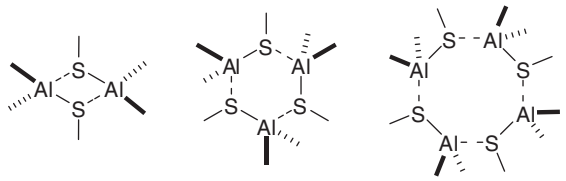


Figure 19 Variation in oligomeric structures involving Al–S bonds.

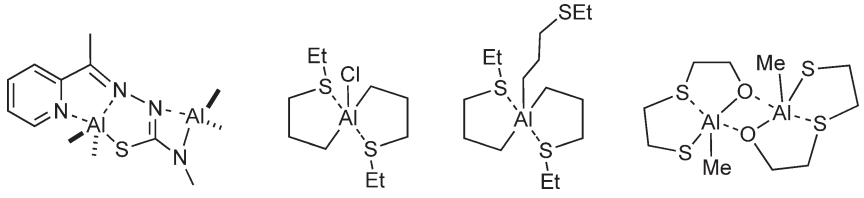
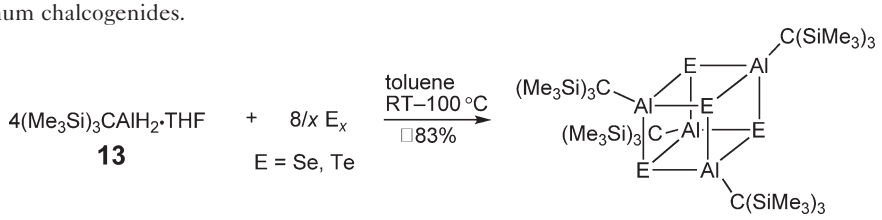


Figure 20 Structure diversity structures imposed by Al–S bonds.

telluride, in good yields. This reaction and those reported by other groups[124] represent new and facile routes to organoaluminum chalcogenides.



(12)

9.06.2.6 Mixed Covalent and Non-covalent Bonding Systems Involving Aluminum(III)–Oxygen, –Nitrogen, and –Sulfur Bonds

Further systematic studies enabled direct comparison among a series of non-covalent (dative) bond properties in the solid-state structure of organoaluminum alkoxides, in which additional amines, oxygen, or sulfur are incorporated into the alkoxide tethers.[125] Five-membered metallacycles were formed with bidentate O–R^1–Y-type ligands (Y = NR_2, OR, SR), most of which imposed again the five-coordinate geometry onto the aluminum center (Figure 21).[125–131] Bond distance of Al···Y decreases in the order of Al···N < Al···O < Al···S. Concerning the donor strength of different elements, the data are consistent with the usually assumed sequence N > O > S (Figure 22).[126] Temperature-dependent lengthening of these dative bonds in the solid state was interpreted as a consequence of thermal excitation rather than the effect of liberation.

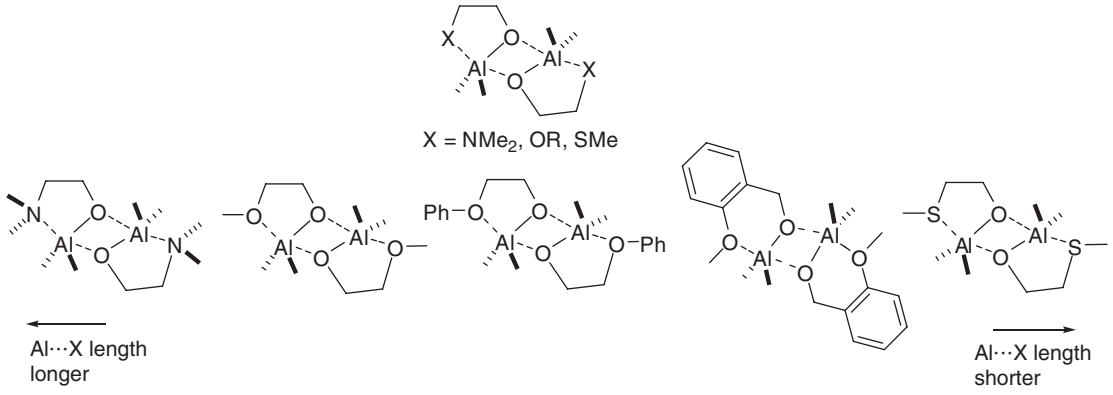


Figure 21 Difference in bond length in the aluminum complexes containing heteroatoms.

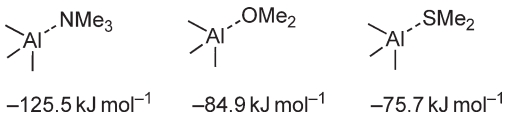


Figure 22 Stability of Al–X (X = N, O, S) dative bonds.

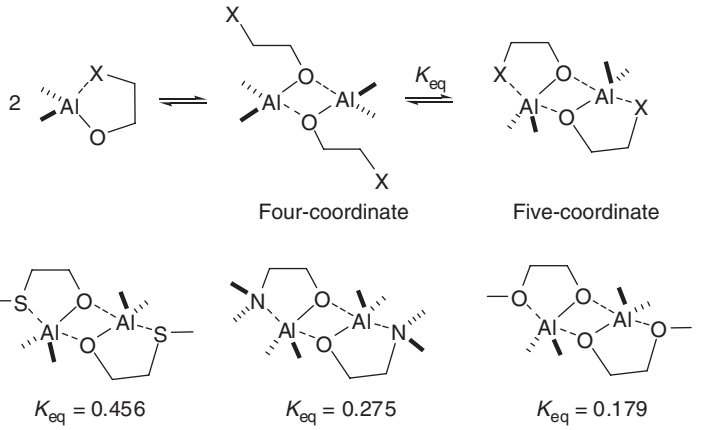


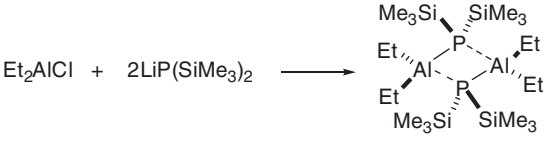
Figure 23 Equilibrium constants of intramolecular association–dissociation dynamics.

It should be noted, however, that a different sequence of bond strength was proposed for this type of compound (Figure 23).[126] Organoaluminums that contain these bidentate ligands exhibit unpredictable geometry and Lewis acid–base interactions dependent upon steric factors and elements embedded in their ligating groups. A three-way equilibrium was proposed in order to shed light on one of the complex dynamic behaviors of the compounds. The equilibrium constant K_{eq} was measured for a set of $[R_2Al(\mu\text{-}OR^1)]_2$ (R = Me, Et, Bu^t; R^1 = Me, Bu^t) compounds. Steric constraint with R groups affected the length of Al···O or Al···N dative bonds: the more increased the steric hindrance of R, the longer the Al···N or Al···O distance.

Development of a more profound understanding of the geometry factors that control the extent of oligomerization and coordination number at the aluminum center should be the subject of future research. The elucidation of structural and dynamic behavior is of great importance for gaining control of the coordination and geometric properties that lead to the fine-tuning of the reactivity of aluminum(III) species in the discovery of latent catalysts or co-catalysts in the future. This control in a diverse group of heteroatom-containing organoaluminum compounds has been the subject of many reports, but it still appears to be difficult to reach a definite, reliable conclusion that clearly explains all of the scattering observations.

9.06.2.7 Aluminum(III)–Phosphine Covalent and Non-covalent Bonds

Simple $AlCl_3$ or R_3Al adducts of small phospines tend to generate four-[132] or five-coordinate species,[133] and consistently favor monomeric, dimeric, or higher oligomeric structures,[132] depending on reaction conditions, including stoichiometry of reagents (Equations (13) and (14)).[134] A multiple[135] or mixed[136] donor system of tridentate ligand reinforced the five-coordinate, monomeric aluminum species, which could serve as the precursors of organoaluminum cations (Figure 24).



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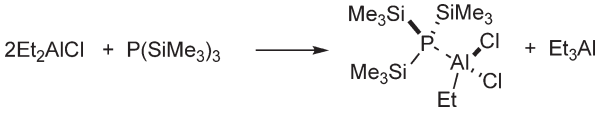


(14)

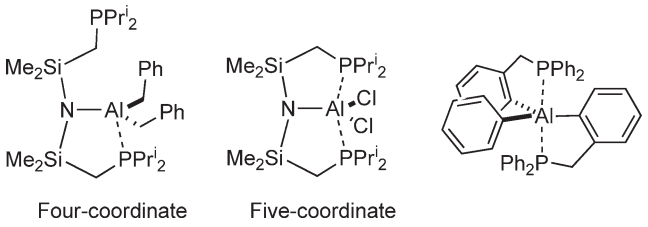
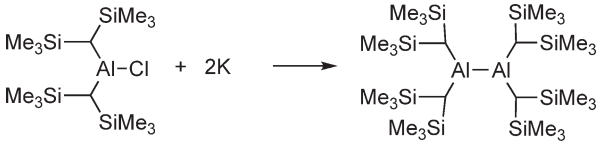


Figure 24 Structure diversity of the aluminum–phosphine complexes.

These fundamental investigations strongly support the strong capability of the aluminum atom for making coordination bonds with the unoccupied lone pairs of halogens, oxygen, nitrogen, sulfur, other chalcogen elements, phosphines, and even with hydrocarbons. Despite the importance of the electronic nature of each element, obviously steric factors sometimes prevail over electronic factors in dynamic behavior, and the preference for some specific interactions and structures, as well as the formation and reaction of heteroatom-containing organoaluminum compounds, is shown.

9.06.2.8 Bonds in Organoaluminum(II) Compounds: Al–Al Bonds

It is interesting that the first compounds containing Al–Al bonds are a relatively recent development in organometallic chemistry.[137] While efforts purporting the synthesis of Al–Al may be traced back to the 1960s–1970s,[138,139] these reports presented neither compelling nor spectroscopic data supporting such a metal–metal interaction. Uhl is credited with unambiguously reporting the first compound **14** containing an Al–Al bond in 1988 (Equation (15)).[140] The tris(trimethylsilyl)methyl group (trisyl group) and 2,4,6-tri-*i*-propylphenyl group are frequently used as a particularly convenient masking group to protect, and for isolation of, relatively unstable aluminum species. The Al–Al bond distance of 2.660(1) Å serves as a benchmark in this field of chemistry. The aluminum atoms in **14** reside in trigonal-planar geometry. An "electronic system delocalized over the Al–Al bond" was suggested as a factor for the planar $C_2Al–AlC_2$ core. The possibility of π-bonding participating in Al–Al bonds was examined through alkali metal reduction of **14**, which gave dark blue and black-violet radical monoanions **15** and **16**, respectively (Equation (16)).[141–143] This π-radical was characterized spectroscopically (ESR, UV–VIS, and IR) and suggests Al–Al one-electron π-bonds. The Al–Al bond distance in the radical anion of 2.53(1)Å is substantially shorter than that observed for the neutral dialane, and this shortening of 0.13 Å was claimed to be the result of an "Al–Al π-bond of partial multiple bond character". It was revealed that mixed valence isomers of dialanes, viz. $RAl–AlR_3$, might be capable of existence if the appropriate substituents were employed. In fact, DFT calculations[144,145] on the prototypical dialane $H_2Al–AlH_2$ revealed that the valence isomer $HAl–AlH_3$ is less stable than $H_2Al–AlH_2$ by 9.17 kcal mol^{-1}.[146] However, replacement of one of the dialane hydride substituents by cyclopentadiene inverted this order and (η^5-C_5H_5)$Al–AlH_3$ is more stable than the dialane (η^5-C_5H_5)$AlH–AlH_2$ by 10.79 kcal mol^{-1}.[146] In contrast to the authenticated structures containing Al–Al bonds, clear evidence for the existence of Al═Al double bonds has not been documented thus far. However, "dialuminene", HAl═AlH, was predicted to have a stronger Al═Al bond (ca. 10 kcal mol^{-1}) than its heavier congeners involving Ga═Ga or In═In bonds (ca. 3 kcal mol^{-1}).[147–149] The Al═Al bond distance was calculated to be 2.613 Å, which is shorter than most Al–Al single bonds in dialanes. Power recently showed that reaction of $ArAlI_2$ with KC_8 afforded the 1,2-diiodoalane **17** and probably, the aluminene **18**, which was subsequently trapped by toluene to give the [4+2]-addition product (Equation (17)).[150] This result is strongly suggestive of the transient nature of **18**, even though it was not isolated in pure form.



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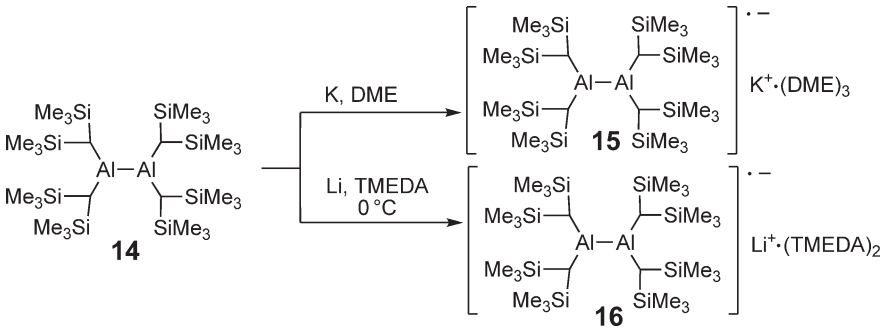

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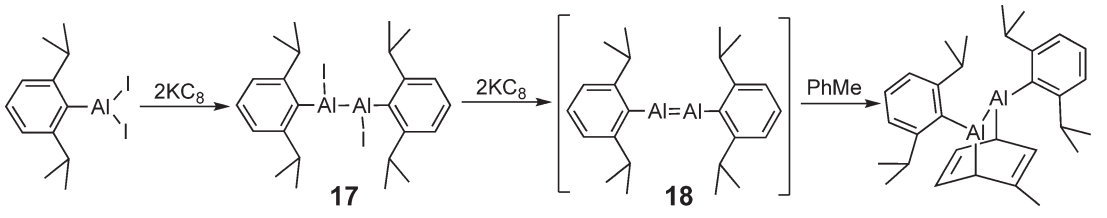
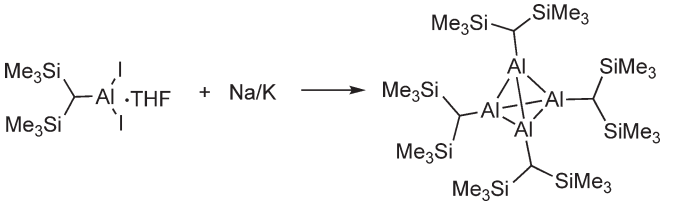


(17)

9.06.2.9 Bonds in Organoaluminum(I) Compounds: Al–Al Bonds

Since aluminum diiodides are susceptible to reduction upon treatment with alkali metals, the reductive dehalogenation of [(trisyl)AlI_2·THF] with Na/K alloy gave a novel tetrahedral structure [Al(trisyl)]$_4$ as orange platelets (Equation (18)).[151] Similarly, an [(η^5-C_5Me_5)Al]$_4$ tetrahedron was synthesized in 1991,[152] which is extremely thermally stable and decomposes at 205 °C, turning to a brown solid. Several additional synthetic routes to this aluminum tetrahedron have been screened (Figure 25).[153] [Cp^*Al]$_4$ was able to be converted into [(η^5-C_5Me_5)Al]–Al(C_6F_5)$_3$, consisting of both strong electron-donating and -accepting aluminum components (Equation (19)).[146] Indeed, the Al–Al bond distance (2.591(3) Å) is shorter than those in typical dialanes (2,4,6-*i*-$Pr_3C_6H_2$)Al_2 (2.647(3) Å),[143] and (*t*-Bu_3Si)$_4Al_2$ (2.751(2) Å),[154] but comparable to that in [RIAl–AlClR] (R = [(Me_3Si)$_2$-PhC(Me_3Si)N], 2.593(3) Å; Figure 26).[155] Exclusively, *N*-based[156] and *Si*-based[157] tetrameric aluminum(I) compounds **19** and **20** have been characterized by XRD (Figure 26).



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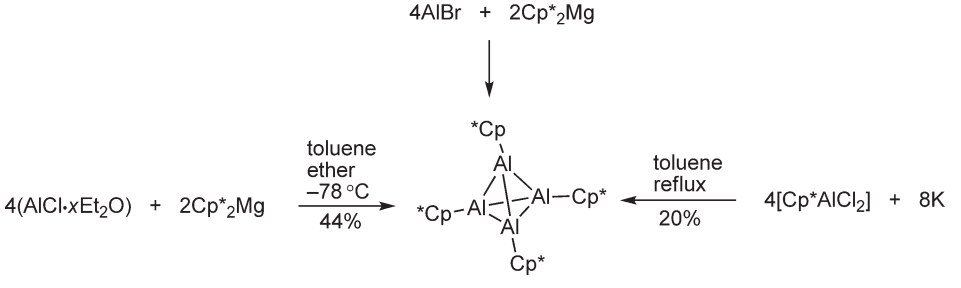


Figure 25 Synthesis of the Al(I) tetrahedron.

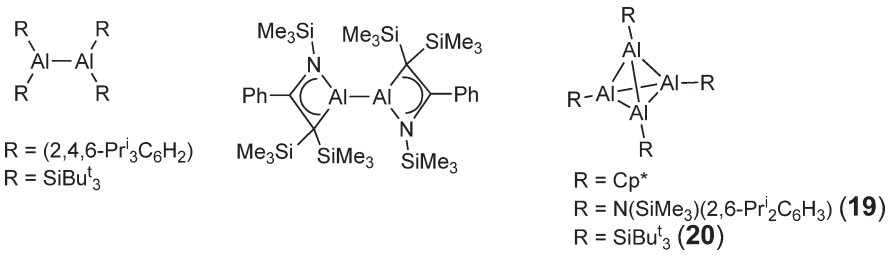
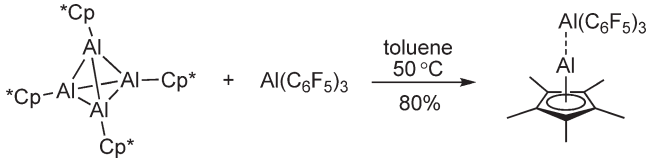
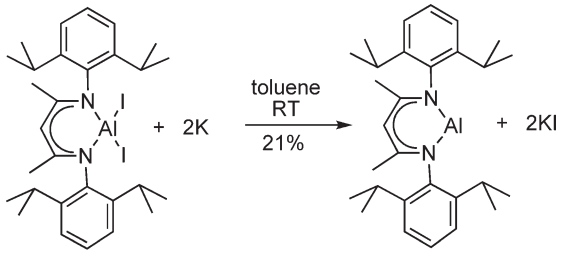


Figure 26 Al(II)–Al(II) and Al(I)–Al(I) bonds.



(19)

The aluminum(I) tetrahedra are easily synthesized following simple synthetic steps, one of which involves reduction of Al(III). The tetrameric interaction in $[Cp^*Al]_4$ is allowed to dissociate in solution by adjustment of the elevated temperature, and in the gas phase, eventually into monomeric form. The tetramerization energy was estimated to be about –150 kJ mol^{-1},[158] and the molecular structure of the monomer was studied using gas-phase electron diffraction.[159] The photoinduced reaction of the Cp^*Al monomer with H_2 in an Ar matrix at 12 K was followed by IR spectroscopy.[160] The Cp^*Al monomer is less stable than its tetramer, so it cannot be kept for more than a few hours at 100 °C. The physical properties of monomeric CpAl and Cp^*Al were also examined in quantum-chemical studies, which suggested that the negative pole is apparently located at the Al center and that there is a significant amount of π-backdonation from Cp to Al.[161] The more kinetically and thermodynamically stable monomeric Al(I) species **21** was first synthesized using a bulky protecting group to ensure kinetic stability as had been done to isolate Al–Al species (Equation (20)).[162]

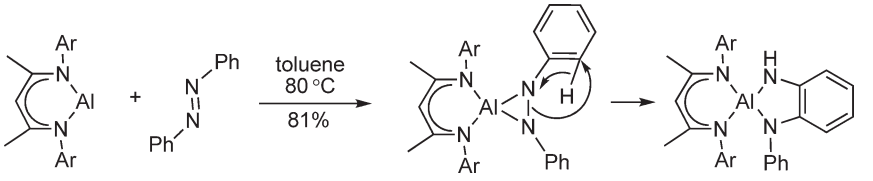


21

(20)

A notable structural aspect of **21** is the coordination number of 2 at the Al center. The lengthening of the N–Al bonds and the nearly 90° acute N–Al–N angle indicate that two 3*p*-orbitals on the Al center are essentially involved in the bonding to the two N atoms. A preliminary insight into the peculiarities of the aluminum-containing metallacycle was gained from *ab initio* calculations by analyzing the Laplacian of electron density. A lone pair of electrons is accommodated on the metal atom and arranged outside of the metallacycle in a quasi-trigonal-planar manner. This non-bonded lone pair also implies a singlet carbene character of the Al atom. These properties allow the argument that the electrons originating from an s^2-configuration of the Al(I) center are stereochemically active, leading to an *sp*-like hybrid. In this conjecture, the "off-cycle" side of the Al(I) atom could be considered as a Lewis base. At the same time, the charge depletion close to the Al atom in the semiplane of the metallacycle can be described as Lewis acid-type behavior.

The reactivity of such bulky monomeric Al(I) species has been further surveyed.[163] The reaction was carried out with diazobenzene (Equation (21)),[164] phenyl azide derivatives,[165] trimethylsilyl azide (Equation (22)),[166] alkynes (Equation (23)),[167] P_4 (Equation (24)),[168] and carbenes.[169]



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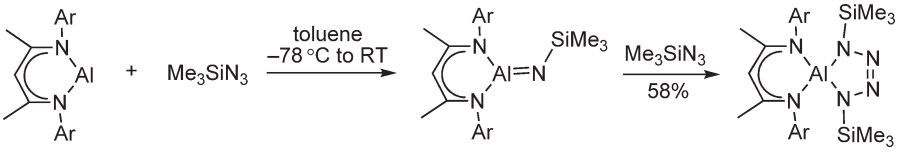

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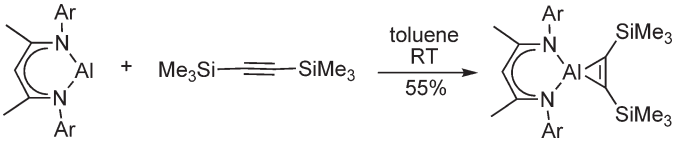

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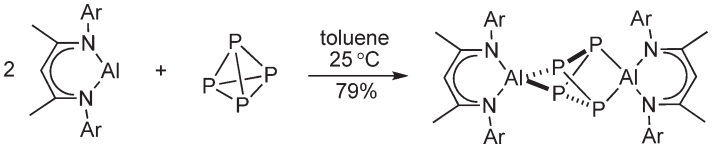
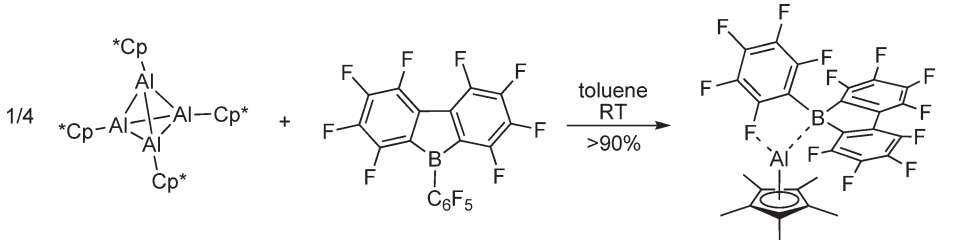


(24)

9.06.2.10 Aluminum(I)–Boron Bonds

The aluminum–boron bond is rarely found in the literature (see one example noted in COMC (1995)) but can be synthesized following a procedure analogous to the mixing of electron-donor Al(I) and -acceptor Al(III) components used to generate $[(\eta^5\text{-}C_5Me_5)Al]\text{–}Al(C_6F_5)_3$. When the low-valent aluminum(I) compound $[Cp^*Al]_4$ was mixed with electron-deficient boron(III) species, novel Al–B bonds were easily formed (Equation (25)).[170] In fact, theoretical studies indicate that the most significant contribution for a bonding interaction involves mixing of the 9-borafluorene LUMO with the CpAl HOMO. Cubic clusters comprising Se and Te were also synthesized from the aluminum(I) tetrahedron (Equation (26)).[153]



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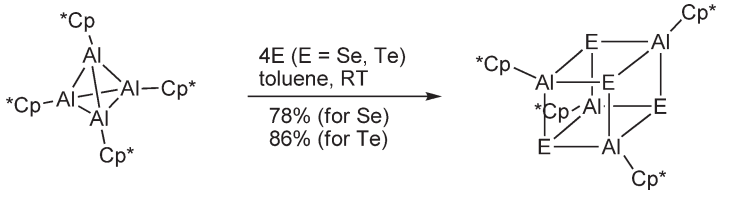


(26)

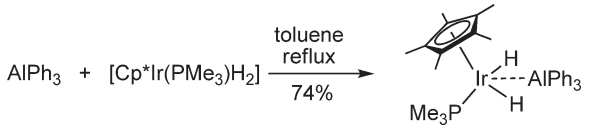
9.06.2.11 Aluminum–Transition Metal Bonds

There are only a few examples reported for Al–M (transition metal) bonds. The first Al–M bond was featured in the synthesis, structure, and bonding of $[(\eta^5\text{-}C_5Me_5)Al\text{–}Fe(CO)_4]$ (Equation (27)).[171]

$$[(Cp^*AlCl_2)_2] + 2K_2[Fe(CO)]_4 \xrightarrow[10\text{–}20\%]{\text{toluene}} 2[Cp^*Al\text{–}Fe(CO)_4] + 4KCl \quad (27)$$

The AlX fragments bonded to transition metals in compounds of the general formula $[(CO)_5M\text{–}AlXL_2]$ (M = Cr, Mo, W; X = H, Cl, alkyl) were extensively investigated both experimentally and theoretically. The electronic structure was analyzed using the natural bond orbital (NBO) analysis, and metal–ligand interactions were characterized with the help of charge-decomposition analysis (CDA).[172] The differences in optimized geometry and electronic distribution in bonding between base-free complexes $(CO)_5W\text{–}AlX$ and base-ligated complexes $(CO)_5W\text{–}[Al(NH_3)_2X]$ (X = H, Cl) were compared, and there were several characteristic features worth mentioning. The bond energies of the base-free complexes are $>30\,kcal\,mol^{-1}$ lower than those calculated for the base-ligated complexes. The aluminum lone pair orbitals of AlH and AlCl have a much higher percent *s*-character (91.5% and 93.8%, respectively) than those of $Al(NH_3)_2H$ and $Al(NH_3)_2Cl$ (77.5% and 84%). These $Al\cdots NH_3$ bonds are clearly stronger (64.0–65.1 kcal mol^{-1} for the two NH_3) than in the free ligands $AlH(NH_3)_2$ (33.1 kcal mol^{-1}) and $AlCl(NH_3)_2$ (30.5 kcal mol^{-1}). These results are all due to electron donation from the Al lone pair orbital to the $W(CO)_5$ fragment. The W–Al bond is further investigated using topological analysis of the electron density distribution. The AlH fragment alone clearly shows an area of electron concentration at Al, which represents the lone pair electrons of Al. In contrast, the base-free complex $(CO)_5W\text{–}AlH$ has a large area of electron density in the area of the W–Al π-bonding, which suggests stronger W-to-Al backdonation in $(CO)_5W\text{–}AlH$ than in $(CO)_5W\text{–}[Al(NH_3)_2H]$. CDA was used to estimate the relative donor and acceptor strength of ligands more quantitatively. In base-ligated complexes $(CO)_5W\text{–}[Al(NH_3)_2X]$, Al-to-W donation is more significant than in $(CO)_5W\text{–}AlX$, which strongly supports the previous arguments. The calculated donation and backdonation indicate that AlH and AlCl are stronger acceptors than $Al[(NH_3)_2H]$ and $Al[(NH_3)_2Cl]$, which is reasonable. The calculated Al-to-N backdonation is negligible in comparison to the N-to-Al donation.

The bond formation between iridium(III) and Al(III) was also reported recently.[173] The synthesis of monomeric $[Cp^*(PMe_3)IrH_2](AlPh_3)$ was achieved by simply mixing $[Cp^*(PMe_3)IrH_2]$ and Ph_3Al (Equation (28)), while the dimeric structure predominates in the corresponding complex of Et_3Al. Compared with the W–Al distance of 3.110(3) Å in $Cp_2WH_2AlMe_3$,[174] which predominates in the η^1-H-type structure (Figure 27), the Ir–$AlPh_3$ distance of 2.684(2) Å proved to be much shorter. The Ir–$AlPh_3$ bond is stronger than Ir–$AlEt_3$ bond. Ni and Al atoms are connected by two-center two-electron bonds in the $(CpNi)_2\text{–}(Cp^*Al)_2$ complex, derived by treatment of Cp^*Al with $[CpNi(CO)]_2$ (Equation (29)).[175] A series of unusual Co–Al cluster complexes[176,177] and Cr–Al(I) bonds[178] was also recently reported (Equations (30) and (31)).



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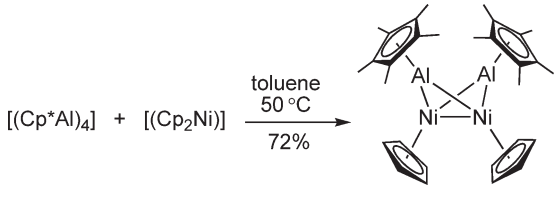

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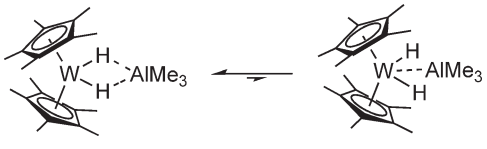
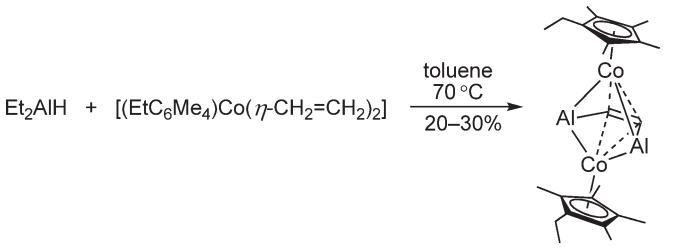


Figure 27 Equilibrium between W–H–Al and W–Al bonding species.



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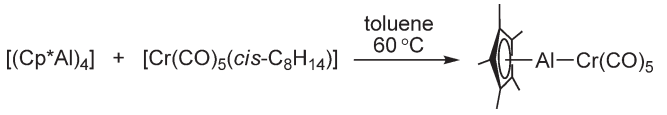


(31)

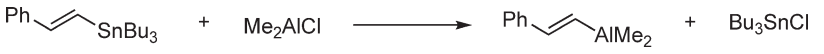
9.06.3 New Aspects in the Synthesis of Organoaluminum Compounds

Early synthetic experiments demonstrated that organoaluminum complexes could be made from aluminum metal. Ethylaluminum sesquiiodide ($EtAlI_2 + Et_2AlI$) was prepared by Hallwachs and Schafarik in 1859 upon combining ethyl iodide with aluminum metal.[28] In 1865, Buckton and Odling prepared aluminum alkyls from mercury alkyls and aluminum metal.[28] Since these milestones concerning organoaluminum syntheses, essentially nothing was improved upon in this area for nearly a century. From 1950 to 1970s, headed by Ziegler's pioneering "synthesis from aluminum metal, olefin, and hydrogen", several other basic syntheses of organoaluminums were established, and the concept-based procedures are summarized in detail in COMC (1982)[3] and COMC (1995),[4,5] among others.[24] The preparation methods developed so far can be roughly classified into seven types: (i) reduction of organoaluminum halides by alkali metals; (ii) hydroalumination; (iii) carboalumination; (iv) direct alumination of carbon acids, including acetylene derivatives; (v) transmetallation from organotin, -magnesium, -lithium, and -boron compounds; (vi) via tetraorganoaluminates; and (vii) homologation of diazoalkanes. Through these procedures, higher organoaluminums with elongated carbon chains or bearing more functional carbons are made accessible. This chapter is limited only to notable improvements accomplished recently along these lines.

9.06.3.1 Aluminum–Metal Exchange

9.06.3.1.1 Aluminum(III)–tin exchange

Early studies of the organotin–chloroaluminum exchange process were carried out by Neumann *et al.*[179] Although aryl–alkyl metathesis between tin and aluminum still remains a possible side-process, this method provides an effective route to unsolvated organoaluminum compounds and is frequently employed because organotin compounds are generally air and moisture stable, and halogenated aluminum compounds constitute good commercial resources. Recent work by Eisch[180] and others[181] has demonstrated the broad applicability of this method for the preparation of a range of organoaluminum compounds bearing allyl-, benzyl-, alkenyl-, alkynyl-, and arylaluminum bonds (Equations (32)–(37)). The work also describes their potential utility as co-catalysts for titanocene-mediated ethylene polymerization.



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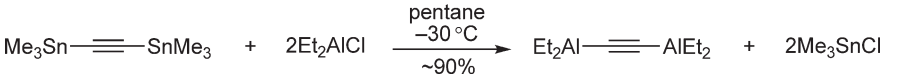

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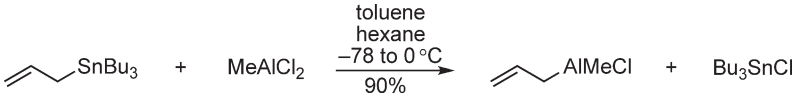

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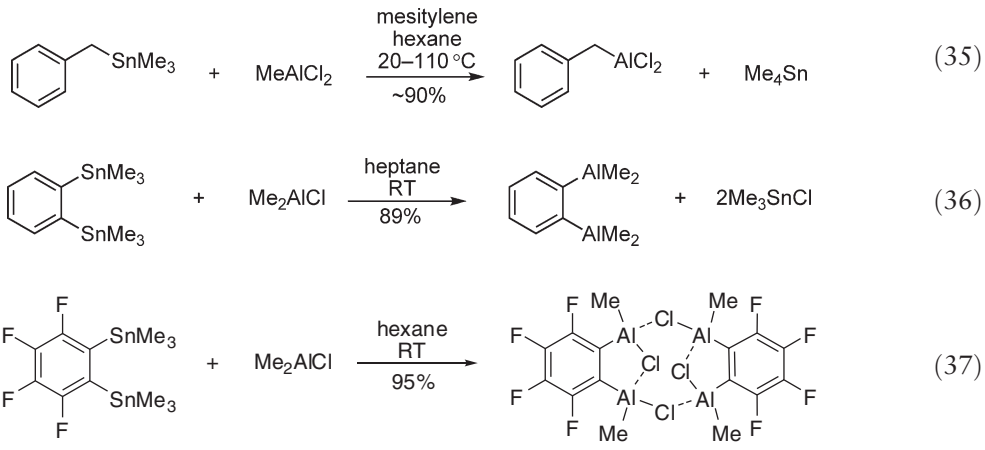
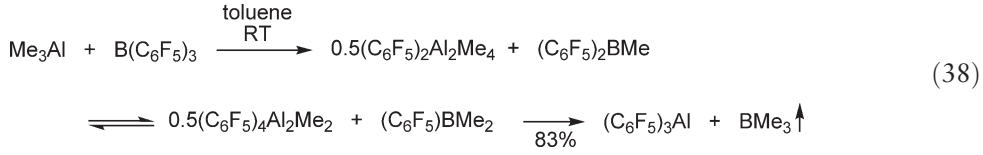


9.06.3.1.2 Aluminum(III)–boron exchange

Organoborons are regarded as soluble, relatively stable, and less toxic than organotin or -mercury compounds, so their usefulness in the preparation of organoaluminum compounds has been well discussed. The equilibrium and the exchange rate of organic groups between organoaluminum and -boron compounds depend strongly on the electronic and steric nature of both the 13-group elements. Me_3Al or Et_3Al is often employed so as to facilitate the spontaneous removal of the resulting volatile organoboron species (i.e., Me_3B or Et_3B; Equation (38)).[182]



Exchange reactions sometimes suffer from undesirable elimination steps to give the corresponding alkenes, along with aluminum hydrides. This method recently offered a major advance in the synthesis of aluminum tris(pentafluorobenzene), ($Al(C_6F_5)_3$), which has found tremendous application as a co-catalyst in olefin polymerization (see also Section 5.2.1).[183] $Al(C_6F_5)_3$ is so extremely electrophilic that it can be isolated as the η^1,π-complex of the hydrocarbon upon exposure to toluene or benzene (Figure 28).[184] NMR studies indicated that the boron/aluminum stoichiometry and solvent used are critical factors in affording high purity $Al(C_6F_5)_3$.[185] It is worth mentioning that early studies on the synthesis of $Al(C_6F_5)_3$ via treatment of Et_3Al with $B(C_6F_5)_3$ without any solvent resulted in an explosion when the reaction temperature reached 70 °C, but at 50 °C no $Al(C_6F_5)_3$ was formed.[186,187] $Al(C_6F_5)_3$ and $B(C_6F_5)_3$ showed distinct reactivity upon treatment with the bis(imide) complex of group IV metals (Figure 29).[188] Trimethylaluminum reacts with $[CPh_3][B(C_6F_5)_3]$ at elevated temperature to give a mixture of $AlMe_{3-n}(C_6F_5)_n$ compounds, depending on Al/B ratio. $Al(Bu^i)_3$ undergoes β-hydride elimination significantly faster than Al/B exchange.

Hydroalumination of 1-alkynes generally proceeds without the aid of transition metal catalysts. However, the reaction sometimes suffers from undesirable side-processes, including the formation of alk-1-ynylalanes or protonolysis of the intermediate alk-1-enylalanes. In particular, these side-products increase significantly in the reaction of

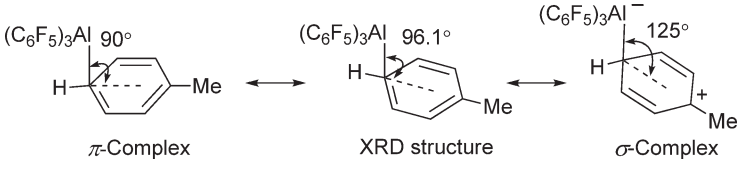


Figure 28 Al–arene σ and π complexes.

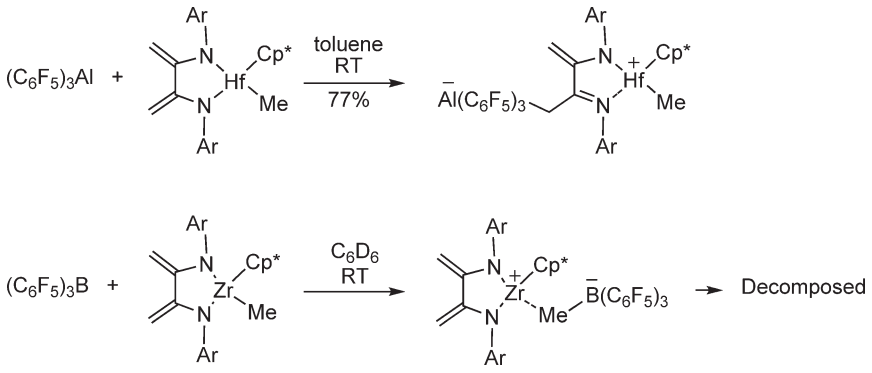
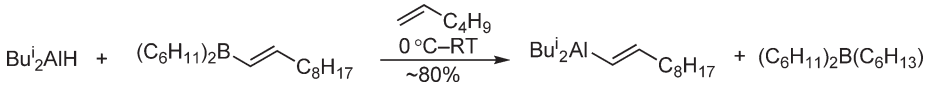


Figure 29 Different reactivity in the reaction of $Al(C_6F_5)_3$ and $B(C_6F_5)_3$.

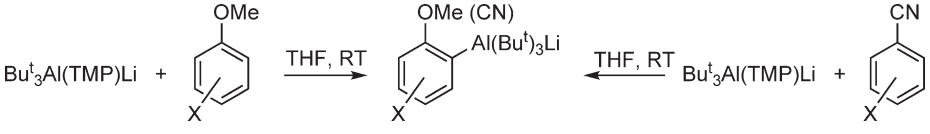
conjugated alk-1-ynes. In contrast, treatment of (*E*)-1-alkenyldicyclohexylboranes with diisobutylaluminum hydride (Bu^i_2AlH) in the presence of 1-hexene resulted in transfer of the alkenyl group from boron to aluminum to give (*E*)-alkenyldiisobutylalanes in high yields with retention of configuration at the double bonds (Equation (39)).[189]



(39)

9.06.3.2 Direct Alumination of Aromatic Rings

Aromatic aluminum compounds are also available by direct alumination of multiply functionalized aromatic rings using aluminum amide ate complexes (Equation (40)).[190] The reaction tolerates various functional groups on an aromatic nucleus, such as bromine, alkoxy, amide, and cyano groups, and even heterocyclic aromatics, including indoles and pyridines, can participate successfully in this deprotonative procedure. Thus, an *o*-bromoaluminum benzene intermediate was stable enough at –78 °C but at RT underwent clean formation of the benzyne, which was subsequently trapped by an enenophile (Equation (41)).



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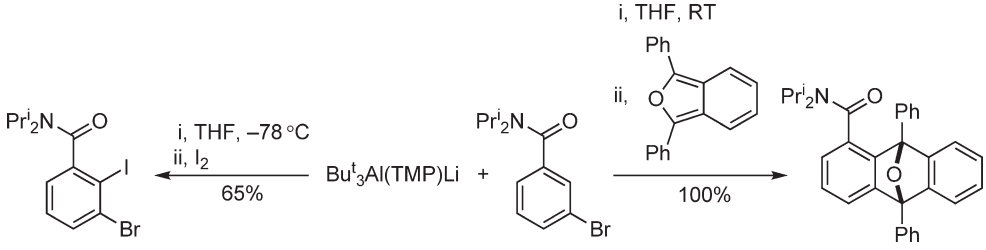


(41)

Aromatic carboxylic acids were obtained in good yield, essentially free of diaryl ketones by carboxylation of aromatics with a carbon dioxide–Al_2Cl_6/Al system at moderate temperature (20–80 °C).[191] It was not possible to distinguish between two possible mechanistic reaction pathways based on the experimental results. According to theoretical DFT calculations, one possible though unlikely pathway involves an initial complexation between benzene and Al_2Cl_6, with subsequent formation of organoaluminum intermediates ($PhAlCl_2$ and $PhAl_2Cl_6$) (Figure 30). A rather superelectrophilic aluminum chloride-activated carbon dioxide species, namely $CO_2AlCl_2^+$, seems to be involved in this typical electrophilic aromatic substitution pathway.

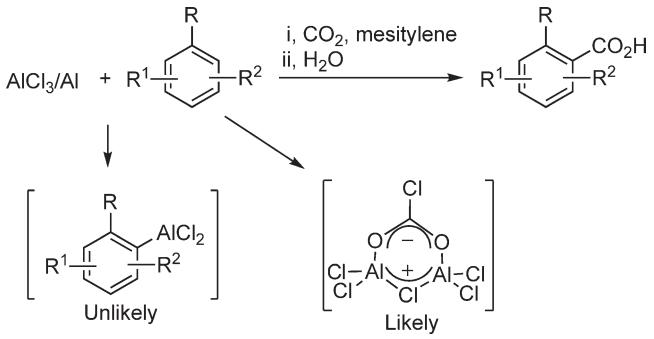
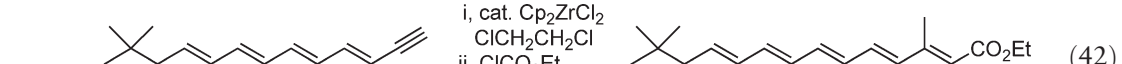


Figure 30 Reaction of arene ring and CO_2.

9.06.3.3 Carboalumination and Hydroalumination

The addition of aluminum hydride and alkyls to non-activated C–C multiple bonds (C≡C or C=C) is referred to as hydroaluminaton and carboalumination, respectively. The reactions involve metathesis of each C–C multiple bond with *Al–H* or *Al–C* bonds, giving an *Al*–C=C–*H* (or *Al*–C–C–*H*) or *Al*–C=C–*C* (or *Al*–C–C–*C*) structure, respectively. These methods are of broad utility in the construction of Al–C linkages, including Al–alkenyl and Al–alkyl bonds, which can be further converted into C–C bonds (Equations (42)–(45)).[192–196] Therefore, a great contribution has been made in synthetic applications, in addition to the mechanistic studies, of hydroalumination and carboalumination since 1993.[197–199]



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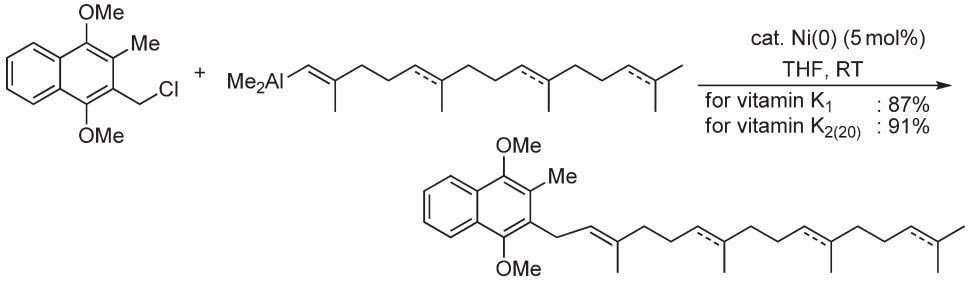

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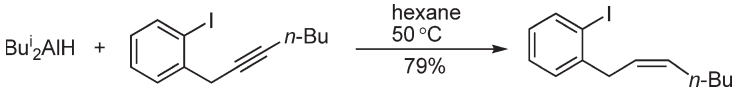

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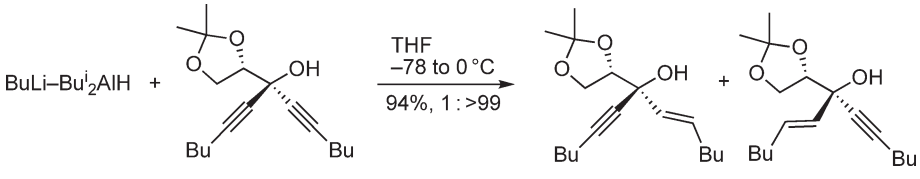
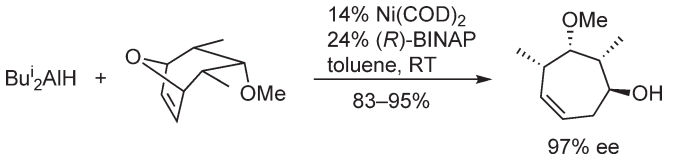


(45)

Carbo- and hydrometallation reactions are frequently catalyzed by group 4 metals (Ti, Zr) and are thus highly associated with the question of how the Ziegler–Natta polymerization or Tebbe processes should be controlled or

modified. While chiral Ni–BINAP catalysts were recently introduced into asymmetric hydroalumination (Equation (46)),[200–203] Cp_2TiCl_2 and Cp_2ZrCl_2 have been most profoundly investigated in the catalytic processes.



(46)

The mechanism of the carboalumination of alkenes falls into either of the following two classes depending on the unsaturated substrates used and the reaction conditions: (i) alkene insertion into a transition metal–carbon or aluminum–carbon bond and (ii) coupling of two alkenes with low-valent metal(II), leading to metallacyclopentanes or -propanes. Yoshida and Negishi have proposed[204] that Cp_2ZrCl_2-catalyzed carboalumination of alkynes involves methylation of Cp_2ZrCl_2 with Me_3Al to give $ZrCp_2Cl(Me)$ and Me_2AlCl. Subsequent carbozirconation of the alkyne yields the corresponding alkenylzirconium derivatives; their transmetallation with Me_2AlCl results in alkenyldimethylalanes, accompanied by regeneration of the catalyst. The reaction mechanism likely involves the existence of a reversible process where the methyl group or methyl radical is transferred from the aluminum atom to the Zr atom, as evidenced by NMR measurements. However, further investigations[205,206] showed that this reaction involves direct carboalumination of alkynes by Me_2AlCl activated by $Cp_2ZrCl(Me)$ (Figure 31). When Et_3Al was used in place of Me_2AlCl, it was proposed that the Cp_2ZrCl_2-catalyzed cyclic carboalumination of alkynes proceeds via bimetallic C–H bond activation and gives **22**, which rearranges to yield $Cp_2ZrEtCl$ and the aluminacyclopentene (Figure 32).[207] This mechanism is based on a series of earlier studies on the reaction of Et_3Al with Cp_2ZrCl_2 by Sinn[208] and Kaminsky[209] in the 1960s and 1970s, and is in good agreement with theoretical data obtained by PM3 calculations.[210]

Related to these metathesis processes, the first report of a regioselective synthesis of a previously unknown five-membered organoaluminum compound was published in 1989 (Equation (47)).[211] Later, it was found that this reaction is versatile and allows for a one-step synthesis of five-membered organoaluminums from Et_3Al and terminal alkenes in nearly quantitative yields.[212] This reaction is termed "catalytic cycloalumination"[213] or "cyclic carboalumination".[214] The synthesis of aluminocyclopentenes was achieved through intramolecular cycloalumination of disubstituted acetylenes with Et_3Al in the presence of catalytic Cp_2ZrCl_2 without any solvents

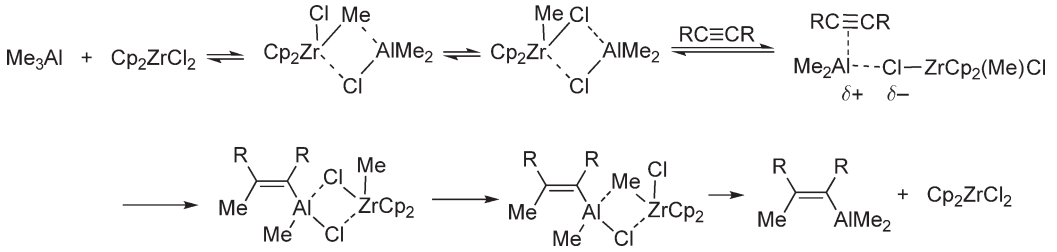


Figure 31 Proposed mechanism of the carboalumination promoted by Me_3Al and cat. Cp_2ZrCl_2.

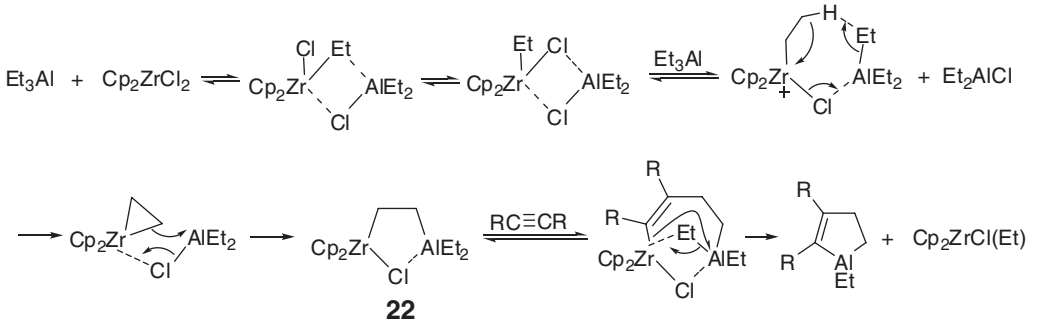
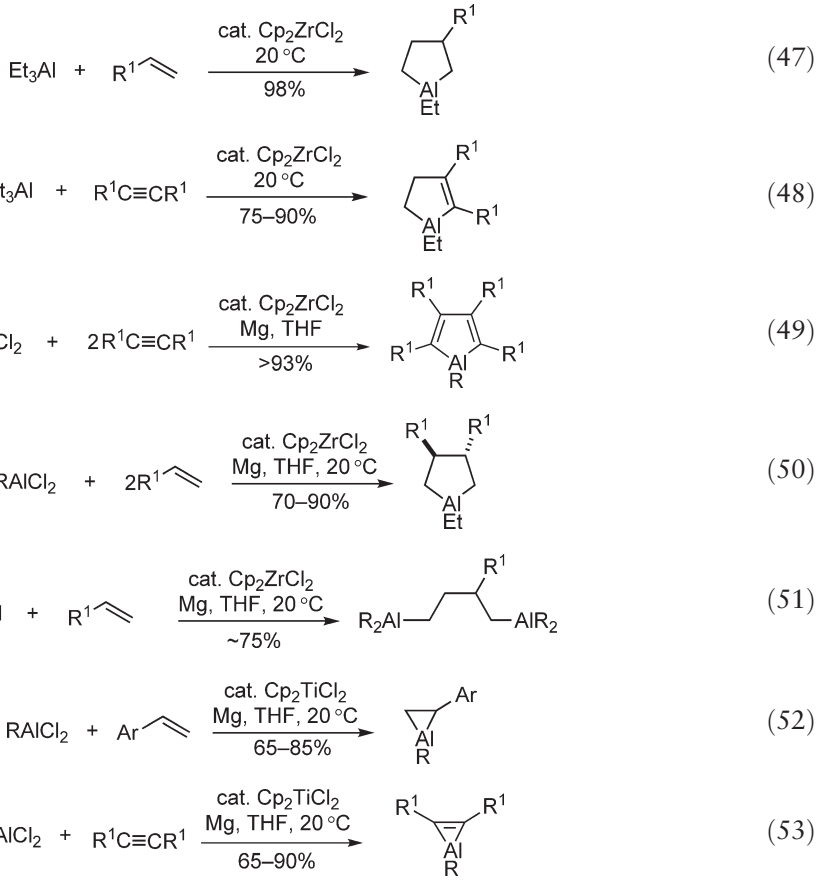


Figure 32 Proposed mechanism of the carboalumination promoted by Et_3Al and cat. Cp_2ZrCl_2.

(Equation (48)).[199] Increasing the internal alkynes by twice the amount and addition of Mg led to the alumino-cyclopentadiene (Equation (49)).[215] Dimerization of terminal alkenes involving an aluminum center resulted in the formation of aluminocyclopentane when the Zr catalyst and Mg used had the proper reaction conditions (Equation (50)).[216] In contrast, 1,4-dialuminobutane was readily formed using a twofold excess of R_2AlCl following a similar reductive process in THF (Equation (51)).[217] In 1997, Dzhemilev and co-workers developed a method for the synthesis of a class of metallacycles named "aluminocyclopropanes" (Equation (52)).[218] The reaction involves the use of alkylaluminum dichlorides ($RAlCl_2$), Mg, and catalytic Cp_2TiCl_2. Mg was used as well for reduction of Ti(IV) to generate low-valent titanium species. Similar adjustment of reaction conditions allowed for the synthesis of alumino-cycropropenes through cycloalumination of 1,2-disubstituted acetylenes using $RAlCl_2$, Mg, and catalytic Cp_2TiCl_2 (Equation (53)).[219] The nature of the solvent had great influence on the formation and reactivity of intermediary titanium- and zirconium-containing metallacycles, the common key species in the synthesis of aluminocycloalkanes and -alkenes.



9.06.4 New Aspects in Reactivity of Organoaluminum Compounds

Organoaluminum(III) compounds can act not only as nucleophiles but also in the electrophilic adhesion and subsequent activation of heteroatom-containing substrates. The dual functions of organoaluminums recall a simplified mechanistic model working with acid–base-type interactions and reactions. The most common geometry around aluminum is tetrahedral, which accommodates typical reactive intermediates, and subsequently initiates coupling at the most electrophilic and nucleophilic intersections. In fact, upon formation of ate complexes with organometallic species (organolithium, organomagnesium, etc.) or coordination complexes with neutral Lewis bases (heteroatom-containing substrates such as carbonyl and imino compounds, ethers, and amines, etc.) (Figure 33), transfer of the alkyl group from aluminum atom begins in either an intra- or an intermolecular fashion. However, contrary to representative alkyl-transfer reactions, the organic chains attached to aluminum are almost inert, given the special

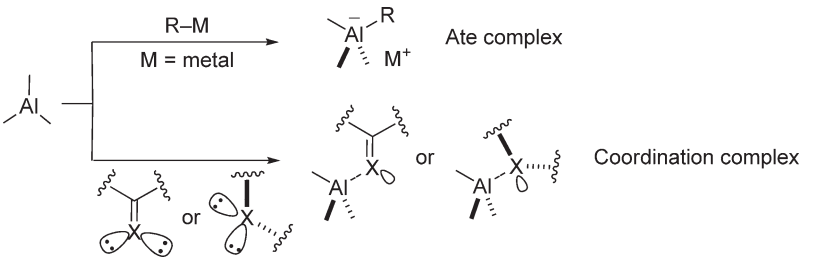


Figure 33 Aluminum ate complex and coordination complex in tetrahedral geometry.

arrangement with the coordination sphere of aluminum. In many cases, this nature could be applied to Lewis acid-promoted reactions, allowing a number of bimolecular and intramolecular carbon–carbon bond-forming reactions. The next section briefly describes some of the notable properties of the reactivity of organoaluminum compounds.

9.06.4.1 Tunable Reactivity of Methyl and Other Alkyl Groups on Aluminum(III)

Organoaluminum(III) reagents commonly have high oxophilicity. Trialkylaluminum compounds, especially Me_3Al and Et_3Al, ignite spontaneously in air at ambient temperature. Most aluminum alkyls react violently with water. Covalent bonds formed between aluminum and oxygen or halogen atoms are extremely strong – the energy of the Al–O bond is estimated to be 138 kcal mol^{-1}. Special care must be taken with their handling; the precautions are explicitly indicated elsewhere. Increasing molecular weight by increasing the number of carbons in the aluminum alkyl chain reduces pyrophoric reactivity. Replacing alkyl groups by alkoxy or other heteroatoms including halogen atoms also reduces the reactivity, that is, the remaining alkyl groups bound to the aluminum(III) center lose their mobility comparatively.

9.06.4.1.1 Aluminum alkyls in reaction with protic groups

Since the most common carbon-bonded ligand for aluminum is the methyl group, it would be most appropriate to begin discussions regarding reactivity differences with various types of Al–Me bonds. For example, the (salen)Al–Me complex is a shelf stable compound (Figure 34). ("Salen" is the name that has historically been used to describe the entire class of such ligands possessing various diamino backbones; however, it is also the specific name of the ethylenediamine derivatives.)[220] The 5,10,15,20-tetraphenylporphyrinato (TPP)-based aluminum reagent (TPP)Al–SPh frequently has higher reactivity in initiating anionic polymerization than (TPP)Al–Me.[221] Me_3Al works as an effective methylating agent for carbonyls, imines, and epoxides, among others,[24] but MAD[92] does not.

In fact, the methyl group of MAD shows intriguing reactivity upon treatment with water.[222] The reaction of MAD with water is slow, and although CH_4 is formed, the primary product of hydrolysis is 2,6-di-*t*-butyl-4-methylphenol (Equation (54)). Before liberating the phenol, the aquo complex **23** was formed by treatment of 1.0 equiv. of H_2O with a THF solution of MAD. Complex **23** was stable at –40 °C but gradually decomposed at 5 °C following first-order kinetics with $k_{obs} = 3.0 \times 10^{-4}$ s^{-1}. This suggests that liberation of phenol overrides the general tendency that aluminum methyl rapidly reacts to enable the entropically favored pathway, that is, evolution of CH_4 gas. In contrast, a 1 : 1 complex of Me_3Al and H_2O was kept inert at −70 °C, while at −40 °C it began decomposing, resulting primarily in $Me_2Al(OH)$.[223] The more inert nature of the Me group of $Me_2Al(OH)$ as opposed to that of Me_3Al is also

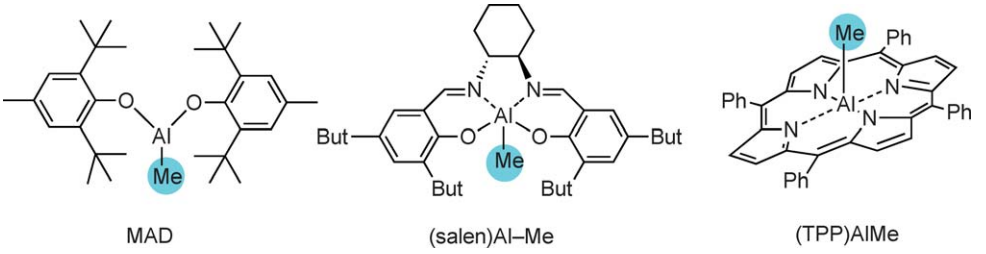
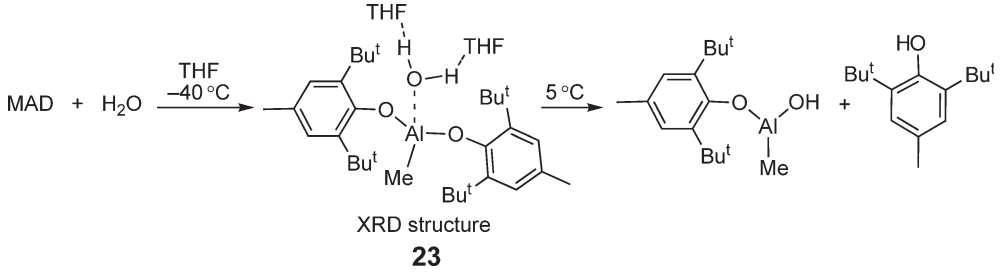


Figure 34 Al–Me bonds in various aluminum complexes.

demonstrated by an experiment employing a 2 : 1 mixture of Me_3Al and H_2O: a second liberation of methane to form $Me_2Al–O–AlMe_2$ starts above −20 °C. Et_3Al was also examined along these lines and found to be consistently less reactive than Me_3Al. Compared with Me_3Al, however, Bu^i_3Al was more reactive and started decomposing at −50 °C, but the second decomposition step was slower. The search for a partial decomposition of organoalanes by water merits identifying the formation mechanism of MAOs or other cage structures comprising repeated Al–O–Al linkages, which has attracted great attention from polymer scientists. Roesky recently reported time-dependent spectral data obtained during the hydrolysis of relatively bulky trialkylalanes and -galliums.[86,224] Bu^t_3Al is rather inert to amino alcohols, giving the hydrogen-bonded coordination complex **24** without formation of any covalent bonds and liberation of hydrocarbon gas (Equation (55)).[225] The thiomorphine complex **25** is stable at 25 °C while gradually decomposing at higher temperatures, eventually forming homodimer **26** (Equation (56)).[226]



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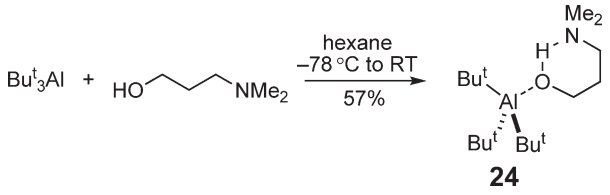

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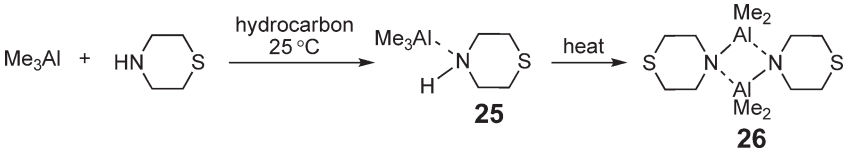


(56)

9.06.4.1.2 Aluminum alkyls in alkylation and deprotonation

The reactivity of Me_3Al can also be altered by coordination of solvent, and this treatment affects the addition mode of Me_3Al to carbonyl, imino, or olefinic substrates. This can be most typically seen in the case of solvated Me_3Al monomer giving axial alcohol predominantly, while the stereochemical reversal was observed in hydrocarbon solvents, in which the "closed" (homo)dimer (Me_6Al_2) predominates (Figures 35 and 36).

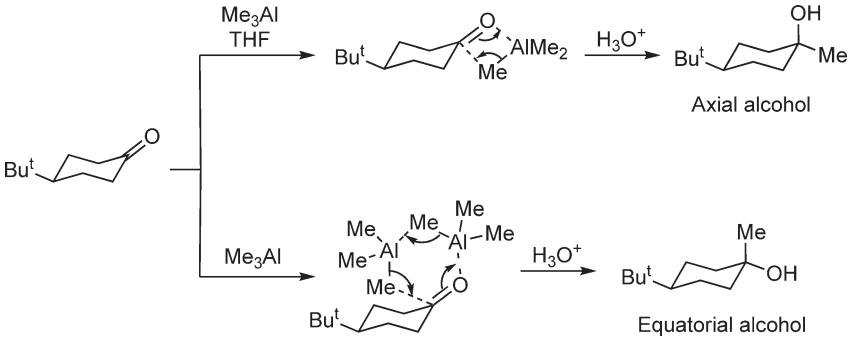


Figure 35 Different stereoselectivity controlled by Me_3Al dimer and monomer.

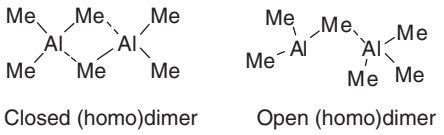


Figure 36 Closed dimer and open dimer of Me_3Al.

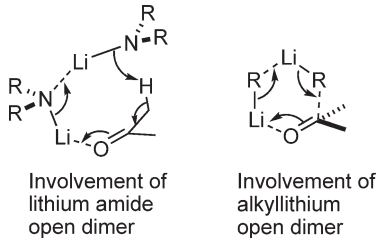


Figure 37 Involvement of open dimer in deprotonation and alkylation reactions.

The importance of the reagent on open dimers was also pointed out in the proposed mechanism of deprotonation by lithium amides and alkylation by organolithiums in carbonyl and imine chemistry (Figure 37).[227,228] This mechanistic basis was further extended to the catalyst-promoted addition of Et_2Zn[229] or BH_3[230] to carbonyl compounds. The involvement of "open" (homo)dimers overriding the monomer mechanism is now the general understanding, and a strong possibility. However, steric demands in a transition state ensemble sometimes favor a monomer pathway. It is reasonable to ascribe this exception to a decrease in steric congestion in the monomers relative to the open dimers. Although MAD alone apparently is not a promising methylating agent, combined use with MeLi or MeMgX (X = Cl, Br, I) affords effective methylation.[231] When a 1 : 1 toluene/Et_2O solution of MAD and MeLi (or MeMgX) was treated with the ketone, smooth addition to the carbonyl group took place with the formation of **27** or **28**, most likely via an open "hetero"-dimer pathway (Ashby transition state) (Figure 38). Thus, MAD might have a role in directing the methyl transfer through a relay mechanism.

The opposite sense of diastereoselectivity has been observed frequently, giving, for example, alcohol **29** or **30** exclusively in the MAD/MeM (M = Li, MgX) system (Equations (57) and (58)).[232,233] For the deprotonation events of the α-proton of ketones, a monomer pathway was proposed (Figure 39),[234] but the open dimer mechanism cannot be ruled out entirely. The relatively bulky aluminum phenoxide may be involved in the monomer pathway due to its

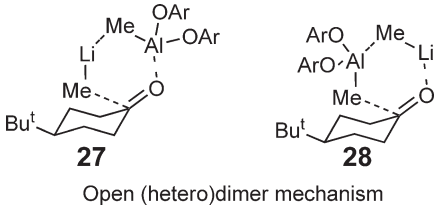


Figure 38 Two different open dimers in alkylation of 4-Bu^t-cyclohexan-1-one.

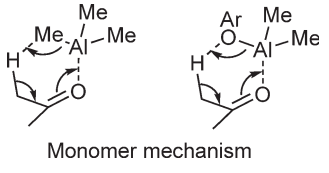
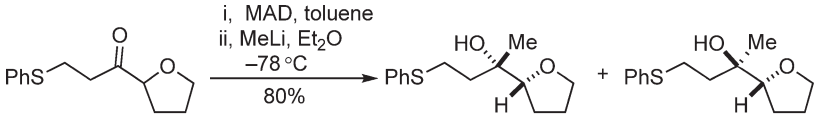


Figure 39 Me_3Al monomer mechanism in deprotonation of acetone.

steric effects.[235] Note that the phenoxy group is likely to be more susceptible to deprotonation and, hence, reacts faster than the alkyl groups but slower than the amide groups, both being attached to an aluminum center.



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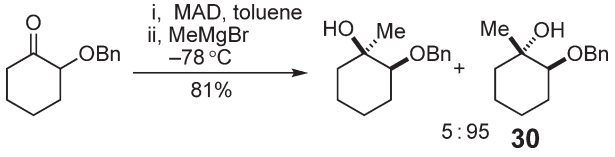
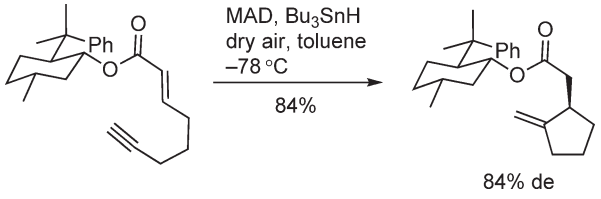


(58)

9.06.4.1.3 Aluminum alkyls in radical reaction

The methyl group of MAD shows another distinct behavior upon exposure to O_2: it works as a radical initiator, presumably through homolytic cleavage of the Me–Al bond. This reaction affords diastereoselective radical cyclization of chiral α,β-unsaturated esters (Equation (59)).[236] There exists rather old though subsequently growing evidence that many of the reactions of organoaluminums involve free-radical and/or peroxo intermediates upon UV or O_2 treatment,[5] one of which was isolated, and its structure was verified recently by XRD (Equation (60)).[237] However, ESR studies of MAD under an O_2 atmosphere revealed that homolytic cleavage of the aluminum–oxygen bond took place with the formation of two free radicals stable at RT. These are the only observable species: one is the phenoxy radical and the other is the more stable radical comprised of aluminum and the phenoxy group.[238] The peroxide–trialkylaluminum system is frequently used in industrial application for initiating radical co-polymerization of ethylene with vinyl acetate.[239]



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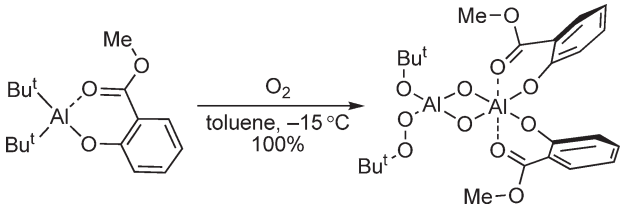


(60)

9.06.4.1.4 Aluminum alkyls in polymerization

The methyl group of (TPP)AlMe is also activated upon exposure to visible light (>350 nm), serving as a methylating agent for α,β-unsaturated esters.[240–242] This behavior was applied in the initiation of polymerization of methyl methacrylate (MMA) in the presence of MAD. The very high-speed chain process seems to start, upon light irradiation, with the conjugate addition of the Al–Me bond of (TPP)AlMe to a methacrylate activated by MAD and reach completion within 30 s (Figure 40). The resulting enolate might further react with a second methacylate activated by a (TPP)Al^+ species, or return to the (TPP)Al^+, generating a second (TPP)Al–enolate complex, followed by conjugate addition to a methacrylate. The Al–enolate complexes formed in each propagation step serve as the nucleophilic growing species, producing the repeating unit and eventually a polymer chain with a narrow molecular weight distribution (MWD ~ 1.1). (TPP)AlEt promotes CO_2 insertion into the Al–Et bond upon visible light irradiation in the presence of 1-methylimidazole.[242]

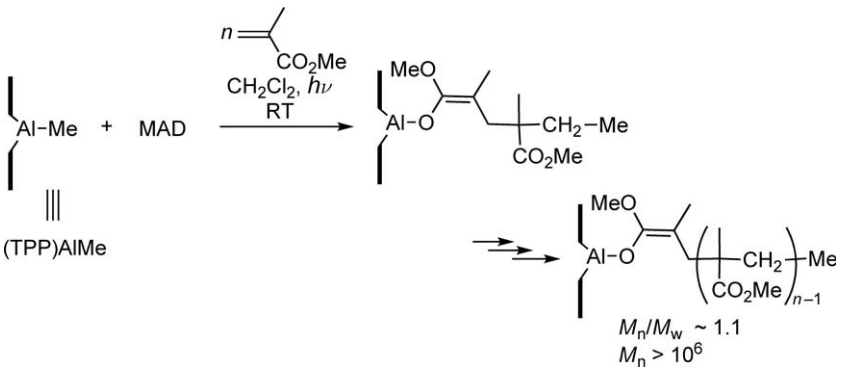
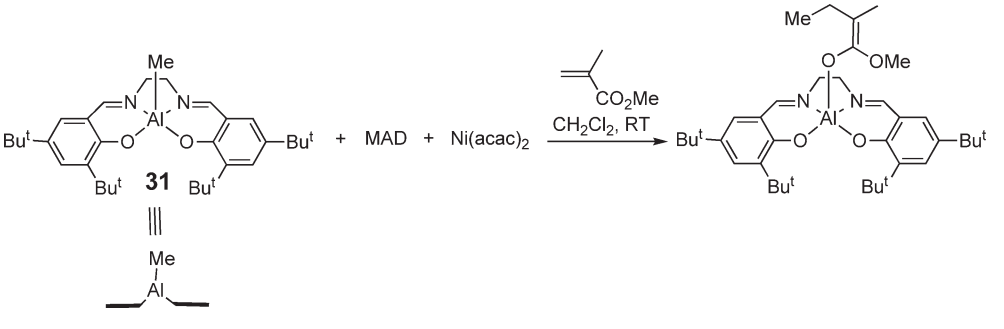


Figure 40 Schematic description of (TPP)AlMe-promoted polymerization of MMA.

A complex reaction mechanism that explains an abnormal feature of MAD, facilitating transfer of the methyl group on its own, was postulated.[243] The (salen)–AlMe complex **31** was used to initiate the polymerization of MMA in the presence of $Ni(acac)_2$ and MAD (Equation (61)). Without MAD, the conversion of the monomer is very low. MAD was suggested to play a dual role: it activates the MMA, and generates the active nickel catalyst responsible for enolate formation (Figure 41). The first step involves transfer of the methyl group of MAD to the Ni center. During the next step, the monomer MMA might insert into the Ni–Me bonds of **32**, generating the Ni–enolate complex **33**. Subsequent group exchange between **33** and the aluminum methyl of **31** gives **34**, which serves as the primary propagating anionic species, and Ni–Me catalyst **32** regenerates spontaneously. This is reminiscent of the "nickel effect", the basic nature of which has been well discussed in COMC (1995). In particular, the Me_3Al– and Et_3Al–$Ni(acac)_2$ catalytic system in conjugate addition events has been studied in detail in many works.[244] CIDNAP effects were analyzed recently in the reaction of Et_3Al with $CHCl_3$ in the presence of $Ni(acac)_2$.[245]



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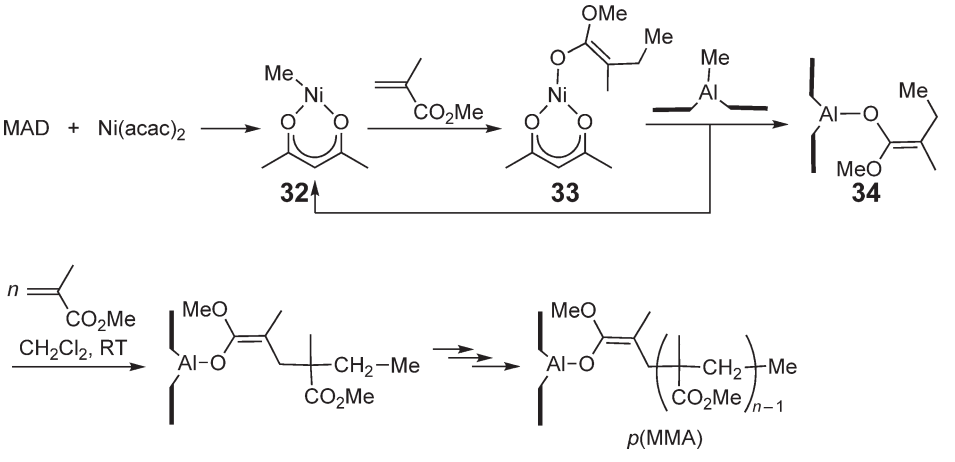


Figure 41 Proposed mechanism of MAD–$Ni(acac)_2$-mediated polymerization of MMA.

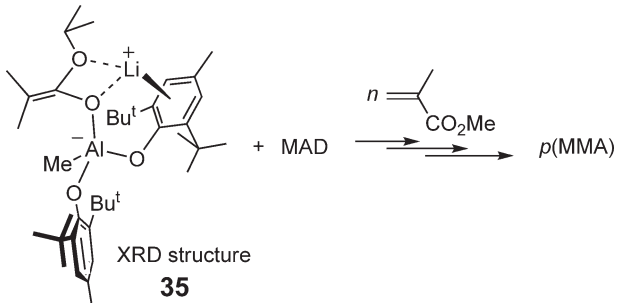


Figure 42 Possible reaction intermediate involved in polymerization of MMA promoted by MAD.

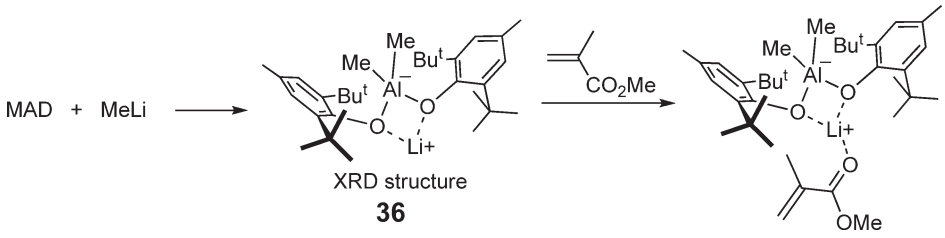
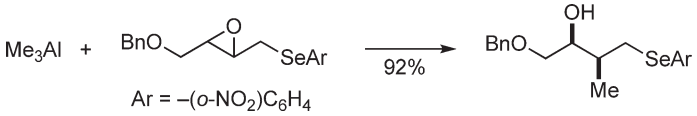


Figure 43 Possible reaction intermediate involved in polymerization of MMA promoted by MAD and cat. MeLi.

The MAD/RLi system and its variants are widely used in the polymerization of methacrylates or acrylates.[246] By taking into account the inertness of the methyl group of MAD, RLi serves as the initiator of polymerization like (TPP)AlMe. The MAD–Li-enolate complex **35**,[247] which might resemble the core structure of the propagating enolate species, was isolated and its structure was determined by XRD (Figure 42).[248] By performing kinetic studies using **35**, MAD, and the monomer MMA, it was suggested that the "single-site anionic propagating center" mechanism is operative, which compares well with the one proposed for the MAD/(TPP)AlMe system. Another mechanistic scenario that involves coordination of conjugated carbonyl compound at the Li^+ of lithium dialkylaluminum bis(2,6-di-*t*-butyl-4-methylphenoxide) **36** was proposed based on XRD (Figure 43).[249] Note that activation of the monomer by MAD is a critical treatment in enabling the polymerization. MAD is also considered to be a nice scavenger of small amounts of H_2O and O_2,[250] which reside in the reaction mixture and possibly prevent high performance of the chain processes.

9.06.4.1.5 Aluminum alkyls in reactions with carbon–carbon multiple bonds, oxiranes, and other functional groups

Me_3Al and Et_3Al have been widely used for alkylation of various functional groups. Very recent examples include the ring-opening methylation of oxiranes (Equations (62) and (63)),[251–253] lactones[254] and aminoacetals (Equation (64)),[255] and the methylation of the anomeric position of sugar derivatives[256–258] (Equations (65) and (66)) and carbamates (Equation (67)).[259] A second alkylation was suppressed to yield ketones in the methylation of esters with Me_3Al/ethylenediamine system (Equation (68)).[260]



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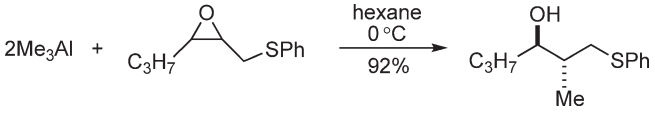

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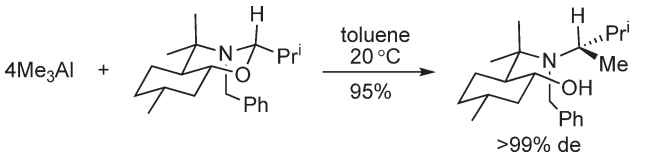

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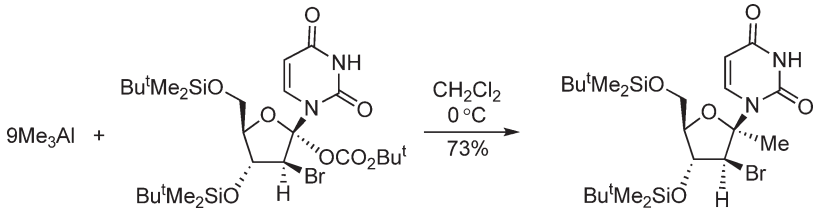

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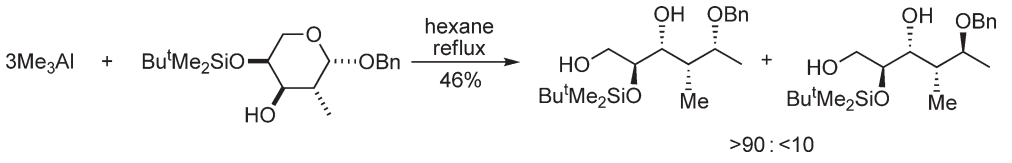

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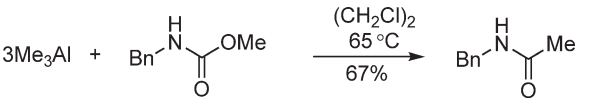

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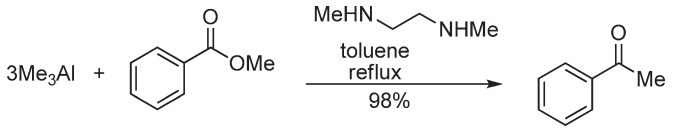
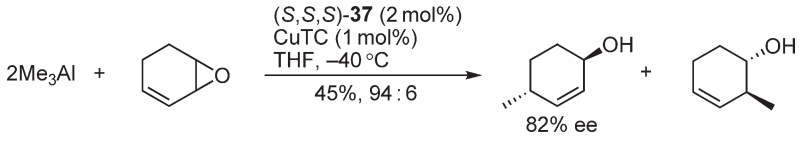
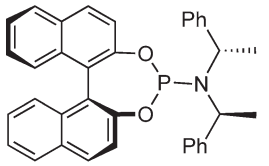


(68)

The use of Me_3Al is generally effective for the methylation of C═C (double) and C≡C (triple) bonds, being promoted by transition metals such as Ti, Zr, Cu, Pd, and Ni species. This rather old chemistry has been well established, achieving carbometallation and conjugate addition to α,β-unsaturated ketones and esters. Alkylation of allylic epoxides proceeded at the C═C double bonds, followed by simultaneous ring opening in the presence of the catalytic Cu–**37** species (Equation (69)).[261] It was subsequently found that the transfer of the methyl group from Al to the transition metal is facilitated, irrespective of whether the several heteroatoms are attached to Al covalently or non-covalently (Equations (70)–(72)).[262–265] Therefore, Me_3Al can be replaced by the more air and moisture insensitive derivatives **38**–**40**, which have found broader utility, due to their easier handling, in various methyl–aryl coupling and conjugate addition processes. It was also elucidated that a small amount of H_2O enhances the reaction rate of the methylalumination of terminal alkynes (Equation (73)).[266]





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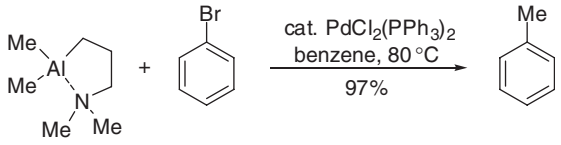

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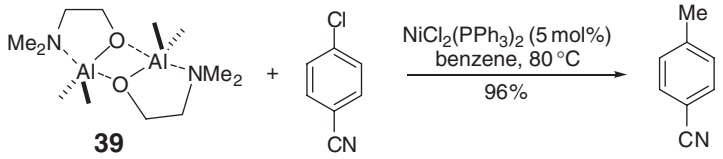

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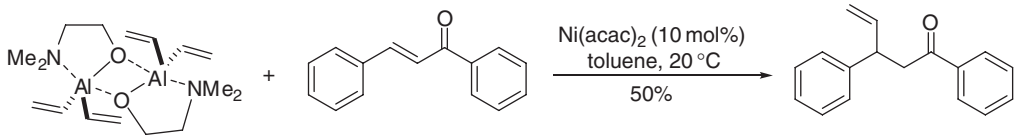

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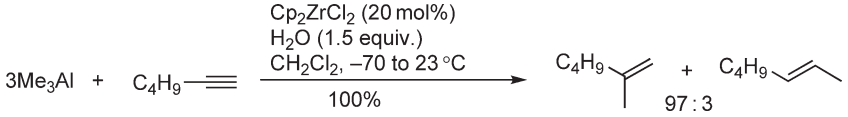
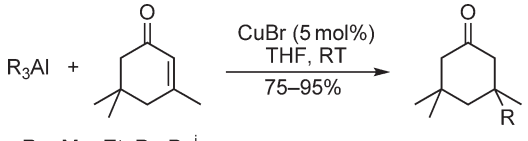


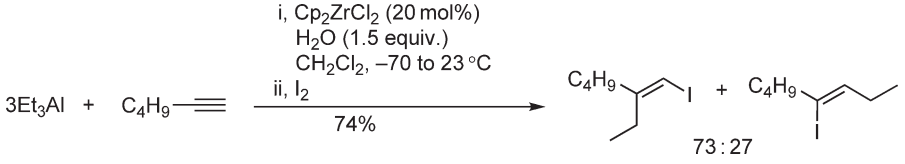
(73)

Et_3Al is sometimes a good ethylating agent with the aid of a transition metal catalyst;[267–271] however, β-hydride elimination frequently competes with ethylation, bringing about reductive processes such as reduction of vinyl phosphates[272] and hydroalumination of alkynes[273] in the presence of Pd(0) catalysts. The use of $Ni(acac)_2$ as a catalyst was shown to be limited to aluminum alkyls without β-hydrogen in the conjugate addition.[274] β-Hydride elimination/transfer is the side-process commonly observed with other organoaluminums incorporating higher alkyl chains. This hampers the synthetic scope of those organoaluminum reagents from further expansion, no matter how they are used, with or even without transition metal species. However, there is significant growing evidence that availability of those higher alkyls could be maintained by the proper choice of transition metal catalyst, ligand, substrates, and/or reaction conditions. The Ni-catalyzed aryl–ethyl coupling was indeed facilitated by Et_3Al in certain cases.[270,271] The Et, Pr, or even Bu^i groups of aluminum are transferable to α,β-enones in Cu(I)-catalyzed conjugate addition (Equation (74)).[267–269] The Zr-catalyzed ethylalumination of terminal alkynes proceeds readily at a low temperature, thereby suppressing the β-hydride elimination from proceeding significantly (Equations (75) and (76)). Negishi found effective methods for methyl-[275] and ethylalumination[276] of terminal olefins, which was further extended to the asymmetric version using a chiral zirconocene-type catalyst **41** (Figure 44).[277]



(74)

R = Me, Et, Pr, Bu^i



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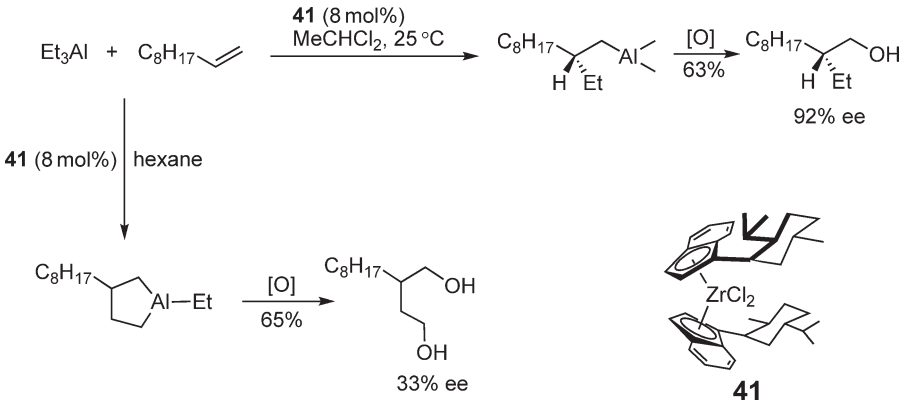
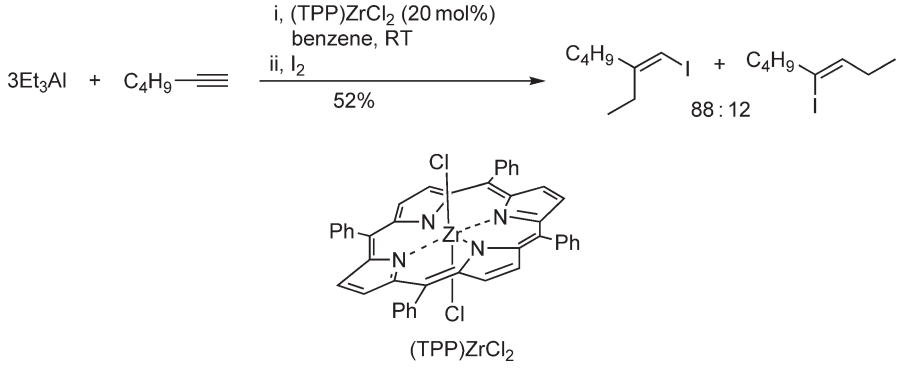


Figure 44 Solvent effects on product distribution in the asymmetric ethylalumination.



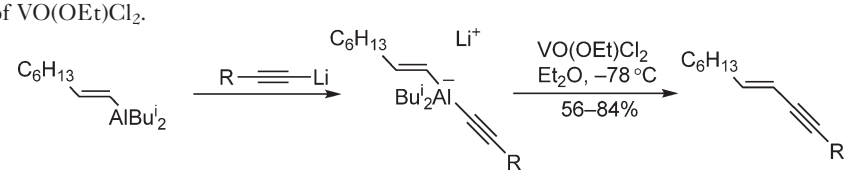
(76)

Although methyl and ethyl groups embedded into the elaborate coordination sphere of aluminum are certain to have potential reactivity, it is obvious that special treatment is necessary for promoting the alkyl transfer, which otherwise is difficult to achieve. Thus, MAD and other elaborate methylaluminum species are finding wider applicability as monomeric Lewis acid reagents in both polymerization and organic synthesis by taking advantages of this rather inert nature of the methyl group and high oxophilicity of the aluminum atom. Some of those catalytic properties will be clearly demonstrated in the forthcoming sections.

9.06.4.2 Organic Group-selective Transfer from Aluminum(III) Ate Complexes to Electrophiles

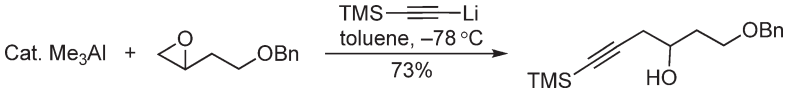
As mentioned above, most trivalent organoaluminum-mediated reactions are initiated by coordination of the substrate to an aluminum atom; thus, significant solvent effects are observed in many cases which affect the reaction rate, pattern, and selectivity. Similarly, the ate complexes of organoaluminum compounds, adopting tetracoordinate geometry, dramatically change the reactivity of the parent trivalent organoaluminums. The complex has already satisfied the octet rule and behaves as a nucleophile rather than a Lewis acid. If different organic groups (e.g., alkyl, alkenyl, alkynyl, or aryl groups) were attached at the same time to an aluminum atom, the question arises as to which organic group would be more reactive. Each covalent bond has discrete covalent nature, and their order of reactivity has been roughly estimated as hydride (H^-) > alkynyl (Csp) > alkenyl (Csp^2) > alkyl (Csp^3). For example, the ate complex of an alkynylaluminum species undergoes alkynyl coupling in the presence of an oxovanadium reagent. The reaction is intriguing in several ways. When the aluminum atom is simultaneously bound to alkynyl, alkenyl, and alkyl groups, the cross-coupling is accommodated with the first two of these groups after delivery to the vanadium center, and thereafter, undergoes reductive elimination (Equation (77)).[278] Neither alkynyl–alkynyl coupling nor alkenyl–alkenyl homo-coupling was detected. This group-selective process depends on the structural and electronic

features of the oxovanadium species and reaction conditions. Although the triorganoaluminum species is less reactive as a nucleophile than the corresponding ate complex, even the former neutral species are capable of cross-coupling under more drastic conditions. At higher temperatures, aryl(diethyl)aluminums undergo ethyl–aryl cross-coupling in the presence of $VO(OEt)Cl_2$.



(77)

In another reaction, alkynyl groups were transferable in the presence of a catalytic amount of Me_3Al (Equation (78)).[279] Preference for the Ph group transfer has been well featured in the competitive alkyl transfer process leading to selective imine arylation (Equation (79)).[280,281] Higher organic chains such as ethyl and butyl are generally less reactive than a methyl group, as evidenced from the reaction of the corresponding aluminum ate complex hybridized with those different alkyl groups. This order of reactivity was validated by recent examples of oxirane ring opening[282] (Equation (80)) and Meerwein pinacol-type rearrangement (Equation (81)),[283] both of which are accompanied by subsequent methylation. A notable discrepancy is evident in light of the dissociation energy of Al–Me (283.6 kJ mol^{-1}), Al–Et (272.5 kJ mol^{-1}), Al–Pr (273.1 kJ mol^{-1}), and Al–Bu (280.3 kJ mol^{-1}).[36] The methylation proceeded with a stoichiometric amount of Me_3Al and a catalytic amount of BuLi. Note that the ethyl group seems to have higher mobility than the butyl group.[284]



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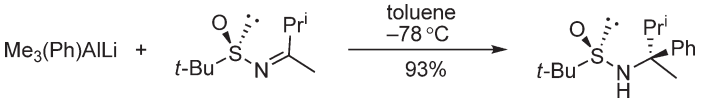

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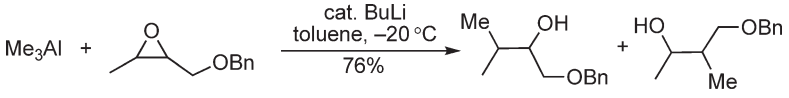

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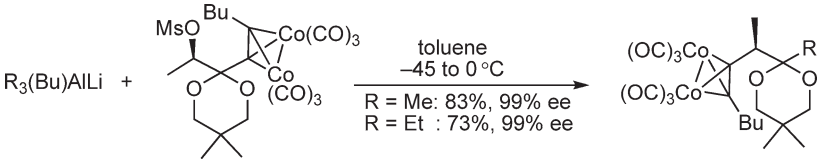
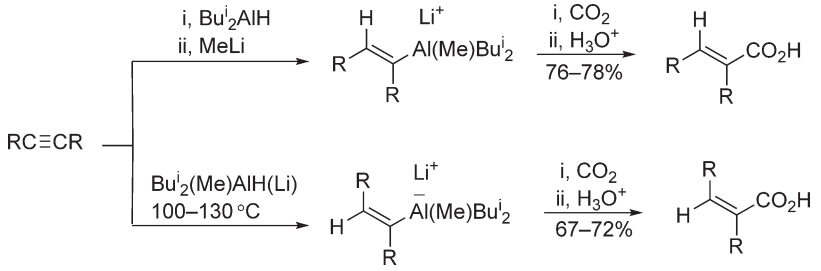
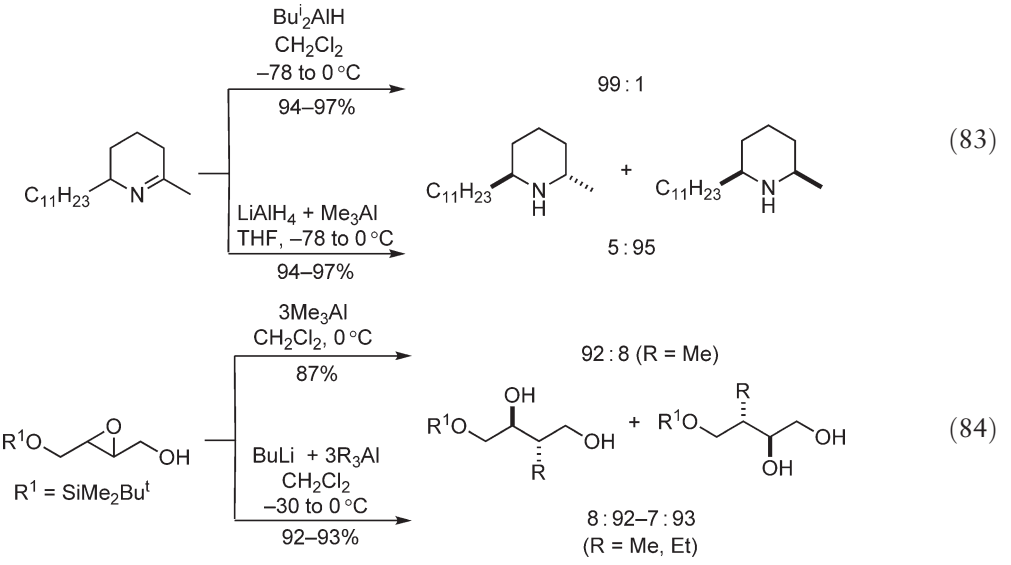


(81)

There exist many other examples that illustrate the reactivity of organic groups as well as hydrides bound to aluminum, which sometimes significantly affect the selectivity of the reaction. Notable results were found in older as well as recent literature, describing hydroaluminations (Equation (82)),[285] Beckmann rearrangements (Equation (83)),[286] and epoxide ring-opening alkylations (Equation (84)).[287]



(82)



9.06.5 Specialized Topics – Recent Advances in Organoaluminum and Related Compounds as Lewis-Acidic Promoter for Organic Transformations

9.06.5.1 Ligand-induced Geometrical Diversity Affording New Reactivity of Organoaluminum(III) Compounds

Aluminum is most stable as a trivalent metal, adopting trigonal geometry with sp^2-hybridization. Upon coordination with a Lewis base, the geometry changes to sp^3-hybridization, with structures adopting tetrahedral geometry. The geometry of aluminum can, however, be altered significantly by the nature of the ligand attached to it, which sometimes is consistent with hybridization other than sp^2 or sp^3, even though d-orbital hybridization is highly unlikely. The XRD structures of various aluminum(III) complexes indeed support the properties of the geometry of aluminum. For instance, all the (salen)AlX species adopt a square-bipyramidal metal-centered geometry, but the potentially electrophilic nature of the complex is preserved, affording typical Lewis acid-promoted reactions. This and other numerical data are indicative of an available vacant orbital in either the equatorial or apical direction that recalls sp^3d^2, but, if not, that invokes an as yet unknown type of quasi-hybridization, presumably the sum of three independent p-orbitals ($p_x + p_y + p_z$), which can also provide octahedral geometry.

Therefore, it should be pointed out that the catalytic nature of aluminum varies substantially with subtle changes in aluminum geometry. Organoaluminum complexes adopting a higher-coordinate geometry, while retaining Lewis-acidic character, have found broad utility as structurally more stable catalysts or co-catalysts in organic and polymer synthesis. Nelson recently disclosed[288–291] that ligands **42** and **43** had entirely different effects not only on the structural geometry, but also on the carbonyl activation capacity of aluminum. The Lewis acidity of **44** and the distored metal coordination geometry were validated by the reactions, which the corresponding methylaluminum catalysts promoted, and by XRD (Figure 45). The geometry of **45** indicated that the expanded chelate size of the propylene triamine-derived ligand conferred sufficient conformational flexibility to enable the Al(III) ion to adopt a

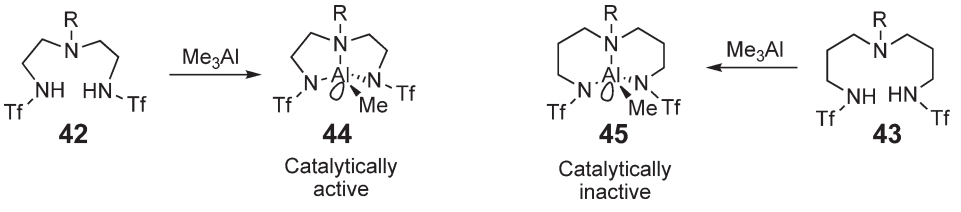


Figure 45 Difference in carbonyl activation capacity imposed by chelation ring size of aluminum reagents.

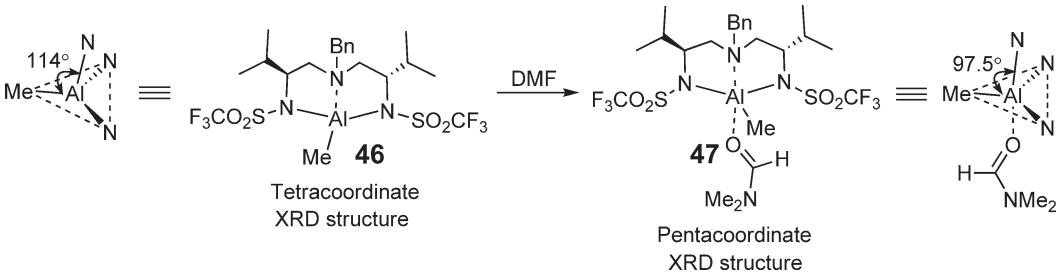


Figure 46 Trigonal bipyramidal geometry accommodated by the fused five-membered rings.

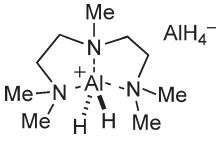
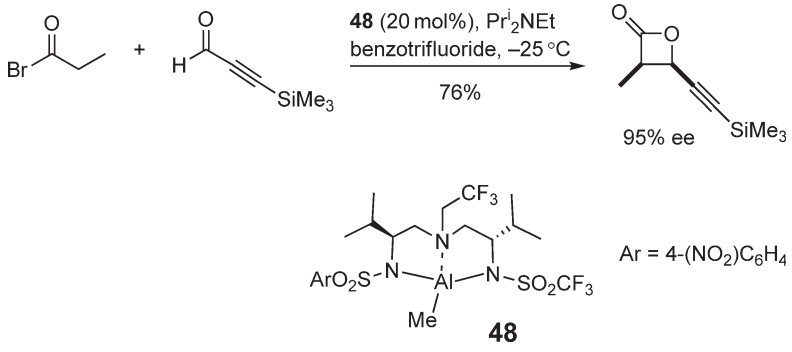


Figure 47 Polyamine-ligated aluminum cation accommodated by the fused five-membered rings.

low-energy, tetrahedral (sp^3-) coordination geometry. The author concluded that other than sp^3, presumably sp^3d-Al(III) hybridization in **44** and **46** furnished a low-lying metal-centered LUMO, thus ideally disposing the Al(III) center to accommodate a fifth ligand in order to complete the trigonal-bipyramidal coordination geometry, and achieving a Lewis acid–base complex such as **47** (Figure 46). Conversely, the electron-rich, highly coordinated complex **45**, lacking any ligand-imposed coordinative distortion, has minimal Lewis-acidic character. Subsequent studies substantiated the catalytic versatility of this type of structure, for example, **48**, in a range of typical Lewis acid-catalyzed reactions (Equation (85)).[289–291] In fact, penta- and even hexacoordinate species, frequently found in organoaluminum complexes, are accommodated by at least one five-membered metallacycle produced from multidentate ligands. An earlier example of a polyamine-ligated aluminum cation represents a higher coordinate, similar to those generated by Nelson (Figure 47).[292]



(85)

In contrast, such higher coordinates seem relatively unusual for a simple six-membered metallacycle, being liberated from a substantial distortion. In some cases, however, a ligand-imposed coordinative distortion arises, exposing an available vacant orbital for the six-membered metallacycle. For example, a 1 : 1 mixture of BnOH and the organoaluminum compound bearing amine bis(phenolate) proved to catalyze the living anionic polymerization of ε-caprolactone with narrow MWD (~1.1).[293] The XRD structure of **49** adopts a distored tetrahedral geometry corresponding to four coordinate; however, to keep the living polymerization nature, each aluminum alkoxide intermediate must accommodate the binding of an incoming substrate, adopting a consistent five-coordinate geometry in each propagation step (Figure 48). The aluminum-centered trigonal-bipyramidal geometry is also explicitly indicated in another example of a seven-membered metallacycle (Figures 49 and 50).[294] This higher-coordination geometry is not as distored as that attained by a five-membered ring; hence, one plausible explanation for the higher

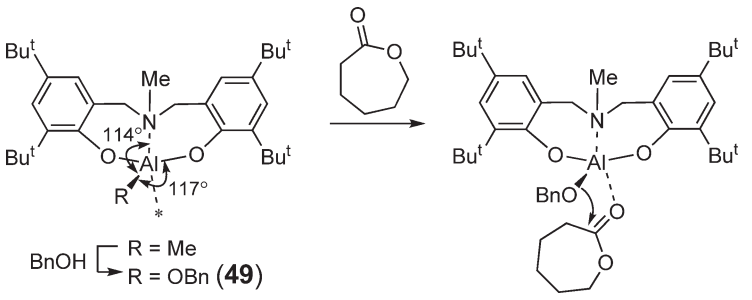


Figure 48 Trigonal bipyramidal geometry possibly accommodated by the strain of fused seven-membered rings.

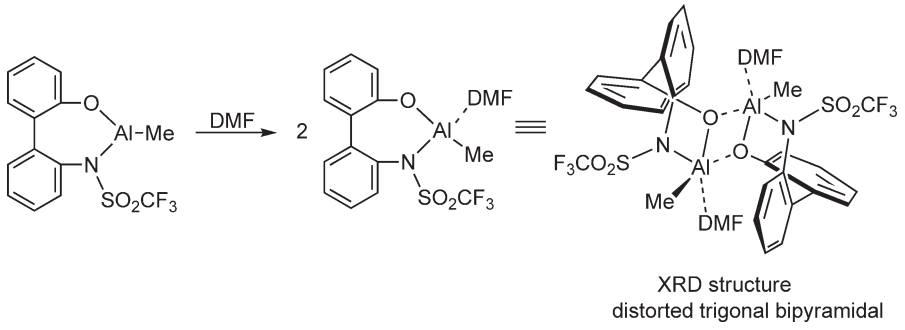


Figure 49 Trigonal bipyramidal geometry possibly accommodated by electron-withdrawing ligand.

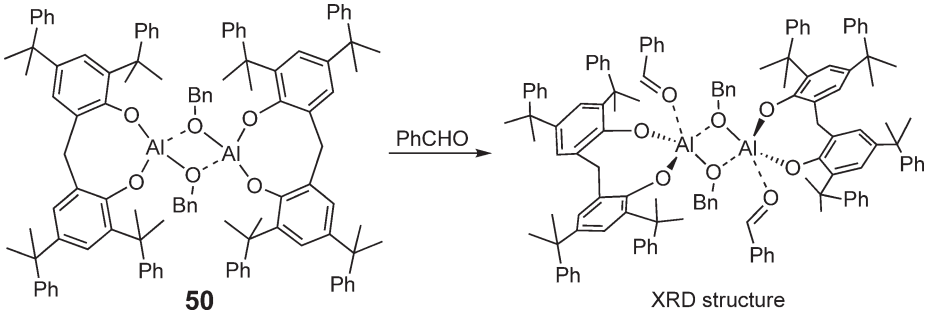


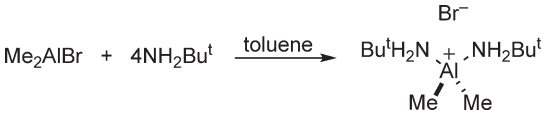
Figure 50 Trigonal bipyramidal geometry possibly accommodated by the strain due to steric bulk of the highly oxygenated seven-membered metallacycle.

coordinate is that it seems to be induced by the additional action of a strong electron-withdrawing ligand. It is well known that by lowering the metal-centered LUMO with more electronegative groups on the metal center, tin and silicon adopt higher-coordination geometry – penta- and hexacoordinates. Similarly, a newly available vacant orbital might be exposed on the aluminum center. According to a survey of the number of XRD structures of aluminum complexes, it would be reasonable to state that the more electronegative the group attached covalently to an aluminum center, the more feasible a higher coordination. The geometrical change from tetra- to pentacoordinate was indeed observed in another example of the highly oxygenated seven-membered metallacycle, upon coordination of benzaldehyde to the tetracoordinated dimer **50** (Figure 50).[295]

9.06.5.2 Cationic Organoaluminum Compounds

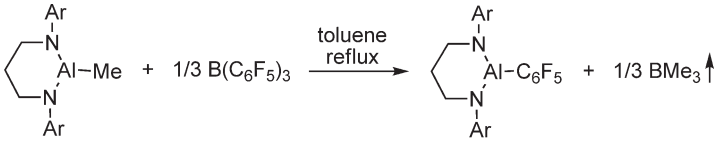
Neutral organoaluminum(III) compounds have broad applicability in organic synthesis as extremely strong Lewis-acidic reaction promoters. However, the exploration of increased reactivity in aluminum is a key subject for expanding their utility, especially in polymer synthesis and in the activation of relatively stable substrates

(e.g., CO and CO_2). One of the first cations structurally characterized and described in early literature were extraordinarily septacoordinate.[296] Multi-oxygen pentacoordinate crown ethers were also introduced.[297] Subsequently, four-coordinate cations started emerging in the literature (Equation (86)).[298–301] They were too reactive and labile to be used broadly in synthetic applications.



(86)

So far, cationic organoaluminum species are likely to be kept more stable if the following conditions are satisfied: (i) the electron richness around the aluminum atom is enhanced by multidentate ligand attachment, or especially by achieving higher coordination at aluminum; and (ii) a vacant aluminum orbital is superimposed on an expanded array of π-orbitals provided by the attachment of a bidentate ligand, where the metallacycle accommodates effective electron delocalization. The significant contribution of the latter criteria can be found in the following examples (Equations (87)–(90)). The imine fragment provides a cyclic π-conjugated system to enable electron delocalization that stabilizes the aluminum cation; otherwise, merely ligand exchange takes place (Equation (87)).[302,303]



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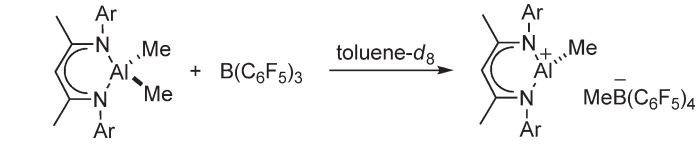

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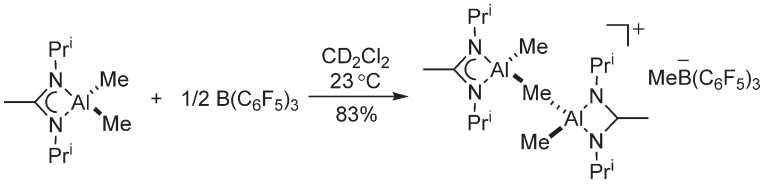

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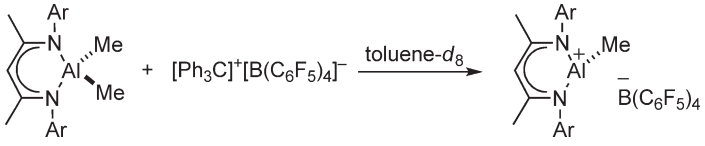


(90)

These electronic and geometrical characteristics can lead to the cationic center persisting for a reasonable lifetime. Representative examples of the general formula denoting the distinct coordination modes of aluminum cations are summarized in Figure 51. Each structure (51(a)–51(j)) was optimized through changes in ligand constituents and/or in the geometry around the aluminum atom. Cationic aluminums incorporating amidinate (Equation (89)),[304] β-diketiminate (Equation (90)),[305–307] and aminotroponiminate (Figure 52),[308–310] have been introduced by Jordan, and their catalytic applications in olefin polymerization have been thoroughly investigated.

Abstraction of one ligating group from an aluminum center is carried out to generate aluminum cations. This has been done in several ingenious ways. For example, protonated amines (Equation (91)) and $B(C_6F_5)_3$ (Equation (92)),[311] as well as carbocations such as trityl cation (Equation (90)), facilitate removal of an alkyl group from the aluminum atom. These processes end up with the favorable liberation of the corresponding hydrocarbons or formation of a strong B–C or C–C bond. In order to detach Al–halogen bonds, an ion pair such as $NaBPh_4$ was used to precipitate the sodium halides out of the solution (Equation (93)).[312] An attempt to prepare low-coordinate aluminum cations, by reaction of the aluminum iodide adducts with $NaBPh_4$, was unsuccessful, and resulted merely

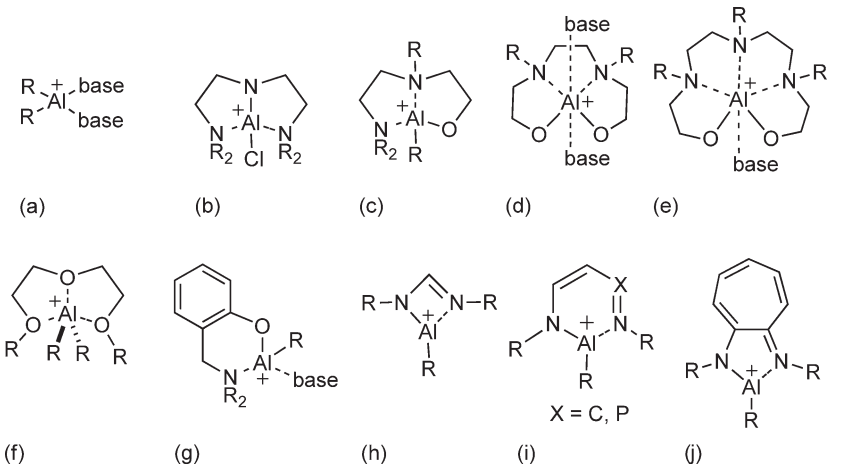


Figure 51 Distinct coordination modes of aluminum cations.

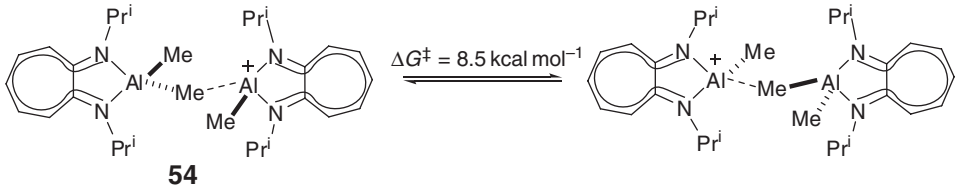
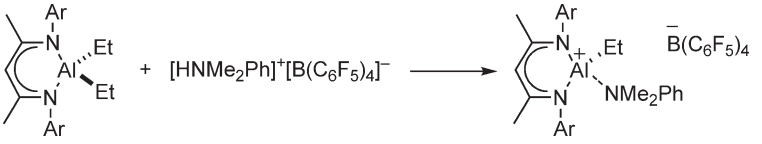
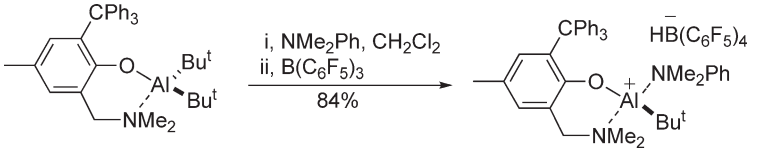


Figure 52 Energy barrier upon conformational change or cation exchange in the complex of neutral and cationic aluminum aminotroponiminate.

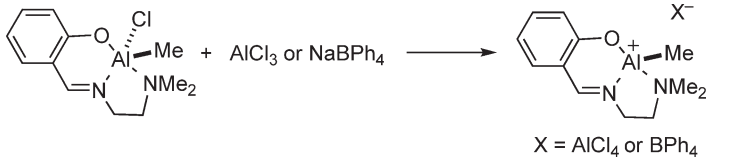
in phenylation products (Equation (94)).[313] In another example, MX_3 (M = Al, Ga; X = alkyl, Cl) was utilized to promote the formation of ate complexes such as $AlCl_4^-$[312] (Equation (93)) and $GaCl_4^-$.[314] In special cases, upon treatment with H_2O, such cations are generated automatically. These cationic species apparently show a Lewis acidity much greater than the parent neutral Al(III) species in many cases.



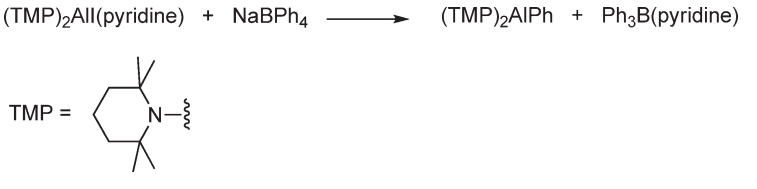
(91)



(92)

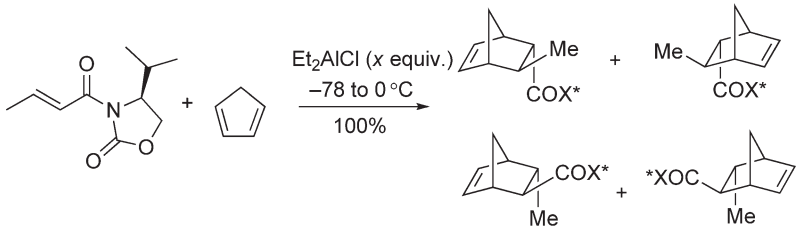


(93)



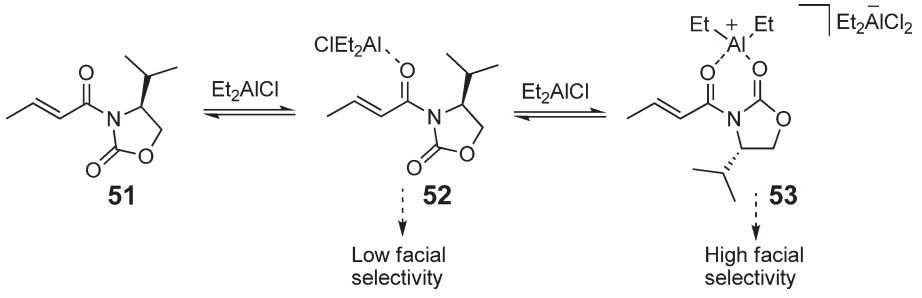
(94)

In 1988, Evans featured the high reactivity and importance of cationic aluminum species in organic synthesis.[315] Excess R_2AlCl (R = Me, Et) was found to behave differently from less than 1 equiv. of R_2AlCl in the Diels–Alder reaction of the oxazolidinone derived from an α,β-unsaturated carboxylic acid (Equation (95)). The reactivity and diastereoselectivity of the reaction strongly depends on the stoichiometry of the organoaluminum Lewis acid used to catalyze the reaction. The equilibrium $2[Et_2AlCl] \rightarrow [Et_2Al]^+ + [Et_2AlCl_2]^-$ is reinforced by unknown factors, and is invoked to account for this unusual observation. Thereafter, Castellino focused on the solution structure of the Et_2AlCl–**51** complex and supported Evans' hypothesis (Equation (96)).[316] The main species formed initially with 1 equiv. of Et_2AlCl was assumed be **52**. The species when 2 equiv. of Et_2AlCl is present was assumed to be **53**. Al-complex **53** was proved to be responsible for the high level of diastereocontrol. This conclusion was reconfirmed by an additional experiment, in which a similar cationic intermediate was generated through a separate pathway (Equation (97)). The formation of cationic aluminum species was facilitated by mixing **52** with sodium tetrakis{[3,5-bis(trifluoromethyl)phenyl]} borate.[316] This protocol to generate cationic aluminum species was subsequently utilized in the chelation-controlled Mukaiyama-aldol reaction, giving high *anti*-selectivity.[317] In all these cases, stabilization of the aluminum center with a multidentate chelation structure, facilitated by no more than two oxygen atoms of reactants and/or products, might help to accommodate the $[Et_2Al]^+$ species. Very recently, icosahedral carboranes of the type $CB_{11}H_6X_6^-$ (X = halide) have proved to stabilize $[Et_2Al]^+$, allowing its isolation and structural characterization.[318]

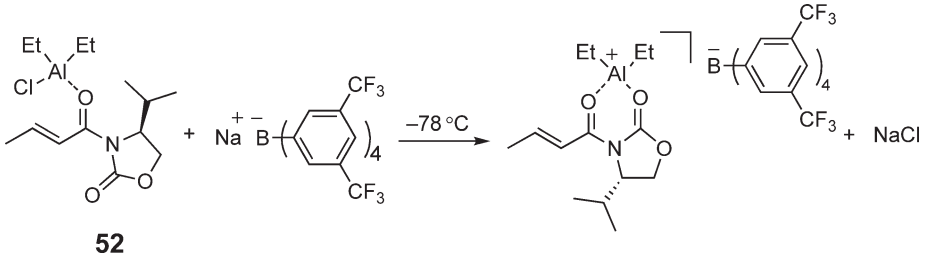


(95)

Et_2AlCl (0.8 equiv.): *endo* : *exo* = 15 : 1, 70% de
Et_2AlCl (1.4 equiv.): *endo* : *exo* = 50 : 1, 90% de



(96)

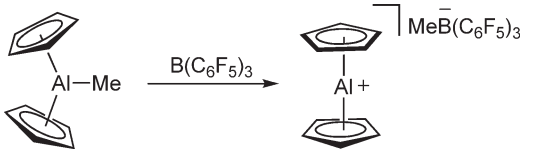


(97)

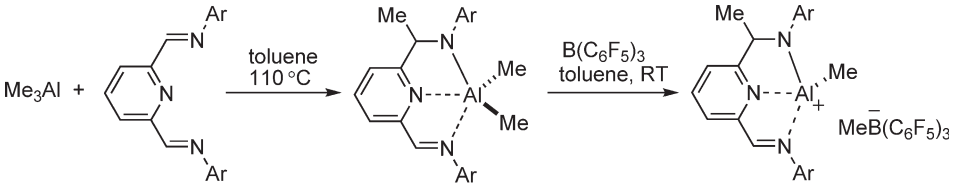
9.06.5.2.1 Low-coordinate cationic organoaluminum(III) compounds (two to four coordinate)

Group 4 elements (e.g., Ti, Zr) are used as typical catalyst precursors for olefin polymerization and serve as potent cationic components for polymer chain growth with the aid of aluminum (e.g., MAO) or boron co-catalysts. It would be more efficient and convenient if organoaluminum cations were used to polymerize olefins. From this viewpoint, following an earlier precedent with two-coordinate cations (Equation (98)),[319,320] some three-coordinate organoaluminum cations hold promise, and their ability to promote polymerization of ethylene or terminal olefins is now

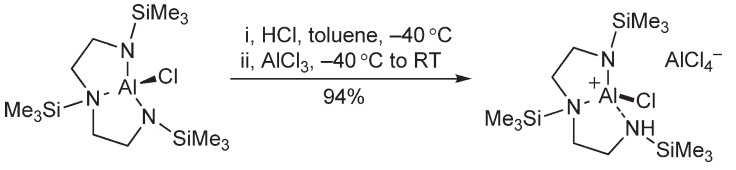
emerging in the literature.[305–310] Very unstable quasi-two-coordinate, cationic aluminum species were also recently characterized.[321] In addition to the three-coordinated species, four-coordinate alkylaluminum cations have begun attracting considerable attention (Equations (99) and (100)).[322,323] A multidentate nitrogen-based structure has now become a platform for these classes of catalyst precursor. Of the two alkyl groups on the cation precursors, one is for abstraction by the co-catalyst (carbocations or $B(C_6F_5)_3$) to form the aluminum cations noted previously. The other can be adjusted in anticipation of insertion of the olefin double bond upon its coordination, that is, for initiation of polymerization. This mechanism is ideal if living polymerization is considered in view of low MWD.



(98)



(99)



(100)

However, there is no clear evidence that supports the living (polymerization) nature. In addition, a theoretical study predicted that none of the proposed active cationic species should give a high molecular mass polymer.[324] The author also concluded that olefin polymerization at a single aluminum center is rather unlikely. Further DFT and *ab initio* calculations agree that the main chain-transfer process is the β-hydrogen transfer to the monomer, and that this is substantially easier than propagation.[325] A renewed interpretation of the NMR studies revealed the predominance of dinuclear aluminum amidinate complexes, for example, **54–57**, formed from the co-addition of the cationic species and the parent neutral species (Figures 52 and 53).[326] From additional theoretical investigations of the simplified model structure (Figure 54), a binuclear complex such as **56** was assumed to be more responsible for the polymerization catalysis,[327] although several issues are thrown into reasonable doubt. A more reliable mechanism awaits for future research.

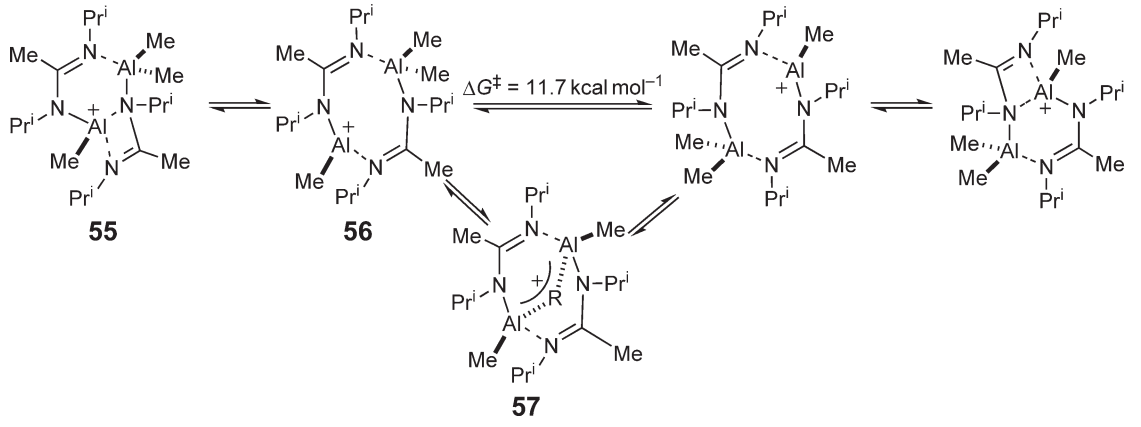


Figure 53 Energy barrier upon conformational change or cation exchange in the complex of neutral and cationic aluminum amidinates.

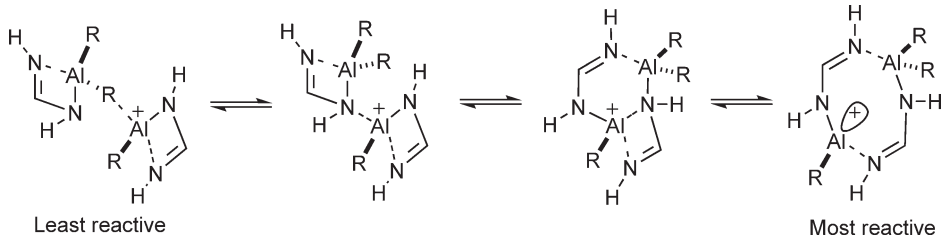


Figure 54 Theoretical results obtained from the calculation of model structure of aluminum amidinates.

9.06.5.2.2 High-coordinate cationic organoaluminum(III) compounds (five or six coordinate)

To date, a range of six-coordinate aluminum cations and their neutral precursors (latent cations) have been synthesized and isolated, and their XRD structures are identified.[328–333] In particular, salen-based aluminum cations and their latent cations are the most widely investigated in terms of substantiating their structures, coordination aptitude, and reactivity in organic synthesis as well as in polymerization processes. Subtle changes in the structure of the salen-based ligand had a significant effect on the coordination sphere in the octahedral geometry of the aluminum atom (Figures 55 and 56).

Although (salen)Al cations **58–61** are bound to two identical molecules that occupy two vacant orbitals to complete the octahedral geometry, a distinct mode of occupation is perceptible. Two H_2O molecules are in a *cis*-relationship for **61**,[328] while two THF,[329] MeOH,[330,331] or H_2O[330,332] molecules are in two apical positions corresponding to a *trans*-relationship in **58–60**. Of particular note is that structure **61** has one of the phenoxy oxygen atoms in the apical direction, whereas neutral species **62** accommodates the two phenoxy oxygen atoms in equatorial positions, or a distored trigonal-bipyramidal geometry. The fact that none of the cations degrades in water or in alcoholic solvents hints at potential aqueous, and thereby environmentally benign, processes. Due to the high oxophilicity of the salen-based aluminum cations, in certain cases, the homodimer formation prevails against solvation that would insufficiently stabilize the monomer, even though steric constraint is more substantial in the dimer (Figure 57).[333] Compound **64** was used as a catalyst precursor for living polymerization of lactide with a very narrow MWD. Production of the oxo-bridged dimer **65** is also possible (Figure 58),[334] and this type of compound has been used as an asymmetric catalyst by Jacobsen (Equation 104).[335] There exist many other organoaluminum variants adopting a five-coordinate geometry,[336,337] in which oxygen and/or nitrogen atoms are incorporated into a bidentate or tridentate ligand. These are strong candidates for the generation of cationic aluminum species, but have not yet been used as such.

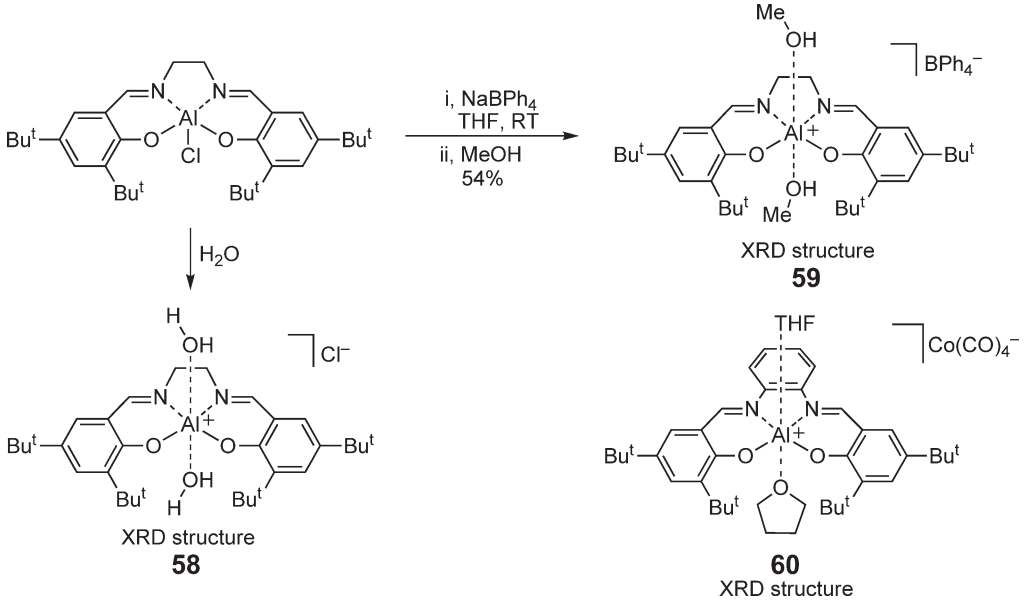


Figure 55 Salen–Al(III) complexes formed upon coordination at the two apical sites.

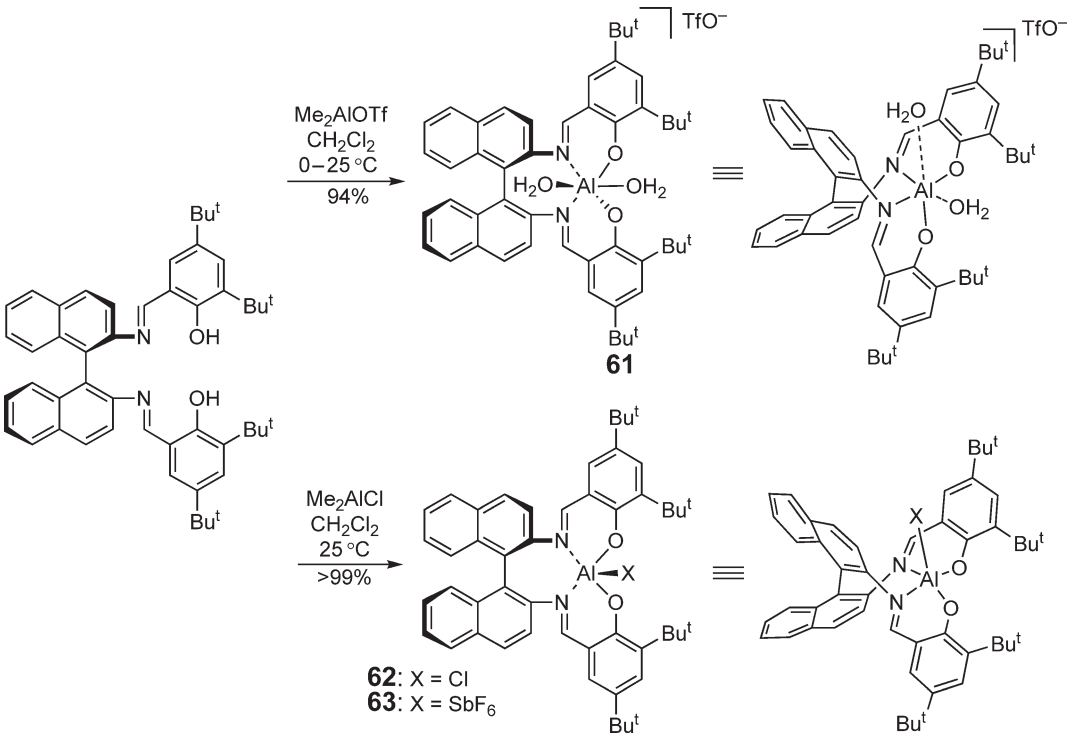


Figure 56 Difference in coordination site for phenoxy ligand.

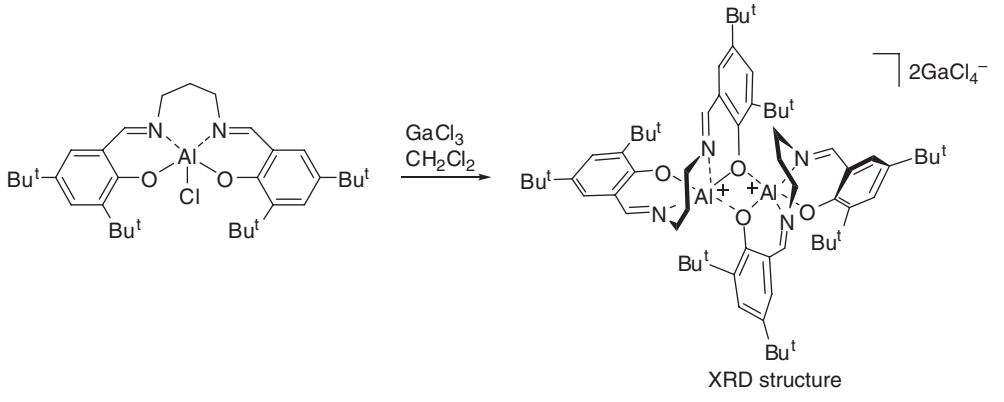


Figure 57 Dimerization of Salen–Al(III) cation.

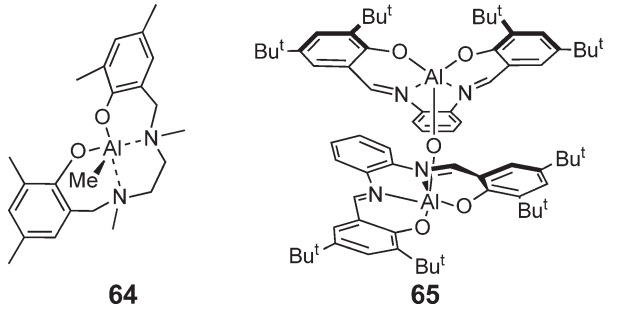
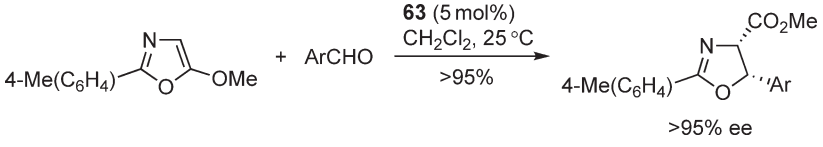
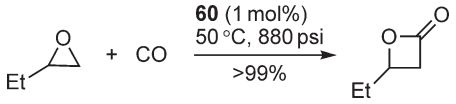


Figure 58 Oxo Salen–Al(III) dimer.

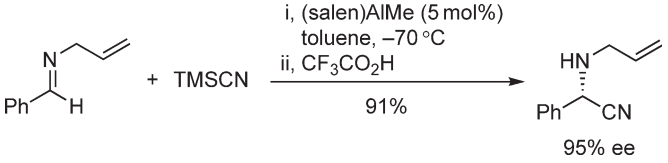
These salen-based, highly coordinated aluminum cations were found to be very versatile catalysts in the asymmetric aldol reaction[328,338] (Equation (101)) and β-lactone formation upon reaction of oxiranes with carbon monoxide (Equation (102)).[329] In contrast, their precursors, that is, latent cations, have been thoroughly investigated as catalysts in the anionic polymerization of lactides,[339–344] and co-polymerization between oxiranes and carbon dioxides.[345,346] A narrow MWD, characteristic of living propagation, is generally attained with (salen)aluminum alkoxides. A series of latent cations were also widely used as effective catalysts in various bimolecular transformations and asymmetric syntheses. These include cyclic carbonate formation,[345] the Strecker reaction (Equation (103)),[220] and conjugate addition (Equations (104) and (105)).[335,347,348] By taking advantage of this rather water and air inert nature, the improvement of turnover number and frequency in the performance of these catalysts remains a significant challenge for the future.



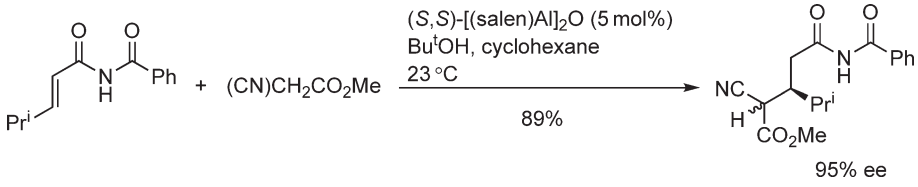
(101)



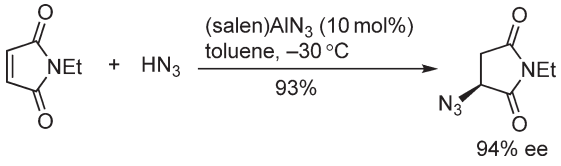
(102)



(103)



(104)



(105)

References

1. Ziegler, K. In *Organometallic Chemistry*; Zeiss, H., Ed.; Reinhold: New York, 1960; p 194.
2. Mole, T.; Jeffery, E. A. *Organoaluminum Compounds*; Elsevier: Amsterdam, 1972; Chapter 5.
3. Eisch, J. J. In *Comprehensive Organometallic Chemistry I*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 6, Chapter 6.
4. Eisch, J. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11, Chapter 6.
5. Eisch, J. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 1, Chapter 10.
6. Mason, M. R.; Song, B.; Kirstin, K. *J. Am. Chem. Soc.* **2004**, *126*, 1182–1183.
7. Sanchez, R.; Arrington, C.; Arrinton, C. *J. Am. Chem. Soc.* **1989**, *111*, 9110–9111.
8. Barron, A. R. In *Metallocene-based Polyoefins*; Scheirs, J., Kaminsky, W., Eds.; Wiley: Chichester, 2000; Vol. 1, pp 33–67.
9. Chen, E. Y.-X.; Marks, T. J. *Chem. Rev.* **2000**, *100*, 1391–1434.
10. Psynkiewicz, S. *Polyhedron* **1990**, *9*, 429–453.
11. Owens, K.; Kyllingstad, V. *Kirk–Othmer Encyclopedia of Chemical Technology*; 4th ed.; Wiley: New York, 1993; Vol. 8, pp 1079–1093.
12. Vadenberg, E. J. In *Catalysis in Polymer Synthesis*; Vandenberg, E. J., Salamone, J. C. Eds.; ACS Symposium Series 496; American Chemical Society: Washington, DC, 1992; Chapter 1.
13. Wilke, G. *Angew. Chem., Int. Ed.* **2003**, *42*, 5000–5008.

14. Lin, B. C.; Cheng, C. P.; You, Z.-Q.; Hsu, C.-P. *J. Am. Chem. Soc.* **2005**, *127*, 66–67.
15. Zhang, J.; Frenking, G. *J. Phys. Chem. A.* **2004**, *108*, 10296–10301.
16. Halls, M. D.; Schlegel, H. B. *Chem. Mater.* **2001**, *13*, 2632–2640.
17. Ashenhurst, J.; Brancaleon, L.; Hassan, A.; Liu, W.; Schmider, H.; Wang, S.; Wu, Q. *Organometallics* **1998**, *17*, 3186–3195.
18. Ashenhurst, J.; Brancaleon, L.; Gao, S.; Kiu, W.; Schmider, H.; Wang, S.; Wu, S.; Wu, Q. G. *Organometallics* **1998**, *17*, 5334–5341.
19. Liu, W.; Wang, S. *Organometallics* **1997**, *16*, 4257–4259.
20. Yamamoto, H. In *Organometallics in Synthesis*, 2nd Ed.; Schlosser, M., Ed.; Wiley: Chichester, 2002; pp 535–577.
21. Saito, S. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley–VCH: Weinheim, 2004; pp 189–306.
22. Ooi, T.; Maruoka, K. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed. Wiley: Chichester, 2000; pp 191–281.
23. Wulff, W. W. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed. Wiley: Chichester, 2000; pp 283–354.
24. Bellus, D., Ley, S. V., Noyori, R., Regitz, M., Reider, R. J., Schaumann, E., Shinkai, I., Thomas, E. J., Trost, B. M., Eds. *Science of Synthesis, Houben-Weyl Methods of Molecular Transformation*; Thieme: Stuttgart, 2004; Vol. 7, pp 5–385.
25. Yamamoto, H.; Nozaki, H. *Angew. Chem., Int. Ed.* **1978**, *17*, 169.
26. Maruoka, K.; Yamamoto, H. *Angew. Chem., Int. Ed.* **1985**, *24*, 668–682.
27. Maruoka, K.; Yamamoto, H. *Tetrahedron* **1988**, *44*, 5001–5032.
28. Atwood, D. A.; Yearwood, B. C. *J. Organomet. Chem.* **2000**, *600*, 186–197.
29. Williams, R. J. P. *Coord. Chem. Rev.* **1996**, *149*, 1–9.
30. Holloway, C. E.; Melnik, M. *J. Organomet. Chem.* **1997**, *543*, 1–37.
31. Holloway, C. E.; Melnik, M. *Main Group Met. Chem.* **1996**, *19*, 411–487.
32. Holloway, C. E.; Melnik, M. *Main Group Met. Chem.* **1996**, *19*, 619–698.
33. Ham, N. S.; Mole, T. *Prog. Nucl. Magn. Reson. Spectrosc.* **1961**, *4*, 91–192.
34. Uhl, W. Z. *Anorg. Allg. Chem.* **1989**, *570*, 37–53.
35. Vitalev, S. E.; Baev, A. K. *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.* **1988**, 46–49.
36. Baev, A. K.; Ahishko, M. A.; Kornev, N. N. *Russ. J. General Chem.* **2002**, *72*, 1389–1395.
37. Schumann, H.; Glanz, M.; Gottfriedsen, J.; Dechert, S.; Wolff, D. *Pure Appl. Chem.* **2001**, *73*, 279–282.
38. Herzog, A.; Roesky, H. W.; Zak, Z.; Noltemeyer, M. *Angew. Chem. Int. Ed.* **1994**, *33*, 967–968.
39. Klimpel, M. G.; Eppinger, J.; Sirsch, P.; Scherer, W.; Anwander, R. *Organometallics* **2002**, *21*, 4021–4023.
40. Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611–3613.
41. Pine, S. H.; Kim, G.; Lee, V. *Org. Synth.* **1990**, *69*, 72.
42. Nicolaou, K. C.; Koumbis, A. E.; Snyder, S. A.; Simonsen, K. B. *Angew. Chem., Int. Ed.* **2000**, *39*, 2529–2533.
43. Francl, M. M.; Hehre, W. J. *Organometallics* **1983**, *2*, 459.
44. Mikami, K.; Motoyama, Y. *Syn. Org. Chem. Jpn.* **1994**, *9*, 716–721.
45. Viciu, M. S.; Nolan, S. P. In *Palladium in Organic Synthesis*. Tuji, J., Ed.; Topics in Organometallic Chemistry; Springer: Berlin, Heidelberg, 2005; Vol. 14, pp 241–278.
46. Arduengo, A. J. III; Dias, H. V. R.; Calabrese, J. C.; Davidson, F. *J. Am. Chem. Soc.* **1992**, *114*, 9725–9726.
47. Stasch, A.; Singh, S.; Roesky, H. W.; Noltemeyer, M.; Schmidt, H.-G. *Eur. J. Inorg. Chem.* **2004**, *43*, 4052–4055.
48. Schiefer, M.; Reddy, N. D.; Ahn, H.-J.; Stasch, A.; Roesky, H. W.; Schlicker, A. C.; Schmidt, H.-G.; Noltemeyer, M.; Vidovic, D. *Inorg. Chem.* **2003**, *42*, 4970–4976.
49. Cowley, A. H.; Gabbaï, F. P.; Carrano, C. J.; Mokry, L. M.; Bond, M. R.; Bertrand, G. *Angew. Chem., Int. Ed.* **1994**, *33*, 578–580.
50. Stucky, G. D.; Mcpherson, A. M.; Rhine, W. E.; Eisch, J. J.; Considine, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 1941–1942.
51. Schiefer, M.; Hatop, H.; Roesky, H. W.; Schmidt, H.-G.; Noltemeyer, M. *Organometallics* **2002**, *21*, 1300–1303.
52. Muslukhov, R. R.; Khalilov, L. M.; Ramazanov, I. R.; Sharipova, A. Z.; Ibragimov, A. G.; Dzhemilev, U. M. *Russ. Chem. Bull.* **1997**, *46*, 2082–2085.
53. Stöckigt, D.; Schwarz, J.; Schwarz, H. *J. Phys. Chem.* **1996**, *100*, 8786–8790.
54. Kemper, P. R.; Bushnell, J.; Bowers, M. T.; Gellene, G. I. *J. Phy. Chem. A* **1998**, *102*, 8590–8597.
55. Alikhani, M. E.; Bouteiller, Y.; Silvi, B. *J. Phys. Chem.* **1996**, *100*, 16092–16097.
56. Kasai, P. H. *J. Am. Chem. Soc.* **1982**, *104*, 1165–1172.
57. Manceron, L.; Andrews, L. *J. Phys. Chem.* **1989**, *93*, 2964–2970.
58. King, E. M.; Clark, S. J.; Verdozzi, C. F.; Ackland, G. J. *J. Phys. Chem. B* **2001**, *105*, 641–645.
59. Duschek, R.; Mettendorfer, F.; Blyth, R. I. R.; Netzer, F. P.; Hafner, J.; Ramsey, M. G. *Chem. Phys. Lett.* **2000**, *318*, 43–48.
60. Chenier, J. H. B.; Howard, J. A.; Mile, B. *J. Am. Chem. Soc.* **1987**, *109*, 4109–4110.
61. Mile, B.; Howard, J. A.; Tse, J. S. *Organometallics* **1988**, *7*, 1278–1282.
62. Chey, J.; Choe, H.-S.; Chook, Y.-M.; Jensen, E.; Seida, P. R.; Francl, M. M. *Organometallics* **1990**, *9*, 2430–2436.
63. Bundens, J. W.; Francl, M. M. *Organometallics* **1993**, *12*, 1608–1615.
64. Bundens, J. W.; Yudenfreund, J.; Francl, M. M. *Organometallics* **1999**, *18*, 3913–3920.
65. Histed, M.; Howard, J. A.; Morris, H.; Mile, B. *J. Am. Chem. Soc.* **1988**, *110*, 5290–5292.
66. Sanderson, R. T. *Polar Covalence;* Academic Press: New York, 1983; p 147.
67. Hoffman, E. Z. *Electrochem.* **1960**, *1*, 144.
68. Tatazona, A.; Koglin, E.; Buda, F.; Coussens, B. B.; Renkema, J.; Heel, S. van; Meier, R. J. *J. Phys. Chem. B* **1997**, *101*, 4370–4378.
69. Pinkas, J.; Roesky, H. W. *J. Fluorine Chem.* **2003**, *122*, 125–150.
70. Hatop, H.; Roesky, H. W.; Labahn, T.; Fischer, A.; Schmidt, H.-G.; Noltemeyer, M. *Organometallics* **2000**, *19*, 937–940.
71. Hammerl, A.; Welch, B. J.; Schwerdtfeger, P. *Inorg. Chem.* **2004**, *43*, 1436–1440.
72. Chen, Y.-X.; Metz, M. V.; Li, L.; Stern, C. L.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 6287–6305.
73. Ooi, T.; Uraguchi, D.; Kagoshima, N.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 5679–5682.
74. Nöth, H.; Schlegel, A.; Knizek, J.; Schwenk, H. *Angew. Chem. Int. Ed.* **1997**, *36*, 2640–2643.
75. Healy, M. D.; Power, M. B.; Barron, A. R. *Coord. Chem. Rev.* **1994**, *130*, 63–135.
76. Kumar, R.; de Mel, V. S. J.; Sierra, M. L.; Hendershot, D. G.; Oliver, J. P. *Organometallics* **1994**, *13*, 2079–2083.
77. Lewínski, J.; Zachara, J.; Justyniak, I. *Organometallics* **1997**, *16*, 3859–3862.
78. Lewíński, J.; Justyniak, I.; Horeglad, P.; Tratkiewicz, E.; Zachara, J.; Ochal, Z. *Organometallics* **2004**, *23*, 4430–4437.
79. Dostál, L.; Jambor, R.; Ruzicka, A.; Císarová, I.; Holecek, J. *Appl. Organomet. Chem.* **2005**, *19*, 797–802.

80. Beard, B. *J. Raman Spectrosc.* **2004**, *35*, 1006–1010.
81. Dostál, L.; Jambor, R.; Ruzicka, A.; Císarová, I. *Appl. Organomet. Chem.* **2005**, *19*, 797–802.
82. Schumann, H.; Dechert, S.; Schutte, S.; Hyeon, J.-Y.; Hummert, M.; Wassermann, B. C. *Organometallics* **2003**, *22*, 1392–1401.
83. Eisenhardt, A.; Heuer, B.; Kaminsky, W.; Köhler, K.; Schumann, H. *Adv. Synth. Catal.* **2003**, *345*, 1299–1304.
84. Bryant, P. L.; Harwell, C. R.; Mrse, A. A.; Emery, E. F.; Gan, Z.; Caldwell, T.; Reyes, A. P.; Kuhns, P.; Hoyt, D. W., Simeral, L. S., *et al. J. Am. Chem. Soc.* **2001**, *123*, 12009–12017.
85. Von Lacroix, K.; Heitmann, B.; Sinn, H. *Macromol. Symp.* **1995**, *97*, 137–142.
86. Roesky, H. W.; Walawalkar M, G.; Murugavel, R. *Acc. Chem. Res.* **2001**, *34*, 201–211.
87. Harlan, C. J.; Mason, M. R.; Barron, A. R. *Organometallics* **1994**, *13*, 2957–2969.
88. Harlan, C. J.; Bott, S. G.; Barron, A. R. *J. Am. Chem. Soc.* **1995**, *117*, 6465–6474.
89. Mason, M. R.; Smith, J. M.; Bott, S. G.; Barron, A. R. *J. Am. Chem. Soc.* **1993**, *115*, 4871–4984.
90. Sinn, H. *Hamburger Makromolekulares Kolloquium*, Hamburg, Germany, September 1994, pp 22–23.

90a. Soga, K.; Shiono, T. *Kagaku* **1995**, *50*, 128–129.

91. Landry, C. C.; Harlan, J. H.; Bott, S. G.; Barron, A. R. *Angew. Chem., Int. Ed.* **1995**, *34*, 1201–1202.
92. Ooi, T.; Maruoka, K. *Syn. Org. Chem. Jpn.* **1996**, *54*, 200.
93. Saito, S.; Yamamoto, H. *Chem. Commun.* **1997**, 1585–1592.
94. Maruoka, K.; Concepcion, A. B.; Hirayama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 3943–3949.
95. Healy, M. D.; Barron, A. R. *Angew. Chem., Int. Ed.* **1992**, *31*, 921–923.
96. Power, M. B.; Bott, S. G.; Clark, D. L.; Atwood, J. L.; Barron, A. R. *Organometallics* **1990**, *9*, 3086–3097.
97. Power, M. B.; Bott, S. G.; Atwood, J. L.; Barron, A. R. *J. Am. Chem. Soc.* **1990**, *112*, 3446–3451.
98. Quinkert, G.; Becker, H.; Grosso, M.; Dambacher, G.; Bats, J. W.; Durner, G. *Tetrahedron Lett.* **1993**, *34*, 6885–6888.
99. Maruoka, K.; Imoto, H.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 4131–4132.
100. Saito, S.; Sone, T.; Murase, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2000**, *122*, 7847–7848.
101. Saito, S.; Nagahara, T.; Siozawa, M.; Nakadai, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2003**, *125*, 6200–6210.
102. Saito, S.; Ito, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1997**, *119*, 611–612.
103. Saito, S.; Shiozawa, M.; Masahiro, I.; Yamamoto, H. *J. Am. Chem. Soc.* **1998**, *120*, 813–814.
104. Saito, S.; Shiozawa, M.; Yamamoto, H. *Angew. Chem., Int. Ed.* **1999**, *38*, 1769–1771.
105. Saito, S.; Shiozawa, M.; Nagahara, T.; Nakadai, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2000**, *122*, 7847–7848.
106. Saito, S.; Yamazaki, S.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2001**, *40*, 3613–3617.
107. Trepanier, S. J.; Wang, S. *Organometallics* **1996**, *15*, 760–765.
108. Reddy, N. D.; Roesky, H. W.; Noltemeyer, M.; Schmidt, H.-G. *Inorg. Chem.* **2002**, *41*, 2374–2378.
109. Zheng, W.; Nösch-Zanetti, N. C.; Blunck, T.; Roesky, H. W.; Noltemeyer, M.; Schmidt, H. G. *Organometallics* **2001**, *20*, 3299–3303.
110. Maruoka, K.; Oishi, M.; Yamamoto, H. *J. Org. Chem.* **1993**, *58*, 7638–7639.
111. Schumann, H.; Dechert, S.; Hummert, M.; Lange, K. C. H.; Schutte, S.; Wassermann, B. C.; Köhler, K.; Eichhorn, J. *Z. Anorg. Allg. Chem.* **2004**, *630*, 1196–1204.
112. Liu, X.; Gao, W.; Mu, Y.; Li, G.; Ye, L.; Xia, H.; Ren, Y.; Feng, S. *Organometallics* **2005**, *24*, 1614–1619.
113. Schumann, H.; Wassermann, B. C.; Schutte, S.; Heymer, B.; Nickel, S.; Seub, T. D.; Wernik, S.; Demtschuk, J.; Girgsdies, F.; Weimann, R. *Z. Anorg. Allg. Chem.* **2000**, *626*, 2081–2095.
114. Abeysekera, D.; Robertson, K. N.; Cameron, T. S.; Clyburne, J. A. C. *Organometallics* **2001**, *20*, 5532–5536.
115. Enders, M.; Kohl, G.; Pritzkow, H. *Organometallics* **2004**, *23*, 3832–3839.
116. Cortright, S. B.; Coalter, J. N., III; Pink, M.; Johnston, J. N. *Organometallics* **2004**, *23*, 5885–5888.
117. Chang, J.-C.; Hung, C.-H.; Huang, J.-H. *Organometallics* **2001**, *20*, 4445–4447.
118. Bensiek, S.; Bangel, M.; Neumann, B.; Stammler, H.-G.; Jutzi, P. *Organometallics* **2000**, *19*, 1292–1298.
119. Li, M.-D.; Chang, C.-C.; Liu, S.-T.; Lee, G.-H.; Wang, Y.; Peng, S.-M. *Organometallics* **1994**, *13*, 1504–1506.
120. Taghiof, M.; Heeg, M. J.; Bailey, M.; Dick, D. G.; Kumar, R.; Hendershot, D. G.; Rahbarnoohi, H.; Oliver, J. P. *Organometallics* **1995**, *14*, 2903–2917.
121. Schumann, H.; Wassermann, B. C.; Heymer, B.; Keitsch, M.; Girgsdies, F. *Z. Anorg. Allg. Chem.* **2001**, *627*, 1828–1835.
122. Paek, C.; Kang, S. O.; Ko, J. *Organometallics* **1997**, *16*, 2110–2115.
123. Klimek, K. S.; Prust, J.; Roesky, H. W.; Noltemeyer, M.; Schmidt, H.-G. *Organometallics* **2001**, *20*, 2047–2051.
124. Grigsby, W. J.; Raston, C. L.; Tolhurst, V. A.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1998**, 2547–2556.
125. Schumann, H.; Girgsdies, F.; Dechert, S.; Gottfriedsen, J.; Hummert, M.; Schutte, S.; Pickardt, J. *Z. Anorg. Allg. Chem.* **2002**, *628*, 2625–2630.
126. Francis, J. A.; McMahon, C. N.; Bott, S. G.; Barron, A. R. *Organometallics* **1999**, *18*, 4399–4416.
127. Atwood, D. A.; Gabbi, F. P.; Lu, J.; Remington, M. P.; Rutherford, D.; Sibi, M. P. *Organometallics* **1996**, *15*, 2308–2313.
128. Hogerheide, M. P.; Wesseling, M.; Jastrzebski, T. B. H.; Boersma, J.; Kooijman, H.; Spek, A. L.; van Koten, G. *Organometallics* **1995**, *14*, 4483–4492.
129. Jones, C.; Lee, F. C.; Koutsantonis, G. A.; Gardiner, M. G.; Raston, C. L. *J. Chem. Soc., Dalton Trans.* **1996**, 829–833.
130. Francis, J. A.; Bott, S. G.; Barron, A. R. *J. Chem. Soc., Dalton Trans.* **1998**, 3305–3310.
131. Janas, Z.; Jerzykiewicz, L. B.; Przybylak, S.; Richards, R. L.; Sobota, P. *Organometallics* **2000**, *19*, 4252–4257.
132. Krannich, L. K.; Watkins, C. L.; Schauer, S. J. *Organometallics* **1995**, *14*, 3094–3097.
133. Bennet, F. R.; Elms, F. M.; Gardiner, M. G.; Koutsantonis, G. A.; Raston, C. L.; Roberts, N. K. *Organometallics* **1992**, *11*, 1457–1459.
134. Wells, R. L.; Mcphail, A. T.; Self, M. F.; Laske, J. A. *Organometallics* **1993**, *12*, 3333–3339.
135. Müller, G.; Kachmann, J.; Rufínska, A. *Organometallics* **1992**, *11*, 2970–2972.
136. Fryzuk, M. D.; Giesbrecht, G. R.; Olovsson, G.; Rettig, S. J. *Organometallics* **1996**, *15*, 4832–4841.
137. Robinson, G. H. *Adv. Organomet. Chem.* **2001**, *47*, 283–294.
138. Schram, E. P. *Inorg. Chem.* **1966**, *5*, 1291–1294.
139. Hoberg, H.; Krause, S. *Angew. Chem., Int. Ed.* **1976**, *15*, 694–695.
140. Uhl, W. *Z. Naturforsch.* **1988**, *43b*, 1113–1118.
141. Uhl, W.; Vester, A.; Kaim, W.; Poppe, J. *J. Organomet. Chem.* **1993**, *454*, 9–13.
142. Pluta, C.; Pörschke, K.-R.; Kruger, C.; Hildenbrand, K. *Angew. Chem., Int. Ed.* **1993**, *32*, 388–390.
143. Wehmshulte, R. J.; Ruhlandt-Senge, K.; Olmstead, M. M.; Hope, H.; Sturgeion, B. E.; Power, P. P. *Inorg. Chem.* **1993**, *32*, 2983–2984.

144. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652.
145. Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098–3100.
146. Gorden, J. D.; Macdonald, C. L. B.; Cowley, A. H. *Chem. Commun.* **2001**, 75–76.
147. Schwerdtfeger, P.; Heath, G. A.; Dolg, M.; Bennett, M. A. *J. Am. Chem. Soc.* **1992**, *114*, 7518–7527.
148. Palágyi, Z.; Schaefer, H. F., III. *Chem. Phys. Lett.* **1993**, *203*, 195–200.
149. Uhl, W.; Schutz, U.; Kaim, W; Waldhör, E. *J. Organomet. Chem.* **1995**, *501*, 79–85.
150. Wright, R. J.; Phillips, A. D.; Power, P. P. *J. Am. Chem. Soc.* **2003**, *125*, 10784–10785.
151. Schnitter, C.; Roesky, H. W.; Röpken, C.; Herbst-Irmer, R.; Schmidt, H.-G.; Noltemeyer, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1952–1955.
152. Dohmeier, C.; Robl, C.; Tacke, M.; Schnöckel, H. *Angew. Chem., Int. Ed.* **1991**, *30*, 564–565.
153. Schultz, S.; Roesky, H. W.; Koch, H. J.; Sheldrick, G. M.; Stalke, D.; Kuhn, A. *Angew. Chem., Int. Ed.* **1993**, *32*, 1729–1731.
154. Wiberg, N.; Amelunxen, K.; Blank, T.; Nöth, H.; Knizek, J. *Organometallics* **1998**, *17*, 5431–5433.
155. Klimek, K. S.; Cui, C.; Roesky, H. W.; Noltemeyer, M.; Schmidt, H.-G. *Organometallics* **2000**, *19*, 3085–3090.
156. Schiefer, M.; Reddy, N. D.; Roesky, H. W.; Vidovic, D. *Organometallics* **2003**, *22*, 3637–3638.
157. Purath, A.; Dohmeier, C.; Ecker, A.; Schnöckel, H. *Organometallics* **1998**, *17*, 1894–1896.
158. Gauss, J.; Schneider, U.; Ahlrichs, R.; Dohmeier, C.; Schnöckel, H. *J. Am. Chem. Soc.* **1993**, *115*, 2402–2408.
159. Haaland, A.; Martinsen, K.-G.; Shlykov, S. A.; Volden, H. V.; Dohmeier, C.; Schnöckel, H. *Organometallics* **1995**, *14*, 3116–3119.
160. Himmel, H.-J.; Vollet, J. *Organometallics* **2002**, *21*, 5972–5977.
161. Ahlrichs, R.; Ehrig, M.; Horn, H. *Chem. Phys. Lett.* **1991**, *183*, 227–233.
162. Cui, C.; Roesky, H. W.; Schmidt, H.-G.; Noltemeyer, M.; Hao, H.; Cimpoesu, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 4274–4276.
163. Roesky, H. W. *Inorg. Chem.* **2004**, *43*, 7284–7293.
164. Zhu, H.; Chai, J.; Fan, H.; Roesky, H. W.; Nehete, U. M.; Schmidt, H.-G.; Noltemeyer, M. *Eur. J. Inorg. Chem.* **2005**, *44*, 2147–2150.
165. Zhu, H.; Chai, J.; Chandrasekhar, V.; Roesky, H. W.; Magull, J.; Vidovic, D.; Schmidt, H.-G.; Noltemeyer, M.; Power, P. P.; Merrill, W. A. *J. Am. Chem. Soc.* **2004**, *126*, 9472–9473.
166. Cui, C.; Roesky, H. W.; Schmidt, H.-G.; Noltemeyer, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 4531–4533.
167. Cui, C.; Köpke, S.; Herbst-Irmer, R.; Roesky, H. W.; Noltemeyer, M.; Schmidt, H.-G.; Wrackmeyer, B. *J. Am. Chem. Soc.* **2001**, *123*, 9091–9098.
168. Peng, Y.; Fan, H.; Zhu, H.; Roesky, H. W.; Magull, J.; Hughes, C. E. *Angew. Chem., Int. Ed.* **2004**, *43*, 3443–3445.
169. Zhu, H.; Chai, J.; Stasch, A.; Roesky, H. W.; Blunck, T.; Vidovic, D.; Magull, J.; Schmidt, H.-G.; Noltemeyer, M. *Eur. J. Inorg. Chem.* **2004**, *43*, 4046–4051.
170. Romero, P. E.; Piers, W. E.; Decker, S. A.; Chau, D.; Woo, T. K.; Parvez, M. *Organometallics* **2003**, *22*, 1266–1274.
171. Weiss, J.; Stetzkamp, D.; Nuber, B.; Fischer, R. A.; Boehme, C.; Frenking, G. *Angew. Chem., Int. Ed.* **1997**, *36*, 70–72.
172. Fischer, R. A.; Schulte, M. M.; Weiss, J.; Zsolnai, L.; Jacobi, A.; Huttner, G.; Frenking, G.; Boehme, C.; Vyboishchikov, S. F. *J. Am. Chem. Soc.* **1998**, *120*, 1237–1248.
173. Golden, J. T.; Peterson, T. H.; Holland, P. L.; Bergman, R. G.; Anderson, R. A. *J. Am. Chem. Soc.* **1998**, *120*, 223–224.
174. Bruno, J. W.; Huffman, J. C.; Kenneth, G. C. *J. Am. Chem. Soc.* **1984**, *106*, 444–445.
175. Dohmeier, C.; Krautsheid, H.; Schnöckel, H. *Angew. Chem., Int. Ed.* **1994**, *33*, 2482–2483.
176. Schneider, J. J.; Kruger, C.; Nolte, M.; Abraham, I.; Ertel, T. S.; Betagnolli, H. *Angew. Chem., Int. Ed.* **1994**, *33*, 2435–2437.
177. Üffing, C.; Ecker, A.; Köppe, R.; Schnöckel, H. *Organometallics* **1998**, *17*, 2373–2375.
178. Yu, Q.; Purath, A.; Donchev, A.; Schnöckel, H. *J. Organomet. Chem.* **1999**, *584*, 94–97.
179. Neumann, W. P.; Scick, R.; Köster, R. *Angew. Chem., Int. Ed.* **1964**, *3*, 385.
180. Eisch, J. J.; Mackenzie, K.; Windisch, H.; Krüger, C. *Eur. J. Inorg. Chem.* **1999**, 153–162.
181. Tschinkl, M.; Bachman, R. E.; Gabbaï, F. P. *Chem. Commun.* **1999**, 1367–1368.
182. Bochmann, M.; Sarfield, M. J. *Organometallics* **1998**, *17*, 5908–5912.
183. Kim, J. S.; Wojcinski, L. M. II; Liu, S.; Sworen, J. C.; Sen, A. *J. Am. Chem. Soc.* **2000**, *122*, 5668–5669.
184. Hair, G. S.; Cowley, A. H.; Jones, R. A.; Mcburnett, B. G.; Voigt, A. *J. Am. Chem. Soc.* **1999**, *121*, 4922–4923.
185. Klosin, J.; Roof, G. R.; Chen, E. Y.-X. *Organometallics* **2000**, *19*, 4684–4686.
186. Pohlmann, J. L. W.; Brinckmann, F. E. *Z. Naturforsch., B* **1965**, *20*, 5–11.
187. Chambers, R. D. *Organomet. Chem. Rev.* **1966**, *1*, 279–304.
188. Kim, Y. H.; Kim, T. H.; Kim, N. Y.; Cho, E. S.; Lee, B. Y.; Shin, D. M.; Chung, Y. K. *Organometallics* **2003**, *22*, 1503–1511.
189. Hoshi, M.; Shirakawa, K. *Chem. Commun.* **2002**, 2146–2147.
190. Uchiyama, M.; Naka, H.; Matsumoto, Y.; Ohwada, T. *J. Am. Chem. Soc.* **2004**, *126*, 10526–10527.
191. Olah, G. A.; Török, B.; Joscheck, J. P.; Bucsi, I.; Esteves, P. M.; Rasul, G.; Prakash, G. K. S. *J. Am. Chem. Soc.* **2002**, *124*, 11379–11391.
192. Lipshutz, B. H.; Bulow, G.; Lowe, R. F.; Stevens, K. L. *J. Am. Chem. Soc.* **1996**, *118*, 5512–5513.
193. Lipshutz, B. H.; Lindsley, C. *J. Am. Chem. Soc.* **1997**, *119*, 4555–4556.
194. Negishi, E.; Copéret, C.; Ma, S.; Mita, T.; Sugihara, T.; Tour, J. M. *J. Am. Chem. Soc.* **1996**, *118*, 5904–5918.
195. Ohmori, K.; Suzuki, T.; Taya, K.; Tanabe, D.; Ohta, T.; Suzuki, K. *Org. Lett.* **2001**, *3*, 1057–1060.
196. Suzuki, T.; Ohmori, K.; Suzuki, K. *Org. Lett.* **2001**, *3*, 1741–1744.
197. Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65–72.
198. Negishi, E.; Kondakov, D. Y. *Chem. Soc. Rev.* **1996**, 417–426.
199. Dzhemilev, U. M.; Ibragimov, A. G. *Russ. Chem. Rev.* **2000**, *69*, 121–135.
200. Lautens, M.; Chiu, P.; Ma, S.; Rovis, T. *J. Am. Chem. Soc.* **1995**, *117*, 532–533.
201. Lautens, M.; Ren, Y.; Delanghe, P.; Chiu, P.; Ma, S. *J. Am. Chem. Soc.* **1995**, *117*, 1251–1252.
202. Lautens, M.; Ma, S.; Chiu, P. *J. Am. Chem. Soc.* **1997**, *119*, 6478–6487.
203. Lautens, M.; Rovis, T. *J. Am. Chem. Soc.* **1997**, *119*, 11090–11091.
204. Yoshida, T.; Negishi, E. *J. Am. Chem. Soc.* **1981**, *103*, 1276–1277.
205. Yoshida, T.; Negishi, E. *J. Am. Chem. Soc.* **1981**, *103*, 4985–4987.
206. Negishi, E.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639–6647.
207. Negishi, E.; Kondakov, D. Y.; Choueiry, D.; Kasai, K.; Takahashi, T. *J. Am. Chem. Soc.* **1996**, *118*, 9577–9588.
208. Rusakov, S. V.; Khalilov, L. M.; Parfenova, L. V.; Ibragimov, A. G.; Ponomarev, O. A.; Dzhemilev, U. M. *Russ. Chem. Bull.* **2001**, *50*, 2336–2345.

209. Sinn, H.; Opermann, G. *Angew. Chem., Int. Ed.* **1966**, *5*, 962–963.
210. Kaminsky, W.; Kopf, J.; Sinn, H.; Vollmer, H. J. *Angew. Chem., Int. Ed.* **1976**, *15*, 629–630.
211. Dzhemilev, U. M.; Ibragimov, A. G.; Zolotarev, A. P.; Muslukov, R. R.; Tolstikov, G. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 194–195.
212. Dzhemilev, U. M.; Ibragimov, A. G. *J. Organomet. Chem.* **1994**, *466*, 1–4.
213. Dzhemilev, U. M. *Tetrahedron* **1995**, *51*, 4333–4346.
214. Negishi, E.; Montchamp, J.-L.; Anastasia, L.; Elizarov, A.; Choueiry, D. *Tetrahedron Lett.* **1998**, *39*, 2503–2506.
215. Dzhemilev, U. M.; Ibragimov, A. G.; Zolotarev, A. P. *Mendeleev Commun.* **1992**, 135–136.
216. Dzhemilev, U. M.; Ibragimov, A. G. *Russ. Chem. Bull.* **1998**, *47*, 786–794.
217. Dzhemilev, U. M.; Ibragimov, A. G.; Azhgaliev, M. N.; Muslukhov, R. R. *Russ. Chem. Bull.* **1995**, *44*, 1501–1507.
218. Dzhemilev, U. M.; Ibragimov, A. G.; Khafizova, L. O.; Rusakov, S. V.; Khalilov, L. M. *Mendeleev Commun.* **1997**, 198–199.
219. Dzhemilev, U. M.; Ibragimov, A. G.; Ramazanov, I. R.; Khalilov, L. M. *Russ. Chem. Bull.* **1997**, *47*, 2150–2151.
220. Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 5315–5316.
221. Adachi, A.; Sugimoto, H.; Aida, T.; Inoue, S. *Macromolecules* **1993**, *26*, 1238.
222. Stapleton, R. A.; Galan, B. R.; Collins, S.; Simons, R. S.; Garrison, J. C.; Youngs, W. J. *J. Am. Chem. Soc.* **2003**, *125*, 9246–9247.
223. Boleslawski, M.; Serwatowski, J. *J. Organomet. Chem.* **1983**, 269–278.
224. Storre, J.; Klemp, A.; Roesky, H. W.; Schmidt, H.-G.; Noltemeyer, M.; Fleischer, R.; Stalke, D. *J. Am. Chem. Soc.* **1996**, *118*, 1380–1386.
225. McMahon, C. N.; Bott, S. G.; Barron, A. R. *J. Chem. Soc., Dalton Trans.* **1997**, 3129–3137.
226. Taghiof, M.; Hendershot, D. G.; Barder, M.; Oliver, J. P. *J. Organomet. Chem.* **1992**, *431*, 271–281.
227. Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1993**, *115*, 11016–11017.
228. Saito, S. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed. Wiley–VCH: Weinheim, 2001; pp 1–58.
229. Kitamura, M.; Okada, S.; Suga, S.; Noyori, R. *J. Am. Chem. Soc.* **1989**, *111*, 4028–4036.
230. Jones, D. K.; Liotta, D. C.; Shinkai, I.; Mathre, D. J. *J. Org. Chem.* **1993**, *58*, 799–801.
231. Maruoka, K.; Itoh, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588–3597.
232. Ahn, Y.; Cohen, T. *J. Org. Chem.* **1994**, *59*, 3142–3150.
233. Maruoka, K.; Oishi, M.; Yamamoto, H. *Synlett* **1993**, 683–684.
234. Jeffrey, E. A.; Meisters, A.; Nole, T. *J. Organomet. Chem.* **1974**, *74*, 365–371.
235. Power, M. B.; Apblett, A. W.; Bott, S. G.; Atwood, J. L.; Barron, A. R. *Organometallics* **1990**, *9*, 2529–2534.
236. Nishida, M.; Hayashi, H.; Yonemitsu, O. *Synlett* **1995**, 1045–1047.
237. Lewinski, J.; Zachara, J.; Grabska, E. *J. Am. Chem. Soc.* **1996**, *118*, 6794–6795.
238. Skowronska-Ptasinska, M.; Starowieyski, K. B.; Pasynkiewicz, S. *J. Organomet. Chem.* **1977**, *141*, 149–156.
239. Luft, G.; Jabbari, M.; Dorn, M. *Angew. Makromol. Chem.* **1996**, *238*, 81–95.
240. Aida, T.; Inoue, S. *Acc. Chem. Res.* **1996**, *29*, 39–48.
241. Inoue, S.; Aida, T. *Chemtech* **1994**, 28–35.
242. Inoue, S.; Aida, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 984.
243. Cameron, P. A.; Gibson, V. C.; Irvine, D. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2141–2144.
244. Kabbara, J.; Flemming, S.; Nickisch, K.; Neh, H.; Westermann, J. *Liebigs Ann.* **1995**, 401–406.
245. Sadykov, R. A.; Dzhemilev, U. M. *Russ. Chem. Bull.* **1999**, *48*, 995–997.
246. Kitayama, T.; Hirano, T.; Hatada, K. *Tetrahedron* **1997**, *53*, 15263–15279.
247. Schlaad, H.; Schmitt, B.; Müller, A. H. E. *Angew. Chem., Int. Ed.* **1998**, *37*, 1389–1391.
248. Rodriguez-Delgado, A.; Chen, E. Y.-X. *J. Am. Chem. Soc.* **2005**, *127*, 961–974.
249. Clegg, W.; Lamb, E.; Liddle, S. T.; Snaith, R.; Wheatley, A. E. H. *J. Organomet. Chem.* **1999**, *573*, 305–312.
250. Williams, V. C.; Dai, C.; Li, Z.; Collins, S.; Piers, W. E.; Clegg, W.; Elsegood, M. R. J.; Marder, T. B. *Angew. Chem., Int. Ed.* **1999**, *38*, 3695–3698.
251. El Kaim, L.; Grimaud, L.; Lee, A.; Perroux, Y.; Tirla, C. *Org. Lett.* **2004**, *6*, 381–383.
252. Fujiwara, T.; Ito, T.; Nishimura, S.; Shimizu, M. *Tetrahedron Lett.* **1998**, *39*, 9735–9738.
253. Itoh, Y.; Haraguchi, K.; Tanaka, H.; Gen, E.; Miyasaka, T. *J. Org. Chem.* **1995**, *60*, 656–662.
254. Haraguchi, K.; Kubota, Y.; Tanaka, H. *J. Org. Chem.* **2004**, *69*, 1831–1836.
255. Andrés, C.; Nieto, J.; Pedrosa, R.; Villamanán, N. *J. Org. Chem.* **1996**, *61*, 4130–4135.
256. Olsson, R.; Berg, U.; Frejd, T. *Tetrahedron Lett.* **1995**, *38*, 5701–5704.
257. Howell, A. R.; Ndakala, A. J. *Org. Lett.* **1999**, *1*, 825–827.
258. Sasaki, M.; Tanino, K.; Miyashita, M. *J. Org. Chem.* **2001**, *66*, 5388–5394.
259. Sasaki, M.; Hatta, M.; Tanino, K.; Miyashita, M. *Tetrahedron Lett.* **2004**, *45*, 1911–1913.
260. Chung, E.-A.; Cho, C.-W.; Ahn, K. H. *J. Org. Chem.* **1998**, *63*, 7590–7591.
261. Equey, O.; Alexakis, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1531–1536.
262. Shumann, H.; Kaufmann, J.; Dechert, S.; Schmalz, H.-G.; Velder, J. *Tetrahedron Lett.* **2001**, *42*, 5405–5408.
263. Blum, J.; Gelman, D.; Baidossi, W.; Shak, E.; Rosenfeld, A.; Aizenshtat, Z.; Wassermann, B. C.; Frick, M.; Heymer, B., Schutte, S., *et al. J. Org. Chem.* **1997**, *62*, 8681–8686.
264. Blum, J.; Gelman, D.; Aizenshtat, Z.; Wernik, S.; Schumann, H. *Tetrahedron Lett.* **1998**, *39*, 5611–5614.
265. Gelman, D.; Schumann, H.; Blum, J. *Tetrahedron Lett.* **2000**, *41*, 7555–7558.
266. Wipf, P.; Lim, S. *Angew. Chem., Int. Ed.* **1993**, *32*, 1068.
267. Westermann, J.; Nickisch, K. *Angew. Chem., Int. Ed.* **1993**, *32*, 1368–1370.
268. Kabbara, J.; Flemming, S.; Nickisch, K.; Neh, H.; Westermann, J. *Synlett* **1994**, 679–680.
269. Kabbara, J.; Flemming, S.; Nickisch, K.; Neh, H.; Westermann, J. *Tetrahedron* **1995**, *51*, 743–754.
270. Hayashi, T.; Katsuro, Y.; Okamoto, Y.; Kumada, M. *Tetrahedron Lett.* **1981**, *22*, 4449–4452.
271. Giacomelli, G.; lardicci, L. *Tetrahedron Lett.* **1978**, 2831–2834.
272. Charbonnier, F.; Moyano, A.; Greene, A. E. *J. Org. Chem.* **1987**, *52*, 2303–2309.
273. Corey, E. J.; Wright, S. W. *J. Org. Chem.* **1990**, *55*, 1670–1675.
274. Kabbara, J.; Flemming, S.; Nickisch, K.; Neh, H.; Westermann, J. *Chem. Ber.* **1994**, *127*, 1489–1493.
275. Kondakov, D. Y.; Negishi, E. *J. Am. Chem. Soc.* **1995**, *117*, 10771–10772.
276. Kondakov, D. Y.; Negishi, E. *J. Am. Chem. Soc.* **1996**, *118*, 1577–1578.

277. Erker, G.; Aulbach, M.; Knickermeier, M.; Wingbermuhle, D.; Krüger, C.; Nolte, M.; Werner, S. *J. Am. Chem. Soc.* **1993**, *115*, 4590–4601.
278. Ishikawa, T.; Ogawa, A.; Hirao, T. *J. Am. Chem. Soc.* **1998**, *120*, 5124–5125.
279. Ooi, T.; Kagoshima, N.; Ichikawa, H.; Maruoka, K. *J. Am. Chem. Soc.* **1999**, *121*, 3328–3333.
280. Cogan, D. A.; Ellmann, J. A. *J. Am. Chem. Soc.* **1999**, *121*, 268–269.
281. Cogan, D. A.; Liu, G.; Ellmann, J. A. *Tetrahedron* **1999**, *55*, 8883–8904.
282. Pfaltz, A.; Mattenberger, A. *Angew. Chem., Int. Ed.* **1982**, *21*, 71–72.
283. Taya, K.; Nagasawa, T.; Kitamura, M.; Suzuki, K. *Synlett* **1997**, 304.
284. Flippin, L. A.; Brown, P. A.; Jalai-Araghi, K. *J. Org. Chem.* **1989**, *54*, 3588–3596.
285. Zweifel, G.; Steele, R. B. *J. Am. Chem. Soc.* **1967**, *89*, 5085–5086.
286. Matsumura, Y.; Maruoka, K.; Yamamoto, H. *Tetrahedron Lett.* **1982**, *23*, 1929–1932.
287. Sasaki, M.; Tanino, K.; Miyashita, M. *Org. Lett.* **2001**, *3*, 1765–1767.
288. Nelson, S. G.; Peelem, T. J.; Wan, Z. *J. Am. Chem. Soc.* **1999**, *121*, 9742–9743.
289. Nelson, S. G.; Kim, B.-K.; Peelen, T. J. *J. Am. Chem. Soc.* **2000**, *122*, 9318–9319.
290. Wan, Z.; Nelson, S. G. *J. Am. Chem. Soc.* **2000**, *122*, 10470–10471.
291. Nelson, S. G.; Zhu, C.; Shen, X. *J. Am. Chem. Soc.* **2004**, *126*, 14–15.
292. Atwood, J. L.; Jones, C.; Raston, C. L.; Robinson, K. D. *J. Chem. Soc. Chem. Commun.* **1991**, 1697–1699.
293. Barybin, M. V.; Diaconescu, P. L.; Cummins, C. C. *Inorg. Chem.* **2001**, *40*, 2892–2897.
294. Ooi, T.; Ichikawa, K.; Maruoka, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 3610–3612.
295. Liu, Y.-C.; Ko, B.-T.; Huang, B.-H.; Lin, C.-C. *Organometallics* **2002**, *21*, 2066–2069.
296. Bott, G. S.; Alvanipour, A.; Morley, S. D.; Atwood, D. A.; Means, C. M.; Coleman, A. W.; Atwood, J. L. *Angew. Chem.* **1987**, *26*, 485–486.
297. Atwood, J. L.; Bott, S. G.; Harvey, S.; Junk, P. C. *Organometallics* **1994**, *13*, 4151–4152.
298. Kynasi, U.; Skelton, B. W.; White, A. H.; Henderson, M. J.; Raston, C. L. *J. Organomet. Chem.* **1990**, *384*, C1–C5.
299. Uhl, W.; Wagner, J.; Fenske, D.; Baum, G. *Z. Anorg. Allg. Chem.* **1992**, *612*, 25–33.
300. Atwood, D. A.; Jegier, J. A.; Rutherford, D. *Inorg. Chem.* **1996**, *35*, 4277–4282.
301. Atwood, D. A.; Jegier, J. A. *Chem. Commun.* **1996**, 1507–1508.
302. Chakraborty, D.; Chen, E. Y.-X. *Organometallics* **2002**, *21*, 1438–1442.
303. Chakraborty, D.; Rodriguez, A.; Chen, E. Y.-X. *Macromolecules* **2003**, *36*, 5470–5481.
304. Radzewich, C. E.; Guzei, I. A.; Jordan, R. F. *J. Am. Chem. Soc.* **1999**, *121*, 8673–8674.
305. Coles, M. P.; Jordan, R. F. *J. Am. Chem. Soc.* **1997**, *119*, 8125–8126.
306. Radzewich, C. E.; Coles, M. P.; Jordan, R. F. *J. Am. Chem. Soc.* **1998**, *120*, 9384–9385.
307. Welch, G. C.; Piers, W. E.; Parvez, M.; Mcdonald, R. *Organometallics* **2004**, *23*, 1811–1818.
308. Ihara, E.; Young, V. G., Jr.; Jordan, R. F., *J. Am. Chem. Soc.* **1998**, *120*, 8277–8278.
309. Korolev, A. V.; Guzei, I. A.; Jordan, R. F. *J. Am. Chem. Soc.* **1999**, *121*, 11605–11606.
310. Korolev, A. V.; Ihara, E.; Guzei, I. A.; Young, V. G., Jr.; Jordan, R. F. *J. Am. Chem. Soc.* **2001**, *123*, 8291–8309.
311. Dagorne, S.; Janowska, I.; Welter, R.; Zakrzewski, J.; Jaouen, G. *Organometallics* **2004**, *23*, 4706–4710.
312. Lewinski, J.; Horeglad, P.; Dranka, M.; Justyniak, I. *Inorg. Chem.* **2004**, *43*, 5789–5791.
313. Krossing, I.; Nöth, H.; Schwenk-Kircher, H. *Eur. J. Inorg. Chem.* **1998**, *37*, 927–939.
314. M.-Hernández, M.-A.; Sannigrahi, B.; Atwood, D. A. *J. Am. Chem. Soc.* **1999**, *121*, 6747–6748.
315. Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238–1239.
316. Castellino, S.; Dwight, W. J. *J. Am. Chem. Soc.* **1993**, *115*, 2986–2987.
317. Evans, D. A.; Allison, B. D.; Yang, M. G.; Masse, C. E. *J. Am. Chem. Soc.* **2001**, *123*, 10840–10852.
318. Kim, K.-C.; Reed, C. A.; Long, G. S.; Sen, A. *J. Am. Chem. Soc.* **2002**, *124*, 7662–7663.
319. Bochmann, M. *Top. Catal.* **1999**, *7*, 9–22.
320. Bochmann, M.; Dawson, D. M. *Angew. Chem., Int. Ed.* **1996**, *35*, 2226–2228.
321. Young, J. D.; Khan, M. A.; Wehmschulte, R. J. *Organometallics* **2004**, *23*, 1965–1967.
322. Bruce, M.; Gibson, V. C.; Redshaw, C.; Solan, G. A.; White, A. J. P.; Wiliams, D. J. *Chem. Commun.* **1998**, 2523–2524.
323. Emig, N.; Nguyen, H.; Krautscheid, H.; Réau, R.; Cazaux, J.-B.; Bertrand, G. *Organometallics* **1998**, *17*, 3599–3608.
324. Talarico, G.; Busico, V. *Organometallics* **2001**, *20*, 4721–4726.
325. Talarico, G.; Budzelaar, P. H. M.; Gal, A. W. *J. Comput. Chem.* **2000**, *21*, 398–410.
326. Dagorne, S.; Guzei, I. A.; Coles, M. P.; Jordan, R. F. *J. Am. Chem. Soc.* **2000**, *122*, 274–289.
327. Meier, R. J.; Koglin, E. *J. Phys. Chem. A* **2001**, *105*, 3867–3874.
328. Evans, D. A.; Janey, J. M.; Magomedov, N.; Tedrow, J. S. *Angew. Chem., Int. Ed.* **2001**, *40*, 1884–1888.
329. Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1174–1775.
330. Atwood, D. A.; Jegier, J. A.; Rutherford, D. *Inorg. Chem.* **1996**, *35*, 63–70.
331. Atwood, D. A.; Jegier, J. A.; Rutherford, D. *J. Am. Chem. Soc.* **1995**, *117*, 6779–6780.
332. Jegier, J. A.; Munoz-Hernandez, M.-A.; Atwood, D. A. *J. Chem. Soc., Dalton Trans.* **1999**, 2583–2587.
333. Munoz-Hernández, M.-Á.; Sannigrahi, B.; Atwood, D. A. *J. Am. Chem. Soc.* **1999**, *121*, 6747–6748.
334. Wang, Y.; Bhandari, S.; Parkin, S.; Atwood, D. A. *J. Organomet. Chem.* **2004**, *689*, 759–765.
335. Taylor, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2003**, *125*, 11204–11205.
336. Kim, Y.; Verkade, J. G. *Inorg. Chem.* **2003**, *42*, 4804–4806.
337. Chen, C.-T.; Huang, C.-A.; Huang, B.-H. *Macromolecules* **2004**, *37*, 7968–7973.
338. Che, C.-M.; Huang, J.-S. *Coord. Chem. Rev.* **2003**, *242*, 97–113.
339. Zhong, Z.; Dijkstra, P. J.; Feijen, J. *J. Am. Chem. Soc.* **2003**, *125*, 11291–11298.
340. Ovitt, T. M.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1316–1326.
341. Ovitt, T. M.; Coates, G. W. *J. Am. Chem. Soc.* **1999**, *121*, 4072–4073.
342. Hormnirun, P.; Marshall, E. L.; Gibson, V. C.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **2004**, *126*, 2688–2689.
343. Nomura, N.; Ishii, R.; Akakura, M.; Aoi, K. *J. Am. Chem. Soc.* **2002**, *124*, 5938–5939.
344. Radano, C. P.; Baker, G. L.; Smith, M. R III *J. Am. Chem. Soc.* **2000**, *122*, 1252–1553.

345. Darensbourg, D. J.; Billodeaux, D. R. *Inorg. Chem.* **2005**, *44*, 1433–1442.
346. Chisholm, M. H.; Zhou, Z. *J. Am. Chem. Soc.* **2004**, *126*, 11030–11039.
347. Myers, J. K.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1999**, *121*, 8959–8960.
348. Sammis, G. M.; Danjo, H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 9928–9929.

9.07
Silicon

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9.07.1 Introduction

9.07.1.1 Scope

This chapter deals with the advances in organic synthesis using organosilicon compounds on the basis of works published from 1994 to 2004. The earlier reviews in COMC (1982) and COMC (1995) described many examples of synthetic use of organosilicon compounds,[1,2] and much attention has been paid continuously to this area until today.[3–17] A large number of synthetic reactions and organosilicon reagents has been developed during the last decade; however, this chapter mainly reviews carbon–carbon bond-forming reactions of alkenyl-, aryl-, alkynyl-, allylsilanes, heteroatom-substituted and strained alkylsilanes, and silyl enolates with carbon electrophiles. Synthetic use of organosilicon compounds having an Si–X (X = H, heteroatoms, and heteroatom groups other than enoxy groups) bond for transformation and protection of functional groups is not included in this work. For recent progress in this field, the reader is referred to other reviews.[3–6]

9.07.1.2 Recent Developments

Organosilicon compounds have unique and moderate reactivities enabling fine control of organic reactions by additives and reaction conditions. Additionally, they are readily available and relatively less toxic. Thus, their synthetic use has intensively been studied for fine organic synthesis. COMC (1982) and COMC (1995) disclosed many fundamental reactivities and synthetic potentials of organosilicon reagents bearing a triorganosilyl group. During the last decade, much effort has been directed to the development of efficient catalysts and catalytic systems for silicon-directed synthetic reactions. The studies on the Mukaiyama aldol reactions of silyl enolates and the Hosomi–Sakurai reactions of allylsilanes for highly efficient and stereoselective transformations led to explosive growth of synthetic utility of Lewis acids.[14,18] Asymmetric Mukaiyama aldol reactions using homochiral Lewis acid catalysts provided reliable methods for highly enantioselective carbon–carbon bond formation.[19,20] New types of organosilicon reagents have also been developed to achieve high efficiency, high selectivity, or rapid synthesis by a tandem process. Substitution of the unreactive carbon ligand(s) on silicon by hydrogen, chlorine, an oxygen ligand, or a more strained carbon ligand was found to introduce novel reactivities into silicon-protected carbon nucleophiles.

9.07.1.3 Literature

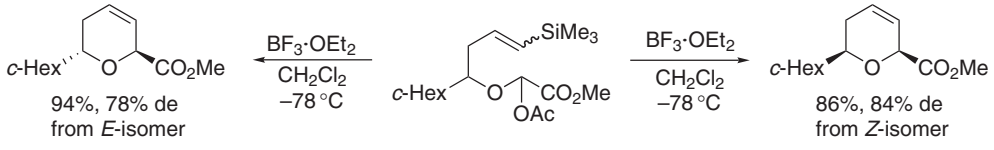
One monograph,[3] three edited multiauthor works,[4–6] several conference proceedings,[7–12] and one symposia-in-print[13] on a wide range of organosilicon chemistry including applications to organic synthesis were published from 1994 to 2004. Some reviews were devoted to a survey of synthetic applications of organosilicon reagents.[14–17]

9.07.2 Alkenylsilanes, Arylsilanes, and Alkynylsilanes

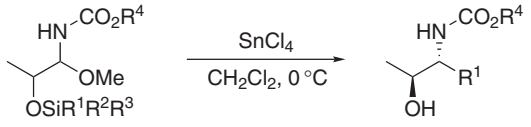
9.07.2.1 Electrophilic Substitution

Electrophilic substitutions of alkenyl-, aryl-, and alkynylsilanes with heteroatom-stabilized cationic carbon species generated by the action of a Lewis or Brønsted acid (acyl cation, oxocarbenium ion, etc.) provide powerful methods for carbon–carbon bond formation. Particularly, intramolecular reactions of alkenylsilanes with oxocarbenium and iminium ions are very valuable for stereoselective construction of cyclic ether and amine units.[21–23] For example, the $BF_3{\cdot}OEt_2$-promoted reaction of (*E*)- and (*Z*)-alkenylsilanes bearing an acetal moiety in the alkenyl ligand gives 2,6-disubstituted dihydropyrans in a stereospecific manner (Scheme 1).[23] Arylsilanes also can be utilized for a similar cyclization.[24]

Another type of intramolecular electrophilic substitution is shown in Equation (1).[25] In this case, the reaction sites are located in different substituents on silicon. This reaction mode is useful for highly diastereoselective alkenylation and phenylation of aminoacetals and hemiaminals.[26] Intramolecular conjugative arylation of α-enals bearing an aryldimethylsilyl group is effectively promoted by tetrabutylammonium fluoride (TBAF) (Equation (2)).[27,27a]

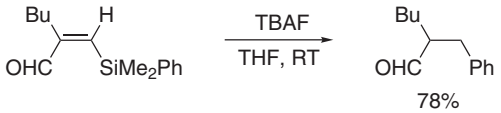


Scheme 1



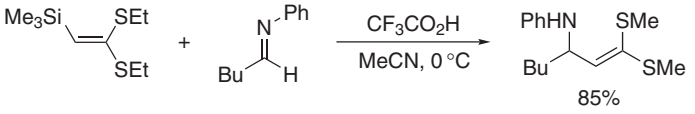
(1)

R^1 = vinyl; R^2 = R^3 = Me; R^4 = Bn: 74%, 90% de
R^1 = R^2 = Ph; R^3 = Bu^t; R^4 = Et: 85%, 97% de



(2)

Intermolecular carbon–carbon bond formation of alkenylsilanes by electrophilic substitution is rather limited except for the reaction with acyl chlorides.[1,28] The alkenylations of imines and epoxides are achieved with electronically activated alkenylsilanes (Equation (3)).[29,29a] Alkynylsilanes have frequently been used for intermolecular alkynylation of carbon electrophiles activated by a Lewis acid.[30,30a–30d]



(3)

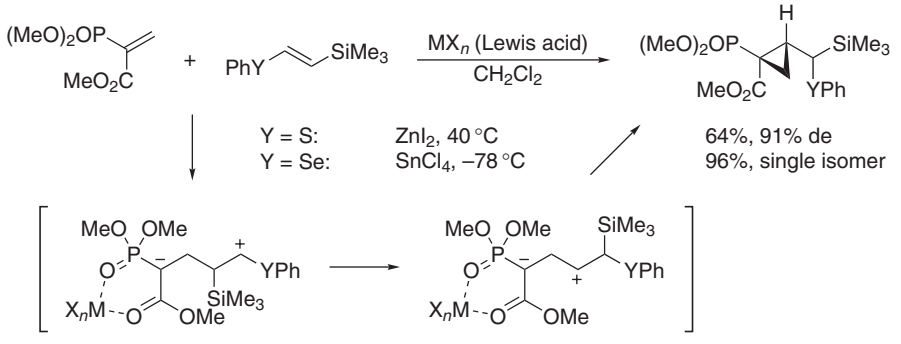
9.07.2.2 Reactions Forming Silylated Products

It is well recognized that β-silylcarbenium ions are prone to desilylation leading to alkenes by nucleophilic attack of the counteranions or a solvent molecule to the silicon center. However, synthetic use of the kinetically unstable carbon species for intramolecular bond formation has intensively been studied in the last decade.

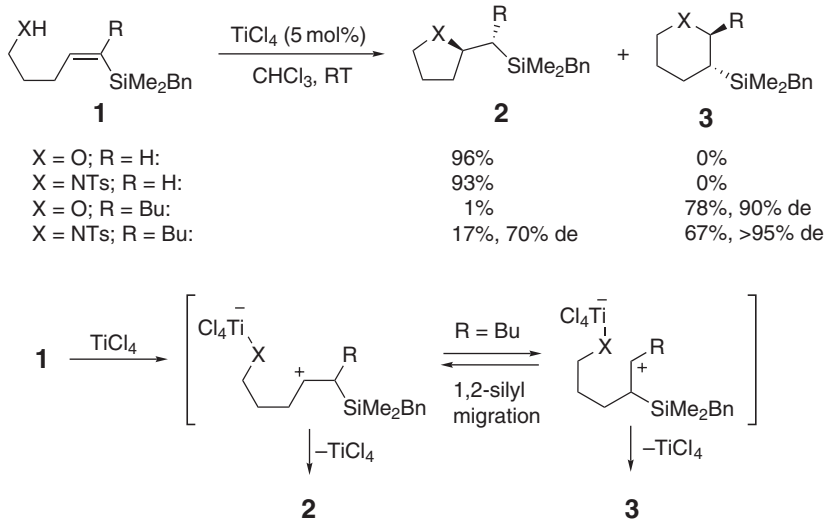
In the presence of a Lewis acid, 1-seleno- and 1-thio-2-silylethenes react with 2-phosphonoacrylates to give cyclopropane products (Scheme 2).[31,31a] The [2 + 1]-cycloaddition would involve 1,2-silyl migration of an α-seleno- or α-thio-β-silylcarbenium ion intermediate and subsequent ring closure.

Alkenylsilanes **1** (R = H), bearing a hydroxy or amino group, are smoothly cyclized to tetrahydrofurans and pyrrolidines under catalysis by a Lewis or Brønsted acid (Scheme 3).[32–34] When a substituent is in the methylene tether, the cyclization shows high diastereoselectivity. Interestingly, α-alkyl-substituted alkenylsilanes **1** (R = Bu) undergo 1,2-silyl-migrative cyclization with high *trans*-selectivity.[35,35a] These cyclizations probably involve the formation of a β-silylcarbenium ion intermediate by protonation of the alkenylsilane moiety. In the cyclization to **2**, the heteronucleophile directly adds to the cationic center. On the other hand, the presence of an alkyl group at the α-position induces 1,2-silyl migration of the intermediate to form thermodynamically favored six-membered heterocycles **3**.

The $BF_3{\cdot}OEt_2$-promoted [3 + 2]-cycloaddition of 1-morpholino-2-trimethylsilylethyne to homochiral epoxides is very valuable for direct asymmetric synthesis of γ-butanolides (Equation (4)).[36] The initial product, a 4-silyl-2,3-dihydrofuran, may be formed by ring closure of the β-silylcarbenium ion generated from a BF_3-activated epoxide and

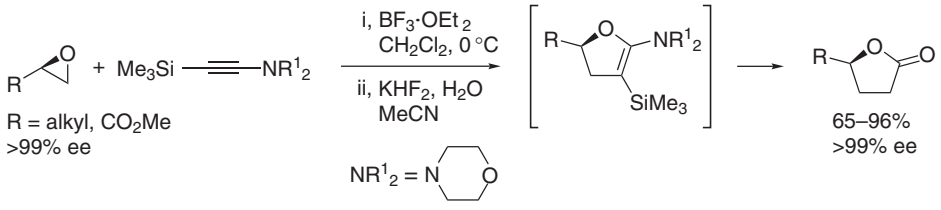


Scheme 2

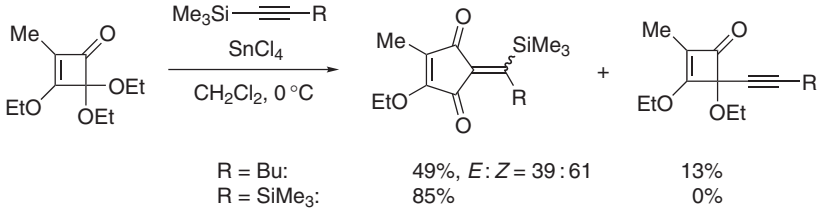


Scheme 3

the alkynylsilane. The $SnCl_4$-promoted reaction of a cyclobutenedione monoacetal with 1,2-bis(trimethylsilyl)ethyne proceeds via 1,2-silyl migration to give a ring-expansion product (Equation (5)).[37] A reaction mechanism via β-silylcarbenium ion intermediates has also been proposed in this case.

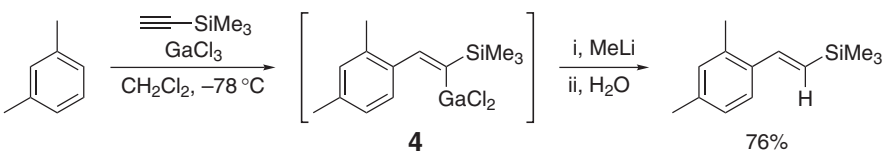


(4)

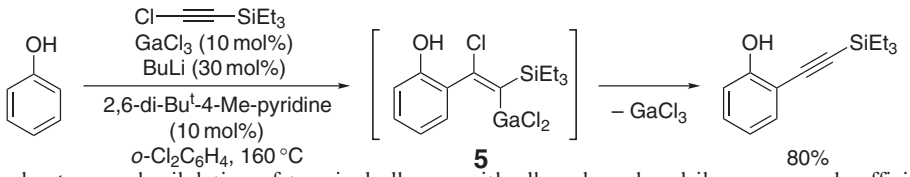


(5)

In the presence of a stoichiometric amount of $GaCl_3$, alkynylsilanes react with arenes to give β-arylated alkenylsilanes after treatment with MeLi followed by hydrolysis (Equation (6)).[38,38a,38b] The proposed mechanism for the formation of the initial product such as **4** consists of the coordination of an alkynylsilane to $GaCl_3$ and electrophilic aromatic substitution of the resultant complex positively charged at the β-position. The $GaCl_3$-catalyzed reaction of phenols with chloro(triethylsilyl)ethyne affords *ortho*-ethynylation products (Equation (7)).[39] The product formation is probably due to β-elimination of an alkenylgallium intermediate such as **5**. The route to such an intermediate can be explained by carbogallation of the alkyne with a dichlorophenoxygallane. The $GaCl_3$-catalyzed ethynylation is applicable to *N*-benzylanilines and ketones.[40,40a] Similar alkenylation and alkynylation reactions of silyl enolates with alkynylsilanes are described in section 9.07.6.2.

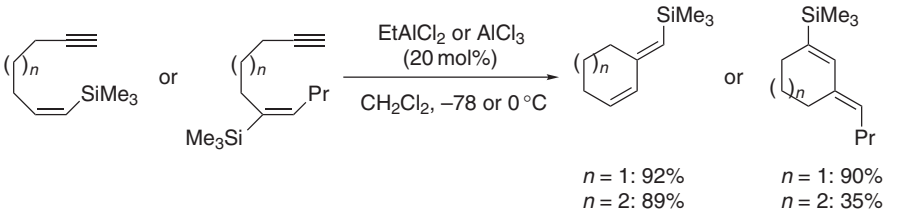


(6)



(7)

Intramolecular *trans*-carbosilylation of terminal alkynes with alkenyl- and arylsilanes proceeds efficiently under catalysis by a Lewis acid (Equation (8)).[41,41a] Alkenyl- and arylsilanes bearing an alkynyl group at the β- or *ortho*-position undergo *exo*-cyclization, while α-alkynyl-substituted alkenylsilanes are converted into *endo*-cyclization products. These cyclizations have been proposed to proceed also via a β-silylcarbenium ion intermediate. However, the cationic center does not participate in bond formation. The intermolecular alkenylsilylation of terminal alkynes is rather limited in applicability.[42]



(8)

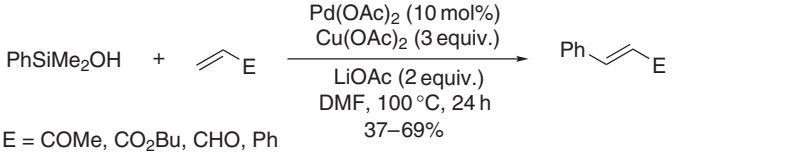
9.07.2.3 Transition Metal-promoted Reactions

9.07.2.3.1 Palladium-catalyzed reactions

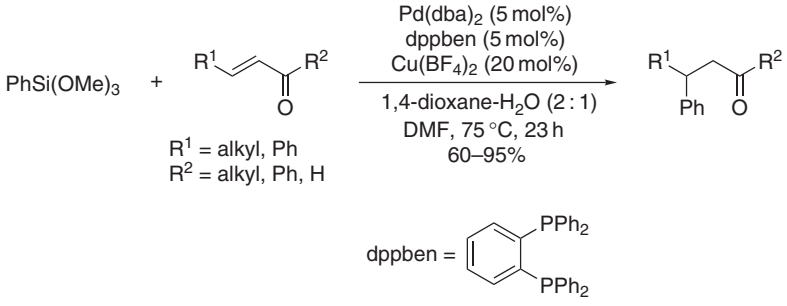
Alkenyl- and arylsilanes as well as the corresponding organoboron compounds have frequently been used as alkenyl and aryl donors for Pd-catalyzed cross-coupling with organic halides and pseudohalides.[43,43a,44] Pioneering works by Hiyama's and Ito's groups demonstrated that alkenyl- and arylsilanes bearing one or more fluorine atoms or alkoxy groups on silicon work as effective donors.[43,43a] In recent years, a variety of silicon-based alkenyl and aryl donors have been developed for efficient cross-coupling between sp^2 carbons (Table 1). For the review on Pd-catalyzed cross-coupling reactions of organosilanes, see *Volume 11* of this work and the recent review by Denmark and Sweis.[44]

With the aid of a fluoride ion source, alkynyltrimethylsilanes work as effective alkynyl donors in the Pd-catalyzed cross-coupling with alkenyl iodides.[43,43a] Recent studies have revealed that the alkynylsilanes react smoothly with aryl iodides and triflates, alkenyl triflates, or alkynyl chlorides under co-catalysis by a Cu or Ag salt.[45–46a] The use of a Pd/imidazolium chloride system in the presence of Cs_2CO_3 and a Cu co-catalyst enables an efficient coupling between alkynyltrimethylsilanes and aryl bromides.[47] In some cases, this catalytic system works well under Cu-free conditions. Alkynylsilanols also can be used as alkynyl donors in the coupling with aryl iodides.[48,49] When TBAF is employed as activator, the coupling proceeds efficiently without co-catalyst.[48]

Hiyama and co-workers have reported that the Mizoroki–Heck-type reaction of aryl- and alkenylsilanols is efficiently promoted by a $Pd(OAc)_2/Cu(OAc)_2/LiOAc$ system (Equation (9)).[50,50a] In contrast, a dicationic Pd(II) complex prepared *in situ* from $Pd(dba)_2$, a diphosphine (dppe or dppben), and $Cu(BF_4)_2$ catalyzes 1,4-addition of aryltrialkoxysilanes to α-enones and α-enals in aqueous media (Equation (10)).[51] The Pd-catalyzed 1,4-addition of the arylsilanes can be achieved also by using excess amounts of $TBAF{\cdot}3H_2O$, $SbCl_3$, and acetic acid.[52]

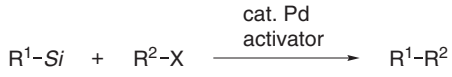


(9)



(10)

Table 1 Pd-catalyzed cross-coupling reactions of alkenyl- and arylsilanes



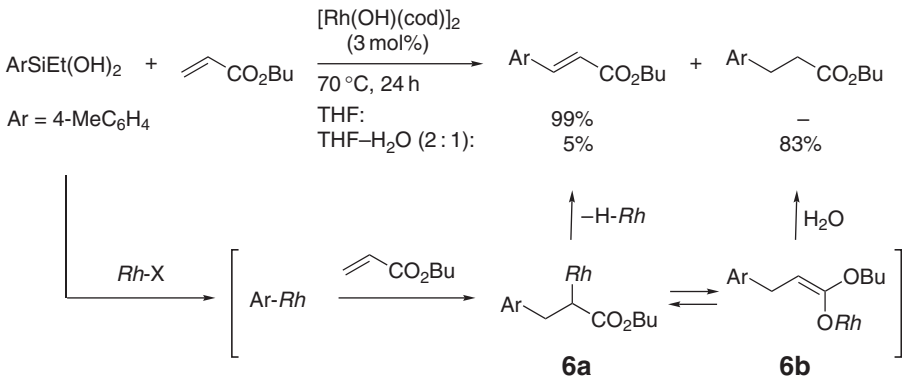
R^1	*Si*	R^2	*Activator*	*References*
Aryl, alkenyl	$SiR(OH)_2SiR_2(OH)$	Aryl, benzyl	Ag_2O	337–339
Alkenyl	$SiR_2(OH)$	Aryl, alkenyl	TBAF	340–344
Alkenyl	$SiMe_2(OH)$	Aryl	$KOSiMe_3$	345,346
Aryl	$SiMe_2(OH)$	Aryl	Cs_2CO_3 or CsOH	347,348
2-Indolyl	$SiMe_2(OH)$	Aryl	$NaOBu^t$, CuI	349
Alkenyl	$(\text{-}SiMe_2)_2O$	Aryl, alkenyl	TBAF	350,351
Aryl, alkenyl	Silicone	Aryl	TBAF	352
Aryl, alkenyl	Silicone	Aryl	K_2CO_3/H_2O	353
Ph, alkenyl	$Si(OMe)_3$	Aryl, allyl	TBAF	354
Ph	$SiF_2Ph_2^{-}$[a]	Aryl	None	355
Alkenyl	$SiHPr^i_2$	Alkenyl	TBAF	342
Alkenyl	1-Me-1-sila-cyclobutyl	Aryl, alkenyl	TBAF	341,356,357
Aryl	1-Cl-1-sila-cyclobutyl	Aryl	TBAF	358
Alkenyl	$SiMe_2$(2-Py)[b]	Aryl	TBAF	359
Alkenyl	$Si(SiMe_3)_3$	Aryl	H_2O_2, NaOH	360
Aryl	$Si(allyl)_3$	Aryl	TBAF	361–363
Alkenyl	$SiMe_2$(2-Th)[c]	Aryl	TBAF	364
Alkenyl	$SiMe_2Ar$	Aryl	TBAF	365
Alkenyl	$SiMe_2Ph$	Aryl	$KOSiMe_3$, 18-crown-6	366
Alkenyl	$SiMe_2Bn$	Aryl, alkenyl	TBAF	367

[a]$[Ph_3SiF_2]NBu_4$ was used as a phenyl donor.
[b]2-Py = 2-pyridyl.
[c]2-Th = 2-thienyl.

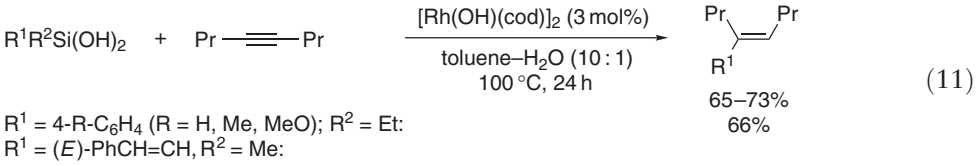
9.07.2.3.2 Rhodium-catalyzed reactions

A rhodium(I)-catalyzed system in THF is also effective in the Mizoroki–Heck-type reaction of arylsilanediols with acrylates (Scheme 4).[53] Interestingly, the use of aqueous THF switches the reaction to 1,4-addition forming β-arylated esters. The proposed catalytic cycles for these reactions involve 1,4-addition of an arylrhodium species to an acrylate. The change of the reaction pathway is probably because, in aqueous THF, the resultant Rh enolate **6** undergoes protonolysis rather than β-elimination. Similar Rh-catalyzed 1,4-additions to α,β-unsaturated carbonyl compounds have been achieved with arylsilicones,[54] arylchlorosilanes,[55] and aryltrialkoxysilanes.[56,57] The use of a cationic Rh–binap complex leads to highly enantioselective 1,4-additions of alkenyl- and arylsilanes.[58,58a]

Under catalysis by an Rh(I)OH complex, alkenyl- and arylsilanes add to aldehydes[56,59] and internal alkynes.[60] The addition to alkynes proceeds in a *cis*-mode, which is indicative of *cis*-addition of an alkenyl- or arylrhodium intermediate (Equation (11)).



Scheme 4

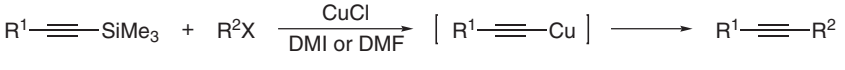


(11)

Acylation of alkenylsilanes with acid anhydrides is efficiently catalyzed by $[RhCl(CO)_2]_2$.[61] Based on the fact that stoichiometric reaction of an alkenylsilane with the Rh complex gives the corresponding alkenylrhodium species, the proposed mechanism involves alkenyl transfer from Si to Rh as the initial step.

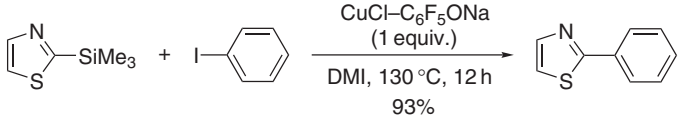
9.07.2.3.3 Copper-promoted reactions

Alkynylsilanes can be converted into alkynylcoppers by treatment with Cu salts in an aprotic polar solvent such as 1,3-dimethyl-2-imidazolidinone (DMI).[62] The Cu-promoted coupling reactions via the Si–Cu transmetallation of alkynylsilanes are valuable for the syntheses of alkynyl ketones, 1,3-diynes, 1,3-enynes, and 1-aryl-1-alkynes from acid chlorides,[62] alkynyl chlorides,[63] alkenyl iodides,[64] and aryl iodides,[64] respectively (Equation (12)). In addition, symmetric 1,3-diynes can be prepared by the CuCl-mediated homocoupling of alkynylsilanes.[65,65a]

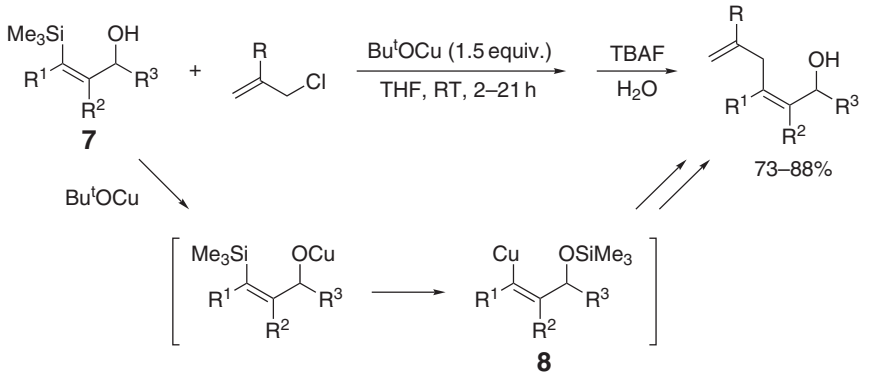


(12)

Synthetic reactions involving activation of alkenyl- and arylsilanes by copper salts have also been reported. A copper-mediated system is effective in the cross-coupling reaction of aryl- and heteroarylsilanes with aryl halides under Pd-free conditions (Equation (13)).[66] Alkenyl- and arylsilanes as well as alkynylsilanes undergo homocoupling in the presence of CuI and air.[65,65a] Functionalized alkenyl- and arylsilanes bearing a coordination site in the vicinity of silicon (e.g., 7) are easily activated by copper salts even at room temperature (Scheme 5).[67,67a–67e,68] The resultant organocoppers such as 8 are useful for carbon–carbon bond-forming reaction with carbon electrophiles.



(13)

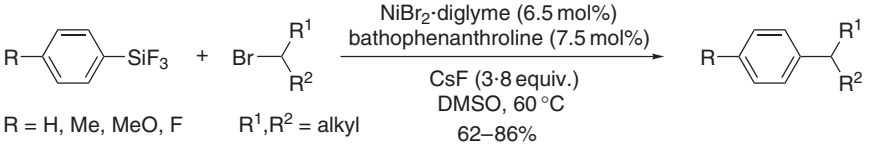


Scheme 5

9.07.2.3.4 Other transition metal-catalyzed reactions

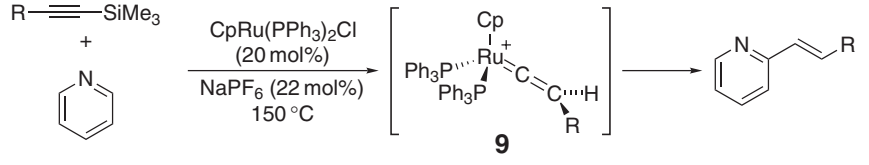
Iridium complexes as well as $[Rh(OH)(cod)]_2$ can catalyze the Mizoroki–Heck-type reaction of arylsilanediols with acrylates. Aryltrialkoxysilanes activated by TBAF also work as the aryl donor in the presence of H_2O. In contrast to the Rh-catalyzed reaction, this reaction does not form β-arylated saturated esters even in aqueous media.[69]

Fu and Powell have reported that a nickel-based catalyst accomplishes an efficient cross-coupling between secondary alkyl bromides and aryltrifluorosilanes activated by CsF (Equation (14)).[70] This arylation is tolerant to a variety of functionalities and applicable to primary alkyl bromides and iodides.



(14)

Under catalysis by an Ru complex, alkynylsilanes react with pyridines to give (*E*)-2-alkenylated pyridines (Equation (15)).[71] This regio- and stereoselective direct alkenylation has been proposed to proceed via cationic Ru vinylidene complex **9**.



(15)

9.07.3 Allylsilanes and Related Compounds

9.07.3.1 Allylation of Aldehydes, Ketones, and Acetals

9.07.3.1.1 Lewis acid-promoted allylation

Lewis acid-promoted allylation with allyltriorganosilanes, the Hosomi–Sakurai reaction, has several advantages over allylations with other allylmetals.[16,72–74] Since these silicon reagents have high thermal stability and low reactivity to water and oxygen, they are isolable, storable, and easily handled without special precautions. The stability also allows synthesis of highly functionalized allylating reagents and their efficient addition to carbon electrophiles. The allylation occurs at the position γ to silicon in a regiospecific manner. In addition, the stereoselectivity can be controlled finely by the choice of Lewis acid and reaction conditions. More importantly from the trend toward environmentally benign synthesis, allylsilanes are less toxic than other allylmetals such as allylstannanes. The great utility of the Hosomi–Sakurai reaction in fine organic synthesis has fully been demonstrated by extensive studies in the last three decades.

The pioneering works by Hosomi and Sakurai described that conventional Lewis acids ($TiCl_4$, $SnCl_4$, and $BF_3{\cdot}OEt_2$) are effective in the allylation of aldehydes, ketones, and acetals with a (sub)stoichiometric quantity.[72]

Since then, much effort has been paid at achieving a catalytic version of the Hosomi–Sakurai reaction. A number of Lewis acids have so far been found to accomplish the catalytic allylation. Among them, Me_3SiNTf_2, prepared *in situ* from allyltrimethylsilane **10** and $HNTf_2$, has exceedingly high activity and realizes high efficient allylation of ketones as well as aldehydes and acetals.[75] Me_3SiI shows high catalytic activity to the carbonyl allylation in MeCN, which stands in sharp contrast with much less activity in CH_2Cl_2.[76] Catalytic use of $FeCl_3$, a very cheap Lewis acid, is valuable particularly for allylation of sterically hindered aliphatic aldehydes (Table 2).[77]

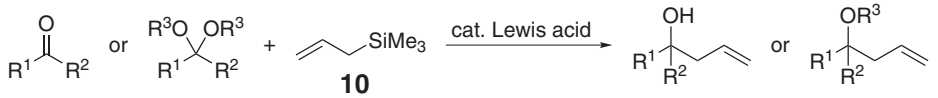
The Hosomi–Sakurai reaction is quite useful for diastereoface-selective allylation of oxocarbenium ions generated from acetals and lactols by treatment with a Lewis acid. The $TiCl_4$-promoted allylation of α-iodo mixed acetals with **10** gives homoallylsilyl ethers with high *anti*-selectivity (Scheme 6).[78] The stereochemical outcomes can be explained by the Felkin–Anh model **11** of the oxocarbenium ion intermediate. Interestingly, catalytic use of Me_3SiOTf results in exclusive replacement of the siloxy group with retention of the diastereoselectivity.

In the $SnBr_4$-promoted allylation of 4-substituted 2-acetoxytetrahydrofurans, the sense of diastereoselectivity strongly depends on the substituent R^2 (Scheme 7).[79] When R^2 is a methyl group, the allylation affords the 2,4-*trans*-isomer of the allylated product predominantly. This stereochemistry is explainable by stereoelectronically favored inside attack of **10** to the stable conformer **12a** of the oxocarbenium ion intermediate. In the case of $R^2 = OBn$, high 2,4-*cis*-diastereoselectivity is observed. The origin of the reversed diastereoselectivity is probably that electrostatic effect between the alkoxy oxygen and the positively charged carbon make the conformer **12b** more stable than **12a**, and **10** attacks **12b** from the inside, that is, the same side of the alkoxy group. Similar stereochemical divergence appears in the allylation of 4- or 5-substituted 2-acetoxytetrahydropyrans.[80,80a]

The $BF_3{\cdot}OEt_2$-promoted allylation of 4-substituted 2-hydroxytetrahydrofurans (γ-lactols) shows high *trans*-selectivity as in the allylation of 4-substituted 2-acetoxytetrahydrofurans.[81]

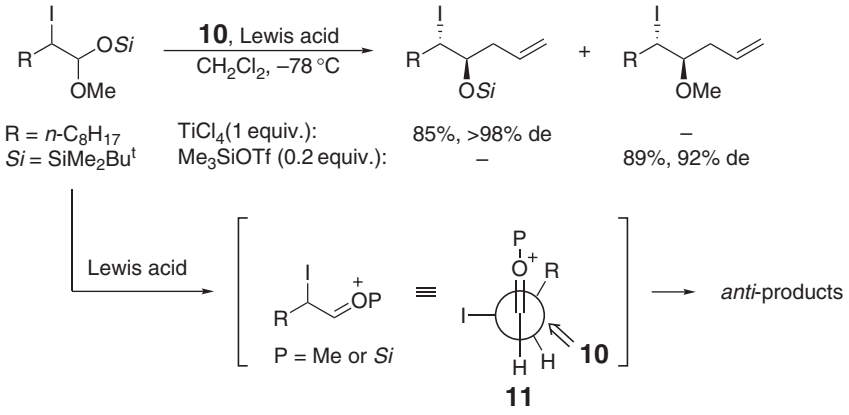
Tandem acetalization–allylation reaction of aldehydes with allylsilanes provides a convenient route to homoallyl ethers.[82] Under catalysis by $Sc(OTf)_3$, various aldehydes can be converted into homoallyl ethers by treatment with

Table 2 Lewis acid-catalyzed allylation with allyltrimethylsilane

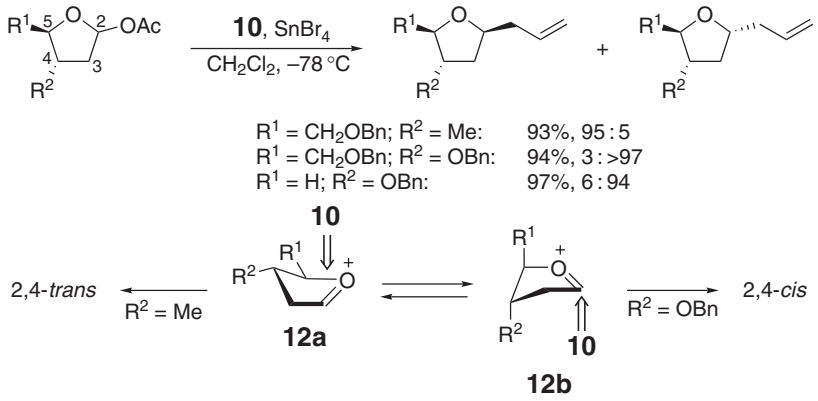


Catalyst	*Substrate*	*Solvent*	*References*
Me_3SiOTf	Acetal	CH_2Cl_2	368
Me_3SiI	Acetal	CH_2Cl_2	369
Ph_3CClO_4	Acetal	CH_2Cl_2	370
Ph_2BOTf	Aldehyde, acetal	CH_2Cl_2	370
Montmorillonites	Aldehyde, acetal	CH_2Cl_2	371
$Me_3SiB(OTf)_4$	Aldehyde	CH_2Cl_2	372
$Me_3SiN(SO_2F)_2$	Acetal	CH_2Cl_2	373
Me_3SiOSO_2F	Acetal	CH_2Cl_2	374
$Cp_2Ti(OTf)_2$	Acetal	CH_2Cl_2, $MeNO_2$	375
$Sc(OTf)_3$	Aldehyde	$MeNO_2$	376
$R_3SiB(OTf)_3Cl$	Aldehyde	CH_2Cl_2	377
$HN(SO_2F)_2$	Aldehyde, ketone	CH_2Cl_2	378
$Yb(OTf)_3$	Aldehyde	CH_2Cl_2, MeCN	379
Me_3SiNTf_2	Acetal	CH_2Cl_2	380
$BiBr_3$	Aldehyde, ketone, acetal	CH_2Cl_2	381
Me_2AlNTf_2	Aldehyde	CH_2Cl_2	382
$Sc(OTf)_3$	Acetal	CH_2Cl_2	83
$HNTf_2$ (Me_3SiNTf_2)	Aldehyde, ketone	CH_2Cl_2, Et_2O, PhCl	75
PS-$C_6F_4CHTf_2$[a]	Aldehyde	CH_2Cl_2	383
I_2 (Me_3SiI)	Aldehyde	MeCN	76
$Bi(OTf)_3$	Acetal	CH_2Cl_2	384
$FeCl_3$	Aldehyde, acetal	$MeNO_2$	77
Me_3SiOTf	Acetal	[bmim][PF_6], [bmim][OTf][b]	385

[a]PS = polystyrene.
[b]bmim = 1-butyl-3-methylimidazolium.

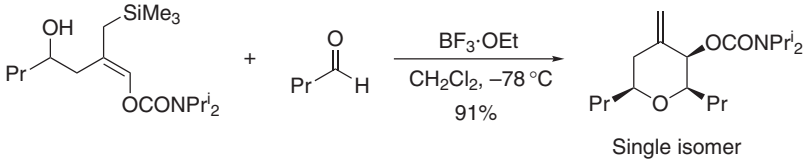


Scheme 6



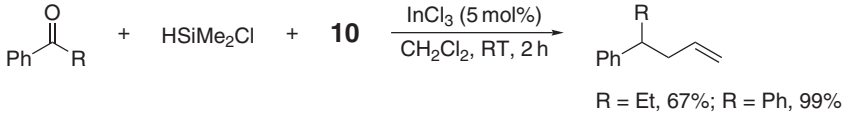
Scheme 7

trimethylorthoformate and **10**.[83] Hydroxy- or siloxy-substituted allylsilanes have frequently been used for stereoselective construction of multisubstituted cyclic ethers by the tandem process.[16,84] A recent example is shown in Equation (16).[84]



(16)

Deoxygenative allylation of aromatic ketones can be performed by the $InCl_3$-catalyzed reaction with $HSiMe_2Cl$ and **10** (Equation (17)).[85]

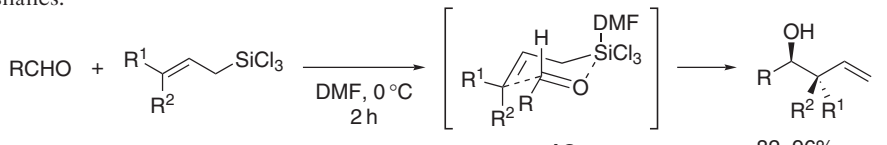


(17)

9.07.3.1.2 New types of carbonyl allylation

Carbonyl allylation using pentacoordinate allylsilicates is valuable for stereospecific synthesis of homoallyl alcohols: the allylations with (*E*)- and (*Z*)-crotylsilicates show high *anti*- and *syn*-selectivity, respectively.[86,86a–86d] Significant

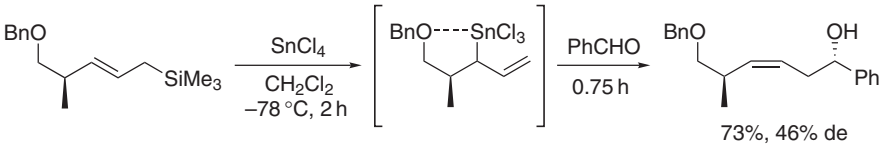
progress in synthetic use of allylsilicates was made by Kobayashi *et al.* They found that allyltrichlorosilanes work for stereospecific allylation of aldehydes in DMF, and proposed that pentacoordinate allylsilicates generated from the allylsilanes and one DMF molecule react with aldehydes via a cyclic transition state such as **13** (Equation (18)).[87,87a,87b] Allyltrichlorosilanes can be prepared in an isomerically pure form by the reaction of allyl chlorides or 1,3-dienes with $HSiCl_3$; therefore, this method provides a convenient, stereoselective route to homoallyl alcohols. Denmark *et al.* demonstrated that HMPA is an efficient base catalyst of the carbonyl allylation with allyltrichlorosilanes.[88]



(18)

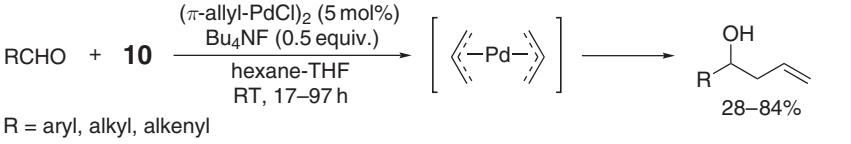
An extended study by Kobayashi *et al.* showed that propargyl- and allenyltrichlorosilanes serve as efficient allenylating and propargylating agents, respectively, in DMF.[89]

Generally, the Lewis acid-promoted allylation of aldehydes with allyltrimethylsilanes proceeds via carbonyl activation. However, the $SnCl_4$-promoted allylation with allylsilanes bearing a coordinate site is rationalized by a transmetallation mechanism, in which allyltrichlorostannanes work as the actual allylating agents (Equation (19)).[90,91,91a] The allylation takes place at the α-position unlike the usual regiochemistry of the Hosomi–Sakurai reaction.[90]



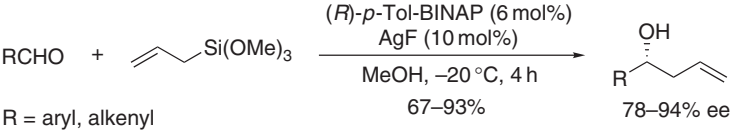
(19)

The TBAF-catalyzed allylation of aldehydes with **10** proceeds efficiently in refluxing THF.[92] In contrast, a Pd–TBAF co-catalyst system enables the allylation at room temperature (Equation (20)).[93] This mild allylation is due to the formation of a bis-π-allylpalladium complex as the actual allylating agent.



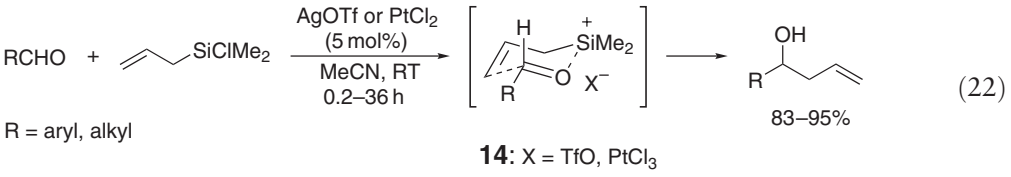
(20)

Allyltrimethoxysilanes are available for carbonyl allylation under catalysis by AgF·(*p*-Tol)BINAP,[94] CuCl–$Bu_4N[Ph_3SiF_2]$,[95] or CdF_2·terpyridine.[96] The Ag-based catalytic system achieves highly enantioselective allylation of aldehydes (Equation (21)), and the proposed mechanism involves a transmetallation step. The Cd-catalyzed allylation can be performed in aqueous media. These Ag- and Cd-based catalytic cycles include regeneration of the metal fluorides as the active catalysts[97] although the TBAF-catalyzed allylation with **10** has been proved to proceed via a fluoride ion-initiated (triggered) mechanism.[98,99]



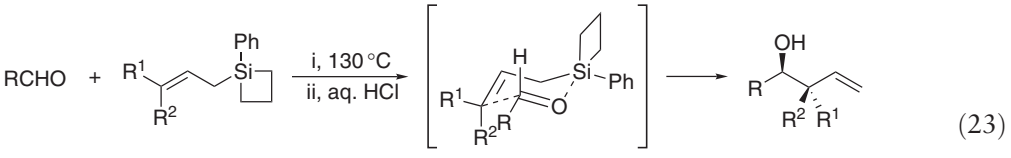
(21)

Allylchlorodimethylsilanes exert the ability to allylate aldehydes and acetals in the presence of a catalytic amount of halophilic transition metal salts such as AgOTf and $PtCl_2$ (Equation (22)).[100] The allylation of aldehydes occurs at the γ-position in a stereospecific manner. This observation is indicative of cyclic transition state **14**. AgOTf is used only for the initial formation of allyldimethylsilyl triflates, the active allylating agents. In contrast, $PtCl_2$ works as the actual catalyst for halophilic activation leading to **14** ($X = PtCl_3$).



(22)

Allylation of aldehydes with allylsilacyclobutanes proceeds spontaneously at 130–160 °C with regio- and stereospecificity (Equation (23)).[101] Under the same conditions, allyldimethylphenylsilane is insensitive to aldehydes. The thermal allylation takes place probably via a six-membered cyclic transition state, which would be assisted by the relatively strong Lewis acidity of the strained silyl group. Allylsilacycles derived from allylchlorosilanes by treatment with 1,2-diols, β-amino-alcohols, and 1,2-diamines are reactive enough for spontaneous allylation at or below room temperature.[102,102a,102b,103]



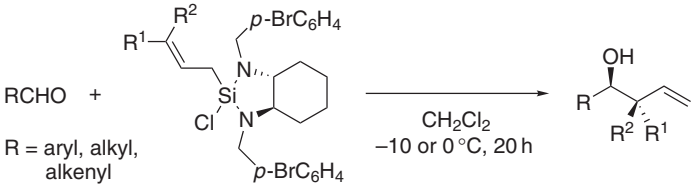
(23)

R = Ph, Hex, PhCH=CH; $R^1 = R^2 = H$: 58–85%
R = Ph; R^1 = Pr; R^2 = H: 68%, 90% de
R = Ph; R^1 = H; R^2 = Pr: 66%, 90% de

9.07.3.1.3 Asymmetric allylation of aldehydes, ketones, and acetals

Oxocarbenium ions bearing a chiral auxiliary are useful for asymmetric allylation with **10**. For example, oxocarbenium ions generated from aldehydes and homochiral Me_3Si ether **15** are allylated with high diastereoselectivity (Scheme 8).[104,104a,104b] The resultant homoallyl ethers can easily be converted into homoallyl alcohols without epimerization. This two-step procedure is applicable to enantioselective allylation of ketones.[105,105a]

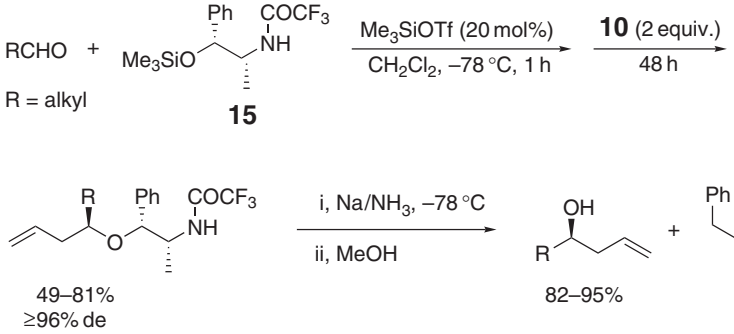
Allylsilacycles bearing a chiral 1,2-diol, β-aminoalcohol, or 1,2-diamine ligand have been utilized for enantioselective allylation of aldehydes.[102,102a,103,106,106a] As mentioned above, they react with aldehydes spontaneously. Among them, allylsilacycles **16** show the highest enantioselectivity (Equation (24)).



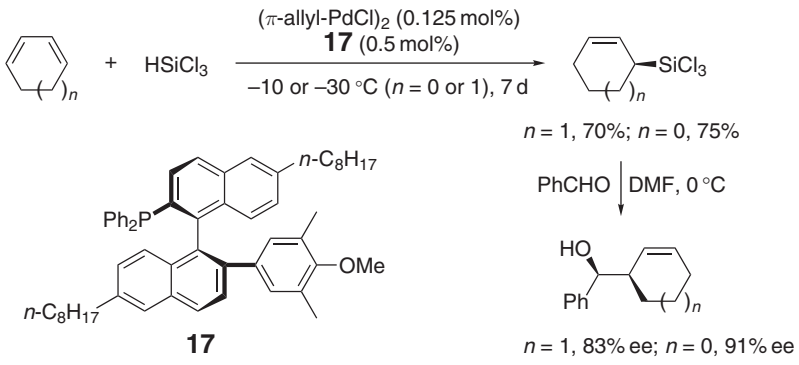
(24)

16

R^1, R^2 = H: 61–93%, 95–98% ee
R^1 = H; R^2 = Me: 61–83%, >88% de, 95–97% ee
R^1 = Me; R^2 = H: 52–83%, >88% de, 93–99% ee



Scheme 8



Scheme 9

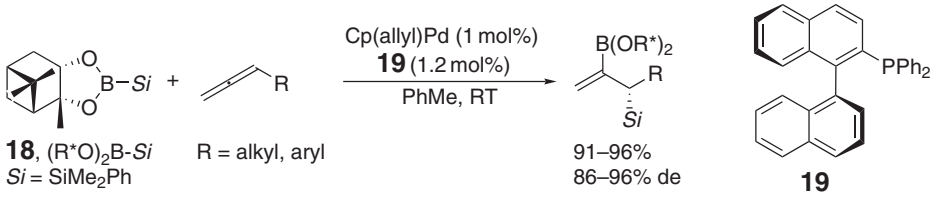
Asymmetric hydrosilylation of 1,3-dienes provides convenient access to optically active α-chiral allylsilanes.[107,107a,107b] The combination of π-allylpalladium chloride dimer with axially chiral monophosphine ligand **17** realizes high catalytic activity and enantioselectivity in the reaction of cyclic 1,3-dienes with $HSiCl_3$.[108,108a] The allyltrichlorosilanes obtained react with aldehydes in a *syn*-S_E' mode to give homoallyl alcohols with high diastereo- and enantioselectivity (Scheme 9).

Similarly, optically active allenyltrichlorosilanes can be prepared from 1,3-enynes and $HSiCl_3$.[109] The DMF-promoted propargylation of aldehydes with allenyltrichlorosilanes effects complete chirality transfer by a *syn*-S_E' process.

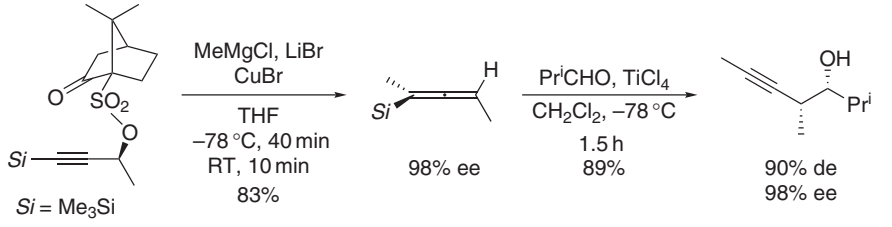
Highly enantioselective synthesis of allenyltrimethylsilanes can be carried out by *anti*-S_N2' reaction of homochiral γ-trimethylsilyl-substituted propargyl sulfonates with a methylcopper reagent (Scheme 10).[110] Under catalysis by a Lewis acid, optically active allenyltrimethylsilanes react with aldehydes via an *anti*-S_E' process. Nucleophilic substitution of homochiral propargyl sulfonates with silylcopper reagents (Cl_3SiCu, $(PhMe_2Si)_2CuLi$) affords optically active propargyl- and allenylsilanes.[111,111a]

The Pd-catalyzed intramolecular bis-silylation of homochiral allyl and propargyl disilanyl ethers and subsequent Peterson-type elimination provide a reliable method for highly enantioselective synthesis of allyl- and allenylsilanes.[112,112a,112b,113] This method enables the synthesis of highly enantioenriched allylsilanes bearing a hydroxyalkyl group, which are very valuable as synthetic intermediates for highly diastereo- and enantioselective construction of heterocycles and carbocycles (Scheme 11).[114,114a,114b]

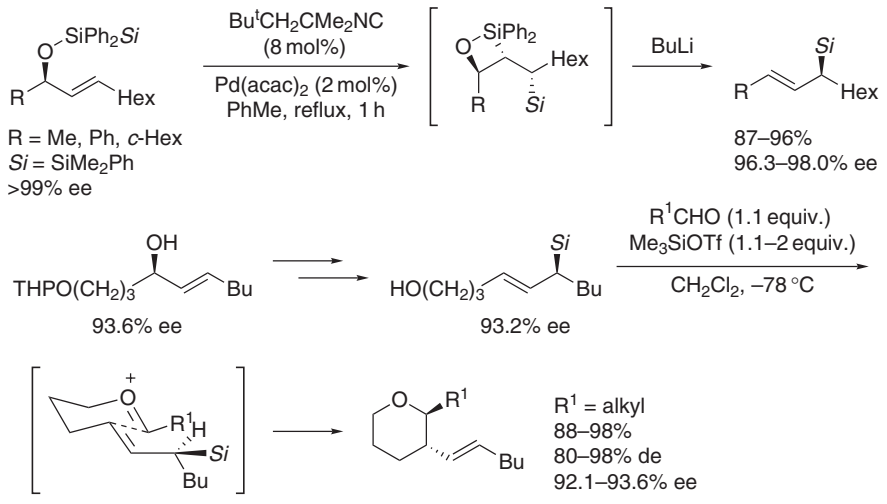
Under catalysis by a Pd complex with homochiral phosphine ligand **19**, silaboration of terminal allenes with homochiral silylborane **18** shows high enantioface-selectivity by double asymmetric induction (Equation (25)).[115] The resultant β-borylated allylsilanes can be used for asymmetric carbonyl allylation.



(25)



Scheme 10

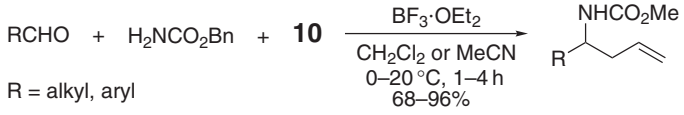


Scheme 11

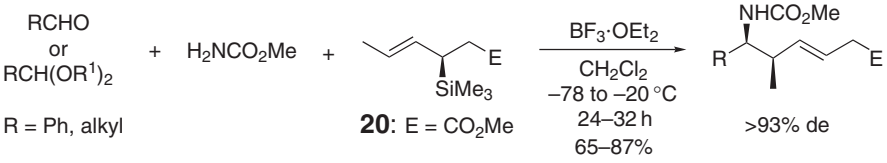
Catalytic asymmetric allylation of aldehydes and ketones with allylsilanes can be achieved by using chiral Lewis acids, transition metal complexes, and Lewis bases. In recent years, much attention has been paid for the chiral Lewis base-catalyzed system using allyltrichlorosilanes. Advances in catalytic asymmetric carbonyl allylation have been described in detail in recent reviews.[116,117,117a]

9.07.3.2 Allylation of Carbon–Nitrogen Double Bonds

Allyltriorganosilanes react with activated C–N double bonds such as iminium salts and Lewis acid-coordinated imines at the γ-position to give homoallylamines.[14,118] For example, in the presence of BF_3, *N*-acylimines generated *in situ* by the reaction of aldehydes or acetals with carbamates are efficiently allylated with allyltrimethylsilanes (Equation (26)).[119,119a,120] The use of homochiral crotylsilanes such as **20** leads to highly diastereo- and enantioselective synthesis of homoallylamines (Equation (27)).[121,121a] Allenylation of the *N*-acylimines can be performed with propargylsilanes.[122] Intramolecular allylation of imines with allylsilanes is useful for the synthesis of substituted piperidines.[123]

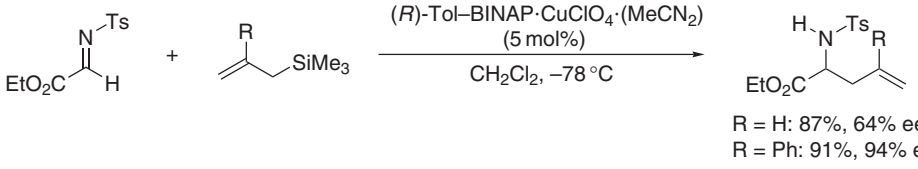


(26)



(27)

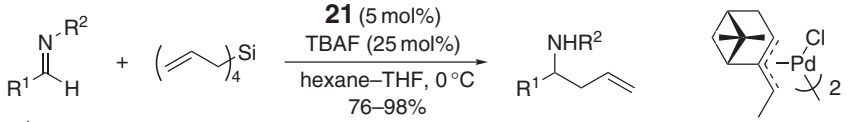
The allylation of α-*N*-tosylimino esters, highly activated imines, proceeds by catalytic use of a Lewis acid. Tol–BINAP–Cu(I) complexes are effective catalysts of asymmetric allylation of these imines with allylsilanes (Equation (28)).[124,125] The presence of an aryl group at the position β to silicon improves the enantioselectivity.



(28)

A catalytic amount of TBAF is effective in the allylation of aromatic imines with **10** in refluxing THF.[99] Similar to the TBAF-catalyzed carbonyl allylation, the imine allylation is promoted by a fluoride-triggered autocatalytic cycle.

The π-allylpalladium–TBAF co-catalyst system described in Equation (20) enables the allylation of aromatic imines as well as aldehydes at room temperature.[93] Chiral π-allylpalladium complex **21** is an efficient asymmetric catalyst of the imine allylation (Equation (29)).[93,126]

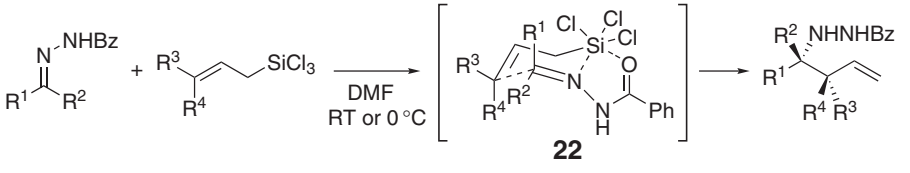


R^1 = aryl, (*E*)-PhCH=CH
R^2 = Bn, 4-$MeOC_6H_4CH_2$

(29)

In the presence of $Bu_4N[Ph_3SiF_2]$ and $In(OTf)_3$, tetraallylsilane adds to *N*-acylhydrazones bearing a chiral oxazolidinone moiety at room temperature to give allylated products with high diastereoselectivity.[127] Dual activation of the reactants by these additives is crucial for the mild allylation.

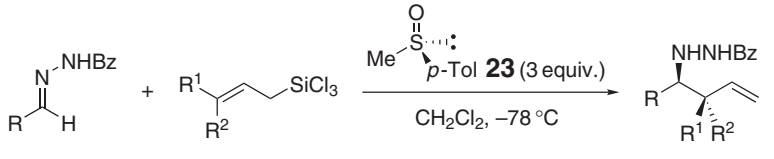
The DMF-promoted allylation with allyltrichlorosilanes is applicable to *N*-benzoylhydrazones and *N*-(2-hydroxyphenyl)imines.[128,128a,128b,129] Various *N*-benzoylhydrazones derived from aldehydes and ketones are efficiently allylated at 0 °C or room temperature (Equation (30)). The crotylation of these hydrazones and imines proceeds in a stereospecific manner as does the carbonyl crotylation in Equation (18). In the hydrazone allylation, bicyclic transition state **22** has been proposed for the stereochemical outcomes and high reactivity of *N*-benzoylhydrazones.



(30)

	R^1 = Ph, (*E*)-PhCH=CH, alkyl; R^2 = H	R^1 = aryl, R^2 = alkyl
R^3 = R^4 = H:	73–96%	87–95%
R^3 = H; R^4 = Me (*E*:*Z* = <1:99):	65–80%, 82–98% de (*anti*)	37–88%, 86–>98% de (*anti*)
R^3 = Me; R^4 = H (*E*:*Z* = 97:3):	59–82%, 56–90% de (*syn*)	46–78%, 72–90% de (*syn*)

In the presence of an excess amount of homochiral sulfoxide **23**, allyltrichlorosilanes react smoothly with *N*-benzoylhydrazones in CH_2Cl_2 to give allylated products with good to high enantioselectivity (Equation (31)).[130] The sulfoxide-promoted crotylation also shows stereospecificity. The use of BINAP and Tol–BINAP dioxides instead of **23** achieves high enantioselectivity in the allylation of α-hydrazono esters.[131]



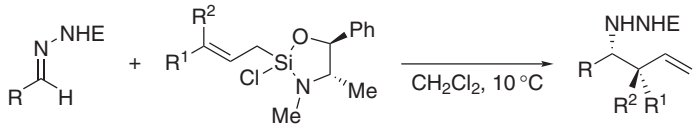
(31)

R = alkyl
R^1 = R^2 = H:
R^1 = H; R^2 = Me (*E*:*Z* = <1:99):
R^1 = Me; R^2 = H (*E*:*Z* = 98:2):

73–81%, 90–98% ee
60–99%, >98% de, 73–91% ee (*anti*)
58–99%, 90-98% de, 82–91% ee (*syn*)

Catalytic enantioselective allylation of α-hydrazono esters with allyltrimethoxysilanes in aqueous media can be accomplished by ZnF_2-chiral diamine complexes.[132]

Homochiral strained allylsilacycles **24** are valuable for uncatalyzed enantioselective allylation of *N*-acylhydrazones derived from aldehydes and ketones (Equation (32)).[133,133a] The crotylation using **24b** and **24c** occurs in the same stereospecific manner as observed in the DMF-promoted crotylation using crotyltrichlorosilanes. A cyclic transition state similar to **22** is reasonable also in the allylation using **24**.

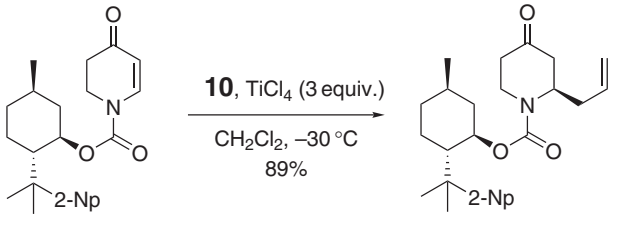


(32)

R = aryl, Bu^t; E = Ac	$R^1 = R^2 = H$ **24a**:	49–96%, 23–97% ee
R = Ph; E = Bz	$R^1 = H$; $R^2 = Me$ **24b**:	81%, 92% de, 95% ee (*anti*)
R = Ph; E = Bz	$R^1 = Me$; $R^2 = H$ **24c**:	89%, 90% de, 97% ee (*syn*)

9.07.3.3 Conjugate Allylation

The Hosomi–Sakurai reaction is valuable for conjugate allylation of α-enones.[134] The conjugate allylation using allylsilanes has been widely utilized for introduction of functionalized carbon chains and construction of carbocycles in natural product synthesis.[16,135] Asymmetric conjugate allylation using chiral auxiliaries is a recent topic in this field.[136,137,137a] For example, homochiral α-enone **25** undergoes $TiCl_4$-promoted allylation with high diastereoselectivity (Equation (33)).[136]

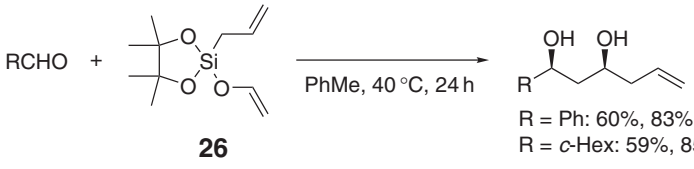


(33)

9.07.3.4 Tandem Carbon-Carbon Bond Formation

Tandem (Domino) reactions, in which two or more bond-forming processes result from a single step, are useful for rapid synthesis of complex molecules.[138] Functionalized allylsilanes and the related silicon compounds have frequently been used for tandem reactions, because of their ease of synthesis and moderate, controllable reactivity. Recently, much attention has been paid to the use of multifunctional allylsilanes bearing another reactive group on silicon.

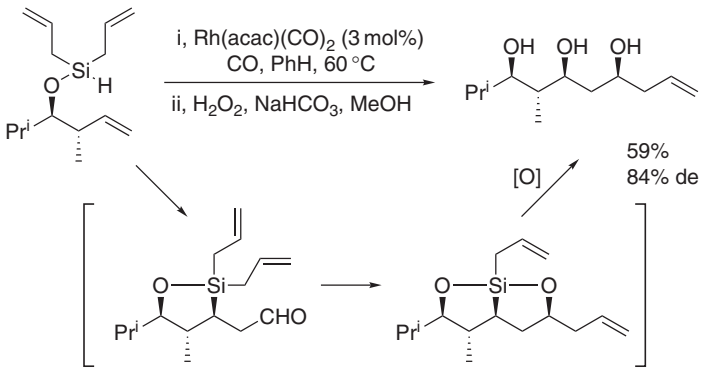
In the presence of $BF_3{\cdot}OEt_2$, allyldimethylsilyl enolates react with acetals to give allylated 1,3-diol monoethers.[139] A similar tandem aldol-allylation reaction can be performed by strained allylsilyl enolates such as **26** without promoter (Equation (34)).[140] Allylsilanes bearing a vinyl ether moiety at the β-position give rise to another type of tandem aldol-allylation reaction in the presence of a Lewis acid.[141]



(34)

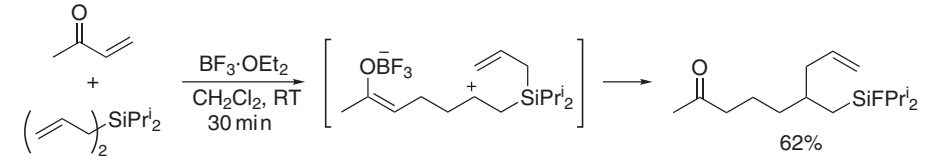
Tandem intramolecular silylformylation–allylation reaction of diallylhydrosilyl ethers derived from homoallyl alcohols is convenient for rapid, stereoselective synthesis of 1,3,5-triols convertible to more oxygen-functionalized compounds (Scheme 12).[142,142a,142b,143] The second uncatalyzed allylation step would be facilitated by the formation of a strained silacycle intermediate, which has enough Lewis acidity to activate the formyl group. A similar tandem reaction via alkyne silylformylation has been reported.[144]

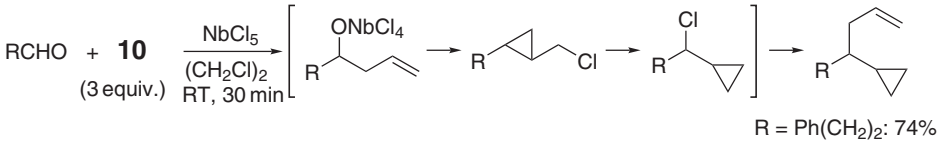
The $BF_3{\cdot}OEt_2$-promoted reaction of α-enones with diallylsilanes forms double allylation products (Equation (35)).[145] The tandem allylation can be rationalized by intramolecular allylation of the β-silylcarbenium



Scheme 12

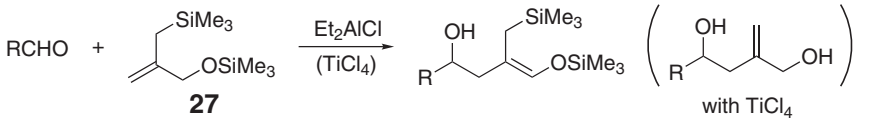
ion intermediate generated by the initial conjugate addition. In the presence of $NbCl_5$, **10** reacts with aldehydes in 2 : 1 stoichiometry to introduce both allyl and cyclopropyl groups (Equation (36)).[146] A plausible mechanism for this tandem process involves cationic isomerization of a cyclopropylmethyl chloride intermediate. A double Hosomi–Sakurai reaction of aldehydes with an allylsilane bearing a silylmethyl group at the β-position is useful for the synthesis of 2,3,5-trisubstituted tetrahydrofurans.[147]



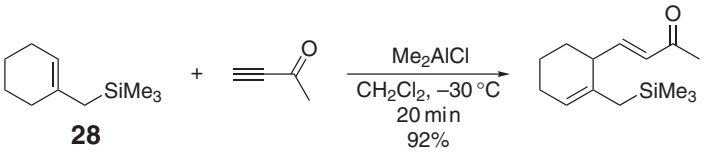


9.07.3.5 Ene Reactions

β-Substituted allylsilanes are subject to ene reaction with aldehydes and α,β-unsaturated carbonyl compounds in the presence of a Lewis acid. The Et_2AlCl-promoted reaction of β-siloxymethyl-substituted allylsilane **27** with aldehydes gives more functionalized allylsilanes (Equation (37)).[148] The use of $TiCl_4$ instead of Et_2AlCl leads to the Hosomi–Sakurai allylation. Catalytic enantioselective carbonyl–ene reactions of methallylsilanes have been achieved by using chiral Ti and Al complexes.[149,150]



In the presence of Me_2AlCl, isocyclic allylsilane **28** adds to 3-butyn-2-one to afford an α-enone bearing an allylsilane moiety (Equation (38)).[151,151a] In contrast, the ZnI_2-promoted ene reaction of an acyclic β-substituted allylsilane with an α-ynone forms a vinylsilane product exclusively.[152]

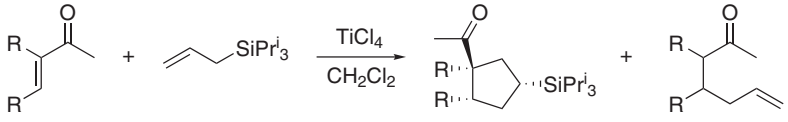


9.07.3.6 Cycloaddition to Electron-deficient Unsaturated Bonds

9.07.3.6.1 1,2-Silyl-migrative cycloaddition

Danheiser and Miginiac reported Lewis acid-promoted [3 + 2]-cycloadditions of allenylsilanes and propargylsilanes to electron-deficient unsaturated bonds in the 1980s.[21,153,153a,153b,154] The 1,2-silyl-migrative cycloadditions provide efficient routes to unsaturated five-membered carbocycles and heterocycles. The reaction mechanism consists of three steps: nucleophilic addition of the silicon reagent to an unsaturated bond activated by Lewis acid, 1,2-silyl migration of the resultant β-silylcarbenium ion intermediate, and intramolecular nucleophilic addition to the cationic center. Knölker and co-workers introduced a similar cycloaddition of allyltrimethylsilane **10** to α-enones in 1990 (Scheme 13).[155] Since then, various allylsilanes and unsaturated compounds have been utilized for the 1,2-silyl-migrative cycloaddition to realize highly selective, highly efficient synthesis of saturated carbocycles and heterocycles.[74,156]

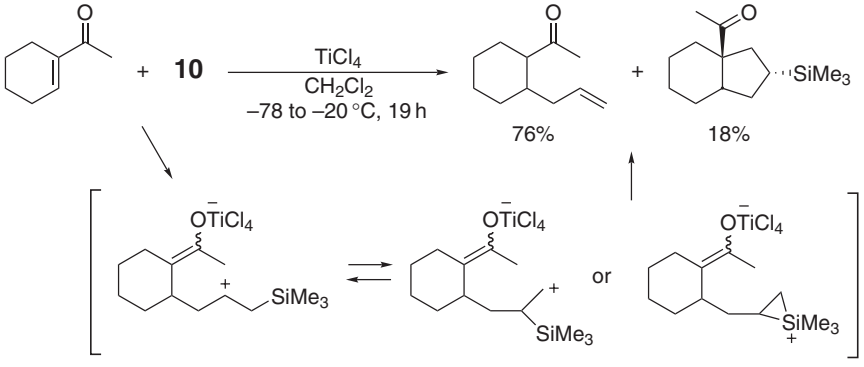
As shown in Scheme 13, the cycloaddition of **10** to α-enones results in low yield due to competitive formation of the allylated product. However, allylsilanes bearing a bulky silyl group such as *i*-Pr_3Si are quite effective in suppression of the Hosomi–Sakurai allylation (Equation (39)).[157,158] In general, the [3 + 2]-cycloaddition of allylsilanes to α-enones proceeds with high *trans*-diastereoselectivity concerning the relationship between the carbonyl and silyl groups. Crotylsilanes add to α-enones in a stereospecific manner.[159]



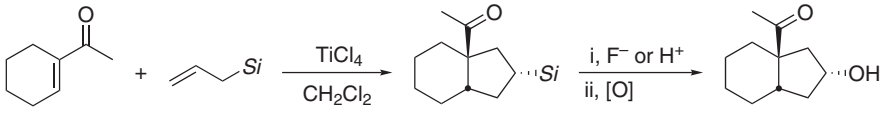
R = H:	–78 °C, 2 h	77%, 98% de	–
R,R = $(CH_2)_4$:	–78 to –20 °C, 19 h	86%, single isomer	2%

(39)

Some silyl groups are known to serve as efficient latent hydroxy groups.[160,160a] Allyltriisopropylsilane achieves an efficient [3 + 2]-cycloaddition to α-enones; however, it is difficult to convert the silyl group of products into a hydroxy group. Therefore, to enhance synthetic utility of silylated cycloadducts, new allylsilanes bearing a bulky, easily oxidizable silyl group have been developed (Scheme 14).



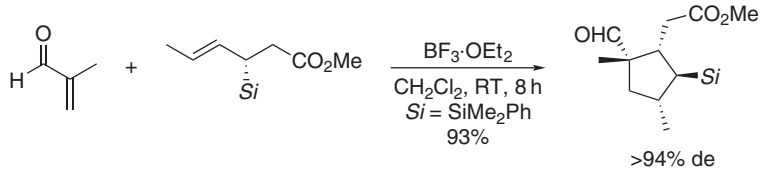
Scheme 13



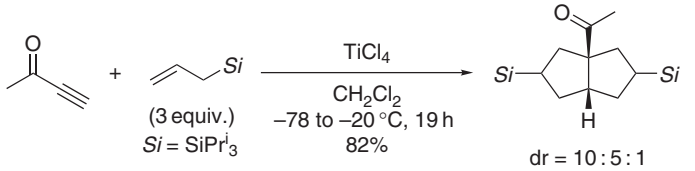
Si = $SiPh_3$:[386]	51%	96%
Si = $SiPh_2Bu^t$:[387]	69%	82%
Si = $SiPhPr^i_2$:[387]	68%	36%
Si = $SiMe_2(CPh_3)$:[388]	85%	67%
Si = $SiMe_2(CHPh_2)$:[389]	92%	83%

Scheme 14

The reaction of homochiral allylsilanes with α-enones and α-enals is very valuable for the asymmetric synthesis of multisubstituted cyclopentanes (Equation (40)).[161,162] The [3 + 2]-cycloaddition of allylsilanes is applicable to *p*-quinones[163] and *p*-quinoneimines.[164] 3-Butyn-2-one undergoes a double cycloaddition with an excess amount of allyltriisopropylsilane to give a bicyclo[3.3.0]octane in good yield (Equation (41)).[165]

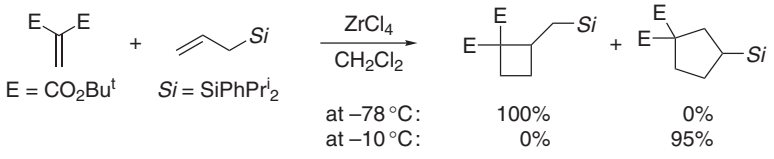


(40)



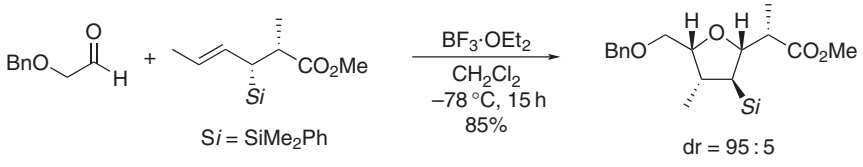
(41)

The Lewis acid-promoted reactions of acrylates and propiolates with allylsilanes usually afford [2 + 2]-cycloadducts rather than [3 + 2]-cycloadducts (*vide infra*). The ratio of the two kinds of cycloadducts depends on the reaction temperature.[166] Particularly, the product ratio in the reaction of alkylidene malonates and their derivatives is markedly temperature dependent.[167,168] Cyclobutanes are major products at low temperature, and [3 + 2]-cycloaddition proceeds predominantly at higher temperature (Equation (42)).



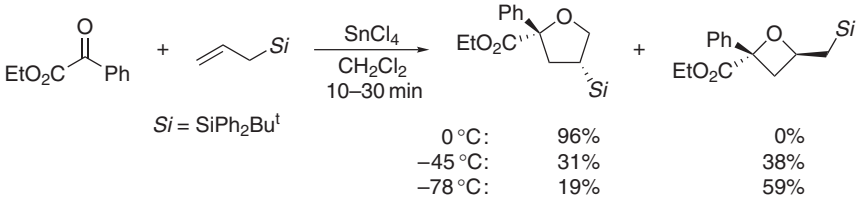
(42)

The Lewis acid-promoted reaction of aldehydes with α-substituted allylsilanes forms 3-silyltetrahydrofurans in good to high yields.[169–172] The use of homochiral allylsilanes is very valuable for highly diastereo- and enantioselective syntheses of tri- and tetrasubstituted tetrahydrofurans (Equation (43)). Catalytic asymmetric [3 + 2]-cycloaddition of α-substituted allenylsilanes to aldehydes can be achieved by a chiral scandium complex.[173]



(43)

Certain ketones are also usable for [3 + 2]-cycloaddition with allylsilanes.[174,174a–174c,175] Interestingly, the reaction of unsubstituted allylsilanes at −78 °C gives 2-silylmethyloxetanes ([2 + 2]-cycloadducts) mainly, although only [3 + 2]-cycloadducts are obtained at 0 °C (Equation (44)).[176]

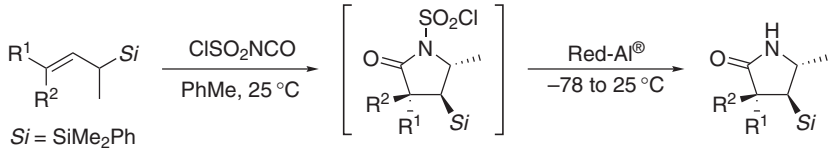


(44)

Imines and iminium salts also undergo [3 + 2]-cycloaddition of allylsilanes to afford 3-silylpyrrolidines with high diastereoselectivity.[121,177,178]

Spontaneous reaction of *N*-chlorosulfonyl isocyanate with α-substituted allylsilanes is valuable for the synthesis of 4-silyl-2-pyrrolidinones.[179–181] The [3 + 2]-cycloaddition of crotylsilanes proceeds stereospecifically as does the

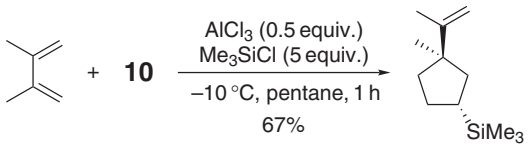
addition to α-enones (Equation (45)). In contrast, α-unsubstituted allylsilanes favor [2 + 2]-cycloaddition. Use of allylsilanes bearing a bulky group at the α-position effects predominant formation of iminolactones by cycloaddition across the carbon–oxygen double bond.[182]



(45)

R^1 = Me; R^2 = H ($E:Z$ = 97 : 3): 68%, 90% de
R^1 = H; R^2 = Me ($E:Z$ = 7 : 93): 63%, 84% de

In the presence of $AlCl_3$ and Me_3SiCl, 1,3-dienes react with **10** to afford *trans*-[3 + 2]-cycloadducts (Equation (46)). A trimethylsilyl cation-mediated mechanism involving 1,2-silyl migration has been proposed.[183]



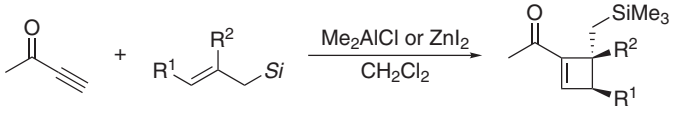
(46)

Benzyl cations generated from benzyl alcohols or quinone methides by the action of $SnCl_4$ undergo [3 + 3]-cycloaddition of allylsilanes leading to tetrahydronaphthalenes.[184] With secondary and tertiary benzyl cations, a competing [3 + 2]-pathway forms dihydro(1*H*)indenes.

9.07.3.6.2 [2 + 2]-Cycloaddition

The first example of Lewis acid-promoted [2 + 2]-cycloaddition of allylsilanes was introduced by Snider *et al.* in 1979.[185] In the last decade, similar cycloadditions to various electron-deficient unsaturated bonds have been developed for efficient syntheses of cyclobutanes, cyclobutenes, oxetanes, and azetidines as described below.

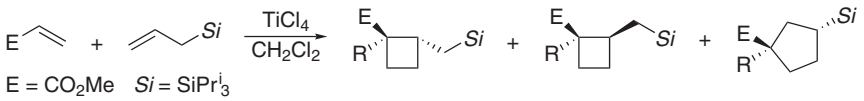
The Me_2AlCl-promoted reaction of naphthoquinone with **10** at −78 °C gives [2 + 2]- and [3 + 2]-adducts in 34% and 23% yields, respectively. At 0 °C, a quantitative formation of the latter product is observed.[163] When Me_2AlCl and ZnI_2 are used as promoters, the reaction of 3-butyn-2-one with certain allylsilanes favors the [2 + 2]-pathway (Equation (47)).[151,151a,186] On the other hand, the $TiCl_4$-catalyzed reaction forms [3 + 2]-adducts as shown in Equation (41).[165]



(47)

R^1,R^2 = $(CH_2)_3$; *Si* = $SiMe_3$, Me_2AlCl, −30 °C, 20 min: 93%
R^1 = R^2 = H; *Si* = $SiPr^i_3$, ZnI_2, RT, 36 h: 56%

The $TiCl_4$-catalyzed reactions of acrylates and maleates with allylsilanes bearing a bulky silyl group furnish diastereomeric mixtures of [2 + 2]-adducts mainly, with small quantities of [3 + 2]-adducts (Equation (48)).[187,187a,188] As shown in Equation (42), the cycloadditions of alkylidene malonates and their derivatives enable selective synthesis of both [2 + 2]- and [2 + 3]-adducts by a proper choice of reaction temperature.[167,168] Methyl propiolate undergoes [2 + 2]-cycloaddition predominantly.[185–187,189] Use of excess allyltriisopropylsilane induces double [2 + 2]-cycloaddition to methyl propiolate, forming a bicyclo[2.2.0]hexane.[187] The [2 + 2]-cycloadditions of (*E*)- and (*Z*)-crotylsilanes proceed stereospecifically.[190]

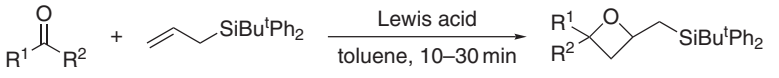


(48)

–40 to 0 °C, 19 h: 100%, 42 : 53 : 5
40 °C, 3 h: 97%, 19 : 70 : 11

Allenylmethylsilanes and propargylsilanes are usable for [2 + 2]-cycloaddition with electron-deficient alkenes and alkynes.[191,192]

The [2 + 2]-cycloaddition of allylsilanes is applicable to the synthesis of substituted oxetanes from aldehydes and ketoesters (Equation (49)).[176,193] The $BF_3{\cdot}OEt_2$-promoted reaction of *N*-tosylaldimines with allylsilanes gives [3 + 2]-cycloadducts, 3-silylpyrrolidines (*vide supra*).[178] In contrast, *N*-acylaldimines are converted into [2 + 2]-cycloadducts under similar conditions.[194]



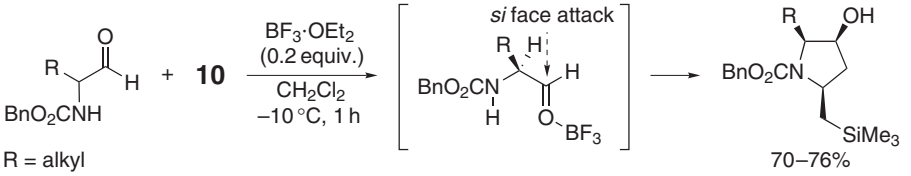
R^1 = Bu^{t}Me$_2$SiOCH$_2$; R^2 = H; $ZrCl_4$, –20 °C: 75%, *cis* : *trans* = 86 : 14
R^1 = Ph; R^2 = CO_2Et; $TiCl_4$, 0 °C: 96%, *trans* only

(49)

9.07.3.6.3 Other cycloaddition without 1,2-silyl migration

In 1990, Sugimura reported that the BF_3-promoted reaction of α-oxyaldehydes with allylsilanes gave substituted tetrahydrofurans with high stereoselectivity (Scheme 15).[195,196,196a] He demonstrated that β-carbenium ions generated from allylsilanes can be used for intramolecular bond-forming reaction with the preexisting heteronucleophile. Since this pioneering work, [3 + 2]- and [4 + 2]-cycloadditions using allylsilanes as 1,2-dipole equivalents have intensively been studied for stereoselective synthesis of oxygen- or nitrogen-containing heterocycles.

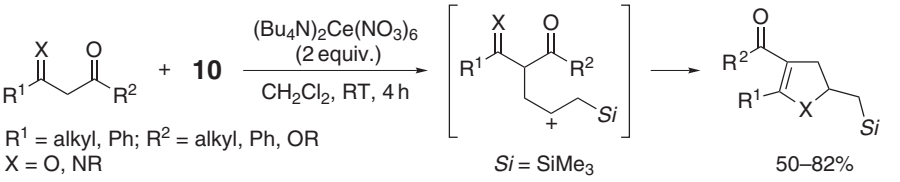
The BF_3-catalyzed reaction of α-aminoaldehydes with **10** is valuable for highly stereoselective synthesis of 2,3,5-trisubstituted pyrrolidines with all-*cis* configurations (Equation (50)).[197] The stereochemical outcome like chelation-controlled stereochemistry might result from the inherent conformational arrangement of the aldehyde–BF_3 complex. *p*-Quinoneimines, *o*-quinones, and α-alkoxyhydroperoxides undergo similar types of [3 + 2]-cycloadditions with allylsilanes to afford dihydroindoles, dihydrobenzofurans, and 1,2-dioxolanes, respectively.[164,175,198]



R = alkyl 70–76%

(50)

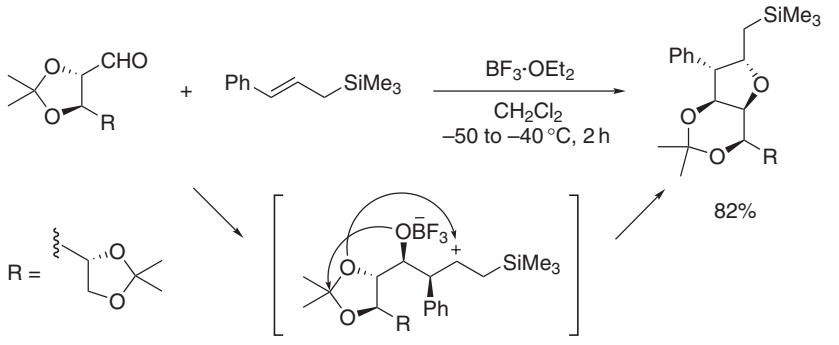
In the presence of $Mn(OAc)_3$ or a Ce(IV) salt, 1,3-dicarbonyl compounds and β-carbonyl imines react with allylsilanes to give silylmethylated dihydrofurans and dihydropyrroles, respectively.[199,200,200a] A proposed mechanism involves the formation of a β-silylcarbenium ion intermediate via two-electron oxidation and subsequent intramolecular nucleophilic attack (Equation (51)).[200,200a]



R^1 = alkyl, Ph; R^2 = alkyl, Ph, OR
X = O, NR

Si = $SiMe_3$ 50–82%

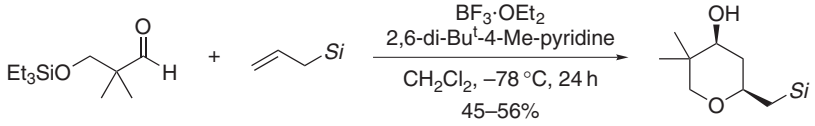
(51)



Scheme 15

Allylsilanes act as good acceptors of nitrones and oxyallyl cations.[201,202] The 1,3-dipole species arising from electronically activated cyclopropanes can be trapped by allylsilanes.[203,204,204a] Epoxides as well as aziridines act as 1,3-dipole precursors for inter- and intramolecular [3 + 2]-cycloadditions with allylsilanes.[205,205a,206,206a]

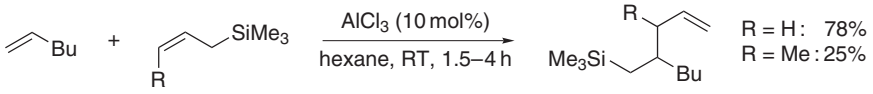
Use of allylsilanes as 1,2-dipole equivalents is valuable also for the construction of six-membered rings. β-Oxyaldehydes undergo Lewis acid-promoted cycloadditions with allylsilanes to provide substituted tetrahydropyrans (Equation (52)).[207,207a] A similar [4 + 2]-cycloaddition of *N*-*t*-butoxycarbonyl-*O*,*N*-acetals is available for the synthesis of oxazinones.[208]



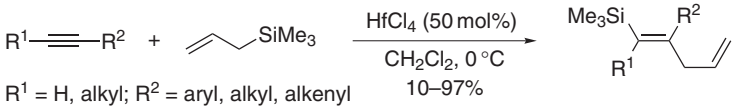
(52)

9.07.3.7 Allylation of Unactivated Alkynes and Alkenes

The Lewis acid-catalyzed reactions of allylsilanes with simple alkenes and alkynes introduce both allyl and silyl groups into the unsaturated bonds (Equations (53) and (54)).[209–210b] These allylsilylations are γ-regiospecific with respect to allylsilanes. The *trans*-addition of allylsilanes occurs in the reaction with alkynes. There are two possible mechanisms for the Lewis acid-promoted allylsilylations, that is, trimethylsilyl cation- and Lewis acid-mediated pathways.

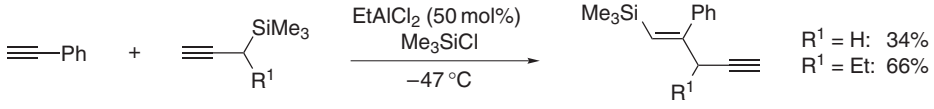


(53)



(54)

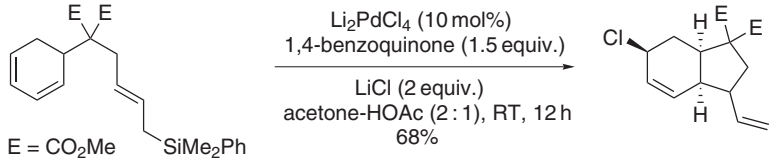
Intramolecular allylsilylation of alkynes is a convenient route to cyclic vinylsilanes.[211] Propargylsilanes are available for Lewis acid-promoted carbosilylation of alkynes.[212] Unlike allylsilanes, both α-substituted and unsubstituted propargylsilanes react at the α-position, which can be rationalized by *in situ* isomerization of these reagents to allenylsilanes (Equation (55)).



(55)

In the presence of $GaCl_3$, allylsilanes add to simple terminal alkynes and silylated alkynes to give *cis*-allylation products.[213] A stepwise mechanism including formation and *cis*-addition of an allylgallium species is plausible for this allylation.

Intramolecular allylation of alkynes with allylsilanes can be catalyzed by electrophilic transition metal halides and complexes (e.g. Pt(II), Pd(II), Ru(II), Au(III), and Ag(I)).[214,214a] A Pd(II)-catalyzed system using a reoxidant is effective in oxidative intramolecular allylation of 1,3-dienes (Equation (56)).[215,215a] These allylations are initiated by coordination of the electrophilic metals to alkynes and 1,3-dienes.

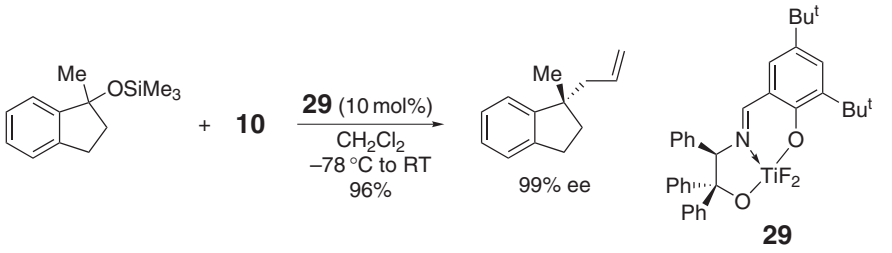


(56)

9.07.3.8 Allylation of Alkyl Esters, Ethers, and Alcohols

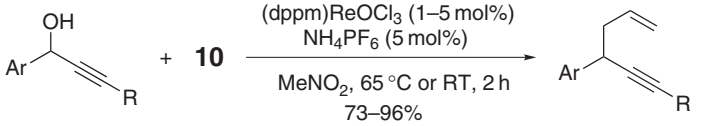
Allylsilanes are available for Lewis acid-promoted allylation of reactive alkyl electrophiles such as allyl halides and esters.[216] Recently, much attention has been focused on catalytic allylation of alkyl esters, ethers, and alcohols with allylsilanes.[217–221]

$B(C_6F_5)_3$ works as an effective catalyst for the allylation of propargylic esters.[217] Allyl and propargyl trimethylsilyl ethers bearing a π-electron-donating group at the α-position are smoothly allylated at the α- or γ-position under catalysis by Me_3SiOTf.[218] Chiral titanium catalyst **29** enables highly enantioselective allylation of racemic benzyl trimethylsilyl ethers by a dynamic kinetic resolution (Equation (57)).[219]



(57)

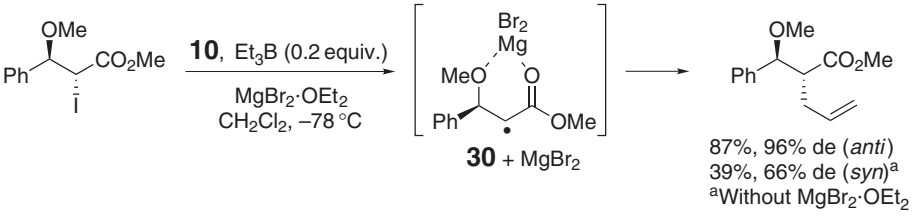
A rhenium catalyst is quite valuable for the direct allylation of α-aryl-substituted propargyl alcohols with **10** (Equation (58)).[220] Benzyl alcohols are efficiently allylated with allylchlorodimethylsilane under catalysis by $InCl_3$.[221]



(58)

9.07.3.9 Allylation via Radical Process

Allyltrimethylsilane **10** serves as an allylating agent in radical-initiated allylation of reactive alkyl halides and selenides.[222–224a] This type of allylation proceeds probably by atom or group-transfer radical addition (Kharasch reaction) of the substrates to **10** and subsequent elimination of silyl halides or selenides. In the allylation of β-alkoxy-α-iodo-esters, $MgBr_2{\cdot}OEt_2$ is effective in improving both yield and diastereoselectivity of the allylation products (Equation (59)).[223] Coordination of the Lewis acid to the radical intermediate **30** would enhance its reactivity to **10** and serve for its conformational fixation leading to high diastereoface selectivity.



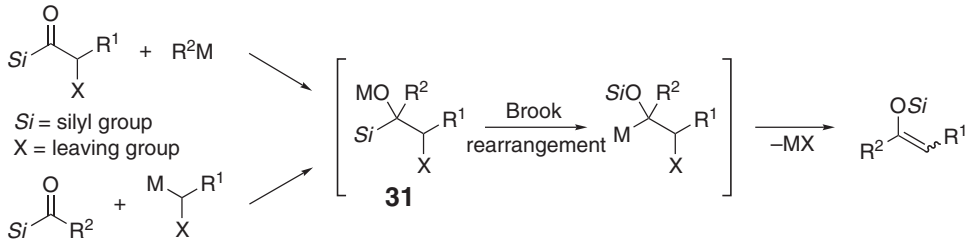
(59)

The radical-initiated allylation of alkyl halides with allyltris(trimethylsilyl)silanes proceeds via an S_H2' process mediated by a tris(trimethylsilyl)silyl radical.[225] The radical-allylating agents react with alkenes, alkynes, and aldehydes via a radical chain process to give the corresponding allylsilylation products.[226]

9.07.4 Heteroatom-Functionalized Organosilanes

9.07.4.1 Acylsilanes

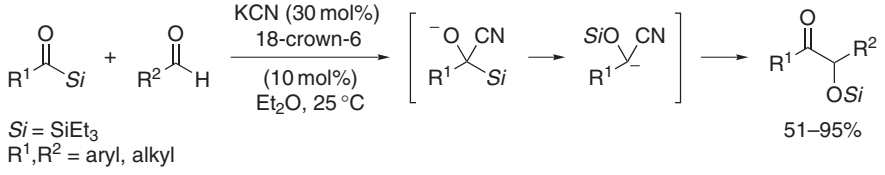
Acylsilanes react with alkylmetals to give α-silylated alcohols, which can be readily desilylated by fluoride ion-induced hydrolysis with stereochemical retention. For this reason, they have been used as aldehyde equivalents for highly stereo- and regioselective synthesis of alcohols.[227–228b] When acylsilanes or alkylmetals have a leaving group at



Scheme 16

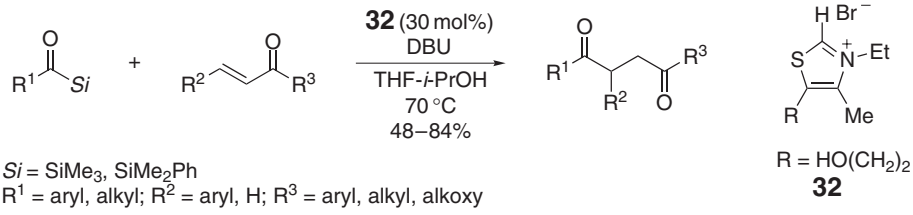
the α-position, the reaction affords silyl enolates via the Brook rearrangement of the α-silyl alkoxide intermediate **31** (Scheme 16).[229,229a–229e]

Nucleophilic addition of anionic species to acylsilanes followed by the Brook rearrangement provides an efficient route to siloxy-substituted carbon nucleophiles valuable for further carbon–carbon bond formation. The reaction of alkenylmetals forms siloxy-substituted allylmetals, which is useful for allylation of carbonyls and halides.[230,231,231a–231c] Cyanide addition to acylsilanes leads to cyano-stabilized carbanions.[232] Cyanide-catalyzed processes via such an anionic species enable a highly selective cross-silyl benzoin reaction of acylsilanes with aldehydes (Equation (60)).[233,233a] The cyanide-catalyzed reaction of cyanoformates with acylsilanes gives α-cyano-α-siloxy esters efficiently.[234] Homochiral metal alkoxides promote the tandem cyanation–acylation reaction enantioselectively (Scheme 17).[235,235a] It has been proposed that metal cyanides generated from metal alkoxides and cyanoformates act as the actual catalysts.

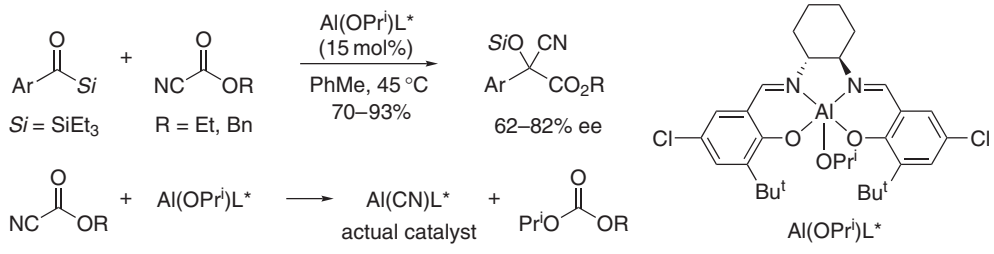


(60)

Lithium phosphites also can catalyze the silyl benzoin reaction of acylsilanes. Its asymmetric version is successfully achieved by a lithium phosphite derived from a homochiral diol.[236] Thiazolium salt **32** effectively promotes conjugate acylation of α,β-unsaturated carbonyls with acylsilanes in the presence of DBU (Equation (61)).[237,237a] The active catalyst of this sila-Stetter reaction would be a carbene species generated from **32** by deprotonation.

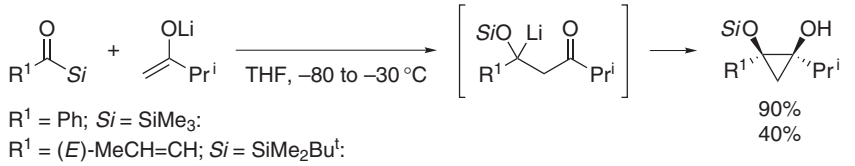


(61)



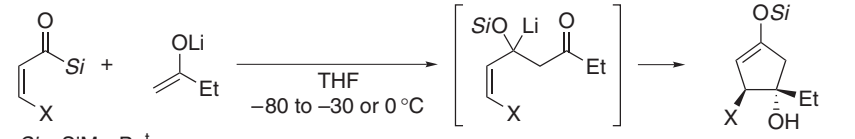
Scheme 17

Carbon nucleophiles generated from acylsilanes are usable also for intramolecular carbon–carbon bond formation.[238–242a] Upon treatment with phenyllithium or lithium dimethyl phosphite, acylsilanes bearing an acrylate moiety are smoothly cyclized to four- to six-membered carbocycles by a tandem carbonyl addition–Brook rearrangement–Michael addition process.[238] The reactions of benzoyl- and crotonylsilanes with lithium enolates of methyl ketones produce 1,2-cyclopropanediol monosilyl ethers via intramolecular carbonyl addition of the rearranged anionic species (Equation (62)).[240] β-Thio- and β-silylacryloylsilanes are converted into cyclopentanone silyl enolates under similar conditions (Equation (63)).[241,241a] Lithium enolates of 1-alkenyl methyl ketones react with α,β-unsaturated acylsilanes to afford 3-cycloheptenones stereospecifically (Equation (64)).[242,242a] The [3 + 4]-annulation can be rationalized by a stepwise mechanism involving the oxy-Cope rearrangement of divinylcyclopropanes **33**.



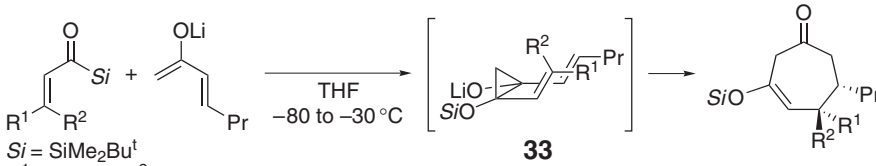
R^1 = Ph; *Si* = $SiMe_3$:
R^1 = (*E*)-MeCH=CH; *Si* = $SiMe_2Bu^t$:

(62)



Si = $SiMe_2Bu^t$
X = SPh; *Z*: *E* = 7.6 : 1:
X = $SiMe_3$; *Z*-isomer:

(63)

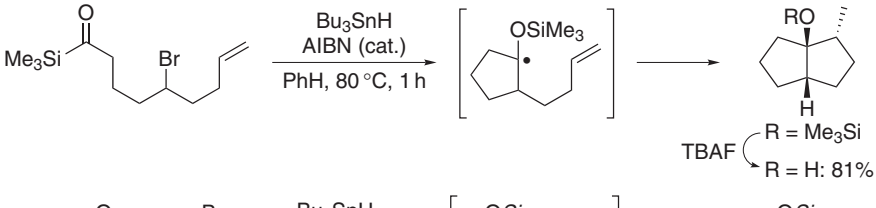


Si = $SiMe_2Bu^t$
R^1 = $SiMe_3$; R^2 = H (*E*):
R^1 = H; R^2 = $SiMe_3$ (*Z*):

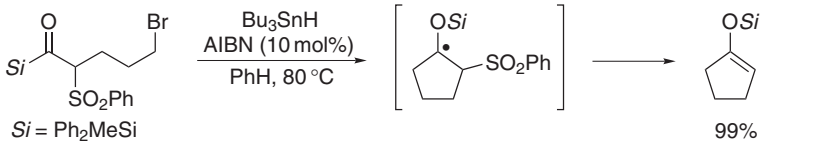
(64)

Acylsilanes serve as acyl donors in the Pd-catalyzed cross-couplings with allyl trifluoroacetates,[243] aryl halides,[244] and alkenyl halides.[245] Intramolecular acylation of alkynes with acylsilanes proceeds under catalysis by $[RhCl(CO)_2]_2$.[246]

The AIBN-initiated reactions of 5- and 6-bromoalkanoylsilanes with Bu_3SnH give cyclopentanol and cyclohexanol silyl ethers, respectively, in moderate to high yields (Scheme 18).[247,247a,248] A plausible mechanism for this radical cyclization involves a Brook-type rearrangement of the α-silylalkoxy radical intermediate **34** generated by intramolecular radical addition to the acylsilane moiety. The resultant α-siloxyalkyl radical abstracts hydrogen from Bu_3SnH to give the cyclized product. Such alkyl radicals generated from acylsilanes are available for carbon–carbon bond formation (Equation (65))[249,250] and β-elimination leading to cyclic silyl enolates (Equation (66)).[251,251a]

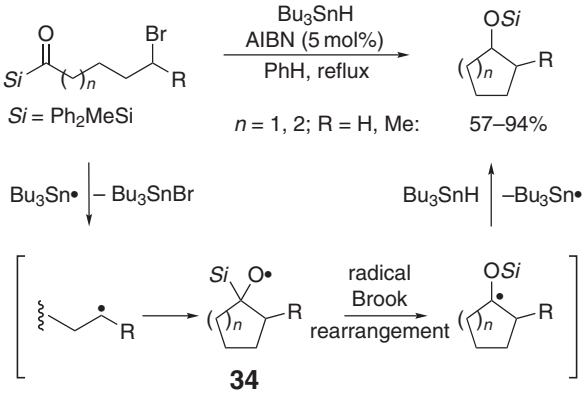


(65)



Si = Ph_2MeSi

(66)

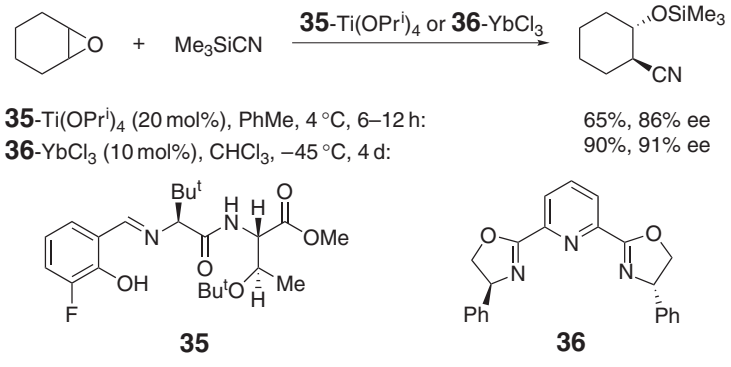


Scheme 18

9.07.4.2 Cyanosilanes

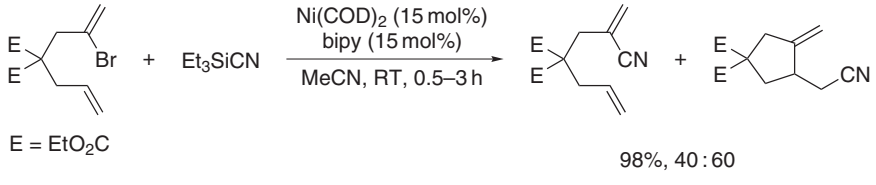
Cyanosilylations of carbon–oxygen and carbon–nitrogen double bonds with cyanosilanes are very important synthetic reactions since the products, cyanohydrin silyl ethers and α-amino nitriles, serve as synthetic intermediates for a variety of natural products. A number of studies on these subjects have been reported in the last decade; however, this review does not deal with carbonyl and imine cyanosilylations due to the availability of recent reviews and limited space.[3,14,252–254a]

The Lewis acid-catalyzed reaction of epoxides with cyanotrimethylsilane (Me_3SiCN) forms β-siloxy nitriles.[252] Highly enantioselective desymmetrization of *meso*-epoxides with Me_3SiCN can be achieved by chiral Ti and Yb catalysts (Equation (67)).[255,256]



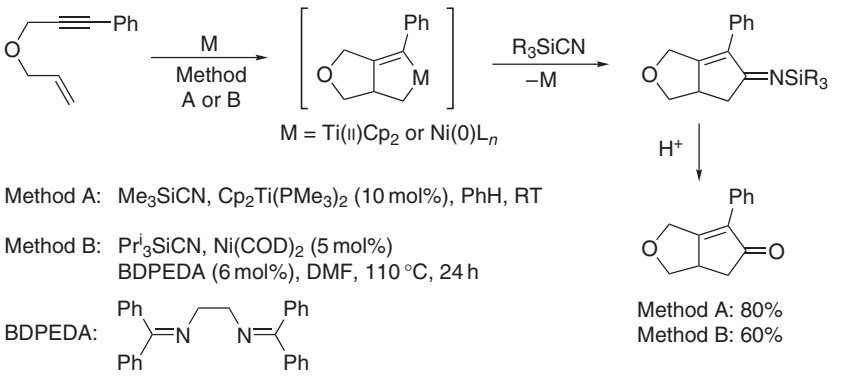
(67)

Me_3SiCN is a convenient, reactive cyanide donor in transition metal-catalyzed processes. The Pd-catalyzed reaction of aryl iodides with Me_3SiCN is useful for the synthesis of aryl cyanides.[257] Me_3SiCN works also as an effective co-catalyst for the Pd-catalyzed cyanation of aryl iodides with KCN.[258] Allylic acetates, carbonates, and the related compounds undergo the Pd-catalyzed cyanation with Me_3SiCN.[259–261] The tandem cyclization–cyanation reaction of 2-bromo-1,6-heptadienes with Me_3SiCN proceeds under catalysis by an Ni complex (Equation (68)).[262]



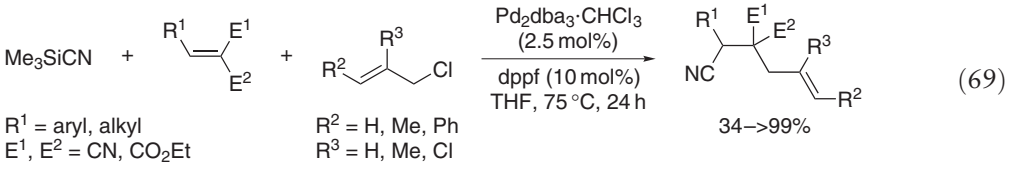
(68)

Cyanosilylation of alkynes with Me_3SiCN is effectively catalyzed by a $PdCl_2$ complex.[263] Its intramolecular version is valuable for the stereo-defined synthesis of tri- and tetrasubstituted alkenes.[264] A Pd-catalyzed system effects an efficient three-component coupling of Me_3SiCN, highly electron-deficient alkenes, and allyl chlorides (Equation (69)).[265] The



Scheme 19

reaction mechanism can be rationalized by alkene cyanation with a π-allylpalladium cyanide intermediate and subsequent reductive elimination.



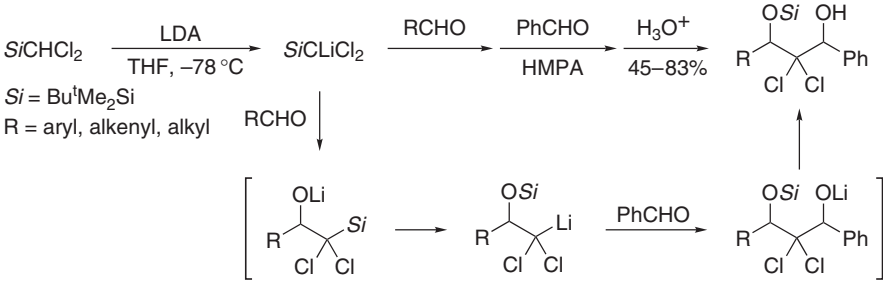
(69)

Cyanosilanes can be isocyanide sources since a tautomeric equilibrium exists between cyanosilanes and the corresponding isocyanides. The equilibrium largely favors the cyano tautomer. The use of such dilute isocyanide donors realizes efficient Ti(II)- and Ni(0)-catalyzed cyclizations of enynes to iminocyclopentenes via metallacyclopentene intermediates (Scheme 19).[266,266a,266b] Treatment of zirconacyclopentanes and -pentenes with Me_3SiCN provides zirconocene–imine complexes, which serve for carbon–carbon bond formation with various unsaturated bonds.[267]

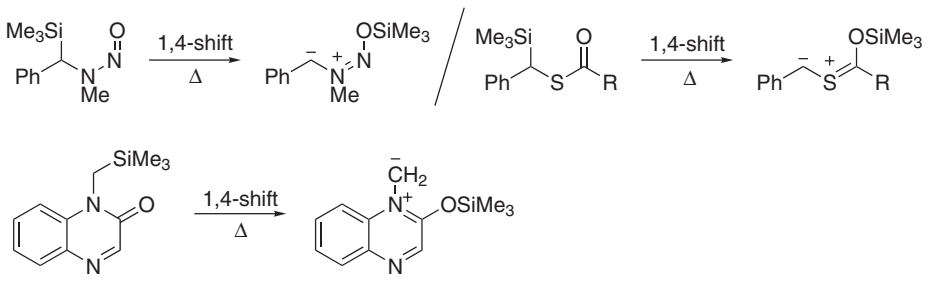
9.07.4.3 Other Functionalized Organosilanes

α-Heteroatom-substituted organosilanes are quite valuable as protected carbon nucleophiles. Nucleophilic activation of the organosilanes effectively promotes their reactions with carbon electrophiles. For example, trimethyl(trifluoromethyl)silane adds to aldehydes by the help of a fluoride ion,[268] and the use of a chiral fluoride source enables asymmetric trifluoromethylation.[269]

Lithiated (dihalomethyl)silanes react successively with two kinds of aldehydes to give 1,3-diol monosilyl ethers (Scheme 20).[270,270a] In this tandem process, the initially formed β-lithioxyalkylsilanes undergo 1,3-silyl migration by intramolecular nucleophilic activation. The resultant lithium carbenoids add to another aldehyde. Haloalkanes can be used as the second electrophile. The reactions of epoxides, esters, and nitriles with lithiated (dihalomethyl)silanes also provide lithium carbenoids via silyl migration from carbon to oxygen.[270–271a] 2-Lithiated 2-silyl-1,3-dithianes as well as the halo analogs react successively with two kinds of electrophiles by a similar tandem process.[272,273,273a]

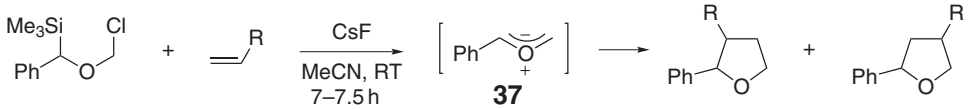


Scheme 20



Scheme 21

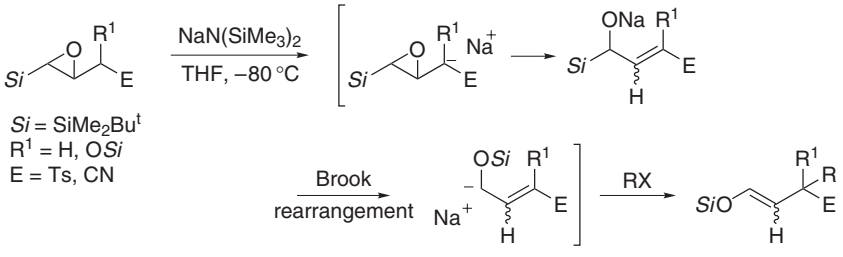
Silyl-protected 1,3-dipoles are quite useful for the synthesis of five-membered heterocycles by [3 + 2]-cycloaddition.[274,275] Thermal 1,4-silyl migrations of α-silylnitrosamines, *S*-α-silylbenzyl thioesters, and *N*-(silylmethyl)pyridones give convenient routes to azomethine imines,[276,276a] thiocarbonyl ylides,[277] and pyridinium methylides,[278] respectively (Scheme 21). These 1,3-dipoles add smoothly to electron-deficient alkynes to give *N*- and *S*-containing heterocycles. In the presence of fluorosilanes, α-silylimidates and α-silylimines react with electron-deficient alkenes and alkynes via *N*-silylated azomethines.[279,279a] Carbonyl ylide **37** can be efficiently generated by CsF-promoted 1,3-elimination of chloromethyl α-trimethylsilylbenzyl ether (Equation (70)).[280,280a] It is reactive enough for cycloaddition to various alkenes, alkynes, allenes, and heterodipolarophiles.



R = Bu: 52%, 66 : 34
R = OAc: 72%, 68 : 32
R = CO_2Me: 74%, 52 : 48

(70)

Nucleophilic substitution of α,β-epoxysilanes followed by the Peterson elimination is valuable for the stereoselective synthesis of alkenes.[3] The reactions with lithium phenylsulfide and diphenylphosphide form alkenyl sulfides and alkenylphosphines, respectively, in a stereospecific manner.[281,281a] γ-Metallo-α,β-epoxysilanes are isomerized to α-siloxyallylmetals by anionic ring opening and subsequent Brook rearrangement (Equation (71)).[282,282a,282b] The allylmetals are useful for allylation of carbon electrophiles. Upon treatment with Lewis acids, α,β-epoxysilanes are converted into allylic alcohols and carbonyl compounds.[283,284] The reaction pathways are governed by the conformation of substrates and the bulkiness of silyl groups.



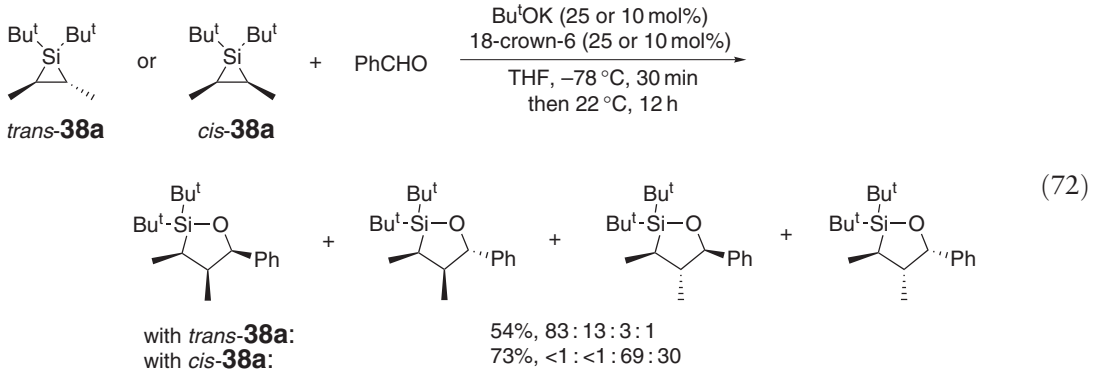
Si = $SiMe_2Bu^t$
R^1 = H, O*Si*
E = Ts, CN

(71)

9.07.5 Strained Alkylsilanes

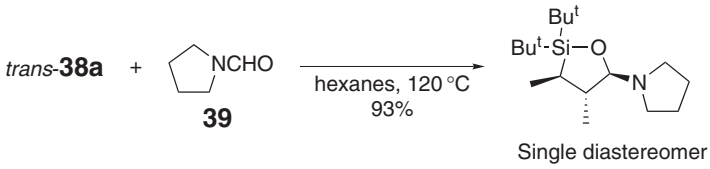
9.07.5.1 Silacyclopropanes

Under catalysis by *t*-BuOK, *cis*- and *trans*-silacyclopropanes **38a** react with benzaldehyde at 22 °C to give diastereomeric mixtures of an oxasilacyclopentane product (Equation (72)).[286,286a] The carbonyl insertion proceeds with inversion of silacyclopropane configuration. A plausible mechanism involves initial formation of a more reactive pentacoordinate silane intermediate. The base-catalyzed system is not applicable to the insertion of enolizable aldehydes.

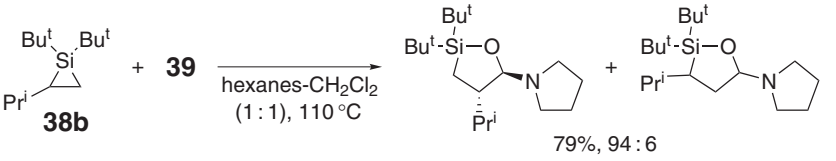


(72)

The thermal reaction of *trans*-**38a** with formamide **39** affords the corresponding insertion product in high yield with high diastereoselectivity (Equation (73)).[287] The *trans*-configuration of the substrate is retained in the product. Unsymmetrical silacyclopropane **38b** undergoes the carbonyl insertion on the more substituted side (Equation (74)). The high reactivity of **39** and these stereo- and regiochemical results can be rationalized by a stepwise mechanism via initial coordination of **39** to **38**. Isocyanides are also inserted into **38** with the retention of stereochemistry.[288,288a]



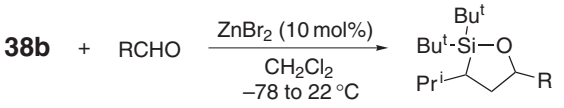
(73)



(74)

In the presence of a copper salt, aromatic aldehydes, α,β-unsaturated aldehydes, formates, and formamides react with **38** at or below room temperature to give the corresponding insertion products in good yield.[289] This catalytic reaction shows similar stereo- and regiochemistry as does the thermal reaction of formamides. A transmetallation mechanism via an organocopper intermediate has been proposed for the Cu-catalyzed insertion.

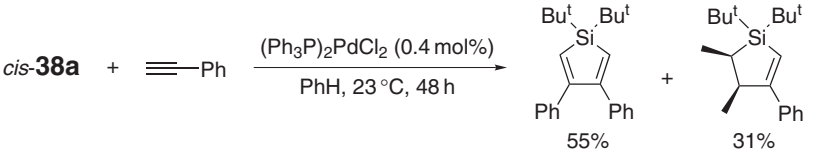
$ZnBr_2$ also is an effective catalyst for the carbonyl insertion (Equation (75)).[290] The Zn-catalyzed reaction is applicable to various aldehydes and ketones including aliphatic compounds. In sharp contrast to the Cu-catalyzed reaction, the carbonyl insertion occurs on the less substituted side with high regioselectivity. $ZnBr_2$ most likely serves as electrophilic activation of carbonyl compounds.



(75)

R = Pr: 70%, 10% de, >99 : 1 regioselectivity
R = MeO: 78%, 34% de, >99 : 1 regioselectivity

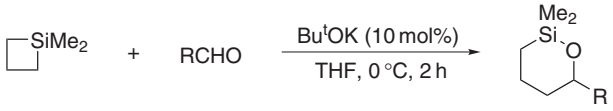
The Pd-catalyzed reaction of silacyclopropanes with terminal or electron-deficient alkynes gives siloles and silacyclopentenes (Equation (76)).[291,291a]



(76)

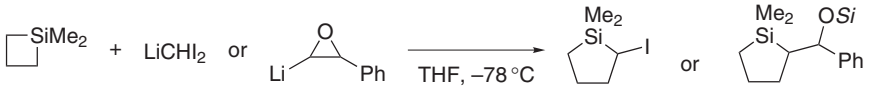
9.07.5.2 Silacyclobutanes

Silacyclobutanes as well as silacyclopropanes undergo aldehyde insertion under catalysis by *t*-BuOK (Equation (77)).[292] The reaction of silacyclobutanes with lithium carbenoids such as dihalomethyllithium and oxiranyllithium gives 2-substituted silacyclopentanes (Equation (78)). Treatment of 1-(1-iodoalkyl)- and 1-oxiranyl-silacyclobutanes with a stoichiometric amount of an alkali alkoxide leads to silacyclopentanes by anionic 1,2-shift of the ring carbon adjacent to silicon. These ring-expansion reactions proceed probably via a pentacoordinate silane intermediate.



R = Ph: 65%
R = Bu^t: 72%

(77)



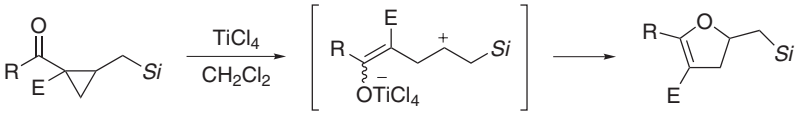
83% 67%, *Si* = $SiMe_2Pr$

(78)

The strained silicon–carbon bonds of silacyclobutanes are subject to activation by Pd and Pt complexes.[293,293a] This reactivity has been used for a catalytic carbon–carbon bond formation.[294,295]

9.07.5.3 Cyclopropylmethylsilanes

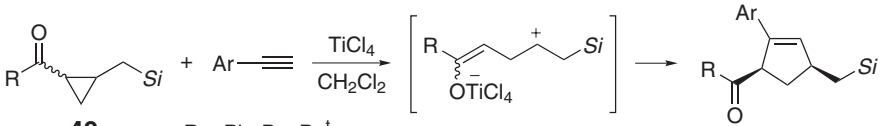
Silylmethyl-substituted cyclopropanes bearing a carbonyl group at the vicinal position are isomerized to dihydrofurans in the presence of $TiCl_4$ (Equation (79)).[296] A plausible mechanism for this ring-expansion reaction consists of two steps: the $TiCl_4$-promoted ring opening to a 1,3-dipole bearing a titanium enolate moiety and ring closure by nucleophilic addition of the enolate oxygen. 1,3-Dipoles generated from cyclopropanes **40** add to arylacetylenes to give [3 + 2]-cycloadducts (Equation (80)).[297] The use of allenylsilanes as dipolarophiles results in [3 + 2]- and [3 + 3]-cycloadditions.[298] The latter cycloaddition is accompanied with 1,2-migration of the silyl group of allenylsilanes. Trimethylsilyl analogs of **40** work as precursors of titanium enolates under similar conditions.[299] Silylmethyl-substituted cyclopropanes bearing a hydroxymethyl group at the vicinal position are converted into silyl-stabilized 3-butenyl cations upon treatment with an acid. The active species are valuable for the Prins annulation with aldehydes (Equation (81)) or intramolecular addition of oxygen nucleophiles.[300,301]



Si = $SiPh_2Bu^t$
R = Me, OMe, OEt
E = electron-withdrawing group

70–96%

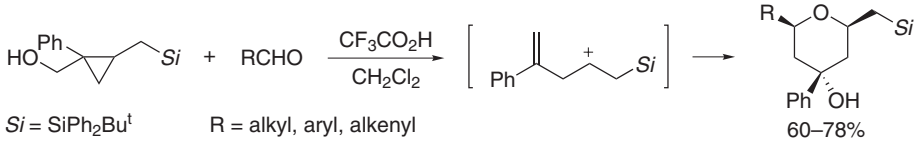
(79)



R = Ph, Bu, Bu^t
Si = $SiPh_2Bu^t$

55–85%
14–90% de

(80)



Si = $SiPh_2Bu^t$ R = alkyl, aryl, alkenyl

60–78%

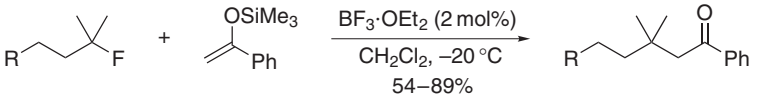
(81)

9.07.6 Silyl Enolates

Silyl enolates are well recognized to be very valuable carbon nucleophiles for highly efficient and selective carbon–carbon bond formation and functionalization introducing a carbonyl group. They add to electron-deficient carbon–carbon and carbon–heteroatom multiple bonds by the aid of Lewis acids or bases, in some cases, without promoter. Recent progress of these polar additions (i.e., Mukaiyama aldol reactions,[19,20] Mannich-type reactions,[302] Mukaiyama–Michael reactions,[303,303a] and hetero-Diels–Alder reactions of siloxy-substituted 1,3-dienes,[304–306] etc.,) are well reviewed;[3,14,307] therefore, this review deals mainly with substitution reactions of carbon electrophiles bearing a leaving group with silyl enolates and the transition metal-catalyzed additions of silyl enolates to unactivated alkenes and alkynes.

9.07.6.1 Alkylation

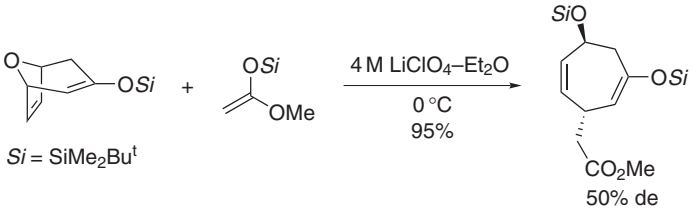
Alkyl fluorides are rarely used for alkylation of metal enolates because of the poor ability of a fluoride ion as a leaving group. However, silyl enolates can be alkylated with *tert*-alkyl fluorides under catalysis by a fluorophilic Lewis acid such as Me_3Al or $BF_3{\cdot}OEt_2$.[308,309] $BF_3{\cdot}OEt_2$ is superior to Me_3Al in catalytic activity and compatibility of functional groups (Equation (82)). The $BF_3{\cdot}OEt_2$-catalyzed system is applicable to allylation with allyl fluorides.



(82)

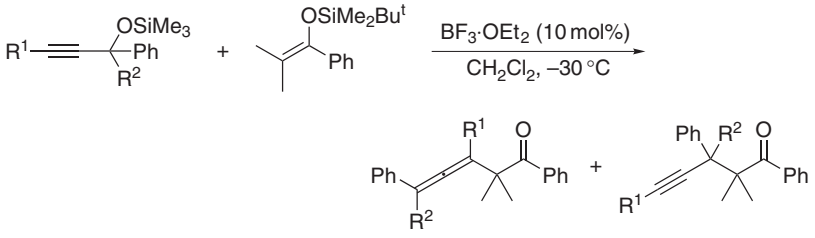
R = Ph, *n*-C_7H_{15}, $PhCOCHMeCH_2$, $BnO(CH_2)_2CHMeCH_2$, $PhCO_2(CH_2)_2CHMeCH_2$

A concentrated solution of $LiClO_4$ in Et_2O is effective in the allylation of silyl enolates with allyl alcohols and acetates.[310] The $LiClO_4$-promoted reaction with silyl enolates enables ring opening of 8-oxabicyclo[3.2.1]octa-2,6-dienes to highly functionalized 1,4-cycloheptadienes, which can be further manipulated for use in natural product synthesis (Equation (83)).[311]



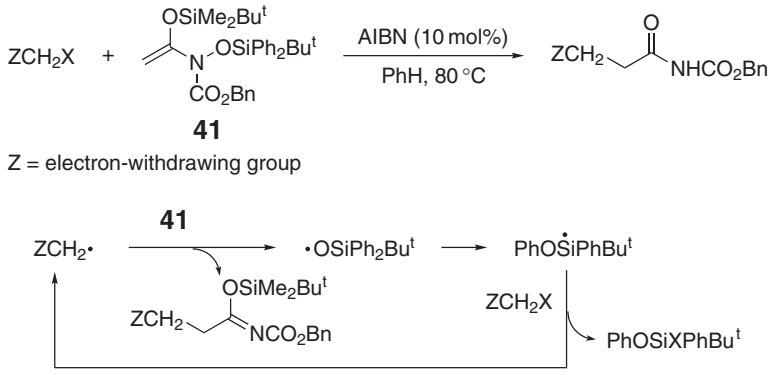
(83)

Allylation of silyl enolates with allyl alcohols is effectively catalyzed by $[Ir(cod)(PPh_3)_2]OTf$ activated by H_2.[312] TfOH has comparable catalytic activity in the allylation. This implies that the Ir complex might work as a source of TfOH. The Ir-catalyzed system is applicable to the propargylation and allenylation of silyl enolates with propargyl acetates.[313] It has also been reported that $BF_3{\cdot}OEt_2$ and Me_3SiOTf catalyze similar reactions with propargyl trimethylsilyl ethers, and that the regiochemistry of nucleophilic attack can be specified depending on the structure of the propargylic ethers (Equation (84)).[218,314]



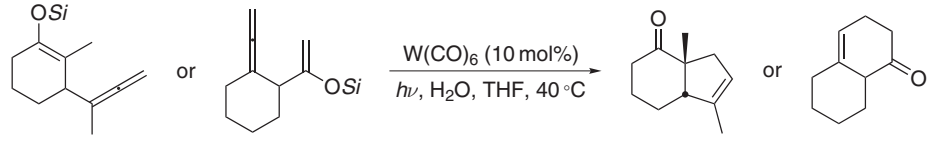
(84)

$R^1 = Me_3Si$, R^2 = Ph:	80%	0%
R^1 = Pr, R^2 = Ph:	67%	0%
$R^1 = Me_3Si$, R^2 = Me:	0%	65%



Scheme 22

Allenylated silyl enolates such as 6-siloxy-1,2,5-trienes and 5-siloxy-1,2,5-trienes undergo $W(CO)_6$-catalyzed 5- and 6-*endo*-cyclizations to give the corresponding cyclopentenes and cyclohexenes, respectively (Equation (85)).[315] These cyclizations proceed via electrophilic activation of the allene moiety by coordination of $W(CO)_5$ photochemically generated from $W(CO)_6$.

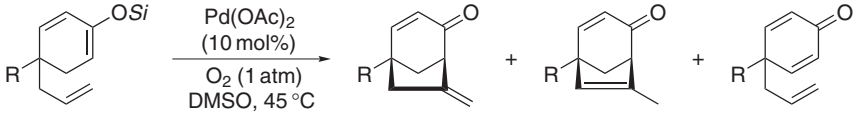


(85)

Silyl enolate **41**, derived from an *N*-siloxyimide, is efficiently alkylated by tin-free radical reactions of active alkyl iodides and bromides (Scheme 22). The propagation mechanism consists of conjugate homolytic substitution (S_H2') of **41** with an alkyl radical, 1,2-rearrangement of the resulting siloxy radical to a silyl radical, and its halogen abstraction to regenerate the alkyl radical.[316,316a]

9.07.6.2 Alkenylation and Alkynylation

In the presence of oxygen as reoxidant, $Pd(OAc)_2$ catalyzes intramolecular alkenylation of silyl enolates with alkenes (Equation (86)).[317,318,318a] This cycloalkenylation is quite useful for natural product synthesis. There are two plausible mechanisms: one is a transmetallation mechanism via intramolecular carbopalladation, and the other involves nucleophilic addition of the internal silyl enolate to a Pd(II)-coordinated alkene moiety.

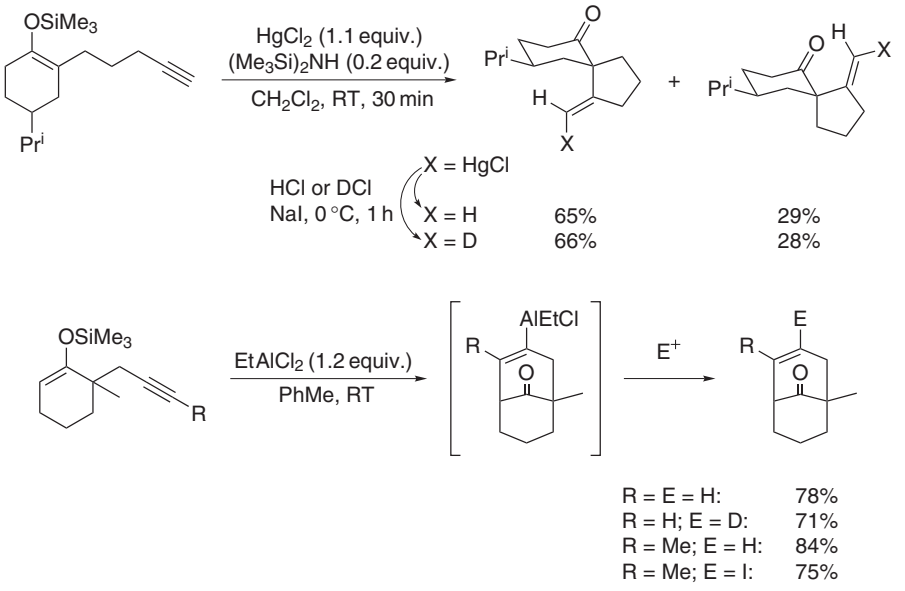


(86)

R = $CH_2CH_2OCH_2OMe$

Si = $SiMe_3$, 0.05 M, 17 h:	62%	trace	21%
Si = $SiMe_2Bu^t$, 0.1 M, 5 h:	89%	2%	3%

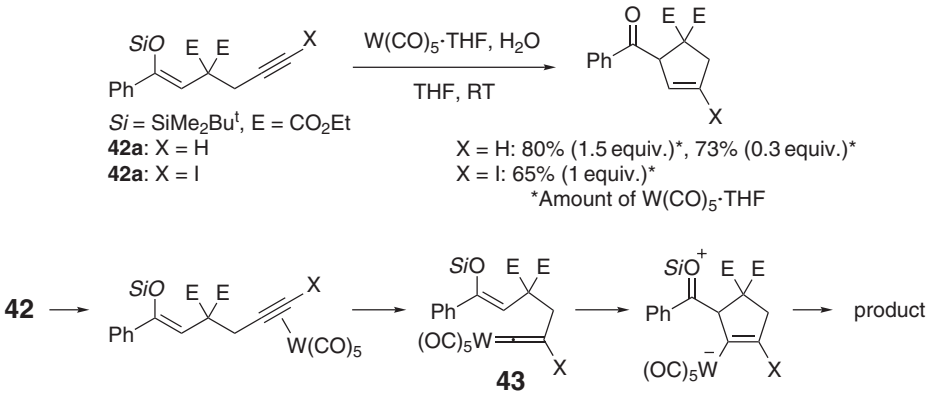
Metal-mediated intramolecular addition of silyl enolates to alkynes is also valuable for the synthesis of cyclic ketones. A stoichiometric amount of $HgCl_2$ or $EtAlCl_2$ effectively promotes the cycloalkenylation via *anti*-addition to alkynes (Equations (87) and (88)).[319–320a] The *anti*-addition mode can be explained by a metal coordination to the triple bond and subsequent attack of the enolate moiety from the opposite side to the metal. The resultant alkenylmetals can be used for carbon–carbon and carbon–heteroatom bond formation as well as protonation.



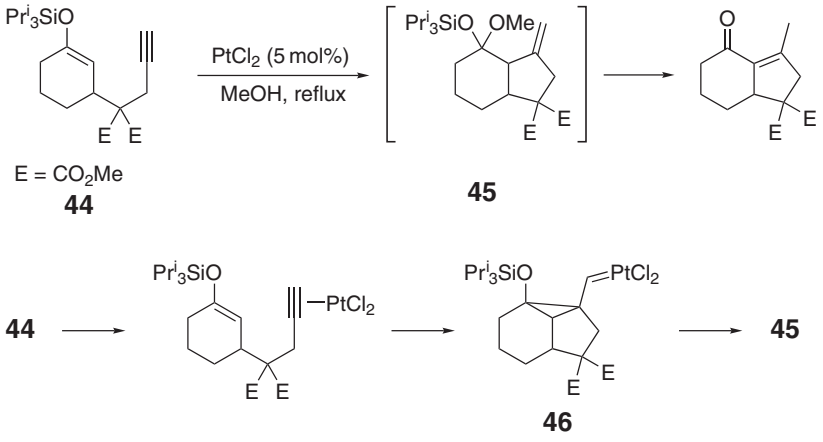
Stoichiometric or catalytic use of $W(CO)_5$·THF leads to successful cycloalkenylation of ω-acetylenic silyl enolates such as **42a** in the presence of water (Scheme 23).[321,321a] The $W(CO)_5$-promoted cyclization of ω-iodoacetylenic silyl enolate **42b** affords the iodine-migrated product in good yield.[322] This observation is indicative of the presence of the vinylidene complex intermediate **43**.

Cycloalkenylation of ω-acetylenic silyl enolates is efficiently catalyzed also by $PtCl_2$.[323] The catalytic reaction of silyl enolate **44** in MeOH gives a bicyclic α-enone, which would be derived from the initially formed acetal **45** (Scheme 24). Cyclopropylmethylene complex **46** has been proposed to be a key intermediate in the transformation of **44** to **45**.

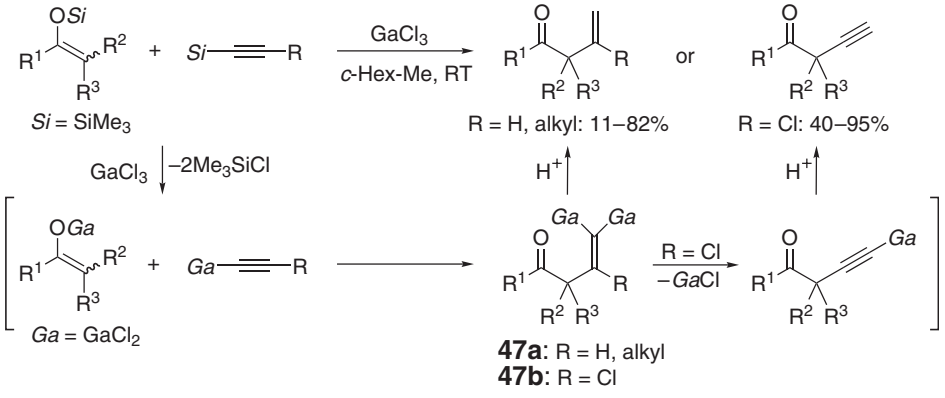
In the presence of $GaCl_3$, trimethylsilyl enolates react with 1-trimethylsilyl-1-alkynes to give β,γ-unsaturated ketones (Scheme 25, R = H, alkyl).[324] The proposed mechanism involves carbometallation of alkynylgalliums with gallium enolates to the *gem*-bismetallated species **47a**. A similar reaction using 1-chloro-2-trimethylsilylethyne forms α-ethynylated ketones (Scheme 25, R = Cl).[325] This ethynylation proceeds probably via β-elimination of **47b**. The use of 1-chloro-2-triethylsilylethyne enables catalytic ethynylation of silyl enolates.[326]The catalytic cycle includes direct carbogallation of the silylethyne and subsequent β-elimination with regeneration of $GaCl_3$.



Scheme 23



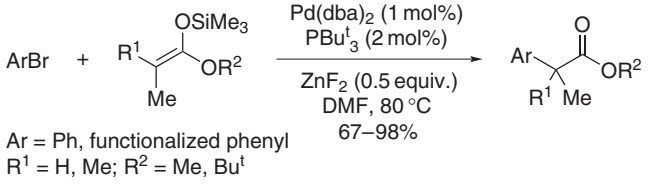
Scheme 24



Scheme 25

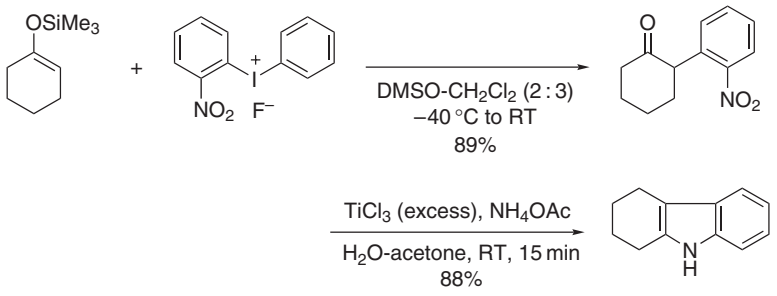
9.07.6.3 Arylation

Silyl enolates undergo Pd-catalyzed arylation with aryl halides in the presence of an additive such as Bu_3SnF,[327] CuF_2,[328] or ZnF_2.[329] The arylation of silyl enolates has higher functional group tolerance than that of alkali metal enolates. The ZnF_2-promoted arylation is valuable for efficient, stereoselective synthesis of α-arylated esters and imides (Equation (89)).



(89)

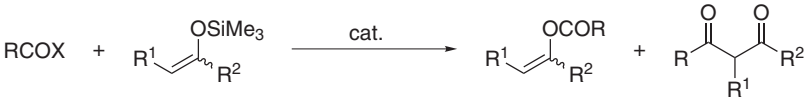
Diaryliodonium fluorides (Ar_2IF) are effective reagents in arylation of silyl enolates.[330] They have been used for the regiocontrolled synthesis of carbocycle-fused indoles (Scheme 26).[331] Ph_4BiF also serves for efficient regioselective α-phenylation of carbonyl compounds via silyl enolates.[332] This approach can be extended to α-alkenylation of carbonyl compounds.



Scheme 26

9.07.6.4 Acylation

Silyl enolates react with acyl cation equivalents to give the *C*- and/or *O*-acylated products (Equation (90)).[333] Fluoride-catalyzed reaction using acyl fluorides is valuable for *O*-acylation of silyl enolates derived from aldehydes and ketones.[334] CuCl also promotes the *O*-acylation with acyl chlorides.[335] The CuCl-promoted reaction of ester silyl enolates results in exclusive *C*-acylation. Combined use of $BiCl_3$ and ZnI_2 (or NaI) effects catalytic *C*-acylation of ketone silyl enolates with acyl chlorides.[336]



X = F; R^2 = alkyl, Ph, H	TBAF (5 mol%)	Major	Minor
X = Cl; R^2 = alkyl, Ph	CuCl (1–3 equiv.)	Major	Minor
X = Cl; R^2 = alkyl, Ph	$BiCl_3$–1.5 ZnI (5 mol%)	Minor	Major

(90)

References

1. Magnus, P. D.; Sarkar, T.; Djuric, S. Organosilicon Compounds in Organic Synthesis. In *Comprehensive Organometallic Chemistry I*; Wilkinson, G., Stone, G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 7, Chapter 48, pp 515–659.
2. Colvin, E. W. Silicon. In *Comprehensive Organometallic Chemistry II*; Stone, G. A., Abel, E. W., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11, Chapter 7, pp 313–354.
3. Brook, M. A. *Silicon in Organic, Organometallic, and Polymer Chemistry*; Wiley: New York, 2000.
4. Rappoport, Z., Apeloig, Y., Eds.; *The Chemistry of Organic Silicon Compounds*, Wiley: Chichester, 2001; Vol. 3.

4a. Rappoport, Z.; Apeloig, Y., Eds.; *The Chemistry of Organic Silicon Compounds*, Wiley: Chichester, 1998; Vol. 2.

4b. Patai, S., Rappoport, Z., Eds.; *The Chemistry of Organic Silicon Compounds*, Wiley: Chichester, 1989; Vol. 1.

5. Larson, G. L., Ed.; *Advances in Silicon Chemistry*, JAI Press: Greenwich, CT, 1996; Vol. 3.

5a. Larson, G. L., Ed.; *Advances in Silicon Chemistry*, JAI Press: Greenwich, CT, 1993; Vol. 2.

5b. Larson, G. L., Ed.; *Advances in Silicon Chemistry*, JAI Press: Greenwich, CT, 1991; Vol. 1.

6. Fleming, I., Ed.; *Science of Synthesis*, Thieme: Stuttgart, Germany, 2001; Vol. 4.
7. Marceniec, B., Chojnowski, J., Eds.; *Progress in Organosilicon Chemistry*, Proceedings of the 10th International Symposium on Organosilicon Chemistry, Poznan, Poland, 1993 Gordon & Breach: Basel, 1995.
8. Auner, N., Weiss, J., Eds., *Organosilicon Chemistry V: From Molecules to Materials*, Proceedings of the Munich Silicon Days, 2001; Wiley-VCH: Weinheim, 2003.
9. Auner, N., Weiss, J., Eds., *Organosilicon Chemistry IV: From Molecules to Materials*, Proceedings of the Munich Silicon Days, 1998; VCH: Weinheim, 2000.
10. Auner, N., Weiss, J., Eds., *Organosilicon Chemistry III: From Molecules to Materials*, Proceedings of the Munich Silicon Days, 1996; Wiley: New York, 1998.
11. Auner, N., Weiss, J., Eds., *Organosilicon Chemistry II: From Molecules to Materials*, Proceedings of the Munich Silicon Days, 1994; VCH: Weinheim, 1996.
12. Auner, N., Weiss, J., Eds., *Organosilicon Chemistry I: From Molecules to Materials*, Proceedings of the Munich Silicon Days, 1992; VCH: Weinheim, 1994.
13. Michl, J., Ed.; Silicon Chemistry *Chem. Rev.* **1995**, *95*, 1135–1673.
14. Miura, K.; Hosomi, A. Silicon in Organic Synthesis. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 2, Chapter 10, pp 409–592.
15. Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063–2192.
16. Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, *95*, 1375–1408.
17. Chatgilialoglu, C. *Organosilanes in Radical Chemistry;* Wiley: Chichester, 2004.

18. Yamamoto, H., Ed.; *Lewis Acids in Organic Synthesis*, Wiley: Weinheim, 2000.
19. Carreira, E. M. Mukaiyama Aldol Reaction. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 1999; Vol. 3, pp 997–1066.
20. Mahrwald, R., Ed.; *Modern Aldol Reactions*, Wiley-VCH: Weinheim, 2004.
21. Panek, J. S. Silicon Stabilization. In *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 1, Chapter 2.5, pp 579–627.
22. Dobbs, A. P.; Guesné, S. J. J.; Hursthouse, M. B.; Coles, S. J. *Synlett* **2003**, 1740–1742.
22a. Dobbs, A. P.; Martinovic, S. *Tetrahedron Lett.* **2002**, *43*, 7055–7057.
23. Semeyn, C.; Blaauw, R. H.; Hiemstra, H.; Speckamp, W. N. *J. Org. Chem.* **1997**, *62*, 3426–3427.
24. Fearnley, S. P.; Tidwell, M. W. *Org. Lett.* **2002**, *4*, 3797–3798.
25. Hioki, H.; Izawa, T.; Yoshizuka, M.; Kunitake, R.; Itô, S. *Tetrahedron Lett.* **1995**, *36*, 2289–2292.
26. Tomooka, K.; Nakazaki, A.; Nakai, T. *J. Am. Chem. Soc.* **2000**, *122*, 408–409.
27. Aronica, L. A.; Raffa, P.; Caporusso, A. M.; Salvadori, P. *J. Org. Chem.* **2003**, *68*, 9292–9298.
27a. For similar 1,2-ligand-shift from silicon to carbon, see: Trost, B. M.; Ball, Z. T. *J. Am. Chem. Soc.* **2004**, *126*, 13942–13944.
28. Fleming, I.; Dunogues, J.; Smithers, R. *Org. React.* **1989**, *37*, 57–575.
29. Yahiro, S.; Shibata, K.; Saito, T.; Okauchi, T.; Minami, T. *J. Org. Chem.* **2003**, *68*, 4947–4950.
29a. Nowak, A.; Bolte, O.; Schaumann, E. *Tetrahedron Lett.* **1998**, *39*, 529–532.
30. Yadav, J. S.; Reddy, B. V. S.; Reddy, M. S.; Parimala, G. *Synthesis* **2003**, 2390–2394.
30a. Yadav, J. S.; Reddy, B. V. S.; Reddy, M. S. *Synlett* **2003**, 1722–1724.
30b. Yadav, J. S.; Reddy, B. V. S.; Raju, A. K.; Rao, C. V. *Tetrahedron Lett.* **2002**, *43*, 5437–5440.
30c. Alvarez, E.; Pérez, R.; Rico, M.; Rodríguez, R. M.; Suárez, M. C.; Martín, J. D. *Synlett* **1996**, 1082–1084.
30d. Hosokawa, S.; Kirschbaum, B.; Isobe, M. *Tetrahedron Lett.* **1998**, *39*, 1917–1920.
31. Yamazaki, S.; Takada, T.; Imanishi, T.; Moriguchi, Y.; Yamabe, S. *J. Org. Chem.* **1998**, *63*, 5919–5928.
31a. Yamazaki, S.; Yanase, Y.; Kamimoto, K.; Yamada, K. *J. Org. Chem.* **2001**, *66*, 5915–5918.
32. Miura, K.; Hosomi, A. *Synlett* **2003**, 143–155.
33. Miura, K.; Okajima, S.; Hondo, T.; Hosomi, A. *Tetrahedron Lett.* **1995**, *36*, 1483–1486.
33a. Miura, K.; Okajima, S.; Hondo, T.; Nakagawa, T.; Takahashi, T.; Hosomi, A. *J. Am. Chem. Soc.* **2000**, *122*, 11348–11357.
33b. Miura, K.; Hondo, T.; Nakagawa, T.; Takahashi, T.; Hosomi, A. *Org. Lett.* **2000**, *2*, 385–388.
34. Adiwidjaja, G.; Floerke, H.; Kirschning, A.; Schaumann, E. *Liebigs Ann.* **1995**, 501–507.
35. Miura, K.; Hondo, T.; Saito, H.; Ito Hosomi, H. A. *J. Org. Chem.* **1997**, *62*, 8292–8293.
35a. Miura, K.; Hondo, T.; Okajima, S.; Nakagawa, T.; Takahashi, T.; Hosomi, A. *J. Org. Chem.* **2002**, *67*, 6082–6090.
36. Movassaghi, M.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 2456–2457.
37. Yamamoto, Y.; Noda, M.; Ohno, M.; Eguchi, S. *J. Org. Chem.* **1997**, *62*, 1292–1298.
38. Yamaguchi, M.; Kido, Y.; Hayashi, A.; Hirama, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1313–1315.
38a. Kido, Y.; Yamaguchi, M. *J. Org. Chem.* **1998**, *63*, 8086–8087.
38b. Yonehara, F.; Kido, Y.; Yamaguchi, M. *Chem. Commun.* **2000**, 1189–1190.
39. Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2002**, *124*, 8528–8529.
40. Amemiya, R.; Fujii, A.; Yamaguchi, M. *Tetrahedron Lett.* **2004**, *45*, 4333–4335.
40a. Amemiya, R.; Nishimura, Y.; Yamaguchi, M. *Synthesis* **2004**, 1307–1314.
41. Asao, N.; Shimada, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3797–3798.
41a. Asao, N.; Shimada, T.; Shimada, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 10899–10902.
42. Asao, N.; Nabatame, K.; Yamamoto, Y. *Chem. Lett.* **2001**, 982–983.
43. Hiyama, T. Organosilicon Compounds in Cross-coupling Reactions. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, 1998; Chap. 10; pp 421–453.
43a. Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845–853.
44. Denmark, S. E.; Sweis, R. F. Organosilicon Compounds in Cross-coupling Reactions. In *Metal-catalyzed Cross-coupling Reactions*, 2nd ed.; De Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; pp 163–216.
45. Nishihara, Y.; Ikegashira, K.; Mori, A.; Hiyama, T. *Chem. Lett.* **1997**, 1233–1234.
45a. Nishihara, Y.; Ikegashira, K.; Hirabayashi, K.; Ando, J.; Mori, A.; Hiyama, T. *J. Org. Chem.* **2000**, *65*, 1780–1787.
45b. Nishihara, Y.; Ando, J.; Kato, T.; Mori, A.; Hiyama, T. *Macromolecules* **2000**, *33*, 2779.
46. Halbes, U.; Pale, P. *Tetrahedron Lett.* **2002**, *43*, 2039–2042.
46a. Koseki, Y.; Omino, K.; Anzai, S.; Nagasaka, T. *Tetrahedron Lett.* **2000**, *41*, 2377–2380.
47. Yang, C.; Nolan, S. P. *Organometallics* **2002**, *21*, 1020–1022.
48. Chang, S.; Yang, S. H.; Lee, P. H. *Tetrahedron Lett.* **2001**, *42*, 4833–4835.
49. Denmark, S. E.; Tymonko, S. A. *J. Org. Chem.* **2003**, *68*, 9151–9154.
50. Hirabayashi, K.; Nishihara, Y.; Mori, A.; Hiyama, T. *Tetrahedron Lett.* **1998**, *39*, 7893–7896.
50a. Hirabayashi, K.; Ando, J.; Kawashima, J.; Nishihara, Y.; Mori, A.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1409–1417.
51. Nishikata, T.; Yamamoto, Y.; Miyaura, N. *Chem. Lett.* **2003**, *32*, 752–753.
52. Denmark, S. E.; Amishiro, N. *J. Org. Chem.* **2003**, *68*, 6997–7003.
53. Mori, A.; Danda, Y.; Fujii, T.; Hirabayashi, K.; Osakada, K. *J. Am. Chem. Soc.* **2001**, *123*, 10774–10775.
54. Koike, T.; Du, X.; Mori, A.; Osakada, K. *Synlett* **2002**, 301–303.
55. Huang, T.-S.; Li, C.-J. *Chem. Commun.* **2001**, 2348–2349.
56. Murata, M.; Shimazaki, R.; Ishikura, M.; Watanabe, S.; Matsuda, Y. *Synthesis* **2002**, 717–719.
57. Oi, S.; Honma, Y.; Inoue, Y. *Org. Lett.* **2002**, *4*, 667–669.
58. Oi, S.; Taira, A.; Honma, Y.; Inoue, Y. *Org. Lett.* **2003**, *5*, 97–99.
58a. Otomaru, Y.; Hayashi, T. *Tetradedron: Asmmetry* **2004**, *15*, 2647–2651.
59. Fujii, T.; Koike, T.; Mori, A.; Osakada, K. *Synlett* **2002**, 298–300.
60. Fujii, T.; Koike, T.; Mori, A.; Osakada, K. *Synlett* **2002**, 295–297.
61. Yamane, M.; Uera, K.; Narasaka, K. *Chem. Lett.* **2004**, *33*, 424–425.
62. Ito, H.; Arimoto, K.; Sensui, H.; Hosomi, A. *Tetrahedron Lett.* **1997**, 3977–3980.

63. Nishihara, Y.; Ikegashira, K.; Mori, A.; Hiyama, T. *Tetrahedron Lett.* **1998**, *39*, 4075–4078.
64. Marshall, J. A.; Chobanian, H. R.; Yanik, M. M. *Org. Lett.* **2001**, *3*, 4107–4110.
65. Ikegashira, K.; Nishihara, Y.; Hirabayashi, K.; Mori, A.; Hiyama, T. *Chem. Commun.* **1997**, 1039–1040.
65a. Nishihara, Y.; Ikegashira, K.; Toriyama, F.; Mori, A.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 985–990.
66. Ito, H.; Sensui, H.; Arimoto, K.; Miura, K.; Hosomi, A. *Chem. Lett.* **1997**, 921–922.
67. Takeda, T.; Uruga, T.; Gohroku, K.; Fujiwara, T. *Chem. Lett.* **1999**, 821–822.
67a. Taguchi, H.; Ghoroku, K.; Tadaki, M.; Tsubouchi, A.; Takeda, T. *Org. Lett.* **2001**, *3*, 3811–3814.
67b. Taguchi, H.; Ghoroku, K.; Tadaki, M.; Tsubouchi, A.; Takeda, T. *J. Org. Chem.* **2002**, *67*, 8450–8456.
67c. Taguchi, H.; Miyashita, H.; Tsubouchi, A.; Takeda, T. *Chem. Commun.* **2002**, 2218–2219.
67d. Taguchi, H.; Tsubouchi, A.; Takeda, T. *Tetrahedron Lett.* **2003**, 5205–5207.
67e. Tsubouchi, A.; Itoh, M.; Onishi, K.; Takeda, T. *Synthesis* **2004**, 1504–1508.
68. Taguchi, H.; Takami, K.; Tsubouchi, A.; Takeda, T. *Tetrahedron Lett.* **2004**, *45*, 429–432.
69. Koike, T.; Du, X.; Sanada, T.; Danda, Y.; Mori, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 89–92.
70. Powell, D. A.; Fu, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 7788–7789.
71. Murakami, M.; Hori, S. *J. Am. Chem. Soc.* **2003**, *125*, 4720–4721.
72. Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200–206.
73. Fleming, I. Allylsilanes, Allylstannanes, and Related Systems. In *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 2.2, pp 563–593.
74. Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293–1316.
75. Ishihara, K.; Hiraiwa, Y.; Yamamoto, H. *Synlett* **2001**, 1851–1854.
76. Yadav, J. S.; Chand, P. K.; Anjaneyulu, S. *Tetrahedron Lett.* **2002**, *43*, 3783–3784.
77. Watahiki, T.; Oriyama, T. *Tetrahedron Lett.* **2002**, *43*, 8959–8962.
78. Maeda, K.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **1997**, *62*, 6429–6431.
79. Larsen, C. H.; Ridgway, B. H.; Shaw, J. T.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 12208–12209.
80. Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. *J. Am. Chem. Soc.* **2000**, *122*, 168–169.
80a. Ayala, L.; Lucero, C. G.; Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. *J. Am. Chem. Soc.* **2003**, *125*, 15521–15528.
81. Schmitt, A.; Reißig, H.-U. *Eur. J. Org. Chem.* **2000**, 3893–3901.
82. Sakurai, H.; Sasaki, K.; Hayashi, J.; Hosomi, A. *J. Org. Chem.* **1984**, *49*, 2808–2809.
83. Yadav, J. S.; Subba, R. B. V.; Srihari, P. *Synlett* **2001**, 673–675.
84. Leroy, B.; Markó, I. E. *J. Org. Chem.* **2002**, *67*, 8744–8752 and references cited therein.
85. Yasuda, M.; Onishi, Y.; Ito, T.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 2425–2428.
86. Sakurai, H. *Synlett* **1989**, 1–8.
86a. Hosomi, A.; Kohra, S.; Tominaga, Y. *J. Synth. Org. Chem. Jpn.* **1989**, *47*, 831–842.
86b. Hosomi, A. *Rev. Heteroatom Chem.* **1992**, *7*, 214–228.
86c. Corriu, R. J. P. *J. Orgnomet. Chem.* **1990**, *400*, 81–106.
86d. Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371–1448.
87. Kobayashi, S.; Nishio, K. *Tetrahedron Lett.* **1993**, *34*, 3453–3456.
87a. Kobayashi, S.; Nishio, K. *J. Org. Chem.* **1994**, *59*, 6620–6627.
87b. Ogawa, C.; Sugiura, M.; Kobayashi, S. *Chem. Commun.* **2003**, 192–193.
88. Denmark, S. E.; Coe, D. M.; Pratt, N. E.; Griedel, B. D. *J. Org. Chem.* **1994**, *59*, 6161–6163.
89. Kobayashi, S.; Nishio, K. *J. Am. Chem. Soc.* **1995**, *117*, 6392–6393.
90. Brain, C. T.; Thomas, E. J. *Tetrahedron Lett.* **1997**, *38*, 2387–2390.
91. Dias, L. C.; Giacomini, R. *Tetrahedron Lett.* **1998**, *39*, 5343–5346.
91a. Dias, L. C.; Meira, P. R. R.; Ferreira, E. *Org. Lett.* **1999**, *1*, 1335–1338.
92. Hosomi, A.; Shirahata, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, 3043–3046.
93. Nakamura, K.; Nakamura, H.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 2614–2615.
94. Yanagisawa, A.; Kageyama, H.; Nakatsuka, Y.; Asakawa, K.; Matsumoto, Y.; Yamamoto, H. *Angew. Chem., Int. Ed.* **1999**, *38*, 3701–3703.
95. Yamasaki, S.; Fujii, K.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2002**, *124*, 6536–6537.
96. Aoyama, N.; Hamada, T.; Manabe, K.; Kobayasi, S. *Chem. Commun.* **2003**, 676–677.
97. Aoyama, N.; Hamada, T.; Manabe, K.; Kobayasi, S. *J. Org. Chem.* **2003**, *68*, 7329–7333.
98. Sakurai, H.; Hosomi, A.; Saito, M.; Sasaki, K.; Iguchi, H.; Sasaki, J.; Araki, Y. *Tetrahedron* **1983**, *39*, 883–894.
99. Wang, D.-K.; Zhou, Y.-G.; Tang, Y.; Hou, X.-L.; Dai, L.-X. *J. Org. Chem.* **1999**, *64*, 4233–4237.
100. Fürstner, A.; Voigtländer, D. *Synthesis* **2000**, 959–969.
101. Matsumoto, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 7152–7155.
102. Wang, Z.; Wang, D.; Sui, X. *Chem. Commun.* **1996**, 2261–2262.
102a. Zhang, L. C.; Sakurai, H.; Kira, M. *Chem. Lett.* **1997**, 129–130.
102b. Wang, D.; Wang, Z. G.; Wang, M. W.; Chen, Y. J.; Liu, L.; Zhu, Y. *Tetrahedron: Asymmetry* **1999**, *10*, 327–338.
103. Kinnaird, J. W. A.; Ng, P. Y.; Kubota, K.; Wang, X.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7920–7921.
104. Tietze, L. F.; Dölle, A.; Schiemann, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1372–1373.
104a. Tietze, L. F.; Schiemann, K.; Wegner, C.; Wulff, C. *Chem. Eur. J.* **1996**, *2*, 1164–1172.
104b. Tietze, L. F.; Wulff, C.; Wegner, C.; Schuffenhauer, A.; Schiemmann, K. *J. Am. Chem. Soc.* **1998**, *120*, 4276–4280.
105. Tietze, L. F.; Schiemann, K.; Wegner, C. *J. Am. Chem. Soc.* **1995**, *117*, 5851–5852.
105a. Tietze, L. F.; Wegner, C.; Wulff, C. *Synlett* **1996**, 471–472.
106. Kubota, K.; Leighton, J. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 946–948.
106a. Hackman, B. M.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2004**, *6*, 4375–4377.
107. Hayashi, T.; Kabeta, K. *Tetrahedron Lett.* **1985**, *26*, 3023–3026.
107a. Kitayama, K.; Tsuji, H.; Uozumi, Y.; Hayashi, T. *Tetrahedron Lett.* **1996**, *37*, 4169–4172.
107b. Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354–362.
108. Han, J. W.; Hayashi, T. *Tetrahedron: Asymmetry* **2002**, *13*, 325–331.
108a. Han, J. W.; Hayashi, T. *Chem. Lett.* **2001**, 976–977.

109. Han, J. W.; Tokunaga, N.; Hayashi, T. *J. Am. Chem. Soc.* **2001**, *123*, 12915–12916.
110. Buckle, M. J. C.; Fleming, I. *Tetrahedron Lett.* **1993**, *34*, 2383–2386.
111. Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1997**, *62*, 8976–8977.
111a. Marshall, J. A.; Maxson, K. *J. Org. Chem.* **2000**, *65*, 630–633.
112. Suginome, M.; Matsumoto, A.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3061–3062.
112a. Suginome, M.; Iwanami, T.; Matsumoto, A.; Ito, Y. *Tetrahedron: Asymmetry* **1997**, *8*, 859–862.
112b. Suginome, M.; Matsumoto, A.; Ito, Y. *J. Org. Chem.* **1996**, *61*, 4884–4885.
113. Suginome, M.; Iwanami, T.; Ito, Y. *J. Am. Chem. Soc.* **2001**, *123*, 4356–4357.
114. Suginome, M.; Iwanami, T.; Ito, Y. *J. Org. Chem.* **1998**, *63*, 6096–6097.
114a. Suginome, M.; Iwanami, T.; Ito, Y. *Chem. Commun.* **1999**, 2537–2538.
114b. Suginome, M.; Iwanami, T.; Yamamoto, A.; Ito, Y. *Synlett* **2001**, 1042–1045.
115. Suginome, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 11174–11175.
116. Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763–2793.
117. Yanagisawa, A. Allylation of Carbonyl Groups. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 1999; Vol. 2, pp 965–982.
117a. Yanagisawa, A. Allylation of Carbonyl Groups. In *Comprehensive Asymmetric Catalysis, Supplement 2*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 2004; pp 97–107.
118. Hiemstra, H.; Speckamp, W. N. Additions to N-acyliminium Ionns. In *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, Chapter 4.5, pp 1047–1082.
119. Veenstra, S. J.; Schmid, P. *Tetrahedron Lett.* **1997**, *38*, 997–1000.
119a. Meester, W. J. N.; Rutjes, F. P. J. T.; Hermkens, P. H. H.; Hiemstra, H. *Tetrahedron Lett.* **1999**, *40*, 1601–1604.
120. Billet, M.; Klotz, P.; Mann, A. *Tetrahedron Lett.* **2001**, *42*, 631–634.
121. Panek, J. S.; Jain, N. F. *J. Org. Chem.* **1994**, *59*, 2674–2675.
121a. Schaus, J. V.; Jain, N.; Panek, J. S. *Tetrahedron* **2000**, *56*, 10263–10274.
122. Billet, M.; Schoenfelder, A.; Klotz, P.; Mann, A. *Tetrahedron Lett.* **2002**, *43*, 1453–1456.
123. Furman, B.; Dziedzic, M. *Tetrahedron Lett.* **2003**, *44*, 8249–8252.
124. Fang, X.; Johannsen, M.; Yao, S.; Gathergood, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **1999**, *64*, 4844–4849.
125. Ferraris, D.; Young, B.; Cox, C.; Dudding, T.; Drury, W. J. III; Ryzhkov, L.; Taggi, A. E.; Lectka, T. *J. Am. Chem. Soc.* **2002**, *124*, 67–77.
126. Fernandes, R. A.; Yamamoto, Y. *J. Org. Chem.* **2004**, *69*, 735–738.
127. Friestad, G. K.; Ding, H. *Angew. Chem., Int. Ed.* **2001**, *40*, 4491–4493.
128. Kobayashi, S.; Hirabayashi, R. *J. Am. Chem. Soc.* **1999**, *121*, 6942–6943.
128a. Hirabayashi, R.; Ogawa, C.; Sugiura, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 9493–9499.
128b. Ogawa, C.; Sugiura, M.; Kobayashi, S. *J. Org. Chem.* **2002**, *67*, 5359–5364.
129. Sugiura, M.; Robvieux, F.; Kobayashi, S. *Synlett* **2003**, 1749–1751.
130. Kobayashi, S.; Ogawa, C.; Konishi, H.; Sugiura, M. *J. Am. Chem. Soc.* **2003**, *125*, 6610–6611.
131. Ogawa, C.; Sugiura, M.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 6491–6493.
132. Hamada, T.; Manabe, K.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 3927–3930.
133. Berger, R.; Rabbat, P. M. A.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 9596–9597.
133a. Berger, R.; Duff, K.; Leighton, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 5686–5687.
134. Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673–1675.
135. Majetich, G.; Song, J.-S.; Ringold, C.; Nemeth, G. A.; Newton, M. G. *J. Org. Chem.* **1991**, *56*, 3973–3988 and references therein.
136. Sato, M.; Aoyagi, S.; Yago, S.; Kibayashi, C. *Tetrahedron Lett.* **1996**, *37*, 9063–9066.
137. Tietze, L. F.; Schünke, C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1731–1733.
137a. Tietze, L. F.; Schünke, C. *Eur. J. Org. Chem.* **1998**, 2089–2099.
138. Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136.
139. Frost, L. M.; Smith, J. D.; Berrisford, D. J. *Tetrahedron Lett.* **1999**, *40*, 2183–2186.
140. Wang, X.; Meng, Q.; Nation, A. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 10672–10673.
141. Kopecky, D. J.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2001**, *123*, 8420–8421.
142. Zacuto, M. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2000**, *122*, 8587–8588.
142a. Zacuto, M. J.; O'Malley, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7890–7891.
142b. Zacuto, M. J.; O'Malley, S. J.; Leighton, J. L. *Tetrahedron* **2003**, *59*, 8889–8900.
143. Dreher, S. D.; Leighton, J. L. *J. Am. Chem. Soc.* **2001**, *123*, 341–342.
144. O'Malley, S. J.; Leighton, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 2915–2917.
145. Akiyama, T.; Asayama, K.; Fujiyoshi, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3655–3656.
146. Naeta, H.; Nagasawa, T.; Handa, Y.; Takei, T.; Osamura, Y.; Suzuki, K. *Tetrahedron Lett.* **1995**, *36*, 899–902.
147. Sarkar, T. K.; Haque, S. A.; Basak, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 1417–1419.
148. Markó, I. E.; Bayston, D. J. *Tetrahedron Lett.* **1993**, *34*, 6595–6598.
149. Mikami, K.; Matsukawa, S. *Tetrahedron Lett.* **1994**, *35*, 3133–3136.
150. Ooi, T.; Ohmatsu, K.; Uraguchi, D.; Maruoka, K. *Tetrahedron Lett.* **2004**, *45*, 4481–4484.
151. Monti, H.; Audran, G.; Feraud, M.; Monti, J.-P.; Léandri, G. *Tetrahedron* **1996**, *52*, 6685–6698.
151a. Monti, H.; Audran, G.; Monti, J.-P.; Léandri, G. *J. Org. Chem.* **1996**, *61*, 6021–6023.
152. O'Brien, M.; Taylor, N. H.; Thomas, E. J. *Tetrahedron Lett.* **2002**, *43*, 5491–5494.
153. Danheiser, R. L.; Carini, D. J.; Basak, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604–1606.
153a. Danheiser, R. L.; Kwasigroch, C. A.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1985**, *107*, 7233–7235.
153b. Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 4407–4413.
154. Pornet, J.; Miginiac, L.; Jaworski, K.; Randrianoelina, B. *Organometallics* **1985**, *4*, 333–338.
155. Knölker, H.-J.; Jones, P. G.; Pannek, J.-B. *Synlett* **1990**, 429–430.
156. Knölker, H.-J. *J. Prakt. Chem.* **1997**, *339*, 304–314.
157. Danheiser, R. L.; Dixon, B. R.; Gleason, R. W. *J. Org. Chem.* **1992**, *57*, 6094–6097.
158. Knölker, H.-J.; Foitzik, N.; Goesmann, H.; Graf, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1081–1083.

159. Danheiser, R. L.; Takahashi, T.; Bertók, B.; Dixon, B. R. *Tetrahedron Lett.* **1993**, *34*, 3845–3848.
160. Tamao, K. Oxidative Cleavage of the Silicon-carbon Bond: Development, Mechanism, Scope, and Limitations. In *Advances in Silicon Chemistry*; Larson, G. L., Ed.; JAI Press: Greenwich, 1996; Vol. 3, pp 1–62.
160a. Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662.
161. Panek, J. S.; Jain, N. F. *J. Org. Chem.* **1993**, *58*, 2345–2348.
162. Knölker, H.-J.; Foitzik, N.; Schmitt, O. *Tetrahedron Lett.* **1999**, *40*, 3557–3560.
163. Murphy, W. S.; Neville, D. *Tetrahedron Lett.* **1997**, *38*, 7933–7936.
164. Nair, V.; Rajesh, C.; Dhanya, R.; Rath, N. P. *Org. Lett.* **2002**, *4*, 953–955.
165. Knölker, H.-J.; Graf, R. *Synlett* **1994**, 131–133.
166. Knölker, H.-J.; Baum, G.; Graf, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1612–1615.
167. Brengel, G. P.; Rithner, C.; Meyers, A. I. *J. Org. Chem.* **1994**, *59*, 5144–5146.
168. Akiyama, T.; Yamanaka, M. *Tetrahedron Lett.* **1998**, *39*, 7885–7888.
169. Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 9868–9870.
170. Micalizio, G. C.; Roush, W. R. *Org. Lett.* **2000**, *2*, 461–464.
171. Panek, J. S.; Beresis, R. *J. Org. Chem.* **1993**, *58*, 809–811.
172. Radetich, B.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 2430–2431.
173. Evans, D. A.; Sweeney, Z. K.; Rovis, T.; Tedrow, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 12095–12096.
174. Akiyama, T.; Ishikawa, K.; Ozaki, S. *Chem. Lett.* **1994**, 627–630.
174a. Akiyama, T.; Yasusa, T.; Ishikawa, K.; Ozaki, S. *Tetrahedron Lett.* **1994**, *35*, 8401–8404.
174b. Schinzer, D.; Panke, G. *J. Org. Chem.* **1996**, *61*, 4496–4497.
174c. Peng, Z.-H.; Woerpel, K. A. *Org. Lett.* **2002**, *4*, 2945–2948.
175. Nair, V.; Rajesh, C.; Dhanya, R.; Rath, N. P. *Tetrahedron Lett.* **2002**, *43*, 5349–5351.
176. Akiyama, T.; Kirino, M. *Chem. Lett.* **1995**, 723–724.
177. Stahl, A.; Steckhan, E.; Nieger, M. *Tetrahedron Lett.* **1994**, *35*, 7371–7374.
178. Akiyama, T.; Sugano, M.; Kagoshima, H. *Tetrahedron Lett.* **2001**, *42*, 3889–3892.
179. Roberson, C. W.; Woerpel, K. A. *J. Org. Chem.* **1999**, *64*, 1434–1435.
180. Isaka, M.; Williard, P. G.; Nakamura, E. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2115–2116.
181. Roberson, C. W.; Woerpel, K. A. *Org. Lett.* **2000**, *2*, 621–623.
182. Peng, Z.-H.; Woerpel, K. A. *Org. Lett.* **2001**, *3*, 675–678.
183. Choi, G. M.; Yeon, S. H.; Jin, J.; Yoo, B. R.; Jung, I. N. *Organometallics* **1997**, *16*, 5158–5162.
184. Angle, S. R.; Boyce, J. P. *Tetrahedron Lett.* **1994**, *35*, 6461–6464.
185. Snider, B. B.; Rodini, D. J.; Conn, R. S. E.; Sealfon, S. *J. Am. Chem. Soc.* **1979**, *101*, 5283–5293.
186. Monti, H.; Audran, G.; Monti, J.-P.; Léandri, G. *Synlett* **1994**, 403–404.
187. Knölker, H.-J.; Baum, G.; Graf, R. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1612–1615.
187a. Knölker, H.-J.; Schmitt, O.; Wanzl, G.; Baum, G. *Chem. Commun.* **1999**, 1737–1738.
188. Organ, M. G.; Dragan, V.; Miller, M.; Froese, R. D. J.; Goddard, J. D. *J. Org. Chem.* **2000**, *65*, 3666–3678.
189. Dang, H.-S.; Davies, A. G. *J. Organomet. Chem.* **1998**, *553*, 67–72.
190. Knölker, H.-J.; Baum, E.; Schmitt, O. *Tetrahedron Lett.* **1998**, *39*, 7705–7708.
191. Hojo, M.; Murakami, C.; Nakamura, S.; Hosomi, A. *Chem. Lett.* **1998**, 331–332.
192. Spence, J. D.; Lowrie, L. E.; Nantz, M. H. *Tetrahedron Lett.* **1995**, *36*, 5499–5502.
193. Akiyama, T.; Yamanaka, M. *Synlett* **1996**, 1095–1096.
194. Uyehara, T.; Yuuki, M.; Masaki, H.; Matsumoto, M.; Ueno, M.; Sato, T. *Chem. Lett.* **1995**, 789–790.
195. Sugimura, H. *Tetrahedron Lett.* **1990**, *31*, 5909–5912.
196. Sugimura, H. *J. Synth. Org. Chem. Jpn.* **1993**, *51*, 884–893.
196a. Osumi, K.; Sugimura, H. *Tetrahedron Lett.* **1995**, *36*, 5789–5792.
197. Kiyooka, S.; Shiomi, Y.; Kira, H.; Kaneko, Y.; Tanimori, S. *J. Org. Chem.* **1994**, *59*, 1958–1960.
198. Dussault, P. H.; Zope, U. *Tetrahedron Lett.* **1995**, *36*, 3655–3658.
199. Hwu, J. R.; Chen, C. N.; Shio, S.-S. *J. Org. Chem.* **1995**, *60*, 856–862.
200. Zhang, Y.; Raines, A. J.; Flowers, R. A. II *Org. Lett.* **2003**, *5*, 2363–2365.
200a. Zhang, Y.; Raines, A. J.; Flowers, R. A. II *J. Org. Chem.* **2004**, *69*, 6267–6272.
201. Arnold, W.; Mohr, P. *Synlett* **1996**, 1215–1217.
202. Giese, S.; Kastrup, L.; Stiens, D.; West, F. G. *Angew. Chem., Int. Ed.* **2000**, *39*, 1970–1973.
203. Sugita, Y.; Yamadori, S.; Hosoya, H.; Yokoe, I. *Chem. Pharm. Bull.* **2001**, *49*, 657–658.
204. Monti, H.; Rizzotto, D.; Leandri, G.; Monti, J.-P. *Tetrahedron Lett.* **1994**, *35*, 2885–2888.
204a. Monti, H.; Rizzotto, D.; Léandri, G. *Tetrahedron* **1998**, *54*, 6725–6738.
205. Nishitani, K.; Harada, Y.; Nakamura, Y.; Yokoo, K.; Yamakawa, K. *Tetrahedron Lett.* **1994**, *35*, 7809–7812.
205a. Sugita, Y.; Kimura, Y.; Yokoe, I. *Tetrahedron Lett.* **1999**, *40*, 5877–5880.
206. Schneider, M.-R.; Mann, A.; Taddei, M. *Tetrahedron Lett.* **1996**, *37*, 8493–8496.
206a. Bergmeier, S. C.; Fundy, S. L.; Seth, P. P. *Tetrahedron* **1999**, *55*, 8025–8038.
207. Angle, S. R.; El-Said, N. A. *J. Am. Chem. Soc.* **1999**, *121*, 10211–10212.
207a. Angle, S. R.; Belanger, D. S.; El-Said, N. A. *J. Org. Chem.* **2002**, *67*, 7699–7705.
208. Brocherieux-Lanoy, S.; Dhimane, H.; Poupon, J.-C.; Vanucci, C.; Lhommet, G *J. Chem. Soc., Perkin Trans. 1* **1997**, 2163–2165.
209. Yeon, S. H.; Han, J. S.; Hong, E.; Do, Y.; Jung, I. N. *J. Organomet. Chem.* **1995**, *499*, 159–165.
209a. Yeon, S. H.; Lee, B. W.; Yoo, B. R.; Suk, M.-Y.; Jung, I. N. *Organometallics* **1995**, *14*, 2361–2365.
209b. Jung, I. N.; Yoo, B. R. *Synlett* **1999**, 519–528.
210. Asao, N.; Yoshikawa, E.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 4874–4875.
210a. Yoshikawa, E.; Gevorgyan, V.; Asao, N.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6781–6786.
210b. Asao, N.; Yamamoto, Y. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1071–1087.
211. Imamura, K.; Yoshikawa, E.; Gevorgyan, V.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 5339–5340.
212. Yoshikawa, E.; Kasahara, M.; Asao, N.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 4499–4502.

213. Yamaguchi, M.; Sotokawa, T.; Hirama, M. *Chem. Commun.* **1997**, 743–744.
214. Fernández-Rivas, C.; Méndez, M.; Echavarren, A. M. *J. Am. Chem. Soc.* **2000**, *122*, 1221–1222.
214a. Fernández-Rivas, C.; Méndez, M.; Nieto-Oberhuber, C.; Echavarren, A. M. *J. Org. Chem.* **2002**, *67*, 5197–5201.
215. Castaño, A. M.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1995**, *117*, 560–561.
215a. Castaño, A. M.; Persson, B. A.; Bäckvall, J.-E. *Chem. Eur. J.* **1997**, *3*, 482–490.
216. Hosomi, A.; Imai, T.; Endo, M.; Sakurai, H. *J. Organomet. Chem.* **1985**, *285*, 95–107.
217. Schwier, T.; Rubin, M.; Gevorgyan, V. *Org. Lett.* **2004**, *6*, 1999–2001 and references therein.
218. Ishikawa, T.; Okano, M.; Aikawa, T.; Saito, S. *J. Org. Chem.* **2001**, *66*, 4635–4642.
219. Braun, M.; Kotter, W. *Angew. Chem., Int. Ed.* **2004**, *43*, 514–517.
220. Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc.* **2003**, *125*, 15760–15761.
221. Yasuda, M.; Saito, T.; Ueba, M.; Baba, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 1414–1416.
222. Sakurai, H.; Hosomi, A.; Kumada, M. *J. Org. Chem.* **1969**, *34*, 1764–1768.
223. Guindon, Y.; Guerin, B.; Chabot, C.; Ogilvie, W. *J. Am. Chem. Soc.* **1996**, *118*, 12528–12535.
224. Porter, N. A.; Wu, J. H.; Zhang, G.; Reed, A. D. *J. Org. Chem.* **1997**, *62*, 6702–6703.
224a. Porter, N. A.; Feng, H.; Kavrakova, I. K. *Tetrahedron Lett.* **1999**, *40*, 6713–6716.
225. Chatgilialoglu, C.; Ferreri, C.; Ballestri, M.; Curran, D. P. *Tetrahedron Lett.* **1996**, *37*, 6387–6390.
226. Miura, K.; Saito, H.; Nakagawa, T.; Hondo, T.; Tateiwa, J.; Sonoda, M.; Hosomi, A. *J. Org. Chem.* **1998**, *63*, 5740–5741.
227. Nakada, M.; Urano, Y.; Kobayashi, S.; Ohono, M. *Tetrahedron Lett.* **1994**, *35*, 741–744.
227a. Bonini, B. F.; Comes-Franchini, M.; Mazzanti, G.; Ricci, A.; Sala, M. *J. Org. Chem.* **1996**, *61*, 7242–7243.
227b. Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Nanni, C.; Ricci, A. *Tetrahedron Lett.* **1998**, *39*, 6737–6740.
227c. Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Gawronski, J.; Mazzanti, G.; Ricci, A.; Varchi, G. *Eur. J. Org. Chem.* **1999**, 437–445.
228. Yanagisawa, A.; Habaue, S.; Yamamoto, H. *Tetrahedron* **1992**, *48*, 1969–1980.
228a. Burns, M. R.; Coward, J. K. *J. Org. Chem.* **1993**, *58*, 528–532.
228b. Molander, G. A.; Siedem, C. S. *J. Org. Chem.* **1995**, *60*, 130–138.
229. Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, *112*, 5609–5617.
229a. Nakajima, T.; Segi, M.; Sugimoto, F.; Hioki, R.; Yokota, S.; Miyashita, K. *Tetrahedron* **1993**, *49*, 8343–8358.
229b. Brigaud, T.; Doussot, P.; Portella, C. *J. Chem. Soc., Chem. Commun.* **1994**, 2117–2118.
229c. Corey, E. J.; Luo, G.; Lin, L. S. *J. Am. Chem. Soc.* **1997**, *119*, 9927–9928.
229d. Saleur, D.; Brigaud, T.; Bouillon, J.-P.; Portella, C. *Synlett* **1999**, 432–434.
229e. Lefebvre, O.; Brigaud, T.; Portella, C. *J. Org. Chem.* **2001**, *66*, 1941–1946.
230. Enda, J.; Kuwajima, I. *J. Am. Chem. Soc.* **1985**, *107*, 5495–5501.
231. Corey, E. J.; Lin, S. *J. Am. Chem. Soc.* **1996**, *118*, 8765–8766.
231a. Corey, E. J.; Lin, S.; Luo, G. *Tetrahedron Lett.* **1997**, *38*, 5771–5774.
231b. Huang, A. X.; Xiong, Z.; Corey, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 9999–10003.
231c. Hu, T.; Corey, E. J. *Org. Lett.* **2002**, *4*, 2441–2443.
232. Takeda, K.; Ohnishi, Y. *Tetrahedron Lett.* **2000**, *41*, 4169–4172.
233. Linghu, X.; Johnson, J. S. *Angew. Chem., Int. Ed.* **2003**, *42*, 2534–2536.
233a. Bausch, C. C.; Johnson, J. S. *J. Org. Chem.* **2004**, *69*, 4283–4285.
234. Linghu, X.; Nicewicz, D. A.; Johnson, J. S. *Org. Lett.* **2002**, *4*, 2957–2960.
235. Nicewicz, D. A.; Yates, C. M.; Johnson, J. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 2652–2655.
235a. Nicewicz, D. A.; Yates, C. M.; Johnson, J. S. *J. Org. Chem.* **2004**, *69*, 6548–6555.
236. Linghu, X.; Potnick, J. R.; Johnson, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 3070–3071.
237. Mattson, A. E.; Bharadwaj, A. R.; Scheidt, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 2314–2315.
237a. Bharadwaj, A. R.; Scheidt, K. A. *Org. Lett.* **2004**, *6*, 2465–2468.
238. Takeda, K.; Tanaka, T. *Synlett* **1999**, 705–708.
239. Saleur, D.; Bouillon, J.-P.; Portella, C. *Tetrahedron Lett.* **2001**, *42*, 6535–6537.
240. Takeda, K.; Nakatani, J.; Nakamura, H.; Sako, K.; Yoshii, E.; Yamaguchi, K. *Synlett* **1993**, 841–843.
241. Takeda, K.; Fujisawa, M.; Makino, T.; Yoshii, E.; Yamaguchi, K. *J. Am. Chem. Soc.* **1993**, *115*, 9351–9352.
241a. Takeda, K.; Yamawaki, K.; Hatakeyama, N. *J. Org. Chem.* **2002**, *67*, 1786–1794.
242. Takeda, K.; Nakajima, A.; Takeda, M.; Okamoto, Y.; Sato, T.; Yoshii, E.; Koizumi, T.; Shiro, M. *J. Am. Chem. Soc.* **1998**, *120*, 4947–4959.
242a. Takeda, K.; Sawada, Y.; Sumi, K. *Org. Lett.* **2002**, *4*, 1031–1033.
243. Obora, Y.; Ogawa, Y.; Imai, Y.; Kawamura, T.; Tsuji, Y. *J. Am. Chem. Soc.* **2001**, *123*, 10489–10493.
244. Cunico, R. F.; Maity, B. C. *Org. Lett.* **2002**, *4*, 4357–4359.
245. Cunico, R. F.; Maity, B. C. *Org. Lett.* **2003**, *5*, 4947–4949.
246. Yamane, M.; Amemiya, T.; Narasaka, K. *Chem. Lett.* **2001**, 1210–1211.
247. Tsai, Y. M.; Cherng, C. D. *Tetrahedron Lett.* **1991**, *32*, 3515–3518.
247a. Chang, S.-Y.; Jiaang, W.-T.; Cherng, C.-D.; Tang, K.-H.; Huang, C.-H.; Tsai, Y.-M. *J. Org. Chem.* **1997**, *62*, 9089–9098.
248. Jiaang, W.-T.; Lin, H.-C.; Tang, K.-H.; Chang, L.-B.; Tsai, Y.-M. *J. Org. Chem.* **1999**, *64*, 618–628.
249. Tsai, Y. M.; Tang, K. H.; Jiaang, W. T. *Tetrahedron Lett.* **1993**, *34*, 1303–1306.
250. Curran, D. P.; Jiaang, W. T.; Palovich, M.; Tsai, Y. M. *Synlett* **1993**, 403–404.
251. Tsai, Y.-M.; Chang, S.-Y. *J. Chem. Soc., Chem. Commun.* **1995**, 981–982.
251a. Huang, C.-H.; Chang, S.-Y.; Wang, N.-S.; Tsai, Y.-M. *J. Org. Chem.* **2001**, *66*, 8983–8991.
252. Rasmussen, J. K.; Heilmann, S. M.; Krepski, L. R. The Chemistry of Cyanotrimethylsilane. In *Advances in Silicon Chemistry*; Larson, G. L., Ed.; JAI Press: Greenwich, CT, 1991; Vol. 1, pp 65–187.
253. Gregory, R. J. H. *Chem. Rev.* **1999**, *99*, 3649–3682.
254. Mori, A.; Inoue, S. Cyanation of Carbonyl and Imino Groups. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 1999; Vol. 2, pp 983–996.
254a. Mori, A.; Inoue, S. Cyanation of Carbonyl and Imino Groups. In *Comprehensive Asymmetric Catalysis, Supplement 1*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 2004; pp 117–130.
255. Cole, B. M.; Shimizu, K. D.; Krueger, C. A.; Harrity, J. P. A.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1668–1671.

256. Schaus, S. E.; Jacobsen, E. N. *Org. Lett.* **2000**, *2*, 1001–1004.
257. Chatani, N.; Hanafusa, T. *J. Org. Chem.* **1986**, *51*, 4714–4716.
258. Anderson, B. A.; Bell, E. C.; Ginah, F. O.; Harn, N. K.; Pagh, L. M.; Wepsiec, J. P. *J. Org. Chem.* **1998**, *63*, 8224–8228.
259. Tsuji, Y.; Yamada, N.; Tanaka, S. *J. Org. Chem.* **1993**, *58*, 16–17.
259a. Tsuji, Y.; Kusui, T.; Kojima, T.; Sugiura, Y.; Yamada, N.; Tanaka, S.; Ebihara, M.; Kawamura, T. *Organometallics* **1998**, *17*, 4835–4841.
260. Tsuji, Y.; Taniguchi, M.; Yasuda, T.; Kawamura, T.; Obora, Y. *Org. Lett.* **2000**, *2*, 2635–2637.
261. Ohe, K.; Matsuda, H.; Ishihara, T.; Ogoshi, S.; Chatani, N.; Murai, S. *J. Org. Chem.* **1993**, *58*, 1173–1177.
262. Hinojosa, S.; Delgado, A.; Llebaria, A. *Tetrahedron Lett.* **1999**, *40*, 1057–1060.
263. Chatani, N.; Takeyasu, T.; Horiuchi, N.; Hanafusa, T. *J. Org. Chem.* **1988**, *53*, 3539–3548.
264. Suginome, M.; Kinugasa, H.; Ito, Y. *Tetrahedron Lett.* **1994**, *35*, 8635–8638.
265. Nakamura, H.; Shibata, H.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 2911–2914.
266. Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912–4913.
266a. Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8593–8601.
266b. Zhang, M.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498–4499.
267. Probert, G. D.; Whitby, R. J. *Tetrahedron Lett.* **1995**, *36*, 4113–4116.
268. Prakash, G. K. S.; Krishnamurti, R.; Olah, G. A. *J. Am. Chem. Soc.* **1989**, *111*, 393–395.
269. Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1994**, *35*, 3137–3138.
270. Shinokubo, H.; Miura, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1993**, *34*, 1951–1954.
270a. Shinokubo, H.; Miura, K.; Oshima, K.; Utimoto, K. *Tetrahedron* **1996**, *52*, 503–514.
271. Shinokubo, H.; Oshima, K.; Utimoto, K. *Chem. Lett.* **1995**, 461–462.
271a. Yagi, K.; Tsuritani, T.; Takami, K.; Shinokubo, H.; Oshima, K. *J. Am. Chem. Soc.* **2004**, *126*, 8618–8619.
272. Tietze, L. F.; Geissler, H.; Gewert, J. A.; Jakobi, U. *Synlett* **1994**, 511–512.
273. Smith, A. B. III; Boldi, A. M. *J. Am. Chem. Soc.* **1997**, *119*, 6925–6926.
273a. Smith, A. B. III; Pitram, S. M.; Boldi, A. M.; Gaunt, M. J.; Sfouggatakis, C.; Moser, W. H. *J. Am. Chem. Soc.* **2003**, *125*, 14435–14445 and references therein.
274. Padwa, A. Intermolecular 1,3-Dipolar Cycloadditions. In *Comprehensive Organic Chemistry*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, Chapter 4.9, pp 1069–1109.
275. Tominaga, Y.; Hojo, M.; Hosomi, A. *J. Synth. Org. Chem. Jpn.* **1992**, *50*, 48–60.
276. Washizuka, K.; Nagai, K.; Minakata, S.; Ryu, I.; Komatsu, M. *Tetrahedron Lett.* **1999**, *40*, 8849–8853.
276a. Washizuka, K.; Nagai, K.; Minakata, S.; Ryu, I.; Komatsu, M. *Tetrahedron Lett.* **2000**, *41*, 691–695.
277. Komatsu, M.; Choi, J.; Mihara, M.; Oderaotoshi, Y.; Minakata, S. *Heterocycles* **2002**, *57*, 1989–1995.
278. Komatsu, M.; Kasano, Y.; Yamaoka, S.; Minakata, S. *Synthesis* **2003**, 1398–1401.
279. Washizuka, K.; Minakata, S.; Ryu, I.; Komatsu, M. *Tetrahedron* **1999**, *55*, 12969–12976.
279a. Komatsu, M.; Okada, H.; Yokoi, S.; Minakata, S. *Tetrahedron Lett.* **2003**, *44*, 1603–1606.
280. Hojo, M.; Ohkuma, M.; Ishibashi, N.; Hosomi, A. *Tetrahedron Lett.* **1993**, *34*, 5943–5946.
280a. Hojo, M.; Ishibashi, N.; Hosomi, A. *Synlett* **1996**, 234–236.
281. Cuadrado, P.; González-Nogal, A. M. *Tetrahedron Lett.* **2000**, *41*, 1111–1114.
281a. Cuadrado, P.; González-Nogal, A. M. *Tetrahedron Lett.* **1997**, *38*, 8117–8120.
282. Sasaki, M.; Kawanishi, E.; Nakai, Y.; Matsumoto, T.; Yamaguchi, K.; Takeda, K. *J. Org. Chem.* **2003**, *68*, 9330–9339.
282a. Tanaka, K.; Takeda, K. *Tetrahedron Lett.* **2004**, *45*, 7859–7861.
282b. Sasaki, M.; Takeda, K. *Org. Lett.* **2004**, *6*, 4849–4851.
283. Kira, K.; Isobe, M. *Chem. Lett.* **2001**, 432–433.
284. Ooi, T.; Kiba, T.; Maruoka, K. *Chem. Lett.* **1997**, 519–520.
285. Franz, A. K.; Woerpel, K. A. *Acc. Chem. Res.* **2000**, *33*, 813–820.
286. Bodnar, P. M.; Palmer, W. S.; Shaw, J. T.; Smitrovich, J. H.; Sonnenberg, J. D.; Presley, A. L.; Woerpel, K. A. *J. Am. Chem. Soc.* **1995**, *117*, 10575–10576.
286a. Bodnar, P. M.; Palmer, W. S.; Ridgway, B. H.; Shaw, J. T.; Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 4737–4745.
287. Shaw, J. T.; Woerpel, K. A. *J. Org. Chem.* **1997**, *62*, 442–443.
288. Kroke, E.; Willms, S.; Weidenbruch, M.; Saak, W.; Pohl, S.; Marsmann, H. *Tetrahedron Lett.* **1996**, *37*, 3675–3678.
288a. Nguyen, P. T.; Palmer, W. S.; Woerpel, K. A. *J. Org. Chem.* **1999**, *64*, 1843–1848.
289. Franz, A. K.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *12*, 949–957.
290. Franz, A. K.; Woerpel, K. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 4295–4299.
291. Palmer, W. S.; Woerpel, K. A. *Organometallics* **1997**, *16*, 1097–1099.
291a. Palmer, W. S.; Woerpel, K. A. *Organometallics* **2001**, *20*, 3691–3695.
292. Matsumoto, K.; Oshima, K.; Utimoto, K. *J. Synth. Org. Chem. Jpn* **1996**, *54*, 289–299 and references therein.
293. Tanaka, Y.; Yamashita, H.; Shimada, S.; Tanaka, M. *Organometallics* **1997**, *16*, 3246–3248.
293a. Yamashita, H.; Tanaka, M.; Honda, K. *J. Am. Chem. Soc.* **1995**, *117*, 8873–8874.
294. Tanaka, Y.; Yamashita, H.; Tanaka, M. *Organometallics* **1996**, *15*, 1524–1526.
295. Chauhan, B. P. S.; Tanaka, Y.; Yamashita, H.; Tanaka, M. *Chem. Commun.* **1996**, 1207–1208.
296. Yadav, V. K.; Balamurugan, R. *Org. Lett.* **2001**, *3*, 2717–2719.
297. Yadav, V. K.; Sriramurthy, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 2669–2671.
298. Yadav, V. K.; Sriramurthy, V. *Org. Lett.* **2004**, *6*, 4495–4498.
299. Yadav, V. K.; Balamurugan, R. *Org. Lett.* **2003**, *5*, 4281–4284.
300. Yadav, V. K.; Kumar, N. V. *J. Am. Chem. Soc.* **2004**, *126*, 8652–8653.
301. Yadav, V. K.; Balamurugan, R. *Chem. Commun.* **2002**, 514–515.
302. Kobayashi, S.; Ueno, M. Mannich Reaction. In *Comprehensive Asymmetric Catalysis, Supplement 1*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 2004; pp 143–150.
303. Yamaguchi, M. Conjugate Addition of Stabilized Carbanions. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 1999; Vol. 3, pp 1121–1142.

303a. Yamaguchi, M. Conjugate Addition of Stabilized Carbanions. In *Comprehensive Asymmetric Catalysis, Supplement 1*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 2004; pp 151–159.
304. Ooi, T.; Maruoka, K. Hetero-Diels–Alder and Related Reactions. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Heidelberg, 1999; Vol. 3, pp 1237–1254.
305. Jørgensen, K. A. Catalytic Enantioselective Cycloaddition Reactions of Carbonyl Compounds. In *Cycloaddition Reactions in Organic Synthesis*; Kobayashi, S., Jørgensen, K. A., Eds.; Wiley-VCH: Weinheim, 2001; pp 151–186.
306. Kobayashi, S. Catalytic Enantioselective Aza Diels-Alder Reactions. In *Cycloaddition Reactions in Organic Synthesis*; Kobayashi, S., Jørgensen, K. A., Eds.; Wiley-VCH: Weinheim, 2001; pp 187–210.
307. Kobayashi, S.; Manabe, K.; Ishitani, H.; Matsuo, J.-I. Product Subclass 16: Silyl Enol Ethers. In *Science of Synthesis*; Fleming, I., Ed. Thieme: Stuttgart, 2001; Vol. 4, pp 317–370.
308. Ooi, T.; Uraguchi, D.; Kagoshima, N.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 5679–5682.
309. Hirano, K.; Fujita, K.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron Lett.* **2004**, *45*, 2555–2557.
310. Grieco, P. A.; Collins, J. L.; Henry, K. J. Jr. *Tetrahedron Lett.* **1992**, *33*, 4735–4738.
310a. Rearson, W. H.; Schkeryantz, J. M. *J. Org. Chem.* **1992**, *57*, 2986–2987.
311. Hunt, K. W.; Grieco, P. A. *Org. Lett.* **2001**, *3*, 481–484.
312. Matsuda, I.; Wakamatsu, S.; Komori, K.; Makino, T.; Itoh, K. *Tetrahedron Lett.* **2002**, *43*, 1043–1046.
313. Matsuda, I.; Komori, K.; Itoh, K. *J. Am. Chem. Soc.* **2002**, *124*, 9072–9073.
314. Ishikawa, T.; Aikawa, T.; Mori, Y.; Saito, S. *Org. Lett.* **2003**, *5*, 51–54.
315. Miura, T.; Kiyota, K.; Kusama, H.; Lee, K.; Kim, H.; Kim, S.; Lee, P. H.; Iwasawa, N. *Org. Lett.* **2003**, *5*, 1725–1728.
316. Kim, S.; Lim, C. J.; Song, C.; Chung, W.-j. *J. Am. Chem. Soc.* **2002**, *124*, 14306–14307.
316a. Kim, S.; Lim, C. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 5378–5380.
317. Toyota, M.; Ihara, M. *Synlett* **2002**, 1211–1222.
318. Toyota, M.; Wada, T.; Fukumoto, K.; Ihara, M. *J. Am. Chem. Soc.* **1998**, *120*, 4916–4925.
318a. Toyota, M.; Odashima, T.; Wada, T.; Ihara, M. *J. Am. Chem. Soc.* **2000**, *122*, 9036–9037.
319. Forsyth, C. J.; Clardy, J. *J. Am. Chem. Soc.* **1990**, *112*, 3497–3505.
319a. Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1995**, *60*, 2773–2779.
319b. Huang, H.; Forsyth, C. J. *J. Org. Chem.* **1995**, *60*, 5746–5747.
319c. Frontier, A. J.; Raghavan, S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 6686–6687.
320. Imamura, K.; Yoshikawa, E.; Gevorgyan, V.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 4081–4084.
320a. Imamura, K.; Yoshikawa, E.; Gevorgyan, V.; Sudo, T.; Asao, N.; Yamamoto, Y. *Can. J. Chem.* **2001**, *79*, 1624–1631.
321. Maeyama, K.; Iwasawa, N. *J. Am. Chem. Soc.* **1998**, *120*, 1928–1929.
321a. Iwasawa, N.; Maeyama, K.; Kusama, H. *Org. Lett.* **2001**, *3*, 3871–3873.
322. Miura, T.; Iwasawa, N. *J. Am. Chem. Soc.* **2002**, *124*, 518–519.
323. Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 2627–2635.
324. Yamaguchi, M.; Tsukagoshi, T.; Arisawa, M. *J. Am. Chem. Soc.* **1999**, *121*, 4074–4075.
324a. Arisawa, M.; Akamatsu, K.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 789–790.
325. Arisawa, M.; Amemiya, R.; Yamaguchi, M. *Org. Lett.* **2002**, *4*, 2209–2211.
326. Amemiya, R.; Fuji, A.; Arisawa, M.; Yamaguchi, M. *J. Organomet. Chem.* **2003**, *686*, 94–100.
327. Kuwajima, I.; Urabe, H. *J. Am. Chem. Soc.* **1982**, *104*, 6831–6833.
328. Agnelli, F.; Sulikowski, G. A. *Tetrahedron Lett.* **1998**, *39*, 8807–8810.
329. Liu, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 5182–5191.
330. Chen, K.; Koser, G. F. *J. Org. Chem.* **1991**, *56*, 5764–5767.
331. Iwama, T.; Birman, V. B.; Kozmin, S. A.; Rawal, V. H. *Org. Lett.* **1999**, *1*, 673–676.
332. Ooi, T.; Goto, R.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 10494–10495.
333. Le Roux, C.; Dubac, J. *Synlett* **2002**, 181–200.
334. Limat, D.; Schlosser, M. *Tetrahedron* **1995**, *51*, 5799–5806.
335. Ito, H.; Ishizuka, T.; Tateiwa, J.; Hosomi, A. *Tetrahedron Lett.* **1998**, *39*, 6295–6298.
336. Le Roux, C.; Mandrou, S.; Dubac, J. *J. Org. Chem.* **1996**, *61*, 3885–3887.
337. Hirabayashi, K.; Kawashima, J.; Nishihara, Y.; Mori, A.; Hiyama, T. *Org. Lett.* **1999**, *1*, 299–301.
338. Hirabayashi, K.; Mori, A.; Kawashima, J.; Suguro, M.; Nishihara, Y.; Hiyama, T. *J. Org. Chem.* **2000**, *65*, 5342–5349.
339. Hirabayashi, K.; Kondo, T.; Toriyama, F.; Nishihara, Y.; Mori, A. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 749–750.
340. Denmark, S. E.; Wehrli, D. *Org. Lett.* **2000**, *2*, 565–568.
341. Denmark, S. E.; Wehrli, D.; Choi, J. Y. *Org. Lett.* **2000**, *2*, 2491–2494.
342. Denmark, S. E.; Neuville, L. *Org. Lett.* **2000**, *2*, 3221–3224.
343. Denmark, S. E.; Sweis, R. F. *Org. Lett.* **2002**, *4*, 3771–3774.
344. Denmark, S. E.; Sweis, R. F.; Wehrli, D. *J. Am. Chem. Soc.* **2004**, *126*, 4865–4875.
345. Denmark, S. E.; Sweis, R. F. *J. Am. Chem. Soc.* **2001**, *123*, 6439–6440.
346. Denmark, S. E.; Sweis, R. F. *J. Am. Chem. Soc.* **2004**, *126*, 4876–4882.
347. Denmark, S. E.; Ober, M. H. *Org. Lett.* **2003**, *5*, 1357–1360.
348. Denmark, S. E.; Ober, M. H. *Adv. Synth. Catal.* **2004**, *346*, 1703–1714.
349. Denmark, S. E.; Baird, J. D. *Org. Lett.* **2004**, *6*, 3649–3652.
350. Denmark, S. E.; Wang, Z. *Org. Lett.* **2001**, *3*, 1073–1076.
351. Denmark, S. E.; Pan, W. *Org. Lett.* **2003**, *5*, 1119–1122.
352. Mori, A.; Suguro, M. *Synlett* **2001**, 845–847.
353. Koike, T.; Mori, A. *Synlett* **2003**, 1850–1852.
354. Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 1684–1688.
355. Mowery, M. E.; DeShong, P. *J. Org. Chem.* **1999**, *64*, 3266–3270.
356. Denmark, S. E.; Choi, J. Y. *J. Am. Chem. Soc.* **1999**, *121*, 5821–5822.
357. Denmark, S. E.; Wang, Z. *Synthesis* **2000**, 999–1003.
358. Denmark, S. E.; Wu, Z. *Org. Lett.* **1999**, *1*, 1495–1498.

359. Itami, K.; Nokami, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 5600–5601.
360. Wnuk, S. F.; Garcia, P. I., Jr.; Wang, Z. *Org. Lett.* **2004**, *6*, 2047–2049.
361. Nakao, Y.; Oda, T.; Sahoo, A. K.; Hiyama, T. *J. Organomet. Chem.* **2003**, *687*, 570–573.
362. Sahoo, A. K.; Nakao, Y.; Hiyama, T. *Chem. Lett.* **2004**, *33*, 632–633.
363. Sahoo, A. K.; Oda, T.; Nakao, Y.; Hiyama, T. *Adv. Synth. Catal.* **2004**, *346*, 1715–1727.
364. Hosoi, K.; Nozaki, K.; Hiyama, T. *Chem. Lett.* **2002**, 138–139.
365. Katayama, H.; Taniguchi, K.; Kobayashi, M.; Sagawa, T.; Minami, T.; Ozawa, F. *J. Organomet. Chem.* **2002**, *645*, 192–200.
366. Anderson, J. C.; Munday, R. H. *J. Org. Chem.* **2004**, *69*, 8971–8974.
367. Trost, B. M.; Machacek, M. R.; Ball, Z. T. *Org. Lett.* **2003**, *5*, 1895–1898.
368. Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 71–74.
369. Sakurai, H.; Sasaki, K.; Hosomi, A. *Tetrahedron Lett.* **1981**, *22*, 745–748.
370. Mukaiyama, T.; Nagaoka, H.; Murakami, M.; Ohshima, M. *Chem. Lett.* **1985**, 977–980.
371. Kawai, M.; Onaka, M.; Izumi, Y. *Chem. Lett.* **1986**, 381–384.
372. Davis, A. P.; Jaspars, M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 470–471.
373. Trehan, A.; Vij, A.; Walia, M.; Kaur, G.; Verma, R. D.; Trehan, S. *Tetrahedron Lett.* **1993**, *34*, 7335–7338.
374. Lipshutz, B. H.; Burgess-Henry, J.; Roth, G. P. *Tetrahedron Lett.* **1993**, *34*, 995–998.
375. Hollis, T. K.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Tetrahedron Lett.* **1993**, *34*, 4309–4312.
376. Aggarwal, V. K.; Vennall, G. P. *Tetrahedron Lett.* **1996**, *37*, 3745–3746.
377. Davis, A. P.; Muir, J. E.; Plunkett, S. J. *Tetrahedron Lett.* **1996**, *37*, 9401–9402.
378. Kaur, G.; Manju, K.; Trehan, S. *Chem. Commun.* **1996**, 581–582.
379. Yang, Y.; Wang, M.; Wang, D. *Chem. Commun.* **1997**, 1651–1652.
380. Ishii, A.; Kotera, O.; Saeki, T.; Mikami, K. *Synlett* **1997**, 1145–1146.
381. Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, *38*, 7215–7218.
382. Marx, A.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2000**, *39*, 178–181.
383. Ishihara, K.; Hasegawa, A.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2001**, *40*, 4077–4079.
384. Wieland, L. C.; Zerth, H. M.; Mohan, R. S. *Tetrahedron Lett.* **2002**, *43*, 4597–4600.
385. Zerth, H. M.; Leonard, N. M.; Mohan, R. S. *Org. Lett.* **2003**, *5*, 55–57.
386. Knölker, H.-J.; Wanzl, G. *Synlett* **1995**, 378–382.
387. Knölker, H.-J.; Jones, P. G.; Wanzl, G. *Synlett* **1998**, 613–616.
388. Brengel, G. P.; Meyers. A. I. *J. Org. Chem.* **1996**, *61*, 3230–3231.
389. Peng, Z.-H.; Woerpel, K. A. *Org. Lett.* **2000**, *2*, 1379–1381.

9.08
Tin

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9.08.1 Introduction

Organotin compound was prepared at first by Frankland in 1849 from ethyl iodide and zinc which were heated together to give diethyltin diiodide.[1] From 1903, a number of simple and mixed tetraalkyl- and tetraarylstannanes from Grignard reagents and tin tetrachloride or alkyltin halides have been prepared, and this type of reaction soon became the standard route to organotin compounds.[2] Subsequently, various allyl-, benzyl-, and alkyltin halides have been obtained by direct synthesis.[3–8] Tin played a full part in the great increase of activity in organometallic chemistry which began in about 1949, and this was stimulated by the discovery of a variety of applications. Structural studies have always been prominent in organotin chemistry. Mössbauer spectroscopy was extensively used during the 1960s and 1970s for investigating structures in the solid state, but it has now largely given place to X-ray crystallography and high resolution tin NMR spectroscopy.[9–11]

In 1962, trialkyltin hydrides have been shown to react with alkyl halides in a radical chain manner involving short-lived trialkyltin radicals, $R_3Sn\cdot$.[12] Also, the reactions with non-polar alkenes and alkynes (hydrostannation) are showed to follow a similar mechanism,[13,14] and these reactions now provide the basis of a number of important organic synthetic methods. A major development in recent years has been the increasing use of organotin reagents and intermediates in organic synthesis, exploiting both their radical and ionic reactivity.[15,16] This section describes the recent development of organotin reagents used in organic synthesis. In particular, tin hydrides, allylic, allenylic and propargyl tins, tin enolates, tin–heteroarom bonds, and tin–metal bonds are focused. These tin reagents are most widely used as mild, easy-to-handle and easy available reagents for chemo-, regio- and stereoselective modern organic syntheses. Organotin reagents such as vinylic tins and aryltins are often used by the combination with transition metal catalysts. For example, the Migita–Stille reactions rank today amongst the most general transformations in organic synthesis.[17–22] These transition metal-catalyzed reactions are not included in this section because they belong to the field of transition metal chemistry. Synthetic utilizations of reactive and activated organotin reagents are mainly discussed here.

Organotin compounds have been applied in industry, agriculture, and medicine. Although in recent years these have been circumscribed by environmental considerations, recent progress of a variety of novel types of tin reagents overcomes these toxic problems and in some tin reagents shows excellent potential for large-scale application in "green" (environmentally friendly) processes.

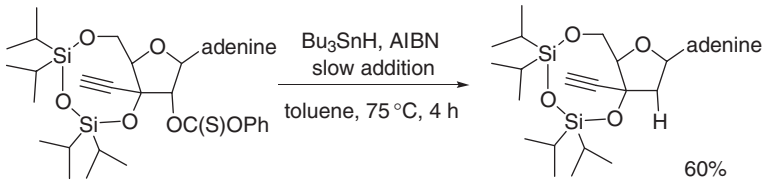
9.08.2 Tin Hydrides

9.08.2.1 Bu_3SnH-promoted Radical Reactions

Organotin hydrides are advantageous as reductants in terms of their facile availability, stability, and reactivity.[23–28] Almost all tin hydrides are liquids, and stoichiometric tin–hydrogen bonds can be used. In general, the tin hydride reductions have been performed under radical conditions using initiators such as azobisisobutyronitrile (AIBN), triethylborane, and UV irradiation. The reduction of organic halides and pseudohalides by tri-*n*-butyltin hydride (Bu_3SnH) proceeds effectively (Equation (1)), and radical cyclizations are representative reactions.[23–25]

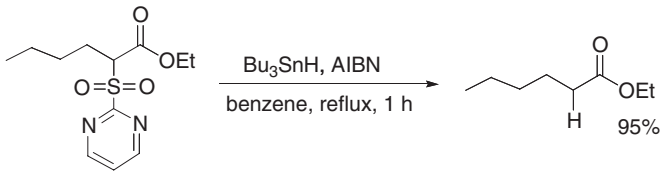
$$Bu_3Sn{-}H \longrightarrow Bu_3Sn\bullet \xrightarrow[-Bu_3SnX]{RX} R\bullet \xrightarrow{Bu_3SnH} R{-}H \qquad (1)$$

Besides carbon–halogen bonds, Bu_3SnH is used routinely for hydrogenolysis of various carbon–heteroatom bonds. The deoxygenation from alcohols has been performed by a Barton–McCombie reaction where the addition of tin hydride to the triple bond is suppressed (Equation (2)).[29–31]



(2)

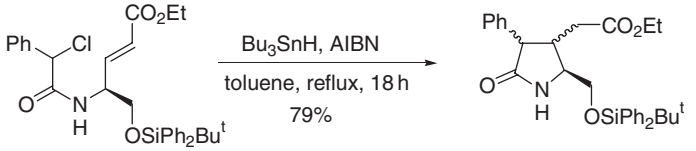
For the cleavage of saturated sulfones, although no change of 2-phenylsulfonyl group takes place, parallel treatment of 2-pyrimidin-2-ylsulfonyl groups leads to a facile reduction (Equation (3)).[32]



(3)

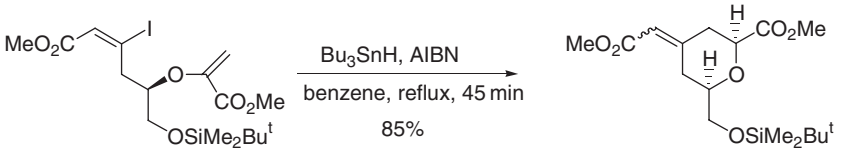
9.08.2.2 Radical Cyclizations

The radical cyclizations are conventionally performed by using Bu_3SnH. Initially, tri-*n*-butyltin radical ($Bu_3Sn\cdot$) reacts with an organic halide to form its carbon radical. Next, the carbon radical attacks to various acceptors such as carbon–carbon double bonds. At last, hydrogen transfer occurs and the tin radical is generated. Recently, various cyclic compounds such as Penitrem D rings[33] and indole alkaloids[34] have been synthesized by radical reactions. For the synthesis of phenyl allokainoids, tin-mediated cyclization of a secondary amide is the key step (Equation (4)).[35,36] Bridgehead nitrogen heterocycles are also synthesized by the similar type of cyclization.[37] Intramolecular additions of aryl radical to a pyridine ring giving quinolines have been shown.[38–40]

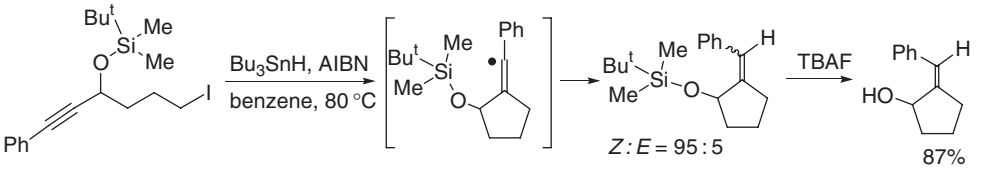


(4)

Vinyl radicals also add to carbon–carbon double bonds intramolecularly to give 2,6-*cis*-disubstituted cyclic ethers (Equation (5)).[41] In the tin hydride-mediated cyclization of the substrates including alkynes, alkyl radicals attack to carbon–carbon triple bonds leading to *exo*-alkylidene allylic alcohols (Equation (6)).[42] The coupling reaction between alkyl radicals may afford cyclization products. Thus, the reduction of 1,3-diiodopropane derivatives with a tin hydride provides substituted cyclopropanes.[43]

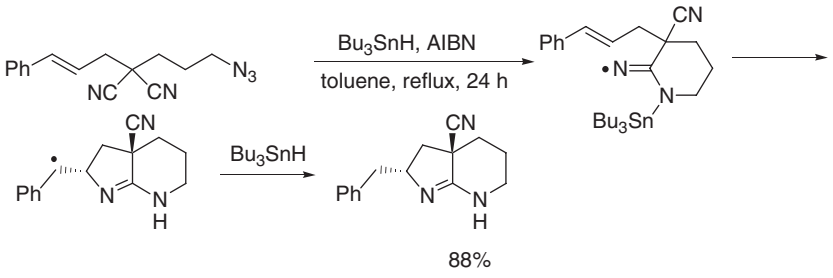


(5)



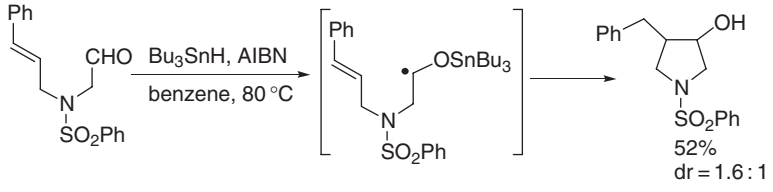
(6)

Stannylaminyl radicals derived from Bu_3SnH and azidoalkyl malononitriles exhibit 6-*exo*-cyclization onto either nitrile group to give aminoiminyl radicals that undergo successive 5-*exo*-cyclization onto an internal alkene (Equation (7)).[44]



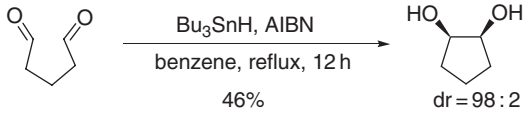
(7)

A tin radical adds to alkynes or allenes to form vinyl radicals which react with intramolecular C═N bonds to give heterocycles.[45–48] The addition of a tin radical to C═O bond forms *O*-stannyl ketyl which affords a cyclic compound via intramolecular radical addition to C═C bond (Equation (8)).[49]



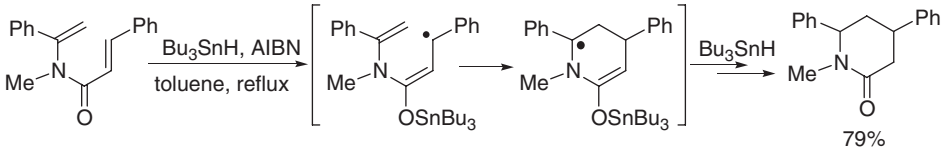
(8)

Analogous reductive cyclization is also established via *O*-stannyl ketyls by using a dicarbonyl compound (Equation (9)).[50]

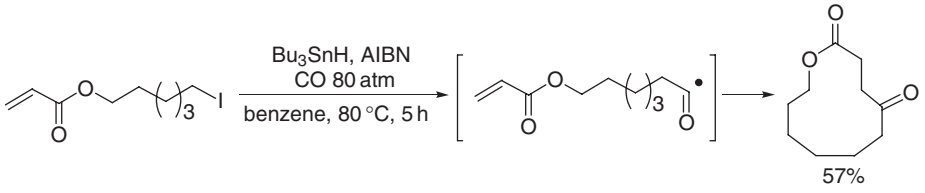


(9)

Cyclization of alkyl radicals derived from acryl enamides gives piperidin-2-ones (Equation (10)).[51] Radical carbonylations have become a promising tool for the introduction of carbon monoxide into organic molecules.[27,28,52,53] Macrocyclic compounds are prepared by intramolecular cyclization via radical carbonylation (Equation (11)).[53]



(10)

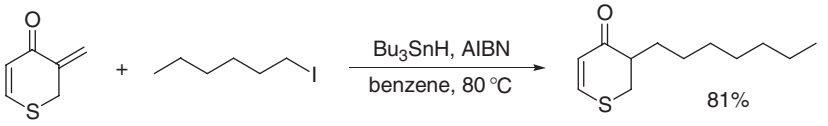


(11)

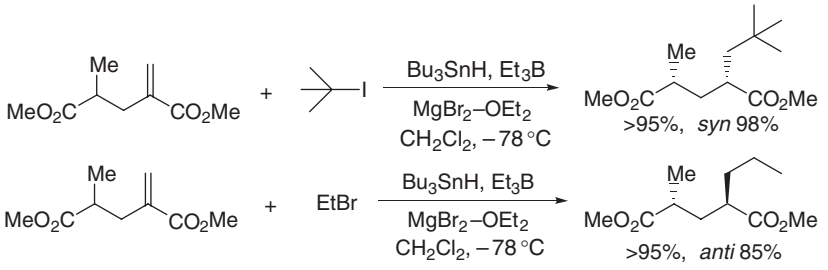
9.08.2.3 Intermolecular Radical Coupling

Radical coupling of organic halides with alkenes or alkynes takes place intermolecularly (Equation (12)).[54] Tin hydride-mediated radical additions to a series of α-methyleneglutarates furnish 2,4-dialkyl-substituted glutarates.[55] Using $MgBr_2{\cdot}OEt_2$ as an additive, exclusive *syn*-selectivities are achieved upon *tert*-butyl radical addition at −78 °C.

On the other hand, high *anti*-selectivities are observed when smaller alkyl radicals such as cyclohexyl, ethyl, and methyl are used (Equation (13)).

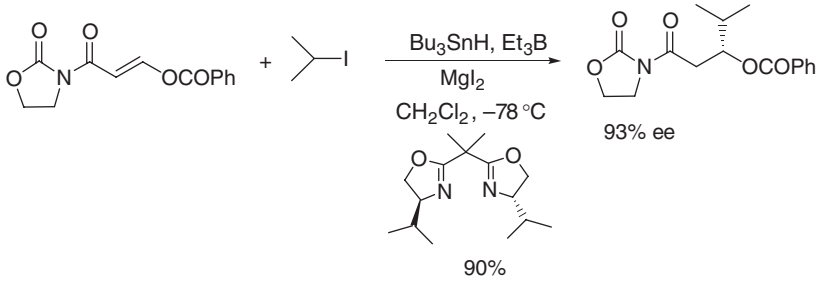


(12)



(13)

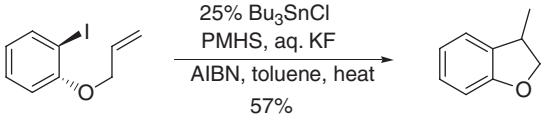
Highly enantioselective couplings have been established by using chiral Lewis acid catalysts (Equation (14)).[56]



(14)

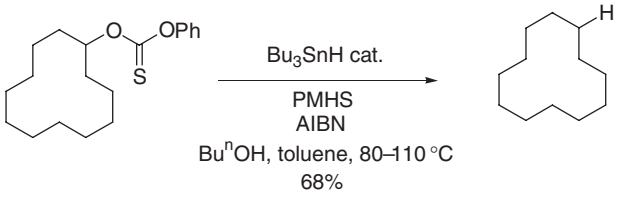
9.08.2.4 Tin Hydrides as Catalytic Use

The *in situ* generation of tin hydrides from inexpensive starting materials, polymethylhydrosiloxane (PMHS; TMSO–$(SiHMeO)_n$–TMS), can be applied to reducing the use of tin compounds (Equation (15)).[57]



(15)

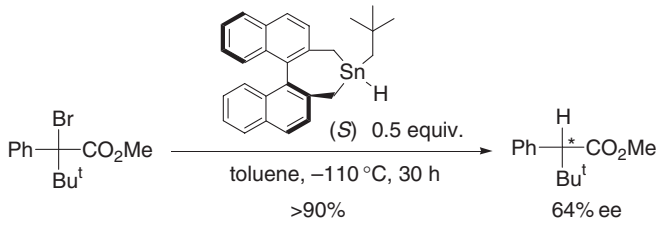
In the conjugate reduction of enals and enones, tin hydride is used catalytically by the combination with $PhSiH_3$.[58] Barton–McCombie deoxygenation reaction is performed by using Bu_3SnH catalyst and PMHS as a stoichiometric reductant (Equation (16)).[59]



(16)

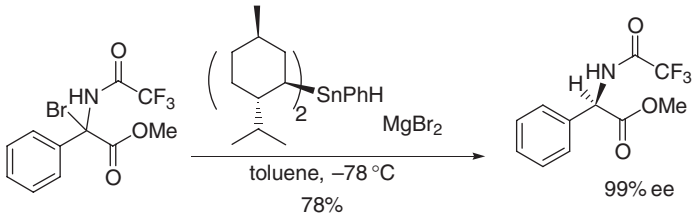
9.08.2.5 Chiral Tin Hydrides

Nanni and Curran initially developed binaphthyl tin hydrides.[60] Their modified reagents accomplish enantioselective hydrogen transfer to organic halides (Equation (17)).[61,62]



(17)

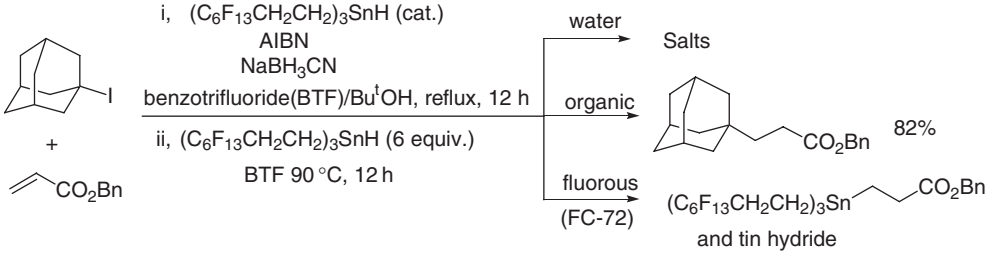
Addition of 1 equiv. of Lewis acid to free-radical reduction by the tin hydride bearing chiral menthyl groups leads to a remarkable increase of the enantioselectivity (Equation (18)).[63,64]



(18)

9.08.2.6 Fluorous Tin Hydrides

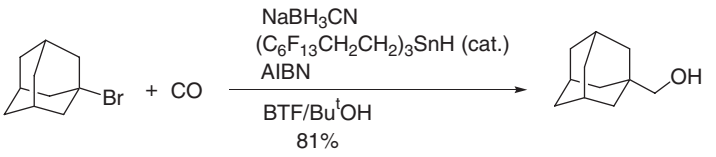
Tin hydrides of the general formulas $[Rf(CH_2)_n]_3SnH$ and $[Rf(CH_2)_n]Me_2SnH$ have been prepared where Rf is C_4F_9, C_6F_{13}, C_8F_{17}, or $C_{10}F_{21}$ and n is 2 or 3. These reagents are highly soluble in fluorinated solvents and generally useful for the reactions that can be conducted typically with Bu_3SnH.[65–67] Fluorous procedures feature very easy separation of fluorous tins from organic products by convenient liquid–liquid or solid–liquid extractions. The tin reagents are recovered from reaction mixtures and routinely reused. This reaction can be used to introduce the technique of "fluorous quenching" whereby a residual undesired organic component is switched to the fluorous phase to allow its removal during workup. As an example, adamantyl iodide and an excess of benzyl acrylate are treated with fluorous tin hydride under the standard catalytic conditions. The resulting mixture is subjected to the hydrostannation with excess fluorous tin hydride followed by perfluorohexane (FC-72)/CH_2Cl_2 extraction. From the organic phase, the desired adduct is isolated free from the starting alkene and tin compounds (Equation (19)).[67]



(19)

Organofluorine compounds are well known to be highly soluble in supercritical CO_2, and so typical radical reactions can be conducted in this media with a fluorous tin hydride.[68] By using a catalytic amount of fluorous tin

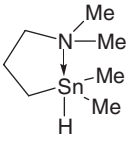
hydride, CO, and $NaBH_3CN$ as a reducing agent, hydroxymethylation of organic halides proceeds smoothly to give one-carbon homologated alcohols (Equation (20)).[69]



(20)

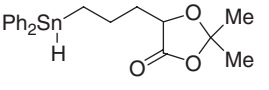
9.08.2.7 Water-soluble Tin Hydrides

Tri-*n*-butyltin hydride is soluble only in typical organic solvents. On the other hand, a polyether-substituted tin hydride, $(CH_3OCH_2CH_2OCH_2CH_2CH_2)_3SnH$, has sufficient water solubility to be a useful reagent in aqueous reactions. In addition, the reaction product of this reagent is the corresponding tin oxide species that can be easily recovered and recycled.[70] Tin hydride $[Me_2Sn(H)(CH_2)_3NMe_2]$ **1** derived from *N*,*N*-dimethylpropargylamine has excellent water solubility thus representing a sevenfold increase in the solubility compared to $(CH_3OCH_2CH_2OCH_2CH_2CH_2)_3SnH$. The internal coordination to the tin hydride **1** causes a high reactivity to promote an effective dehalogenation of simple iodobenzoic acids in water at ambient temperature without addition of an initiator.[71]



1

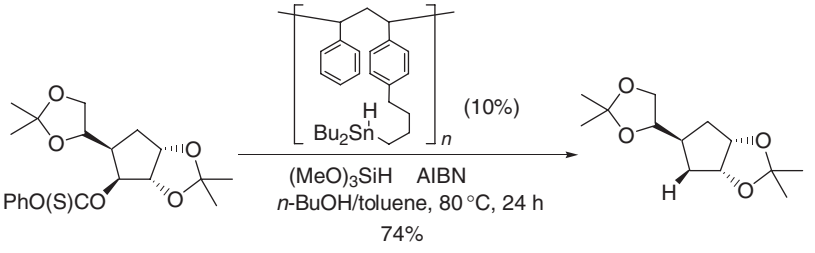
Tin hydride **2** prepared from hydroxyl acid behaves like the conventional Bu_3SnH in standard free-radical reactions, but the tin-containing by-products are easily removed by mild hydrolysis which converts them into base-soluble materials. The performance of these tin hydrides is evaluated for a range of radical reactions involving halides, selenides, Barton–McCombie deoxygenation, and enyne cyclizations.[72]



2

9.08.2.8 Polymer-supported Tin Hydrides

The use of polystyrene beads-supported organotin hydride and the catalytically generated tin hydride from the polymer-bound organotin halide reduces the tin pollution level while keeping a high reduction power.[73,74] Secondary alcohols are deoxygenated by the Barton–McCombie procedure involving a catalytic amount of supported tin hydride in the presence of trimethoxysilane (Equation (21)). The products are then separated from the catalyst by a simple filtration avoiding pollution by toxic tin by-products.[75]

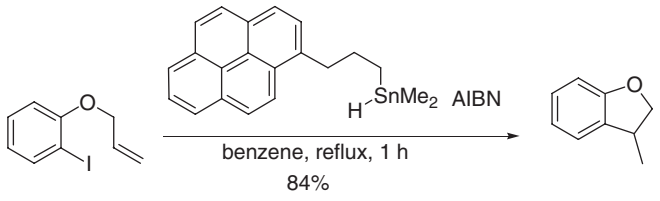


(21)

The porous polymer-supported tin hydride is also good alternative to Bu_3SnH to prevent tin contamination and to facilitate product separation.[76]

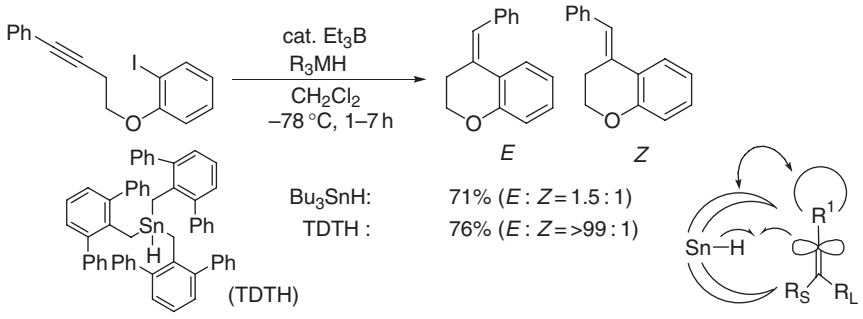
9.08.2.9 Tin Hydrides with Bulky Substituents

The tin hydride having 3-pyrenylpropyl side chain simplifies tin removal and product isolation (Equation (22)). Tin side-products would be easily removable by adsorption on activated carbon.[77]



(22)

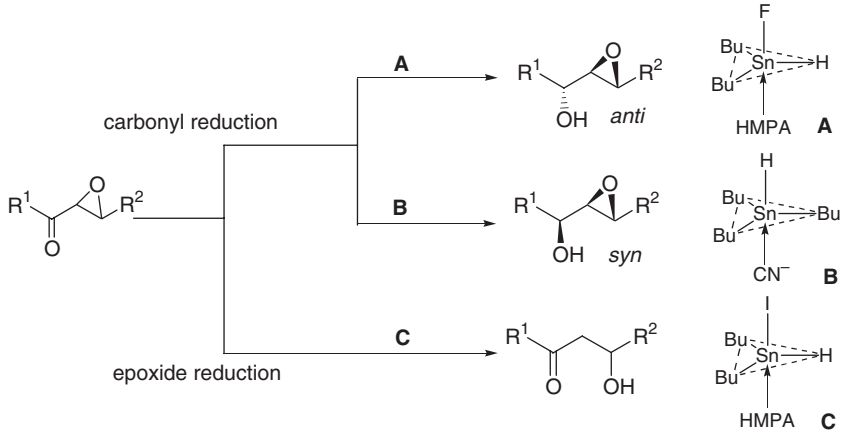
The bowl-shaped tin hydride, tris(2,6-diphenylbenzyl)tin hydride (TDTH), and catalytic Et_3B effect the radical cyclization of *o*-iodophenyl 3-phenylpropynyl ether with excellent stereoselectivity, implying remote stereochemical control (Equation (23)).[78]



(23)

9.08.2.10 Halogenotin Hydrides

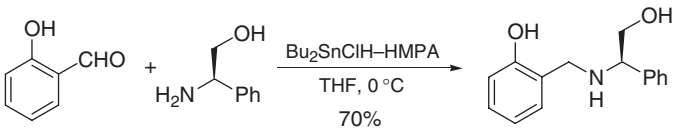
Stereoselective reduction of α-substituted β-keto acid derivatives is of great synthetic value because the aldol reaction is not always satisfactory.[79] Various reagents such as borohydrides are used for the selective reduction.[80] Using $R_2SnH_2/Bu_2Sn(OTf)_2$ system improves the chelation-controlled stereoselectivity.[81] In the reduction of α,β-epoxy ketones, Bu_2SnFH–HMPA system **A** reduces only the carbonyl groups to *anti*-alcohols without cleavage of the epoxy rings. Bu_3SnH–Bu_4NCN **B** affords the highest level of *syn*-selectivities.[82] β-Hydroxy ketones are produced from α,β-epoxy ketones by Bu_2SnIH–HMPA system **C** (Equation (24)).[83]



(24)

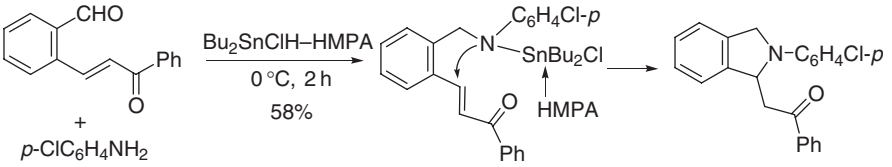
The reduction of 2-imino ketones is performed with Bu_2SnClH–HMPA to give 2-amino ketones where no reduction of the carbonyl group takes place.[84] The reductive amination of carbonyl compounds is one of the most convenient routes to various secondary amines. The high imine selectivity of Bu_2SnClH–HMPA can be applied to

reductive amination (Equation (25)).[85] Compared with the conventional reductant $NaBH_3CN$, Bu_2SnClH–HMPA is useful in the reactions involving weakly basic amines.



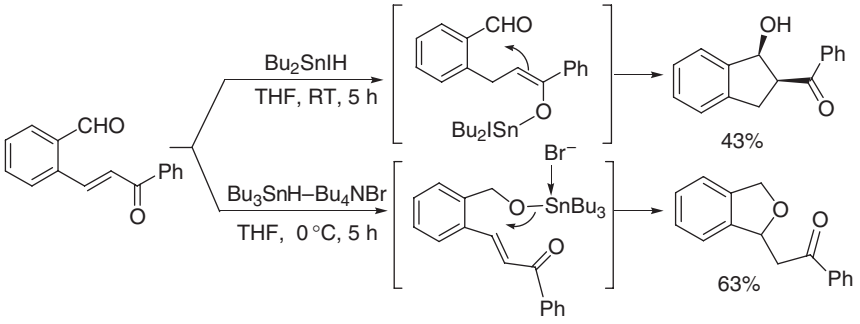
(25)

By using the substrates involving both formyl and enone moieties, a tandem reaction of reductive amination Michael addition gives isoindoline derivatives (Equation (26)).[86]



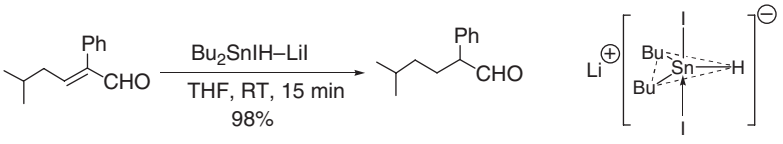
(26)

The general order of reactivity among carbonyl groups is enones < ketones < enals < aldehydes as exhibited in the reductions with $NaBH_4$.[87] This result indicates the difficulty in reversing the reactivity order between aldehydes and enones. Bu_2SnIH, however, promotes the selective 1,4-reduction of an enone group over formyl one to produce an aldol as a final product. In contrast, the combination of Bu_3SnH and Bu_4NBr effects aldehyde-selective reduction, and a subsequent Michael addition gives a cyclic ether (Equation (27)).[88]



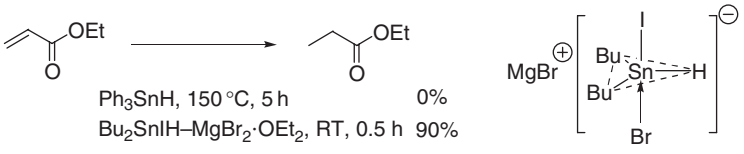
(27)

Iododi-*n*-butyltin hydride–LiI system allows the conjugate hydrostannation of enals under mild and neutral conditions without the assistance of transition metal catalysts (Equation (28)).[89] Bu_2SnIH alone gives a mixture of hexanal and the allylic alcohol derived from both 1,4- and 1,2-reductions, respectively. The formation of an ate complex $Li^+[Bu_2SnI_2H]^-$ and its TBP structure are confirmed by ^{119}Sn NMR spectra.[89]



(28)

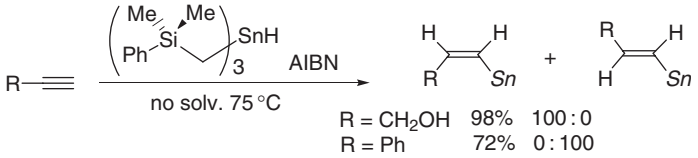
The ate complex $[MgBr]^+[Bu_2SnBrIH]^-$ promotes the conjugate addition to α,β-unsaturated esters (Equation (29)).[90] The results that non-substituted alkenes are more reactive than the substituted ones indicate an ionic mechanism for this hydrogenation, because the reactivity order is reverse in the radical reactions where the non-substituted unsaturated esters are unreactive.[91]



(29)

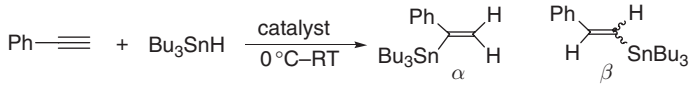
9.08.2.11 Hydrostannation to Alkynes

Hydrostannation of alkynes is one of the simplest and direct routes to vinylstannanes which have great versatility as building blocks in syntheses. However, a variety of regio and stereo isomers are usually formed.[17–22] Until now, the selectivities are controlled by using different types of tin hydrides described above.[26,92] For aryl-subsutituted alkynes, radical stannylation leads to the regioselective formation of the β-adducts but with poor stereoselectivity. The addition of bulky tris[(phenyl dimethylsilyl)methyl]tin hydride indicates that these reactions take place with complete kinetic or thermodynamic stereoselectivity (Equation (30)).[93]



(30)

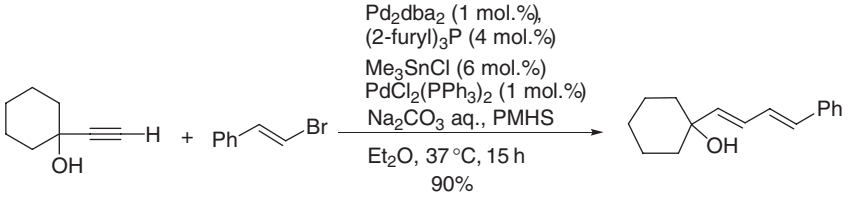
The $RhCl(PPh_3)_3$-catalyzed *syn*-hydrostannation occurs with a preference for α-addition of the tin moiety.[94] Contrary to the transition metal catalysts, the use of Lewis acids such as $ZrCl_4$ leads to *anti*-addition of the Bu_3SnH, furnishing the β-(*Z*)-isomer (Equation (31)).[95]



Catalyst	*Yield* (%)	$\alpha:\beta$ (*E*:*Z*)
$RhCl(PPh_3)_3$	86	88 : 12 (100 : 0)
$ZrCl_4$	73	0 : 100 (5 : 95)

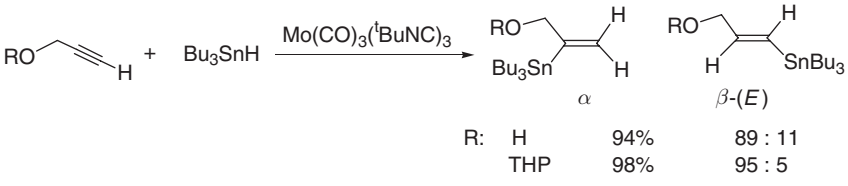
(31)

In the hydrostannation of propagylic alcohols and ethers, Pd catalysts afford slight α-selectivity probably due to electronic and/or coordinative effects. The presence of an oxygen functionality can influence the regioselectivity. The degree of this influence decreases as the functional group is moved away from the alkyne moiety.[96] A bulky substituent at the propargylic position leads to a preference for β-addition products.[97] The highly β-selective hydrostannation is applicable to subsequent Stille coupling reaction. By recycling the organotin halide formed in Stille couplings into the corresponding organotin hydride, a hydrostannylation/cross-coupling sequence can be carried out with catalytic amounts of tin (Equation (32)).[98]



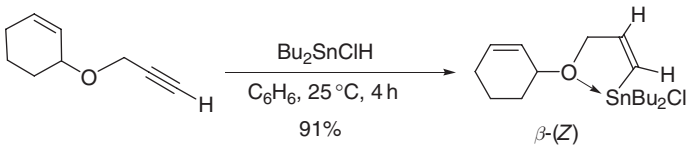
(32)

In the case using $Mo(CO)_3(Bu^tNC)_3$ as a catalyst, propargylic alcohols and ethers undergo highly regioselective α-hydrostannation regardless of their substitution pattern (Equation (33)).[99]



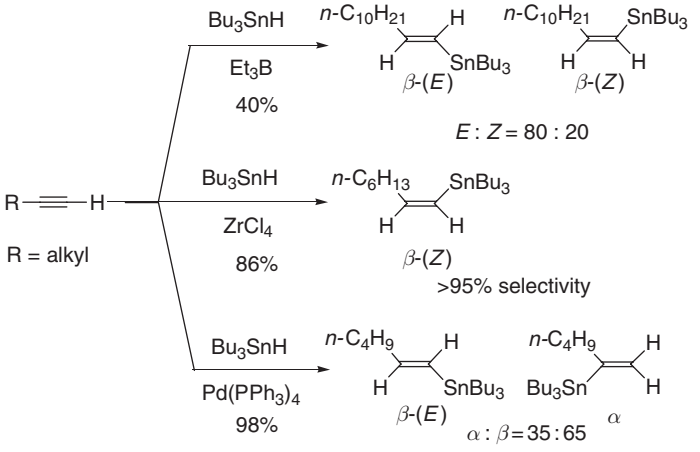
(33)

Chlorodi-*n*-butyltin hydride (Bu_2SnClH) promotes regio- and stereo-selective hydrostannation of propargylic ethers without any additives or catalysts to give β-(*Z*) adduct as single isomer (Equation (34)). Effective coordination of ether oxygen to tin moiety determines the selectivity.[100,101]



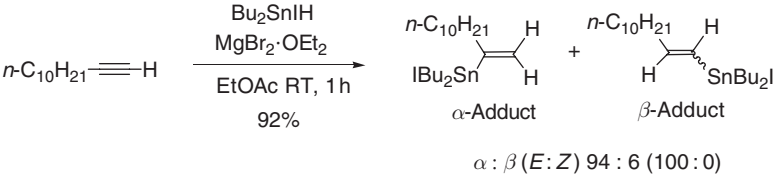
(34)

In the Bu_3SnH-promoted radical reactions to aliphatic alkynes, using initiators such as AIBN,[102] Et_3B,[103] and ultrasound[104] furnishes β-adducts as a mixture of (*E*)- and (*Z*)-isomers. Lewis acid catalysts give β-(*Z*) isomers,[96] whereas transition metal catalysts furnish the predominant formation of β-(*E*) isomers.[105] The α-stannylation of simple aliphatic alkynes, however, is particularly difficult because of the absence of anchor substituents such as ethers. In the general hydrostannations of aliphatic alkynes, α-adducts are obtained only as minor adducts in the Pd-catalyzed reaction (Equation (35)).



(35)

When the hydrostannation of 1-*n*-dodecyne is performed with Bu_2SnIH systems, the sole use of Bu_2SnIH gives a mixture of *E*/*Z* isomers. The tin hydride ate complex, Bu_2SnIH–$MgBr_2{\cdot}OEt_2$ shows the highest effect where an α-stannylated alkene is obtained (Equation (36)).[106] The employment of EtOAc as a solvent sharply increases the yield of the α-stannylated adduct.



(36)

9.08.3 Allylic Tins

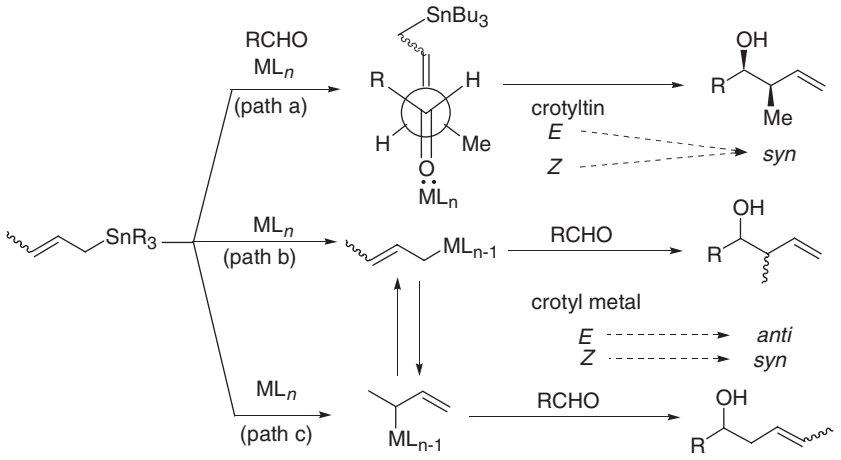
9.08.3.1 General

Allylation of carbonyl and imino groups is one of the most convenient methods for the introduction of allylic functions.[107–110] Allylic tin compounds have high σ–π interaction between C=C and C–Sn bonds which makes them more reactive than the corresponding silicon derivatives.[111,112] In spite of their high reactivity, tin compounds are stable enough to be isolated and to react at ambient temperature under aerobic conditions. These factors allow them to be applicable to various types of reactions, for example, thermal,[113] high-pressure,[116] transition metal-catalyzed,[117,118] radical,[119,120] photochemical,[121,122] tin–lithium exchange reactions,[108,113] and so on. A broad

approach toward their numerous applications to chemo-, regio-, and stereoselective reactions has been established. Recently, selectivity in Lewis acid-promoted reactions has been highlighted,[123] which are classified in two modes: (i) activation of the electrophilic substrates and (ii) activation of the tin reagents.

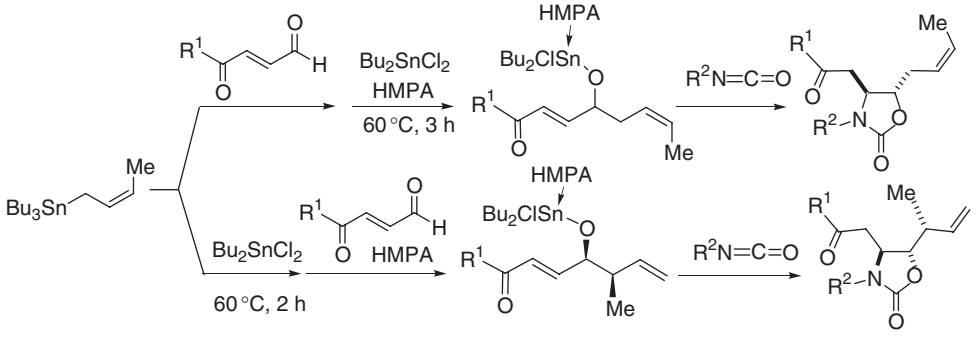
9.08.3.2 Equimolar Lewis Acid-promoted Reactions

The effect of addition modes upon product distribution has been investigated in the reaction of (*E*)- and (*Z*)-crotyltributyltins with aromatic or aliphatic aldehydes in the presence of Lewis acids (Equation (37)).



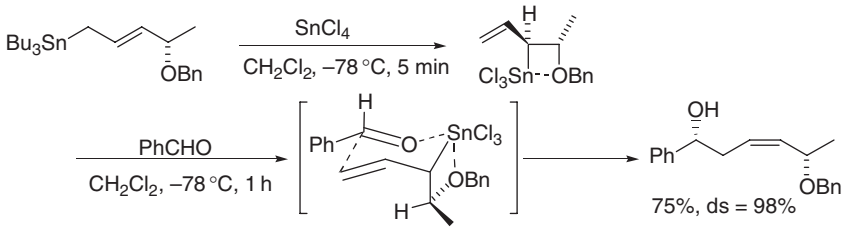
(37)

The detailed experimental results indicate that the crotyltributyltin-aldehyde condensation via the RCHO–Lewis acid complex primarily proceeds through the acyclic mechanism. Either *cis*- or *trans*-crotyltributyltins react with aldehydes in the presence of $BF_3{\cdot}Et_2O$ to yield predominantly *syn*-products. The coordination of BF_3 to the carbonyl oxygen prevents the interaction between the tin center and the oxygen atom. Consequently, the most sterically favorable antiperiplanar conformation leads to the *syn*-isomers (path a).[124] In some cases, the transmetallation between crotyltributyltin and Lewis acids takes place, and the resulting new allylic species participate in the condensation reaction. The balance between the former and latter mechanism depends upon the mode of mixing, a feature of Lewis acids, and reactivity of aldehydes. When a normal addition order [(i) RCHO, (ii) Lewis acid, (iii) crotyltin] is used, high *syn*-selectivity is obtained in the presence of $TiCl_4$. On the other hand, dropwise addition of crotyltributytin to a solution of $TiCl_4$ in CH_2Cl_2 at −78 °C, stirring at that temperature for 8–10 min, and then dropwise addition of aldehyde affords the *anti*-adduct with excellent selectivity (21 : 1).[125] Clearly, the inverse addition produces crotyltitanium intermediate via transmetallation from tin to titanium, which reacts with an aldehyde through a six-membered chairlike cyclic transition state (path b). If a transmetallation is involved, the product may consist of a mixture of regioisomers due to allylic rearrangement of the allylic metal intermediate. For example, transmetallation of crotytributyltin with Bu_2SnCl_2 would proceed via SE′ process to produce the α-methallyltin intermediate, which reacts with aldehydes to give the α-adducts (path c).[126] At elevated temperature, α-methallyltin intermediate rearranges to a crotyltin derivative. This procedure is applied to the one-pot synthesis of nitrogen heterocyclic compounds, in which changing the timing of Bu_2SnCl_2 addition induces different structure of the side chain on the rings (Equation (38)).[127]



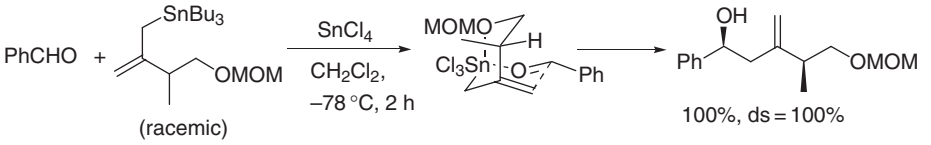
(38)

Transmetallation with $SnCl_4$ is well used for the control of regio- and stereoselectivities.[128] As an example of 1,5-induction, tin(IV) chloride-promoted reactions betweeen aldehydes and alkoxy-substituted allyltins give the linear adducts 1,5-*syn*(*Z*)-alkenols with excellent stereoselectivity (Equation (39)).[129–133]



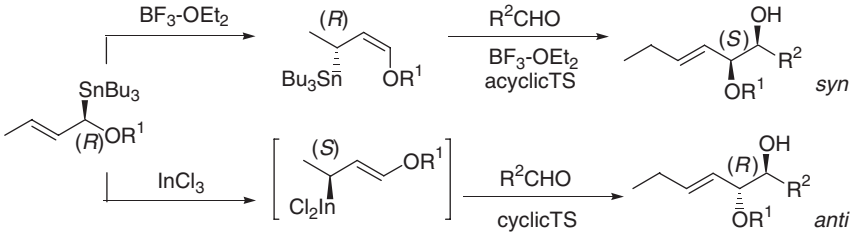
(39)

Chelation between tin and oxygen atoms also plays a role for the formation of 1,4- *syn* isomers from *δ*-oxygenated allylic tin (Equation (40)).[134,135]



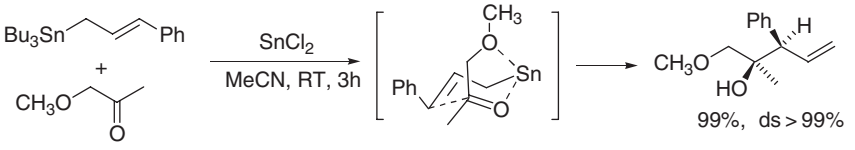
(40)

Enantioenriched (*R*)-alkoxy allylic tins are readily transformed to the *γ*-isomers by a stereospecific intermolecular *anti*-process catalyzed by $BF_3{\cdot}OEt_2$. Treatment of allylic tin reagents with various aldehydes in the presence of stoichiometric amounts of $BF_3{\cdot}OEt_2$ leads to *syn*-adducts with high diastereoselectivity. $InCl_3$ effects a stereospecific *anti*-S_E2' transmetallation of alkoxy stannanes to give a transient allylic indium reagent which provides a stereospecific cyclic transient state mechanism to give the *anti*-adducts (Equation (41)).[136–138]



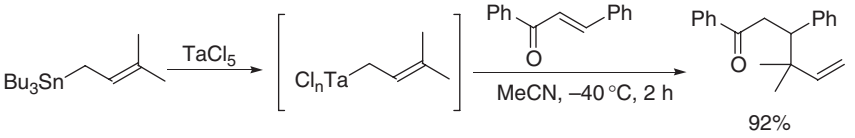
(41)

Transmetallation between cinnamyl tri-*n*-butyltin with $SnCl_2$ leads to an active cinnamyltin(II) species (Equation (42)). A bicyclic transition state favorably promotes highly regioselective additions since the chlorinated tin(II) center is highly capable of accepting ligands.[139]



(42)

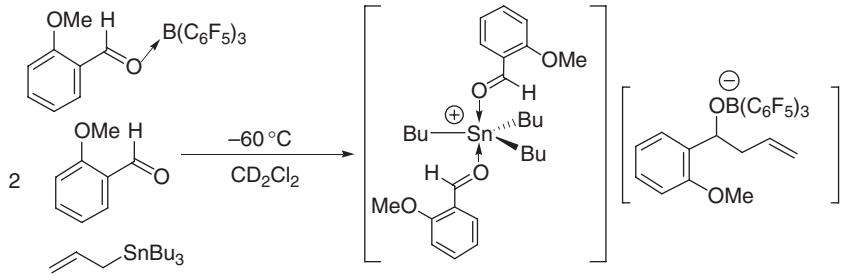
Compared with the direct allylation of carbonyl groups, little has been reported on the selective conjugate allylation of enones. Allylic tantalum species, generated by the Sn–Ta exchange, is the choice of tools for performing conjugate addition of sterically hindered allylic groups (Equation (43)).[140]



(43)

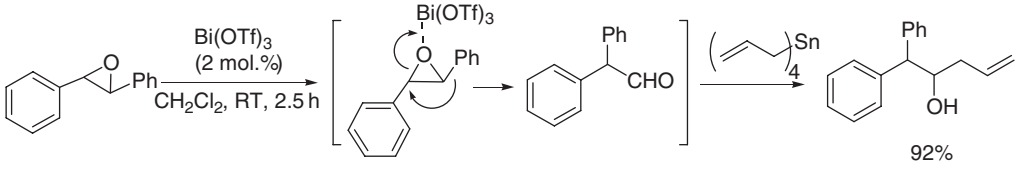
9.08.3.3 Lewis Acid-catalyzed Reactions

Recently, catalytic amounts of Lewis acids have been used in the reaction of allyllic tri-*n*-butyltins with carbonyl compounds. Maruoka *et al.* report the remarkably chemoselective allylstannation of *o*-anisaldehyde over *p*-anisaldehyde, catalyzed by $B(C_6F_5)_3$.[141,142] Piers *et al.* report that the chemoselectivity observed does not rely on classical chelation control. They conclude that stannylium ion pair $[Bu_3Sn(o\text{-anisaldehyde})_2]^+[o\text{-ArCH(allyl)OB}(C_6F_5)_3]^-$ is the active species which is preferentially formed over the complex of *p*-anisaldehyde with $B(C_6F_5)_3$ (Equation (44)).[143] Lambert *et al.* report a similar formation of stannyl cation from allyltri-*n*-butyltin and trityl $(C_6F_5)_4B^-$.[144]



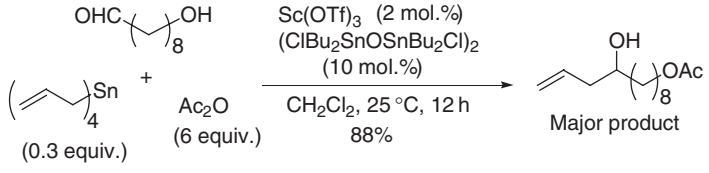
(44)

As Lewis acid catalysts, lanthanide trifrates have been developed for allyltri-*n*-butyltin-promoted reactions.[145,146] $Sc(OTf)_3$ can be used in water containing acetonitrile ($MeCN/H_2O = 9/1$) for the allylation by reactive tetraallyltin.[147] PbI_2–HMPA works as a catalyst for the chemoselective allylation to carbonyls of α-haloketones to afford acid-sensitive vinylepoxydes directly.[148] In the reaction of aromatic aldehydes with crotyltri-*n*-butyltin, Bu_4NBr/PbI_2 catalyst gives high *syn*-selectivity irrespective of *E*/*Z* geometry of the crotyltins in water without any aprotic solvents.[149] Epoxides react smoothly with tetraallyltin in the presence of 2 mol.% of $Bi(OTf)_3$ under mild reaction conditions to afford the homoallylic alcohols via the rearrangement to aldehydes in excellent yields with high regioselectivity (Equation (45)), while aryl aziridines underwent cleavage in a regioselective manner with direct attack at the benzylic position.[150]



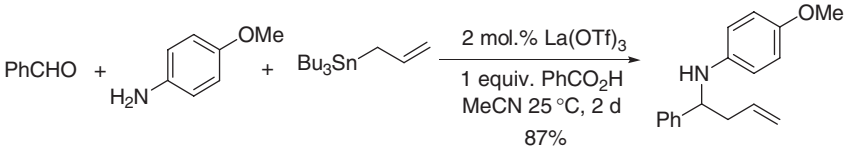
(45)

The combined catalyst of $Sc(OTf)_3$ and distannoxane gives the one-treatment process. Namely, in the reaction of ϖ-hydroxy alkanal, one-pot aldehyde allylation and acetylation of a primary alcohol are achieved without protection/deprotection procedures. The unwanted acetylation of a secondary homoallyl alcohol by $Sc(OTf)_3$ is suppressed by hybridization with distannoxane (Equation (46)).[151]



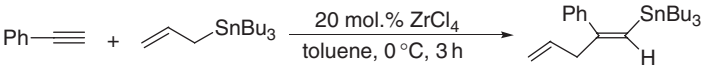
(46)

Lewis acid-mediated nucleophilic additions to carbon–nitrogen double bond have been applied to the synthesis of homoallylic amines.[152,153] Three-component syntheses of homoallylic amines starting from aldehydes, amines, and allyltributyltin are realized in the presence of Lewis acids such as $La(OTf)_3$, $Bi(OTf)_3$, $LiClO_4$ (Equation (47)).[154–156]



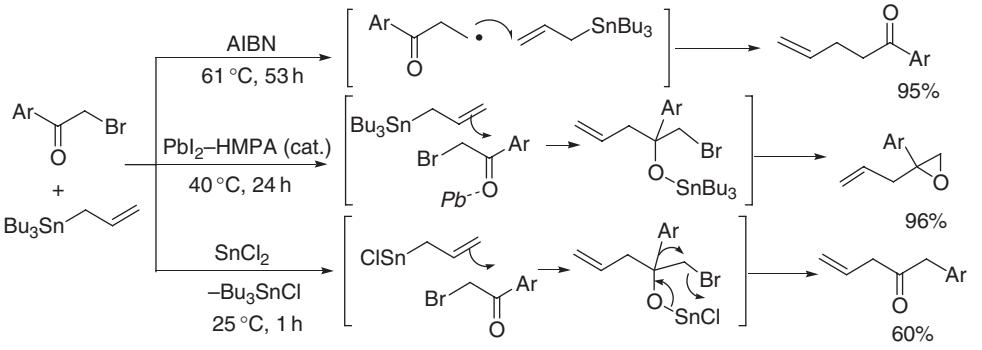
(47)

The use of $Sc(OTf)_2$ and $SnCl_2$/SDS systems enables the reaction with imines in water.[157,158] The allylmetallation of simple unactivated alkynes is not easy, and proceeds usually with poor regio- and stereoselectivity. $ZrCl_4$-catalyzed allylstannylation of unactivated alkynes, however, proceeds with high regio- and stereoselectivities (*anti*-addition) (Equation (48)).[159]



(48)

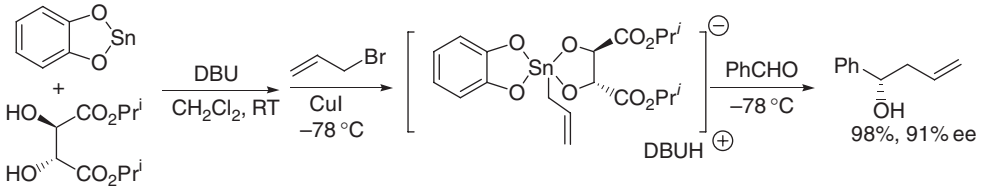
In the reaction of *α*-halo ketones with allyltri-*n*-butyltin, the choice of accelerators determines the reaction course (Equation (49)). Radical reaction affords the coupling at the halogen moiety.[160,161] PbI_2-HMPA acts as a mild Lewis acid to afford the allylation of the carbonyl group. Subsequent cyclization gives allyl epoxides in one-pot reaction.[162] The treatment with $Sn(II)Cl_2$ causes transmetallation to give allytin(II) species. Carbonyl allylation followed by the rearrangement of aromatic substituent gives allylketones.[163]



(49)

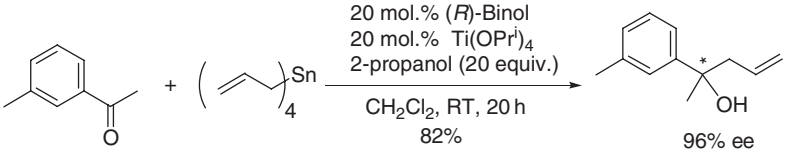
9.08.3.4 Asymmetric Reactions

Asymmetric allylation is performed by chiral allylating reagents. The chiral allyltin generated *in situ* from benzodiostannole [$Sn(O_2C_6H_4)$], allyl halide, chiral dialkyl tartrates and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) reacts with aromatic aldehydes in the presence of copper salts to afford the chiral homoallyl alcohols (Equation (50)).[164]



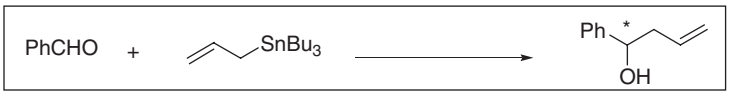
(50)

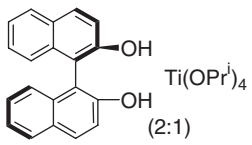
Practical and efficient asymmetric allylation of aldehydes is successfully promoted by Lewis acid catalysts bearing chiral auxiliaries to afford high levels of enantioselectivity.[165] The effective catalysts for asymmetric allylation to benzaldehyde are shown below (Scheme 1).[166–176] The catalytic asymmetric allylation of ketones has proved to be a more challenging transformation owing to the significantly low reactivity compared to aldehydes. In 2002, a catalyst based on titanium complex was developed (Equation (51)).[177,178]



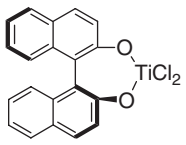
(51)

The first catalytic asymmetric allylation of imines has been reported using allyltri-*n*-butyltin in the presence of a chiral π-allylpalladium complex.[179] Zirconium is also demonstrated as a metal center for the design of chiral Lewis acid catalysts that are suitable for the activation of bidentate imino compounds.[180] Jørgensen reports high enantioselective allylation of α-imino esters (Equation (52)).[181]

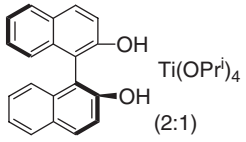




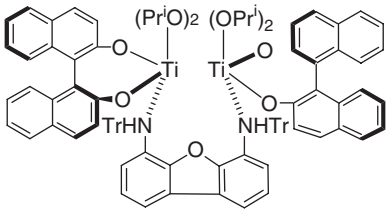
10 mol.%, CH_2Cl_2, –20 °C, 50 h
98%, 96% ee (*R*)[166]



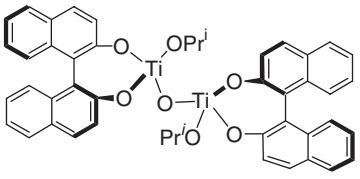
20 mol.%, CH_2Cl_2, MS4A, RT, 48 h
96%, 82% ee (*S*)[167]



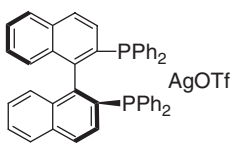
10 mol.% Et_2BSPr^i (1.2“——Ê)
CH_2Cl_2, MS4A, –20 °C, 5 h
89%, 96% ee (*S*)[168,169]



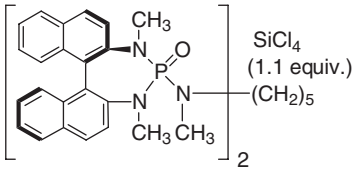
10 mol.%, CH_2Cl_2, MS4A, 0 °C, 2.5 h
94%, 98% ee (*S*)[170]



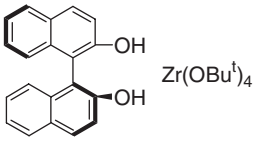
10 mol.%, CH_2Cl_2, 0 °C, 7 h
90%, 96% ee (*S*)[171]



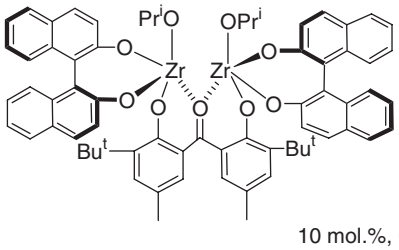
5 mol.%, THF, –20 °C, 8 h
88%, 96% ee (*S*)[172]



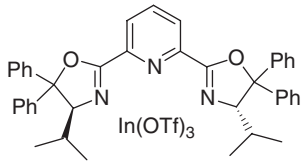
5 mol.%, CH_2Cl_2, –78 °C, 6 h
91%, 94% ee(*R*)[173]



10 mol.%, toluene–pivalonitrile,
MS4A, –20 °C, 1.5 h
90%, 85–90% ee[174]

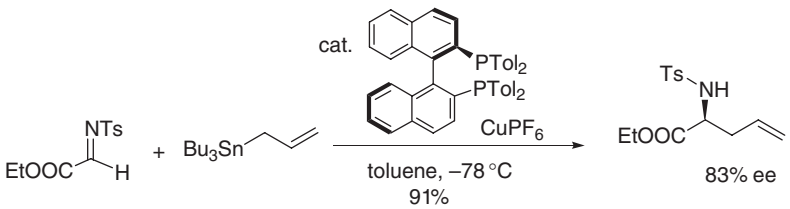


10 mol.%, CH_2Cl_2, MS4A, 0 °C, 4–6 h
91%, 94% ee (*S*)[175]



20 mol.%, CH_2Cl_2, –80 °C, 3 h
81%, 92% ee (*R*)[176]

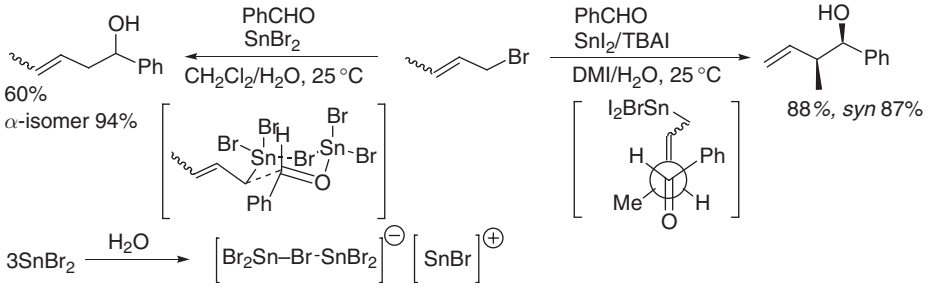
Scheme 1



(52)

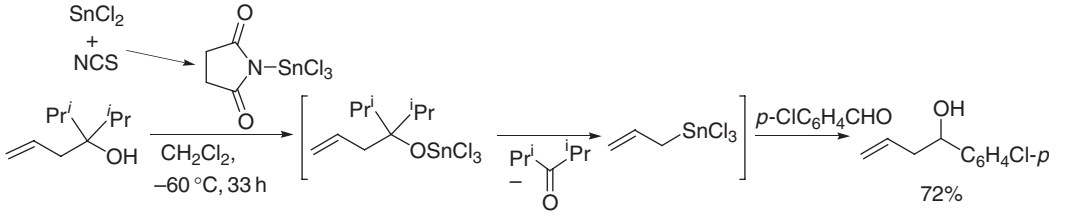
9.08.3.5 Barbier-type Reactions

Barbier-type carbonyl allylation with tin halides is one of the most convenient methods for introduction of allylic functions, because of easy operation, availability, and tractability of starting allylic substrates such as allylic halides, esters, and alcohols, from which allylic tin intermediates are usually prepared *in situ*. Allylic halides react with tin(IV) chloride and tetrabutylammonium iodide (TBAI) in dichloromethane to form allylic tin species which cause nucleophilic addition to aldehydes to produce the corresponding homoallylic alcohols.[182] Tin(II) chloride, $SnCl_2$, can mediate the coupling between an allyl halide and a carbonyl compound in water when Pd(II),[183] Cu(I),[184,185] or $TiCl_3$[186] catalyst is introduced. Bishomoallylic alcohols are prepared in water by $SnCl_2$-mediated allylation of dialdehydes in the presence of excess potassium iodide.[187,188] Under ultrasonication, $SnCl_2$ mediates the aqueous Barbier reactions without any assistance of Lewis acid catalysts.[189] Tin(II) bromide in a CH_2Cl_2–H_2O biphasic system is a reagent for unusual α-regioselective carbonyl allylation by 1-bromobut-2-ene to produce 1-substituted pent-3-en-1-ols. Thus, slightly nucleophilic μ-bromoditin anion $[Br_2Sn–Br–SnBr_2]^-$ may be derived from $3SnBr_2$. The reaction of the μ-bromoditin with 1-bromobut-2-ene forms a but-2-enyl(μ-bromo)ditin intermediate which causes α-regioselective carbonyl allylation. On the other hand, the addition of TBAI produces 1-substituted 2-methylbut-3-en-1-ols via usual γ-addition (Equation (53)).[190]



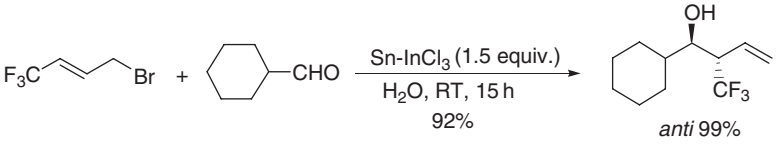
(53)

α,α-Diisopropy homoallylic alcohols react with tin(II) chloride and NCS in CH_2Cl_2 to produce allylic tins and diisopropyl ketone, and the resulting allylic tins cause nucleophilic addition to aldehydes to afford α-substituted homoallylic alcohols (Equation (54)).[191]



(54)

The same reagent also acheives imine allylation to produce the corresponding homoallylic amines.[192] 1-Substituted or 3-substituted prop-2-en-1-ols (allylic alcohols) cause a diastereoselective carbonyl allylation with SnI_2 and Bu_4NI/NaI in DMI/H_2O to produce *syn*-1,2-disubstituted but-3-en-1-ols.[193] Sn metal can mediate the coupling between allyl halides and carbonyl compounds. Allyl bromide and tin react in aqueous media to give allyltin(II) bromide and diallyltin(IV) dibromide. Either organotin intermediate can react with carbonyl compounds to give the corresponding homoallylic alcohols. Competitive experiment shows that allyltin(II) bromide is more reactive than diallyltin(IV) dibromide.[194,195] Ultrasonic irradiation under the solvent-free conditions allylates carbonyl compounds in the presence of metallic Sn and excess allyl bromide.[196] Effective allylation is caused by nanometer tin particles for which the surface is more active and enhances the reaction selectivity.[197] A combination of β-SnO and catalytic Cu_2O promotes the reaction of allylic halides with carbonyl compounds, providing the corresponding homoallylic alcohols with γ-regioselectivity.[198] Indium trichloride ($InCl_3$) promotes tin-mediated coupling reactions of allylic bromides with carbonyl compounds in water, and affords the allylation products in high regio- and diastereo (*anti*)-selectivities (Equation (55)).[199–201]



(55)

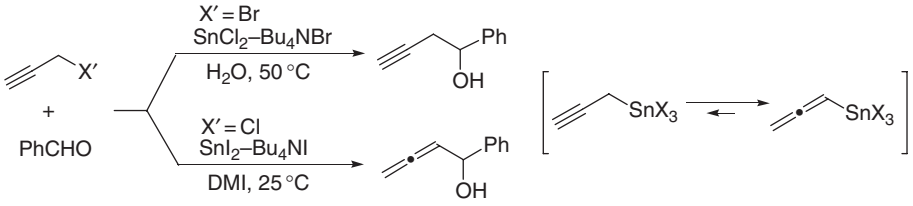
9.08.3.6 Alcohol-activated Reactions

Besides Lewis acids, tetraallyltin is activated by methanol to promote the reaction with aldehydes or activated ketones in which easy separation of the products from tin residues is an advantage.[202–203] Asymmetiric allylation of ketones is performed by using binaphthyl alcohol.[204]

9.08.4 Allenyl Tins, Propargyl Tins

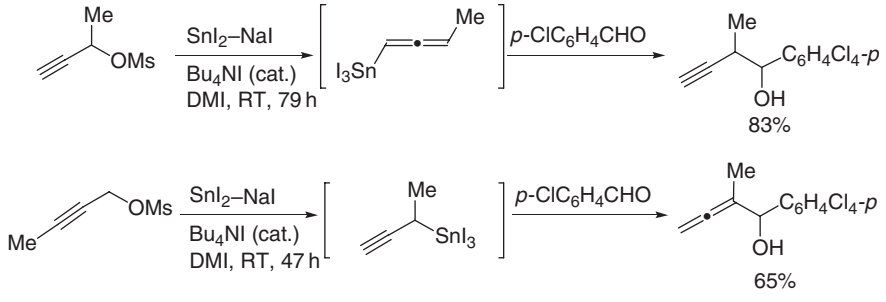
9.08.4.1 Barbier-type Reactions

Similar to allylations, an analogous scenario is applicable to allenyltin reagents. The interconversion of allenic and propargylic isomers can lead to the formation of propargylic and allenic adducts. These adducts have the potential for further elaborations of the alkynyl and allenyl functions. Propargyl bromide is used for carbonyl propargylation with $SnCl_2$ and Bu_4NBr in water to produce 1-substituted but-3-yn-1-ols, while allenylation takes place by propargyl chloride with SnI_2 and Bu_4NI in 1,3-dimethylimidazolidin-2-one (DMI) to produce 1-substituted buta-2,3-dien-1-ols (Equation (56)).[205]



(56)

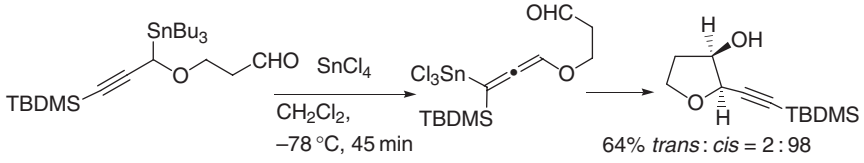
1-Substituted prop-2-ynyl mesylates cause propargylation of aldehydes with SnI_2, Bu_4NI, and NaI in DMI to furnish 2-substituted but-3-yn-1-ols, while 3-substituted prop-2-ynyl mesylates promote allenylation under the same conditions to produce 2-substituted buta-2,3-dien-1-ols (Equation (57)).[206]



(57)

9.08.4.2 Lewis Acid-promoted Reactions

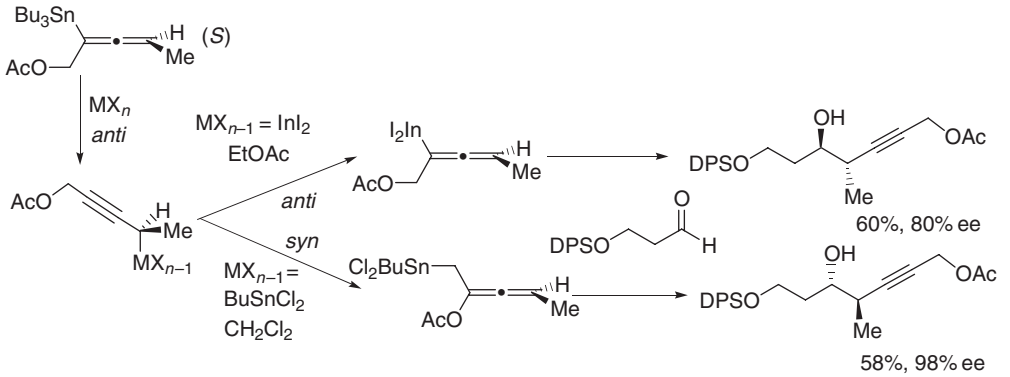
The treatment of propargyltins with Lewis acids such as $SnCl_4$ induces isomerization to allenylmetal species, which undergo cyclization to the corresponding five-membered cyclic ethers (Equation (58)).[207]



(58)

Indium triiodide (InI_3) yields a transient allenylindium species from (*S*)-allenyltin with mainly retention of configuration. In contrast, transmetallation with $BuSnCl_3$ affords an intermediate allenyl species with inverted

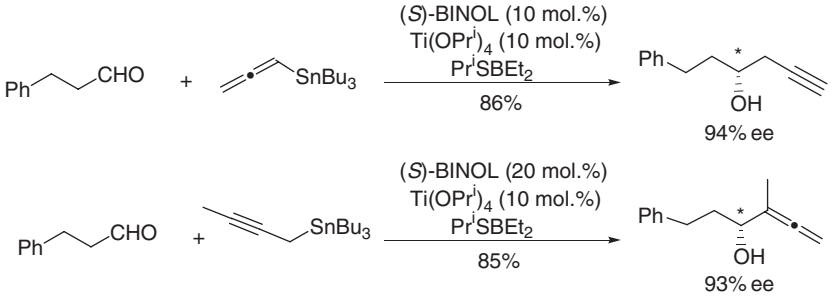
configuration (Equation (59)). The transmetallation with InI_3 proceeds mainly by *anti*, *anti* S_E2' processes. On the other hand, the transmetallation with $BuSnCl_3$ proceeds by sequential *anti*,*syn* processes.[208–211]



(59)

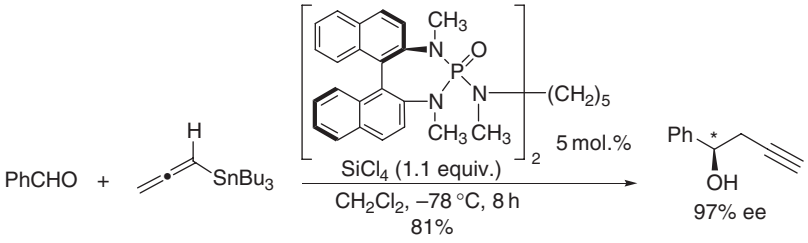
9.08.4.3 Catalytic Asymmetric Reactions

The first enantioselective propargylation of achiral aldehydes with allenyltin promoted by a stoichiometric amount of the BINOL/Ti(IV) complex has been reported by Keck.[212] High yields and enantioselectivities have been obtained using either 100 or 50 mol.% of the promoter although the reaction is much slower than the allylation due to the development of positive charge at the *sp* carbon during the electrophilic addition to the allenyl moiety.[212] As can be seen in the allylation reactions, the rate of propargylation is significantly enhanced when a stoichiometric amount of Pr^iSBEt_2 is added (Equation (60)).[213,214] Under similar conditions, propargylic tins also successfully react with aldehydes to provide the allenic alcohols in high yields and selectivities.[215]



(60)

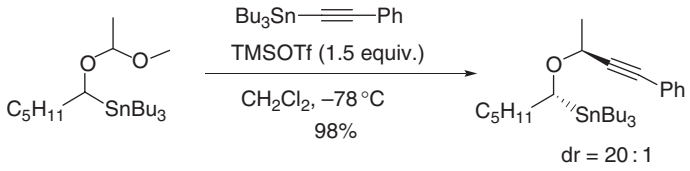
A highly enantioselective propargylation of aldehydes using the strong chiral Lewis acid generated from $SiCl_4$ and a chiral phosphoramide has been reported.[173] With 5 mol.% of (*R*,*R*)-bisphosphoramide and a stoichiometric amount of $SiCl_4$, the addition of allenyltin to aldehydes proceeds at −78 °C to give the homopropargylic alcohols in high yields and enantioselectivities (Equation (61)).



(61)

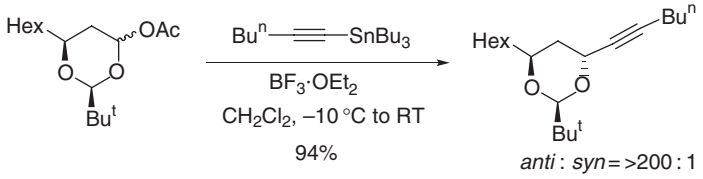
9.08.5 Alkynyltins

The regio- and stereoselective addition of alkynyltins to tin-substituted acetals produces propargylic ether derivatives (Equation (62)).[216]



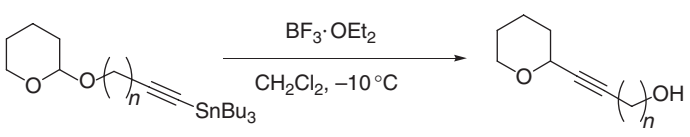
(62)

Alkynyltins couple with 4-acetoxy-l,3-dioxane in the presence of $BF_3{\cdot}OEt_2$ to give acetal protected propargylic *anti*-l,3-diols (Equation (63)).[217]



(63)

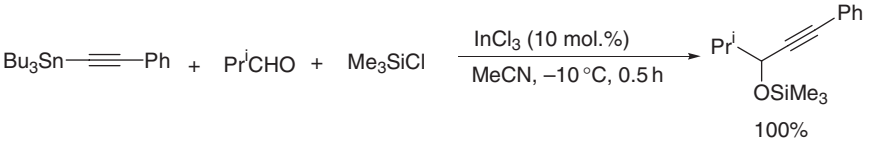
Treatment of alkynyl tri-*n*-butyltin tetrahydropyranyl ether derivatives with $BF_3{\cdot}OEt_2$ effects an anomeric oxygen to carbon rearrangement, furnishing the corresponding carbon-linked alkynol products (Equation (64)).[218]



n	*Yield* (%)
1	49
2	50
3	62
4	58

(64)

Indium trichloride catalytically promotes the alkynylation of aldehydes in which $InCl_3$ plays two roles: transmetallation with tin compounds and activation of aldehydes as a Lewis acid (Equation (65)).[219]

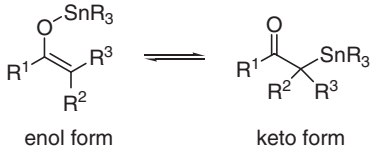


(65)

9.08.6 Tin Enolates

9.08.6.1 General

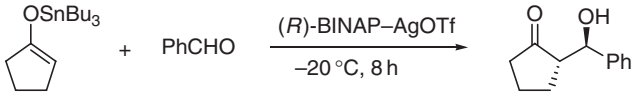
Tin enolates are one of the most versatile reagents for carbon–carbon bond formation. They are used either in ionic or radical reaction manner. Organotin enolates exist as equilibrium mixtures of keto and/or enol forms, and their ratio largely depends on their substituents and conditions (Equation (66)).[220] In general, an enol form has high nucleophilicity in ionic system and thus only the enol form is often shown in a reaction scheme.



(66)

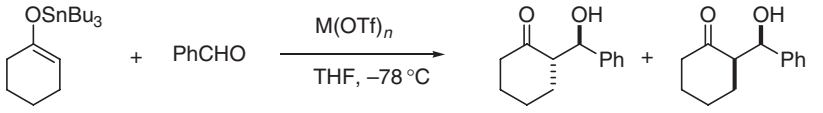
9.08.6.2 Aldol and Its Related Reactions

Enantioselective aldol reaction of tin enolates with aldehydes catalyzed by BINAP–AgOTf complex has been accomplished. This reaction proceeds through a cyclic transition state with the aid of chiral silver complex (Equation (67)).[221]



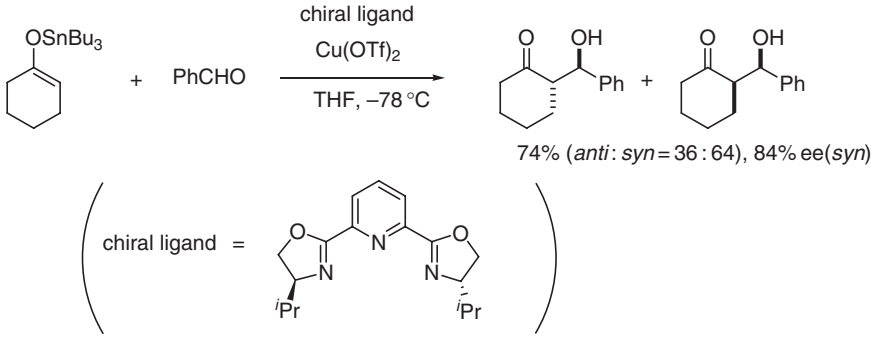
92% (*anti*: *syn* = 89 : 11) 92% ee(*anti*) (67)

The diastereoselective aldol reaction of the tributyltin enolate of cyclohexanone with benzaldehyde in the presence of a catalytic amount of various metal triflates has been studied. The highest *anti*-selectivity is observed with $Pd(OTf)_2$, while $Zn(OTf)_2$ in THF shows moderate *syn*-selectivity (Equation (68)).[222]



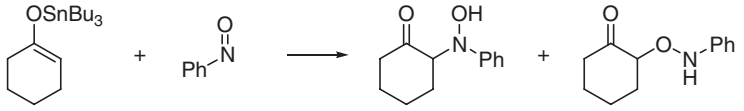
$Pd(OTf)_2$ 77% (92 : 8)
$Zn(OTf)_2$ 59% (35 : 65) (68)

The use of (*S*,*S*)-*i*-Pr-pybox-$Cu(OTf)_2$ complex as a catalyst preferentially produces the optically active *syn*-aldol adduct with 84% ee (Equation (69)).[222]



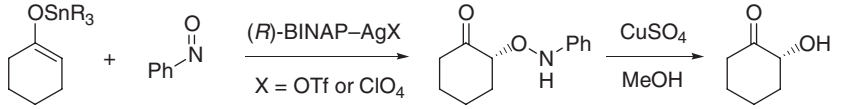
(69)

The reaction of nitroso compounds with typical metal enolates, "the nitroso aldol reaction," occurs in high yields to generate α-hydroxyamino carbonyl compounds. Exclusive *N*-selectivity > 99 : 1 is observed to give hydoroxyamino ketone in the reaction with tin enolates (Equation (70)).[223]



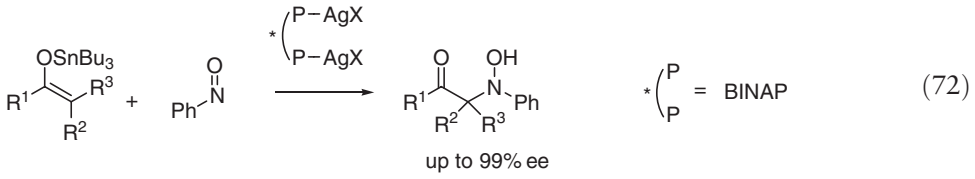
91% (>99 : 1) (70)

The use of Lewis acid drastically changes the regioselectivity. The highly enantioselective and *O*-selective nitroso aldol reactions of tin enolates with nitrosobenzene have been developed with the use of (*R*)-BINAP–silver complexes as catalysts. AgOTf and $AgClO_4$ complexes are optimal in the *O*-selective nitroso aldol reaction in both asymmetric induction (up to 97% ee) and regioselection (*O*/*N* = > 99/1), affording amino-oxy ketone. The product can be transformed to α-hydroxy ketone without any loss of enantioselectivity (Equation (71)).[224]



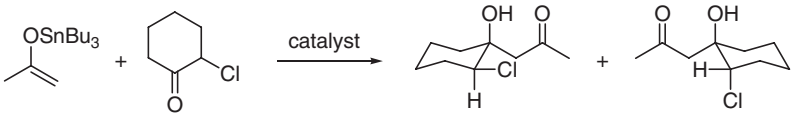
R = Bu, Me 92–97% (71)

The asymmetric synthesis of *N*-adduct is accomplished by BINAP–AgOTf (0.4/1) complex. The complex has the structure with 1 : 1 P–Ag moieties which is confirmed by NMR. The *in situ* generated catalyst gives hydroxyamino ketones in high enantioselectivity (Equation (72)).[225]



(72)

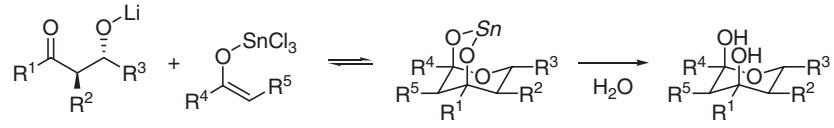
The reaction of tin enolate with α-chlorocyclohexanone gives chlorohydrins bearing chloro and hydroxyl groups in the *cis*-conformation in the presence of catalytic amount of Bu_3SnBr–Bu_4NBr complex or Ph_4SbBr. No selectivity is obtained in the reaction without those catalysts (Equation (73)).[226]



none	95% (48 : 52)
Bu_3SnBr–Bu_4NBr	59% (100 : -)
Ph_4SbBr	68% (95 : 5)

(73)

Three different carbonyl components are assembled to tetrahydropyran-2,4-diols by two successive diastereoselective aldol reactions. Tin(IV) enolates provide high selectivity as compared with other metals (Equation (74)).[227,228]



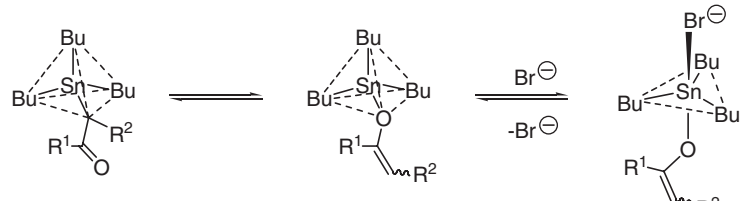
initial aldol product

(74)

9.08.6.3 Highly Coordinated Tin Enolates

Organotin(IV) compounds commonly exist as a tetrahedral structure around the tin metal. Variation in the ligands added can change the hybridization state to give trigonal bipyramidal and octahedral structures including five- and six-coordinated tin centers, which are highly coordinated. High coordination of tin enolates provides a novel synthetic reaction pathway as compared with non-coordinated one.

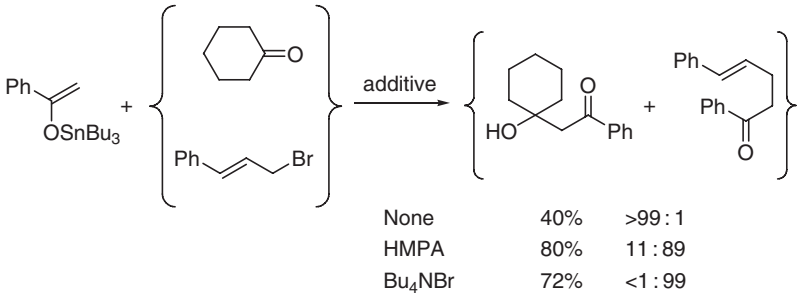
An anionic tin complex, five-coordinated tin enolate, is formed by the coordination of bromide anion from tetrabutylammonium bromide (Bu_4NBr) to a neutral four-coordinated tin(IV) enolates (Equation (75)).



(75)

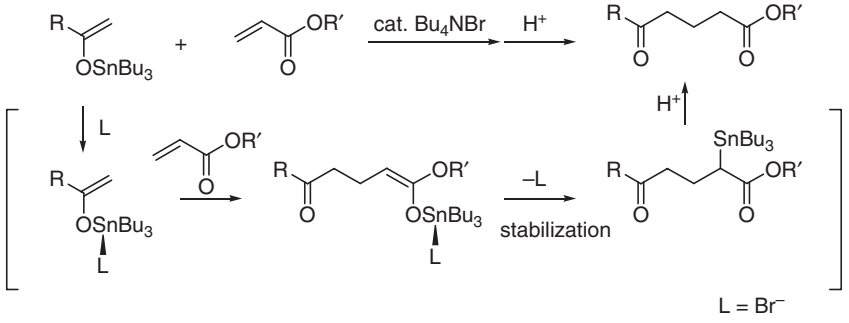
The highly coordinated enolates which show a marked change in chemoselectivity have higher nucleophilicity to organic halides. In addition, they show low nucleophilicity toward carbonyl moieties by the coordination of the bromide anion, whereas carbonyl addition readily proceeds using the usual four-coordinated tin enolate. The effective control of chemoselectivity in the intermolecularly competitive reaction between organic halides and carbonyl compounds is demonstrated using two types of tin enolates, four-coordinated enolate and highly coordinated

anionic enolate; halide displacement reaction exclusively takes place using the bromide-anion-coordinated enolates, and the usual four-coordinated enolates react with only carbonyl compounds (Equation (76)).[229] An *ab initio* computational study reveals the mechanism of the reaction between tin enolates and aldehydes or organic halides in both cases with and without a bromide anion as a coordinating ligand to tin. The reaction of high-coordinated tin enolate with halides is favored both kinetically and thermodynamically as compared with that of non-coordinated enolates. The high nucleophilicity of high-coordinated tin enolate is due to coordination of an anionic ligand.[230]



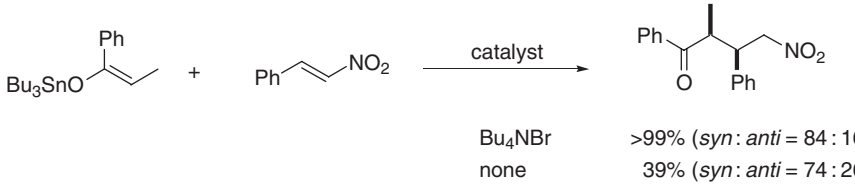
(76)

Michael addition of tin enolates to α,β-unsaturated esters is accomplished in the presence of catalytic amount of Bu_4NBr. Other typical system using lithium enolates or silyl enolates with catalysts (Lewis acid or Bu_4NF) fails to give the Michael products. An *ab initio* calculation reveals that higher reactivity is caused by high coordination of the tin enolate and the keto enol tautomerization for Michael adducts contributes to thermodynamical stabilization (Equation (77)).[231,232]



(77)

One-pot system starting from parent ketones, *sec*-BuLi, Bu_3SnBr, and Michael acceptor is accomplished for various types of substrates.[233] The reaction of tin enolates with nitroalkenes is effectively catalyzed by Bu_4NBr to give γ-nitroketones. The catalyzed reaction provides higher yield and selectivity as compared with the uncatalyzed reactions (Equation (78)).[234]



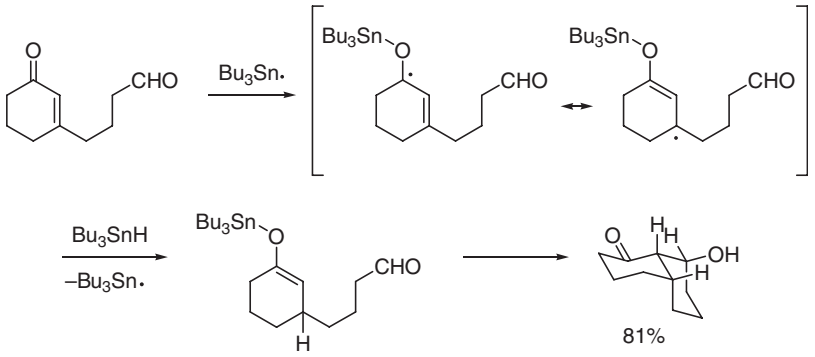
(78)

9.08.6.4 Tin Enolate Generation from Enone with Bu_3SnH

The reaction of α,β-unsaturated carbonyls with tin hydride directly gives tin enolates that can be utilized for further reactions.

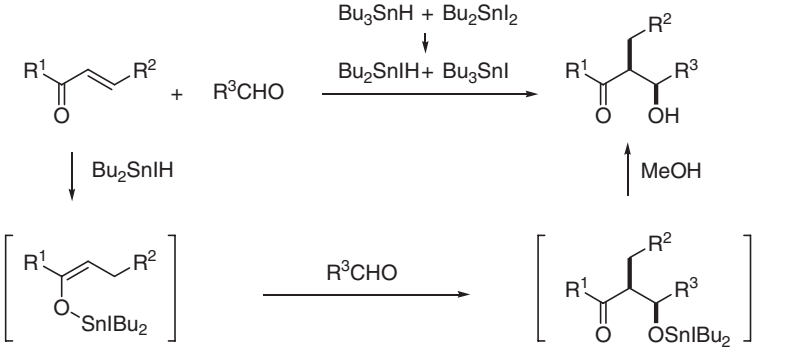
Allylic *O*-stannyl ketyl, a resonance-stabilized radical species, is produced under mild free-radical conditions by the reaction of a conjugated aldehyde or ketone with a tributyltin radical. The formed radical abstracts a hydrogen from

Bu_3SnH and gives a tin enolate, which undergoes an intramolecular aldol reaction with the tethered aldehyde leading to a bicyclic structure (Equation (79)).[235]



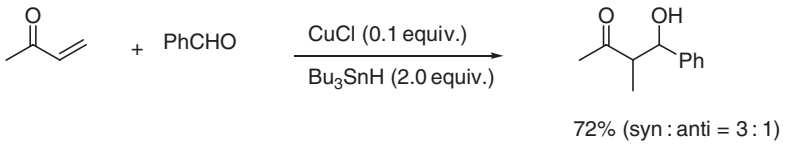
(79)

The substituents on the tin center can be easily modified by this system, giving new type of tin enolates *in situ*. Organotin iodide hydride (Bu_2SnIH) selectively reduces conjugated enones in the presence of aldehydes at ambient temperature, giving dibutyliodotin enolates. A subsequent aldol reaction proceeds with *syn*-selectivity (Equation (80)).[236]



(80)

Copper(I) chloride in combination with tributyltin hydride shows unique character as an initiator of certain radical reactions. Hydrostannation of α,β-unsaturated ketones with Bu_3SnH is initiated by CuCl and the resulting tin enolates react with aldehydes under the influence of CuCl as a Lewis acid catalyst (Equation (81)).[237]

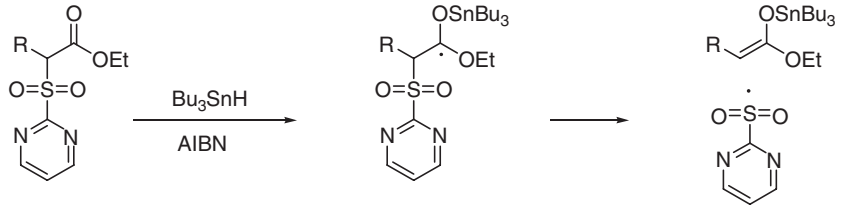


(81)

9.08.6.5 Micellaneous Generation of Tin Enolates

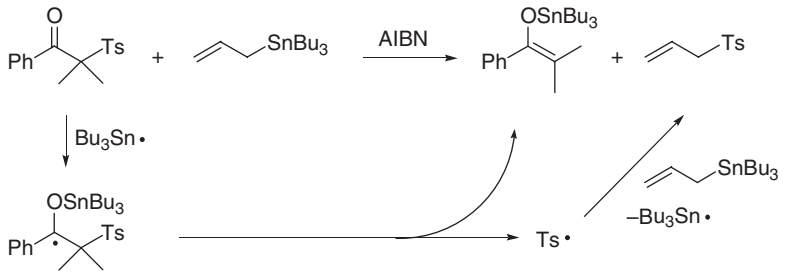
Tin(IV) enolates are normally generated by transmetallation from lithium enolates with trialkyltin halides or transesterification between enol acetates with trialkyltin alkoxides.[220] Other types of generation systems are described below.

Treatment of pyrimidinylsulfonyl esters with Bu_3SnH in the presence of AIBN gives tin enolates *in situ* by the substitution of the sulfonyl group (Equation (82)).[32]



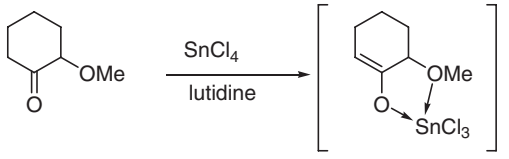
(82)

The reactions of α-(arylsulfonyl)acetophenones with allylstannane in the presence of AIBN give a nearly 1 : 1 mixture of allyl tosyl sulfone and the corresponding ketone. NMR studies reveal the generation of tin enolate during the reaction course (Equation (83)).[238]



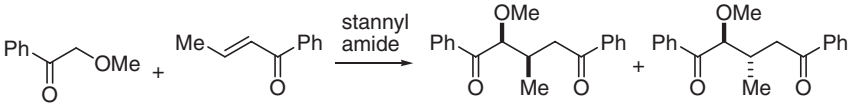
(83)

Low-temperature NMR studies of the reaction of 2-methoxycyclohexanone with $SnCl_4$ in the presence of a base confirm the formation of a chelated tin enolate (Equation (84)). A synthetic application, a high stereoselective synthesis of sanfetrinem, has been described.[239]



(84)

The stannyl amides as bases react with ketones to give tin enolates *in situ*. The generated alkoxy ketone-enolates enable Michael reaction with unsaturated ketones. The stereoselectivity is effectively controlled by substituents on the tin center (Equation (85)).[240,241]

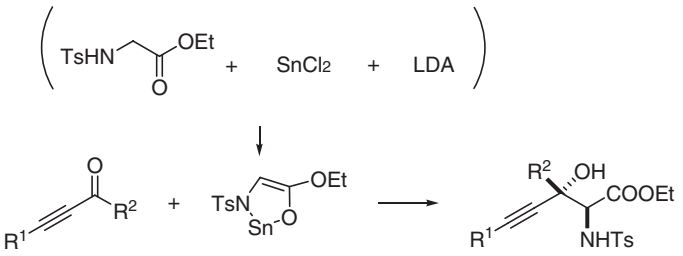


(85)

$Bu_3SnNPr^i_2$	66%	22 : 78
$Cl_2BuSnNPr^i_2$	99%	82 : 18

9.08.6.6 Tin(II) Enolates

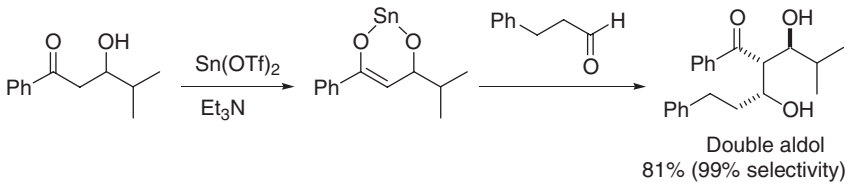
The tin(II) enolate is generated from the ethyl *N*-tosylglycinate/LDA/$SnCl_2$ system and reacts with conjugated ynals and ynones to give amino alcohols in high *anti*-diastereoselectivities (Equation (86)).[242]



(86)

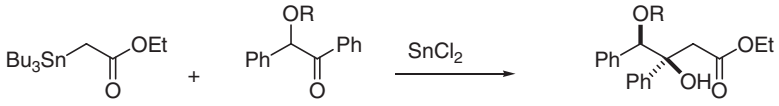
The similar type of generation of tin(II) enolate provides a diastereoselective aldol reaction for the asymmetric synthesis of α-substituted serines using $Sn(OTf)_2$/*N*-ethylpiperizine.[243]

Double aldol reaction proceeds stereoselectively at the α-carbon of ketones to give α-(1-hydroxyalkyl)-β-hydroxyalkylketones (double aldols) in good to high yields. *In situ* generated tin(II) enolates play a key role in this reaction (Equation (87)).[244]



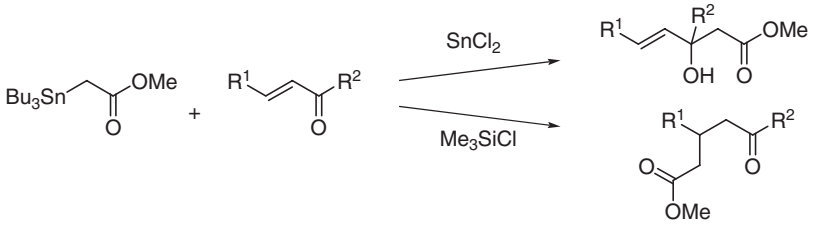
(87)

Transmetallation between stannyl esters and $SnCl_2$ affords tin(II) enolate equivalents. The reaction of α-stannyl esters with α-alkoxy or hydroxyl ketones in the presence of $SnCl_2$ gives aldol-type products with high selectivities in a chlelation-controlled manner (Equation (88)).[245]



(88)

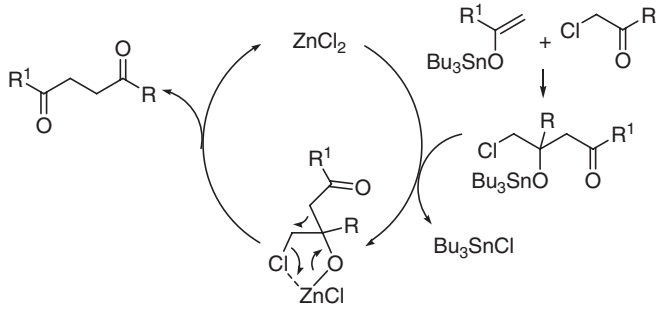
The reaction of α-stannyl esters with α,β-unsaturated ketones in the presence of $SnCl_2$ and chlorosilanes gives 1,2- and 1,4-addition products, respectively (Equation (89)).[246]



(89)

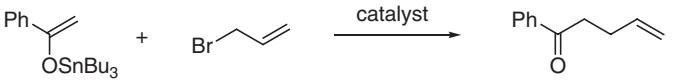
9.08.6.7 Coupling with Halides

The reaction of tin enolates with α-chloro or bromoketones gives γ-diketones (1,4-diketones) catalyzed by zinc halides. In contrast to the exclusive formation of 1,4-diketones under catalytic conditions, uncatalyzed reactions afford aldol-type products. NMR studies indicate that the catalyzed reaction includes precondensation between tin enolates and α-haloketones providing aldol-type species and its rearrangement of the oxoalkyl group with the substitution of the halogen to produce 1,4-diketones (Equation (90)).[247,248]



(90)

In addition, copper halides show high catalytic activity for the coupling between tin enolates and active halides (Equation (91)).[248]



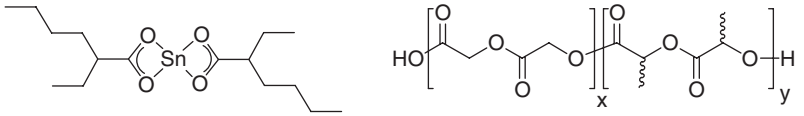
Halides	*Yield* (%)
$ZnCl_2$	0
$NiCl_2$	10
CuCl	>99

(91)

9.08.7 Reaction of Tin–Heteroatom Bonds

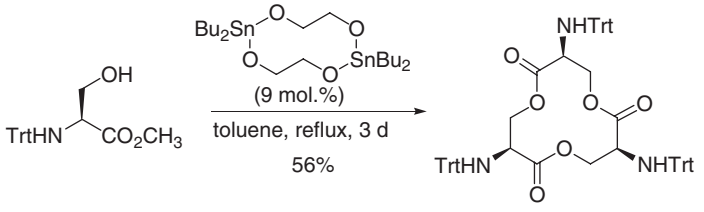
9.08.7.1 Tin Alkoxides

Among the variety of biodegradable polymers, linear aliphatic polyesters derived from lactic acid (PLA), glycolic acid (PGA), and their copolymers (PLGA) are particularly attractive.[249] The most widely used complex catalyst for the industrial preparation of PLA and PLGA is tin(II) bis(2-ethyl hexanoate) ($Sn(Oct)_2$). It is highly active (typical reaction times in bulk at 140–180 °C range from minutes to a few hours) and allows the preparation of high molecular weight polymers (up to 105 or even 106 Da in the presence of an alcohol) (Equation (92)).[250] The polymerization is found to be even faster and better controlled when $Sn(Oct)_2$ is combined with a protic reagent such as an alcohol.[251–253]



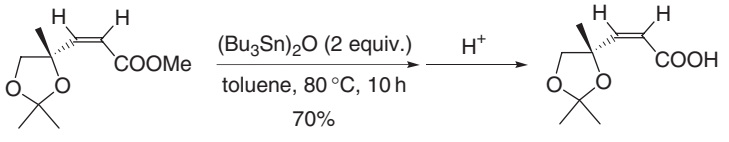
(92)

The effect of a stannoxane template leads to the effective preparation of macrocyclic lactones (Equation (93)).[254–256]



(93)

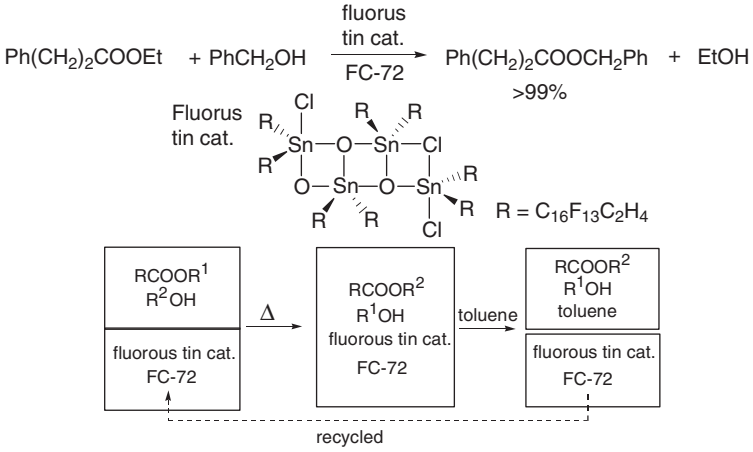
Methyl and ethyl esters of carboxylic acids are successfully cleaved with bis(tri-*n*-butyltin) oxide to give the free carboxylic acids even in the presence of other functional groups and/or protecting groups (Equation (94)).[257]



(94)

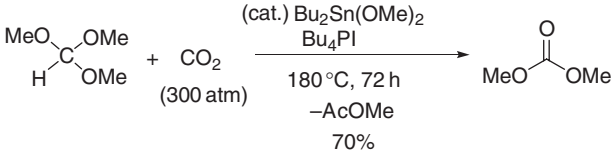
Both esterification and transesterification are classical reactions that still find great demands in modern synthetic chemistry.[258,259] 1,3-Disubstituted tetrakis(fluoroalkyl) distannoxanes, $(XR_2SnOSnR_2Y)_2$ ($R = C_6F_{13}C_2H_4$ and

$C_4F_9C_2H_4$), are highly fluorophilic and exhibit large partition coefficients in favor of fluorocarbon solvents over common organic solvents due to a double-layered structure where the stannoxane core is covered by fluoroalkyl groups. Fluorous technology allows transesterification and esterification in which 100% yield of the desired esters is achievable with reactants in a strict 1 : 1 ratio. The tin catalysts are recovered from the fluorous phase quantitatively (Equation (95)).[260]



(95)

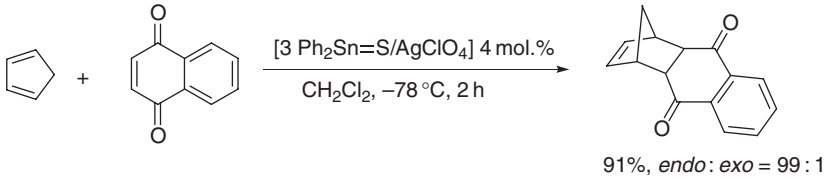
A considerable amount of effort has already been devoted to producing dimethyl carbonate (DMC) from methanol and CO_2, and some of the reactions have been catalyzed by organotin alkoxides. However, the catalytic activities so far obtained have been very low due to the decomposition of the catalysts by water generated during the reaction. The supercritical CO_2 reaction with trimethyl orthoacetate leads to the desired reaction and gives DMC and methyl acetate. Although di-*n*-butyltin dimethoxide is less effective, the addition of tetrabutylphosphonium iodide substantially enhances the catalytic activity of the system (Equation (96)).[261,262]



(96)

9.08.7.2 Tin Sulfides

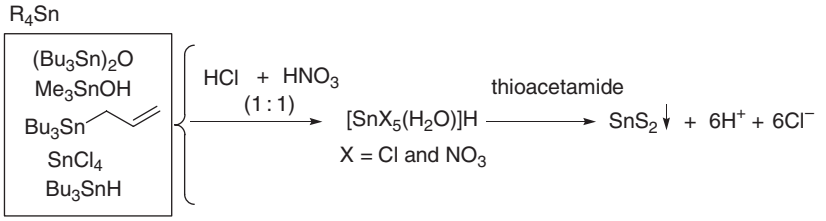
Catalytic Diels–Alder reactions between 1,3-dienes and α,β-unsaturated ketones are promoted by the combined use of diphenyltin sulfide ($Ph_2Sn{=}S$) and silver perchlorate (Equation (97)).[263]



(97)

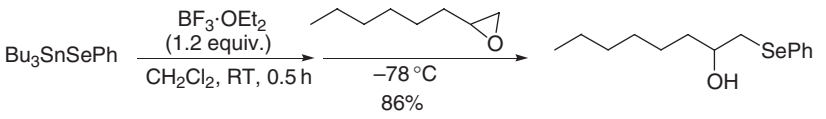
Tin compounds have great affinity to sulfur. To convert the triorganotin compounds into inorganic tin compounds of low toxicity, the degradation of bis(tri-*n*-butyltin) oxide, trimethyltin hydroxide, allyltri-*n*-butyltin, tin

tetrachloride, and tri-*n*-butyltin hydride is has been investigated in aqueous solution with a mixture of HCl and HNO_3 for 1 h at 85 °C (Equation (98)). The acidic solutions are neutralized with ammonium hydroxide to pH 6.8 and stirred at room temperature with thioacetamide which acts as a hydrogen sulfide equivalent, and insoluble and easy removable SnS_2 (which is yellow) is precipitated.[264]



(98)

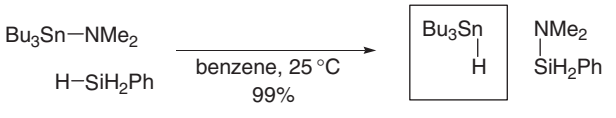
When $Bu_3SnSePh$ is allowed to react with epoxides in the presence of $BF_3{\cdot}OEt_2$, the ring-opening reaction of epoxides proceeds with complete regioselectivity to afford the β-hydroxy phenylselenides (Equation (99)).[265]



(99)

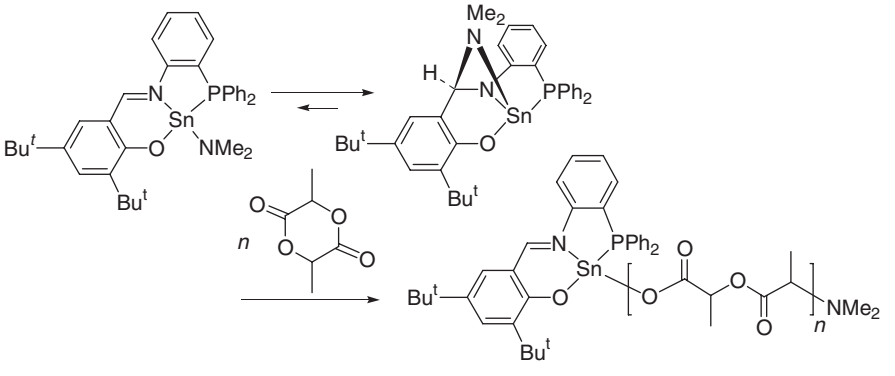
9.08.7.3 Tin Amides

The use of a silicon hydride to reduce Bu_3SnNR_2 to Bu_3SnH is an attractive prospect, since most silicon hydrides are non-toxic and relatively inert toward organic functionalities. However, Bu_3SnNMe_2 does not react with silanes such as Et_3SiH or Ph_3SiH even at elevated temperature. In contrast, $PhSiH_3$ easily converts Bu_3SnNMe_2 to Bu_3SnH at room temperature (Equation (100)).[266]



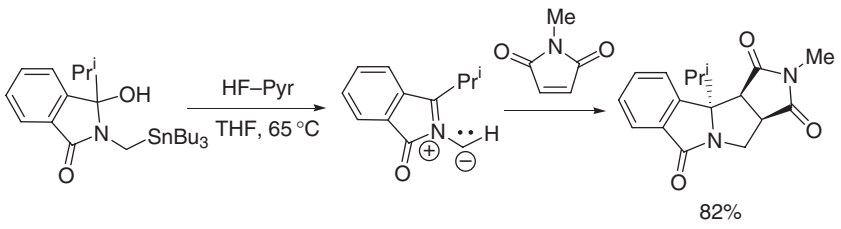
(100)

In tin amide complexes including Shiff base ligand, unprecedented attack by the amide moiety to the imine carbon atoms of tridentate Schiff base ligands gives unusual tetradentate ligand systems. The so-formed complexes act as latent single-site initiators for the controlled polymerization of *rac*-lactide (Equation (101)).[267]



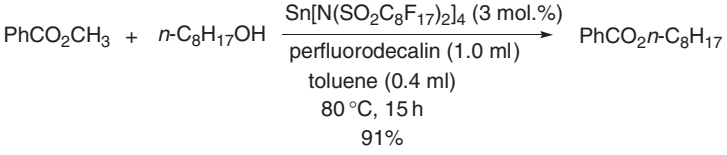
(101)

N-(tri-*n*-butylstannylmethyl) cyclic carbinol amides form azomethine ylides upon treatment with HF-pyridine, which gives highly functionalized pyrrolizidines (Equation (102)).[268]



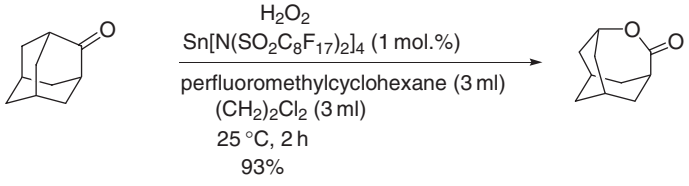
(102)

Tin(IV) bis(perfluorooctanesulfonyl)amide is a practical catalyst for transesterification and direct esterification using an equimolar ratio of the reactants in a fluorous biphase system (Equation (103)). The tin amide is completely recovered and reused in the immobilized fluorous phase without loss of its catalytic activity.[269]



(103)

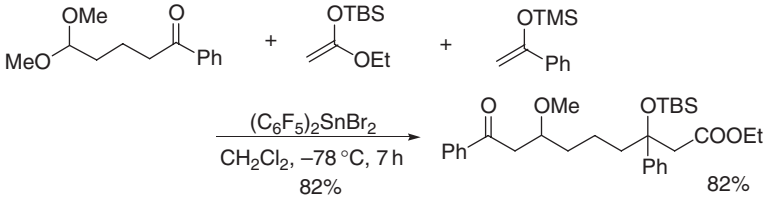
$Sn[N(SO_2C_8F_{17})_2]_4$ catalyst in a similar system also gives an excellent yield and selectivity for Baeyer–Villiger oxidation of cyclic ketones using 35% aqueous hydrogen peroxide (Equation (104)).[270]



(104)

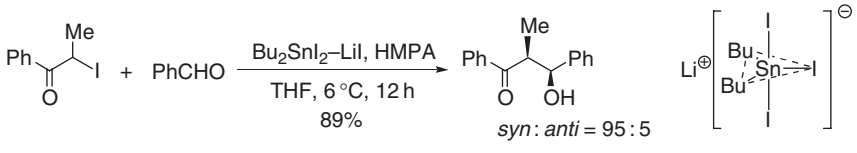
9.08.7.4 Tin Halides

Bis(pentafluorophenyl) tin dibromide effects the Mukaiyama aldol reaction of ketene silyl acetal with ketones, but promotes no reaction with acetals under the same conditions. On the other hand, reaction of silyl enol ether derived from acetophenone leads to the opposite outcome, giving acetal aldolate exclusively. This protocol can be applied to a bifunctional substrate (Equation (105)). Keto acetal is exposed to a mixture of different types of enol silyl ethers, in which each nucleophile reacts chemoselectively to give a sole product.[271]



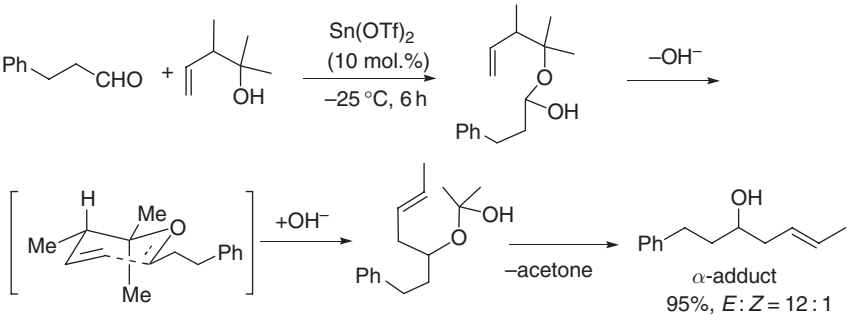
(105)

Highly *syn*-selective aldol synthesis from α-iodo ketones is promoted under aqueous conditions by a distannane system, $(Bu_3Sn)_2$, Bu_2SnF_2, and HMPA. Aqueous solutions of acetaldehyde or formaldehyde provide β-hydroxy ketones.[272] The ate complex $Li^+[n\text{-}Bu_2SnI_3]^-$ generated from LiI and $n\text{-}Bu_2SnI_2$ leads to the highest class of *syn*-diastereoselectivity in the Reformatsky-type reaction (Equation (106)).[273]



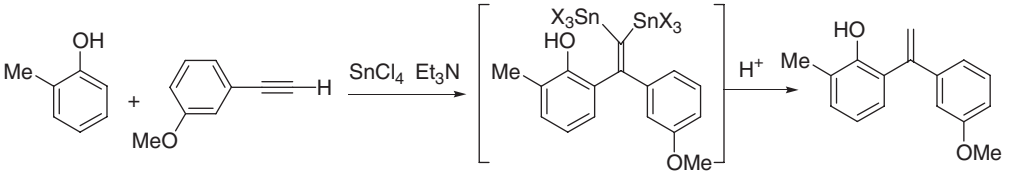
(106)

As a conceptually new allylation of aldehydes, an allylic functionality of the homoallyl alcohols is transferred to aldehydes via the formation of a hemiacetal and the elimination of acetone to give α-adduct homoallylic alcohols in the presence of a catalytic amount of $Sn(OTf)_2$ (Equation (107)).[274]



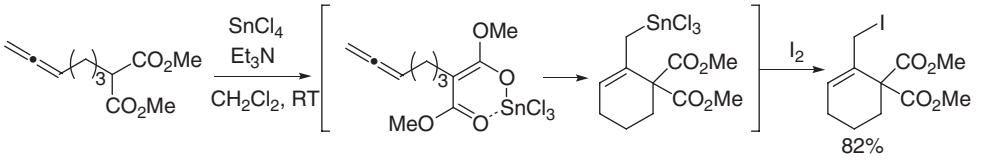
(107)

In the presence of $SnCl_4$ and Et_3N, phenols react with 1-alkynes and are alkenylated at *ortho*-positions, in which the C–C bond formation takes place via carbostanylation of trichlorophenoxytins to alkynyltrichlorotins generated *in situ* (Equation (108)).[275–277]



(108)

Intramolecular carbometallation of active methylene compounds having allenyl group proceeds in a complete regioselectivity in the presence of $SnCl_4$ and Et_3N to give a cyclohexene derivative (Equation (109)).[278]

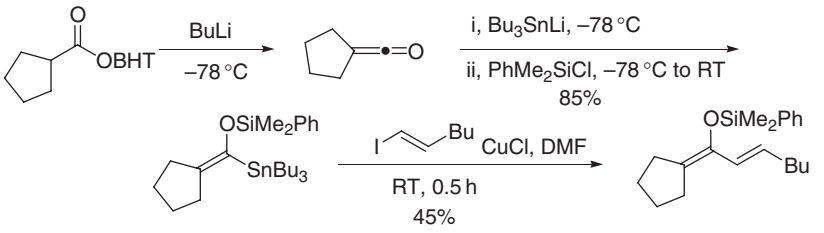


(109)

9.08.8 Reaction of Tin–Metal Bonds

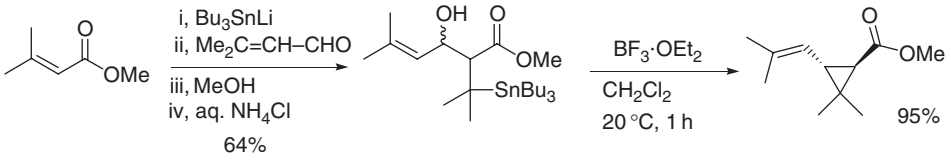
9.08.8.1 Stannyllithiums

Stannyllithiums are synthetic equivalent of stannyl anions. The reaction of 2,6-di-*tert*-butyl-4-methylphenyl(BHT) esters with BuLi, followed by the addition of Bu_3SnLi, and trapping of the resulting lithium enolate with phenyldimethylchlorosilane leads to silyloxyvinylstannanes, which are allowed to the subsequent coupling with vinyl iodides (Equation (110)).[279]



(110)

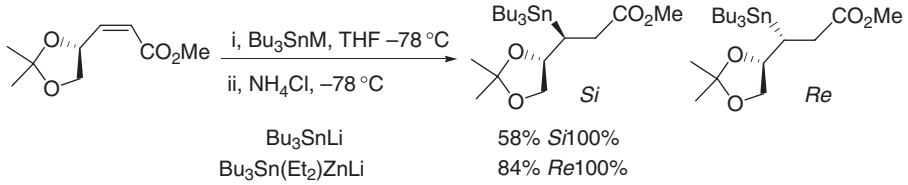
Bu_3SnLi adds to α,β-unsaturated esters, and the resulting Li-enolate reacts with 3-methyl-2-butenal to afford γ-hydroxyalkyl tins which are treated with $BF_3{\cdot}OEt_2$ to produce vinyl cyclopropane carboxylic esters (chrysanthemic acid) (Equation (111)).[280]



(111)

9.08.8.2 Stannylzincates

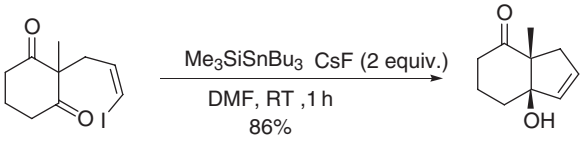
Bu_3SnLi reacts quite efficiently with (*Z*)-α,β-unsaturated esters to provide compounds that arise from the attack on the *Si* face. On the other hand, stannylzincates add to (*Z*)-α,β-unsaturated esters with complete stereocontrol in favor of the *Re* adducts.[281] The differences can be explained by the ability to form chelates with the counter metal species (Equation (112)).



(112)

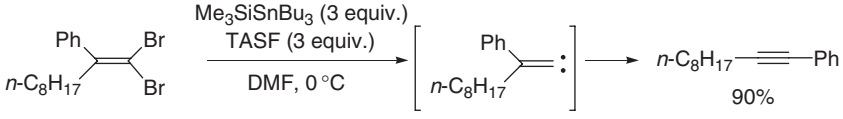
9.08.8.3 Stannylsilanes

When $Me_3SiSnBu_3$ is treated with CsF, the fluoride anion should coordinate to the silyl group and not the stannyl group to produce a hypervalent silicate, and as a result, a stannyl anion would be generated.[282] The stannyl anion reacts with vinyl iodide to produce a vinyl anion via a halogen–metal exchange and it reacts with the carbonyl group intramolecularly (Equation (113)). Aryl halides or allyl halides are also used in similar cyclizations.[283,284]



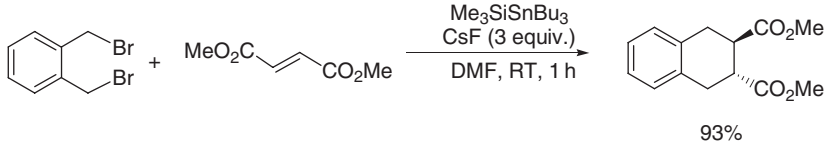
(113)

If a vinyl halide having an appropriate leaving group at the α-position is treated with $Me_3SiSnBu_3$ and F^-, an 1,1-elimination will occur to give an alkylidene carbene. When dibromoalkene, $Me_3SiSnBu_3$, and TASF $[(Et_2N)_3S^+SiMe_3F_2^-]$ are reacted, the 1,2-migration occurs to give internal alkynes (Equation (114)).[285]



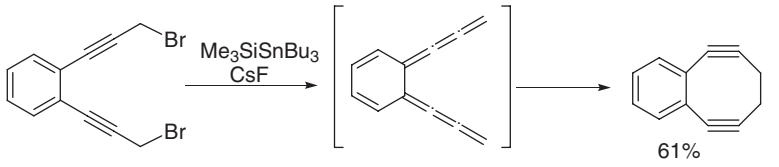
(114)

o-Quinodimethane is thought to be produced by 1,4-elimination. Thus, α,α′-dibromo-*o*-xylene is treated with $Me_3SiSnBu_3$ and CsF in the presence of dimethyl fumarate to produce a tetrahydronaphthalene derivative (Equation (115)).[285,286]



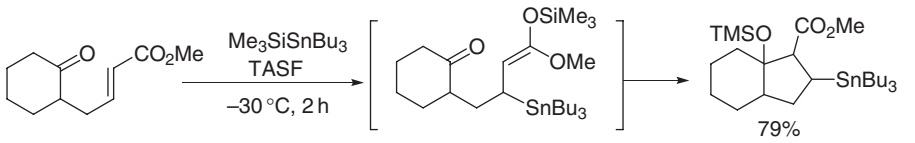
(115)

The reaction of a propargylic bromide derivative with $Me_3SiSnBu_3$ and CsF gives 3,4-benzocycloocten-1,5-diyne. This is the first example of the highly strained diyne (Equation (116)).[287,288]



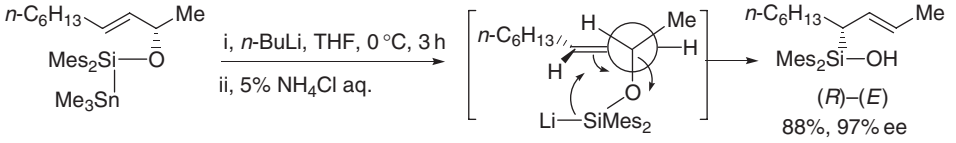
(116)

A stannyl anion reacts with an unsaturated ester to give β-stannylated esters. In this reaction, the intermediate is a silyl enolate. When a ketoester is employed, an intramolecular cyclization takes place (Equation (117)).[289]



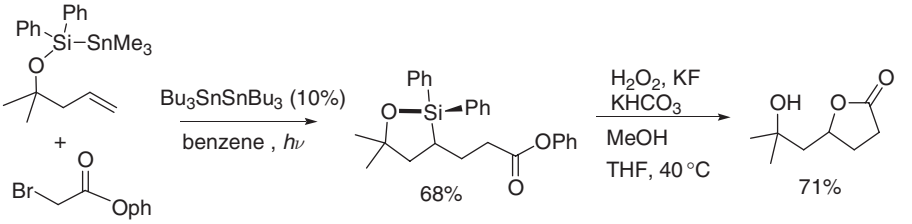
(117)

Treatment of the (*S*)–(*E*)-[(*sec*-allyloxy)dimesitylsilyl]stannane with *n*-BuLi provides a (*R*)–(*E*)-allylsilane with high enantioselectivity, in which 1,3-chirality transfer occurs during the [2,3]-sila-Wittig rearrangement (Equation (118)).[290]



(118)

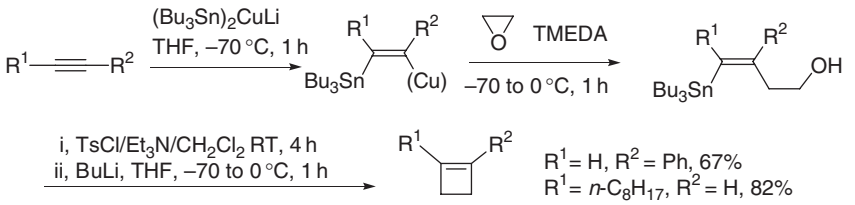
A radical approach to cyclization is offered by the intramolecular homolytic substitution (S_Hi) reaction at a silicon center. Reaction of phenyl bromoacetate with a stannylated silyl homoallyl ether under atom transfer conditions provides cyclic alkoxysilanes (Equation (119)).[291]



(119)

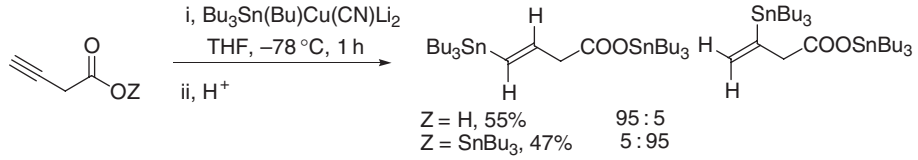
9.08.8.4 Stannylcuprates

The stannylcupration of alkynes has been widely studied.[292,293] Reaction of alkynes with lithium bis(tributylstannyl) cuprate leads to *cis*-2-(tributylstannyl)vinyl cuprates, which are synthetically equivalent to *cis*-1,2-ethylene dianions. Addition of the tin–copper reagent across the triple bond occurs *syn*-stereospecifically, thus providing *Z*-vinylstannanes. Phenylacetylene reacts with the tin cuprate with a regiochemistry opposite to that of 1-decyne.[294] The intermediate cuprates react well with the various electrophiles.[295] For example, the reaction with ethylene oxide gives primary alcohols, and further treatment of their *p*-toluenesulfonates with butyllithium gives 1-substituted cyclobutenes (Equation (120)).[294]



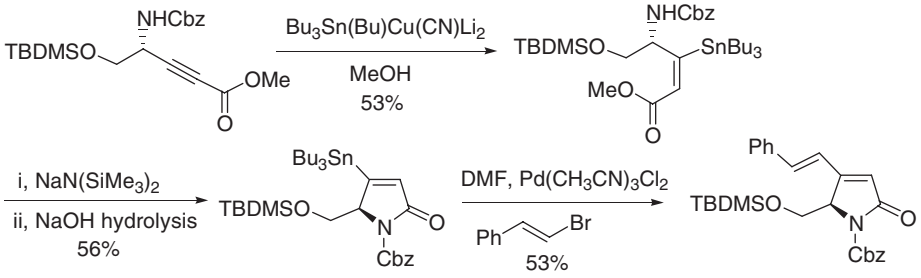
(120)

In the stannylmetallation of β–γ alkynoic acids, the best results are obtained with the high-order cuprate, $Bu_3Sn(Bu)Cu(CN)Li_2$, which affords the terminally tin-substituted isomer. In contrast, tributylstannyl ester of but-3-ynoic acid reacts with complete reverse regioselectivity (Equation (121)).[296,297]



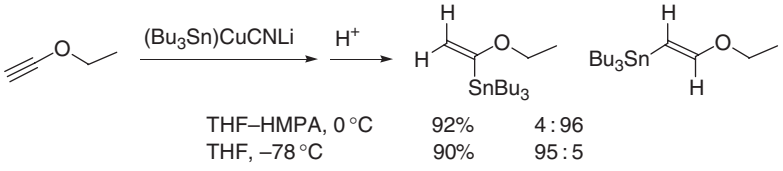
(121)

The addition of tributylstannylcuprate to γ-aminoalkynoate provides a methodology to 4-alkylated unsaturated γ-lactame (Equation (122)).[298]



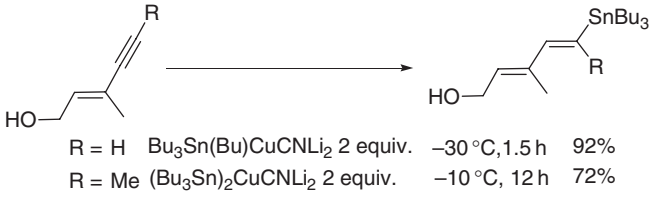
(122)

The addition of $(Bu_3Sn)(PhS)CuLi$ to alkynones (acetylenic ketones) proceeds in high yield and with excellent stereoselectivity for the (*Z*)-isomer of the product (> 95%).[299] The reaction of alkynyl ethers gives different regioisomers. Both kinetically and thermodynamically controlled products are obtained depending on the reaction conditions (Equation (123)).[300]



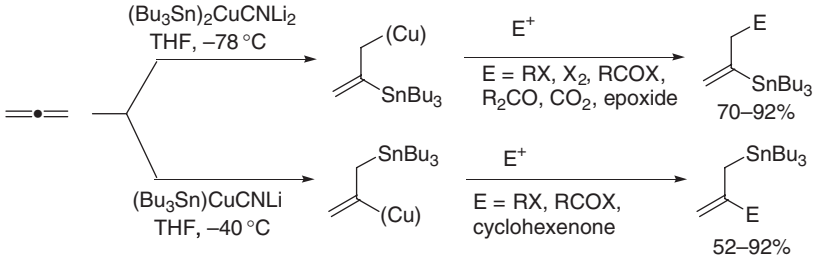
(123)

N-Protected propargylamines upon reaction with $Bu_3Sn(Bu)\ Cu(CN)Li_2$ afford, after quenching with electrophiles, the corresponding 2-substituted allylamines stannylated at position 3 in a stereoselective fashion.[301] Stannylcupration of silicon-substituted alkynes affords differently metallated vinylcuprate intermediates which react with electrophiles, affording silyl- and tin-trisubstituted alkenes.[302] Stannylcupration of enyols has been well performed,[303–306] where highly regio- and stereoselective formation of dienylstannanes is achieved (Equation (124)). Results are explained in terms of steric interactions between the enyne substituents and the cuprate moieties.



(124)

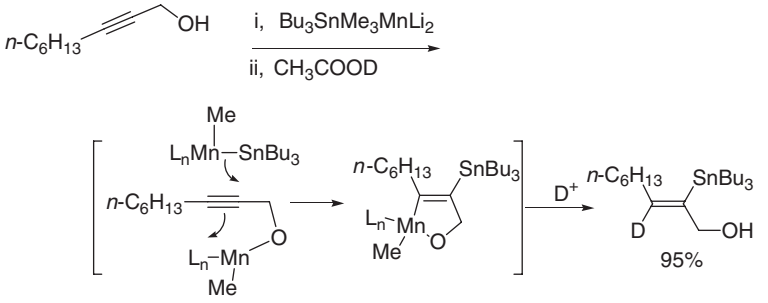
Stannylcupration of allenes has also been studied.[307,308] The higher-order cuprate $(Bu_3Sn)_2CuCNLi_2$ reacts with allene to produce exclusively 2-tributylstannylpropene after protonation.[307] The lower-order cuprate $(Bu_3Sn)CuCNLi$ shows a regiochemistry opposite to higher-order stannylcuprates. Capture of the intermediate allylstannane–vinylcuprate species with electrophiles allows the selective formation of allyltins with different substitution patterns (Equation (125)).[308]



(125)

9.08.8.5 Stannylmanganates

Stannylmanganate is generated by treatment of $Bu_3SnSnBu_3$ with Me_4MnLi_2 or Me_3MnLi. These reagents show *trans*-addition behavior to propargylic alcohols (Equation (126)).[309]



(126)

References

1. Frankland, E. *Liebigs Ann.* **1849**, *71*, 171–213.
2. Edgell, W. F.; Ward, C. H. *J. Am. Chem. Soc.* **1954**, *76*, 1169.
3. Sisido, K.; Takeda, Y.; Kinugawa, Z. *J. Am. Chem. Soc.* **1961**, *83*, 538–541.
4. Sisido, K.; Kojima, S. *J. Organomet. Chem.* **1968**, *11*, 503–513.
5. Matsuda, H.; Matsuda, S. *Kogyo Kagaku Zassi* **1960**, *63*, 114–118.
6. Matsuda, H.; Taniguchi, H.; Matsuda, S.; Sato, R. *Kogyo Kagaku Zassi* **1961**, *64*, 541–543.
7. Matsuda, H.; Hayasi, J.; Matsuda, S. *Kogyo Kagaku Zassi* **1961**, *64*, 1951–1954.
8. Matsuda, H.; Nakamura, M.; Matsuda, S. *Kogyo Kagaku Zassi* **1961**, *64*, 1948–1951.
9. Omae, I. *Organotin Chemistry (J. Organomet. Chem. Library)*; Elsevier: Amsterdam, **1989**; Vol. 21.
10. Davies, A. G.; Smith, P. J. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 2, Chapter 11, pp 519–627.
11. Smith, P. J., Ed. *Chemistry of Tin* 2nd. ed.; Blackie: London, 1998.
12. Kuivila, H. G.; Menapace, L. W.; Warner, C. R. *J. Am. Chem. Soc.* **1962**, *84*, 3584–3586.
13. Neumann, W. P.; Sommer, R. *Liebigs Ann. Chem.* **1964**, *675*, 10–18.
14. Kuivila, H. G. *Adv. Organomet. Chem.* **1964**, *1*, 47–87.
15. Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, **1987**.
16. Davies, A. G. *Organotin Chemistry*; Wiley-VCH: Weinheim, **2004**.
17. Espinet, P.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 4704–4874.
18. Stille, J. K. *Angew. Chem. Int. Ed.* **1986**, *25*, 508–524.
19. Farina, V. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 12.
20. Mitchell, T. N. *Synthesis* **1992**, 803–818.
21. Mitchell, T. N. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998.
22. Neumann, W. P. *Synthesis* **1987**, 665–682.
23. Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541–3676.
24. Bowman, W. R.; Bridge, C. F.; Brookes, P. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1–14.
25. Shibata, I.; Baba, A. *Curr. Org. Chem.* **2002**, *6*, 665–693.
26. Ryu, I.; Sonoda, N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177–194.
27. Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, I. *Chem. Rev.* **1999**, *99*, 1991–2070.
28. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574–1585.
29. Wroblewski, A. E.; Halłajewska-Wosik, A. *Tetrahedron: Asymmetry* **2004**, *15*, 2075–2077.
30. Jung, P. M. J.; Burger, A.; Biellmann, J. F. *J. Org. Chem.* **1997**, *62*, 8309–8314.

31. Wnuk, S. F.; Rios, J. M.; Khan, J.; Hsu, Y. L. *J. Org. Chem.* **2000**, *65*, 4169–4174.
32. Baker, S. R.; Burton, K. I.; Parsons, A. F.; Pons, J.-F.; Wilson, M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 427–436.
33. Rivkin, A.; Turiso, F. G.; Nagashima, T.; Curran, D. P. *J. Org. Chem.* **2004**, *69*, 3719–3725.
34. Bryans, J. S.; Large, J. M.; Parsons, A. F. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2897–2904.
35. Bryans, J. S.; Large, J. M.; Parsons, A. F. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2905–2910.
36. Della, E. W.; Smith, P. A. *J. Org. Chem.* **1999**, *64*, 1798–1806.
37. Harrowven, D. C.; Suttona, B. J.; Coulton, S. *Tetrahedron Lett.* **2001**, *42*, 2907–2910.
38. Harrowven, D. C.; Suttona, B. J.; Coulton, S. *Tetrahedron* **2002**, *58*, 3387–3400.
39. Harrowven, D. C.; Suttona, B. J.; Coulton, S. *Org. Biomol. Chem.* **2003**, *1*, 4047–4057.
40. Maguire, R. J.; Munt, S. P.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2853–2863.
41. Martinez-Grau, A.; Curran, D. P. *Tetrahedron* **1997**, *53*, 5679–5698.
42. Curran, D. P.; Gabarda, A. E. *Tetrahedron* **1999**, *55*, 3327–3336.
43. Benati, L.; Bencivenni, G.; Leardini, R.; Minozzi, M.; Nanni, D.; Scialpi, R.; Spagnolo, P.; Zanardi, G.; Rizzoli, C. *Org. Lett* **2004**, *3*, 417–420.
44. Marco-Contelles, J.; Destabel, C.; Chiara, J. L.; Ber, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1547–1550.
45. Ryu, I.; Ogura, S.; Minakata, S.; Komatsu, M. *Tetrahedron Lett.* **1999**, *40*, 1515–1518.
46. Depature, M. I.; Jacques Grimaldi, J.; Hatem, J. *Eur. J. Org. Chem.* **2001**, 941–946.
47. Marco-Contelles, J.; Balme, G.; Bouyssi, D.; Destabel, C.; Henriet-Bernard, C. D.; Grimaldi, J.; Hatem, J. M. *J. Org. Chem.* **1997**, *62*, 1202–1209.
48. Parsons, A. F.; Pettifer, A. M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 651–660.
49. Hays, D. S.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 6375–6381.
50. Flisińska-Łłuczak, J.; Leśniaka, S.; Nazarskib, R. B. *Tetrahedron* **2004**, *60*, 8181–8188.
51. Ryu, I.; Sonoda, N. *Angew. Chem. Int. Ed.* **1996**, *35*, 1050–1066.
52. Nagahara, K.; Ryu, I.; Yamazaki, H.; Kambe, N.; Komatsu, M.; Sonoda, N.; Baba, A. *Tetrahedron* **1997**, *53*, 14615–14626.
53. Ward, D. E.; Gai, Y.; Lai, Y. *Synlett* **1996**, 261–267.
54. Hayen, A.; Koch, R.; Saak, W.; Haase, D.; Metzger, J. O. *J. Am. Chem. Soc.* **2000**, *122*, 12458–12468.
55. Sibi, M. P.; Zimmerman, J.; Rheault, T. *Angew. Chem. Int. Ed.* **2003**, *42*, 4521–4523.
56. Terstiege, I.; Maleczka, R. E., Jr. *J. Org. Chem.* **1999**, *64*, 342–343.
57. Hays, D. S.; Scholl, M.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 6751–6752.
58. Lopez, R. M.; Hays, D. S.; Fu, G. C. *J. Am. Chem. Soc.* **1997**, *119*, 6949–6950.
59. Nanni, D.; Curran, D. P. *Tetrahedron*: *Asymmetry* **1996**, *7*, 2417–2422.
60. Blumenstein, M.; Schwarzkopf, K.; Metzger, J. O. *Angew. Chem. Int. Ed.* **1997**, *36*, 235–236.
61. Blumenstein, M.; Lemmler, M.; Hayen, A.; Metzger, J. O. *Tetrahedron*: *Asymmetry* **2003**, *14*, 3069–3077.
62. Dakternieks, D.; Dunn, K.; Perchyonok, V. T.; Schiesser, C. H. *Chem. Commun.* **1999**, 1665–1666.
63. Dakternieks, D.; Perchyonok, V. T.; Schiesserb, C. H. *Tetrahedron: Asymmetry* **2003**, *14*, 3057–3068.
64. Curran, D. P.; Hadida, S. *J. Am. Chem. Soc.* **1996**, *118*, 2531–2532.
65. Homer, J. H.; Martinez, F. N.; Newcomb, M.; Hadida, S.; Curran, D. P. *Tetrahedron Lett.* **1997**, *38*, 2783–2786.
66. Curran, D. P.; Hadida, S.; Kim, S-Y.; Luo, Z. *J. Am. Chem. Soc.* **1999**, *121*, 6607–6615.
67. Hadida, S.; Super, M. S.; Beckman, E. J.; Curran, D. P. *J. Am. Chem. Soc.* **1997**, *119*, 7406–7407.
68. Ryu, I.; Niguma, T.; Minakata, S.; Komatsu, M. *Tetrahedron Lett.* **1997**, *38*, 7883–7886.
69. Light, J.; Breslow, R. *Org. Synth.* **1995**, *72*, 199–207.
70. Han, X.; Hartmann, G. A.; Brazzale, A.; Gaston, R. D. *Tetrahedron Lett.* **2001**, *42*, 5837–5839.
71. Clive, D. L. J.; Wang, J. *J. Org. Chem.* **2002**, *67*, 1192–1198.
72. Dumartin, G.; Pourcel, M.; Delmond, B.; Donard, O.; Pereyre, M. *Tetrahedron Lett.* **1998**, *39*, 4663–4666.
73. Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Murphy, F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2534–2537.
74. Boussaguet, P.; Delmond, B.; Dumartin, G.; Pereyre, M. *Tetrahedron Lett.* **2000**, *41*, 3377–3380.
75. Chemin, A.; Mercier, A.; Deleuze, H.; Maillard, B.; Mondain-Monval, O. *J. Chem. Soc., Perkin Trans. 1* **2001**, 366–370.
76. Gastaldia, S.; Stienb, D. *Tetrahedron Lett.* **2002**, *43*, 4309–4311.
77. Sasaki, K.; Kondo, Y.; Maruoka, K. *Angew. Chem. Int. Ed.* **2001**, *40*, 411–414.
78. Oishi, T.; Nakata, T. *Acc. Chem. Res.* **1984**, *17*, 338–344.
79. Davis, A. P. In *Stereoselective Synthesis*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1996; Vol. 7, pp 3988–4040.
80. Sato, T.; Otera, J. *Appl. Organomet. Chem.* **1994**, *8*, 431.
81. Kawakami, T.; Shibata, I.; Baba, A.; Matsuda, H.; Sonoda, N. *Tetrahedron Lett.* **1994**, *35*, 8625.
82. Kawakami, T.; Shibata, I.; Baba, A. *J. Org. Chem.* **1996**, *61*, 82–87.
83. Shibata, I.; Suwa, T.; Moriuchi-Kawakami, T.; Tanizawa, D.; Sugiyama, E.; Matsuda, H.; Baba, A. *J. Org. Chem.* **1998**, *63*, 383–385.
84. Suwa, T.; Sugiyama, E.; Shibata, I.; Baba, A. *Synthesis* **2000**, 789–800.
85. Suwa, T.; Shibata, I.; Nishino, K.; Baba, A. *Org. Lett.* **1999**, *1*, 1579–1581.
86. Ward, D. E.; Rhee, C. K. *Can. J. Chem.* **1989**, *67*, 1206–1211.
87. Suwa, T.; Nishino, K.; Miyatake, M.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 3403–3406.
88. Suwa, T.; Shibata, I.; Baba, A. *Organometallics* **1999**, *18*, 3965–3967.
89. Shibata, I.; Suwa, T.; Ryu, K.; Baba, A. *J. Org. Chem.* **2001**, *66*, 8690–8692.
90. Pereyre, M.; Colin, G.; Valade, J. *Tetrahedron Lett.* **1967**, *8*, 4805–4808.
91. Smith, N. D.; Mancuso, J.; Lautens, M. *Chem. Rev.* **2000**, *100*, 3257–3282.
92. Dodero, V. I.; Mitchell, T. N.; Podesta, J. C. *Organometallics* **2003**, *22*, 856–860.
93. Kikukawa, K.; Umekawa, H.; Wada, F.; Matsuda, T. *Chem. Lett.* **1988**, 881–884.
94. Asao, N.; Liu, J.-X.; Sudoh, T.; Yamamoto, Y. *J. Org. Chem.* **1996**, *61*, 4568–4571.
95. Rice, M. B.; Whitehead, S. L.; Horvath, C. M.; Muchnij, J. A.; Maleczka, R. E., Jr. *Synthesis* **2001**, 1495.
96. Miyake, H.; Yamamura, K. *Chem. Lett.* **1989**, 981–982.
97. Gallagher, W. P.; Terstiege, I.; Maleezka, R. E., Jr. *J. Am. Chem. Soc.* **2001**, *123*, 3194–3204.
98. Kazmaier, U.; Pohlman, M.; Schauß, D. *Eur. J. Org. Chem.* **2000**, 2761–2766.
99. Thiele, C. M.; Mitchell, T. N. *Eur. J. Org. Chem.* **2004**, 323–329.

100. Miura, K.; Wang, D.; Matsumoto, Y.; Fujisawa, N.; Hosomi, A. *J. Org. Chem.* **2003**, *68*, 8730–8732.
101. Leusink, A. J.; Budding, H. A. *J. Organomet. Chem.* **1968**, *11*, 533–539.
102. Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547–2549.
103. Nakamura, E.; Imanishi, Y.; Machii, D. *J. Org. Chem.* **1994**, *59*, 8178–8186.
104. Zhang, H. X.; Guibe, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857–1867.
105. Shibata, I.; Suwa, T.; Ryu, K.; Baba, A. *J. Am. Chem. Soc.* **2001**, *123*, 4101–4102.
106. Kumar Das, V. G.; Chu, C.-K. In *Chemistry of the Metal Carbon Bond*; Hartley, F. R., Patai, S., Eds.; Wiley: New York, 1985; Vol. 3, pp 1–97.
107. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
108. Bloch, R. *Chem. Rev.* **1998**, *98*, 1407–1438.
109. Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069–1094.
110. Yamamoto, Y., Ed. *Tetrahedron (Symsia-in-Print, No. 36, Organotin Compounds in Organic Synthesis)* **1989**, *45*, 909–1230.
111. Nishigaichi, Y.; Takuwa, A.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1993**, *49*, 7395–7426.
112. Pereyre, M.; Quintard, J.-P. *Pure Appl. Chem.* **1981**, *53*, 2401–2417.
113. Hoffmann, R. W. *Angew. Chem. Int. Ed.* **1982**, *21*, 555–566.
114. Yamamoto, Y. *Acc. Chem. Res.* **1987**, *20*, 243–249.
115. Yamamoto, Y. *Si Ge Sn Pb Comp.* **1986**, *9*, 279–304.
116. Stille, J. K. *Angew. Chem. Int. Ed.* **1986**, *25*, 508–524.
117. Mitchell, T. N. *J. Organomet. Chem.* **1986**, *304*, 1–16.
118. Giese, B. *Angew. Chem. Int. Ed.* **1985**, *24*, 553–565.
119. Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*; Pergamon: Oxford, 1986; pp 98–102.
120. Fox, M. A., Chanon, M., Eds.; *Photoinduced Electron Transfer, Part C*; Elsevier: Amsterdam, 1988.
121. Takuwa, A.; Nishgaichi, Y.; Yamaoka, T.; Iihama, K. *Chem. Commun.* **1991**, 1359–1360.
122. Schinxer, D., Ed. *Selectivities in Lewis Acid Promoted Reactions*; Kluwer Academic: Dordrecht, 1989.
123. Yamamato, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107.
124. Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. *Tetrahedron Lett.* **1984**, *25*, 3927–3930.
125. Yano, K.; Baba, A.; Matsuda, A. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 66.
126. Shibata, I.; Kato, H.; Kanazawa, N.; Yasuda, M.; Baba, A. *J. Am. Chem. Soc.* **2004**, *126*, 466–467.
127. Dubost, C.; Leroy, B.; Marko, I. E.; Tinant, B.; Declercq, J.-P.; Bryansc, J. *Tetrahedron* **2004**, *60*, 7693–7704.
128. Thomas, E. J. *Chem. Commun.* **1997**, 411–418.
129. Carey, J. S.; Coulter, T. S.; Hallett, D. J.; Maguire, R. J.; McNeill, A. H.; Stanway, S. J.; Teerawutgulrag, A.; Thomas, E. J. *Pure Appl. Chem.* **1996**, *68*, 707–710.
130. Bradley, G. W.; Hallett, D. J.; Thomas, E. J. *Tetrahedron: Asymmetry* **1995**, *6*, 2579.
131. Hobson, L. A.; Vincent, M. A.; Thomas, E. J.; Hillier, I. H. *Chem. Commun.* **1998**, 899–900.
132. McNeill, A. H.; Thomas, E. J. *Synthesis* **1994**, 322.
133. Nishigaichi, Y.; Kuramoto, H.; Takuwa, A. *Tetrahedron Lett.* **1995**, *36*, 3353–3356.
134. Nishigaichi, Y.; Yoshikawa, M.; Takigawa, Y.; Takuwa, A. *Chem. Lett.* **1996**, 961–962.
135. Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31–48.
136. Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1996**, *61*, 105–108.
137. Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1995**, *60*, 1920–1921.
138. Yasuda, M.; Hirata, K.; Nishino, M.; Yamamoto, A.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 13442–13447.
139. Shibata, I.; Kano, T.; Kanazawa, N.; Fukuoka, S.; Baba, A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1389–1392.
140. Ooi, T.; Uraguchi, D.; Kagushima, N.; Maruoka, K. *J. Am. Chem. Soc.* **1998**, *120*, 5327–5328.
141. Ooi, T.; Uraguchi, D.; Maruoka, K. *Tetrahedron Lett.* **1998**, *39*, 8105.
142. Blackwell, J. M.; Piers, W. E.; McDonald, R. *J. Am. Chem. Soc.* **2002**, *124*, 1295–1306.
143. Lambert, J. B.; Zhao, Y.; Hongwei, T.; Winston, C.; Kuhlmann, B. *J. Am. Chem. Soc.* **1999**, *121*, 5001–5008.
144. Aspinall, H. C.; Browning, A. F.; Greeves, N.; Ravenscroft, P. *Tetrahedron Lett.* **1994**, *35*, 4639–4640.
145. Aspinall, H. C.; Greeves, N.; McIver, E. G. *Tetrahedron Lett.* **1998**, *39*, 9283–9286.
146. Kobayashi, S. *Eur. J. Org. Chem.* **1999**, 15–27.
147. Shibata, I.; Fukuoka, S.; Baba, A. *J. Org. Chem.* **1997**, *62*, 3790–3791.
148. Shibata, I.; Yoshimura, N.; Yabu, M.; Baba, A. *Eur. J. Org. Chem.* **2001**, 3207–3211.
149. Yadav, J. S.; Reddy, B. V. S.; Satheesh, G. *Tetrahedron Lett.* **2003**, *44*, 6501–6504.
150. Nagano, Y.; Orita, A.; Otera, J. *Tetrahedron* **2002**, *58*, 8211–8217.
151. Kobayashi, S.; Iwamoto, S.; Nagayama, S. *Synlett* **1997**, 1099–1101.
152. Marshall, J. A.; Gill, K.; Seletsky, B. M. *Angew. Chem. Int. Ed.* **2000**, *39*, 953–956.
153. Aspinall, H. C.; Bissett, J. S.; Greeves, N.; Levin, D. *Tetrahedron Lett.* **2002**, *43*, 323–325.
154. Choudary, B. M.; Chidara, S.; Sekhar, C. V. R. *Synlett* **2002**, 1694–1696.
155. Yadav, J. S.; Reddy, B. V. S.; Reddy, P. S. R.; Rao, M. S. *Tetrahedron Lett.* **2002**, *43*, 6245–6247.
156. Kobayashi, S.; Butsujma, T.; Nagayama, S. *Chem. Commun.* **1998**, 19–20.
157. Akiyama, T.; Onuma, Y. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1157–1158.
158. Matsukawa, Y.; Asao, N.; Kitahara, H.; Yamamoto, Y. *Tetrahedron* **1999**, *55*, 3779–3790.
159. Li, X.; Chen, J. J.; Tanner, D. D. *J. Org. Chem.* **1996**, *61*, 4314–4318.
160. Enholm, E. J.; Gallagher, M. E.; Moran, K. M.; Lombardi, J. S.; Schulte, J. P. II *Org. Lett.* **1999**, *1*, 689–691.
161. Yasuda, M.; Tsuchida, M.; Baba, A. *Chem. Commun.* **1998**, 563–564.
162. Shibata, I.; Fukuoka, S.; Baba, A. *Chem. Lett.* **1998**, 533–534.
163. Nishida, M.; Tozawa, T.; Yamada, K.; Mukaiyama, T. *Chem. Lett.* **1995**, 1125–1126.
164. Denmark, S. E.; Fu, J.-P. *Chem. Rev.* **2003**, *103*, 2763–2794.
165. Keck, G. E.; Tarbet, K. H.; Geraci, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 8467–8468.
166. Costa, A. L.; Piazza, M. G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Am. Chem. Soc.* **1993**, *115*, 7001–7002.
167. Yu, C.-M.; Choi, H.-S.; Jung, W.-H.; Kim, H.-J.; Shin, J. *Chem. Commun.* **1997**, 761–762.
168. Yu, C.-M.; Kim, J.-M.; Shin, M.-S.; Cho, D. *Tetrahedron Lett.* **2003**, *44*, 5487–5490.

169. Hanawa, H.; Kii, S.; Maruoka, K. *Adv. Synth. Catal.* **2001**, *343*, 57–60.
170. Hanawa, H.; Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 1708–1709.
171. Yanagisawa, A.; Nakashima, H.; Ishiba, A.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 4723–4724.
172. Denmark, S. E.; Wynn, T. *J. Am. Chem. Soc.* **2001**, *123*, 6199–6200.
173. Kurusu, M.; Lorca, M. *Tetrahedron Lett.* **2002**, *43*, 1765–1769.
174. Hanawa, H.; Kii, S.; Asao, N.; Maruoka, K. *Tetrahedron Lett.* **2000**, *41*, 5543–5546.
175. Lu, L.; Ji, S.-J.; Teo, Y.-C.; Loh, T.-P. *Org. Lett.* **2005**, *7*, 159–161.
176. Casolari, S.; D'Addario, D.; Tagliavini, E. *Org. Lett.* **1999**, *1*, 1061–1063.
177. Waltz, K. M.; Gavenonis, J.; Walsh, P. J. *Angew. Chem. Int. Ed.* **2002**, *41*, 3697–3699.
178. Nakamura, H.; Nakamura, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4242–4251.
179. Gastner, T.; Ishitani, H.; Akiyama, R.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2001**, *40*, 1896–1898.
180. Fang, F.; Johannsen, M.; Yao, S.; Gathergood, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **1999**, *64*, 4844–4849.
181. Masuyama, Y.; Suga, T.; Watabe, A.; Kurusu, Y. *Tetrahedron Lett.* **2003**, *44*, 2845–2847.
182. Okano, T.; Kiji, J.; Doi, T. *Chem. Lett.* **1998**, 5–6.
183. Kundu, A.; Prabhakar, S.; Vairamani, M.; Roy, S. *Organometallics* **1997**, *16*, 4796–4799.
184. Tan, X. H.; Shen, B.; Liu, L.; Guo, Q. X. *Tetrahedron Lett.* **2002**, *43*, 9373–9376.
185. Tan, X. H.; Shen, B.; Deng, W.; Zhao, H.; Liu, L.; Guo, Q. X. *Org. Lett.* **2003**, *5*, 1833–1835.
186. Samoshin, V. V.; Gremyachinskiy, D. E.; Smith, L. L.; Bliznets, I. V.; Gross, P. H. *Tetrahedron Lett.* **2002**, *43*, 6329–6330.
187. Houllemare, D.; Outurquin, F.; Paulmier, C. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1629–1632.
188. Wang, J.; Yuan, G.; Dong, C.-Q. *Chem. Lett.* **2004**, *33*, 286–289.
189. Ito, A.; Kishida, M.; Kurusu, Y.; Masuyama, Y. *J. Org. Chem.* **2000**, *65*, 494–498.
190. Masuyama, Y.; Saeki, K.; Horiguchi, S.; Kurusu, Y. *Synlett* **2001**, 1802–1804.
191. Masuyama, Y.; Yamamoto, N.; Kurusu, Y. *Synlett* **2002**, 2113–2115.
192. Masuyama, Y.; Ito, T.; Tachi, K.; Ito, A.; Kurusu, Y. *Chem. Commun.* **1999**, 1261–1262.
193. Chan, T. H.; Yang, Y.; Li, C. J. *J. Org. Chem.* **1999**, *64*, 4452–4455.
194. Zhang, J.; Blazecka, P. G.; Berven, H.; Belmont, D. *Tetrahedron Lett.* **2003**, *44*, 5579–5582.
195. Andrews, P. C.; Peatta, A. C.; Rastonb, C. L. *Tetrahedron Lett.* **2002**, *43*, 7541–7543.
196. Wang, Z.; Zha, Z.; Zhou, C. *Org. Lett.* **2002**, *4*, 1683–1685.
197. Sinha, P.; Roy, S. *Organometallics* **2004**, *23*, 67–71.
198. Li, X.-R; Loh, T.-P. *Tetrahedron: Asymmetry* **1996**, *7*, 1535–1538.
199. Loh, T.-P.; Li, X.-R. *Tetrahedron* **1999**, *55*, 5611–5622.
200. Loh, T.-P.; Li, X.-R. *Eur. J. Org. Chem.* **1999**, 1893–1899.
201. Cokley, T. M.; Harvey, P. J.; Marshall, R. L.; McCluskey, A.; Young, D. J. *J. Org. Chem.* **1997**, *62*, 1961–1964.
202. McCluskey, A.; Muderawan, I. W.; Muntari.; Young, D. J. *J. Org. Chem.* **2001**, *66*, 7811–7817.
203. Yasuda, M.; Kitahara, N.; Fujibayashi, T; Baba, A. *Chem. Lett.* **1998**, 743–744.
204. Masuyama, Y.; Ito, A.; Fukuzawa, M.; Terada, K.; Kurusu, Y. *Chem. Commun.* **1998**, 2025–2026.
205. Masuyama, Y.; Watabe, A.; Ito, A.; Kurusu, Y. *Chem. Commun.* **2000**, 2009–2010.
206. Kadota, I.; Hatakeyama, D.; Seki, K.; Yamamoto, Y. *Tetrahedron Lett.* **1996**, *37*, 3059–3062.
207. Marshall, J. A.; Yu, R. H.; Perkins, J. F. *J. Org. Chem.* **1995**, *60*, 5550–5555.
208. Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 8214–8219.
209. Marshall, J. A.; Palovich, M. *J. Org. Chem.* **1997**, *62*, 6001–6005.
210. Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1995**, *60*, 1920–1921.
211. Keck, G. E.; Krishnamurthy, D.; Chen, X. *Tetrahedron Lett.* **1994**, *35*, 8323–8324.
212. Yu, C.-M.; Yoon, S.-K.; Choi, H.-S.; Baek, K. *Chem. Commun.* **1997**, 763–764.
213. Yu, C.-M.; Choi, H.-S.; Yoon, S.-K.; Jung, W.-H. *Synlett* **1997**, 889–890.
214. Yu, C.-M.; Yoon, S.-K.; Baek, K.; Lee, J.-Y. *Angew. Chem. Int. Ed.* **1998**, *37*, 2392–2395.
215. Linderman, R. J.; Chen, S. *Tetrahedron Lett.* **1996**, *37*, 3819–3822.
216. Powell, N. A.; Rychnovsky, S. D. *Tetrahedron Lett.* **1998**, *39*, 3103–3106.
217. Buffet, M. F.; Dixon, D. J.; Ley, S. V.; Tate, E. W. *Synlett* **1998**, 1091–1092.
218. Yasuda, M.; Miyai, T.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1995**, *36*, 9497–9500.
219. Pereyre, M.; Bellegarde, B.; Mendelsohn, J.; Valade, J. *J. Organomet. Chem.* **1968**, *11*, 97–110.
220. Yanagisawa, A.; Matsumoto, Y.; Nakanishi, H.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1997**, *119*, 9319–9320.
221. Yanagisawa, A.; Kimura, K.; Nakatsuka, Y.; Yamamoto, H. *Synlett* **1998**, 958–960.
222. Momiyama, N.; Yamamoto, H. *Org. Lett.* **2002**, *4*, 3579–3582.
223. Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2003**, *125*, 6038–6039.
224. Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2004**, *126*, 5360–5361.
225. Yasuda, M.; Oh-hata, T.; Shibata, I.; Baba, A.; Matsuda, H.; Sonoda, N. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1180–1186.
226. Schmittel, M.; Haeuseler, A.; Nilges, T.; Pfitzner, A. *Chem. Commun.* **2003**, 34–35.
227. Haeuseler, A.; Henn, W.; Schmittel, M. *Synthesis* **2003**, 2576–2589.
228. Yasuda, M.; Hayashi, K.; Katoh, Y.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **1998**, *120*, 715–721.
229. Yasuda, M.; Chiba, K.; Baba, A. *J. Am. Chem. Soc.* **2000**, *122*, 7549–7555.
230. Yasuda, M.; Ohigashi, N.; Shibata, I.; Baba, A. *J. Org. Chem.* **1999**, *64*, 2180–2181.
231. Yasuda, M.; Chiba, K.; Ohigashi, N.; Katoh, Y.; Baba, A. *J. Am. Chem. Soc.* **2003**, *125*, 7291–7300.
232. Yasuda, M.; Shigeyoshi, Y.; Shibata, I.; Baba, A. *Synthesis* **2005**, 233–239.
233. Yasuda, M.; Ohigashi, N.; Baba, A. *Chem. Lett.* **2000**, 1266–1267.
234. Enholm, E. J.; Xie, Y.; Abboud, K. A. *J. Org. Chem.* **1996**, *60*, 1112–1113.
235. Kawakami, T.; Miyatake, M.; Shibata, I.; Baba, A. *J. Org. Chem.* **1996**, *61*, 376–379.
236. Ooi, T.; Doda, K.; Sakai, D.; Maruoka, K. *Tetrahedron Lett.* **1999**, *40*, 2133–2136.
237. Li, X.; Chen, J. J.; Tanner, D. D. *J. Org. Chem.* **1996**, *61*, 4314–4318.
238. Rossi, T.; Marchioro, C.; Paio, A.; Thomas, R. J.; Zarantonello, P. *J. Org. Chem.* **1997**, *62*, 1653–1661.

239. Shibata, I.; Yasuda, K.; Tanaka, Y.; Yasuda, M.; Baba, A. *J. Org. Chem.* **1998**, *63*, 1334–1336.
240. Shibata, I.; Mori, Y.; Yamasaki, H.; Baba, A.; Matsuda, H. *Tetrahedron Lett.* **1993**, *34*, 6567–6570.
241. Gridley, J. J.; Coogan, M. P.; Knight, D. W.; Malik, K. M. A.; Sharland, C. M.; Singkhonrat, J.; Williams, S. *Chem. Commun.* **2003**, 2550–2551.
242. Sano, S.; Miwa, T.; Liu, X.-K.; Ishii, T.; Takehisa, T.; Shiro, M.; Nagao, Y. *Tetrahedron: Asymmetry* **1998**, *9*, 3615–3618.
243. Mukaiyama, T.; Pudhom, K.; Yamane, K.; Arai, H. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 413–425.
244. Yasuda, M.; Okamoto, K.; Sako, T.; Baba, A. *Chem. Commun.* **2001**, 157–158.
245. Yasuda, M.; Matsukawa, Y.; Okamoto, K.; Sako, T.; Kitahara, N.; Baba, A. *Chem. Commun.* **2000**, 2149–2150.
246. Yasuda, M.; Tsuji, S.; Shibata, I.; Baba, A. *J. Org. Chem.* **1997**, *62*, 8282–8283.
247. Yasuda, M.; Tsuji, S.; Shigeyoshi, Y.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 7440–7447.
248. Dechy-Cabaret, O.; Martin-Vaca, B.; Bourissou, D. *Chem. Rev.* **2004**, *104*, 6147–6176.
249. Degèe, P.; Dubois, P.; Jerome, R.; Jacobsen, S.; Fritz, H.-G. *Macromol. Symp.* **1999**, *144*, 289–302.
250. Kricheldorf, H. R.; Kreiser-Saunders, I.; Stricker, A. *Macromolecules* **2000**, *33*, 702–709.
251. Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **2000**, *33*, 7359–7370.
252. Ryner, M.; Stridsberg, K.; Albertsson, A.-C.; von Schenk, H.; Svensson, M. *Macromolecules* **2001**, *34*, 3877–3881.
253. Marinez, E. R.; Salmassian, E. K.; Lau, T. T.; Gutierrez, C. G. *J. Org. Chem.* **1996**, *61*, 3548–3550.
254. Ramirez, R. J. A.; Karamanukyan, L.; Ortiz, S.; Gutierrez, C. G. *Tetrahedron Lett.* **1997**, *38*, 749–752.
255. Meyer, M.; Telford, J. R.; Cohen, S. M.; White, D. J.; Xu, J.; Raymond, K. N. *J. Am. Chem. Soc.* **1997**, *119*, 10093–10103.
256. Salomon, C. J.; Mata, E. G.; Mascaretti, O. A. *J. Org. Chem.* **1994**, *59*, 7259–7266.
257. Otera, J. *Chem. Rev.* **1993**, *93*, 1449–1470.
258. Otera, J. *Angew. Chem. Int. Ed.* **2001**, *40*, 2044–2045.
259. Otera, J. *Acc. Chem. Res.* **2004**, *37*, 288–296.
260. Sakakura, T.; Saito, Y.; Okano, M.; Choi, J.-C.; Sako, T. *J. Org. Chem.* **1998**, *63*, 7095–7096.
261. Choi, J.-C.; Sakakura, T.; Sako, T. *J. Am. Chem. Soc.* **1999**, *121*, 3793–3794.
262. Mukaiyama, T.; Watanabe, K.; Shiina, I. *Chem. Lett.* **1995**, 1.
263. Salomon, C. J.; Danelon, G. O.; Mascaretti, O. A. *J. Org. Chem.* **2000**, *65*, 9220–9222.
264. Nishiyama, Y.; Ohashi, H.; Itoh, K.; Sonoda, N. *Chem. Lett.* **1998**, 159–160.
265. Hays, D.; Fu, G. C. *J. Org. Chem.* **1997**, *62*, 7070–7071.
266. Nimitsiriwat, N.; Marshall, E. L.; Gibson, V. C.; Elsegood, M. R. J.; Dale, S. H. *J. Am. Chem. Soc.* **2004**, *126*, 13598–13599.
267. Pearson, W. H.; Dietz, A.; Stoy, P. *Org. Lett.* **2004**, *6*, 1005–1008.
268. Hao, X.; Yoshida, A.; Nishikido, J. *Tetrahedron Lett.* **2004**, *45*, 781–785.
269. Hao, X.; Yamazaki, O.; Yoshida, A.; Nishikido, J. *Tetrahedron Lett.* **2003**, *44*, 4977–4980.
270. Chen, J.-X.; Otera, J. *Angew. Chem. Int. Ed.* **1998**, *37*, 91–93.
271. Shibata, I.; Kawasaki, M.; Yasuda, M.; Baba, A. *Chem. Lett.* **1999**, 689–690.
272. Shibata, I.; Suwa, T.; Sakakibara, H.; Baba, A. *Org. Lett.* **2002**, *4*, 301–303.
273. Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S. *J. Am. Chem. Soc.* **1998**, *120*, 6609–6610.
274. Yamaguchi, M.; Hayashi, A.; Hirama, M. *J. Am. Chem. Soc.* **1993**, *115*, 3362–3363.
275. Yamaguchi, M.; Hayashi, A.; Hirama, M. *J. Synth. Org. Chem. Jpn.* **1996**, *54*, 267–279.
276. Yamaguchi, M.; Hayashi, A.; Hirama, M. *Chem. Commun.* **1995**, *117*, 1151–1152.
277. Kitagawa, O.; Suzuki, T.; Fujiwara, H.; Taguchi, T. *Tetrahedron Lett.* **1999**, *40*, 2549–2552.
278. Barbero, A.; Pulido, F. L. *Synlett* **2001**, 827–829.
279. Krlef, A.; Provins, L. *Tetrahedron Lett.* **1998**, *39*, 2017–2020.
280. Krief, A.; Provins, L.; Dumont, W. *Angew. Chem. Int. Ed.* **1999**, *38*, 1946–1948.
281. Mori, M.; Isono, N.; Wakamatsu, H. *Synlett* **1999**, 269–280.
282. Mori, M.; Isono, N.; Kaneta, N.; Shibasaki, M. *J. Org. Chem.* **1993**, *58*, 2972–2976.
283. Kinoshita, A.; Mori, M. *Chem. Lett.* **1994**, 1475–1478.
284. Sato, H.; Isono, N.; Miyoshi, I.; Mori, M. *Tetrahedron* **1996**, *52*, 8143–8158.
285. Sato, H.; Isono, N.; Okamura, K.; Date, T.; Mori, M. *Tetrahedron Lett.* **1994**, *35*, 2035–2038.
286. Hopf, H.; Jones, P. G.; Bubenitschek, P.; Werner, C. *Angew. Chem. Int. Ed.* **1995**, *34*, 2367–2368.
287. Dolbier, W. R., Jr.; Rong, X. X.; Xu, Y. *J. Org. Chem.* **1997**, *62*, 7500–7502.
288. Honda, T.; Mori, M. *Chem. Lett.* **1994**, 1013–1016.
289. Kawachi, A.; Maeda, H.; Nakamura, H.; Doi, N.; Tamao, K. *J. Am. Chem. Soc.* **2001**, *123*, 3143–3144.
290. Studer, A. *Angew. Chem. Int. Ed.* **1998**, *37*, 462–465.
291. Barbero, A.; Cuadrado, P.; Gonza'lez, A. M.; Pulido, F. J.; Fleming, I. *J. Chem. Soc., Chem. Commun.* **1992**, 351–352.
292. Barbero, A.; Cuadrado, P.; Gonza'lez, A. M.; Pulido, F. J.; Rubio, R.; Fleming, I. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1657–1662.
293. Barbero, A.; Cuadrado, P.; Garcia, C.; Rincon, J. A.; Pulido, F. J. *J. Org. Chem.* **1998**, *63*, 7531–7533.
294. Barbero, A.; Cuadrado, P.; Rincon, J. A.; Pulido, F. J.; Galisteo, D.; Martinez-Garcia, H. *Angew. Chem. Int. Ed.* **2001**, *40*, 2101–2103.
295. Thibonnet, J.; Abarbri, M.; Parrain, J.-L.; Duchêne, A. *Tetrahedron* **2003**, *59*, 4433–4441.
296. Thibonnet, J.; Launay, V.; Abarbri, M.; Duchêne, A.; Parrain, J.-L. *Tetrahedron Lett.* **1998**, *39*, 4277–4280.
297. Reginato, G.; Mordini, A.; Degl'Innocenti, A.; Manganiello, S.; Capperucci, A.; Poli, G. *Tetrahedron* **1998**, *54*, 10227–10238.
298. Nielsen, T. E.; Cubillo de Dios, M. A.; Tanner, D. *J. Org. Chem.* **2002**, *67*, 7309–7313.
299. Cabezas, J. A.; Oehlschlager, A. C. *Synlett* **1994**, 432–442.
300. Ricci, A.; Blart, E.; Comes-Franchini, M.; Reginato, G.; Zani, P. *Pure Appl. Chem.* **1996**, *68*, 679–682.
301. Cuadrado, P.; González-Nogal, A. M.; Sánchez, A. *J. Org. Chem.* **2001**, *66*, 1961–1965.
302. Betzer, J. F.; Delaloge, F.; Muller, B.; Pancrazi, A.; Prunet, J. *J. Org. Chem.* **1997**, *62*, 7768–7780.
303. Betzer, J. F.; Pancrazi, A. *Synthesis* **1999**, 629–634.
304. Betzer, J. F.; Pancrazi, A. *Synlett* **1998**, 1129–1131.
305. Betzer, J. F.; Ardisson, J.; Lallemand, J.-Y.; Pancrazi, A. *Tetrahedron Lett.* **1997**, *38*, 2219–2282.
306. Barbero, A.; Cuadrado, P.; Gonzalez, A. M.; Pulido, F. J.; Fleming, I. *J. Chem. Soc., Perkin Trans. 1* **1992**, 327–332.
307. Barbero, A.; Pulido, F. J. *Tetrahedron Lett.* **2004**, *45*, 3765–3767.
308. Usugi, S.; Tang, J.; Shinokubo, H.; Oshima, K. *Synlett* **1999**, 1417–1419.

9.09
Lead

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9.09.1 Introduction

Since the first preparation of tetraethyllead in 1853,[1,1a] the interest for organolead compounds has grown up to mid-twentieth century, largely due to the discovery of the antiknock properties of Et_4Pb, used as an additive for motor gasoline.[2] In the 1970s it became the most important organometallic compound produced in the world. Other organolead compounds also found various applications, such as polymerization catalysts, polymer stabilizers, etc. However, the toxicity of tetraalkyllead derivatives causing environmental hazards and damage to human health became an important environmental issue in the 1980s. Therefore, as an important representative of the heavy metals, the application of organolead derivatives has declined in the past 30 years. In particular, in the last decade, since the previous COMC(1995) review published by J. T. Pinhey,[3] organic chemists have been cautious about employing lead compounds. However, this general tendency toward less frequent uses of the organolead compounds should be balanced by their high reactivity, the high selectivity of their reactions, and the cheap price of lead as a raw material. Moreover, the toxicity issue should not be overestimated.[4] Indeed, despite general public perception, lead(II) salts are about 10 times less toxic than palladium(II) salts.[5,5a] It is also worth noting that lead reagents are easily handled and the levels of residual lead in reactions using lead(IV) reagents are very low.[6] Thus, organolead compounds should not be excluded systematically but instead considered as valuable selective reagents for organic synthesis, particularly if

catalytic systems were to be designed and discovered in the future. Few such examples have been disclosed, but the use of electrochemical methods deserve further investigation and should lead to new applications.[7,7a]

In this chapter, only the reactions of well-defined organolead reagents will be considered. The word "*organolead*" will refer only to compounds bearing at least one clearly demonstrated covalent C–Pb bond. Other reagents containing four Pb–heteroatom bonds, such as $Pb(OAc)_4$ and its congeners, will not be considered. Since Pinhey's review in 1995, a number of other reviews have been published on various aspects of the application of lead to organic synthesis.[8–14] Many methods have been reported for the synthesis of the different types of organolead compounds. As they have been known for a number of years, the reader is referred to Pinhey's review for a comprehensive coverage of the general methods of synthesis.[3]

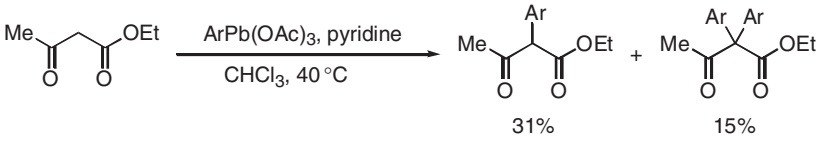
9.09.2 Base-catalyzed Reactions of Organolead Triacetates

Pinhey *et al.* have shown that aryllead tricarboxylates react with soft nucleophiles to afford *C*-arylation products. In most cases, the reactions proceed in chloroform, at 40–60 °C in the presence of pyridine as a base, with a ratio of substrate to organolead derivative to pyridine of 1 : 1 : 3. The substrates which easily undergo *C*-arylation include phenols, β-dicarbonyl compounds and their vinylogs, α-cyanoesters, α-heterosubstituted ketones, enamines and nitroalkanes. Non-carbon nucleophiles have also been reported to react, although in a very limited number.[3] These aryllead derivatives behave as aryl cation equivalents in reactions which involve a ligand coupling mechanism.[3,8,15] These aryl coupling reactions have been further investigated in reactivity studies as well as key steps in the synthesis of natural products. The reactions of organolead triacetates with carbonyl-containing substrates have been among the most extensively studied, due to the wide range of transformations that can be subsequently performed on the derived ketonic compounds. A less important series of applications deals with the reactivity of organolead(IV) compounds with phenolic and aniline substrates.

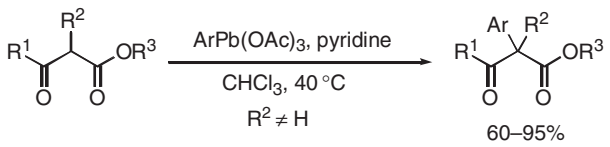
9.09.2.1 Arylation of Dicarbonyl Compounds

A variety of enolized compounds react with aryllead triacetate to afford the corresponding α-arylcarbonyl derivatives. Due to the lower reactivity of aryllead(IV) triacetate compared to lead(IV) tetraacetate, the range of compounds affected by organolead compounds is narrower and, for the most part, restricted to substrates with pK_a values similar or less than that of phenol. The usual reaction conditions are closely similar to the reactions with phenols, that is a ratio of substrate to organolead derivative to pyridine of 1 : 1 : 3 in chloroform solution at 40–60 °C. Although pyridine is usually preferred, bases that coordinate more strongly to lead, such as 2,2′-bipyridine, 1,10-phenanthroline or 4-dimethylaminopyridine (DMAP) can be advantageously used. Generally, β-dicarbonyl compounds with one α-hydrogen give the α-aryl derivatives in good to high yields, and β-dicarbonyl compounds with two α-hydrogen give variable mixtures of mono- and di-arylated derivatives, in modest to moderate yield.[3] The substrates which easily react with aryllead triacetates include β-diketones, β-ketoaldehydes, α- and β-ketoesters, β-ketoester vinylogs, and malonic acid derivatives such as their esters, amides, or nitriles.

Arylation of β-ketoesters by aryllead triacetates has been one of the most active fields of investigation in the chemistry of organolead compounds. β-Ketoesters behave similarly to β-diketones in their reactions with aryllead triacetate. Acyclic β-ketoesters possessing two α-hydrogen afford mixtures of mono and diaryl derivatives (Equation (1)),[16] when consistently good to high yields (60–95%) are obtained with β-ketoesters possessing only one α-hydrogen (Equation (2)).[16]

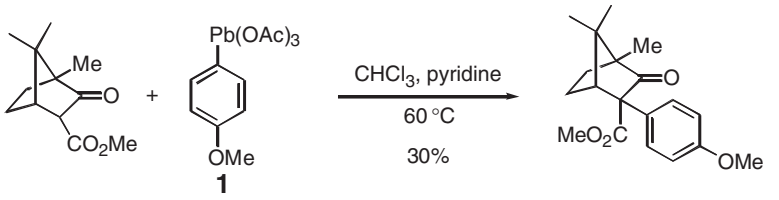


(1)

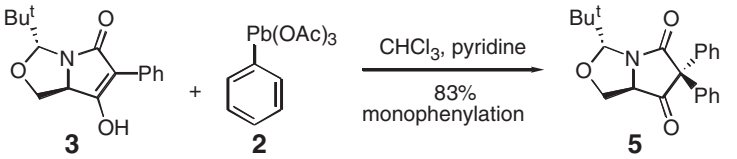


(2)

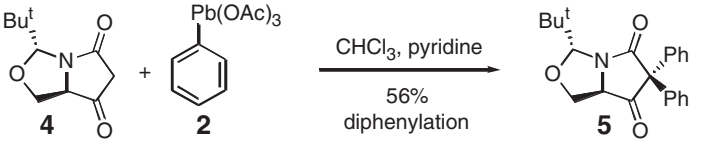
However, it requires rather hindered β-ketoesters to observe a significant drop in the yield of the arylation reaction with *p*-methoxyphenyllead triacetate **1** (Equation (3)).[16] On the other hand, if the β-dicarbonyl moiety is inserted into a cyclic structure, this difference disappears. For example, in the synthesis of functionalized tetramic acid derivatives, reaction of phenyllead triacetate **2** with the two five-membered cyclic pyrrolidinediones **3** and **4** afforded the diphenyl derivative **5** with a similar efficiency of the arylation step (Equations (4) and (5)).[17]



(3)

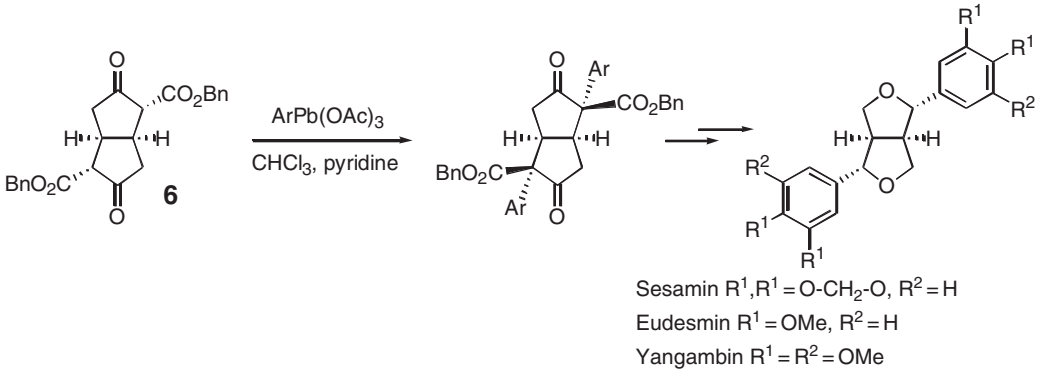


(4)

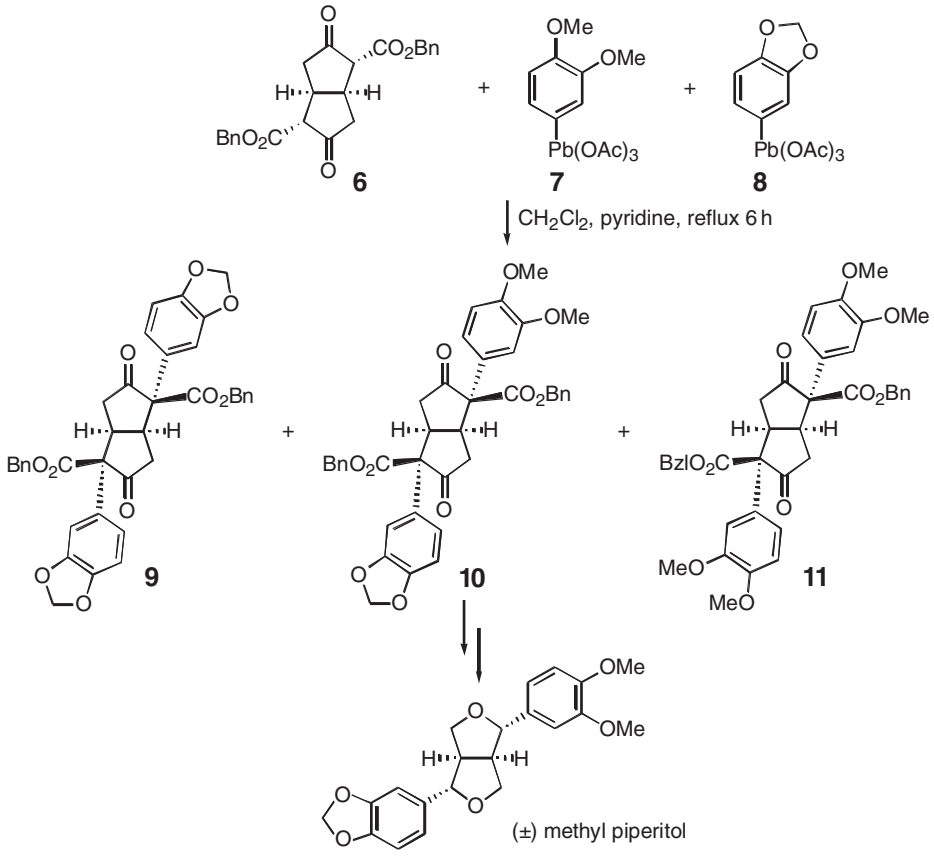


(5)

Aryllead triacetate reagents are generally used as a purified compound. However, *in situ* generated reagents can also be conveniently used as efficient alternatives, particularly in the case of relatively unstable reagents. The *in situ* synthesis of the aryllead triacetate can be done either by mercury–lead exchange[18,18a] or more preferably by boron–lead exchange.[19] Combined with the Krapcho decarboxylation,[20] the arylation of methyl β-ketoesters constitutes an efficient method for the synthesis of α-arylketones.[21] However, difficulties are sometimes encountered with sterically rigid or demanding tetrasubstituted α-aryl β-ketoesters.[22] Prolonged heating at 180 °C can result in low yields either by decomposition of the product or by oxidation to α,β-unsaturated ketones.[21] This drawback can be avoided by using a modified β-ketoester, such as the benzyl[23] or allyl[24] esters. The reaction of arylation of β-ketoesters with aryllead triacetates has been used as a key step in the synthesis of a number of natural products or analogs. Thus, carbocyclic β-ketoesters were key substrates in the synthesis of various lignan structures (Scheme 1). Substrates bearing two β-ketoester moieties, such as dibenzyl 3,7-dioxobicyclo [3.3.0]-octane-2,6-dicarboxylate **6**, can be bisarylated with aryllead triacetate. Further elaboration of the carbon skeleton led to the total synthesis of natural products possessing an aryltetrahydrofuran structure: (±) sesamin, (±) eudesmin, (±) yangambin.[23]



Scheme 1

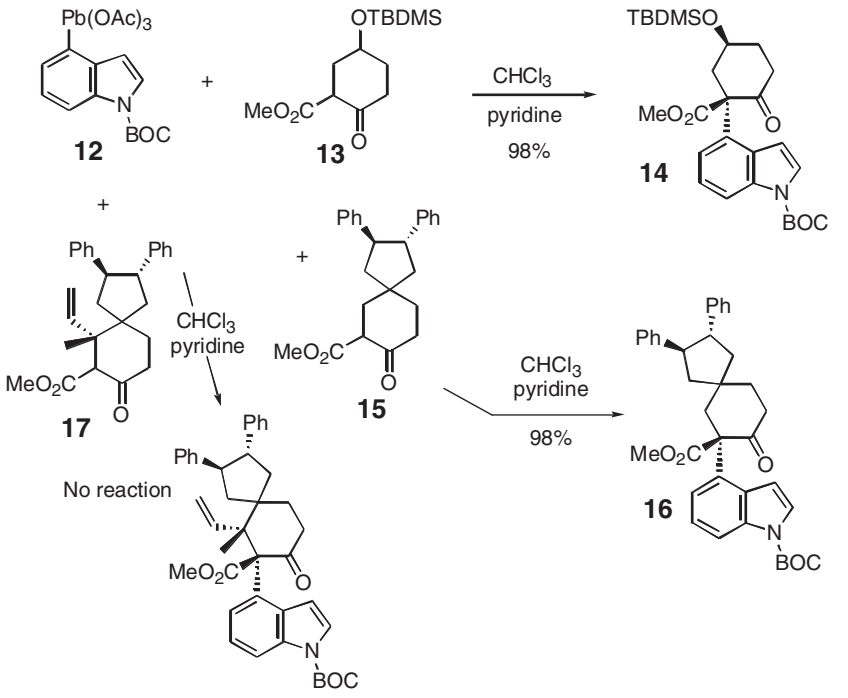


Scheme 2

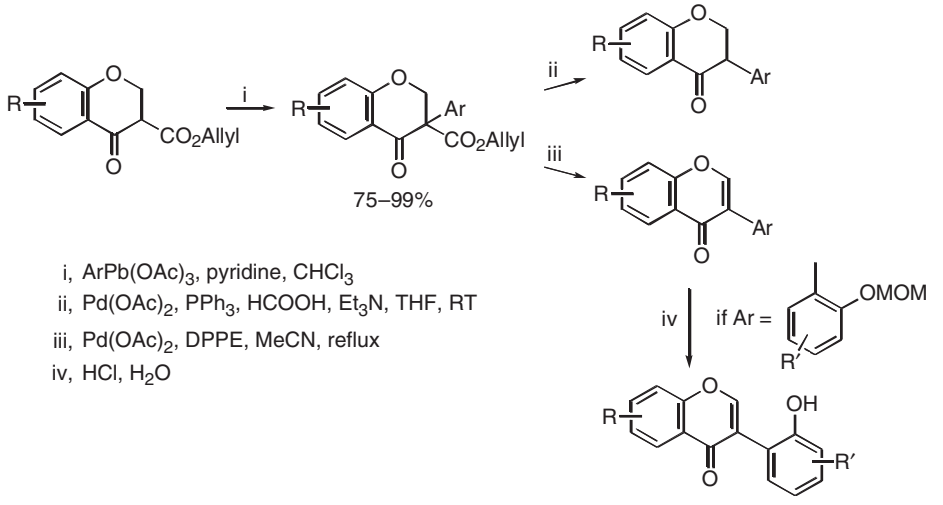
Mixed arylation of bifunctional substrates, such as those containing two β-ketoester groups in their structure can be made. This possibility was used to synthesize unsymmetrically substituted compounds containing two different aryl groups (Scheme 2). One-pot treatment of the dibenzyl 3,7-dioxobicyclo [3.3.0]-octane-2,6-dicarboxylate **6** with a mixture of two aryllead triacetates **7** and **8** afforded a mixture of the unsymmetrical diaryl derivative **10** with the two symmetrical diaryl compounds **9** and **11**. When the arylation was performed with 1.1 equiv. of each aryllead reagents **7** and **8**, a mixture of **9**–**11** in a ratio 0.46 : 1 : 0.72 was obtained. This ratio became 0.43 : 1 : 0.49, when 0.86 equiv. of **7** and 1.33 equiv. of **8** were used. This compound **10**, isolated in a 33% yield, was eventually elaborated to complete a total synthesis of (±) methyl piperitol.[25]

The reaction of 4-indolyllead triacetate **12** was explored with a number of β-ketoesters in a study directed toward the total synthesis of welwistatin *D* (Scheme 3).[26] However, while the model ketone derivatives **13** and **15** could be arylated in high yields with lead reagent **12** to give **14** and **16** respectively, the reaction with the more highly substituted welwistatin precursor **17** failed, probably because of the steric hindrance imposed by the methyl and vinyl substituents.

The reactions of arylation of heterocyclic β-ketoesters were employed in the synthesis of a number of isoflavanones and isoflavones.[27,28] α-Methylene α-arylketones can be easily and selectively obtained by arylation of allyl β-ketoesters which are eventually deprotected by the Tsuji's procedures.[29,29a] Deallyloxycarbonylation was performed by treatment of the allyl α-aryl-β-ketoesters with catalytic amounts of palladium(II) acetate, triethylammonium formate and triphenylphosphane in THF at room temperature and afforded the α-arylketones in 75–97% yield.[27] Deallyloxycarbonylation–dehydrogenation can be realized with the same allyl esters by treatment with catalytic amounts of palladium(II) acetate and 1,2-bis(diphenylphosphino)ethane (DPPE) in acetonitrile under reflux and affords the α-aryl α,β-unsaturated ketones in 60–90% yield (Scheme 4).[28] In particular, this reaction was used in a direct convergent synthesis of 2′-hydroxyisoflavones involving arylation of an appropriate allyl β-ketoester with the MOM-protected (2-methoxymethoxyphenyl)lead triacetate derivative (Scheme 4). The reaction of the isomeric

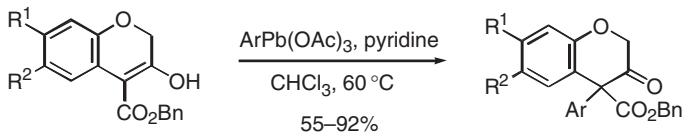


Scheme 3



Scheme 4

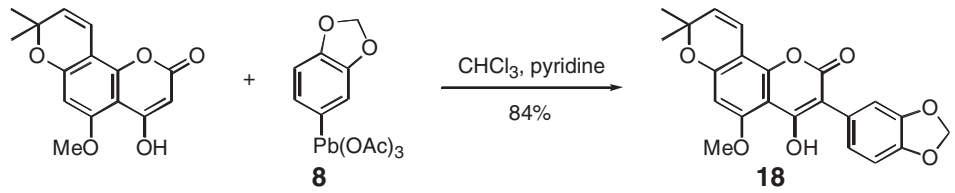
system, 4-alkoxycarbonylchroman-3-one, with aryllead triacetates afforded the 4-aryl derivatives in moderate to good yields, which led, after further elaboration, to neoflavenes (Equation (6)).[30]



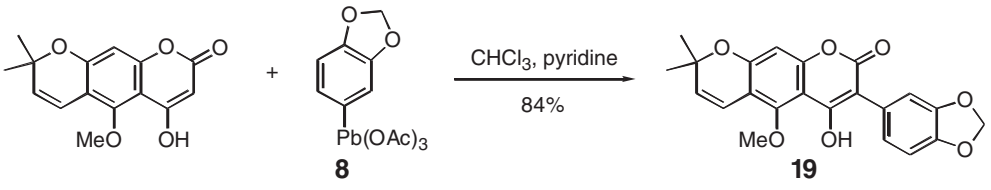
(6)

4-Hydroxycoumarins are cyclic, completely enolized β-ketoesters. In their reactions with aryllead triacetates, they behave more like phenols than like β-ketoesters bearing two α-hydrogens. Indeed monoarylation took place

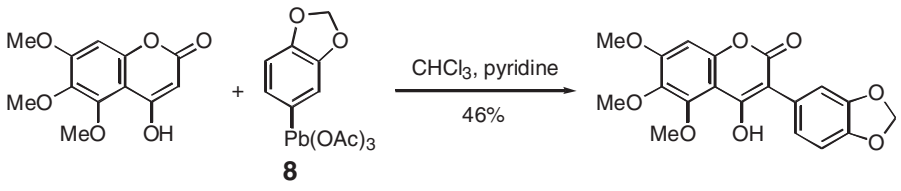
to provide a convenient access to 3-aryl-4-hydroxycoumarins, which belong to a group of highly oxygenated isoflavonoids.[31] This was applied, for example, to the synthesis of isorobustin **18**, robustin **19**, and robustic acid.[31,32] (Equations (7) and (8)) However, in a more recent study,[33] the reaction of 4-hydroxycoumarins with aryllead triacetates showed a less simple behavior, more similar to that of cyclic β-ketoesters than to the behavior of phenolic compounds (Equation (9)). Monoarylation appears to be dependent upon the reaction conditions and the number and position of the methoxy groups present on the A-ring of the coumarin and on the aryllead triacetate, and α,α-diarylation can occur to a significant extent (Equation (10)). When a bifunctional aryllead reagent, *ortho*-bromophenyllead triacetate, containing a benzylic reactive center was used, tetracyclic isochromanocoumarins were easily obtained in a one-pot reaction, provided the proper combination of bases was selected (Equation (11)).[34,35]



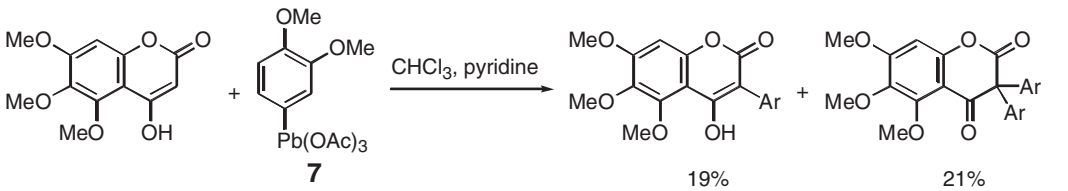
(7)



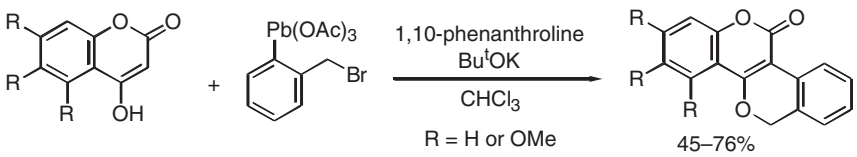
(8)



(9)

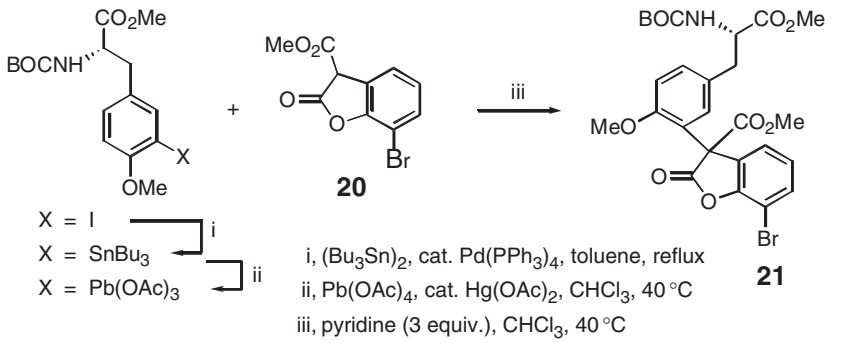


(10)



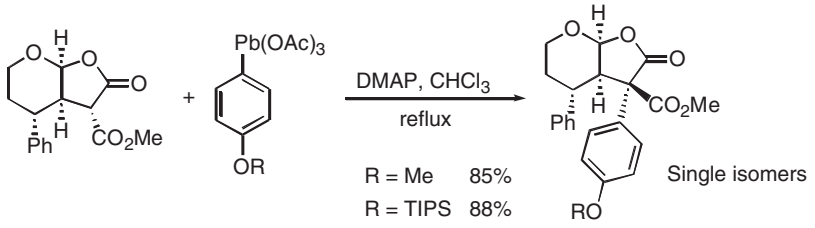
(11)

In an approach toward the synthesis of the marine natural product cytotoxin Diazonamide A, the arylation of a lactonic β-diester **20** with a tyrosinyllead triacetate was realized and afforded **21** as a mixture of diastereomers in 85% overall yield from 3-iodotyrosine (Scheme 5).[36] It later appeared that the first suggested structure of Diazonamide A[37] was in fact erroneous[38,38a] and that the organolead-based approach could not be used for the total synthesis of this natural product.



Scheme 5

In the course of model studies for the synthesis of Blapharocalyxin E, Cakir *et al.* reported that arylation of bicyclic lactones for the synthesis of aryl-substituted pyranoside derivatives led to highly diastereoselective arylation, only one isomer of the arylated derivative being detected and isolated (Equation (12)).[39]

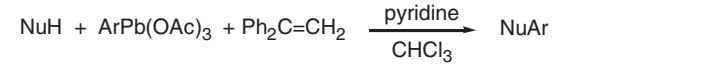


(12)

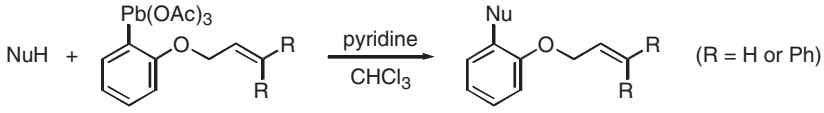
9.09.2.1.1 Mechanism and influence of the ligands and of the reaction conditions

In the cross-coupling reactions involving organolead triacylate reagents, the lead compound reacts as a carbocationic equivalent. An elusive covalent substrate-lead intermediate undergoes a reductive elimination at the lead center (Scheme 6).

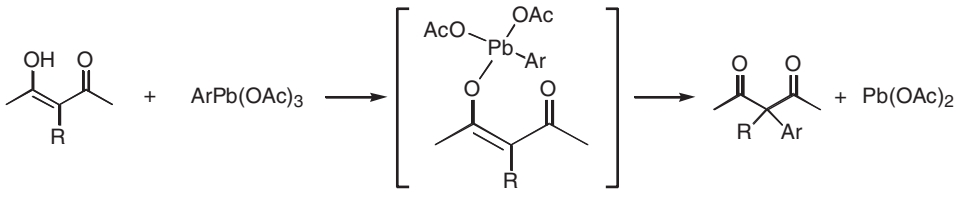
The mechanism of the ligand coupling or reductive elimination step is not well understood and rather speculative. However, the possible intermediacy of radical species, either free or in-cage, has been considered unlikely, since the use of free-radical traps did not alter the outcome of the reactions. The use of an external trap (1,1-diphenylethylene)[31,40] (Equation (13)) or the use of the classical internal intramolecular free-radical probe [(*o*-allyloxy)phenyl radical][41] or its diphenyl analog [(*o*-2,2-diphenylallyloxy)phenyl radical][42] (Equation (14)) did not interfere with the outcome of the arylation reaction, thus excluding the possibility of the intermediacy of free radicals.



(13)

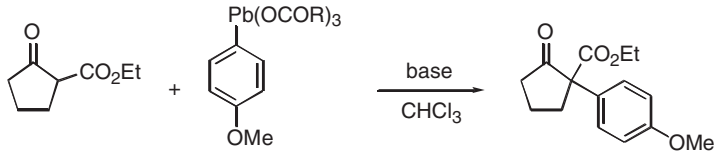


(14)



Scheme 6

In metal-mediated reactions, the importance of the nature of the ligands is well demonstrated. In the case of the lead-mediated reactions, two types of ligands can play a determinant role: (i) the bidentate covalently bound acyl groups, and (ii) the coordinating ligands containing electron-donating nitrogen centers. Modification of the ligands may be used to influence the efficiency of the cross-coupling reactions and even extend the scope to a wider range of nucleophiles or to allow enantioselective couplings. The nature of the acyl groups, substituting the lead atom, may be expected to play a significant role due to its vicinity to the reactive metallic center. Indeed, although lead tetraacetate is generally used for metal–metal exchange to generate organolead reagents, lead tetrabenzoate afforded more efficient reagents.[43] The steric hindrance of the acyl group can have a beneficial influence on the yields, up to a certain level (Equation (15)).[44]



R	*Base*	*Yield* (%)
Ac		65
Ac	DABCO	75
Pivaloyl	Pyridine	52
2,6-$Cl_2C_6H_3CO_2$	Pyridine	74
Thiophen-2-CO_2	Pyridine	40
3-Butenoyl	Pyridine	18
4-Pentenoyl	Pyridine	37
Tropolonyl	Pyridine	0

(15)

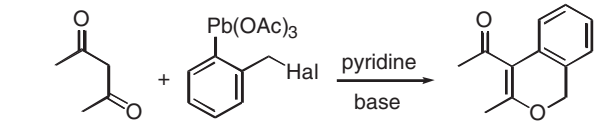
Pyridine is an important cofactor in the reaction system that leads to cleaner reactions and better yields of products than in its absence.[15] It can act either as a σ-donor for Pb(IV) or as a base catalyzing the keto-enol tautomerism. The σ-donor effect was evidenced spectroscopically by the formation of adducts of pyridine with lead tetraacetate.[45,45a] Moreover, pyridine catalyzed the ligand redistribution of *ortho*-methoxyphenyllead triacetate to bis(*ortho*-methoxyphenyl)lead diacetate.[46] Other σ-donor catalysts can be used and their nature is highly important for the success of the reaction. NaOMe and HOBT showed a modest effect, but a thousand-fold increase in rate over the uncatalyzed reaction was observed when 1,10-phenanthroline was employed and near quantitative yields of arylation products were obtained (Equation (16)).[44]

Base	*Rate*	*Yield* (%)
None	1	2
NaOMe	18	60
1-HOBT	40	35
Pyridine	133	70
Imidazole	180	90
DMAP	284	95
1,10-Phenanthroline	980	100

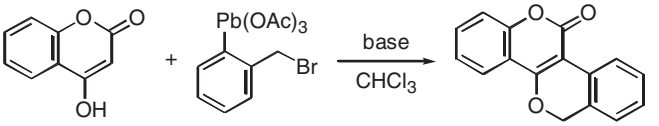
(16)

The role of pyridine as a σ-donor more than as a base was examplified by the use of *ortho*-chloro- or bromobenzyllead triacetate reagents, which required addition of a strong base to reach good to high yields of tricyclic derivatives resulting from the cascade arylation and base-catalyzed cyclization (Equation (17)).[34] The influence of the

σ-donor ligand was even more striking with the use of 1,10-phenanthroline and Bu^{t}OK that leads to the highest yields (Equation (18)).



(17)



(18)

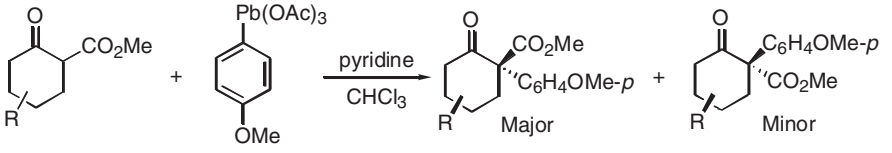
σ-donor ligand	*Yield* (%)
Pyridine	15
Pyridine – DMAP	20
1,10-Phenanthroline–Bu^{t}OK	76

9.09.2.1.2 Diastereoselectivity studies

The stereochemistry of aryllead reactions has not been extensively investigated. A small number of observations were in favor of a possible diastereoselectivity of the arylation reaction. For example, Pinhey *et al.* reported diastereoselectivity for the arylation of two compounds,[16,47] and Moloney *et al.* have done the same for a single compound.[48] Cakir *et al.* also reported diastereoselective arylation in the case of rigid bicyclic heterocyclic systems.[39] However, it is in the course of preparatory model studies aimed at the synthesis of natural products (Diazonamide A and *N*-methylwelwitindolinonje C isothiocyanate)[26,36] that Konopelski *et al.* investigated carefully the diastereoselectivity of the organolead-mediated arylation of various ring-substituted methyl 2-oxo-1-cyclohexanecarboxylate compounds (Table 1, entries 1–4) with 1.1 equiv. of *p*-methoxyphenyllead triacetate. Selectivities ranged from poor for the ketal-protected (Table 1, entry 6) to good for the *tert*-butyl derivative (Table 1, entry 5). Increasing the amount of lead reagent to 1.4 equiv. results in better isolated yields that could reach up to over 90% in the best cases.[49]

When the 3-, 4-, 5-, and 6-methyl derivatives of methyl 2-oxo-1-cyclohexanecarboxylates are used as substrates, the selectivities ranged from moderate to excellent, with the 3-methyl derivative showing the best selectivity (Table 1,

Table 1 Arylation of various ring-substituted methyl 2-oxo-1-cyclohexanecarboxylate compounds with *p*-methoxyphenyllead triacetate[49]



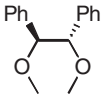
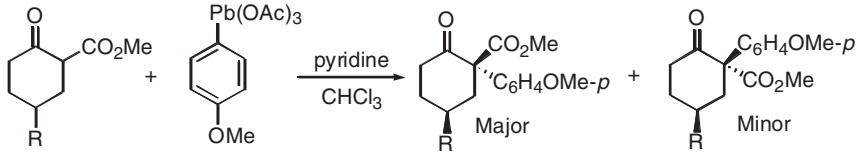
Entry	*R*	*Yield* (%)	dr
1	3-Me	16	15 : 1
2	4-Me	65	3 : 1
3	5-Me	74	7 : 1
4	6-Me	23	9 : 2
5	5-Bu^t	96	9 : 1
6		92	3 : 2

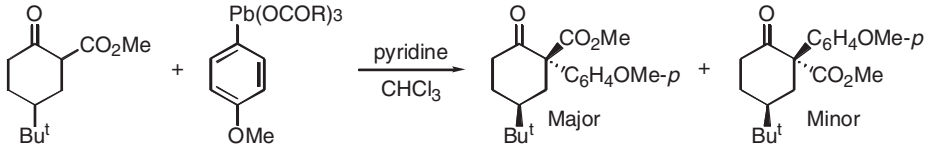
Table 2 Arylation of various 5-substituted methyl 2-oxo-1-cyclohexanecarboxylate compounds with *p*-methoxyphenyllead triacetate[49,50]



Entry	*R*	*Yield* (%)	dr	*References*
1	Me	74	7 : 1	49
2	Bu^t	96	9 : 1	49
3	OMe	96	4 : 1	50
4	OBn	85	6 : 1	50
5	OAc	64	4 : 1	50
6	OPiv	68	6 : 1	50
7	OTIPS	92	15 : 1	50
8	OTBDMS	97	20 : 1	50
9	OTBDPS	95	99 : 1	50

entry 1).[49] The yield of the reaction with the 3-methyl derivative was poor with no recovered starting material. The poor overall mass recovery was attributed to over-oxidation at the C3 center, with concomitant formation of water-soluble compounds. No evidence of α-acetoxylation, a classical side-reaction in aryllead reactions, was obtained in this case. Complexation of the β-ketoester functionality with a lead species functioning as a Lewis acid is expected to increase the acidity of the C3 proton, and that could be involved in the low yield as well as in the high diastereoselectivity. By contrast, in entry 4 (Table 1), the yield of arylated product is also low, but starting material makes up the remainder of material isolated. This low yield is most likely attributed to enhanced steric interactions in that system. In a comparison of 5-substituted methyl 2-oxo-1-cyclohexanecarboxylates (Table 2), the extraordinary selectivity of the TBDMS silyl protecting group compared to the more bulky *tert*-butyl group (compare entry 2 with entry 8 in Table 2) was unexpectedly discovered. This effect is consistently observed with other silyl-protection groups and in the reactions of different aryllead(IV) reagents with the TBDMS-protected 5-hydroxy derivative. This high diastereoselectivity was attributed to an enolate carbanion stabilization by a distal siloxy group. This interaction is thought to direct the silyloxy group to the axial position thereby orienting the aryllead(IV) triacetate complex to attack *anti* to the siloxyether group furnishing α,α-disubstituted β-ketoester in high diastereomeric excess.[49–51]

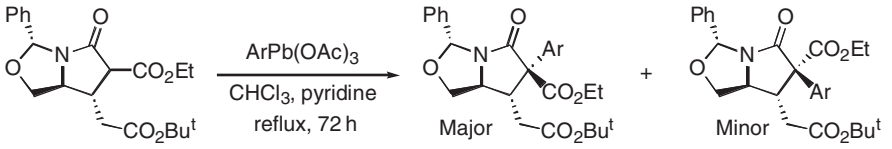
The nature of the acyl ligand of the aryllead triacetate has no influence on the diastereomeric ratio (Equation (19)). It is interesting to note that, when the sodium salt of the β-ketoesters was treated with *p*-$MeOC_6H_4Pb(OCOR)_3$ at 25 °C, the arylated product was obtained in 60% yield with a 9 : 1 diastereomeric ratio.[49]



(19)

R	*Temp* (°C)	*Yield* (%)	dr
Me	25	66	9 : 1
Me	70	59	6 : 1
Ph	25	62	9 : 1
$CHCl_2$	25	65	9 : 1

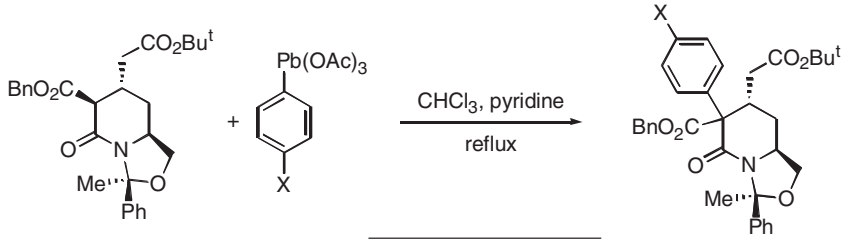
Moloney *et al.* studied the arylation of constrained glutamate analogs. The diastereoselectivities were moderate, varying from 2.4 : 1 with Ph to 1.7 : 1 for *ortho*-methoxyphenyl (Equation (20)). The best diastereoselectivity (4 : 1) was obtained in the case of the *meta*-methoxyphenyl derivative. Overall, these reactions with bicyclic substrates were more challenging, requiring higher reaction temperatures and longer reaction times than usually needed.[52,53]



Ar	*Yield* (%)	dr
C_6H_5	86	2.44 : 1
p-BrC_6H_4	74	2.36 : 1
o-$MeOC_6H_4$	72	1.67 : 1
m-$MeOC_6H_4$	84	4 : 1
p-$MeOC_6H_4$	38	2.17 : 1
p-MeC_6H_4	60	2.33 : 1
p-$CF_3C_6H_4$	72	2.27 : 1

(20)

Slightly better stereoselectivities were observed in the case of the analogous bicyclic piperidinone derivatives (Equation (21)).[54]



X	*Yield* (%)	dr
H	69	3 : 1
Br	93	5 : 1
MeO	59	2 : 1

(21)

9.09.2.1.3 Enantioselective arylation reactions

The asymmetric coupling of aryllead(IV) reagents with β-ketoesters by replacement of one or more of the labile acetate ligands with enantiomerically pure carboxylic acids was studied by three groups, but without great efficiency. Moloney employed camphoric anhydride to develop a series of enantiomerically pure diacid derivatives.[55] The formation of novel aryllead reagents proceeded from lead acetate through a ligand exchange process (Figure 1). In a one-pot two-step process, *in situ* generation of phenyllead tricarboxylate is followed by the addition of a nucleophile along with pyridine (3 equiv.). Unfortunately, the asymmetric induction was very low for this reaction, the best enantiomeric excess obtained was 10% with a 69% chemical yield. The poor asymmetric induction may be due to facile ligand exchanges of mixed ligand complex intermediates, influenced by the differences in electronic stabilization, and/or the steric encumbrance inducing a deceleration of the rate of the ligand coupling step. This conclusion was further supported by the complete absence of ligand coupling when the arylation of β-ketoesters was performed with aryllead containing camphoric acid monoesters, with a tethered pyridine subunit.[56]

Two other examples of asymmetric arylation couplings, described in Equations (22)[11] and (23),[57] have been claimed in review articles.

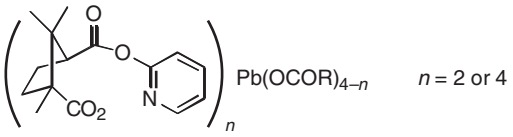
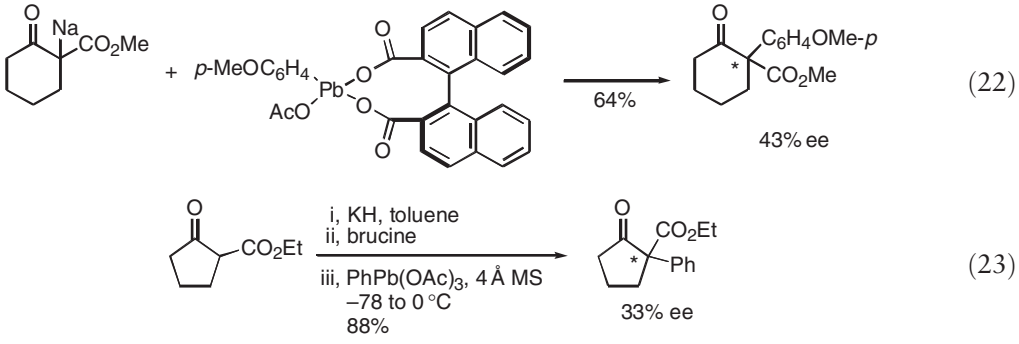


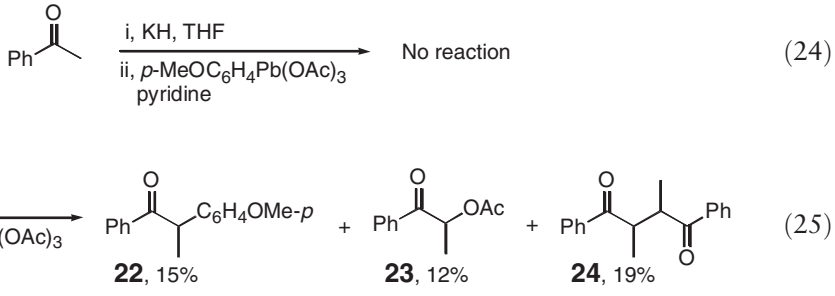
Figure 1

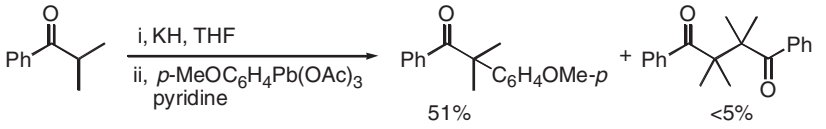


9.09.2.2 Arylation of Ketone Derivatives

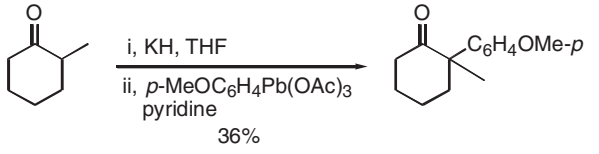
The reactivity of ketones toward aryllead(IV) triacetates is quite different from the reaction of these ketones with lead(IV) tetraacetate, which gives the α-acetoxyketones. Under the usual conditions for arylation (pyridine, $CHCl_3$), simple ketones remain unaffected. Only ketone enolates and some specially activated ketones have been successfully arylated with aryllead reagents.

The enolate salts of simple ketones react with aryllead reagents, but the reaction is of little practical value, as only trisubstituted α-carbon atoms are reactive.[47] The study of the reaction of the potassium enolates of acetophenone derivatives with *p*-methoxyphenyllead triacetate [*p*-$MeOC_6H_4Pb(OAc)_3$] **1** in THF in the presence of pyridine is significant. While there was no reaction with the acetophenone enolate (Equation (24)), the reaction of the propiophenone enolate led to a mixture of the α-arylation product **22**, the α-acetoxylation product **23** and the product of oxidative dimerization **24** (Equation (25)). The more substituted isobutyrophenone gave essentially the α-arylation product in considerably higher yield (51%) with only minor amounts of the dimerization product (Equation (26)). The effect of α-methylation was further demonstrated by the reactions of the potassium enolate of cyclohexanone derivatives. With *p*-methoxyphenyllead triacetate in THF in the presence of pyridine, no reaction occurred with the potassium enolate of cyclohexanone. Metallation of 2-methylcyclohexanone by KH gives a mixture of enolates which reacted with the aryllead compound to afford exclusively the most substituted 2-methyl-2-*p*-methoxyphenylcyclohexanone in a 36% yield (Equation (27)). The more substituted 2,6-dimethylcyclohexanone enolate gave a 75% yield of a mixture of diastereoisomers in a *cis-trans* ratio of 95 : 5 (Equation (28)). On the other hand, the presence of a 2-phenyl group had only a moderately favorable influence on the yield of the 2,2-diarylcyclohexanone (Equation (29)).

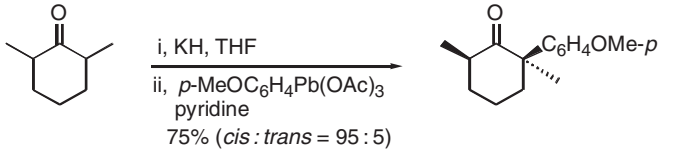




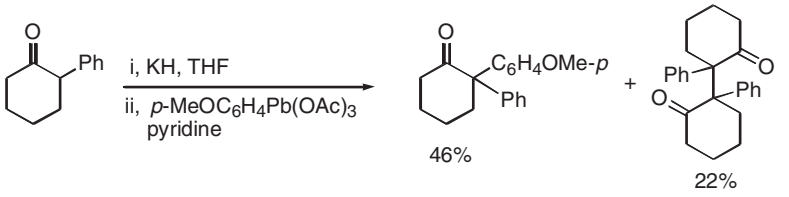
(26)



(27)

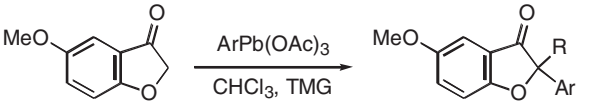


(28)



(29)

Variable results were obtained with a special type of ketone, bearing an arylheteroatom group on the α-carbon, which can present a high degree of enolization. The heteroatom can be, for example, nitrogen (3-oxo-2,3-dihydroindole),[58] oxygen (3-benzofuranone),[24] or sulfur [(3-arylthio-3-benzofuranone,[59] 3-(arylthio)flavanone.[60,61] The simple unsubstituted 3-(*2H*)-benzofuranone reacted with aryllead triacetate to afford either the mono or the diaryl derivative. In the usual system (chloroform, pyridine), only modest yields were obtained, but use of *N*,*N*,*N*′,*N*′-tetramethylguanidine (TMG) allowed the reaction to proceed in better yields (Equation (30)). However, the scope of this reaction is narrow, as only the diphenyl and the mono-2,4,6-trimethoxyphenyl derivatives were obtained in moderate to relatively good yields.[24,59]

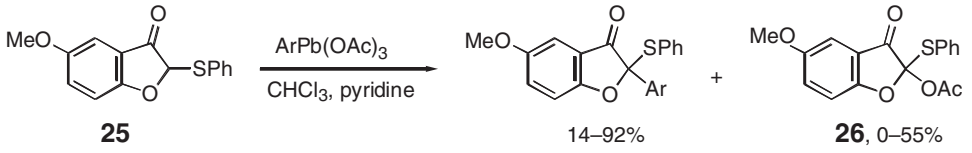


R = Ar = Ph; 84%
R = H, Ar = 2,4,6-(MeO)$_3$C$_6$H$_2$; 31%

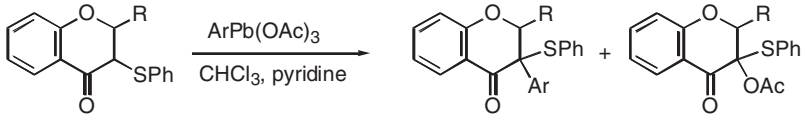
(30)

The trisubstituted α-carbon of α-phenylthioketones reacted with aryllead triacetates under classical conditions to afford good to high yields of the α-aryl α-phenylthio derivatives, without competing oxidation of the sulfur atom of the phenylthio group.[60,62,63] However, α-acetoxylation was sometimes a competing side-reaction, particularly in the case of *ortho*-substituted aryllead derivatives. For example, a 55% yield of the α-acetoxy derivative **26** was reached in the reaction of 2-phenylthio-3-(*2H*)-benzofuranone **25** with the 2,4,6-trimethoxyphenyllead compound (Equation (31)).[59,60] The diastereoselectivity of the arylation of 3-phenylthioflavanones was observed by Donnelly *et al.*, but the stereochemistry of the product of arylation was not rigorously determined (Equation (32)).[60,61] However, recently Chen *et al.* used an X-ray crystal structure determination to reveal the *trans* relationship between the 2-aryl and 3-aryl groups (Equation (33)).[62] The activating α-phenylthio group can

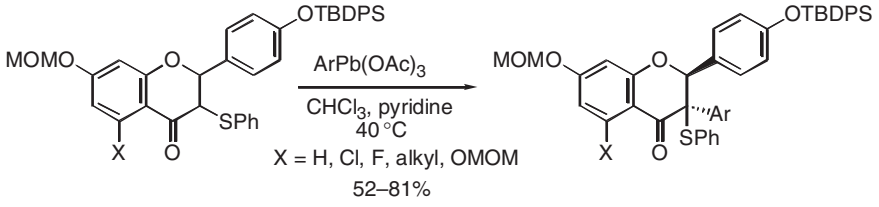
then be removed either by oxidation with dimethyldioxirane followed by thermolysis to afford the isoflavones[60] or through reduction by nickel boride or by Raney nickel catalyzed hydrogenation[62,63] to give the corresponding isoflavanones.[60] These reactions were used in the synthesis of biflavonoid structures **27**, that are simpler analogs of natural compounds isolated from *Garcinia* species, members of the Guttiferae family (Equation (34)).[61,64] In this case, the masked flavanonyllead triacetate acted as an efficient arylation reagent and the dioxolanyl group did not interfere with the synthesis and reactivity of the lead functionality. The α-phenylsulfonylketone analogs of the 3-(phenylthio)chromanones reacted similarly with different aryllead triacetates to yield the corresponding α-aryl derivatives in good yields (69–74%), except in the case of 2,4,6-trimethoxyphenyllead triacetate with which no reaction took place.[61]



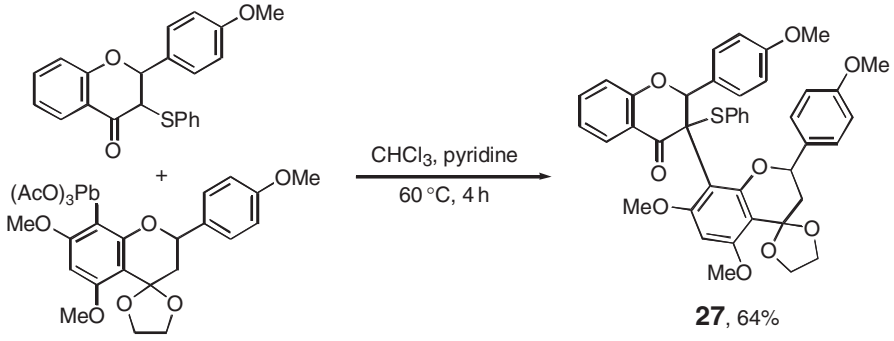
(31)



(32)

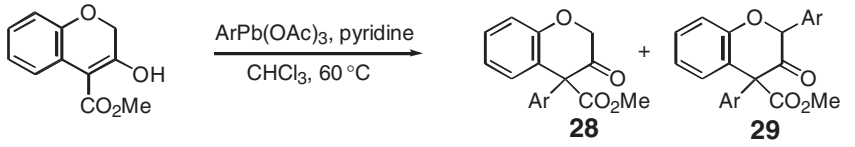


(33)



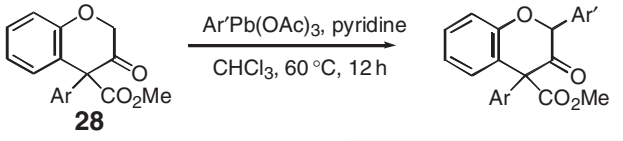
(34)

The reaction of 4-(methoxycarbonyl)chroman-3-one with aryllead triacetates afforded the expected 4-aryl derivatives **28** in moderate to good yields (see Section 9.09.2.1, Equation (6)). However, with longer reaction times the products of bis-arylation **29** were obtained in moderate yields (Equation (35)). Unsymmetrically disubstituted chroman-3-ones were obtained by treatment of the pure product of monoarylation, the 4-monosubstituted compound, with a second aryllead triacetate (Equation (36)).[30]



Ar	Time (h)	Yield (%) 28	29
4-MeOC$_6$H$_4$	4	65	
	12	40	36
2,4-(MeO)$_2$C$_6$H$_3$	3	86	
	12	43	38

(35)

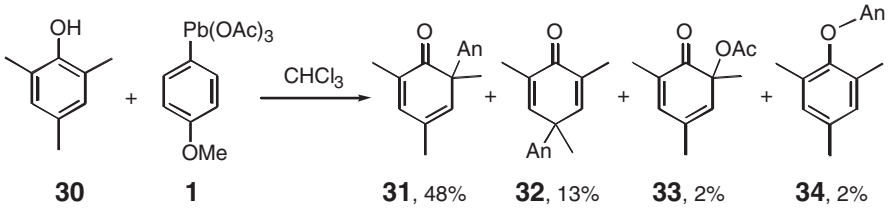


Ar′	Yield (%)
4-MeOC$_6$H$_4$	46
2,4-(MeO)$_2$C$_6$H$_3$	21
2,4,6-(MeO)$_3$C$_6$H$_2$	16

(36)

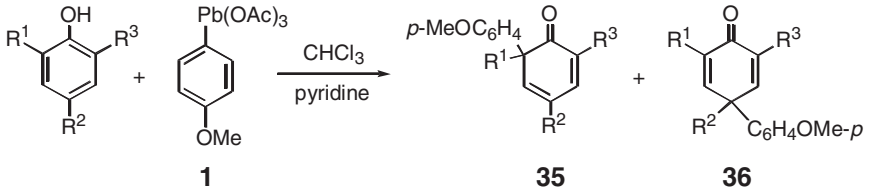
9.09.2.3 Arylation of Phenols

Aryllead(IV) triacetates react with phenols to give mainly products of *ortho*-*C*-arylation, formed by ligand coupling mechanisms.[45,45a,65] In an attempt to extend the arylation of polymethylbenzenes to phenolic substrates, Pinhey *et al.* treated mesitol **30** with *p*-methoxyphenyllead triacetate **1** in $CHCl_3$ (Equation (37)). The reaction afforded a mixture of the *C*-arylated products **31** and **32** together with minor amounts of the *C*-acetoxylated product **33** and *O*-aryl ether **34**.[45,45a]



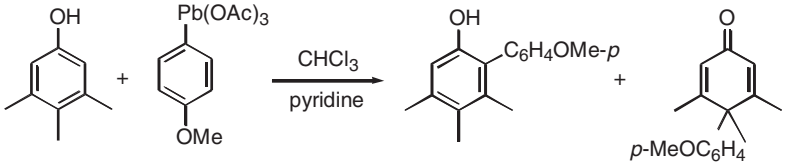
(37)

In their early studies, Pinhey *et al.* showed that, when the reaction of a phenol with an aryllead triacetate is performed in the presence of pyridine, only the *C*-arylated dienones **35** and **36** are formed in a nearly quantitative yield (90%; *ortho* : *para* ratio of 4 : 1) (Equation (38)). Under their classical conditions (phenol : organolead triacetate : base in a ratio 1 : 1 : 3), the reaction of methylated phenols only proceeded in high yield when both *ortho*-positions are substituted. There is a preference for attack *ipso* to a methoxyl group compared to a methyl group.[45,45a]



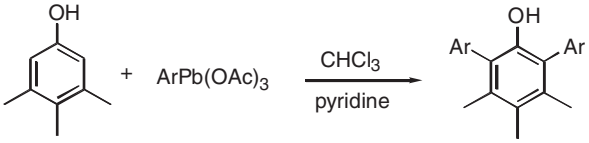
1 **35** **36** (38)

In the arylation of methyl-substituted phenols, the rate of *ortho*-arylation increases with the number of methyl groups. Moreover, *ortho*-methyl groups show a much greater effect than *meta*- or *para*-methyl groups. ^{13}C NMR studies have shown that the *ipso*-carbon of the aryllead reagent presents an electrophilic character.[66] Therefore it reacts with the more electron-rich site, an overlap of the two π-systems of the phenolate ligand and of the Pb-bound aryl group facilitating the *ortho*-arylation.[8,66,67] The presence of two or more alkyl groups on the phenolic substrate is required but they do not necessarily have to be on either of the *ortho*-positions. Indeed, 3,4,5-trimethylphenol **37** was reported to yield a modest amount of 2-(*p*-methoxyphenyl)-3,4,5-trimethylphenol **38** in the reaction with *p*-methoxyphenyllead triacetate **1** (Equation (39)).[45,45a]

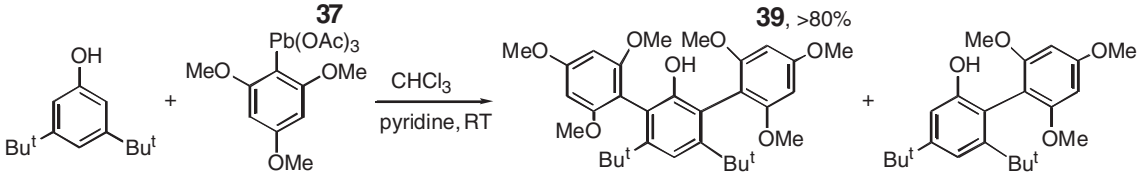


37 **1** **38**, 22% 12% (39)

However, under more forcing conditions, high yields of the 2,6-diaryl derivatives **39** can be obtained, and particularly with more reactive aryllead derivatives, such as 2,4,6-trimethoxyphenyllead triacetate **41** (Equation (40)).[8] Highly hindered structures of the 2′-hydroxy-1′,3′-terphenyl type can be obtained. For example, 3,5-di-*tert*-butylphenol **40** reacted with 2,4,6-trimethoxyphenyllead triacetate **41** (3 equiv.) and pyridine (10 equiv.) to afford the very sterically hindered 2,6-diarylphenol **42** in 87% yield together with 10% of the monoarylated product (Equation (41)).[66]

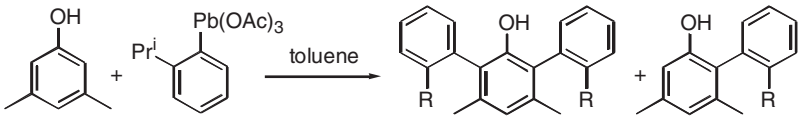


37 **39**, >80% (40)



40 **41** **42**, 87% 10% (41)

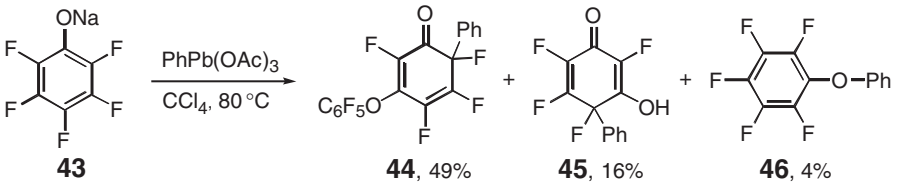
The influence of the nature of the amine that plays a role of base and/or coordinating ligand is essential for the outcome of the reaction. Although pyridine-type compounds are more frequently used and the most suitable, other types of amines can also be employed successfully (Equation (42)).[68]



	Yield (%)	*dl : meso*	*Yield* (%)
Pr^iNH_2	75	>99 : 1	7%
DABCO	78	>99 : 1	
Quinuclidine	95		

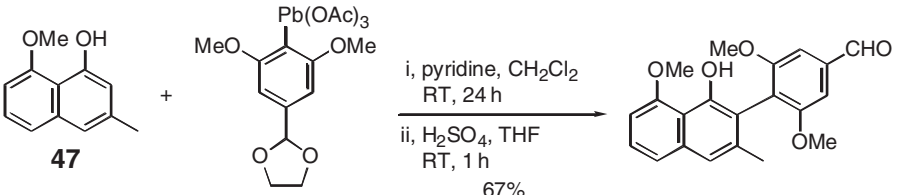
(42)

In general, the rate of the reaction of arylation of phenols by aryllead triacetate increases with the electron density of the phenolic substrate. When pyridine is used as a base, no reaction takes place with electron-poor phenols, such as 2,6-dichlorophenol or 2,6-dichloro-4-nitrophenol.[45,45a] However, the reaction of the sodium salt of perfluorophenol **43** with phenyllead triacetate under more forcing conditions led to a range of products: the product of *ortho*-arylation, the 6-aryl-2,4-cyclohexadienone **44** together with minor amounts of the product of *para*-arylation **45** and the unsymmetrical diaryl ether **46** (Equation (43)).[69]



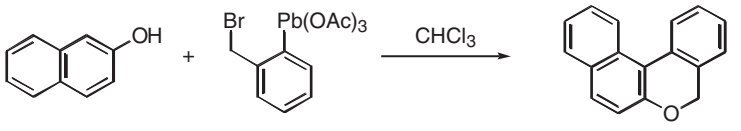
43 **44**, 49% **45**, 16% **46**, 4% (43)

An interesting application of the biaryl coupling is the synthesis of ancistrocladine, a 7,3′-linked naphthylisoquinoline alkaloid, in which the key step, the formation of the biaryl linkage, was realized by coupling of the naphthol **47** with the protected aryllead reagent **48** (Equation (44)).[70]



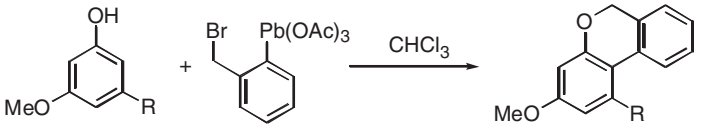
47 **48** (44)

When an *ortho*-halomethylphenyllead triacetate such as **49** was treated with phenolic substrates in the presence of pyridine, only poor yields of dibenzo[b,d]-6*H*-pyrans were obtained (Equation (45)). However, with a carefully selected combination of bases, relatively good yields of the arylation–cyclization products were then isolated. In the case of 3-methoxyphenol, only one product was isolated, although in a moderate yield (38%) (Equation (46)). It is worth noting that, with this ambident organolead reagent, the aromatic *ipso*-carbon bearing the lead atom is more reactive toward the soft nucleophile than the benzylic center. A complete reversal of the order of reactivity is realized. In contrast to the classical order toward the nucleophilic substitution, benzylic ≫ aromatic, the reaction of a soft nucleophile with the lead-substituted carbon atom is faster than with the benzylic center.[34]



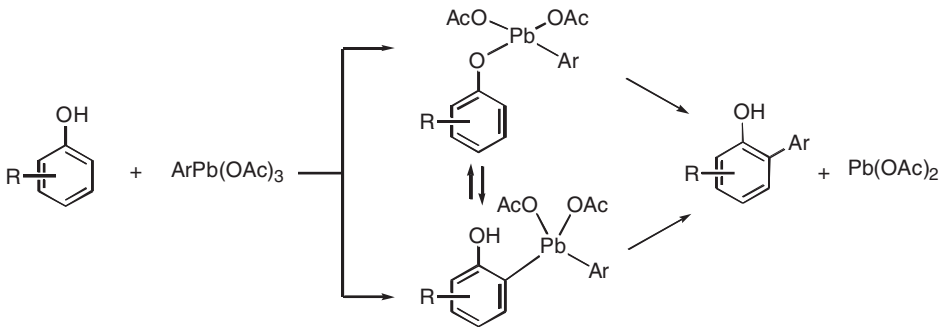
49 (45)

Condition	*Yield* (%)
pyridine, 45 °C, 10 h	20–25
pyridine + Et_3N, RT, 1 h	55
DMAP + Et_3N, RT, 1 h	65



49 (46)

R	*Condition*	*Yield* (%)
OMe	pyridine, 50 °C, 5 h	27
	DMAP + Et_3N, RT, 1 h	60
H	DMAP + Et_3N, RT, 4 h	38

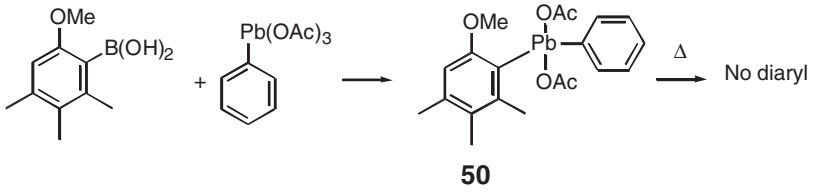


Scheme 7

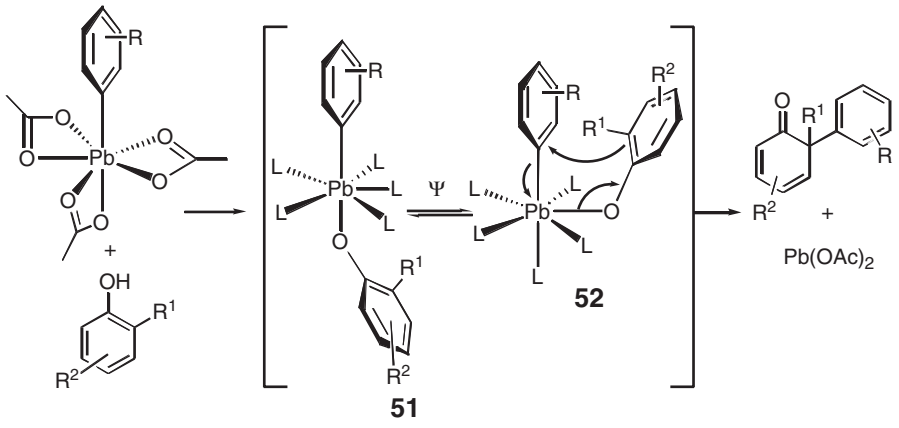
A ligand coupling mechanism has been proposed to explain the arylation reactions. For ambident substrates, two types of intermediates, resulting from ligand exchange in the first step, can be postulated. For phenols and β-dicarbonyl compounds, either an oxygen–lead or a carbon–lead intermediate are possible. In the second step, ligand coupling then affords the products (Scheme 7).[8,31,66,67,71]

For the detection of an intermediate, either spectroscopic or synthetic approaches can be used. Unfortunately, all attempts to detect such an intermediate by ^{1}H or ^{207}Pb NMR failed in the case of phenols as well as in the case of β-dicarbonyl compounds.[8,31,66] Pinhey *et al.* have prepared stable unsymmetrical diaryllead diacetates by boron–lead exchange.[72] They used this boron–lead exchange reaction to prepare a diaryllead-type intermediate such as the *O*-methyl ether analog **50** of a possible intermediate bearing a carbon–lead bond, which was supposed to occur in the easy arylation of 3,4,5-trimethylphenol **37** (Scheme 8). However, the compound also appeared to be quite stable in $CHCl_3$ in the presence of pyridine at 60 °C even after 6 days as in DMSO under reflux.[67] The intermediate involved in the phenol arylation is therefore more likely to be the oxygen-bound (aryloxy)aryllead diacetate analogous to the intermediate postulated in the Wessely α-acetoxylation of phenols.

Thus, in the reaction of aryllead triacetate with phenols, an initial ligand exchange affords an aryl-(aryloxy)lead diacetate intermediate which can have the aryloxy ligand either in the axial position **51** or in the equatorial position **52** (Scheme 9). If the aryloxy group is in the axial position, pseudorotation can easily interconvert this conformer with



Scheme 8

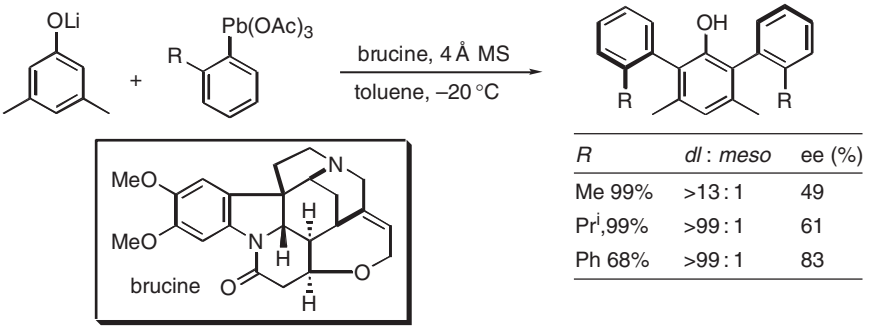


Scheme 9

the conformer possessing the aryloxy ligand in the equatorial position **52**. In this spatial arrangement, the favorable overlap between the π-systems of the two aryl groups makes the ligand coupling process possible.[8,67]

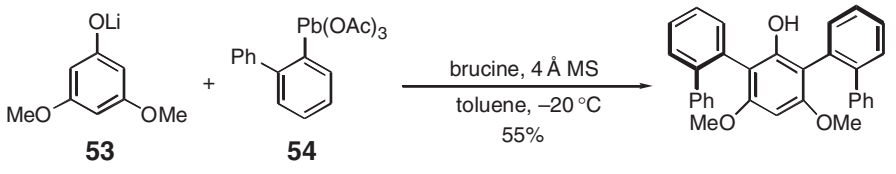
9.09.2.3.1 Asymmetric arylation

Yamamoto *et al.* reported an enantioselective coupling of simple aryllead reagents with phenols to provide a diverse set of axially chiral triaryl compounds (Equation (47)). The reaction conditions are unusual as toluene is preferred to chloroform and the reactions are performed at low temperature (−40 to −20 °C). The preformed lithium phenoxides were found superior to the free phenols and the presence of 4 Å molecular sieves (MS) is crucial for the success. Among a range of enantiomerically pure nitrogen bases used as additives, brucine provided the highest yields and enantiomeric excesses. Six equivalents of the optically active brucine afforded the best results, although a catalytic amount of brucine (0.2 equiv.) could be used without loss of enantiomeric excess. Under these conditions, the isolated yields were lower. With some reaction partners, monoarylation products can constitute a significant fraction of the final mixture. The highest enantiomeric excess was obtained in the reaction of 3,5-dimethoxyphenol **53** with 2-biphenylyllead triacetate **54** (Equation (48)).[68,73]



R	*dl* : *meso*	ee (%)
Me 99%	>13 : 1	49
Pr^i,99%	>99 : 1	61
Ph 68%	>99 : 1	83

(47)

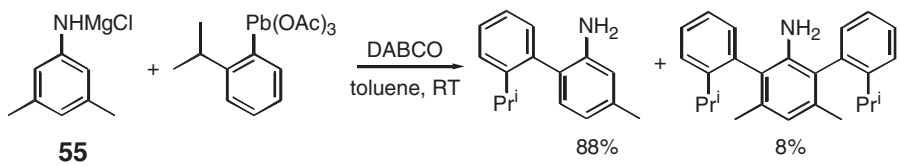


(48)

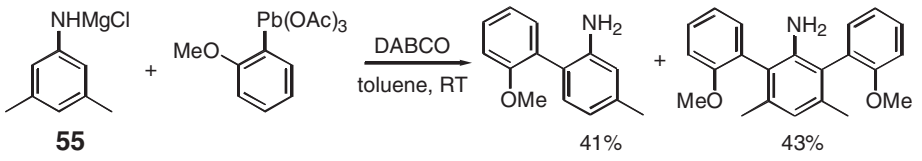
dl : *meso* : 6.9 : 1, 93% ee

9.09.2.4 Arylation of Aniline and other Nitrogen Derivatives

In the presence of pyridine alone, anilines and anilides do not react with aryllead(IV) triacetates.[74] However, the reactivity was modified upon magnesation of the aniline nitrogen (Equation (49)). Reaction of the magnesium salt of an aniline with an aryllead triacetate gives the product of aryl–aryl coupling, that takes place regioselectively at the *ortho*-position with no reaction at the *para*-position.[75] Among a variety of metalating agents, only Bu^tMgCl led to high yields of arylation products. The optimum conditions involved a combination of the aniline, the aryllead triacetate, Bu^tMgCl and DABCO in a ratio 1.3 : 1 : 1.3 : 1 in toluene. With the more reactive *ortho*-methoxyphenyllead triacetate derivatives, the second arylation of 3,5-dimethylaniline **55** takes place significantly (Equation (50)). However, for a range of other anilines, the arylation with all the aryllead triacetates afforded only the product of monoarylation in good to high yields. This is in sharp contrast with the analogous reaction with phenols which leads preferentially to *ortho*–*ortho*′-diarylation products.

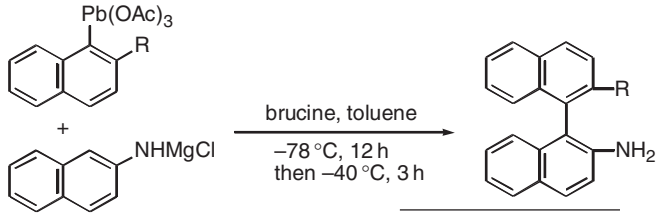


(49)



(50)

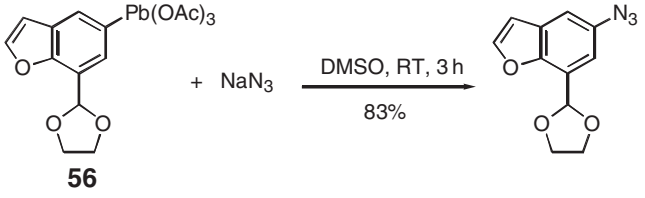
When DABCO is replaced by brucine, enantioselective *ortho*-arylation of the aniline takes place at low temperature (−78 to −40 °C) to afford the chiral biaryl with moderately good enantioselectivity (Equation (51)).[68]



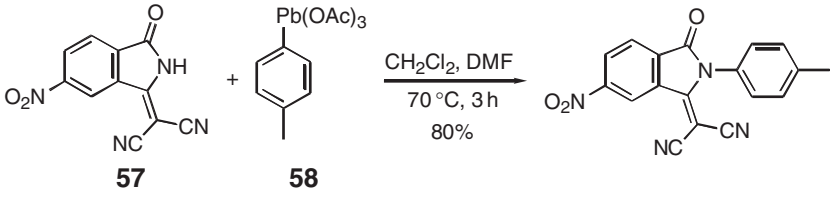
(51)

R	*Yield* (%)	*ee* (%)
Me	90	41
MeO	68	46

Two other examples of *N*-arylation under basic conditions were reported. One is the azidation of a 7-[1,3]dioxan-2-yl-benzofuran-5-yllead triacetate **56** in the synthesis of tachykinin antagonists (Equation (52)).[76] The second one is the efficient *N*-*p*-tolylation of (3-oxoisoindolin-1-ylidine)propandinitrile **57** by reaction with *p*-tolyllead triacetate **58** under mild neutral non-catalyzed conditions (Equation (53)).[77,77a]



(52)



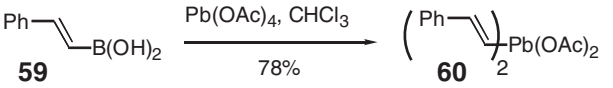
(53)

9.09.2.5 Alkenylation Reactions

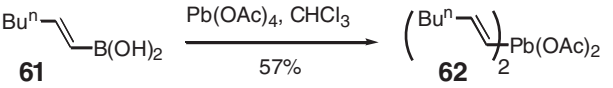
Vinyllead triacetates are easily obtained through metal–lead exchange by treatment of the corresponding vinylmercury, vinylboronic acids, and vinylstannanes with lead tetraacetate in $CHCl_3$. Vinyllead triacetates are generally very unstable and decompose by a vinyl cation pathway to give either enol acetates or acetylenes, depending on the precursor and the reaction conditions.[78–80] Although vinyllead triacetates are not isolable, their formation was demonstrated by ^{1}H NMR experiments.[81]

Symmetrical divinyllead diacetates can be obtained directly from the corresponding vinylboronic compound through reaction with lead tetraacetate in chloroform at room temperature. Thus, the reaction of (*E*)-styrylboronic acid **59** with lead tetraacetate in chloroform afforded the bis-(*E*)-styryllead diacetate **60** and the reaction of (*E*)-hex-1-enylboronic acid **61** led to the relatively unstable bis-[(*E*)-hex-1-enyl]lead diacetate **62** (Equations (54) and (55)).

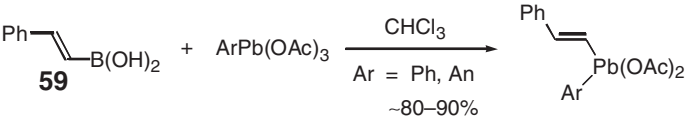
Treatment of an aryllead triacetate with a vinylboronic acid affords relatively stable mixed lead diacetate compounds in good yields (Equations (56) and (57)).[72]



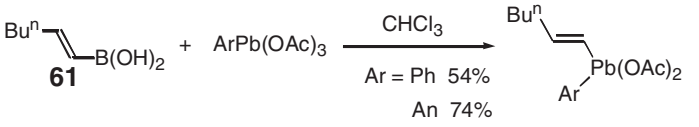
(54)



(55)

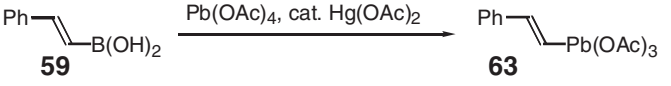


(56)



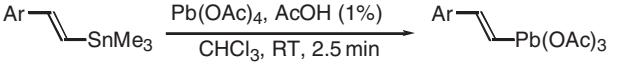
(57)

However, when the transmetallation is performed in the presence of Hg(II) salts, the (*E*)-styrylboronic acid **59** reacts with lead tetraacetate to afford the monoorganolead derivative, styryllead triacetate **63** (Equation (58)).[81]



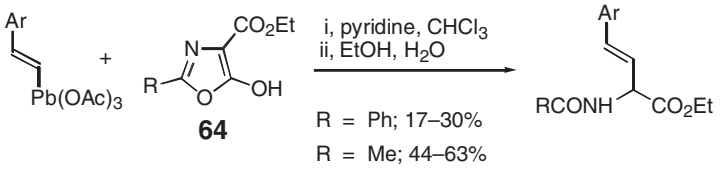
(58)

The reaction of styrylstannane derivatives with lead tetraacetate generates *in situ* the corresponding styryllead triacetate that subsequently can be treated with a nucleophilic substrate to afford the vinylated derivative in good yields. A small amount of acetic acid must be present during the transmetallation step. In the absence of acetic acid, the yield of coupling products drops significantly due to a lower reaction rate of the Sn–Pb exchange. (Equation (59)).[82]



(59)

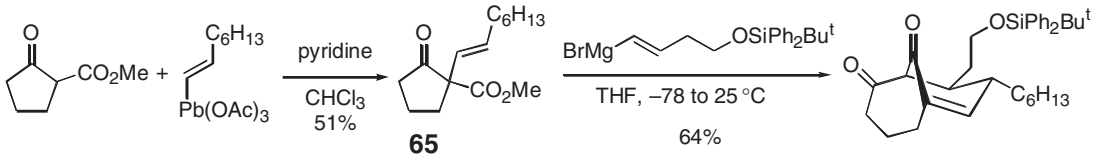
These *in situ* generated unstable vinyllead triacetates react with soft carbon nucleophiles to give moderate to good yields of *C*-vinylated products. This method is potentially very useful in organic synthesis. As an example, styryllead triacetates reacted with 4-ethoxycarbonyl-2-phenyl-4,5-dihydrooxazol-5-one (**64**, R = Ph) to afford, after hydrolysis, the α-styryl-*N*-benzoylaminoesters in relatively modest yields.[82] Better yields were obtained with the 2-methyl-4,5-dihydrooxazol-5-one analog (**64**, R = Me) (Equation (60)).[83]



(60)

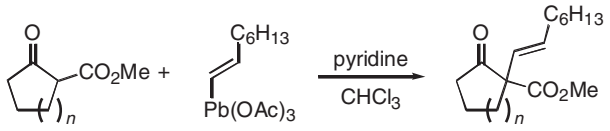
This selective α-alkenylation method was also used for the preparation of a number of other α-(1-alkenyl)-β-ketoesters, for example, in the direct synthesis of the CP-263,114 core system by a bicyclic ring-forming process, starting from readily available β-ketoesters (Scheme 10). Treatment of the vinylstannane by lead tetraacetate followed directly by exposure to the methyl β-ketoester led to the derived ketone **65** in 51% yield.[84]

Various convergent Pb(IV)-promoted coupling reactions between vinylstannanes and cyclic β-keto esters were used to prepare tetrasubstituted α-alkyl-β-ketoesters which underwent subsequently a tandem alkylation, anion-accelerated oxyCope rearrangement and a *trans*-annular Dieckmann cyclization to afford bridgehead enone-containing

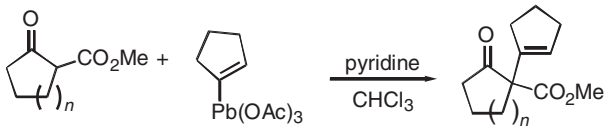


Scheme 10

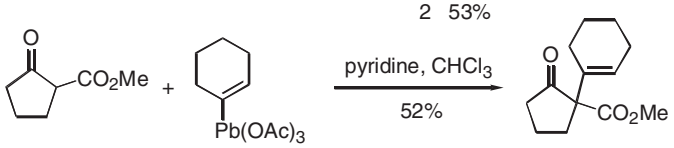
polycyclic ring systems (Equations (61)–(63)). The cycloalkenyllead triacetate reagents were prepared by reaction of the adequate cycloalkenyllithium with trimethylchlorostannane in ether followed directly by treatment with lead tetraacetate in chloroform and treated immediately with the required methyl β-ketoester.[85]



(61)

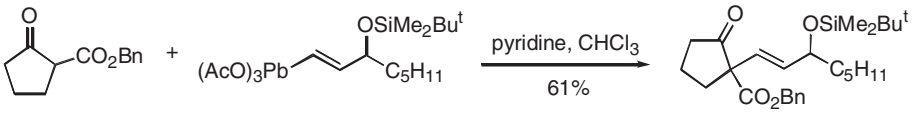


(62)

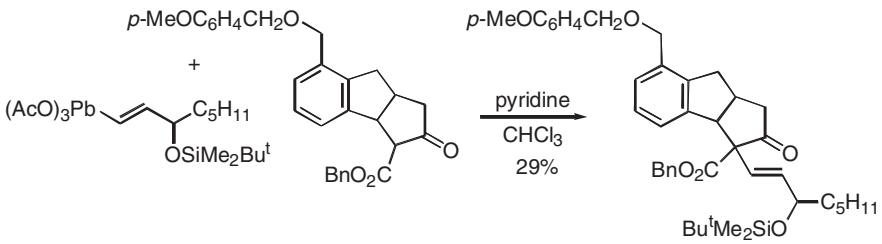


(63)

In 1988, Ikegami *et al.* reported an efficient alkenylation reaction involving a vinyllead triacetate reagent containing a protected allylic alcohol (Equation (64)).[86] When this reagent was used with a more rigid polycyclic system toward the synthesis of benzocarbacyclines, only a modest yield (29%) of the expected alkenylated product was isolated (Equation (65)).[87]



(64)



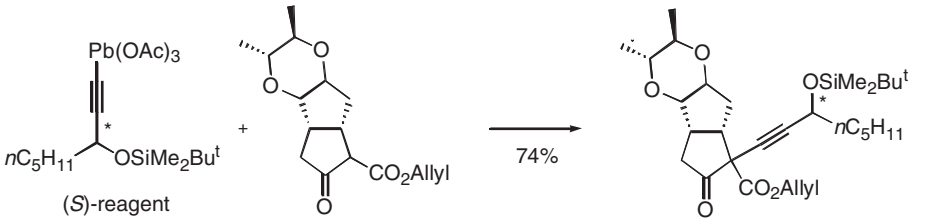
(65)

9.09.2.6 Alkynylation Reactions

Alkynyllead triacetates can be prepared by tin–lead or by mercury–lead exchange.[88,88a] However, more convenient methods were subsequently devised. *In situ* transmetallation can be directly realized by lithium–lead or zinc–lead exchange. This avoids the isolation of unstable alkynylmetal derivatives. Ikegami *et al.* found that, if a THF solution of

a lithium acetylide is added at low temperature to lead tetraacetate in methylene dichloride, the resulting mixture reacts with benzyl β-ketoesters to give the corresponding benzyl α-alkynyl-β-ketoesters.[89] Later, Pinhey *et al.* found that an optimum way of generating a lead-based alkynylating reagent was to use a zinc–lead exchange. Under carefully controlled conditions for the transmetallation step, a number of side-reactions can be avoided or at least significantly reduced.[90]

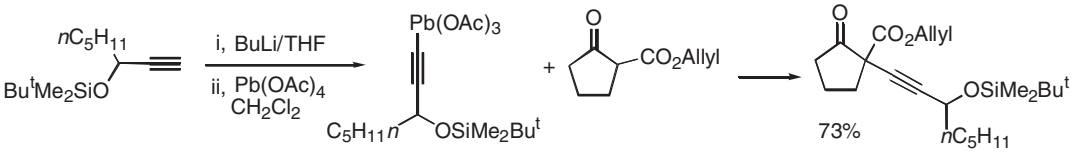
Alkynylation of enolates was used to prepare optically active 13,14-didehydroisocarbacyclin. Preparation of the optically active (*S*)-alkynyllead triacetate was compatible with the lithium–lead tetraacetate metal–metal exchange (Scheme 11 and Equation (66)).[91]



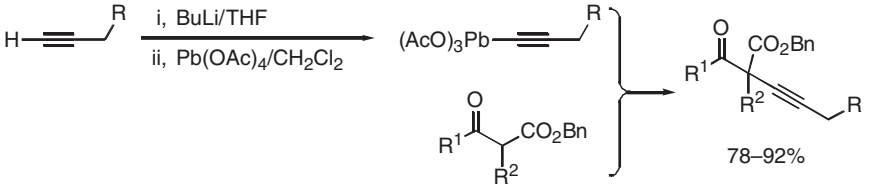
(66)

This alkynylation reaction was also used for an indirect synthesis of (*Z*)-alkenyl-β-ketoesters. Indeed, α-(*E*)-alkenylation of enolates was easily realized by direct alkenylation with the *in situ* generated (*E*)-alkenyllead triacetate for the synthesis of isocarbacyclin reported by Hashimoto *et al.*[86,92] However, introduction of a (*Z*)-alkenyl group by reaction with a (*Z*)-alkenyllead reagent met with failure. Thus a three-step procedure was developed by Ikegami *et al.* to solve this problem (Scheme 12).[89] The sequence involves α-alkynylation, semihydrogenation and debenzyloxycarbonylation.

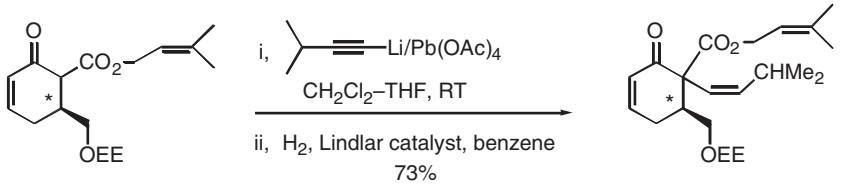
This sequence was used later in the synthesis of Mori's intermediate in the course of the total synthesis of (−)-Periplanone-B (Scheme 13).[93]



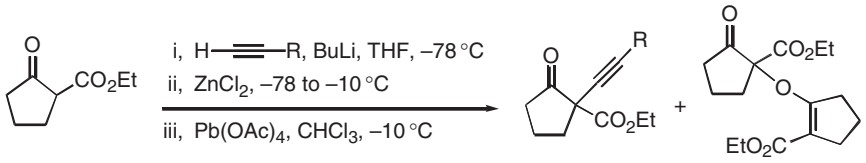
Scheme 11



Scheme 12

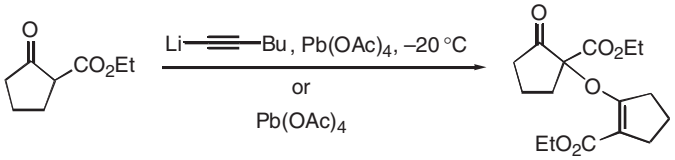


Scheme 13



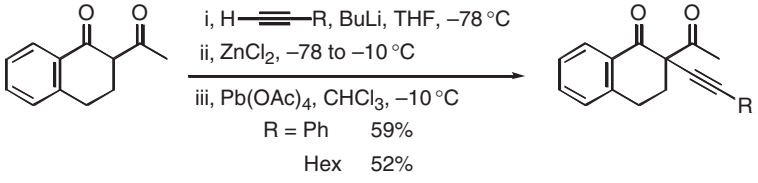
Scheme 14

The nature of the alcoholic group of the β-ketoester plays an important role on the efficiency of the alkynylation reaction, in a way reminiscent of what was observed in the alkenylation reaction.[86] Good yields are obtained with methyl or benzyl esters.[90] In the case of ethyl 2-oxocyclopentanecarboxylate, the reaction with an alkynyllead reagent prepared by the Li–Pb exchange did not yield any expected alkynylation product. Instead, the only product was a dimer, formed by lead tetraacetate oxidation, a fact that indicates a disproportionation of the alkynyllead reagent leading to lead tetraacetate and a tetraalkynyllead compound (Equation (67)). However, this competitive reaction can be suppressed by using the zinc–lead generated reagent (Scheme 14).

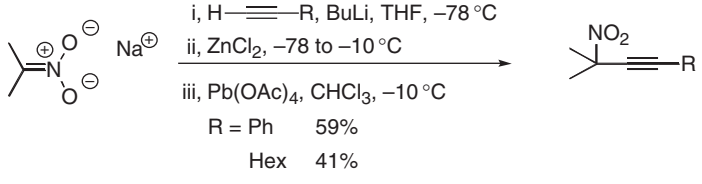


(67)

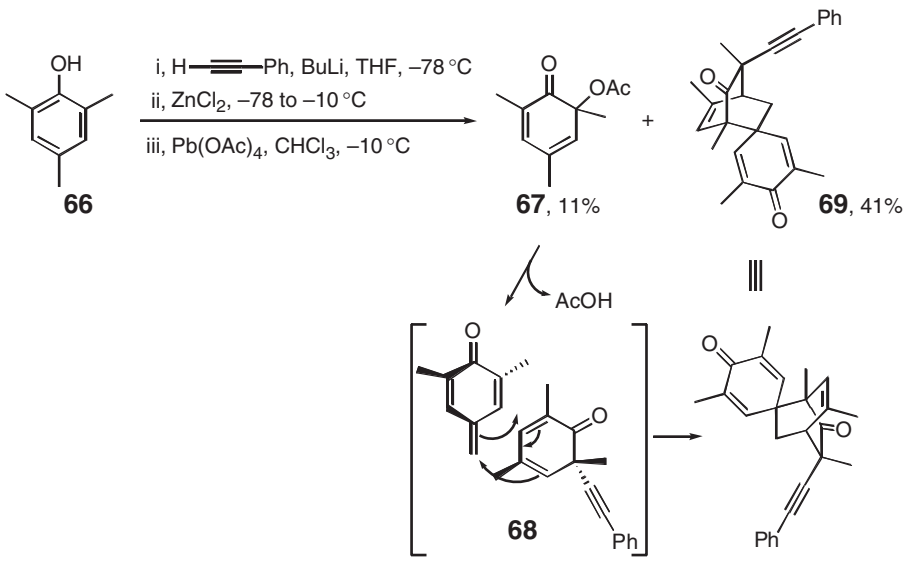
Different soft nucleophiles were alkynylated by the zinc–lead exchange generated reagents (Schemes 15–17).[90] In the case of mesitol **66**, reaction with the *in situ* generated phenylethynyllead derivative did not afford any 6-phenylethynyldienone nor any dimer, as previously observed in the reaction using a tin–lead exchange derived reagent.[94] Instead, the Wessely acetoxylation product **67** was formed as a minor byproduct besides a new dimeric structure **69** resulting from a Diels–Alder reaction between the 6-phenylethynyldienone **68** and a mesitol oxidation–elimination product, which could derive from the 6-acetoxydienone **67** (Scheme 17).



Scheme 15



Scheme 16



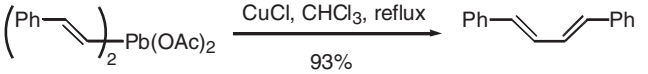
Scheme 17

9.09.3 Metal-catalyzed Reactions

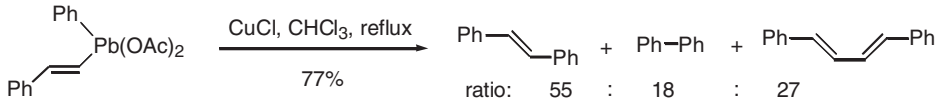
Metal-catalyzed reactions constitute the second major type of reactions in which organolead compounds act as major partners of the reacting systems. The study of these reactions has considerably increased since COMC (1995) review and they can be divided in two subtypes: reactions in which the organolead reactant acts as a stoichiometric partner and reactions in which the organolead is only a catalytic species. In this section, only the reactions with stoichiometric organolead will be reviewed, and these reactions are catalyzed by copper, palladium or rhodium species. The second type is the metathesis reactions where the lead compound acts only as a promoter in a complex catalytic system and is reviewed in Section 9.09.4.

9.09.3.1 Copper-catalyzed Reactions

Some copper-catalyzed reactions are of limited synthetic interest as they involve diorganolead diacetates with copper(I) salts. Diaryllead, arylvinyllead or divinyllead diacetates can be prepared by transmetallation between the appropriate organoboronic acid and the organolead triacetate or lead tetraacetate (for the synthesis of the diaryl and divinyl compounds). They undergo a copper(I)-catalyzed coupling reaction to afford biaryls, vinylaromatics or buta-1,3-dienes in high yields (Equation (68)). With unsymmetrical diorganolead reagents, the three possible coupling products are obtained, resulting either from ligand exchange in the lead compounds or from a non-exclusively bimolecular process in the transmetallation step leading to statistical mixtures of organocopper intermediates (Equation (69)).[72]



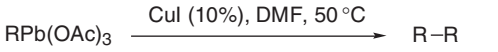
(68)



(69)

Kang *et al.* compared the organolead homocoupling reactions catalyzed by either copper or palladium sources.[95] Both reactions proceed at room or moderate temperature. Yields were good with both metal catalysts, although differences were noted both in the solvent and the amount of catalyst employed. The reactions with copper(I) iodide

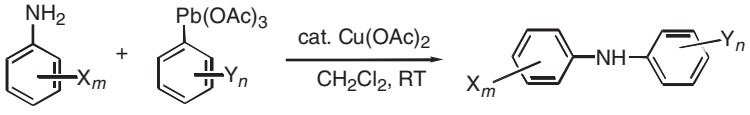
took place at 50 °C in DMF to afford generally good yields of homocoupling products (Equation (70)). Under these conditions, (phenylalkynyl)lead triacetate gave 1,4-diphenylbutadiyne in a lower yield (53%).



R	*Yield* (%)
Ph	68
p-MeC_6H_4	62
p-$MeOC_6H_4$	80
Ph–C≡C	53

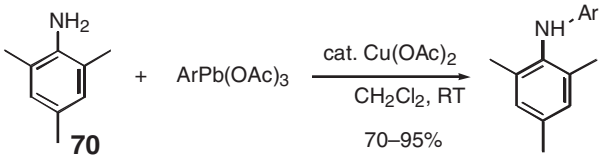
(70)

The most extensively studied group of copper-catalyzed reactions of lead derivatives is the copper(II) diacylates catalyzed *N*-arylation reactions of amine derivatives with aryllead triacetates, although the range of amine substrates is narrower than in the case of the analogous reactions with organobismuth reagents.[3,9,11–13a] With aryllead triacetate reagents, the best yields are obtained either with aniline derivatives or with amide derivatives. Aliphatic and alicyclic amines are not so efficiently arylated than by the analogous arylbismuth reagents. However, the main characteristics of aryllead reagents is that *N*-arylation reactions with reagents containing highly electron-rich arene groups, such as 2,4,6-trimethoxyphenyllead triacetate **41**, can be performed in preparatively useful yields. In the presence of a catalytic amount of a copper salt, most generally copper diacetate, anilines react with aryllead triacetates in methylene dichloride to give the product of *N*-monoarylation.[74,96–102a] Under these conditions, moderate to good yields were usually obtained for a variety of anilines (Equation (71)).

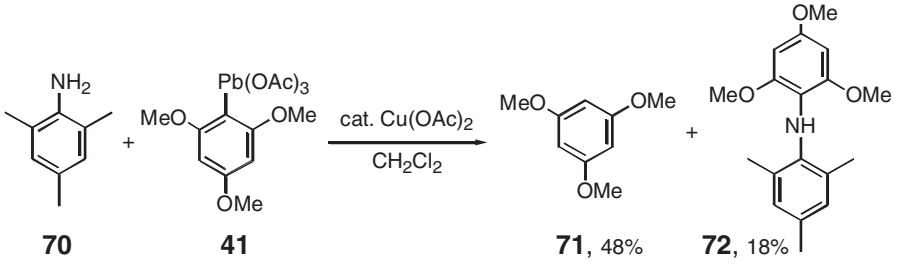


(71)

The efficiency of the arylation is very dependent upon the basicity of the amines. Electron-poor anilines such as *p*-nitroaniline did not react, while electron-rich anilines gave high yields of *N*-arylation products. However, in the case of easily oxidized anilines, oxido-reduction of the aryllead reagent can compete with the *N*-arylation, when the steric compression becomes too important. For example, in the case of mesitylamine **70**, the copper-catalyzed reaction with a variety of substituted phenyllead derivatives led generally to high yields of the diarylamines[100,101] (Equation (72)). However, in the reaction of mesitylamine **70** with the sterically hindered 2,4,6-trimethoxyphenyllead triacetate **41**, the predominant product **71** resulted from oxido-reduction of the aryllead reagent, the diarylamine **72** being isolated in only a poor 18% yield[101] (Equation (73)).



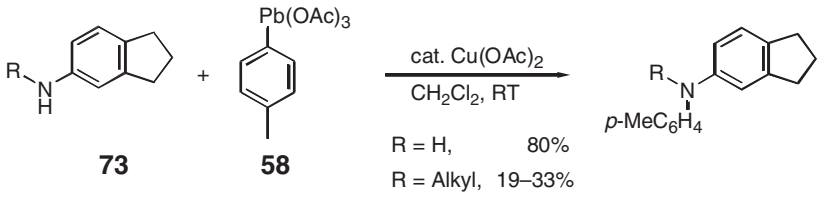
(72)



(73)

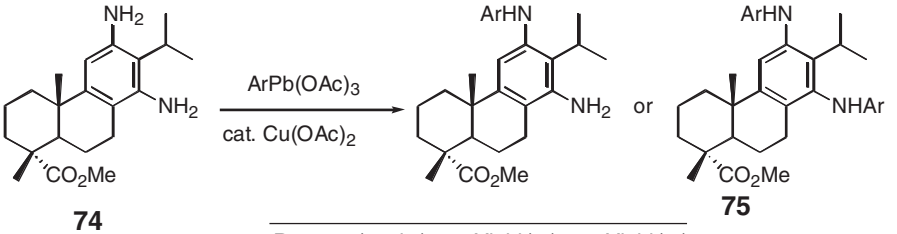
The reaction of *N*-alkylaniline derivatives with aryllead triacetates led to the trisubstituted *N*-alkyl-*N*,*N*-diarylamine in modest yields. For example, arylation of 5-aminoindane (**73**, R = H) with *p*-tolyllead triacetate **58** gave the

N-tolyl derivative in a good 80% yield,[96,96a] but arylation of various 5-(*N*-monoalkylamino)indanes afforded the corresponding *N*-alkyl-*N*-aryl-5-aminoindanes in low yields (19–33%)[97] (Equation (74)).



(74)

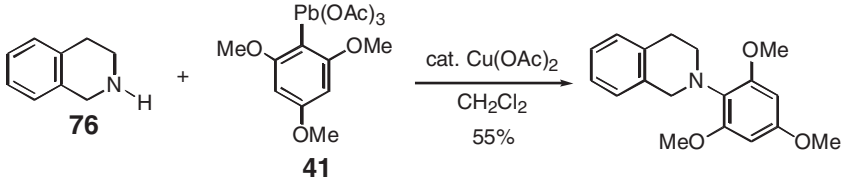
Arylation of methyl 12,14-diaminodehydroabietate **74**, a *meta*-phenylenediamine derivative, afforded the mono *N*-12-arylamino derivatives in good yields in the reaction with 1 equiv. of various aryllead triacetate reagents (Equation (75)).[103] The 12,14-diarylamino compound **75** was formed in moderate yields when 2 equiv. of the lead reagent were used. In contrast to *p*-nitroaniline which does not react, the *m*-nitroaniline analog, 12-amino-14-nitrodehydroabietate reacted with aryllead triacetates to give the 12-arylamino derivatives, although in modest yields (25–32%).



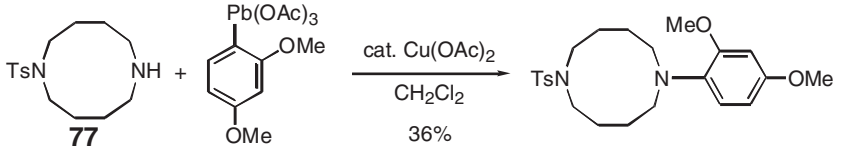
Reagent (equiv.)	*Yield* (%)	*Yield* (%)
1	67–70%	
2		36–41%

(75)

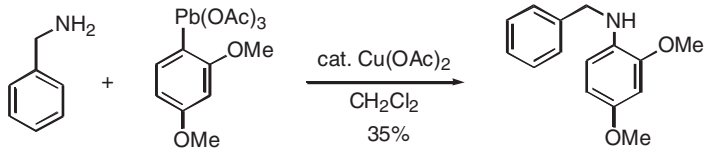
Copper diacetate-catalyzed arylation of heterocyclic amines such as piperidine, tetrahydroisoquinoline **76**[101] or 1,6-diazacyclodecane **77**[104] by aryllead triacetates gave only modest to moderately good yields of the *N*-aryl derivatives (Equation (76) and (77)). The reactions with aliphatic amines lead to particularly poor yields of the derived anilines[101] (Equations (78) and (79)), although the arylation of cyclooctylamine **78** with an electron-rich aryllead triacetate afforded the aniline derivative **79** in a moderately good yield (52%) (Equation (80)).[105,105a]



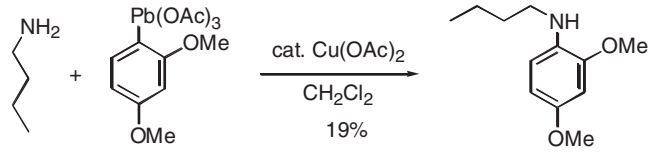
(76)



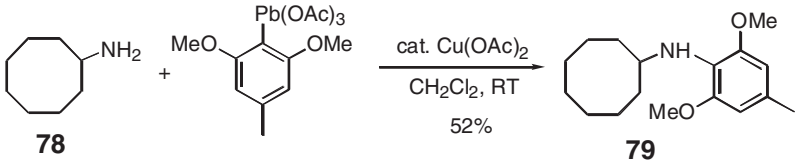
(77)



(78)

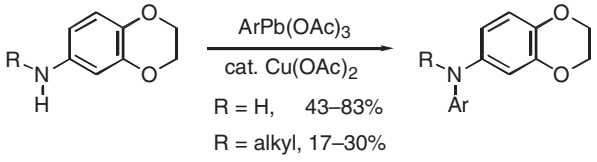


(79)



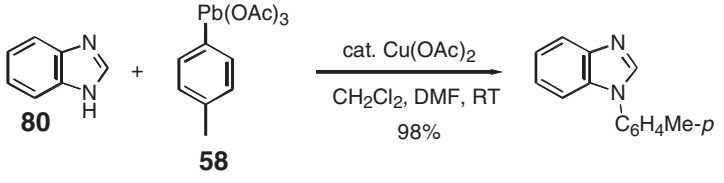
(80)

A number of heterocyclic aniline derivatives afforded moderate to good yields of the diarylamines. Among the reported systems were amino-indazole,[106,106a] aminobenzodioxole,[107] and aminobenzodioxanne.[98,108] In the latter series, good to excellent yields were obtained with the primary aniline, but modest yields were observed after monoalkylation of the amino group (Equation (81)).[98]

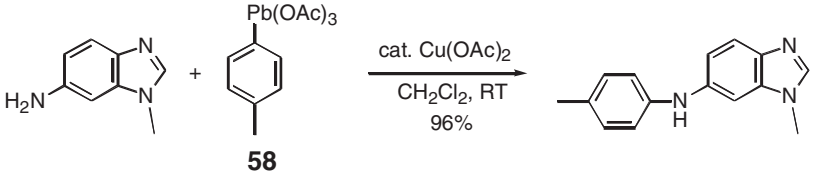


(81)

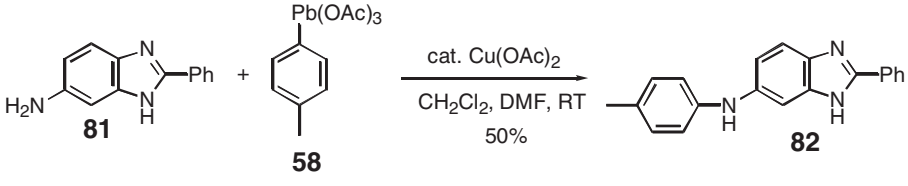
A variety of azole derivatives reacted with *p*-tolyllead triacetate **58** in the presence of copper diacetate to afford the *N*-monoaryl derivatives in good to excellent yields (Equations (82)–(84)).[106,106a,109,109a,110] Benzimidazole **80** was arylated in 98% yield by *p*-tolyllead triacetate. In the case of the 5-aminobenzimidazole **81**, excellent chemoselectivity was observed in favor of the primary aromatic amine with exclusive formation of the *N*-*p*-tolylaminobenzimidazole **82** in 50% yield.[110]



(82)

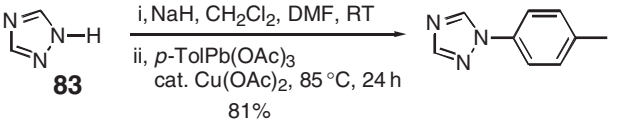


(83)



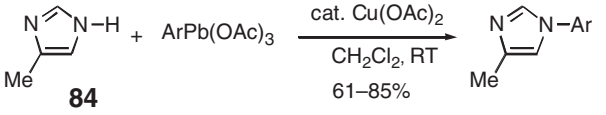
(84)

3-Methylindole, imidazole, and various triazoles were also *N*-arylated. In the case of 1,2,4-triazole **83**, 1,2,3-benzotriazole and indole derivatives, good yields of the *N*-aryl derivatives were only obtained upon treatment of the sodium salt of the substrate with *p*-tolyllead triacetate **58** in the presence of copper diacetate at 50–90 °C (Equation (85)).[110]



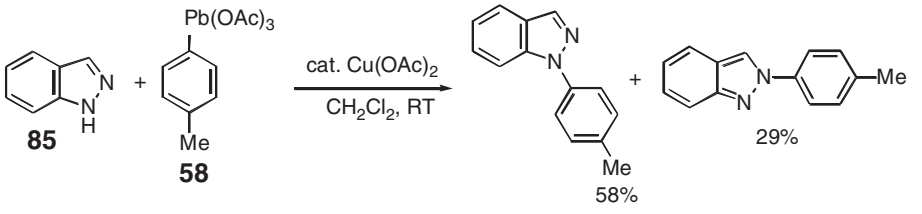
(85)

A good regioselectivity was observed with unsymmetrical imidazoles such as **84**, the less hindered nitrogen being the only one to be *N*-arylated[111] (Equation (86)).

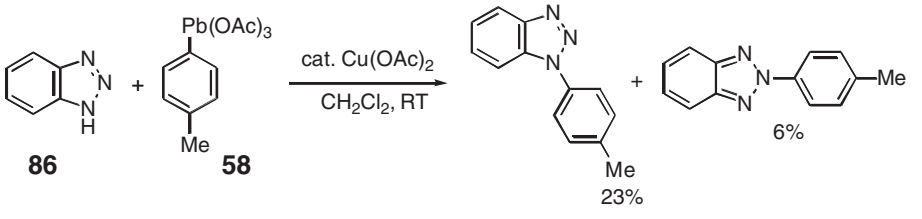


(86)

In the case of the indazole **85** and benzotriazole **86**, the reaction with *p*-tolyllead triacetate **58** led to mixtures of the arylation products on both nitrogen atoms[110] (Equations (87) and (88)).

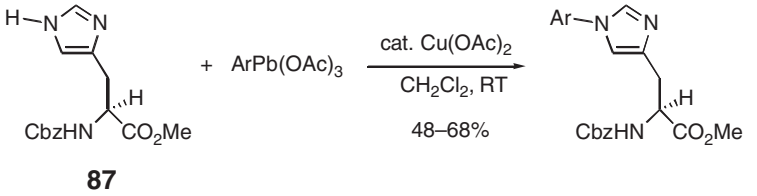


(87)

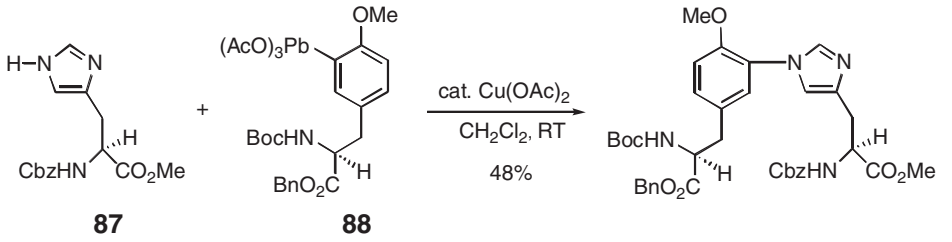


(88)

The mildness of the conditions of reaction and the regioselectivity of the *N*-arylation of imidazoles allowed the *N*-arylation of the azolic nitrogen of a protected histidine **87**, even with the organolead reagent **88** derived from tyrosine, thus realizing the link between two aminoacid derivatives moieties (Equations (89) and (90)).[111,112]



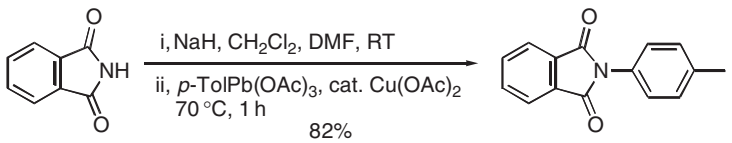
(89)



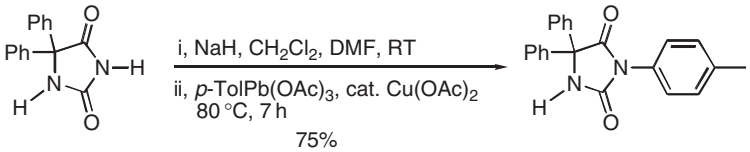
(90)

In the second major class of amine derivatives, the amidic nitrogen atom can also be *N*-arylated when the sodium salt of the amides is treated with *para*-tolyllead triacetate **58** in CH_2Cl_2–DMF at 60–80 °C under mild conditions[113,114] (Equations (91)–(93)). Amides as well as sulfonamides, imides, or hydantoins reacted with aryllead triacetates under copper(II) catalysis, to afford good to excellent yields of the derived *N*-arylamides. In general, better yields were obtained when the sodium salt of the amide was used. For these amidic substrates, the reactions are

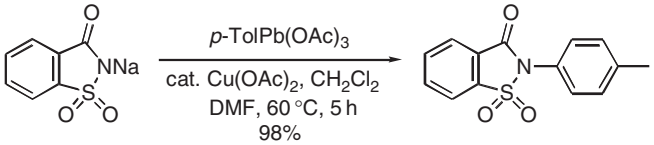
generally performed under harsher conditions than with anilines, at temperatures ranging from 60 to 80 °C. However, in the case of succinimide **89**, the arylation was performed without addition of sodium hydride (Equation (94)).



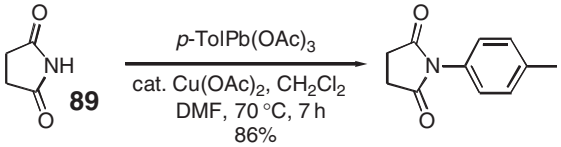
(91)



(92)

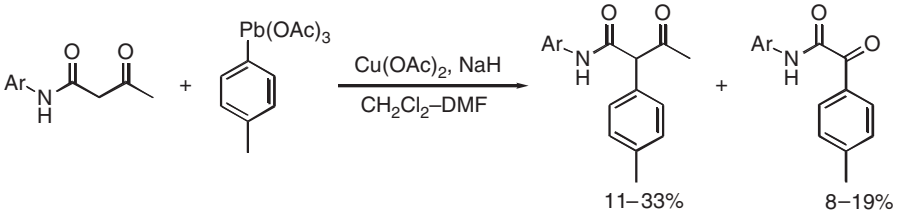


(93)



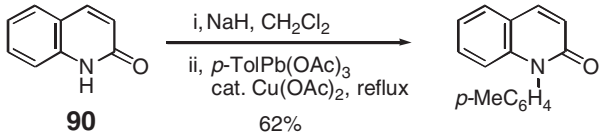
(94)

When a competition between an amido group and a potentially more reactive group is possible, chemoselectivity is observed, so that amino or β-diketone groups are selectively *N*- or *C*-arylated, respectively (Equation (95)).[114]

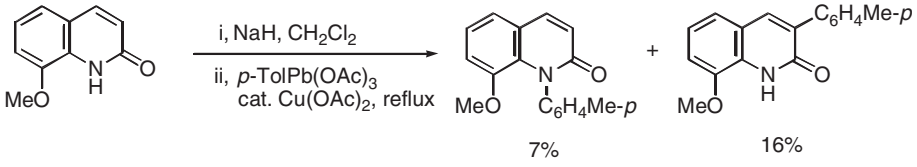


(95)

The unsubstituted 1,2-dihydroquinolin-2-one **90** afforded good yields of the *N*-arylation product, but the presence of a methoxy group on the *ortho*-position relative to the nitrogen atom reduced considerably the yields of the *N*-arylation products (Equations (96)–(98)). In the absence of a copper catalyst, the *C*-3-aryl derivative was the only formed product.[115]



(96)



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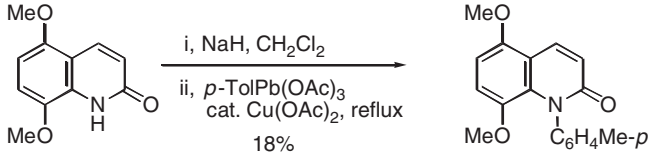
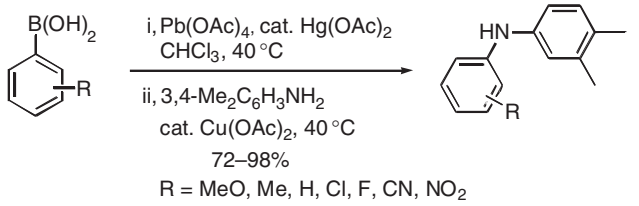


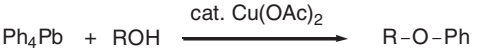
(98)

All the copper-catalyzed amine or amide arylation reactions with aryllead triacetates involve the use of previously isolated aryllead reagents. However, this can be considered as a serious inconvenience for organic chemists. *In situ* generated aryllead reagents have been extensively employed in *C*-arylation reactions, but few examples considered applying the *in situ* generation of aryllead triacetates to the copper-catalyzed amine arylation reactions. Such a system was used with success for the arylation of an aniline derivative with a range of electron-rich as well as electron-depleted arylboronic acid derivatives used as precursors of the active aryllead species, in generally excellent yields (Equation (99)).[116,116a]



(99)

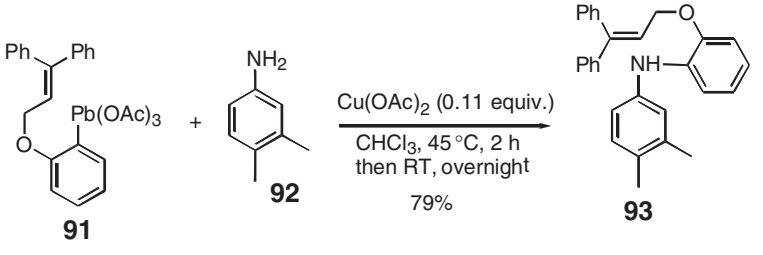
O-Arylation of alcohols or phenols cannot be performed by copper diacetate-catalyzed reactions using aryllead triacetates as the source of the aryl ligand. However, Dodonov *et al.* reported that tetraphenyllead reacts with primary and secondary alcohols in the presence of copper diacetate to afford the derived *O*-phenyl ethers in moderate yields ranging from 1.25 to 1.8 mol. of ether per mole of the lead reagent (Equation (100)). Phenol and *tert*-butyl alcohol afforded lower yields of the ethers (0.72–0.95 mole per mole of the lead reagent).[117]



(100)

9.09.3.1.1 Mechanism of the copper diacylate-catalyzed arylations

As the copper diacylate-catalyzed arylation reactions have been mostly investigated for synthetic purposes, only a limited number of mechanistic studies tried to shed some light on the nature of the copper intermediates. The occurrence of free-radical species has been excluded by using a reagent with an internal free-radical trap **91**. Copper-catalyzed reaction of this compound **91** with the aniline **92** afforded only the linear coupling product **93**. Similarly, in the reaction with benzimidazole **80**, the *N*-arylbenzimidazole **94** was formed together with a side-product **95**, resulting from decomposition of the lead reagent (Equations (101) and (102)).[42]



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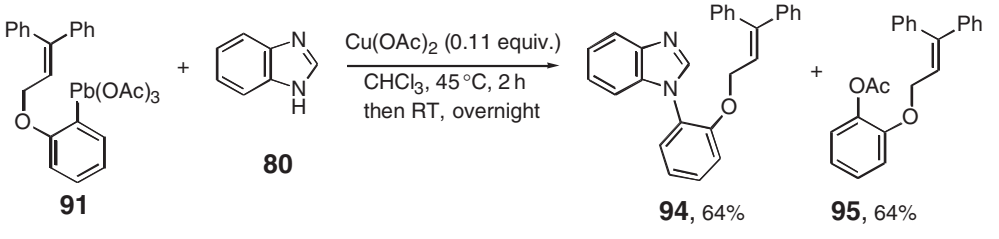
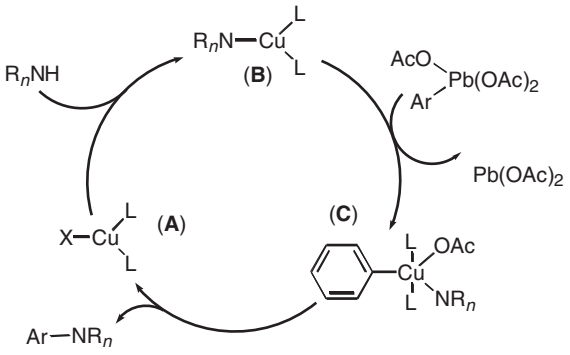


(102)

In the copper-catalyzed *N*-arylation reactions, transmetallation between the organolead reagent and a Cu(I) species is the key step (Scheme 18). The active catalyst is postulated to be a Cu(I) species, that can be generated in the early stages of the reaction through reduction of the original Cu(II) diacylate by an oxidizable component of the reacting system. This copper(I) intermediate (**A**) reacts with the substrate to give a new substrate-copper(I) intermediate (**B**). Oxidative addition of the organolead reagent leads to an hypervalent copper(III) intermediate (**C**), which eventually



Scheme 18

undergoes reductive elimination to afford the modified Ullmann condensation type product with regeneration of the initial catalytic copper(I) species (**A**).[101]

9.09.3.2 Palladium Cross-coupling with Organolead Reagents

Kang *et al.* explored the homocoupling reaction of organolead compounds, catalyzed by either palladium or copper sources. Among the various palladium-based catalysts that were tested, $Pd_2(dba)_3$ appeared to be the most active. Yields were good with either metal catalyst, although differences were noted both in the solvent and the amount of catalyst employed (Equation (103)). Both reactions proceed at room or moderate temperature.[95]

$$\mathrm{ArPb(OAc)_3} \xrightarrow[\mathrm{CHCl_3,\ RT}]{\mathrm{Pd_2(dba)_3{\cdot}CHCl_3\ (5\%)}} \mathrm{Ar{-}Ar} \qquad (103)$$

Ar	*Yield* (%)
Ph	68
p-MeC$_6$H$_4$	65
p-MeOC$_6$H$_4$	75

When the homocoupling reaction is performed in the presence of carbon monoxide, the palladium-catalyzed carbonylative coupling of organolead compounds takes place (Equation (104)). Thus, organolead triacetates can be carbonylated in the presence of $Pd_2(dba)_3$, $CHCl_3$ (5 mol%) and NaOMe (5 equiv.) in acetonitrile under atmospheric pressure of carbon monoxide at room temperature to afford good yields of the symmetrical ketones.[118]

$$\mathrm{ArPb(OAc)_3} \xrightarrow[\mathrm{CO,\ NaOMe,\ MeCN,\ RT}]{\mathrm{Pd_2(dba)_3{\cdot}CHCl_3\ (5\%)}} \mathrm{Ar{-}C(=O){-}Ar} \qquad (104)$$

A variety of palladium-catalyzed coupling reactions involving organolead triacetates and a second organometallic or organoheteroatomic reagent have been also reported by Kang *et al.* Stille-type reactions, normally taking place between organostannanes and aryl halides or triflates, were shown to proceed also with organolead reagents.[119] These reactions were accomplished with palladium and copper(I) iodide as co-catalyst, and in the presence of 5 equiv. of sodium methoxide that appeared essential (Equation (105)). The copper species was suggested to reduce the rate of the competing homocoupling reaction. Phenyllead triacetate coupled with vinyltributylstannane in 80% yield with only trace amounts of biphenyl, the product of homocoupling reaction. Similarly, *p*-methoxyphenyllead triacetate **1** was coupled with 2- and 3-furyltributyltin in 73% and 70% yield, respectively.

$$ArPb(OAc)_3 + RSnBu_3 \xrightarrow[CuI\ (10\%),\ NaOMe\ (5\ equiv.)]{Pd_2(dba)_3\cdot CHCl_3\ (5\%)} Ar\text{–}R + Ar\text{–}Ar \quad (105)$$

Ar	*R*	*Ar–R* (%)	*Ar–Ar* (%)
Ph	Vinyl	80	Trace
p-$MeOC_6H_4$	2-Furyl	73	10
p-$MeOC_6H_4$	3-Furyl	70	Trace

Suzuki-type reactions are also possible with aryllead reagents (Equation (106)).[120] As in the previous system, there is a need for a mixed catalyst system. In addition, 6 equiv. of base are also required. The cross-coupling yielded products in the 70–80% range. The generality of the procedure, toward the electronic nature of the coupling partners, was demonstrated by a comparison of the reaction of phenyllead triacetate with *p*-methoxyphenylboronic acid (75%) with the reaction of phenylboronic acid with *p*-methoxyphenyllead triacetate (76%): both reactions gave the same product, 4-methoxybiphenyl, in identical yields (75–76%).

$$ArPb(OAc)_3 + Ar'B(OH)_2 \xrightarrow[\substack{CuI\ (10\%),\ NaOMe\ (6\ equiv.)\\ DME,\ MeCN,\ 60\ ^\circ C}]{Pd_2(dba)_3\cdot CHCl_3\ (5\%)} Ar\text{–}Ar' \quad (106)$$

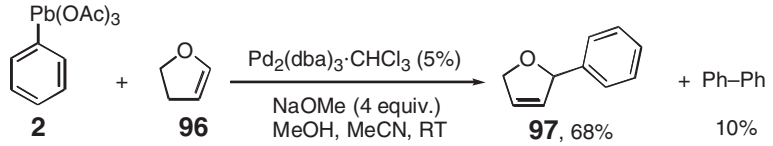
Ar	*R*	*Yield* (%)
Ph	*p*-$MeOC_6H_4$	75
p-$MeOC_6H_4$	Ph	76
2,4-$(MeO)_2C_6H_3$	*p*-MeC_6H_4	74

Cross-coupling reactions between iodonium salts and organolead reagents can be catalyzed by palladium (Equation (107)).[121] These reactions required 2 equiv. of base. In this system, homocoupling of the reagent could not be completely suppressed (Ar–Ar, 10–20%), and the reported yields for the products of the heterocoupling pathway (Ar–Ar′) were moderate (62–75%).

$$ArPb(OAc)_3 + Ar'I^+Ph\ BF_4^- \xrightarrow[\substack{NaOMe\ (2\ equiv.)\\ CHCl_3,\ RT}]{Pd_2(dba)_3\cdot CHCl_3\ (5\%)} Ar\text{–}Ar' + Ar\text{–}Ar \quad (107)$$

Ar	*Ar′*	*Yield* (%)	*Yield* (%)
Ph	*p*-$MeOC_6H_4$	75	10
p-$MeOC_6H_4$	Ph	62	20
p-$MeOC_6H_4$	2-Thiophen	72	10

The third type of classical cross-coupling reaction between organolead reagents and unsaturated alkenes or alkynes was also investigated. Coupling between an aryllead(IV) reagent and an olefin catalyzed by palladium (Heck-type reaction) was reported. As in the previous three reactions, NaOMe must be added to achieve success. Phenyllead triacetate **2** was coupled with 2,3-dihydrofuran **96** to provide the 2-phenyl-2,5-dihydrofuran **97** in 68% yield together with 10% of homocoupling product (Equation (108)). With *p*-methoxyphenyllead triacetate **1**, the yield of 2-(*p*-methoxyphenyl)-2,5-dihydrofuran **98** was 80% with no formation of the homodimer (Ar–Ar) (Equation (109)). Coupling of *p*-methoxyphenyllead triacetate **1** with a vinyl cyclic carbonate **99** gave the Heck-type product **100** in 75% yield without opening of the cyclic carbonate (Equation (110)). The conditions of these Heck-type reactions are slightly different from the Suzuki- and Stille-type coupling with organolead reagents, in that these couplings do not need the copper(I) iodide co-catalyst. The aryllead reagent active in the transformations requiring methoxide was suggested to be either $RPb(OMe)_3$ or one of the possible acetate/methoxide mixed ligand species $RPb(OMe)_x(OAc)_{3-x}$.[122]



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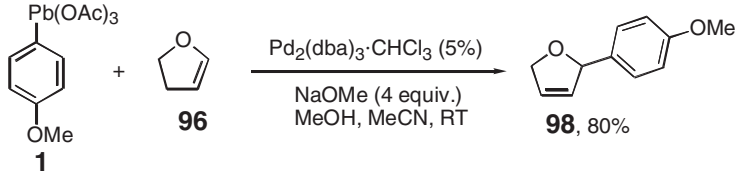

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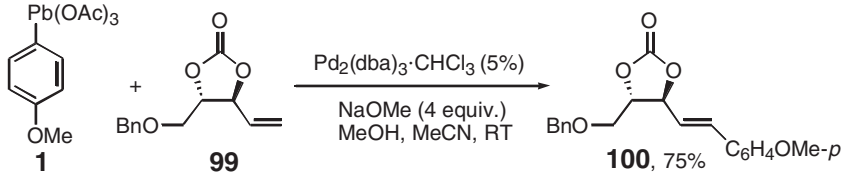
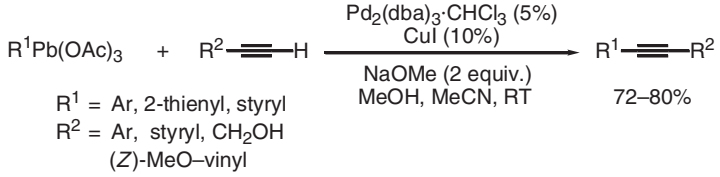


(110)

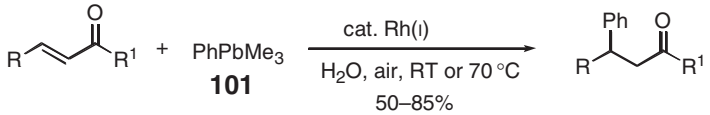
Similarly, arylacetylene derivatives can be prepared by palladium-catalyzed cross-coupling of an organolead(IV) triacetate with terminal alkynes. The coupling of a number of organolead(IV) triacetates with terminal alkynes was accomplished with $Pd_2(dba)_3$, $CHCl_3$ (5 mol%) and CuI (10 mol%) in the presence of NaOMe (2 equiv.) in a mixture of methanol and acetonitrile (1 : 1) at room temperature. This reaction is compatible with the presence of primary alcohol, as well as styryl groups (Equation (111)).[123]



(111)

9.09.3.3 Rhodium-catalyzed Reactions

Transition metal-catalyzed transformations using organometallic reagents are of great importance in modern organic chemistry.[124] One of the recent variety of such transformations is the rhodium-catalyzed addition of the organometallic reagents to a carbon–heteroatom double bonds such as in aldehydes or imines as well as the 1,4-addition to α,β-unsaturated carbonyl compounds.[125] The organorhodium complex active species are generated by transmetallation between a rhodium catalyst and an organometallic reagent. Li *et al.* have reported some such rhodium-catalyzed reactions involving organolead reagents. In the presence of a rhodium catalyst, α,β-unsaturated esters and ketones react with aryllead reagents in aqueous media in an air atmosphere to give the corresponding products of conjugate addition (Equation (112)).[126] With phenyltrimethyllead **101**, high yields of the conjugate addition products were obtained. Chlorotriphenyllead or dichlorodiphenyllead did not react and tetraphenyllead afforded only a poor yield of the addition product. With crotonaldehyde **102**, the bisphenylation product **103**, resulting from C=C and C=O addition, was obtained in a 70% yield (Equation (113)).



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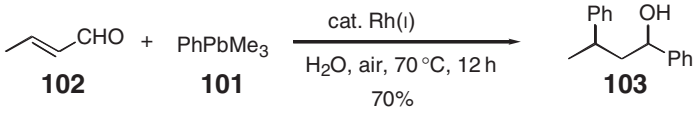
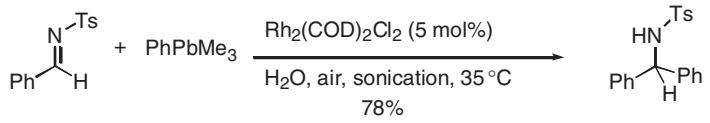


(113)

Similarly, imines react with phenyltrimethyllead **101** in the presence of a rhodium catalyst, in water and air under ultrasonic irradiation at 35 °C, to give the corresponding diarylmethylamines in good yields (Equation (114)). A moderate diastereoselectivity was observed when the rhodium catalyzed addition of (*ortho*-chlorophenyl)trimethyllead **105** was done on a chiral *p*-toluenesulfinylimine **104** (Equation (115)).[127]



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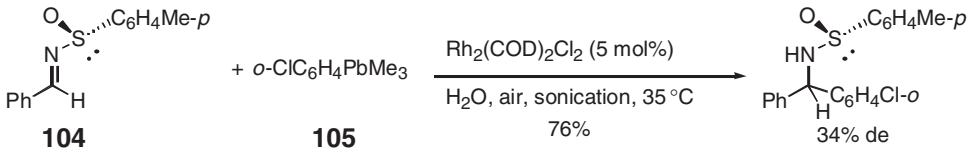
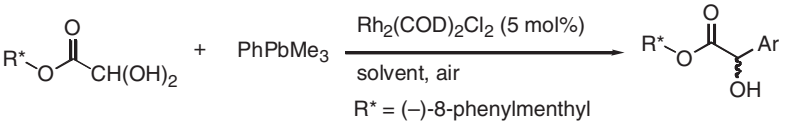


(115)

When the rhodium-catalyzed reaction of aryllead reagents in water and under an atmosphere of air was applied to a chiral glyoxylate hydrate, it gave the corresponding addition products in high yields (Equation (116)). The diastereoselectivity of the reactions were remarkably improved by using water as the solvent.[128]



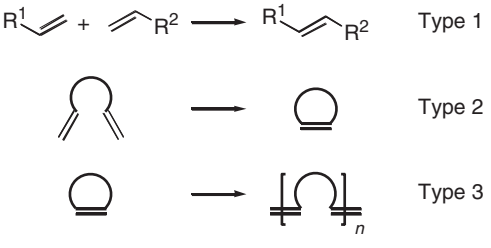
(116)

Solvent	*Yield* (%)	de%
H_2O	73	77
CH_2Cl_2	75	48

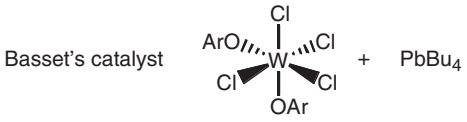
9.09.4 Alkyllead in Co-catalyzed Metathesis Reactions

Olefin metathesis can be categorized in three major types (Scheme 19): (i) acyclic cross metathesis in which two alkenes undergo intermolecular coupling to form a new olefin or a polymer when carried out on dienes (ADMET), (ii) ring-closing metathesis (RCM) in which a diene is transformed into a ring, (iii) ring-opening metathesis polymerization (ROMP), which involves the metathetic opening of cyclic olefins, generally strained although not always, to give polymeric compounds.[129,129a,129b]

Tetraalkyllead derivatives play a determinant role in a number of catalytic combinations that realize these transformations, in heterogeneous or homogeneous systems. The lead compound plays a crucial role for the efficient generation of metal carbene intermediates, that are considered to be the active catalytic species. Among the heterogeneous catalytic systems, a small number involving rhenium oxide on alumina alone or with silica (Re_2O_7, Al_2O_3–SiO_2) require the presence of a promoter such as tetraalkyltin or tetraalkyllead derivative to perform the

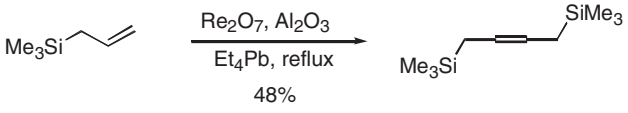


Scheme 19



Scheme 20

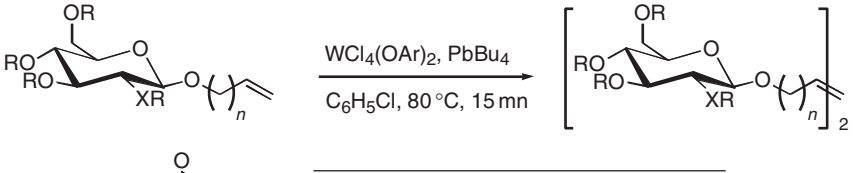
reaction of metathesis of functionalized olefins in moderately good yields.[130,130a] However, the interest of these rhenium oxide-based systems is relatively limited in organic synthesis. Among the alkenes that were submitted to this heterogeneous catalytic system, methyl oleate,[131,131a,131b] 3-trimethylsilyl-1-propene (Equation (117)),[132] norbornene,[133] 6-nitro-1-hexene,[134] or methyl erucate[135] can be mentioned as examples.

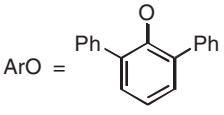


(117)

Heterogeneous tungsten-based catalysts derived from WCl_6, $WOCl_4$, or WBr_5 on supported silica or alumina activated by tetralkyltin or tetraalkyllead promoters were applied to the metathesis of 1-pentene.[136] However, the development of homogeneous tungsten-based catalysts by Basset *et al.* increased the attention devoted to olefin metathesis.[137,137a] The combination of a well-defined tungsten complex, either $WCl_4(OAr)_2$ or $W(O)Cl_2(OAr)_2$, with a tetraalkyllead or tetraalkyltin promoter, gives efficient metathesis catalytic systems (Scheme 20).[138] These catalysts show a relatively good functional groups tolerance, in particular, to sulfur, silicon, tin, and phosphorus.[139] However, they are limited by the steric demand toward shorter alkenes, such as allyl groups. A metal alkylidene intermediate has been suggested as the active catalytic species, although there is no evidence for it.

Descotes *et al.* applied Basset's catalyst for the intermolecular metathesis of di- and tri-substituted ω-unsaturated glucose and glucosamine derivatives bearing different protecting groups to lead to bolaamphiphiles in good yields (Equation (118)). Acetate and silyl-protected sugars were superior to the corresponding benzyl-protected glucosides. The catalyst was active with long-chain alkenes, but allyl glycosides did not react due to a competitive coordination of the ether oxygen to the metallocarbenes. The yields of metathesized products were generally good, but the *cis* : *trans* ratios were not determined.[140,140a]

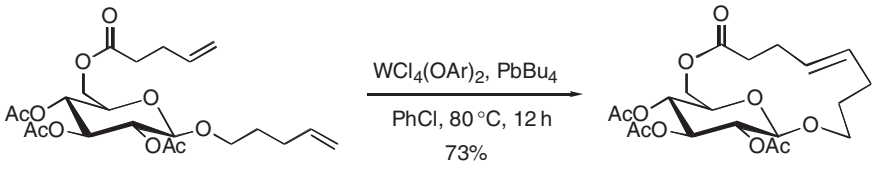




n	*X*	*R*	*Yield* (%)
3	O	Ac	65
9	O	Ac or TBDMS	51–52
9	O	Bn	37
9	NH	Ac	62

(118)

Basset's catalyst was also used for the intramolecular metathesis of diluted solutions of di- and tri-substituted ω-unsaturated glucose and glucosamine derivatives, affording bicyclic carbohydrate-based structures in reasonable yields (Equations (119)–(122)).[141]



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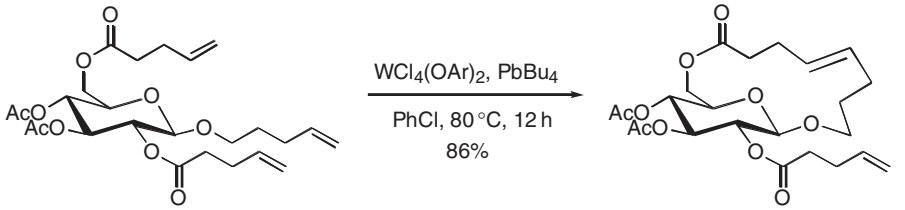

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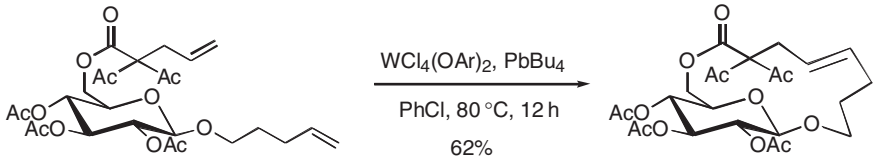

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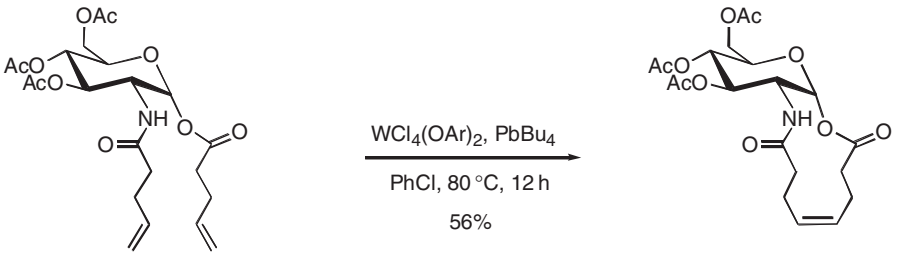
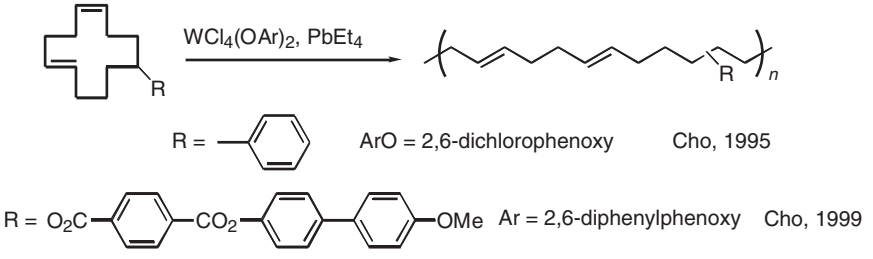


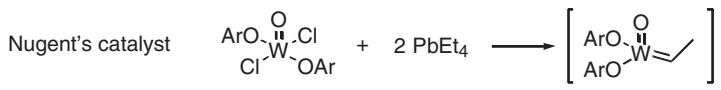
(122)

On the other hand, Basset's catalyst can be used for the preparation of highly regular polymers by ring-opening metathesis polymerization.[139] This system gave high molecular weight polymers in high conversion, whereas other systems (WCl_6–Et_2AlCl; $MoCl_5$–Et_3Al) showed little or no activity.[142] The reaction gave also quantitative conversion of 3-phenyl-1,5-cyclododecadiene with a slightly different tungsten complex, $WCl_4(OAr)_2$ with Ar = 2,6-dichlorophenyl, in the presence of tetraethyllead (Scheme 21). It gave a sequence-controlled 2 : 1 : 1 terpolymer of butadiene, styrene, and ethylene. In this metathesis reaction, the tetraalkyltin-promoted system was much less efficient.[143] Polymerization of 4-methyl-6-phenylcyclooctene with the catalytic system $WCl_4(OAr)_2$–Et_4Pb (ArO = 2,6-diphenylphenoxy) gave high molecular -weight polymers having the *mer*-sequence of butadiene, propylene, and styrene in 1 : 1 : 1 alternating fashion.[144,144a] The reaction was also applied to the metathesis of 4,6-diphenylcyclooctene[145] and of methyl (*Z*,*E* or *E*,*Z*)-3,7-cyclodecadienecarboxylate.[146]

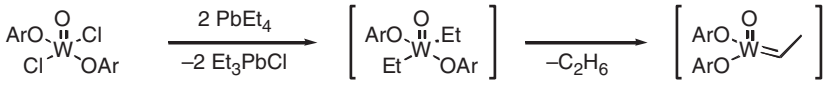
A slightly different tungsten-based complex system, *trans*-$WOCl_2(OAr)_2$ (Ar = 2,6-dibromophenyl), was prepared by Nugent *et al.* and its utility tested as a metathesis catalyst for the cyclization of dienes (Scheme 22).[147] The *oxo*-tungsten complex alone does not perform any metathesis, unless 2 equiv. of tetraethyllead is added. A variety of non-conjugated dienes were cleanly cyclized to the corresponding cycloalkenes using 2 mol% of the catalyst in the



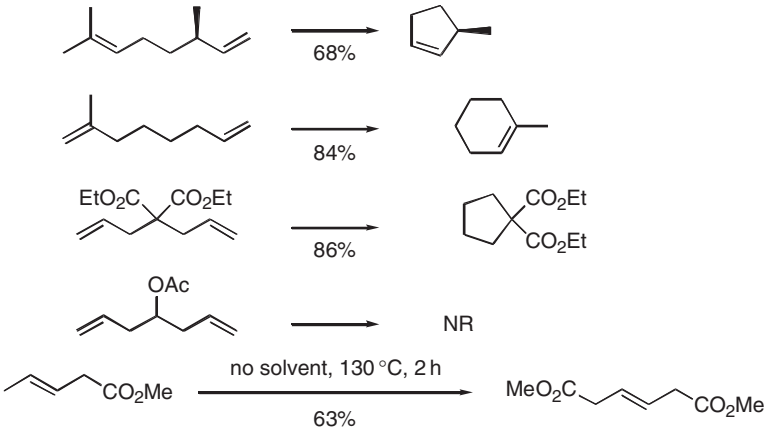
Scheme 21



Scheme 22



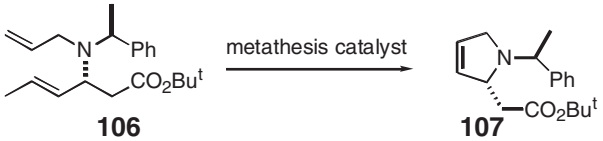
i, catalyst (2 mol%); ii, $PbEt_4$ (4 mol%); iii, 1,2,4-$Cl_3C_6H_3$ or toluene; iv, 90 °C, 1 h



Scheme 23

presence of 4 mol% of tetraethyllead (Scheme 23). This promoter is presumed to replace two chloride ligands with ethyl groups, ultimately leading to the catalytically active ethylidene complex via α-hydride elimination. Relatively high temperature is required to effect the metathesis with the tungsten precursor in the presence of tetraethyllead. The synthesis of chiral cycloalkenes took place with little or no loss in optical activity. For example, (*R*)- and (*S*)-citronellene gave the corresponding (*R*)- and (*S*)-3-methylcyclopentenes in 97% enantiomeric excess. This cyclization is compatible with some functional groups (ester, amide, and ether derivatives), but it lacks the wider compatibility available with other catalysts. This catalytic system was used for the preparation of a key intermediate during the synthesis of carbocyclic nucleosides.[148]

Nugent's catalyst, however, failed to effect the cyclization of the aminodiene **106**, that was cyclized to the pyrroline **107** either by Grubbs' ruthenium alkylidene catalyst, $PhCH{=}Ru(PCy_3)_2Cl_2$, in 77% yield or by Schrock's catalyst, $PhC(Me)_2CH{=}Mo{=}N[2,6\text{-}(iPr)_2C_6H_3]\{[OCMe(CF_3)_2]_2\}$ in 60% yield (Equation (123)).[149]



106 **107** (123)

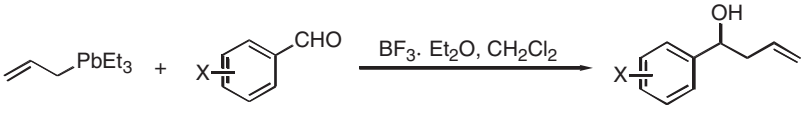
Grubbs' catalyst	77%
Schrock's catalyst	60%
Nugent's catalyst	0%

9.09.5 Miscellaneous Reactions of Organolead Compounds

A small number of other reactions involving organolead compounds have been studied in the past decade. However, their synthetic interest is relatively limited.

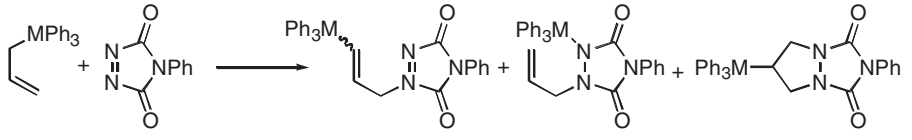
9.09.5.1 Allylation Reactions

In contrast to the numerous applications of allyltrialkylstannanes in organic synthesis, only one report describes the reaction of allyltriethyllead with benzaldehyde in the presence of BF_3. OEt_2 in CH_2Cl_2 to afford homoallylic benzylic alcohols (Equation (124)). The reaction is considered to occur by a polar pathway and not by an alternative ET process. The Hammett ρ values were small and positive at 25 °C and negative at −78 °C.[150] This reaction leads to the same result as the Barbier-type lead-mediated allylation of carbonyl compounds or imines, that however does not involve allyltriorganolead reagents.[151–151b] In these Barbier-type reactions, the structure of the reagent is not well defined, but some allyllead species was postulated to react under a direct nucleophilic addition mechanism.[152]



(124)

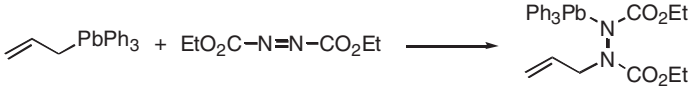
Metalloene reactions can lead to two main types of condensation products, the ene products (H-ene or M-ene) and the [2 + 3]-cycloaddition products.[153] In a series of reactions of allylMPh$_3$ with phenyltriazolinedione, the lead derivative afforded only the H-ene product (Equation (125)).[154]



	H-ene	*M-ene*	*Cycloaddition*
M	*Yield* (%)	*Yield* (%)	*Yield* (%)
Si	0	100	0
Ge	20	30	50
Sn	55	0	45
Pb	100	0	0

(125)

On the other hand, the reaction of allyltriphenyllead with diethyl azodicarboxylate afforded quantitatively only one product, the M-ene product. A strong effect of lithium perchlorate catalysis was noted (Equation (126)).[155]

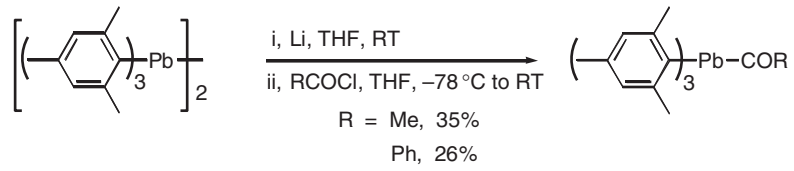


Solvent	*LiClO$_4$*	*Time*
Ether	0	1 h
	4 M	1 min
CH_2Cl_2	0	1.75 h
	0.2 M	40 min

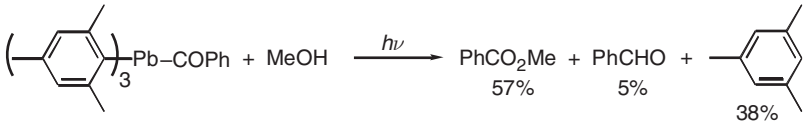
(126)

9.09.5.2 Reactions of Triaryllead Anions

Trimesitylplumbyllithium, generated by reaction of hexamesityldiplumbane with lithium, reacts with acyl chlorides to afford isolable air-stable acylplumbanes in modest yields (Equation (127)). Under ultraviolet irradiation as well as thermal decomposition, the benzoylplumbane reacted with methanol to afford methyl benzoate (Equation (128)).[156] The simpler acetyl- and benzoyl-triphenylplumbane were only detected as transient species in solution, the acetyltriphenylplumbane decomposing at 50 °C to give acetophenone.[157]

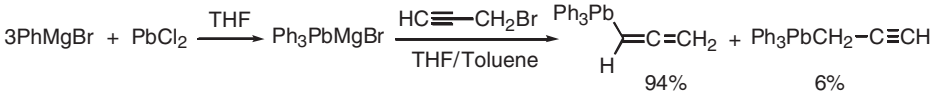


(127)



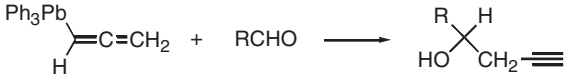
(128)

Cadiot *et al.* reported a synthesis of triphenylallenylplumbane by reaction of propargylmagnesium bromide with triphenyllead chloride. Although the reaction was efficient (70% yield), it suffered from the necessary but tedious preparation of the triphenyllead chloride.[158] In contrast, triphenylallenylplumbane can be easily prepared in 75–80% yields by reaction of *in situ* generated $Ph_3PbMgBr$ with propargyl bromide (Equation (129)).[159]



(129)

Allenyltriphenylplumbane is an efficient propargyl anion equivalent.[159] In the presence of a Lewis acid ($BF_3 \cdot OEt_2$ or $TiCl_4$), it reacts with various types of aldehyde to give homopropargylic alcohols in good yields (Equation (130)). As catalyst, BF_3 afforded generally acceptable yields of the derived alcohol except with propionaldehyde and isobutyraldehyde that required $TiCl_4$ to react correctly. In the case of acrolein, an α,β-unsaturated aldehyde, only the 1,2-addition product was formed. Propargylation of ketones required transmetallation with PhLi to $CH_2{=}C{=}CHLi$ which then reacted with the ketones.



Aldehyde	*Catalyst*	*Yield* (%)
PhCHO	BF_3	80
p-MeC_6H_4CHO	BF_3	77
Octylaldehyde	BF_3	53
Acrolein	BF_3	55
Propionaldehyde	$TiCl_4$	65
Isobutyraldehyde	$TiCl_4$	66

(130)

9.09.5.3 Trifluoromethylation Reaction

The bis(trifluoromethyl)cadmium glyme complex, $[Cd(CF_3)_2.MeOCH_2CH_2OMe]$, reacts with various organolead(IV) halides to afford by a ligand exchange process, the corresponding trifluoromethyllead compounds (Equation (131)).[160] The mono and bis-trifluoromethyl lead compounds have extended shelf lives and could therefore appear as useful trifluoromethylating agents. Indeed, the mono(trifluoromethyl)-substituted compound Ph_3PbCF_3 reacted by ligand exchange with a representative main group derivative (Equation (132)) and a transition metal complex (Equation (133)). Thus, this mono-substituted lead compound reacts more effectively than $Hg(CF_3)_2$ but is less reactive than $Cd(CF_3)_2 \cdot$glyme. Presumably, the disubstituted compound $Ph_2Pb(CF_3)_2$ should prove more reactive. Trifluoromethyl-subsituted aromatic derivative can be prepared by CuCl-catalyzed reaction of hexaphenyldiplumbane with bis(trifluoromethyl)cadmium glyme complex (Equation (134)). This reaction takes place under very mild conditions (room temperature, atmospheric pressure), compared to the alternative methodologies that require elevated temperature and pressure.[161,161a,161b]

$$Ph_nPbCl_{4-n} + Cd(CF_3)_2.(MeOCH_2CH_2OMe) \longrightarrow Ph_nPb(CF_3)_{4-n}$$

$PhPb(CF_3)_3$ 51%
$Ph_2Pb(CF_3)_2$ 61%
Ph_3PbCF_3 81% (131)

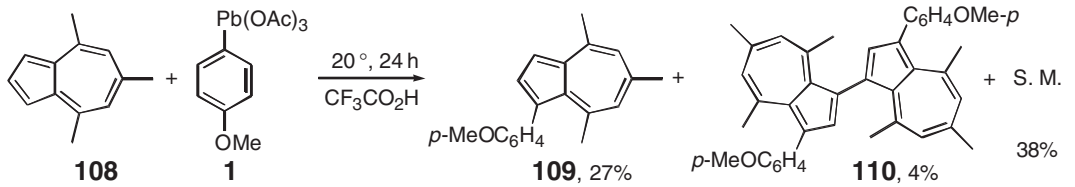
$$Ph_3PbCF_3 + SbI_3 \xrightarrow[61\%]{THF,\ RT,\ 72\,h} Sb(CF_3)_2 \quad (132)$$

$$Ph_3PbCF_3 + Pd(PEt_3)_2Cl_2 \xrightarrow[62\%]{THF,\ RT,\ 48\,h} Pd(PEt_3)_2Cl(CF_3) \quad (133)$$

$$Ph_6Pb_2 + Cd(CF_3)_2.(MeOCH_2CH_2OMe) \xrightarrow[95\%]{cat.\ CuCl,\ THF,\ RT,\ 7\,d} PhCF_3 \quad (134)$$

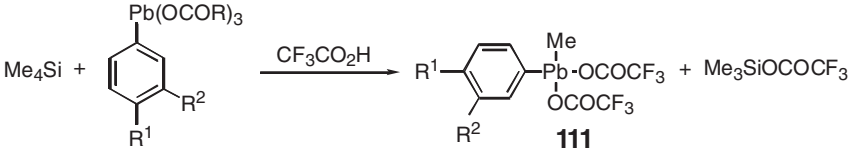
9.09.5.4 Electrophilic Reactions

The reaction of arenes with aryllead tricarboxylates performed in trifluoroacetic acid, affording biarenes, takes place via a cationic π-complex.[162] Since azulenes form π-donor/acceptor complexes with various π-acids, the arylation of 4,6,8-trimethylazulene **108** was attempted with *p*-methoxyphenyllead triacetate **1** (Equation (135)).[163] Only one isomer of 1-arylazulene **109** was formed although in a modest 27% isolated yield. Based on recovered unreacted azulene, the effective yield was 43%. A dimer **110**, 3,3′-dianisyl-1,1′-biazulene (4% yield), was suggested to result from the one-electron oxidation of the intermediate 4-methoxyphenyl cation in the π-complex.



108 **1** **109**, 27% **110**, 4% (135)

Although ^{1}H NMR spectra of aryllead triacetates can be recorded in $CDCl_3$ solution in the presence of tetramethylsilane, cleavage of the methyl–silicon bond takes place when tetramethylsilane is treated with an aryllead(IV) tricarboxylate in trifluoroacetic acid.[164] When the aryl moiety is substituted with an electron-withdrawing group, quantitative conversion of TMS was observed to give aryl(methyl)lead dicarboxylates **111**, (Equation (136)) that were even isolated in two instances, although in modest to moderate yields : 55% yield for the 4-fluorophenyl compound and 23% yield for the 4-trifluoroacetamidophenyl compound.



111 (136)

R^1 = F, Cl, Br, CF_3CONH,CF_3, H
R^2 = H, Cl, Br

References

1. Löwig, C. *J. Prakt. Chem.* **1853**, *60*, 304.
1a. Löwig, C. *Liebigs Ann. Chem.* **1853**, *88*, 318.
2. Midgley, T.; Boyd, T. A. *J. Ind. Chem. Eng.* **1922**, *14*, 894–898.
3. Pinhey, J. T. Lead. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11, pp 461–485.
4. Moloney, M. G. *Main Group Met. Chem.* **2001**, *24*, 653–660.

5. Lewis, R. J., Sr. *Sax's Dangerous Properties of Industrial Materials*, 8th ed.; Van Nostrand Reinhold: New York, 1992.
5a. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety*, 2nd ed.; Sigma-Aldrich: Milwaukee, 1988.
6. Paquette, L. A.; Schloss, J. D.; Efremov, I.; Fabris, F.; Gallou, F.; Méndez-Andino, J.; Yang, J. *Org. Lett.* **2000**, *2*, 1259–1261.
7. Marken, F.; Squires, A. M.; Alden, J. A.; Compton, R. G.; Buston, J. E. H.; Moloney, M. G. *J. Phys. Chem. B* **1998**, *102*, 1186–1192.
7a. Siu, T.; Yudin, A. K. *J. Am. Chem. Soc.* **2002**, *124*, 530–531.
8. Pinhey, J. T. *Pure Appl. Chem.* **1996**, *68*, 819–824.
9. Finet, J.-P. *Ligand Coupling Reactions with Heteroatomic Compounds*; Pergamon: Oxford, 1998, Chapter 7; 205–247.
10. Omae, I. *Applications of Organometallics Compounds*; Wiley: Chichester, 1998, Chapter 11; pp 215–228.
11. Elliott, G. I.; Konopelski, J. P. *Tetrahedron* **2001**, *57*, 5683–5705.
12. Finet, J.-P.; Fedorov, A. Y.; Combes, S.; Boyer, G. *Curr. Org. Chem.* **2002**, *6*, 597–626.
13. Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 5400–5449.
13a. Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 1043.
14. Kano, T.; Saito, S. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, pp 721–751.
15. Pinhey, J. T. *Aust. J. Chem.* **1991**, *44*, 1353–1382.
16. Pinhey, J. T.; Rowe, B. A. *Aust. J. Chem.* **1980**, *33*, 113–120.
17. Andrews, M. D.; Brewster, A. G.; Crapnell, K. M.; Ibbett, A. J.; Jones, T.; Moloney, M. G.; Prout, K.; Watkin, D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 223–235.
18. Kozyrod, R. P.; Pinhey, J. T. *Tetrahedron Lett.* **1982**, *23*, 5365–5366.
18a. Kozyrod, R. P.; Pinhey, J. T. *Aust. J. Chem.* **1985**, *38*, 1155–1161.
19. Morgan, J.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1990**, 715–720.
20. Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, 957–960.
21. Pinhey, J. T.; Rowe, B. A. *Aust. J. Chem.* **1983**, *36*, 789–794.
22. Bonjoch, J.; Casamitjana, N.; Quirante, J.; Garriga, C.; Bosch, J. *Tetrahedron* **1992**, *48*, 3131–3138.
23. Suginome, H.; Orito, K.; Yorita, K.; Ishikawa, M.; Shimoyama, N.; Sasaki, T. *J. Org. Chem.* **1995**, *60*, 3052–3064.
24. Barton, D. H. R.; Donnelly, D. M. X.; Finet, J.-P.; Guiry, P. J.; Kielty, J. M. *Tetrahedron Lett.* **1990**, *31*, 6637–6640.
25. Orito, K.; Sasaki, T.; Suginome, H. *J. Org. Chem.* **1995**, *60*, 6208–6210.
26. Deng, H.; Konopelski, J. P. *Org. Lett.* **2001**, *3*, 3001–3004.
27. Donnelly, D. M. X.; Finet, J.-P.; Rattigan, B. A. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1729–1735.
28. Donnelly, D. M. X.; Finet, J.-P.; Rattigan, B. A. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1679–1683.
29. Shimizu, I.; Tsuji, J. *J. Am. Chem. Soc.* **1982**, *104*, 5844–5846.
29a. Tsuji, J.; Nisar, M.; Shimizu, I. *J. Org. Chem.* **1985**, *50*, 3416–3417.
30. Donnelly, D. M. X.; Finet, J.-P.; Guiry, P. J.; Nesbitt, K. *Tetrahedron* **2001**, *57*, 413–423.
31. Barton, D. H. R.; Donnelly, D. M. X.; Finet, J.-P.; Guiry, P. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1365–1375.
32. Donnelly, D. M. X.; Molloy, D. J.; Reilly, J. P.; Finet, J.-P. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2531–2534.
33. Combes, S.; Finet, J.-P.; Siri, D. *J. Chem. Soc., Perkin Trans. 1* **2002**, 38–44.
34. Fedorov, A. Y.; Carrara, F.; Finet, J.-P. *Tetrahedron Lett.* **2001**, *42*, 5875–5877.
35. Naumov, M. I.; Ganina, O. G.; Shavirin, A. S.; Beletskaya, I. P.; Finet, J.-P.; Fedorov, A. Y. *Synthesis* **2005**, 1178–1182.
36. Konopelski, J. P.; Hottenroth, J. M.; Oltra, H. M.; Véliz, E. A.; Yang, Z.-C. *Synlett* **1996**, 609–611.
37. Lindquist, N.; Fenical, W.; Van Duyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1991**, *113*, 2303–2304.
38. Li, J.; Jeong, S.; Esser, L.; Harran, P. G. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 4765–4770.
38a. Nicolaou, K. C.; Chen, D. Y.-K.; Huang, X.; Ling, T.; Bella, M.; Snyder, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 12888–12896.
39. Cakir, S. P.; Mead, K. T. *J. Org. Chem.* **2004**, *69*, 2203–2205.
40. Barton, D. H. R.; Finet, J.-P.; Giannotti, C.; Halley, F. *J. Chem. Soc., Perkin Trans. 1* **1987**, 241–249.
41. Morgan, J.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1673–1676.
42. Federov, A. Y.; Finet, J.-P. *Eur. J. Org. Chem.* **2004**, 2040–2045.
43. Parkinson, C. J.; Pinhey, J. T.; Stoermer, M. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1911–1915.
44. Buston, J. E. H.; Moloney, M. G.; Parry, A. V. L.; Wood, P. *Tetrahedron Lett.* **2002**, *43*, 3407–3409.
45. Bell, H. C.; May, G. L.; Pinhey, J. T.; Sternhell, S. *Tetrahedron Lett.* **1976**, *47*, 4303–4306.
45a. Bell, H. C.; Kalman, J. R.; Pinhey, J. T.; Sternhell, S. *Aust. J. Chem.* **1979**, *32*, 1551–1560.
46. Buston, J. E. J.; Compton, R. G.; Leech, M. A.; Moloney, M. G. *J. Organomet. Chem.* **1999**, *585*, 326–330.
47. Morgan, J.; Pinhey, J. T.; Rowe, B. A. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1005–1008.
48. Dyer, J.; Keeling, S.; Moloney, M. G. *Chem. Commun.* **1998**, 461–462.
49. Elliott, G. I.; Konopelski, J. P.; Olmstead, M. M. *Organic Lett.* **1999**, *1*, 1867–1870.
50. Konopelski, J. P.; Lin, J. Z.; Wenzel, P. J.; Deng, H. B.; Elliott, G. I.; Gerstenberger, B. S. *Org. Lett.* **2002**, *4*, 4121–4124.
51. Gerstenberger, B. S.; Konopelski, J. P. *J. Org. Chem.* **2005**, *70*, 1467–1470.
52. Dyer, J.; Keeling, S.; Moloney, M. G. *Chem. Commun.* **1998**, 461–462.
53. Dyer, J.; King, A.; Keeling, S.; Moloney, M. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2793–2804.
54. Brewster, A. G.; Broady, S.; Hughes, M.; Moloney, M. G.; Woods, G. *Org. Biomol. Chem.* **2004**, *2*, 1800–1810.
55. Moloney, M. G.; Paul, D. R.; Prottey, S. C.; Thompson, R. M.; Wright, E. *J. Organomet. Chem.* **1997**, *534*, 195–205.
56. Moloney, M. G.; Paul, D. R.; Thompson, R. M.; Wright, E. *J. Organomet. Chem.* **1998**, *560*, 77–88.
57. Kano, T.; Saito, S. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, p 725.
58. Mérour, J.-Y.; Chichereau, L.; Finet, J.-P. *Tetrahedron Lett.* **1992**, *33*, 3867–3870.
59. Donnelly, D. M. X.; Kielty, J. M.; Cormons, A.; Finet, J.-P. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2069–2073.
60. Donnelly, D. M. X.; Fitzpatrick, B. M.; O'Reilly, B. A.; Finet, J.-P. *Tetrahedron* **1993**, *49*, 7967–7976.
61. Donnelly, D. M. X.; Fitzpatrick, B. M.; Ryan, S. M.; Finet, J.-P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1797–1801.
62. Chen, H. Y.; Dykstra, K. D.; Birzin, E. T.; Frisch, K.; Chan, W.; Yang, Y. T.; Mosley, R. T.; DiNinno, F.; Rohrer, S. P., Schaeffer, J. M., *et al. Bioorg. Med. Chem. Lett.* **2004**, *14*, 1417–1421.
63. DiNinno, F.; Chen, H. Y.; Tan, Q. *PCT Int. Appl.* WO 2004091488, 2004 (*Chem. Abstr.* **2004**, *141*, 395331).
64. Donnelly, D. M. X.; Fitzpatrick, B. M.; Finet, J.-P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1791–1795.

65. Greenland, H.; Kozyrod, R. P.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1986**, 2011–2015.
66. Barton, D. H. R.; Donnelly, D. M. X.; Guiry, P. J.; Finet, J.-P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2921–2926.
67. Morgan, J.; Hambley, T. W.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2173–2177.
68. Kano, T.; Ohyabu, Y.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc.* **2002**, *124*, 5365–5373.
69. Kovtonyuk, V. N.; Kobrina, L. S. *J. Fluorine Chem.* **1993**, *63*, 243–251.
70. Bungard, C. J.; Morris, J. C. *Org. Lett.* **2002**, *4*, 631–633.
71. Morgan, J.; Buys, I.; Hambley, T.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1677–1681.
72. Morgan, J.; Parkinson, C. J.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3361–3365.
73. Saito, S.; Kano, T.; Muto, H.; Nakadai, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1999**, *121*, 8943–8944.
74. Barton, D. H. R.; Yadav-Bhatnagar, N.; Finet, J.-P.; Khamsi, J. *Tetrahedron Lett.* **1987**, *28*, 3111–3114.
75. Saito, S.; Kano, T.; Ohyabu, Y.; Yamamoto, H. *Synlett* **2000**, 1676–1678.
76. Naylor, A.; Evans, B. *PCT Int. Appl.* WO 9506645, 1995 (*Chem. Abstr.* **1995**, *123*, 339709).
77. Suh, D. H.; Choi, H. C.; Rhee, T. H. *Fr. Demande* FR 2769627, 1999 (*Chem. Abstr.* **1999**, *131*, 18927).

77a. Suh, D. H.; Choi, H. C.; Rhee, T. H. US Pat. US 5,962,658, 1999.

78. Corey, E. J.; Wollenberg, J. *J. Am. Chem. Soc.* **1974**, *96*, 5581–5583.

78a. Larock, R. C.; Oertle, K.; Beatty, K. M. *J. Am. Chem. Soc.* **1980**, *102*, 1966–1974.

78b. Shibasaki, M.; Torisawa, Y.; Ikegami, S. *Tetrahedron Lett.* **1982**, *23*, 4607–4610.

79. Moloney, M. G.; Pinhey, J. T.; Stoermer, M. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2645–2655.
80. Pinhey, J. T.; Stoermer, M. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2455–2460.
81. Parkinson, C. J.; Stoermer, M. J. *J. Organomet. Chem.* **1996**, *507*, 207–214.
82. Koen, M. J.; Morgan, J.; Pinhey, J. T.; Sherry, C. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 487–491.
83. Morgan, J.; Pinhey, J. T.; Sherry, C. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, 613–619.
84. Chen, C.; Layton, M. E.; Shair, M. D. *J. Am. Chem. Soc.* **1998**, *120*, 10784–10785.
85. Sheehan, S. M.; Lalic, G.; Chen, J. S.; Shair, M. D. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 2714–2715.
86. Hashimoto, S.; Shinoda, T.; Ikegami, S. *J. Chem. Soc., Chem. Commun.* **1988**, 1137–1139.
87. Tomyama, T.; Ikegami, S.; Hashimoto, S.; Imamaki, T. *Jpn. Kokai Tokkyo Koho* JP 07076550, 1995 (*Chem. Abstr.* **1995**, *123*, 111743).
88. Moloney, M. G.; Pinhey, J. T.; Roche, E. G. *Tetrahedron Lett.* **1986**, *27*, 5025–5027.

88a. Moloney, M. G.; Pinhey, J. T.; Roche, E. G. *J. Chem. Soc., Perkin Trans. 1* **1989**, 333–341.

89. Hashimoto, S.; Miyazaki, Y.; Shinoda, T.; Ikegami, S. *J. Chem. Soc., Chem. Commun.* **1990**, 1100–1103.
90. Parkinson, C. J.; Hambley, T. W.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1465–1468.
91. Hashimoto, S.; Miyazaki, Y.; Ikegami, S. *Synlett* **1996**, 324–326.
92. Hashimoto, S.; Miyazaki, Y.; Shinoda, T.; Ikegami, S. *Tetrahedron Lett.* **1989**, *30*, 7195–7198.
93. Hashimoto, S.; Miyazaki, Y.; Shiro, M.; Ikegami, S. *Chem. Lett.* **1995**, 1091–1092.
94. Hambley, T. W.; Holmes, R. J.; Parkinson, C. J.; Pinhey, J. T. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1917–1922.
95. Kang, S.-K.; Shivkumar, U.; Ahn, C.; Choi, S.-C.; Kim, J.-S. *Synth. Commun.* **1997**, *27*, 1893–1897.
96. Morel, S.; Chatel, F.; Boyer, G.; Galy, J.-P. *J. Chem. Res. (S)* **1998**, 4–5.

96a. Morel, S.; Chatel, F.; Boyer, G.; Galy, J.-P. *J. Chem. Res. (M)* **1998**, 0115–0125.

97. Chatel, F.; Boyer, G.; Galy, J.-P. *Synth. Commun.* **2002**, *32*, 2893–2901.
98. Chatel, F.; Morel, S.; Boyer, G.; Galy, J.-P. *Heterocycles* **2000**, *53*, 2535–2552.
99. Boyer, G.; Chatel, F.; Galy, J.-P. *Arkivoc* **2000**, *1*, 563–575.
100. Barton, D. H. R.; Donnelly, D. M. X.; Finet, J.-P.; Guiry, P. J. *Tetrahedron Lett.* **1989**, *30*, 1377–1380.
101. Barton, D. H. R.; Donnelly, D. M. X.; Finet, J.-P.; Guiry, P. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2095–2102.
102. Mainagashev, I. Ya.; Klimenko, L. S.; Gritsan, N. P. *Iz. Akad. Nauk, Ser. Khim.* **1998**, 2519–2522.

102a. Mainagashev, I. Ya.; Klimenko, L. S.; Gritsan, N. P. *Russ. Chem. Bull.* **1998**, *47*, 2437–2440.

103. Esteves, M. A.; Narender, N.; Marcelo-Curto, M. J.; Gigante, B. *J. Nat. Prod.* **2001**, *64*, 761–766.
104. Schneider, R.; Hosseini, M. W.; Planeix, J.-M. *Tetrahedron Lett.* **1996**, *37*, 4721–4724.
105. Bras, J.-P.; de Cointet, P.; Despeyroux, P.; Frehel, D.; Gully, D.; Maffrand, J.-P.; Bignon, E. *Eur. Pat. Appl.* EP 697403, 1996 (*Chem. Abstr.* **1996**, *124*, 343106);

105a. Bras, J.-P.; de Cointet, P.; Despeyroux, P.; Frehel, D.; Gully, D; Maffrand, J.-P.; Bignon, E. US Pat. US 5,731,340, 1998.

106. Boyer, G.; Galy, J.-P.; Barbe, J. *Heterocycles* **1995**, *41*, 487–496.

106a. Morel, S.; Boyer, G.; Coullet, F.; Galy, J.-P. *Synth. Commun.* **1996**, *26*, 2443–2447.

107. Boyer, G.; Giorgi, M.; Chatel, F.; Galy, J.-P. *J. Chem. Cryst.* **1998**, *28*, 735–739.
108. Boyer, G.; Galy, J.-P. *Molecules* **1998**, *3*, M89.
109. López-Alvarado, P.; Avendaño, C.; Menéndez, J. C. *Heterocycles* **1991**, *32*, 1003–1012.

109a. López-Alvarado, P.; Avendaño, C.; Menéndez, J. C. *Tetrahedron Lett.* **1992**, *33*, 659–662.

110. López-Alvarado, P.; Avendaño, C.; Menéndez, J. C. *J. Org. Chem.* **1995**, *60*, 5678–5682.
111. Elliott, G. I.; Konopelski, J. P. *Org. Lett.* **2000**, *2*, 3055–3057.
112. Cappuccio, J. A.; Ayala, I.; Elliot, G. I.; Szundi, I.; Lewis, J.; Konopelski, J. P.; Barry, B. A.; Einarsdottir, O. *J. Am. Chem. Soc.* **2002**, *124*, 1750–1760.
113. López-Alvarado, P.; Avendaño, C.; Menéndez, J. C. *Tetrahedron Lett.* **1992**, *33*, 6875–6878.
114. López-Alvarado, P.; Avendaño, C.; Menéndez, J. C. *J. Org. Chem.* **1996**, *61*, 5865–5870.
115. López-Alvarado, P.; Avendaño, C.; Menéndez, J. C. *J. Chem. Soc., Perkin Trans. 1* **1997**, 229–233.
116. Shimi, K.; Boyer, G.; Finet, J.-P.; Galy, J.-P. *Lett. Org. Chem.* **2004**, *1*, 34–36.

116a. Shimi, K.; Boyer, G.; Finet, J.-P.; Galy, J.-P. *Lett. Org. Chem.* **2005**, *2*, 407–409.

117. Dodonov, V. A.; Starostina, T. I.; Gushchin, A. V.; Egorova, T. A. *Metalloorg. Khim.* **1989**, *2*, 682–683.
118. Kang, S.-K.; Ryu, H.-C.; Choi, S.-C. *Synth. Commun.* **2001**, *31*, 1035–1039.
119. Kang, S.-K.; Ryu, H.-C.; Choi, S.-C. *Chem. Commun.* **1998**, 1317–1318.
120. Kang, S.-K.; Ryu, H.-C.; Son, H.-J. *Synlett* **1998**, 771–773.
121. Kang, S.-K.; Choi, S.-C.; Baik, T.-G. *Synth. Commun.* **1999**, *29*, 2493–2499.
122. Kang, S.-K.; Choi, S.-C.; Ryu, H.-C.; Yamaguchi, T. *J. Org. Chem.* **1998**, *63*, 5748–5749.

123. Kang, S.-K.; Ryu, H.-C.; Lee, S.-H. *Synth. Commun.* **2001**, *31*, 1059–1064.
124. Knight, D. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, pp 481–520.
125. Review: Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169–196.
126. Ding, R.; Chen, Y.-J.; Wang, D.; Li, C.-J. *Synlett* **2001**, 1470–1472.
127. Ding, R.; Ge, C.-S.; Chen, Y.-J.; Wang, D.; Li, C.-J. *Tetrahedron Lett.* **2002**, *43*, 7789–7791.
128. Ding, R.; Zhao, C. H.; Chen, Y. J.; Liu, L.; Wang, D.; Li, C. J. *Tetrahedron Lett.* **2004**, *45*, 2995–2998.
129. Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450.
129a. Fürstner, A. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3013–3043.
129b. Astruc, D. *New J. Chem.* **2005**, *29*, 42–56.
130. Mol, J. C. *J. Mol. Catal.* **1991**, *65*, 145–162.
130a. Mol, J. C. *Catal. Today* **1999**, *51*, 289–299.
131. Xu, X.; Imhoff, P.; van den Aardweg, G. C. N.; Mol, J. C. *J. Chem. Soc., Chem. Commun.* **1985**, 273–275.
131a. Xu, X.; Mol, J. C. *J. Chem. Soc., Chem. Commun.* **1985**, 631–633.
131b. Xu, X.; Benecke, J. I.; Boelhouwer, C.; Mol, J. C. *Appl. Catal.* **1986**, *28*, 271–283.
132. Finkel'shtein, E. Sh.; Portnykh, E. B.; Antipova, I. V.; Vdovin, V. M. *Izv. Akad. Nauk SSSR Ser. Khim.* **1989**, 1358–1361.
133. Makovetsky, K. L.; Finkel'shtein, E. Sh.; Ostrovskaya, I. Ya.; Portnykh, E. B.; Gorbacheva, L. I.; Golberg, A. I.; Ushakov, N. V.; Yampolsky, Y. *J. Mol. Catal.* **1992**, *76*, 107–121.
134. Zarzecki, S.; Zawadzki, J.; Skupinski, W. *React. Kinet. Catal. Lett.* **2001**, *72*, 29–33.
135. Zawadzki, J.; Skupinski, W. *React. Kinet. Catal. Lett.* **2001**, *74*, 51–56.
136. Maksimowski, P.; Skupinski, W. *J. Mol. Catal.* **1991**, *65*, 187–192.
137. Couturier, J.-L.; Paillet, C.; Leconte, M.; Basset, J.-M.; Weiss, K. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 628–631.
137a. Couturier, J.-L.; Tanaka, K.; Leconte, M.; Basset, J.-M.; Ollivier, J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 112–115.
138. Quignard, F.; Leconte, M.; Basset, J.-M. *J. Mol. Catal.* **1986**, *36*, 13–29.
139. Lefebvre, F.; Leconte, M.; Pagano, S.; Mutch, A.; Basset, J.-M. *Polyhedron* **1995**, *14*, 3209–3226.
140. Descotes, G.; Ramza, J.; Basset, J.-M.; Pagano, S. *Tetrahedron Lett.* **1994**, *35*, 7379–7382.
140a. Ramza, J.; Descotes, G.; Basset, J.-M.; Mutch, A. *J. Carbohyd. Chem.* **1996**, *15*, 125–136.
141. Descotes, G.; Ramza, J.; Basset, J.-M.; Pagano, S.; Gentil, E.; Banoub, J. *Tetrahedron* **1996**, *52*, 10903–10920.
142. Cho, I.; Jo, S.-Y. *Macromolecules* **1999**, *32*, 521–523.
143. Cho, I.; Moon, G. S. *J. Polym. Sci. A-Polym. Chem.* **1995**, *33*, 1823–1828.
144. Cho, I.; Jeong, S. W.; Hwang, K. M. *Korea Polym. J.* **1993**, *1*, 1–8 (*Chem. Abstr.* **1994**, *121*, 231540).
144a. Cho, I.; Hwang, K. M. *J. Polym. Sc., Part A: Polym. Chem.* **1993**, *31*, 1079–1081.
145. Cho, I.; Hwang, K. M. *Polym. J.* **1993**, *25*, 111–113.
146. Cho, I.; Bae, S. S. *Polym. J.* **1991**, *23*, 1283–1286.
147. Nugent, W. A.; Feldman, J.; Calabrese, J. C. *J. Am. Chem. Soc.* **1995**, *117*, 8992–8998.
148. Martinez, L. E.; Nugent, W. A.; Jacobsen, E. N. *J. Org. Chem.* **1996**, *61*, 7963–7966.
149. Chippindale, A. M.; Davies, S. G.; Iwamoto, K.; Parkin, R. M.; Smethurst, C. A. P.; Smith, A. D.; Rodriguez-Solla, H. *Tetrahedron* **2003**, *59*, 3253–3265.
150. Yamataka, H.; Nishikawa, K.; Takatsuka, T.; Hanafusa, T. *J. Phys. Org. Chem.* **1995**, *8*, 35–40.
151. Tanaka, H.; Yamashita, S.; Ikemoto, Y.; Torii, S. *Chem. Lett.* **1987**, 673–674.
151a. Tanaka, H.; Yamashita, S.; Hamatani, T.; Ikemoto, Y.; Torii, S. *Synth. Commun.* **1987**, *17*, 789–794.
151b. Zhou, J.-Y.; Jia, Y.; Sun, G.-F.; Wu, S.-H. *Synth. Commun.* **1997**, *27*, 1899–1906.
152. Yamataka, H.; Nishikawa, K.; Hanafusa, T. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2145–2150.
153. Davies, A. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1997–2010.
154. Cai, J.; Davies, A. G. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1743–1746.
155. Kinart, W. J.; Tylak, I.; Kinart, C. M. *J. Chem. Res., Synop.* **1999**, 46–47.
156. Villazana, R. S.; Sharma, H.; Cervantes-Lee, F.; Pannell, K. H. *Organometallics* **1993**, *12*, 4278–4279.
157. Willemsens, L. C. *J. Organomet. Chem.* **1971**, *27*, 45–51.
158. Masson, J.-C.; Le Quan, M.; Cadiot, P. *Bull. Soc. Chim. Fr.* **1967**, 777–780.
159. Seyferth, D.; Son, D. Y.; Shah, S. *Organometallics* **1994**, *13*, 2105–2108.
160. Galiotos, J. K.; Morrison, J. A. *Organometallics* **2000**, *19*, 2603–2607.
161. Burton, D. J.; Yang, Z.-Y. *Tetrahedron* **1992**, *48*, 189–275.
161a. Adams, D. J.; Clark, J. H.; Hansen, L. B.; Sanders, V. C.; Tavener, S. J. *J. Fluorine Chem.* **1998**, *92*, 123–125.
161b. McClinton, M. A.; McClinton, D. A. *Tetrahedron* **1992**, *48*, 6555–6566.
162. Bell, H. C.; Kalman, J. R.; May, G. L.; Pinhey, J. T.; Sternhell, S. *Aust. J. Chem.* **1979**, *32*, 1531–1550.
163. Briquet, A. A. S.; Hansen, H.-J. *Helv. Chim. Acta* **1994**, *77*, 1577–1584.
164. Kalman, J. R.; Morgan, J.; Pinhey, J. T.; Sternhell, S. *Tetrahedron* **1999**, *55*, 3615–3624.

9.10 Antimony and Bismuth

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9.10.1 Introduction

Antimony and bismuth lie at the fifth and sixth rows of the 15th group in the periodic table, and a variety of trivalent and pentavalent organic compounds derived from these elements have been reported. As shown in Table 1, antimony and bismuth have relatively small ionization potentials and electronegativities as well as large orbital radii. Due to these properties, elemental antimony and bismuth behave as metals, and the respective organic compounds possess relatively weak and polarized element–carbon bonds. These characteristics of antimony and bismuth have been

Table 1 Selected physical properties of antimony and bismuth

	Sb	*Bi*
Atom number	51	83
Atomic weight	121.757	208.980
Melting point (°C)	630.7	271.4
First ionization potential (eV)	8.64	7.287
Electronegativity (Allred–Rochow)	1.82	1.67
Ionic radius (Å)	0.90 (3+)	1.17 (3+)
	0.74 (5+)	0.90 (5+)
Covalent radius (Å)	1.41 (3+)	1.52 (3+)
Bond dissociation energy (kJ mol^{-1})	268 (Sb–C)	194 (Bi–C)

Data from Emsley, J. *The Elements*, 3rd ed.; Oxford University Press: Oxford, 1998.

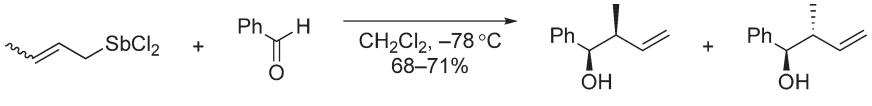
utilized in carbon–carbon bond-forming reactions, carbon–heteroatom bond-forming reactions, oxidations, reductions, and others. In this chapter, recent advances of organoantimony and organobismuth compounds in organic synthesis are overviewed with selected examples. The literatures cited here are those published from 1993 to 2004, including not only organic compounds bearing the Sb–C or Bi–C bonds but also some inorganic compounds of the types MX_n (M = Sb, Bi; X denotes an anionic ligand; $n = 3, 5$) because these salts have been widely used as Lewis acid catalysts. The following two sections are divided into two main parts, trivalent compounds and pentavalent compounds, and each part is subdivided based on reaction types. Due to space limitations, whole results on the reactivity, selectivity, and mechanism are not provided. Therefore, it is recommended that readers refer to the original references when the reactions described here need to be examined or studied in detail. Previous works published before 1993 are summarized in COMC(1982)[1] by Wardell and COMC(1995)[2] by Huang and Zhou, respectively. Additional information is also available in some recent reviews and monographs that deal with the summary of antimony and bismuth in organic synthesis,[3–5] the special topics of antimony[6] and bismuth[7–17] in organic synthesis, and the general aspects of organoantimony[18–22] and organobismuth[23–29] chemistry. Wardell and Jones also reported on an annual survey in the *Organometallic Chemistry*.[30–34]

9.10.2 Antimony in Organic Synthesis

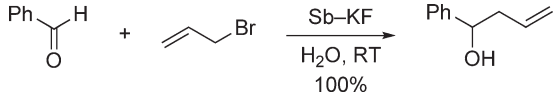
9.10.2.1 Organoantimony(III) Compounds

9.10.2.1.1 Barbier-type reactions

Elemental antimony is known to mediate the Barbier-type allylation of aldehydes by allylic halides.[35] The active intermediates are believed to be allylic antimony(III) species, which are generated from the antimony(0) and the halides. In fact, allylic dichlorostibanes, produced by metathesis of $SbCl_3$ with the corresponding allylic stannanes, react with benzaldehyde to give homoallyl alcohols, where the C–C bond is constructed with *syn*-selectivity (Equation (1)).[36] Fluoride salts such as KF, NaF, RbF, and CsF accelerate the Sb-mediated Barbier-type allylation with allyl bromide in aqueous media (Equation (2)).[37] In the absence of the fluoride ion, no allylation occurs. Although aromatic and aliphatic aldehydes are allylated in good yields by a combined use of Sb–KF, acetophenone, cyclohexanone, and methyl pyruvate remain untouched.



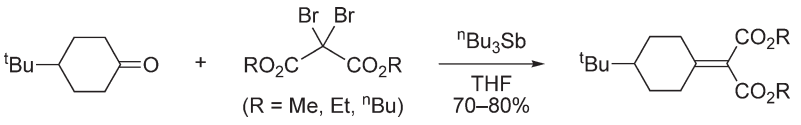
syn : *anti* = 80 : 20 (1)



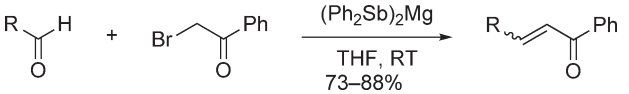
(2)

9.10.2.1.2 Organoantimony(III)-mediated carbon–carbon bond forming reactions

In the presence of 2–3 equiv. of tri-*n*-butylstibane, the Knoevenagel condensation between ketones and α,α-dibromomalonic esters provides the corresponding alkylidenemalonic esters (Equation (3)).[38] Probably, the initially formed stibonium halides recombine to generate zwitterionic species, which undergo nucleophilic addition on the carbonyl carbon. The olefination between α-bromoacetophenone and aldehydes is also promoted by $(Ph_2Sb)_2Mg$, where diphenylantimony(III) enolates are generated as active nucleophiles (Equation (4)).[39]

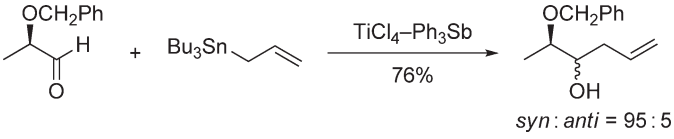


(3)

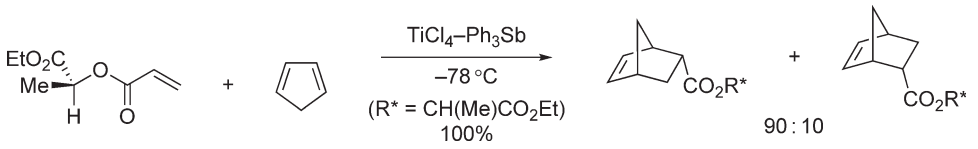


(4)

A Lewis acid–base complex, $TiCl_4$–$SbPh_3$, mediates the allylation of 2-(benzyloxy)propanal with allyltributylstannane, where a homoallyl alcohol is obtained with a high *syn*-selectivity (Equation (5)).[40] The same complex is also effective for Diels–Alder reaction of an acrylate of (*S*)-ethyl lactate with cyclopentadiene, where an *endo*-adduct is formed predominantly with high diastereoselectivity and without polymerization of cyclopentadiene (Equation (6)).



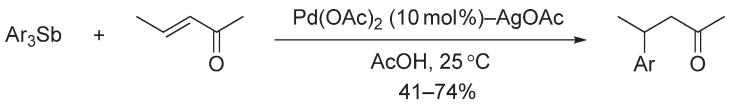
(5)



(6)

9.10.2.1.3 Pd-catalyzed carbon–carbon bond-forming reactions

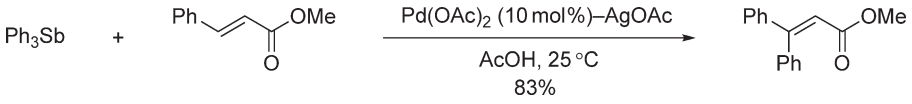
In the presence of AgOAc and a catalytic amount of $Pd(OAc)_2$, α,β-unsaturated ketones and aldehydes react with triarylstibanes (Ar_3Sb) in acetic acid to afford the corresponding conjugate addition products in moderate to good yields (Equation (7)).[41] The similar hydroarylation proceeds more efficiently with Ar_2SbCl, $ArSbCl_2$, and Ph_2SbOAc in the absence of AgOAc. A palladium or antimony enolate has been proposed as an intermediate, which would be produced via metathesis between PdX_2 (X = OAc, Cl) and arylantimony(III) species.



(7)

On the other hand, under the same conditions, styrene, acrylonitrile, and α,β-unsaturated esters undergo the Heck-type reaction with Ph_3Sb to give stilbene, β-phenylacrylonitrile, and β-phenyl-α,β-unsaturated esters, respectively (Equation (8)). Ph_2SbCl and $PhSbCl_2$ also react with a variety of olefins such as allylic alcohols, allylic acetates, and styrenes in the presence of a catalytic amount of $Pd(OAc)_2$ under air to give the corresponding phenylated alkenes (Heck-type products) (Equation (9)).[42] It has been suggested that oxygen mediates the regeneration of PhPdOAc species from Ph_2SbCl and HPd(OAc) in the catalytic cycle. A combination of Ar_3Sb, an equimolar amount of *t*-BuOOH, and a catalytic amount of Li_2PdCl_4 or $PdCl_2$ is also effective for the Heck-type arylation of methyl

acrylate in acetic acid (Equation (10)).[43,43a] The principal role of the peroxide in this reaction is believed to oxidize Ar_3Sb to $Ar_3Sb(OAc)_2$.



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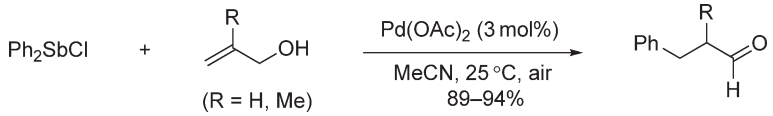
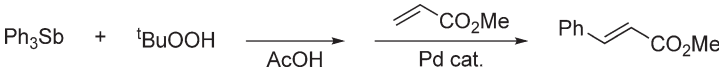
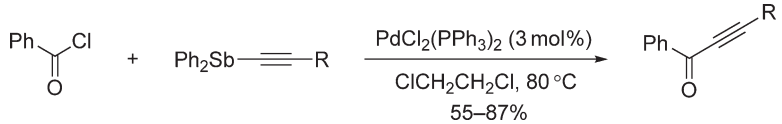


(9)

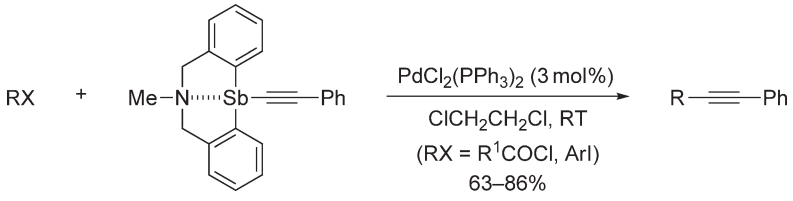


(10)

Alkynyldiphenylstibanes react with acyl chlorides under Pd catalysis at 80 °C to afford the corresponding alkynyl ketones, in which the phenyl transfer from the antimony species does not take place even in the presence of a large excess of acyl chlorides (Equation (11)).[44] Alkynyl-1,5-azastibocines also transfer the alkynyl moiety to acid chlorides in the presence of 3 mol% of $PdCl_2(PPh_3)_2$ at room temperature (Equation (12)).[45] Similarly, the cross-coupling reaction between the phenylethynyl-1,5-azastibocine and aryl iodides occurs at room temperature within 5–20 min to yield diarylacetylenes as the major products. The alkynyl transfer from the alkynyl-1,5-azastibocines takes place more efficiently than that from alkynyldiphenylstibanes, and the higher reactivity of the former Sb(III) reagents is ascribed to the hypervalent coordination between Sb and N atoms.



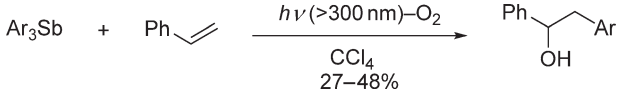
(11)



(12)

9.10.2.1.4 Carbon–heteroatom bond-forming reactions

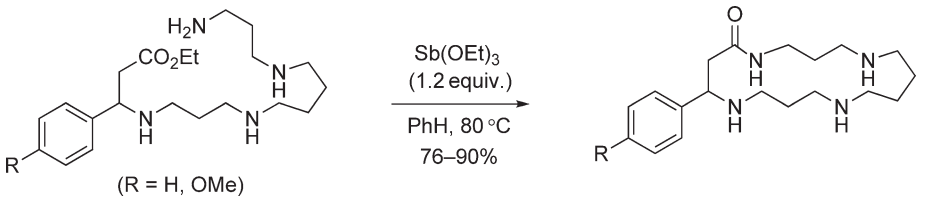
The photochemical reaction of triarylstibanes with styrene in the presence of O_2 results in the formation of 1-phenyl-2-arylethanols in moderate yields (Equation (13)).[46] A key intermediate is considered to be $Ar_3Sb{\cdot}O_2$ complex, which would be formed from photoexcited triarylstibane and oxygen. Then, the complex undergoes oxidative 1,2-addition to the carbon–carbon double bond of styrene via peroxyantiomny(V) intermediate.



(13)

Antimony(III) ethoxide ($Sb(OEt)_3$) promotes the intermolecular amidation of esters and carboxylic acids with amines under azeotropic conditions.[47,48] When tetramino esters are used, the antimony(III)-templated intramolecular macrolactamization provides macrocyclic spermine alkaloids in good yields (Equation (14)). Under the same

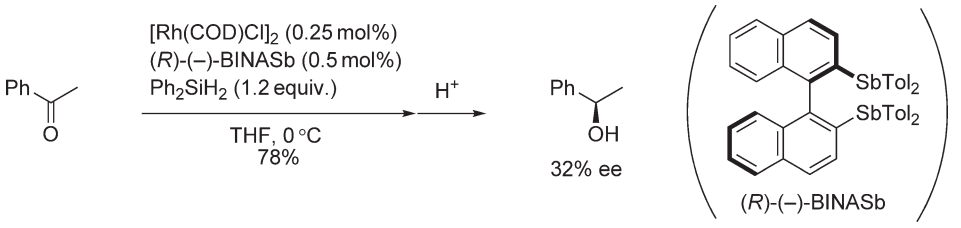
conditions, $Sb(OEt)_3$ does not provide satisfactory results in the cyclization of a triamino ester, indicating that the Sb(III)-templated cyclization is size selective.



(14)

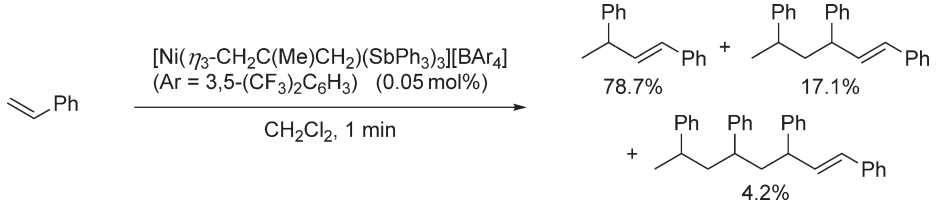
9.10.2.1.5 Miscellaneous reactions

The optically active (*S*)-(+)- and (*R*)-(−)-2,2′-bis[diarylstibano]-1,1′-binaphthyls (BINASb) have been prepared and used as chiral auxiliaries in the Rh-catalyzed asymmetric hydrosilylation of ketones with diphenylsilane.[49,49a] When acetophenone is reduced using 0.25 mol% of $[Rh(COD)Cl]_2$ as the catalyst and 0.5 mol% of (*R*)-BINASb (aryl = *p*-tolyl) as the ligand, (*R*)-1-phenylethanol is formed in 78% yield and in 32% ee (Equation (15)). When (*R*)-BINAP is used as the chiral ligand instead of (*R*)-BINASb, the yield and enantiomeric excess of (*R*)-1-phenylethanol are 42% and 0.6%, respectively.



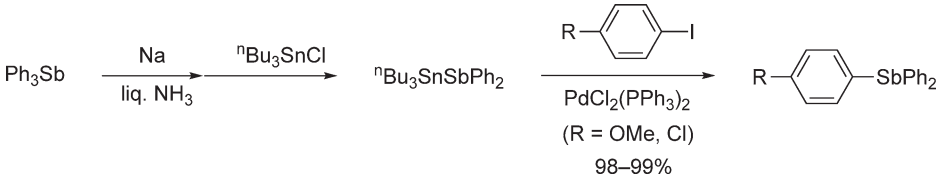
(15)

The five-coordinate cationic nickel(II) complex having the triphenylstibane ligand, $[Ni(\eta_3\text{-}CH_2\text{-}C(Me)CH_2)(SbPh_3)_3][BAr_4]$ (Ar = 3,5-$(CF_3)_2C_6H_3$), catalyzes oligomerization of styrene to the dimer, trimer, and tetramer.[50] The oligomerization is complete within 1 min in CH_2Cl_2 at room temperature, reaching a turnover frequency of 1965 min^{-1} (Equation (16)).



(16)

Treatment of Ph_3Sb with sodium metal in liquid ammonia produces a Ph_2Sb^- ion, which readily reacts with *n*-Bu_3SnCl to give *n*-$Bu_3SnSbPh_2$.[51] The stannylantimony(III) species further undergo the Sb–C coupling reaction with aryl iodides in the presence of a catalytic amount of $PdCl_2(PPh_3)_2$ in toluene at 80 °C to afford the corresponding aryldiphenylstibanes (Equation (17)).



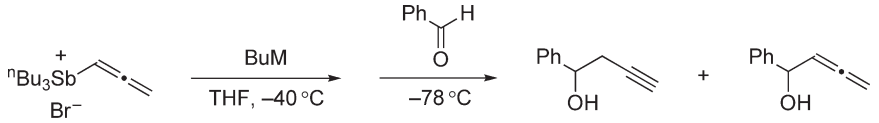
(17)

9.10.2.2 Organoantimony(V) Compounds

9.10.2.2.1 Carbon–carbon bond-forming reactions using tetraorganylantimony(V) compounds

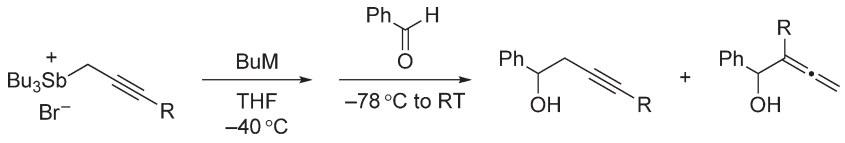
Subsequent treatment of allenyltributylstibonium bromide with BuMgBr and benzaldehyde at low temperatures yields a homopropargyl alcohol exclusively (Equation (18)).[52,52a] The active nucleophile is considered to be a

pentaorganylantimony (Bu_3SbRR'), which is generated from the stibonium salt and the Grignard reagent.[53] When BuLi is used instead of BuMgBr, however, both homopropargyl and homoallenyl alcohols are produced in a 1 : 1 ratio. Similar treatment of γ-substituted propargyltributylstibonium bromides affords a mixture of homopropargyl and homoallenyl alcohols, the regioselectivity being dependent on the γ-substituents and the cations (Equation (19)).



(18)

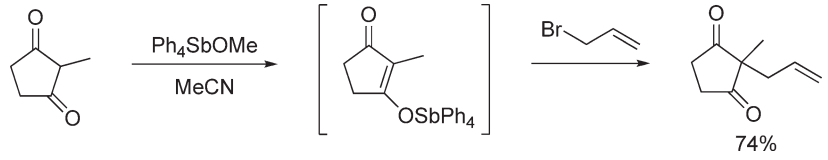
M = MgBr; 92% (100 : 0)
M = Li; 50% (50 : 50)



(19)

R = $SiMe_3$ (M = Li) 80% (94 : 6)
R = Me (M = MgBr) 89% (3 : 97)

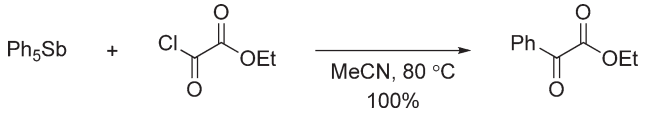
Tetraphenylantimony methoxide (Ph_4SbOMe) reacts with 1,3-dicarbonyl compounds to generate tetraphenylantimony(V) enolates, which are readily alkylated by allyl, propargyl, and benzyl bromides as well as by ethyl bromoacetate (Equation (20)).[54]



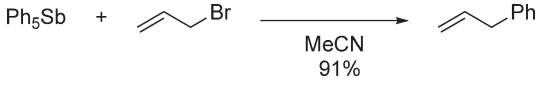
(20)

9.10.2.2.2 Carbon–carbon bond-forming reactions using pentaarylantimonys

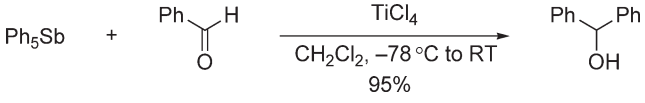
Without any additives, pentaarylantimonys (Ar_5Sb) react with aroyl chlorides, cinnamyl chloride, and ethyl oxalyl chloride in refluxing acetonitrile to give the corresponding aromatic ketones (Equation (21)).[55] Under the same conditions, triphenylstibane and tetraphenylstibonium bromide do not transfer the phenyl group. Pentaphenylantimony also reacts with allyl halides in acetonitrile to give allylbenzene as the major product (Equation (22)).[56] 1-Bromopentane, benzyl bromide, and ethyl bromoacetate do not give any coupling products under the same conditions. It has been suggested that the reaction involves nucleophilic attack of the polarized Sb–C bond to the allylic carbon. When the reaction is carried out in benzene or THF, only a trace amount of the cross-coupling product is formed. Although no direct addition of Ar_5Sb to aldehyde and ketone occurs, the nucleophilic phenylation of benzaldehyde, 1-hexanal, and cyclohexanone with Ph_5Sb can be achieved by adding a stoichiometric amount of $TiCl_4$ (Equation (23)).



(21)



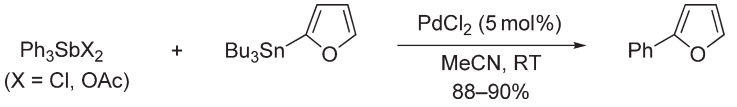
(22)



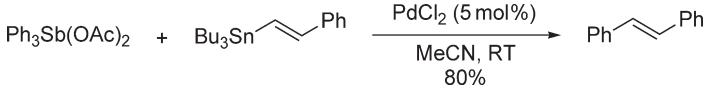
(23)

9.10.2.2.3 Pd-catalyzed carbon–carbon bond-forming reactions

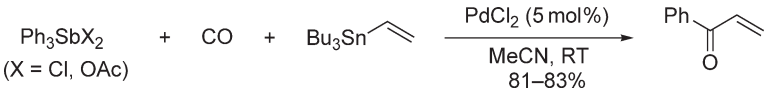
Triarylantimony dichlorides and diacetates (Ar_3SbX_2; X = Cl, OAc) undergo cross-coupling reactions with aryl- and styrylstannanes in the presence of 5 mol% of $PdCl_2$ in acetonitrile at room temperature to give biaryls and stilbenes, respectively (Equations (24) and (25)).[57] When the reactions are carried out under an atmospheric pressure of CO, the corresponding aromatic ketones are obtained (Equation (26)). The diacetates also undergo the Pd(0)–Cu(I)-catalyzed cross-coupling and carbonylative cross-coupling reactions with alkynyltrimethylsilanes (Equation (27)).[58] Of the catalysts tested, $Pd_2(dba)_3{\cdot}CHCl_3$ has been found to be the most efficient.



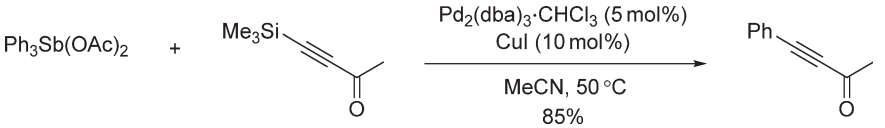
(24)



(25)



(26)

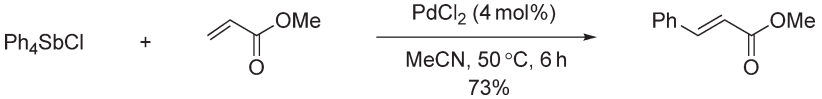


(27)

Triphenylantimony(V) dicarboxylates are used for the Heck-type phenylation of various olefins under palladium catalysis, with $PdCl_2$, $LiPdCl_4$, $Pd(OAc)_2$, $Pd_2(dba)_3{\cdot}CHCl_3$ being effective (Equation (28)).[59,59a] The efficiency of the phenylation slightly increases in air or under an O_2 atmosphere, whereas copper(II) salts do not increase the yield. In this system, Sb(V) species act not only as the donor of phenyl groups but also as the reoxidant for Pd(0) to Pd(II). When $Pd(OAc)_2$ and acetonitrile are used as the catalyst and solvent, respectively, the Heck-type arylation of methyl acrylate with $Ph_3Sb(OAc)_2$ proceeds much more efficiently than those with Ph_3SbCl_2 and $Ph_3Bi(OAc)_2$.[60] Tetraphenylantimony(V) halides and carboxylates have also been examined as phenyl sources, and a combination of Ph_4SbCl–$PdCl_2$ (1 : 0.04) has been found to be most effective in the Heck-type reaction with methyl acrylate (Equation (29)).[61] In the presence of *t*-BuOOH or $(PhCO_2)_2$, the Pd-catalyzed *C*-phenylation with Ph_4SbOH in acetic acid proceeds under mild conditions, in which the peroxides promote a cascade participation of the organoantimony species.[62]

	Yield (%)
	92
In air	135
In O_2	153

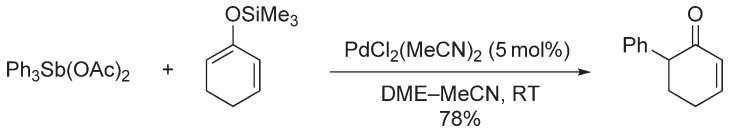
(28)



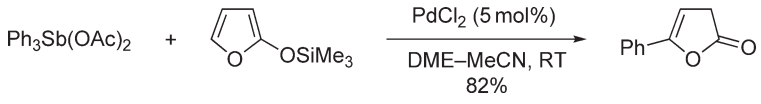
(29)

In the presence of a palladium catalyst, Ar_3SbX_2 (X = OAc, Cl) react with silyl enol ethers in DME–MeCN at room temperature to give the corresponding α-arylketones (Equation (30)).[63] When 2-furyloxytrimethylsilane is used as

substrate, 5-arylfuran-2(3H)-one is formed as the final product (Equation (31)). In the Pd-catalyzed reaction of Ar_5Sb with allyl acetate in acetonitrile, a significant amount of biaryl (homo-coupling product) is formed predominantly with a small amount of allylbenzene (cross-coupling product).



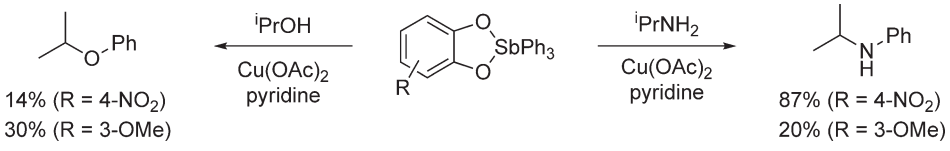
(30)



(31)

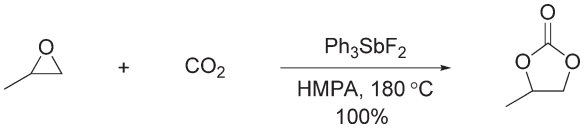
9.10.2.2.4 Carbon–heteroatom bond-forming reactions

Triphenylantimony(v) *ortho*-phenylenedioxides react with amines, alcohols, and phenols in the presence of $Cu(OAc)_2$ and pyridine to afford the corresponding *N*-phenylamines and *O*-phenyl ethers (Equation (32)).[64] The yield of the phenylated products strongly depends on the substituents of the dioxastibolane moiety: the Sb(v) dioxide bearing an electron-withdrawing group is more effective for the *N*-phenylation, whereas that bearing an electron-donating group is more effective for the *O*-phenylation.



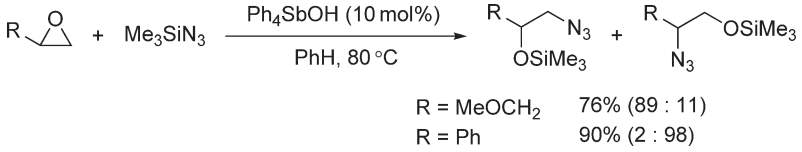
(32)

Triphenylantimony difluoride (Ph_3SbF_2) catalyzes the formation of cyclic carbonates from oxiranes and CO_2 (Equation (33)).[65] The best result is obtained when the reaction is conducted using a high pressure of CO_2 at 180 °C in HMPA. Under similar reaction conditions, Ph_3BiF_2 shows only a low catalytic activity.



(33)

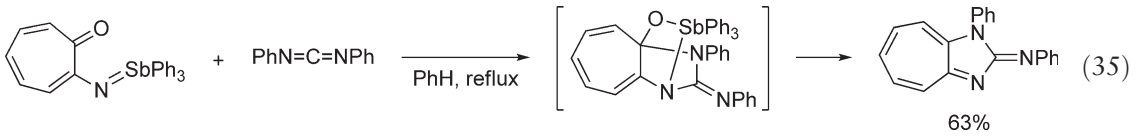
Tetraphenylantimony hydroxide (Ph_4SbOH) catalyzes the C–N bond-forming reaction between oxiranes and trimethylsilyl azide (Equation (34)).[66] The real species of this ring-cleavage azidation is Ph_4SbN_3, and the regioselectivity is dependent on the substituents of oxiranes employed. Ph_4SbOH also mediates the β-lactam synthesis from β-halo amides.[67]



(34)

(Tropon-2-ylimino)triphenylstibane, prepared by the Kirsanov reaction between Ph_3SbCl_2 and 2-aminotropone, undergoes a formal [8 + 2]-type electrocyclization with carbon disulfide, phenyl isocyanate, phenyl isothiocyanate, and diphenylcarbodiimide to give the corresponding cyclized products in moderate yields (Equation (35)).[68]

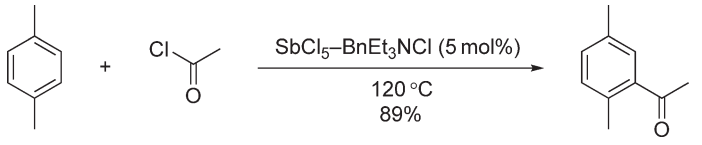
(Tropon-2-ylimino)triphenylbismuthane reacts with these heterocumulenes more rapidly than the antimony counterparts, but the yields of products are lower.



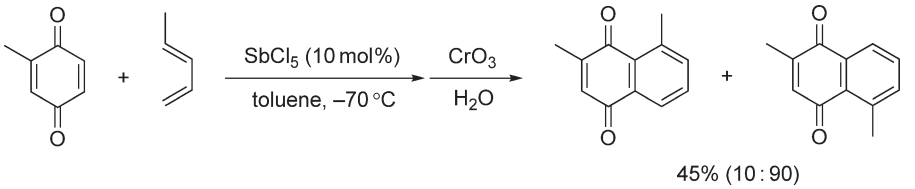
(35)

9.10.2.2.5 Miscellaneous reactions

A complex of $SbCl_5$ and benzyltriethylammonium chloride, which is insensitive to air and moisture, catalyzes the Friedel–Crafts acylation of arenes with acyl chlorides and sulfonyl chlorides (Equation (36)).[69] The Diels–Alder reaction of toluquinone with 1,3-dienes is catalyzed by $SbCl_5$ with high regioselectivity (Equation (37)).[70]



(36)



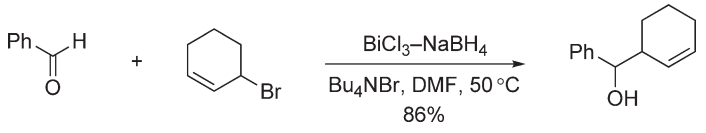
(37)

9.10.3 Bismuth in Organic Synthesis

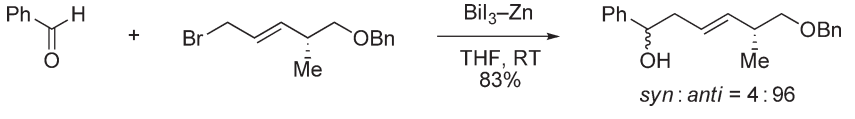
9.10.3.1 Organobismuth(III) Compounds

9.10.3.1.1 Barbier-type and related reactions

Metallic bismuth promotes the Barbier-type allylation of aromatic and aliphatic aldehydes to give homoallylic alcohols in good yields.[71,71a] It has been suggested that the elemental bismuth inserts into the carbon–halogen bond of the allylic halides to generate intermediary allylic bismuth(III) species. A combination of $BiCl_3$ or BiI_3 with a suitable reducing agent such as Zn, Fe, Al, Mg, and $NaBH_4$ has also been used for generating activated bismuth metal (Equation (38)).[72,72a] Based on the stereochemical outcome (*syn*-selectivity) observed in the reaction with crotyl bromide, an acyclic transition state has been proposed for the carbon–carbon bond-forming step. When an allylic bromide bearing a benzyloxy group at the ε-position is used, the 1,5-remote stereocontrol can be achieved (Equation (39)).[73]



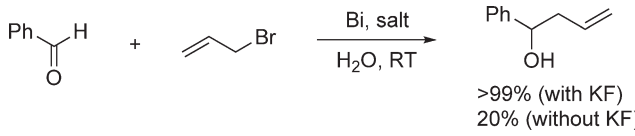
(38)



(39)

An interesting aspect of the Bi-mediated Barbier-type allylation is that the reaction can be conducted in aqueous media. When the reaction is carried out using metallic bismuth powder in water, addition of an equimolar amount of potassium fluoride improves the yield of homoallyl alcohol (Equation (40)).[74] The reaction is also compatible with hydroxyl and carboxyl groups of the carbonyl substrates. When succinaldehydic acid, 4-oxopentanoic acid,

5-oxohexanoic acid, 3-benzoylpropionic acid, and phthalaldehydic acid are used as substrates, the corresponding lactones formed via intramolecular dehydration of the homoallylic alcohols are obtained (Equation (41)).[75,76]



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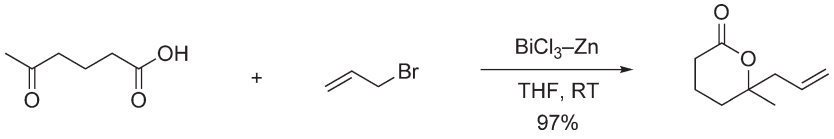
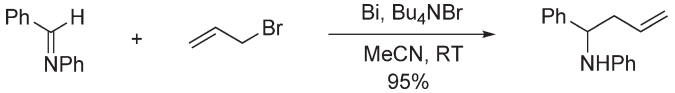
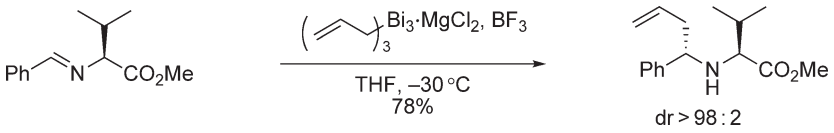


(41)

Aldimines react with allyl bromide in the presence of metallic bismuth and tetrabutylammonium bromide in acetonitrile to give homoallyl amines (Equation (42)).[77] When a chiral imine derived from benzaldehyde and (*S*)-valine methyl ester is used as the substrate, the allylation with allylic bismuth(III) species takes place smoothly by the assistance of a Lewis acid such as $BF_3{\cdot}OEt_2$ and $AlCl_3$ to afford a chiral homoallylic amine with high diastereoselectivity (Equation (43)).[78]

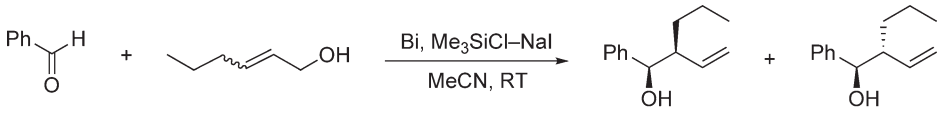


(42)



(43)

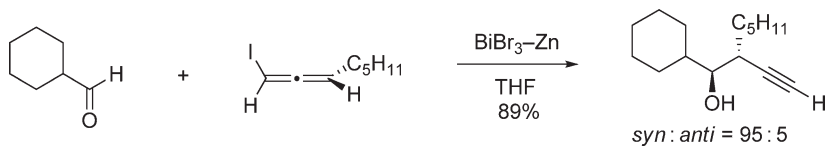
The Bi-mediated allylation also proceeds with allylic alcohols in the presence of Me_3SiCl–NaI in acetonitrile, where the alcohols are initially converted to the corresponding iodides by metathesis with Me_3SiI generated *in situ*.[79] When α- or γ-substituted allylic alcohols are used, the *syn*-adducts are formed preferentially, regardless of the stereochemistry of the substrates (Equation (44)).



	Yield (%)	*syn* : *anti*
From (*E*)	87	75 : 25
From (*Z*)	90	75 : 25

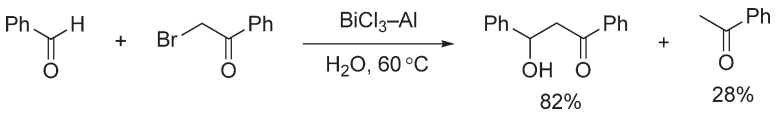
(44)

The $BiBr_3$–Zn couple mediates the diastereoselective propargylation of cyclohexanecarboaldehyde with an allenyl iodide (Equation (45)).[80] The $BiCl_3$–Al binary system is applicable to the Reformatsky-type reaction of α-bromoketones with aldehydes in water, though significant amounts of dehalogenated byproducts are formed simultaneously (Equation (46)).[81] The $BiCl_3$–Al system also promotes the alkylation of *L*-proline and pipecolinic esters using benzotriazole as a synthetic auxiliary in aqueous THF (Equation (47)).[82]

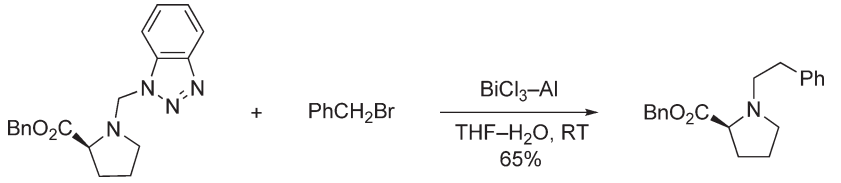


syn : *anti* = 95 : 5

(45)

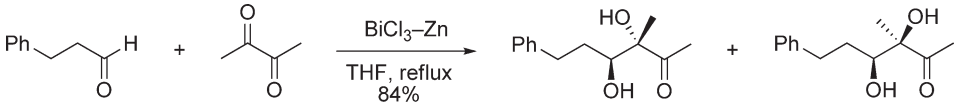


(46)



(47)

In the presence of metallic zinc and a catalytic amount of $BiCl_3$, the reductive coupling between α-diketones and aldehydes takes place to yield α,β-dihydroxyketones with moderate *anti*-selectivity (Equation (48)).[83] The reaction proceeds even in aqueous media. Phenylglyoxal and methylglyoxal can be converted to the corresponding coupling products. The reductive coupling of aldimines to vicinal diamines can also be accomplished by the action of Bi–KOH in methanol at room temperature.[84]



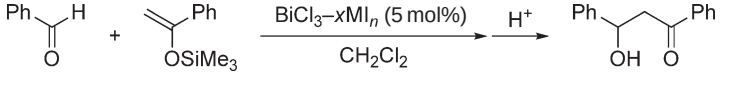
(48)

anti : *syn* = 74 : 26

9.10.3.1.2 BiX_3-catalyzed carbon–carbon bond-forming reactions

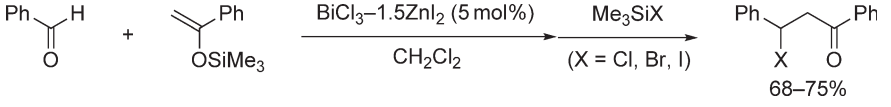
Bismuth(III) salts, such as $BiCl_3$, $BiBr_3$, $Bi(OCOR)_3$, $Bi(NO_3)_3$, $Bi(OTf)_3$, and $Bi(NTf_2)_3$, have been used as Lewis acid catalysts to mediate a variety of carbon–carbon bond-forming reactions.[85] In some cases, true catalysts differ from the bismuth salts initially added. The most effective and frequently used catalyst is $Bi(OTf)_3$, which is obtained as a hydrated or dehydrated form depending on the preparation methods.[86,86a,86b] Like lanthanide triflates, $Bi(OTf)_3$ is water stable and reusable.

The catalytic Mukaiyama-aldol reactions of aldehydes and ketones with silyl enolates proceed efficiently by assist of $BiCl_3$ or by a combined use of $BiCl_3$ and metal iodides (MI_n = NaI, ZnI_2, SnI_2) (Equation (49)).[87,87a,87b] The latter binary system is more efficient than $BiCl_3$ alone, and the catalytic power is activated significantly by ultrasound. When the reaction mixture is treated with a trimethylsilyl halide before aqueous workup, the corresponding β-halo carbonyl compounds are formed (Equation (50)).[88] This result shows that the C–O bond in the alkoxysilane can be cleaved by the silyl halide in the presence of BiX_3. The Mukaiyama-aldol reaction is also catalyzed by $Bi(OTf)_3$ with higher catalytic activity compared to $BiCl_3$, $Sc(OTf)_3$, and $Ln(OTf)_3$.[89] However, the true catalyst in this system is believed to be trimethylsilyl triflate that is generated from $Bi(OTf)_3$ and silyl enolates at the initial stage. The Mannich-type reaction of aldimines with silyl enolates in a three-component process takes place rapidly in the presence of $Bi(OTf)_3$ (Equation (51)).[90]

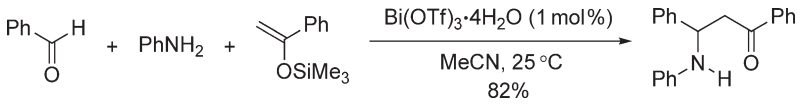


xMI_n	*Reation time*	*Yield* (%)
None	25 min at RT	94
3NaI	5 min at RT	97
$1.5ZnI_2$	10 min at –30 °C	98

(49)

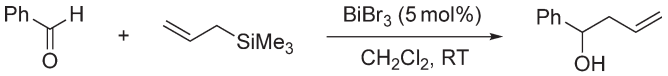


(50)

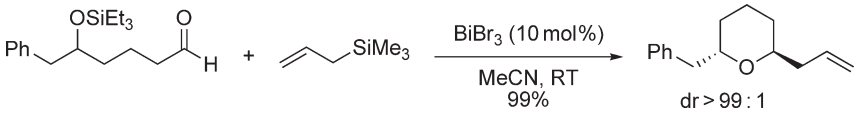


(51)

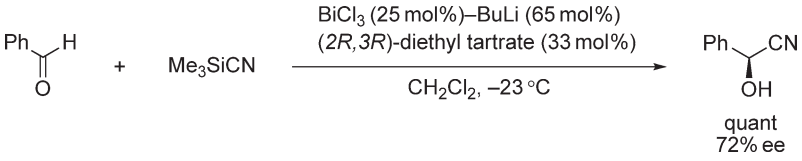
Aldehydes, ketones, and acetals react with allyltrimethylsilane in the presence of a catalytic amount of BiX_3 (X = Cl, Br, OTf) to give homoallyl alcohols or homoallyl alkyl ethers (Equation (52)).[91–93] The BiX_3-catalyzed allylation of aldehydes and sequential intramolecular etherification of the resulting homoallylic silyl ethers are involved in the stereoselective synthesis of polysubstituted tetrahydropyrans (Equation (53)).[94,95] Similarly, these Lewis acids catalyze the cyanation of aldehydes and ketones with cyanotrimethylsilane. When a chiral bismuth(III) catalyst is used in the cyanation, cyanohydrines are obtained in up to 72% ee (Equation (54)). α-Aminonitriles are prepared directly from aldehydes, amines, and cyanotrimethysilane by the $BiCl_3$-catalyzed Strecker-type reaction.[96]



(52)

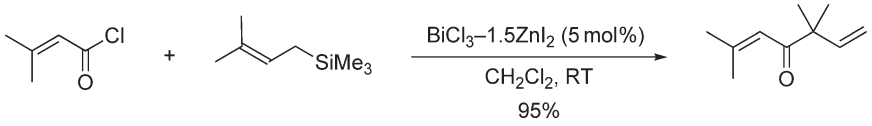


(53)

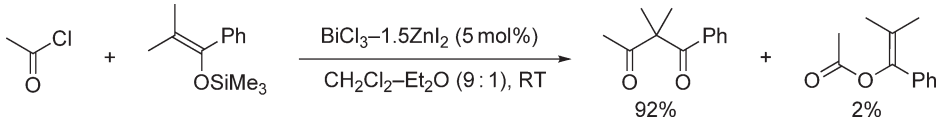


(54)

In the presence of the $BiCl_3$–xMI_n binary catalyst, allylic trimethylsilanes are acylated by acyl chlorides to give allylic ketones with little or no isomerization of the carbon–carbon double bond (Equation (55)).[97] When silyl enolates are reacted with acyl chlorides, *C*-acylation is preferred to *O*-acylation under $BiCl_3$ catalysis to give β-diketones as the sole or major products (Equation (56)).[98] The $BiCl_3$-catalyzed Michael addition of 1,3-dicarbonyl compounds toward methyl vinyl ketone and benzal acetophenone occurs efficiently under microwave irradiation (Equation (57)).[99] Indoles are also used as the nucleophile under the catalysis of $Bi(NO_3)_3$.[100] $BiCl_3$ and $Bi(OTf)_3$ are excellent catalysts for Diels–Alder reaction (Equation (58))[101,101a] and the carbonyl Diels–Alder or ene reaction (Equation (59))[102,102a] without diene polymerization.



(55)



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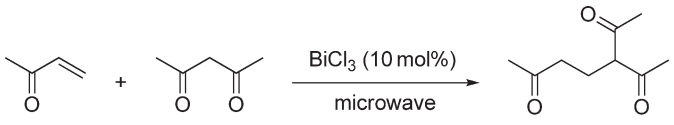

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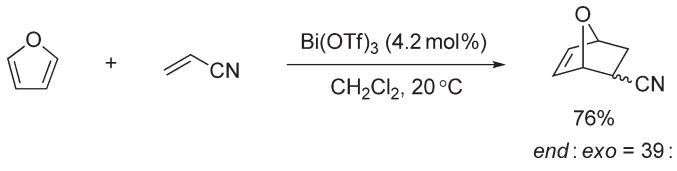
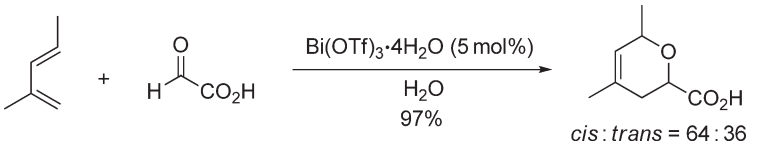
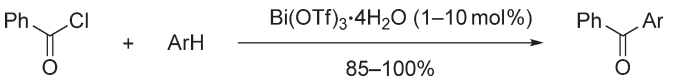


(58)

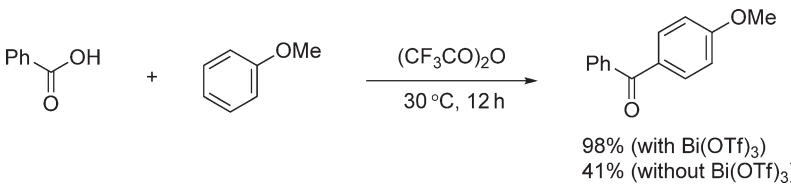


(59)

Bismuth salts such as $BiCl_3$, Bi_2O_3, $Bi(OTf)_3$, and $Bi(NTf_2)_3$ have proved to be efficient catalysts for the Friedel–Crafts acylation by acyl chlorides and acid anhydrides.[103–105] Even deactivated benzenes such as chlorobenzene and fluorobenzene are acylated in high yields by using acyl chlorides and a catalytic amount of $Bi(OTf)_3$ (Equation (60)). Carboxylic acids can also be used as acyl cation equivalents by the combined use of perfluoroalkanoic anhydride and $Bi(OTf)_3$ under solventless conditions (Equation (61)).[106] The rate of acylation is accelerated in the presence of $Bi(OTf)_3$. Dubac and co-workers have investigated the mechanism of the BiX_3-catalyzed Friedel–Crafts acylation and characterized some key intermediates.[107,107a] With benzoyl anhydride as an acylating reagent, $Bi(OTf)_3$ acts as the Lewis acid and is almost completely recovered. On the other hand, with benzoyl chloride, $Bi(OTf)_3$ promotes an exchange reaction to generate benzoyl triflate, which is the active species for benzoylation. Under microwave irradiation, the catalytic activity of BiX_3 (X = Cl, OTf) for the acylation of aromatic compounds is enhanced.[108,108a] The catalytic system becomes recyclable when ionic liquids are used as the reaction media.[109]

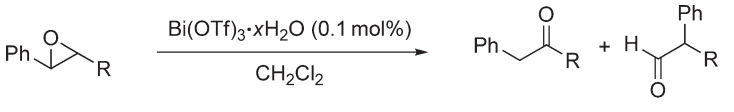


(60)



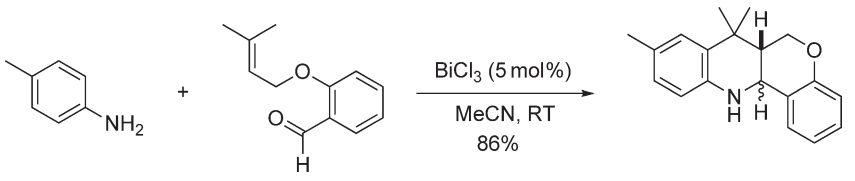
(61)

In the presence of 0.01–0.1 mol% of $Bi(OTf)_3 \cdot H_2O$, aryl-substituted epoxides are converted to 2-arylketones with high regioselectivity (Equation (62)).[110] $BiOClO_4 \cdot xH_2O$ can also be used as catalyst for the rearrangement of epoxides, but the catalyst loading is much higher (10–50 mol%) as compared to $Bi(OTf)_3$.[111] The tandem [4 + 2]-cycloaddition reaction (Equation (63))[112,112a] and the Erlenmeyer synthesis of azalactones (Equation (64))[113] take place under catalysis of $BiCl_3$ and $Bi(OAc)_3$, respectively. $Bi(OTf)_3$ catalyzes the condensation of δ-hydroxy-α,β-unsaturated aldehydes with aryl amines (Equation (65)).[114]

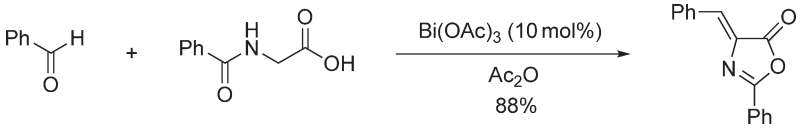


R = Ph; 92% (0 : 100)
R = Me; 77% (100 : 0)

(62)



(63)



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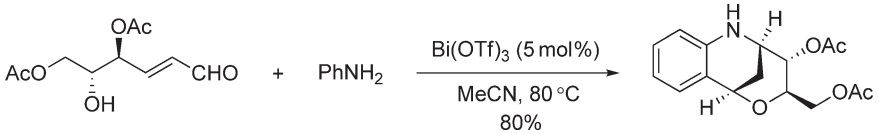
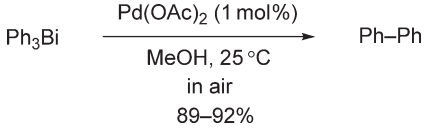


(65)

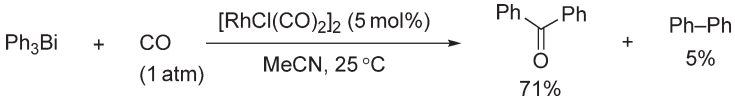
9.10.3.1.3 Pd- and Rh-catalyzed carbon–carbon bond-forming reactions

The Bi–C bonds of organobismuth(III) compounds can be cleaved by late transition metals such as palladium and rhodium under mild conditions. Triarylbismuthanes (Ar_3Bi) readily react with a catalytic amount of $Pd(OAc)_2$, $Pd_2(dba)_3$, or $Pd(O_2)$ $(PPh_3)_2$ in methanol under air to give biaryls (Ar–Ar) in good yields (Equation (66)).[115] When the reaction is carried out under a nitrogen atmosphere, biaryl formation becomes quite slow. The key steps of the catalytic cycle are proposed as follows: the transmetallation between arylbismuth(III) compounds and PdX_2 occurs twice to give Ar–Pd–Ar species, which undergo reductive elimination to give biaryls and Pd(0). Then, Pd(0) is oxidized by oxygen to regenerate Pd(II) via a Pd–oxygen complex. Triarylbismuthanes bearing a methyl group at the *ortho*-position are inert in this catalytic coupling reaction.

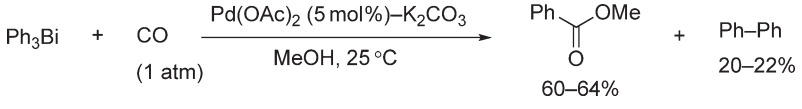


(66)

In the presence of 5 mol% of $[RhCl(CO)_2]_2$, triarylbismuthanes (Ar_3Bi) react with carbon monoxide (CO) in acetonitrile to give the corresponding diaryl ketones (Ar_2CO) together with a small amount of biaryls (Ar–Ar) (Equation (67)).[116] If methanol is used as the solvent, benzoic acid methyl esters ($ArCO_2Me$) are also formed. When treated with a catalytic amount of $Pd(OAc)_2$ in the presence of a base in methanol under a CO atmosphere, Ar_3Bi are converted to $ArCO_2Me$ in good yields (Equation (68)). In most cases, however, biaryls are also formed as side-products.

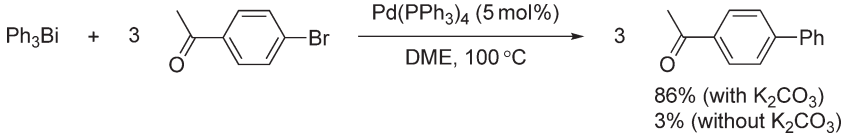


(67)



(68)

All the aryl groups of triarylbismuthanes are available as aryl anion sources in the Pd-catalyzed cross-coupling reactions. In the presence of a palladium catalyst and a base, Ph_3Bi reacts with aryl bromides, iodides, and triflates (ArX) to give unsymmetrical biaryls (Ar–Ph) (Equation (69)).[117] The addition of base is indispensable for enhancing the reactivity. The yield of the cross-coupling product and the selectivity of Ar–Ph/Ph–Ph are higher for the aryl groups bearing an electron-withdrawing substituent such as acetyl, benzoyl, or cyano group. In the presence of 10 mol% of $Pd(PPh_3)_4$, cyclic organobismuth(III) dialkoxides, prepared from $RBi(OEt)_2$ and 2,6-pyridinedimethanol, react with aryl and vinyl triflates in NMP to afford the corresponding cross-coupling products (Equation (70)).[118]



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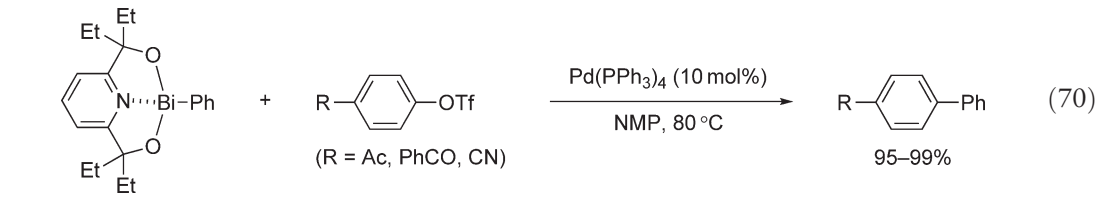
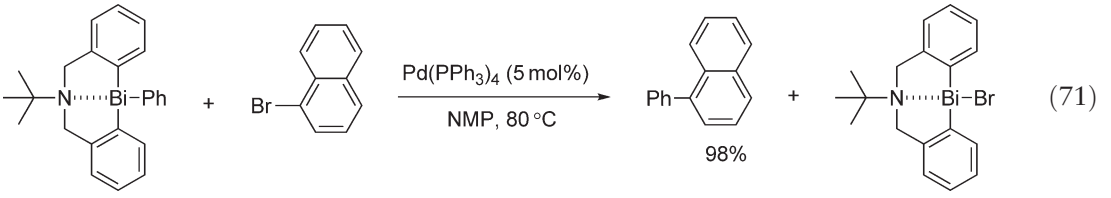


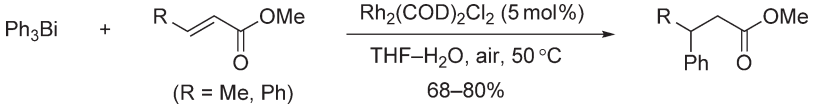
(70)

Azabismocine derivatives, a kind of hypervalent heterocyclic organobismuth(III) compounds, are highly reactive reagents for the Pd-catalyzed cross-coupling reaction with aryl bromides and chlorides in NMP (Equation (71)).[119,120] Of the catalysts examined, $Pd(PPh_3)_4$ has proved to be most effective for the bromides and $Pd(OAc)_2$/dppf for the chlorides, respectively. In these reactions, air-stable haloazabismocines are recovered as bismuth(III) byproducts, which can be converted to tertiary bismuthanes by treatment with the appropriate Grignard reagents. It has been suggested that the higher efficiency of the azabismocine derivatives as compared to triphenylbismuthane is partly derived from the higher ability to transfer the organic group from Bi(III) to Pd(II) in the transmetallation step.



(71)

The Rh-catalyzed reaction of triphenylbismuthane with α,β-unsaturated carbonyl compounds in aqueous media under air gives the corresponding conjugated addition products (β-phenyl carbonyl compounds) in moderate to good yields (Equation (72)).[121,122] Dimethyl(phenyl)bismuthane also transfers the phenyl group exclusively.[123] In the presence of KOH, dichloro(phenyl)bismuthane and dibromo(phenyl)bismuthane undergo similar rhodium-catalyzed hydroarylations in water. Asymmetric 1,4-addition reaction of triarylbismuthanes to enones has been achieved by a combined use of a dicationic palladium(II) salt and a chiral diphosphane ligand, providing optically active β-aryl-ketones of up to 95% ee (Equation (73)).[124]



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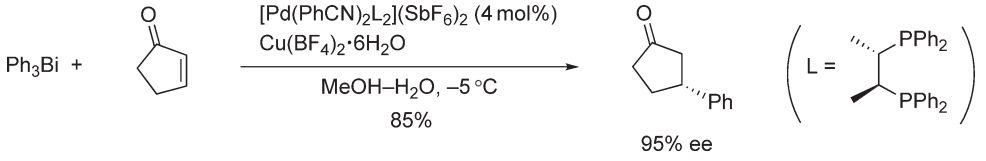
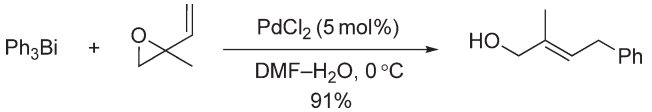


(73)

Triarylbismuthanes react with vinyloxiranes with a palladium catalysis to afford arylated allylic alcohols via ring opening of oxiranes (Equation (74)).[125] When diol acetonides and carbonates are used as substrates, the Pd-catalyzed arylation proceeds at the terminal vinylic carbon without ring opening. In the presence of a catalytic amount of $[Rh(COD)Cl]_2$, a chiral glyoxylate hydrate reacts with Ar_3Bi to give the corresponding α-aryl-α-hydroxy esters (Equation (75)).[126] The diastereoselectivity is improved by using water as the solvent.



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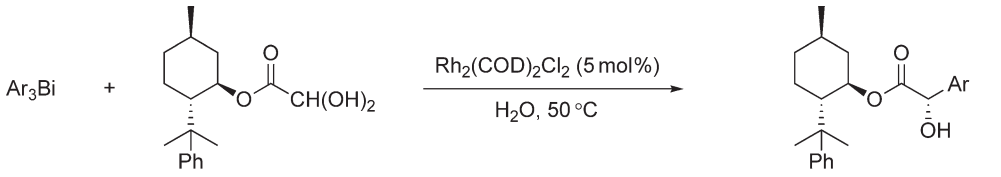
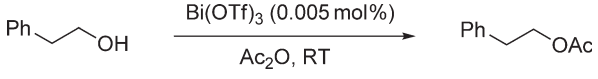


Ar = 1-$C_{10}H_7$; 81% (85% de)
Ar = Ph; 70% (67% de)

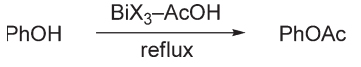
(75)

9.10.3.1.4 BiX_3-mediated carbon–heteroatom bond-forming reactions

Bismuth(III) salts are efficient Lewis acid catalysts for esterification. Acetylation, formylation, and benzoylation of various primary and secondary alcohols with the respective acids (acetic acid or anhydride, ethyl formate, and benzoic anhydride) are catalyzed by $BiCl_3$, $Bi(OCOCF_3)_3$, and $Bi(OTf)_3$ (Equation (76)).[127,127a,128,128a] Phenols are also *O*-acylated under the catalysis of BiX_3 to give phenyl esters. Among these bismuth(III) salts, $Bi(OTf)_3$ is the most effective in terms of the reaction conditions and the yield of esters (Equation (77)).[129] The $Bi(OTf)_3$–acid anhydride system can be used for the acylation of sterically demanding alcohols and phenols. Aliphatic and aromatic aldehydes are converted to the corresponding acylals by treatment with acetic anhydride in the presence of 0.1 mol% of $Bi(OTf)_3{\cdot}xH_2O$ (Equation (78)).[130,130a] Acylation of amines and thiols is catalyzed by BiOCl.[131] In the presence of a catalytic amount of $Bi(OTf)_3$, transcarbamoylation proceeds efficiently.[132] Tertiary and benzylic bromides react with $Bi(OCOR)_3$ (R = Me, Ph) to afford the corresponding esters.[133]

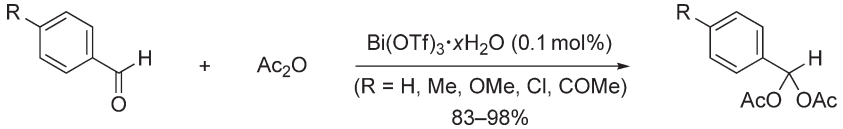


(76)



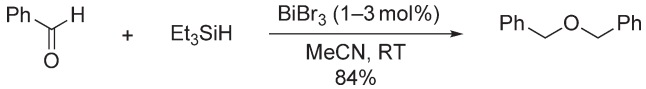
	Yield (%)
$Bi(OTf)_3$ (5 mol%)	98
$BiCl_3$ (10–20 mol%)	97
$Bi(OCOCF_3)_3$ (30 mol%)	0

(77)

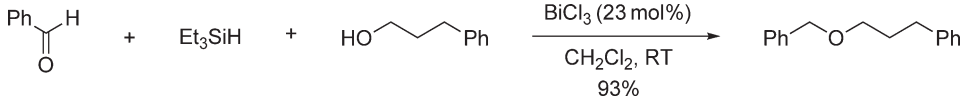


(78)

Aromatic aldehydes undergo reductive homocoupling with Et_3SiH in the presence of a catalytic amount of $BiBr_3$ to afford dibenzyl ethers (Equation (79)).[134,134a] Similarly, reductive heterocoupling of carbonyl compounds with non-protected alcohols/Et_3SiH is catalyzed by $BiCl_3$ to give unsymmetrical ethers (Equation (80)).[135] These methods are utilized in one-pot syntheses of crownophanes and homooxacalixarenes. $BiBr_3$ promotes the *O*-benzylation of aliphatic alcohols with benzylic alcohols.[136,136a]



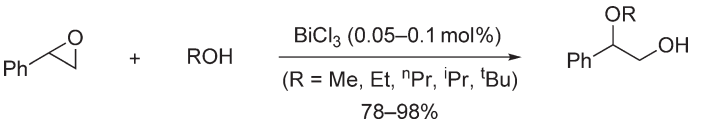
(79)



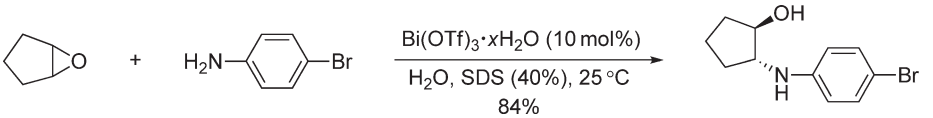
(80)

In the presence of $BiCl_3$, epoxides undergo ring-opening addition reactions with alcohols, acetic acid, and water to afford α-alkoxy, α-acetoxy, and α-hydroxy alcohols, respectively (Equation (81)).[137] In the presence of $BiCl_3$ or

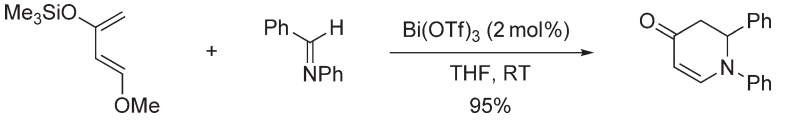
$Bi(OTf)_3$, cyclic epoxides also react with amines, Me_3SiN_3, and Me_3SiCl to afford the corresponding α-functionalized alcohols (Equation (82)).[138,138a] $BiCl_3$ and $Bi(OTf)_3$ catalyze aza-Diels–Alder reactions of *N*-arylimines with both Danishefsky's diene and dienophiles (Equation (83))[139] and the intramolecular aza-Diels–Alder reaction of *N*-vinyloxypropyl-2-cyano-1-azadienes (Equation (84)).[140]



(81)



(82)



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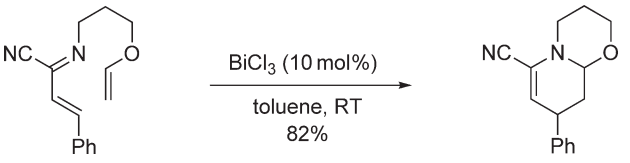
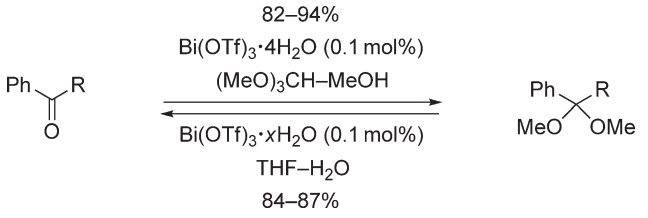
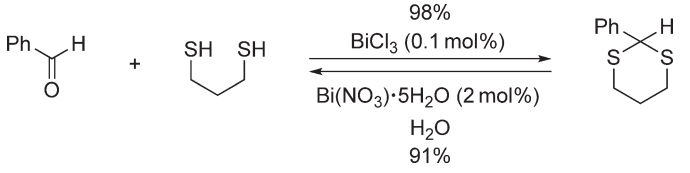


(84)

O,O-acetals are formed from aldehydes and ketones in good yields under catalysis of $Bi(OTf)_3$ (Equation (85)).[141] *S,S*-acetalization of aldehydes and ketones and transacetalization of *O,O*-acetals to the corresponding *O,S*- and *S,S*-acetals are catalyzed by BiX_3 (X = Cl, Br, I) and $Bi_2(SO_4)_3$ (Equation (86)).[142] The reverse reactions, deprotection of the *O,O*- and *S,S*-acetals, are efficiently catalyzed by $Bi(OTf)_3$ and $Bi(NO_3)_3{\cdot}5H_2O$, respectively.

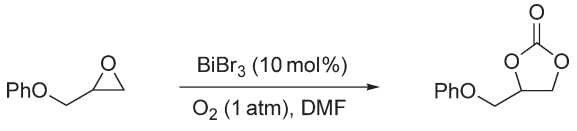


(85)

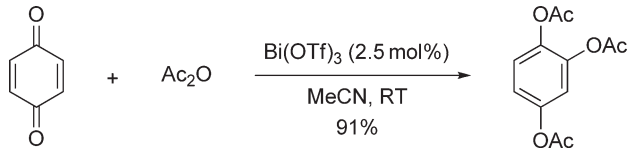


(86)

Terminal epoxides react with DMF in the presence of $BiBr_3$ under an O_2 atmosphere to afford cyclic carbonates (Equation (87)).[143] *Para*-quinones react with acetic anhydride under the catalysis of $Bi(OTf)_3$ to give acetoxy-1,4-hydroquinone diacetates (Equation (88)).[144]

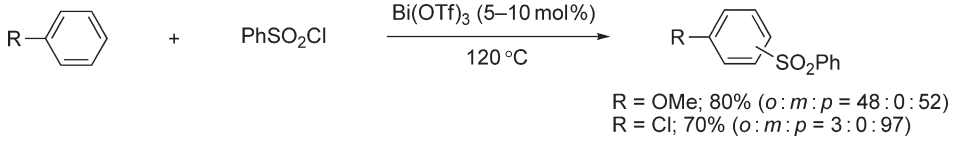


(87)

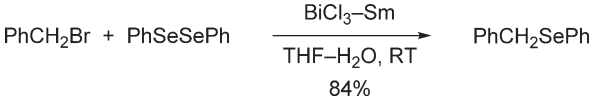


(88)

Friedel–Crafts sulfonylation of arenes with sulfonyl chlorides and sulfonic anhydrides is efficiently catalyzed by BiX_3 (Equation (89)).[145,145a,145b] In the presence of bismuth metal, alkyl and arylsulfonyl chlorides react with allylic halides to afford the corresponding allylic sulfones.[146] Both activated and deactivated arenes are converted to unsymmetrical sulfones. The $BiCl_3$–Sm binary reagent mediates the reductive C–S and C–Se bond formations of benzyl[147] and allyl bromides[148] with diorganyl disulfies and diselenides in aqueous media, affording the corresponding sulfides and selenides, respectively (Equation (90)).

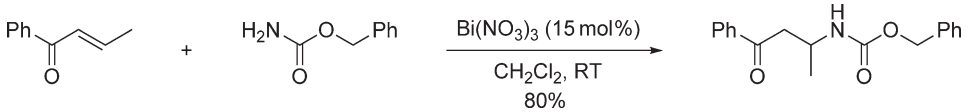


(89)

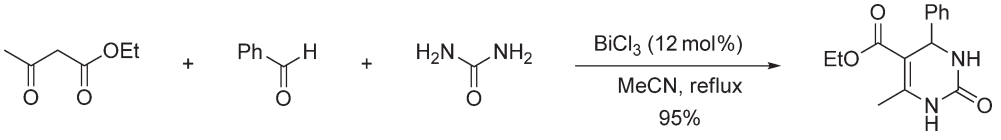


(90)

Bismuth(III) nitrate catalyzes Michael addition of α,β-unsaturated ketones with amines, thiols, and carbamates, although the promoting role of $Bi(NO_3)_3$ is not fully understood (Equation (91)).[100] The Biginelli cyclocondensation of a mixture of β-keto esters, aldehydes, and urea is mediated by $BiCl_3$, affording 3,4-dihydropyrimidin-2(1H)-ones (Equation (92)).[149] $Bi(OCOCF_3)_3$ is an efficient catalyst for the regio- and chemoselective synthesis of β-enaminones in water.[150]

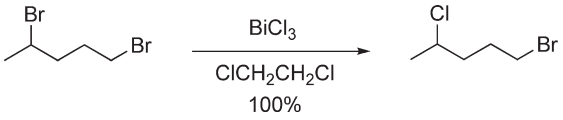


(91)



(92)

The conversion of cyclic secondary and tertiary alcohols to the corresponding chlorides can be achieved by treatment with $BiCl_3$ or Me_3SiCl–$BiCl_3$.[151,152] A mechanism involving the formation of a complex between the alcohol and the Lewis-acidic Bi(III) salts has been proposed.[153] When allylic alcohols are used as substrates, a mixture of regioisomers is formed. Secondary and tertiary alkyl bromides and iodides undergo the halogen exchange reaction with BiX_3 (X = Cl, Br) to afford the corresponding chlorides and bromides in high yields with high regioselectivity (Equation (93)).[154]

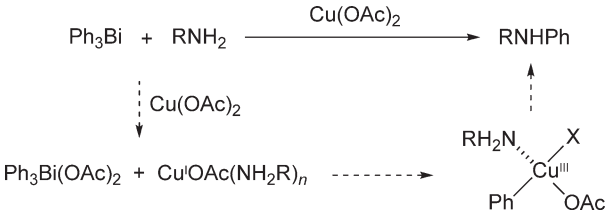


(93)

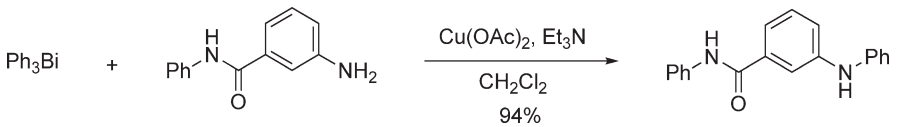
9.10.3.1.5 Cu-mediated carbon–heteroatom bond-forming reactions

A variety of N–H containing compounds are *N*-arylated by Ar_3Bi in the presence of a stoichiometric amount of $Cu(OAc)_2$,[155–161] which plays dual important roles: it oxidizes Ar_3Bi to $Ar_3Bi(OAc)_2$ and mediates the arylation via transmetallation (Equation (94)). In the presence of Et_3N or pyridine, the $Cu(OAc)_2$-promoted *N*-arylation of amides, sulfonamides, ureas, carbamates, and anilines with Ar_3Bi occurs much more efficiently than the reaction without a

base.[162,163] It is suggested that the tertiary amines help to enhance the solubility of the copper species and to buffer the reaction media. When aminobenzanilides are used as the substrates, *N*-arylation occurs selectively on the primary amino group (Equation (95)).[164]

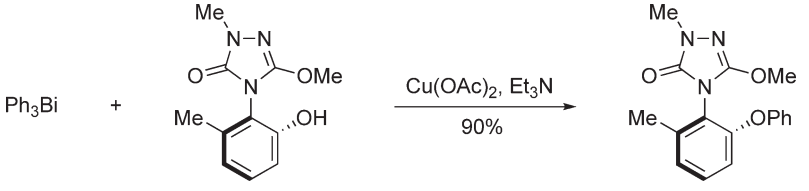


(94)

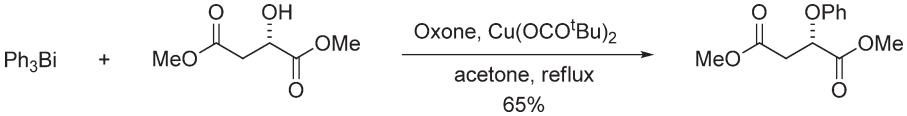


(95)

The *O*-phenylation of phenols has also been performed using a Ph_3Bi-$Cu(OAc)_2$-Et_3N system (Equation (96)).[165] The copper-mediated *O*-alkylation of alcohols and phenols with R_3Bi (R = *n*-Bu, $PhCH_2$) gives a mixture of alkyl ethers, dialkyls (R–R), alkanes (RH), and aldehydes derived from the R group.[166] Hydroxy esters and amides are *O*-arylated by a combined use of Ar_3Bi and Oxone^{TM} in the presence of copper(II) pivalate (Equation (97)).[167] 1,2-Cyclohexanediol is also *O*-arylated to give the corresponding α-hydroxy ether, whereas cyclohexanol and 1-octanol are not arylated under the same reaction conditions.



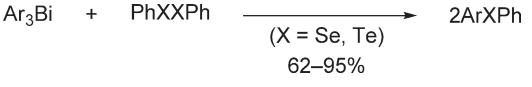
(96)



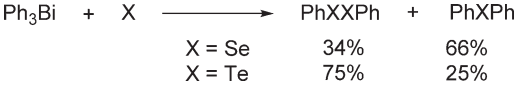
(97)

9.10.3.1.6 Non-catalyzed carbon–heteroatom bond-forming reactions

Triarylbismuthanes (Ar_3Bi) react with diphenyl diselenide (Ph_2Se_2) and diphenyl ditelluride (Ph_2Te_2) to give the corresponding aryl phenyl chalcogenides (ArXPh; X = Se, Te) in good yields based on the PhX moiety (Equation (98)).[168] The reaction of Ar_3Bi with elemental chalcogen (Se, Te) affords a mixture of the respective dichalcogenides (Ar_2X_2) and monochalcogenides (Ar_2X) (Equation (99)). The ratio of Ar_2X_2/Ar_2X depends on the aryl ligand (Ar), chalcogen (X), and reaction conditions.



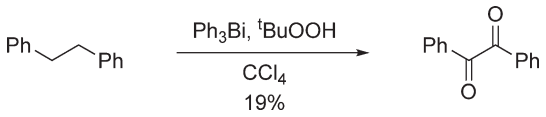
(98)



(99)

9.10.3.1.7 Oxidations

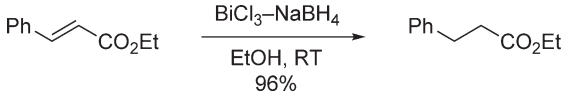
When treated with a mixture of Ph_3Bi and *t*-BuOOH in CCl_4 or toluene, dibenzyl is oxidized to benzil (Equation (100)). The active oxidant is assumed to be an O_2-coordinated bismuthane complex ($Ph_3Bi{\cdot}O_2$).[169] Triphenylmethane and 1,1-diphenylethane are oxidized by this complex to the corresponding hydroperoxides.



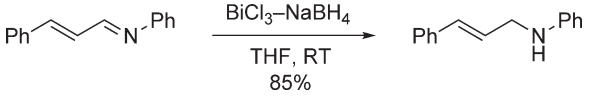
(100)

9.10.3.1.8 Reductions

The $BiCl_3$–$NaBH_4$ binary reagent selectively reduces the C═C bond of α,β-unsaturated carbonyl compounds (Equation (101)) and the C═N bond of α,β-unsaturated imines (Equation (102)).[170,170a,170b,171] Aromatic α-bromo and α-iodo ketones are reduced by $BiCl_3$–$NaBH_4$ in aqueous media to their parent ketones via insertion of Bi(0) into the carbon–halogen bond.[170b]



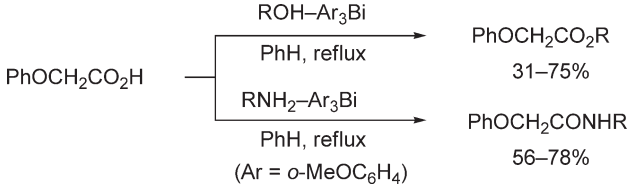
(101)



(102)

9.10.3.1.9 Miscellaneous reactions

When heated in benzene in the presence of a triarylbismuthane bearing *ortho*-methoxy groups, α-monosubstituted carboxylic acids react with alcohols and amines to afford the corresponding esters and amides, respectively (Equation (103)).[172,172a,172b] Macrocyclic esters are synthesized by the Ar_3Bi-templated reaction of diols with dicarboxylic acid derivatives (Equation (104)).[172b,173] Based on the IR and mass spectral data, it is suggested that the complexing ability of the diol with Ph_3Bi is much higher than those with Ph_3Sb and Ph_3As. Tris(4-methoxyphenyl)bismuthane and triphenylbismuthane catalyze the cyanation of aromatic and aliphatic aldehydes with Me_3SiCN in refluxing THF.



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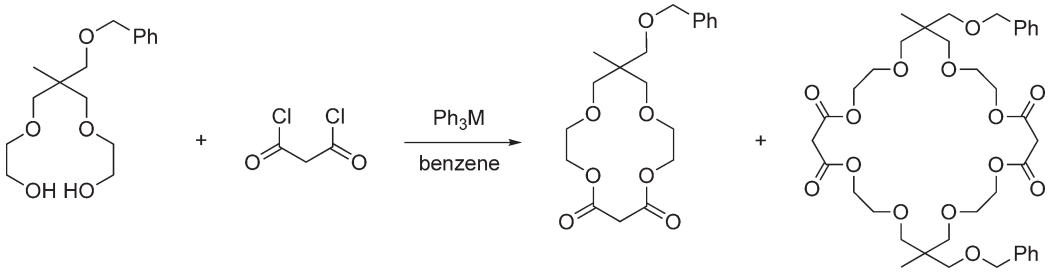


(104)

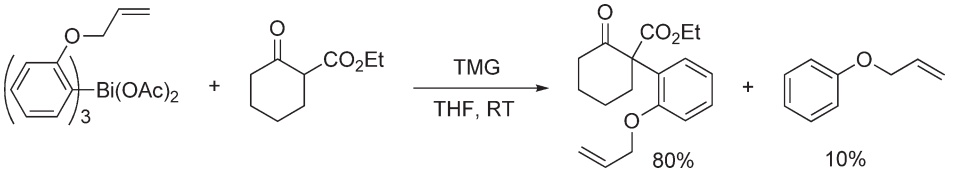
M = As 25% 21%
M = Sb 40% 15%
M = Bi 40% 44%

9.10.3.2 Organobismuth(v) Compounds

9.10.3.2.1 C-arylation of enolisable substrates

In the 1980s, Barton and co-workers developed a useful method for *C*-arylation of enolisable substrates using polyarylbismuth(v) compounds of the types Ar_3BiX_2, Ar_4BiX, and Ar_5Bi. Under basic conditions, the arylation occurs

through a typical ligand coupling mechanism, a non-synchronous concerted process from polyarylbismuth(V) intermediates. This mechanism has recently been supported by the results of reactions using tris(2-allyloxyphenyl)bismuth diacetate, an internal-trap containing reagent (Equation (105)).[174] Thus, no cyclized products are formed, and the intervention of radical species is excluded. Influence of the steric hindrance of the aryl group of triarylbismuth(V) derivatives in *C*-, *O*-, and *N*-arylations has also been investigated.[175,176] *ortho*-Tolyl and 2,4-xylyl derivatives transfer their aryl ligands to the substrates more easily than mesityl (2,4,6-trimethylphenyl) derivatives (Equation (106)). This result indicates that the steric hindrance plays an inhibitory role in the ligand-coupling step. In the presence of DBU or TMG, an α-nitrocarboxylic acid methyl ester is *C*-arylated by Ph_3BiCl_2 (Equation (107)).[177]



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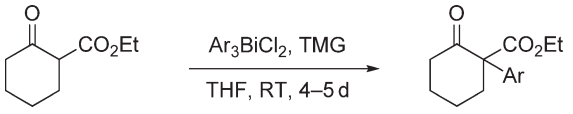
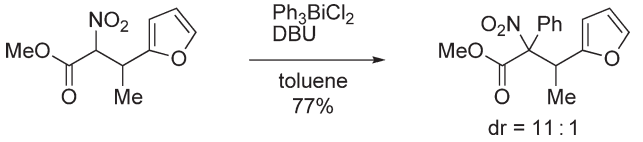


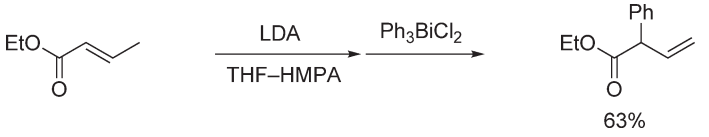
Ar	*Yield* (%)
2-MeC_6H_4	64
2,4-$Me_2C_6H_3$	63
2,4,6-$Me_3C_6H_2$	25

(106)

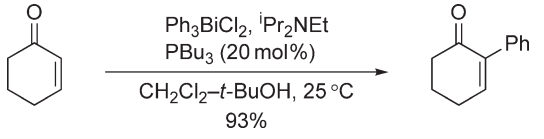


(107)

Treatment of α,β-unsaturated carbonyl compounds and 1-nitrocyclohexene with LDA–HMPA generates the corresponding enolates, which undergo α-arylation with Ph_3BiCl_2 to afford α-aryl-β,γ-unsaturated carbonyl compounds (Equation (108)).[178] In the case of 2-cyclohexenone, however, the classical α-arylation is privileged. The regioselective α-arylation of enones and enals using triarylbismuth dichlorides is catalyzed by tributylphosphane in the presence of Hunig's base (Equation (109)).[179] The reaction is initiated by a Michael addition of the phosphane to the substrate, resulting in the formation of β-phosphonioenolates. Then, enolates react with Ar_3BiCl_2 to give bismuth(V) enolates, which undergo ligand coupling to afford the α-aryl-α,β-unsaturated carbonyl compounds.

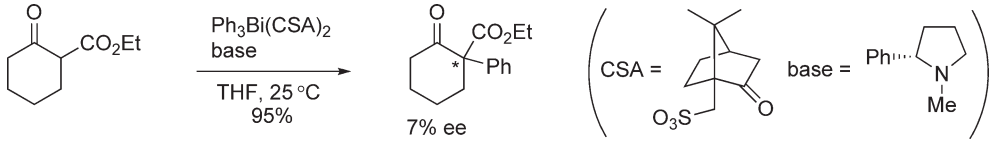


(108)



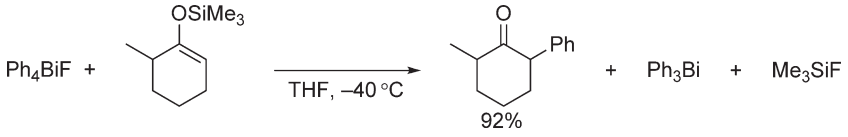
(109)

Recently, enantioselective *C*-arylation of enolisable compounds with chiral triarylbismuth(v) reagents bearing optically active apical ligands has been attempted (Equation (110)).[180] Although the observed enantioselectivity is low, it has been suggested that addition of a chiral base is necessary for enhancing the enantioselectivity.



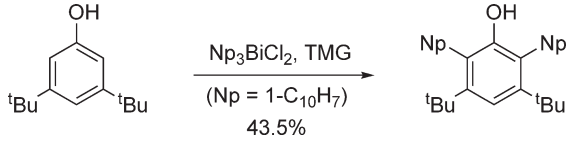
(110)

Silyl enol ethers and ketene silyl acetals react with tetraphenylbismuth fluoride under neutral conditions to give the corresponding α-monophenylated carbonyl compounds in good yields together with triphenylbismuthane and fluorotrimethylsilane (Equation (111)).[181] The reaction is likely to be initiated by the nucleophilic attack of the fluoride ion on the silicon atom, and the regiochemistry of arylation is governed by the structure of silyl enolates.

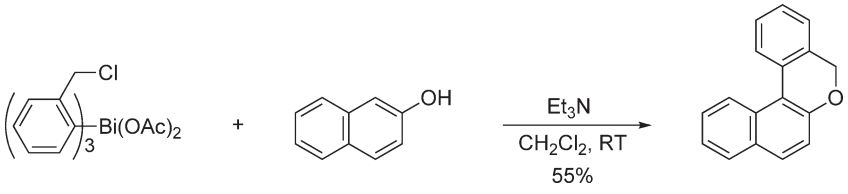


(111)

Phenols undergo *C*- or *O*-arylation with arylbismuth(v) reagents to yield the corresponding arylated phenols. In general, the *C*-arylation occurs for the phenols bearing electron-donating substituents and under basic conditions (Equation (112)),[182,182a] whereas the *O*-arylation occurs for those bearing electron-withdrawing substituents and under acidic conditions. One-pot synthesis of benzo[b]pyran compounds can be performed via arylation of phenols with tris(*o*-chloromethylphenyl)bismuth diacetate (Equation (113)).[183]



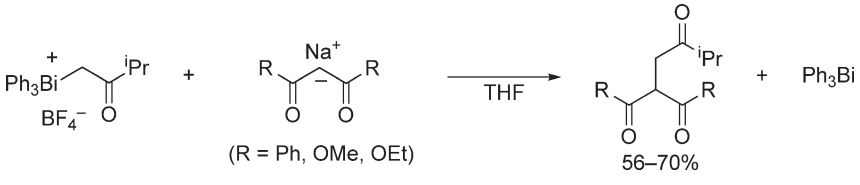
(112)



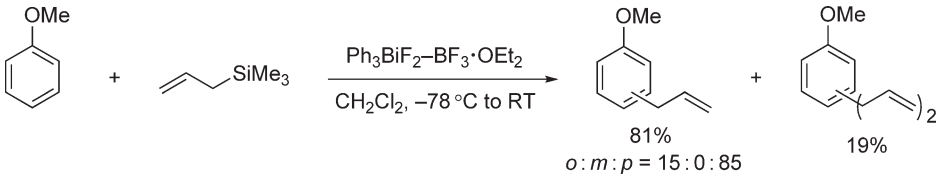
(113)

9.10.3.2.2 Carbon–carbon bond-forming reactions using bismuthonium salts

Alkyltriarylbismuthonium salts are easily prepared from triarylbismuth difluorides, $BF_3{\cdot}OEt_2$, and the corresponding alkylmetals such as silyl enolates and alkylboronic acids. When treated with a sodium salt of dibenzoylmethane, 2-oxoalkyltriphenylbismuthonium salts selectively transfer the alkyl group under mild conditions to the active methylene carbon (Equation (114)).[184,184a] In this reaction, triphenylbismuthane is recovered in good yield, suggesting the high nucleofugality of the triphenylbismuthonio group. Treatment of a mixture of Ph_3BiF_2 and allyltrimethylsilane with $BF_3{\cdot}OEt_2$ in the presence of excess electron-rich arenes yields a mixture of allylated arenes (Equation (115)).[185] The high *p*/*o*-selectivity indicates that the Friedel–Crafts-type allylation occurs via highly electrophilic allylbismuthonium(v) species.

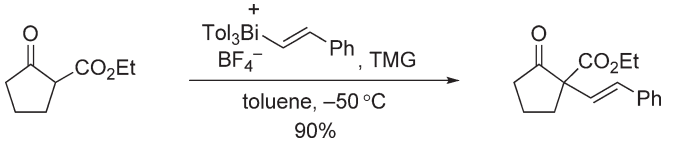


(114)

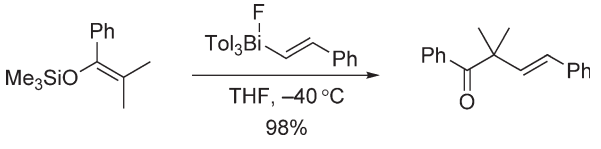


(115)

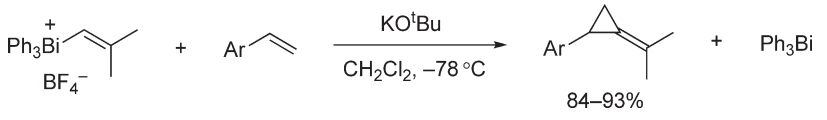
Direct nucleophilic α-alkenylation of β-keto esters, β-diketones, and phenols with alkenyltriarylbismuthonium tetrafluoroborates proceeds smoothly in the presence of TMG, affording the corresponding β,γ-unsaturated carbonyl compounds as the major product (Equation (116)).[186] The selectivity of alkenyl versus aryl transfer depends on the substituents of the vinyl moiety, and the transferring ability of the alkenyl group is in the order: β-alkyl > β-phenyl > β-methyl > β,β-dimehyl. The regioselective α-monoalkenylation of carbonyl compounds is achieved by the reaction of styryltri(*p*-tolyl)bismuth fluoride with silyl enolates (Equation (117)).[181] The addition of KO-*t*-Bu to a mixture of alkenylbismuthonium salt and styrenes affords alkylidenecyclopropanes together with triphenylbismuthane (Equation (118)).[187] Based on the Hammett study, the generation of a free alkylidene carbene intermediate is suggested.



(116)



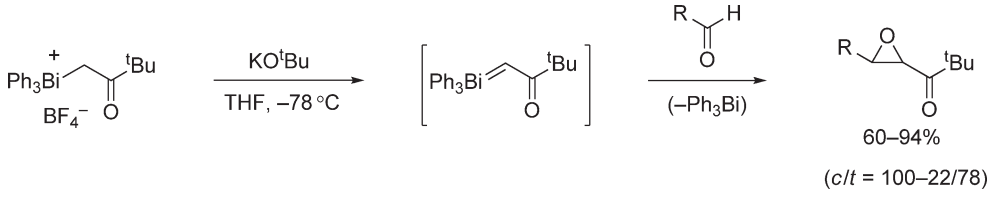
(117)



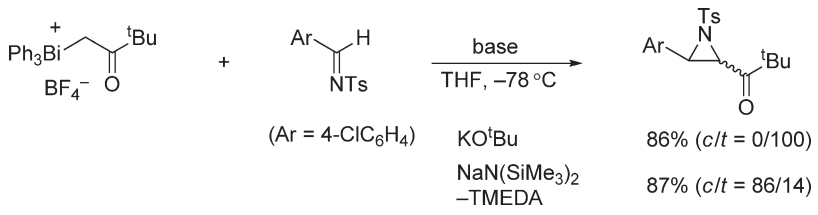
(118)

9.10.3.2.3 Carbon–carbon bond-forming reactions using bismuth ylides

Treatment of 2-oxoalkyltriphenylbismuthonium salts with KO-*t*-Bu in THF at −78 °C generates the corresponding α-monocarbonyl bismuth ylides of the type $Ph_3Bi{=}CHCOR$. In marked contrast to the phosphorus counterparts, the bismuth ylides thus generated are thermally unstable and highly reactive. For example, $Ph_3Bi{=}CHCOR$ readily reacts with aromatic and aliphatic aldehydes at low temperatures to yield α,β-epoxy ketones with high *trans*-selectivity (Equation (119)).[188] In this reaction, α,β-unsaturated ketones (Wittig products) are not formed, indicating the high leaving ability of the triphenylbismuthonio group. The bismuth ylides ($Ph_3Bi{=}CHCOR$) also react with *N*-sulfonylaldimines to give α,β-aziridinoketones. Interestingly, the *cis*/*trans* selectivity of the aziridines can be controlled by a suitable choice of base and additive (Equation (120)).[189]

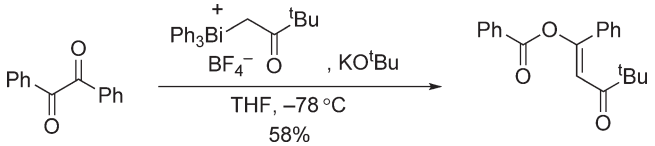


(119)

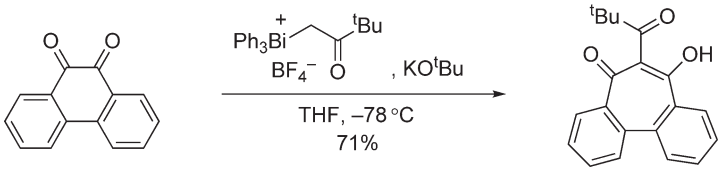


(120)

Simple ketones such as benzophenone and acetophenone do not undergo the C–C bond-forming reaction with $Ph_3Bi{=}CHCOR$. On the other hand, activated ketones such as α-keto esters,[190,190a] benzils (Equation (121)),[191] and *ortho*-quinones (Equation (122))[192] readily react with $Ph_3Bi{=}CHCOR$ to afford epoxides, *O*-aroyl enolates, and 2-acyl-3-hydroxytropones, respectively. Both the transposition and the ring expansion are unprecedented in the ylide chemistry and characteristic of bismuth. When treated with 1,2-dibenzoylethene, cyclopropanation occurs to give 1,2,3-acylcyclopropanes in moderate yields.[188]



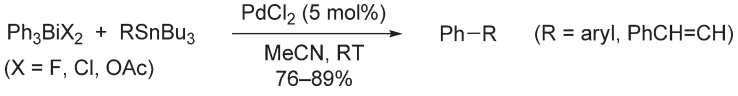
(121)



(122)

9.10.3.2.4 Pd-catalyzed carbon–carbon bond-forming reactions

In the presence of a catalytic amount of $PdCl_2$, Ar_3BiX_2 (X = F, Cl, OAc) react with aryl- and styrylstannanes in acetonitrile at room temperature to give biaryls and stilbene, respectively (Equation (123)).[193] When similar reactions are conducted under an atmospheric pressure of CO, the carbonylative cross-coupling reactions afford the corresponding aromatic ketones (Equation (124)). Unsymmetrical biaryls are also prepared by the Pd-catalyzed cross-coupling reaction of diaryliodonium salts with Ar_3BiX_2 (X = F, Cl, OAc) (Equation (125)).[194] Terminal acetylenes are phenylated by Ph_3BiF_2 under CuCl catalysis to afford phenyl-substituted acetylenes via ligand coupling (Equation (126)).[195] Other organobismuth(V) reagents such as Ph_3BiCl_2 and Ph_3BiCO_3 give much lower yields.



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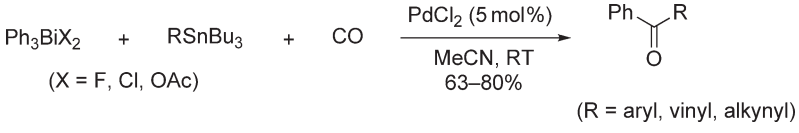
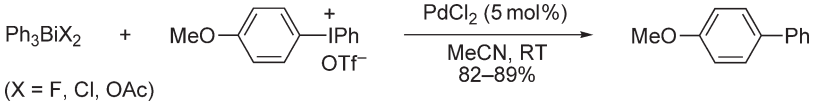
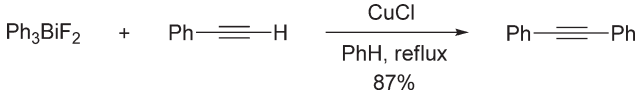


(124)



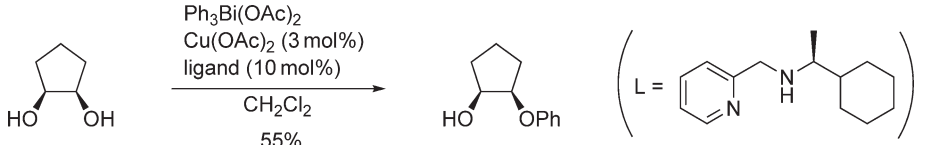
(125)



(126)

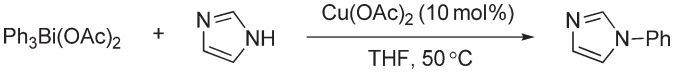
9.10.3.2.5 O-arylations and N-arylations

In the presence or absence of a copper catalyst, *O*-arylation of alcohols and phenols by $Ph_3Bi(OAc)_2$ proceeds to give the corresponding aryl ethers.[196–198] The monophenylation of *cis*-1,2-cyclopentanediol with $Ph_3Bi(OAc)_2$ in the presence of a Cu(II) complex bearing a chiral triamine or diamine ligand affords an α-hydroxy phenyl ether with moderate enantiomeric excesses up to 38% (Equation (127)).[199] The copper-catalyzed *O*-arylation has been successfully applied to the synthesis of immunosuppressive macrolides.[200–202]

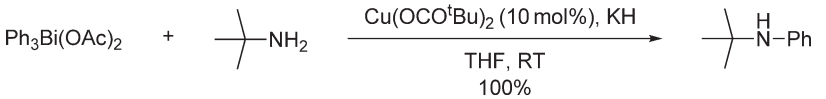


(127)

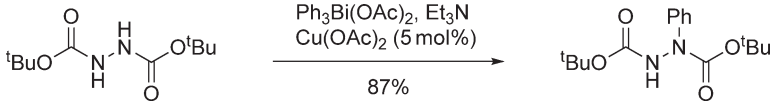
Amines, amides, and N–H containing heteroarenes smoothly react with $Ar_3Bi(OAc)_2$ in the presence of $Cu(OAc)_2$ to give *N*-arylated products (Equation (128)).[203–208] In general, primary amines are monoarylated, because the resulting products, secondary amines, are much less reactive than the parent primary amines. Thus, the selective *N*-arylation can be achieved by controlling the amount of reagents and the reaction conditions. With copper(II) pivalate and KH, the *N*-arylation of sterically hindered aromatic and aliphatic amines proceeds efficiently under mild conditions (Equation (129)).[209] 1,2-Di-Boc-hydrazine is selectively *N*-phenylated with $Ph_3Bi(OAc)_2$ in the presence of a catalytic amount of $Cu(OAc)_2$ (Equation (130)). When the reaction is carried out in the absence of $Cu(OAc)_2$, 1,2-di-Boc-hydrazone is formed as the only product.



(128)

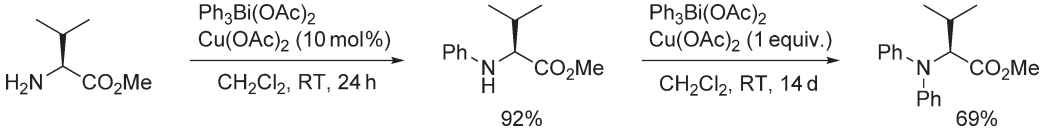


(129)



(130)

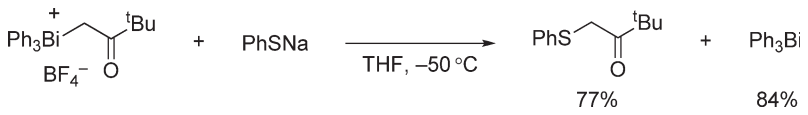
Amino acid methyl esters are *N*-phenylated by $Ph_3Bi(OAc)_2$ in the presence of $Cu(OAc)_2$. For example, monophenylatino of (*S*)-valine methyl ester is complete within 24 h by the combined use of $Ph_3Bi(OAc)_2$ and 10 mol% of $Cu(OAc)_2$, and the second *N*-phenylation can be achieved by using an equimolar amount of $Cu(OAc)_2$ (Equation (131)).[210,210a,211] Triarylbismuth diacetates, generated *in situ* from the corresponding triarylbismuthanes and $PhI(OAc)_2$, can be used for the *N*-arylation without isolation.[212] Polymer-supported triarylbismuth(V) reagents are used for the *N*-, *C*-, and *O*-arylations.[213]



(131)

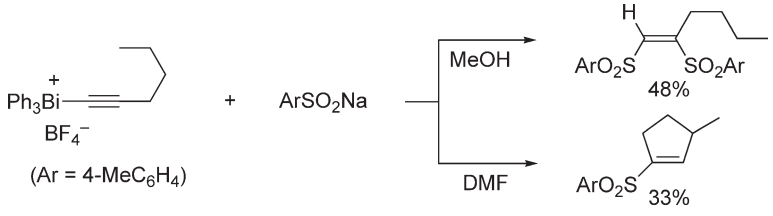
9.10.3.2.6 Carbon–heteroatom bond-forming reactions using bismuthonium salts

2-Oxoalkyl- and 3-oxoalkyl-triphenylbismuthonium salts transfer the alkyl groups to various hetero nucleophiles such as piperidine, triphenylphosphane, arylsulfinates, alcohols, arylthiolates, dimethyl sulfide, and metal halides under mild conditions (Equation (132)).[214,215] Methyl- and allyl-triphenylbismuthonium salts also alkylate some heteronucleophiles.[216] The leaving ability of the triphenylbismuthonio group has been found to be higher than that of the triflate anion.



(132)

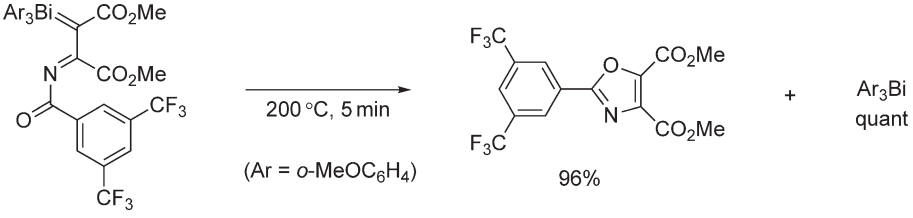
Alkynyltriphenylbismuthonium salts react with sodium *p*-toluenesulfinate in dual reaction modes depending on the solvents employed (Equation (133)).[217] When the reaction is conducted in DMF, 1-tosylcyclopentene is formed through 1,5-C–H insertion of an alkylidene carbene intermediate, generated via Michael addition of the sulfinate anion to the *β*-carbon. When the reaction is carried out in MeOH, 1,2-bis(sulfonyl)alkenes are produced via sequential Michael addition and nucleophilic substitution of the sulfinate anion.



(133)

9.10.3.2.7 Carbon–heteroatom bond-forming reactions using bismuth ylides

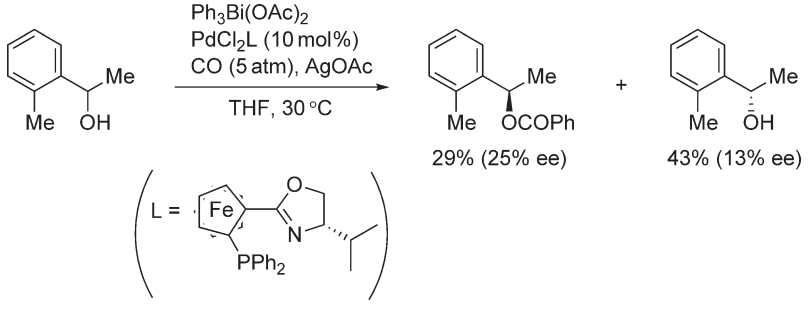
Triarylbismuth *N*-acylimides ($Ar_3Bi{=}NCOR$) react with dialkyl acetylenedicarboxylate to afford highly conjugated triarylbismuth ylides, which eliminate Ar_3Bi by heating or by treating with a catalytic amount of a copper salt to produce trisubstituted oxazoles via intramolecular cyclization (Equation (134)).[218] Triphenylbismuth (tropon-2-yl)imide reacts with heterocumulenes to give cycloheptaannulated heterocycles.[219]



(134)

9.10.3.2.8 Pd-catalyzed carbon–heteroatom bond-forming reactions

The kinetic resolution of racemic secondary alcohols via enantioselective benzoylation using $Ph_3Bi(OAc)_2$, CO, AgOAc, and a chiral Pd(II) catalyst has been investigated (Equation (135)).[220,220a] Of the chiral *P*- and *N*-ligands tested, the planar chirality of an optically active oxazolynylferrocenylphosphane has shown some positive effects on the enantioselectivity.

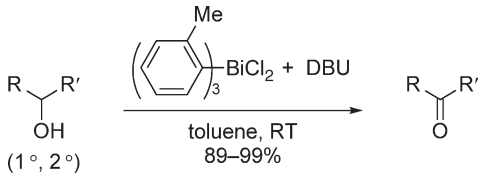


(135)

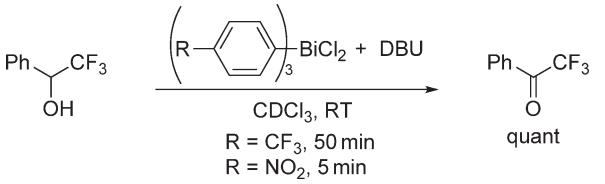
9.10.3.2.9 Oxidations

Organobismuth(V) compounds are potential oxidants due to the facile Bi(V)/Bi(III) redox process. Primary and secondary alcohols are oxidized by Ph_3BiCO_3 or by a $(Ph_3BiCl)_2O$–base system to aldehydes and ketones,

respectively.[221,222] When the reaction is carried out by the combined use of tris(*o*-tolyl)bismuth dichloride and DBU in toluene, the oxidation proceeds rapidly to give desired carbonyl compounds in good yields (Equation (136)).[223] The oxidation of simple alcohols by triarylbismuth(v) reagents is considered to proceed via two main steps: the formation of alkoxybismuth(v) intermediates and the subsequent α-hydrogen abstraction by the aryl ligand. The substituent effects of the aryl ligands of Ar_3BiCl_2 on each step have been examined by means of competition experiments.[224] It has been found that the electron-withdrawing substituent at the *para*-position accelerates the first step electronically and that the *ortho*-methyl group accelerates the second step sterically. For instance, tri(*p*-nitrophenyl)bismuth dichloride and tri(*p*-trifluoromethylphenyl)bismuth dichloride oxidize a trifluoromethylcarbinol within 5–50 min at room temperature (Equation (137)).

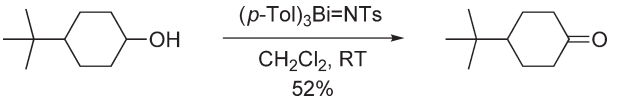


(136)

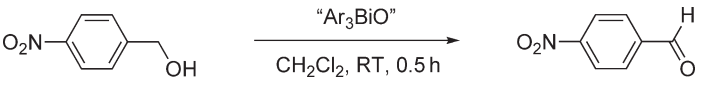


(137)

Triarylbismuthane imides ($Ar_3Bi{=}NR$)[225–227] and triarylbismuthane oxides (Ar_3BiO)[228,229] oxidize alcohols to carbonyl compounds under mild conditions in the absence of a base (Equation (138)). The *ortho*-effect is observed for the oxidation with Ar_3BiO; the oxides bearing *o*-methoxy or *o*-methyl groups oxidize alcohols much more rapidly than the respective *para*-substituted derivatives (Equation (139)).[230] The C–C bond of α-glycols is oxidatively cleaved by a variety of triarylbismuth(v) oxidants to yield two molecules of carbonyl compounds together with triarylbismuthane (Equation (140)).[231,232]

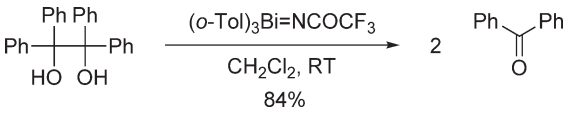


(138)



(139)

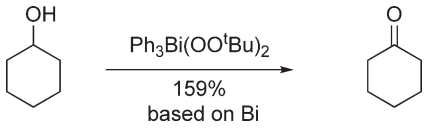
Ar	*Conv.* (%)	*Yield* (%)
2-$MeOC_6H_4$	99	91
4-$MeOC_6H_4$	25	17



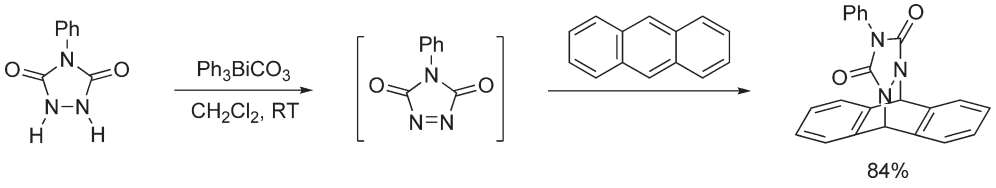
(140)

Aliphatic alcohols and benzyl alcohol are oxidized by $Ph_3Bi(OO^tBu)_2$ to the corresponding carbonyl compounds (Equation (141)).[233] It has been suggested that the oxidation occurs via dehydrogenation of alcohols by phenyl or *tert*-butoxy radical. When treated with diethyl ether, $Ph_3Bi(OO^tBu)_2$ oxidizes the methyl group to afford ethoxyacetic

acid as the initial product.[234] Urazoles are oxidized by Ph_3BiCO_3 to triazolinediones, which subsequently undergo cycloaddition reaction with anthracene derivatives (Equation (142)).[235]



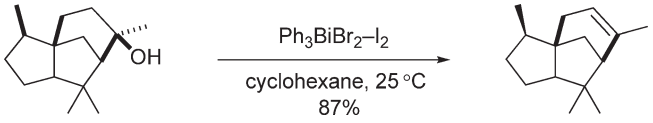
(141)



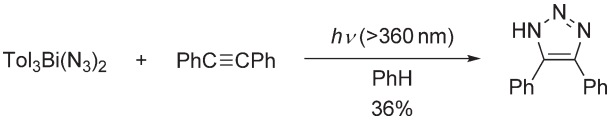
(142)

9.10.3.2.10 Miscellaneous reactions

When treated with a mixture of triphenylbismuth dibromide (Ph_3BiBr_2) and iodine, tertiary and secondary alcohols are converted to the corresponding most stable alkenes under mild conditions. Sesquiterpinic alcohol is dehydrated to cedrene by this binary system (Equation (143)).[236] Irradiation of tri(*p*-tolyl)bismuth diazide in benzene in the presence of acetylenes results in the transfer of one of the azido ligands to the triple bond, affording 1,2,3-triazoles in moderate yields (Equation (144)).[237]



(143)



(144)

References

1. Wardell, J. L. In *Comprehensive Organometallic Chemistry I*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 2, pp 681–707.
2. Huang, Y.-Z.; Zhou, Z.-L. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Chapter 12, pp 487–513.
3. Lloyd, D.; Gosney, I. In *The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds*; Patai, S., Ed.; Wiley: New York, 1994; Chapter 16, pp 657–693.
4. Suzuki, H.; Ikegami, T.; Matano, Y. *Synthesis* **1997**, 249–267.
5. Matano, Y. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004; Chapter 14, pp 753–811.
6. Antimony salts in organic synthesis: Ishihara, K. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; VCH-Verlag: Weinheim, 2000; Vol. 2, Chapter 11, pp 523–541.
7. Arylation and oxidation: Dodonov, V. A.; Gushchin, A. V. *Russ. Chem. Bull. (Engl. Transl.)* **1993**, *42*, 1955.
8. Bismuthonium salts, ylides, and imides: Matano, Y.; Suzuki, H. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2673–2681.

8a. Matano, Y. *Yuki Gosei Kagaku Kyokaishi* **2001**, *59*, 834–844.

9. Bismuth molybdate catalysts: Bettahar, M. M.; Costentin, G.; Savary, L.; Lavalley, J. C. *Appl. Catal., A* **1996**, *145*, 1–48.
10. Bismuth compounds in oxidation: Postel, M.; Duñach, E. *Coord. Chem. Rev.* **1996**, *155*, 127–144.
11. Bismuth(III) salts in Friedel–Crafts acylation: Desmurs, J.-R.; Labrouillere, M.; Dubac, J.; Laporterie, A.; Gaspard, H.; Metz, F. *Ind. Chem. Libr.* **1996**, *8* (*Roots of Organic Development*), 15–28.
12. Bismuth(III) compounds in organic synthesis: Marshall, J. A. *Chemtracts* **1997**, *10*, 1064–1075.
13. Bismuth(III) compounds in organic synthesis in water: Wada, M.; Miyoshi, N. *Yuki Gosei Kagaku Kyokaishi* **1999**, *57*, 689–697.
14. Organobismuth reagents in arylation: Elliott, G. I.; Konopelski, J. P. *Tetrahedron* **2001**, *57*, 5683–5705.
15. Bismuth(III) compounds in organic synthesis: Leonard, N. M.; Wieland, L. C.; Mohan, R. S. *Tetrahedron* **2002**, *58*, 8373–8397.
16. Bismuth(III) triflate in organic synthesis: Gaspard-Iloughmane, H.; Le Roux, C. *Eur. J. Org. Chem.* **2004**, 2517–2532.
17. Bismuth in SOHIO process: Hanna, T. A. *Coord. Chem. Rev.* **2004**, *248*, 429–440.
18. Akiba, K.; Yamamoto, Y. In *The Chemistry of Organic Arsenic, Antimony and Bismuth Compounds*; Patai, S., Ed.; Wiley: New York, 1994; Chapter 20, pp 761–812.

19. Cross, W. I.; Godfrey, S. M.; McAuliffe, C. A.; Mackie, A. G.; Pritchard, R. G. In *Chemistry of Arsenic, Antimony and Bismuth*; Norman, N. C., Ed., Blackie Academic & Professional: London, 1998; Chapter 5, pp 207–282.
20. Burton, J. W. In *Science of Synthesis*; Fleming, I., Ed.; Georg Thieme Verlag: Stuttgart, 2002; pp 53–75.
21. Freedman, L. D.; Doak, G. O. *J. Organomet. Chem.* **1994**, *477*, 1–29.
22. Freedman, L. D.; Doak, G. O. *J. Organomet. Chem.* **1995**, *496*, 137–152.
23. Silvestru, C.; Breunig, H. J.; Althaus, H. *Chem. Rev.* **1999**, *99*, 3277–3327.
24. Suzuki, H.; Matano, Y. In *Chemistry of Arsenic, Antimony and Bismuth*; Norman, N. C., Ed.; Blackie Academic & Professional: London, 1998; Chapter 6, pp 283–343.
25. Suzuki, H.; Matano, Y., Eds., *Organobismuth Chemistry*; Elsevier: New York, 2001.
26. Suzuki, H.; Ikegami, T. In *Science of Synthesis*; Fleming, I., Ed.; Georg Thieme Verlag: Stuttgart, 2002; pp 77–116.
27. Doak, G. O.; Freedman, L. D. *J. Organomet. Chem.* **1994**, *477*, 31–44.
28. Doak, G. O.; Freedman, L. D. *J. Organomet. Chem.* **1995**, *485*, 1–9.
29. Doak, G. O.; Freedman, L. D. *J. Organomet. Chem.* **1995**, *496*, 1–17.
30. Wardell, J. L. *Organomet. Chem.* **1993**, *22*, 138–143.
31. Wardell, J. L. *Organomet. Chem.* **1994**, *23*, 138–143.
32. Wardell, J. L. *Organomet. Chem.* **1995**, *24*, 151–156.
33. Wardell, J. L. *Organomet. Chem.* **1996**, *25*, 143–149.
34. Jones, C. *Organomet. Chem.* **2000**, *28*, 138–152.
35. Huang, Y.-Z.; Zhou, Z.-L. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Chapter 12.2.2.3, and references therein.
36. Serre, S. L.; Guillemin, J.-C.; Karpati, T.; Soos, L.; Nyulászi, L.; Veszprémi, T. *J. Org. Chem.* **1998**, *63*, 59–68.
37. Li, L.-H.; Chan, T. H. *Tetrahedron Lett.* **2000**, *41*, 5009–5012.
38. Davis, A. P.; Bhattarai, K. M. *Tetrahedron* **1995**, *51*, 8033–8042.
39. Zhang, L.-J.; Huang, Y.-Z. *J. Organomet. Chem.* **1993**, *454*, 101–103.
40. Suzuki, I.; Yamamoto, Y. *J. Org. Chem.* **1993**, *58*, 4783–4784.
41. Cho, C. S.; Motofusa, S.; Ohe, K.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2341–2348.
42. Matoba, K.; Motofusa, S.; Cho, C. S.; Ohe, K.; Uemura, S. *J. Organomet. Chem.* **1999**, *574*, 3–10.
43. Moiseev, D. V.; Morugova, V. A.; Gushchin, A. V.; Dodonov, V. A. *Tetrahedron Lett.* **2003**, *44*, 3155–3157.

43a. Moiseev, D. V.; Gushchin, A. V.; Morugova, V. A.; Dodonov, V. A. *Russ. Chem. Bull. (Engl. Transl.)* **2003**, *52*, 2081–2082.

44. Kakusawa, N.; Yamaguchi, K.; Kurita, J.; Tsuchiya, T. *Tetrahedron Lett.* **2000**, *41*, 4143–4146.
45. Kakusawa, N.; Tobiyasu, Y.; Yasuike, S.; Yamaguchi, K.; Seki, H.; Kurita, J. *Tetrahedron Lett.* **2003**, *44*, 8589–8592.
46. Kakusawa, N.; Tsuchiya, T.; Kurita, J. *Tetrahedron Lett.* **1998**, *39*, 9743–9746.
47. Ishihara, K.; Kuroki, Y.; Hanaki, N.; Ohara, S.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 1569–1570.
48. Kuroki, Y.; Ishihara, K.; Hanaki, N.; Ohara, S.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1221--1230.
49. Yasuike, S.; Okajima, S.; Yamaguchi, K.; Seki, H.; Kurita, J. *Tetrahedron: Asymmetry* **2000**, *11*, 4043–4047.

49a. Yasuike, S.; Okajima, S.; Yamaguchi, K.; Seki, H.; Kurita, J. *Tetrahedron* **2003**, *59*, 4959–4966.

50. Jiménez-Tenorio, M.; Puerta, M. C.; Salcedo, I.; Valerga, P.; Costa, S. I.; Gomes, P. T.; Mereiter, K. *Chem. Commun.* **2003**, 1168–1169.
51. Bonaterra, M.; Martín, S. E.; Rossi, R. A. *Org. Lett.* **2003**, *5*, 2731–2734.
52. Zhang, L. J.; Mo, X. S.; Huang, J. L.; Huang, Y.-Z. *Tetrahedron Lett.* **1993**, *34*, 1621–1624.

52a. Zhang, L. J.; Mo, X. S.; Huang, Y.-Z. *J. Organomet. Chem.* **1994**, *471*, 77–85.

53. Huang, Y.-Z.; Zhou, Z.-L. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Chapter 12.2.2.2, and references therein.
54. Fujiwara, M.; Hitomi, K.; Baba, A.; Matsuda, H. *Chem. Lett.* **1994**, 875–876.
55. Fujiwara, M.; Tanaka, M.; Baba, A.; Ando, H.; Souma, Y. *J. Organomet. Chem.* **1996**, *508*, 49–52.
56. Fujiwara, M.; Tanaka, M.; Baba, A.; Ando, H.; Souma, Y. *J. Organomet. Chem.* **1996**, *525*, 39–42.
57. Kang, S.-K.; Ryu, H.-C.; Lee, S.-W. *J. Organomet. Chem.* **2000**, *610*, 38–41.
58. Kang, S.-K.; Ryu, H.-C.; Hong, Y.-T. *J. Chem. Soc., Perkin Trans. 1* **2001**, 736–739.
59. Gushchin, A. V.; Moiseev, D. V.; Dodonov, V. A. *Russ. Chem. Bull. (Engl. Transl.)* **2001**, *50*, 1291–1294.

59a. Moiseev, D. V.; Gushchin, A. V.; Shavirin, A. S.; Kursky, Y. A.; Dodonov, V. A. *J. Organomet. Chem.* **2003**, *667*, 176–184.

60. Gushchin, A. V.; Moiseev, D. V.; Dodonov, V. A. *Russ. Chem. Bull. (Engl. Transl.)* **2002**, *51*, 1571–1575.
61. Gushchin, A. V.; Grunova, E. V.; Moiseev, D. V.; Morozov, O. S.; Shavyrin, A. S.; Dodonov, V. A. *Russ. Chem. Bull. (Engl. Transl.)* **2003**, *52*, 1376–1379.
62. Moiseev, D. V.; Morugova, V. A.; Gushchin, A. V.; Shavirin, A. S.; Kursky, Y. A.; Dodonov, V. A. *J. Organomet. Chem.* **2004**, *689*, 731–737.
63. Kang, S.-K.; Ryu, H.-C.; Hong, Y.-T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3350–3351.
64. Stolyarova, T. E.; Shavyrin, A. S.; Finet, J.-P.; Fedorov, A. Y. *Russ. Chem. Bull. (Engl. Transl.)* **2003**, *52*, 1736–1739.
65. Lermontov, S. A.; Shkavrov, S. V.; Lermontov, A. S.; Zavorin, S. I. *Russ. Chem. Bull. (Engl. Transl.)* **1998**, *47*, 1607–1609.
66. Fujiwara, M.; Tanaka, M.; Baba, A.; Ando, H.; Souma, Y. *Tetrahedron Lett.* **1995**, *36*, 4849–4852.
67. Fujiwara, M.; Tanaka, M.; Baba, A.; Ando, H.; Souma, Y. *Main Group Chem.* **1997**, *2*, 111.
68. Nitta, M.; Mitsumoto, Y.; Yamamoto, H. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1901–1907.
69. Huang, A.; Liu, X.; Li, H.; Wu, X.; Liu, W.; Liang, Y. *Adv. Synth. Catal.* **2004**, *346*, 599–602.
70. Nunes, R. L.; Bieber, L. W. *Tetrahedron Lett.* **2001**, *42*, 219–222.
71. Huang, Y.-Z.; Zhou, Z.-L. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Chapter 12.3.1.1.

71a. Chan, T. H.; Isaac, M. B. *Pure Appl. Chem.* **1996**, *68*, 919–924, and references therein.

72. Ren, P.-D.; Pan, S.-F.; Dong, T.-W.; Wu, S.-H. *Chin. J. Chem.* **1996**, *14*, 462–466.

72a. Ren, P.-D.; Shao, D.; Dong, T.-W. *Synth. Commun.* **1997**, *27*, 2569–2576.

73. Donnelly, S.; Thomas, E. J.; Fielding, M. *Tetrahedron Lett.* **2004**, *45*, 6779–6782.
74. Smith, K.; Lock, S.; El-Hiti, G. A.; Wada, M.; Miyoshi, N. *Org. Biomol. Chem.* **2004**, *4*, 935–938.
75. Wada, M.; Honna, M.; Kuramoto, Y.; Miyoshi, N. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2265–2267.
76. Wada, M.; Fukuma, T.; Morioka, M.; Takahashi, T.; Miyoshi, N. *Tetrahedron Lett.* **1997**, *38*, 8045–8048.

77. Bhuyan, P. J.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **1993**, *34*, 7975–7976.
78. Basile, T.; Bocoum, A.; Savoia, D.; Umani-Ronchi, A. *J. Org. Chem.* **1994**, *59*, 7766–7773.
79. Miyoshi, N.; Nishio, M.; Murakami, S.; Fukuyama, T.; Wada, M. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 689–692.
80. Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 8214–8219.
81. Shen, Z.; Zhang, J.; Zou, H.; Yang, M. *Tetrahedron Lett.* **1997**, *38*, 2733–2736.
82. Katritzky, A. R.; Allin, S. M. *Synth. Commun.* **1995**, *25*, 2751–2762.
83. Miyoshi, N.; Fukuma, T.; Wada, M. *Chem. Lett.* **1995**, 999–1000.
84. Baruah, B.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **1995**, *36*, 6747–6750.
85. Vidal, S. *Synlett* **2001**, 1194–1195.
86. Louër, M.; Le Roux, C.; Dubac, J. *Chem. Mater.* **1997**, *9*, 3012–3016.
86a. Labrouillère, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J.; Desmurs, J. R. *Tetrahedron Lett.* **1999**, *40*, 285–286.
86b. Répichet, S.; Zwick, A.; Vendier, L.; Le Roux, C.; Dubac, J. *Tetrahedron Lett.* **2002**, *43*, 993–995.
87. Le Roux, C.; Gaspard-Iloughmane, H.; Dubac, J.; Jaud, J.; Vignaux, P. *J. Org. Chem.* **1993**, *58*, 1835--1839.
87a. Le Roux, C.; Gaspard-Iloughmane, H.; Dubac, J. *Bull. Soc. Chim. Fr.* **1993**, *130*, 832–842.
87b. Peidro, L.; Le Roux, C.; Laporterie, A.; Dubac, J. *J. Organomet. Chem.* **1996**, *521*, 397–399.
88. Le Roux, C.; Gaspard-Iloughmane, H.; Dubac, J. *J. Org. Chem.* **1994**, *59*, 2238–2240.
89. Le Roux, C.; Ciliberti, L.; Laurent-Robert, H.; Laporterie, A.; Dubac, J. *Synlett* **1998**, 1249–1251.
90. Ollevier, T.; Nadeau, E. *J. Org. Chem.* **2004**, *69*, 9292–9295.
91. Komatsu, N.; Uda, M.; Suzuki, H.; Takahashi, T.; Domae, T.; Wada, M. *Tetrahedron Lett.* **1997**, *38*, 7215–7218.
92. Wada, M.; Takahashi, T.; Domae, T.; Fukuma, T.; Miyoshi, N.; Smith, K. *Tetrahedron: Asymmetry* **1997**, *8*, 3939–3946.
93. Wieland, L. C.; Zerth, H. M.; Mohan, R. S. *Tetrahedron Lett.* **2002**, *43*, 4597–4600.
94. Evans, P. A.; Cui, J.; Gharpure, S. J.; Hinkle, R. J. *J. Am. Chem. Soc.* **2003**, *125*, 11456–11457.
95. Leroy, B.; Markó, I. E. *Tetrahedron Lett.* **2001**, *42*, 8685–8688.
96. De, S. K.; Gibbs, R. A. *Tetrahedron Lett.* **2004**, *45*, 7407–7408.
97. Le Roux, C.; Dubac, J. *Organometallics* **1996**, *15*, 4646–4648.
98. Le Roux, C.; Mandrou, S.; Dubac, J. *J. Org. Chem.* **1996**, *61*, 3885–3887.
99. Baruah, B.; Boruah, A.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **1997**, *38*, 1449–1450.
100. Srivastava, N.; Banik, B. K. *J. Org. Chem.* **2003**, *68*, 2109–2114.
101. Garrigues, B.; Gonzaga, F.; Robert, H.; Dubac, J. *J. Org. Chem.* **1997**, *62*, 4880–4882.
101a. Garringues, B.; Oussaid, A. *J. Organomet. Chem.* **1999**, *585*, 253–255.
102. Laurent-Robert, H.; Le Roux, C.; Dubac, J. *Synlett* **1998**, 1138–1140.
102a. Robert, H.; Garrigues, B.; Dubac, J. *Tetrahedron Lett.* **1998**, *39*, 1161–1164.
103. Desmurs, J. R.; Labrouillère, M.; Le Roux, C.; Gaspard, H.; Laporterie, A.; Dubac, J. *Tetrahedron Lett.* **1997**, *38*, 8871–8874.
103a. Répichet, S.; Le Roux, C.; Dubac, J.; Desmurs, J.-R. *Eur. J. Org. Chem.* **1998**, 2743–2746.
104. Torisawa, Y.; Nishi, T.; Minamikawa, J. *Org. Process Res. Dev.* **2001**, *5*, 84–88.
105. Picot, A.; Répichet, S.; Le Roux, C.; Dubac, J.; Roques, N. *J. Fluorine Chem.* **2002**, *116*, 129–134.
106. Matsushita, Y.; Sugamoto, K.; Matsui, T. *Tetrahedron Lett.* **2004**, *45*, 4723–4727.
107. Mazieres, S.; Le Roux, C.; Peyronneau, M.; Gornitzka, H.; Roques, N. *Eur. J. Inorg. Chem.* **2004**, 2823–2826.
107a. Peyronneau, M.; Boisdon, M.-T.; Roques, N.; Mazieres, S.; Le Roux, C. *Eur. J. Org. Chem.* **2004**, 4636–4640.
108. Laporte, C.; Baulès, P.; Laporterie, A.; Desmus, J.-R.; Dubac, J. *C. R. Acad. Sci., Ser. iic* **1998**, *1*, 141–150.
108a. Laporte, C.; Marquié, J.; Laporterie, A.; Desmus, J.-R.; Dubac, J. *C. R. Acad. Sci., Ser. iic* **1999**, *2*, 455–465.
109. Gmouh, S.; Yang, H.; Vaultier, M. *Org. Lett.* **2003**, *5*, 2219–2222.
110. Bhatia, K. A.; Eash, K. J.; Leonard, N. M.; Oswald, M. C.; Mohan, R. S. *Tetrahedron Lett.* **2001**, *42*, 8129–8132.
111. Anderson, A. M.; Blazek, J. M.; Garg, P.; Payne, B. J.; Mohan, R. S. *Tetrahedron Lett.* **2000**, *41*, 1527–1530.
112. Sabitha, G.; Reddy, E. V.; Yadav, J. S. *Synthesis* **2001**, 1979–1984.
112a. Sabitha, G.; Reddy, E. V.; Maruthi, C.; Yadav, J. S. *Tetrahedron Lett.* **2002**, *43*, 1573–1575.
113. Monk, K. A.; Sarapa, D.; Mohan, R. S. *Synth. Commun.* **2000**, *30*, 3167–3170.
114. Yadav, J. S.; Reddy, B. V. S.; Parimala, G.; Raju, A. K. *Tetrahedron Lett.* **2004**, *45*, 1543–1546.
115. Ohe, T.; Tanaka, T.; Kuroda, M.; Cho, C. S.; Ohe, K.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1851–1855.
116. Cho, C. S.; Yoshimori, Y.; Uemura, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 950–957.
117. Rao, M. L. N.; Yamazaki, O.; Shimada, S.; Tanaka, T.; Suzuki, Y.; Tanaka, M. *Org. Lett.* **2001**, *3*, 4103–4105.
118. Rao, M. L. N.; Shimada, S.; Tanaka, M. *Org. Lett.* **1999**, *1*, 1271–1273.
119. Shimada, S.; Yamazaki, O.; Tanaka, T.; Rao, M. L. N.; Suzuki, Y.; Tanaka, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 1845–1848.
120. Yamazaki, O.; Tanaka, T.; Shimada, S.; Suzuki, Y.; Tanaka, M. *Synlett* **2004**, 1921–1924.
121. Venkatraman, S.; Li, C.-J. *Tetrahedron Lett.* **2001**, *42*, 781–784.
122. Huang, T.-S.; Li, C.-J. *Org. Lett.* **2001**, *3*, 2037–2039.
123. Huang, T.; Meng, Y.; Venkatraman, S.; Wang, D.; Li, C.-J. *J. Am. Chem. Soc.* **2001**, *123*, 7451–7452.
124. Nishikawa, T.; Yamamoto, Y.; Miyaura, N. *Chem. Commun.* **2004**, 1822–1823.
125. Kang, S.-K.; Ryu, H.-C.; Hong, Y.-T.; Kim, M.-S.; Lee, S.-W.; Jung, J.-H. *Synth. Commun.* **2001**, *31*, 2365–2371.
126. Ding, R.; Ge, C.-S.; Chen, Y.-J.; Wang, D.; Li, C.-J. *Tetrahedron Lett.* **2002**, *43*, 7789–7791.
127. Orita, A.; Tanahashi, C.; Kakuda, A.; Otera, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 2877–2879.
127a. Orita, A.; Tanahashi, C.; Kakuda, A.; Otera, J. *J. Org. Chem.* **2001**, *66*, 8926–8934.
128. Mohammadpoor-Baltork, I.; Khosropour, A. R.; Aliyan, H. *J. Chem. Res., Synop.* **2001**, 280–282.
128a. Mohammadpoor-Baltork, I.; Aliyan, H.; Khosropour, A. R. *Tetrahedron* **2001**, *57*, 5851–5854.
129. Carrigan, M. D.; Freiberg, D. A.; Smith, R. C.; Zerth, H. M.; Mohan, R. S. *Synthesis* **2001**, 2091–2093.
130. Carrigan, M. D.; Eash, K. J.; Oswald, M. C.; Mohan, R. S. *Tetrahedron Lett.* **2001**, *42*, 8133–8135.
130a. Aggen, D. H.; Arnold, J. N.; Hayes, P. D.; Smoter, N. J.; Mohan, R. S. *Tetrahedron* **2004**, *60*, 3675–3679.
131. Ghosh, R.; Maiti, S.; Chakraborty, A. *Tetrahedron Lett.* **2004**, *45*, 6775–6778.
132. Jousseaume, B.; Laporte, C.; Toupance, T.; Bernard, J.-M. *Tetrahedron Lett.* **2002**, *43*, 6305–6307.
133. Keramane, E.-M.; Boyer, B.; Roque, J.-P. *Tetrahedron Lett.* **2001**, *42*, 855–857.

134. Komatsu, N.; Ishida, J.; Suzuki, H. *Tetrahedron Lett.* **1997**, *38*, 7219–7222.
134a. Komatsu, N.; Chishiro, T. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1532–1537.
135. Wada, M.; Nagayama, S.; Mizutani, K.; Hiroi, R.; Miyoshi, N. *Chem. Lett.* **2002**, 248–249.
136. Boyer, B.; Keramane, E.-M.; Roque, J.-P.; Pavia, A. A. *Tetrahedron Lett.* **2000**, *41*, 2891–2894.
136a. Keramane, E. M.; Boyer, B.; Roque, J.-P. *Tetrahedron* **2001**, *57*, 1917–1921.
137. Mohammadpoor-Baltork, I.; Tangestaninejad, S.; Aliyan, H.; Mirkhani, V. *Synth. Commun.* **2000**, *30*, 2365–2374.
138. Oussaid, A.; Boukherroub, R.; Dejean, V.; Garrigues, B. *Phosphorus Sulfur Silicon* **2000**, *167*, 81–92.
138a. Ollevier, T.; Lavie-Compin, G. *Tetrahedron Lett.* **2004**, *45*, 49–52.
139. Laurent-Robert, H.; Garrigues, B.; Dubac, J. *Synlett* **2000**, 1160–1162.
140. Motorina, I. A.; Grierson, D. S. *Tetrahedron Lett.* **1999**, *40*, 7215–7218.
141. Leonard, N. M.; Oswald, M. C.; Freiberg, D. A.; Nattier, B. A.; Smith, R. C.; Mohan, R. S. *J. Org. Chem.* **2002**, *67*, 5202–5207.
142. Komatsu, N.; Uda, M.; Suzuki, H. *Synlett* **1995**, 984–986.
143. Le Boisselier, V.; Postel, M.; Duñach, E. *Chem. Commun.* **1997**, 95–96.
144. Yadav, J. S.; Reddy, B. V. S.; Swamy, T.; Rao, K. R. *Tetrahedron Lett.* **2004**, *45*, 6037–6039.
145. Répichet, S.; Le Roux, C.; Hernandez, P.; Dubac, J.; Desmurs, J.-R. *J. Org. Chem.* **1999**, *64*, 6479–6482.
145a. Répichet, S.; Le Roux, C.; Dubac, J. *Tetrahedron Lett.* **1999**, *40*, 9233–9234.
145b. Marquié, J.; Laporterie, A.; Dubac, J.; Roque, J.-P.; Desmurs, J.-R. *J. Org. Chem.* **2001**, *66*, 421–425.
146. Baruah, M.; Boruah, A.; Prajapati, D.; Sanghu, J. S. *Synlett* **1998**, 1083–1084.
147. Lu, G.; Zhang, Y. *Synth. Commun.* **1998**, *28*, 4479–4484.
148. Zhan, Z.; Lu, G.; Zhang, Y. *J. Chem. Res., Synop.* **1999**, 280–281.
149. Ramalinga, K.; Vijayalakshmi, P.; Kaimal, T. N. B. *Synlett* **2001**, 863–865.
150. Khosropour, A. R.; Khodaei, M. M.; Kookhazadeh, M. *Tetrahedron Lett.* **2004**, *45*, 1725–1728.
151. Boyer, B.; Keramane, E. M.; Montero, J.-L.; Roque, J.-P. *Synth. Commun.* **1998**, *28*, 1737–1741.
152. Labrouillére, M.; Le Roux, C.; Gaspard-Iloughmane, H.; Dubac, J. *Synlett* **1994**, 723–724.
153. Keramane, E. M.; Boyer, B.; Roque, J.-P. *Tetrahedron* **2001**, *57*, 1909–1916.
154. Boyer, B.; Keramane, E. M.; Arpin, S.; Montéro, J.-L.; Roque, J.-P. *Tetrahedron* **1999**, *55*, 1971–1976.
155. Banfi, A.; Bartoletti, M.; Bellora, E.; Bignotti, M.; Turconi, M. *Synthesis* **1994**, 775–776.
156. Vassileva, E.; Shopova, M.; Fugier, C.; Basch, E. H. *Synth. Commun.* **1997**, *27*, 1669–1675.
157. Naito, R.; Takeuchi, M.; Morihira, K.; Hayakawa, M.; Ikeda, K.; Shibanuma, T.; Isomura, Y. *Chem. Pharm. Bull.* **1998**, *46*, 1274–1285.
158. Aoki, Y.; Saito, Y.; Sakamoto, T.; Kikugawa, Y. *Synth. Commun.* **2000**, *30*, 131–140.
159. Loog, O.; Mäeorg, U.; Ragnarsson, U. *Synthesis* **2000**, 1591–1597.
160. Fukuda, Y.; Furuta, H.; Kusama, Y.; Ebisu, H.; Oomori, Y.; Terashima, S. *Heterocycles* **1998**, *49*, 53–58.
161. Meigh, J.-P.; Álvarez, M.; Joule, J. A. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2012–2021.
162. Chan, D. M. T. *Tetrahedron Lett.* **1996**, *37*, 9013–9016.
163. Tsubrik, O.; Mäeorg, U.; Sillard, R.; Ragnarsson, U. *Tetrahedron* **2004**, *60*, 8363–8373.
164. Sorenson, R. J. *J. Org. Chem.* **2000**, *65*, 7747–7749.
165. Brown, R. J.; Annis, G.; Casalnuovo, A.; Chan, D.; Shapiro, R.; Marshall, W. J. *Tetrahedron* **2004**, *60*, 4361–4375.
166. Dodonov, V. A.; Starostina, T. I.; Belukhina, E. V.; Vorob'eva, N. V. *Russ. Chem. Bull. (Engl. Transl.)* **1993**, *42*, 2023–2025.
167. Sheppard, G. S. *Synlett* **1999**, 1207–1210.
168. Arnauld, T.; Barton, D. H. R.; Normant, J.-F. *J. Org. Chem.* **1999**, *64*, 3722–3725.
169. Dodonov, V. A.; Zaburdaeva, E. A.; Dolganova, N. V.; Stepovik, L. P.; Zinov'eva, T. I. *Russ. J. Gen. Chem. (Engl. Transl.)* **1997**, *67*, 927–931.
170. Ren, P.-D.; Pan, S.-F.; Dong, T.-W.; Wu, S.-H. *Synth. Commun.* **1995**, *25*, 3395–3399.
170a. Ren, P.-D.; Pan, S.-F.; Dong, T.-W.; Wu, S.-H. *Synth. Commun.* **1996**, *26*, 763–767.
170b. Ren, P.-D.; Jin, Q.-H.; Yao, Z.-P. *Synth. Commun.* **1997**, *27*, 2577–2581.
171. Borah, H.; Prajapati, D.; Sandhu, J. S. *J. Chem. Res. Synop.* **1994**, 228–229.
172. Ogawa, T.; Hikasa, T.; Ikegami, T.; Ono, N.; Suzuki, H. *Chem. Lett.* **1993**, 815–818.
172a. Ogawa, T.; Hikasa, T.; Ikegami, T.; Ono, N.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3473–3478.
172b. Ogawa, T.; Yoshikawa, A.; Wada, H.; Ogawa, C.; Ono, N.; Suzuki, H. *J. Chem. Soc., Chem. Commun.* **1995**, 1407.
173. Habata, Y.; Fujishiro, F.; Akabori, S. *J. Chem. Soc., Perkin Trans. 1* **1996**, 953–957.
174. Combes, S.; Finet, J.-P. *Tetrahedron* **1999**, *55*, 3377–3386.
175. Fedorov, A. Y.; Finet, J.-P. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3775–3778.
176. Fedorov, A.; Combes, S.; Finet, J.-P. *Tetrahedron* **1999**, *55*, 1341–1352.
177. Fornicola, R. S.; Oblinger, E.; Montgomery, J. *J. Org. Chem.* **1998**, *63*, 3528–3529.
178. Arnauld, T.; Barton, D. H. R.; Normant, J.-F.; Doris, E. *J. Org. Chem.* **1999**, *64*, 6915–6917.
179. Koech, P. K.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 5350–5351.
180. Finet, J.-P.; Fedorov, A. Y. *Russ. Chem. Bull. (Engl. Transl.)* **2004**, *53*, 1488–1495.
181. Ooi, T.; Goto, R.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 10494–10495.
182. Vilardo, J. S.; Thorn, M. G.; Fanwick, P. E.; Rothwell, I. P. *Chem. Commun.* **1998**, 2425–2426.
182a. Riley, P. N.; Thorn, M. G.; Vilardo, J. S.; Lockwood, M. A.; Fanwick, P. E.; Rothwell, I. P. *Organometallics* **1999**, *18*, 3016–3024.
183. Bolshakov, A. V.; Ganina, O. G.; Shavirin, A. S.; Kurskii, Y. A.; Finet, J.-P.; Fedorov, A. Y. *Tetrahedron Lett.* **2002**, *43*, 8245–8248.
184. Matano, Y.; Azuma, N.; Suzuki, H. *Tetrahedron Lett.* **1993**, *34*, 8457–8460.
184a. Matano, Y.; Azuma, N.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1739–1747.
185. Matano, Y.; Yoshimune, M.; Suzuki, H. *Tetrahedron Lett.* **1995**, *36*, 7475–7478.
186. Matano, Y.; Imahori, H. *J. Org. Chem.* **2004**, *69*, 5505–5508.
187. Matano, Y.; Yoshimune, M.; Azuma, N.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1971–1977.
188. Matano, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2703–2709.
189. Matano, Y.; Yoshimune, M.; Suzuki, H. *J. Org. Chem.* **1995**, *60*, 4663–4665.
190. Matano, Y.; Suzuki, H. *Chem. Commun.* **1996**, 2697–2698.
190a. Rahman, M. M.; Matano, Y.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1533–1542.
191. Rahman, M. M.; Matano, Y.; Suzuki, H. *Chem. Commun.* **1998**, 1359–1360.

192. Rahman, M. M.; Matano, Y.; Suzuki, H. *Synthesis* **1999**, 395–397.
193. Kang, S.-K.; Ryu, H.-C.; Lee, S.-W. *Synth. Commun.* **2001**, *31*, 1027–1034.
194. Kang, S.-K.; Ryu, H.-C.; Kim, J.-W. *Synth. Commun.* **2001**, *31*, 1021–1026.
195. Lermontov, S. A.; Rakov, I. M.; Zefirov, N. S.; Stang, P. J. *Tetrahedron Lett.* **1996**, *37*, 4051–4054.
196. Harada, T.; Ueda, S.; Yoshida, T.; Inoue, A.; Takeuchi, M.; Ogawa, N.; Oku, A.; Shiro, M. *J. Org. Chem.* **1994**, *59*, 7575–7576.
197. Dodonov, V. A.; Starostina, T. I.; Kuznetsova, Y. L.; Gushchin, A. V. *Russ. Chem. Bull. (Engl. Transl.)* **1995**, *44*, 151.
198. Coles, S. J.; Costello, J. F.; Hursthouse, M. B.; Smith, S. *J. Organomet. Chem.* **2002**, *662*, 98–104.
199. Brunner, H.; Chuard, T. *Monatsh. Chem.* **1994**, *125*, 1293–1300.
200. Sinclair, P. J.; Wong, F.; Wyvratt, M.; Staruch, M. J.; Dumont, F. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 1035–1038.
201. Sinclair, P. J.; Wong, F.; Staruch, M. J.; Wiederrecht, G.; Parsons, W. H.; Dumont, F.; Wyvratt, M. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2193–2196.
202. Jos Brands, K. M.; Dolling, U.-H.; Jobson, R. B.; Marchesini, G.; Reamer, R. A.; Williams, J. M. *J. Org. Chem.* **1998**, *63*, 6721–6726.
203. Fedorov, A. Y.; Finet, J.-P. *Tetrahedron Lett.* **1999**, *40*, 2747–2748.
204. Boyer, G.; Galy, J. P.; Barbe, J. *Heterocycles* **1995**, *41*, 487–496.
205. Fan, P.; Ablordeppey, S. Y. *J. Heterocycl. Chem.* **1997**, *34*, 1789–1794.
206. Tsubrik, O.; Mäeorg, U.; Ragnarsson, U. *Tetrahedron Lett.* **2002**, *43*, 6213–6215.
207. Chatel, F.; Boyer, G.; Galy, J.-P. *Synth. Commun.* **2002**, *32*, 2893–2901.
208. Miloudi, A.; El-Abed, D.; Boyer, G.; Finet, J.-P.; Galy, J. P.; Siri, D. *Eur. J. Org. Chem.* **2004**, 1509–1516.
209. Arnauld, T.; Barton, D. H. R.; Doris, E. *Tetrahedron* **1997**, *53*, 4137–4144.
210. Anderson, J. C.; Harding, M. *Chem. Commun.* **1998**, 393–394.
210a. Anderson, J. C.; Cubbon, R.; Harding, M.; James, S. D. *Tetrahedron: Asymmetry* **1998**, *9*, 3461–3490.
211. Balsamini, C.; Bedini, A.; Spadoni, G.; Tarzia, G.; Tontini, A.; Balduini, W.; Cimino, M. *Il Farmaco* **1998**, *53*, 181–188.
212. Combes, S.; Finet, J.-P. *Tetrahedron* **1998**, *54*, 4313–4318.
213. Rasmussen, L. K.; Begtrup, M.; Ruhland, T. *J. Org. Chem.* **2004**, *69*, 6890–6893.
214. Matano, Y.; Azuma, N.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2543–2549.
215. Matano, Y.; Rahman, M. M.; Yoshimune, M.; Suzuki, H. *J. Org. Chem.* **1999**, *64*, 6924–6927.
216. Matano, Y. *Organometallics* **2000**, *19*, 2258–2263.
217. Matano, Y. *Chem. Commun.* **2000**, 2233–2234.
218. Matano, Y.; Nomura, H.; Suzuki, H. *J. Organomet. Chem.* **2000**, *611*, 89–99.
219. Nitta, M.; Mitsumoto, Y. *Heterocycles* **2001**, *55*, 629–633.
220. Miyake, Y.; Iwata, T.; Chung, K.-G.; Nishibayashi, Y.; Uemura, S. *Chem. Commun.* **2001**, 2584–2585.
220a. Iwata, T.; Miyake, Y.; Nishibayashi, Y.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1548–1554.
221. Clive, D. L. J.; Kong, X.; Paul, C. C. *Tetrahedron* **1996**, *52*, 6085–6116.
222. Huang, Y.-Z.; Zhou, Z.-L. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995. 12.3.2.1, and references therein.
223. Matano, Y.; Nomura, H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3028–3031.
224. Matano, Y.; Hisanaga, T.; Yamada, H.; Kusakabe, S.; Nomura, H.; Imahori, H. *J. Org. Chem.* **2004**, *69*, 8676–8680.
225. Suzuki, H.; Ikegami, T. *J. Chem. Res. Synop.* **1996**, 24–25.
226. Matano, Y.; Nomura, H.; Shiro, M.; Suzuki, H. *Organometallics* **1999**, *18*, 2580–2582.
226a. Matano, Y.; Nomura, H.; Suzuki, H.; Shiro, M.; Nakano, H. *J. Am. Chem. Soc.* **2001**, *123*, 10954–10965.
227. Mitsumoto, Y.; Nitta, M. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 1029–1034.
228. Suzuki, H.; Ikegami, T.; Matano, Y. *Tetrahedron Lett.* **1994**, *35*, 8197–8200.
229. Matano, Y.; Nomura, H. *J. Am. Chem. Soc.* **2001**, *123*, 6443–6444.
230. Matano, Y.; Nomura, H.; Hisanaga, T.; Nakano, H.; Shiro, M.; Imahori, H. *Organometallics* **2004**, *23*, 2471–5480.
231. Dolganova, N. V.; Dodonov, V. A.; Zinov'eva, T. I.; Prezhbog, I. G. *Russ. Chem. Bull. (Engl. Transl.)* **1997**, *46*, 1164.
232. Ikegami, T.; Suzuki, H. *Organometallics* **1998**, *17*, 1013–1017.
233. Zinov'eva, T. I.; Dolganova, N. V.; Dodonov, V. A.; Prezhbog, I. G. *Russ. Chem. Bull. (Engl. Transl.)* **1998**, *47*, 659–662.
234. Dodonov, V. A.; Zinov'eva, T. I.; Dolganova, N. V. *Russ. Chem. Bull. (Engl. Transl.)* **1995**, *44*, 764.
235. Ménard, C.; Doris, E.; Mioskowski, C. *Tetrahedron Lett.* **2003**, *44*, 6591–6593.
236. Dorta, R. L.; Suárez, E.; Betancor, C. *Tetrahedron Lett.* **1994**, *35*, 5035–5038.
237. Suzuki, H.; Nakaya, C.; Matano, Y. *Tetrahedron Lett.* **1993**, *34*, 1055–1056.

9.11 Selenium

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9.11.1 Introduction and General Aspects

Selenium was discovered in 1817 by Berzelius in the sludge of the lead chambers of the sulfuric acid chamber process of a plant at Gripsholm in Sweden.[1] Organoselenium compounds have been known since 1847, when Wöhler and Siemens reported the synthesis of ethyl selenol.[2] Other early examples include alkyl selenides, selenoxides as well as diselenides, but some of these compounds are unstable, highly malodorous, and unpleasant to handle. In 1929, the first patent on the use of selenium dioxide in oxidation reactions appeared,[3] but most organic chemists were not interested in selenium chemistry due to the properties of organoselenium compounds. After the discovery of the toxic properties of selenium (>5–15 mg kg^{-1}) and the fact that selenium is an essential trace element in the diet and plays an important role in living systems, the interest in the chemistry of selenium grew. In 1973, selenocysteine, the 21st essential amino acid, was discovered in the active site of glutathione peroxidase, an important enzyme in the thiol metabolism and responsible for the destruction of peroxides and oxygen radicals.[4,5] A first extensive overview by Klayman and Günther appeared in 1973 at a time when organic chemists had just realized the potential of selenium reagents and compounds for organic synthesis.[6] Up to that time, selenium-based reagents were not popular in organic synthesis; only selenium dioxide,[7] a reagent which is also used for the purification of selenium due to its volatility,[8] with oxidizing properties,[9] and elemental selenium as a dehydrating agent were used by organic chemists for synthetic purposes. In the early 1970s it became obvious after initial observations[10,11] that the *syn*-elimination of selenoxides is a powerful method for the generation of carbon–carbon double bonds and systematic investigations followed the initial findings.[12–16] The required selenoxides were easily available by oxidation of the corresponding selenides, which were accessible by using either nucleophilic or electrophilic selenium species with appropriate

organic substrates. First conference reports on different aspects of selenium chemistry were published[17] and this pioneering work can be regarded as the start of various investigations in the field of organoselenium chemistry. Since that time many selenium-containing reagents and a variety of different selenium-based reactions have been discovered and many of them have found their way into the repertoire of organic chemists.

This chapter concentrates on the developments in organoselenium chemistry from 1993 to 2004 and is therefore a continuation and extention of the chapter "Selenium" by Krief in the previous edition of *Comprehensive Organometallic Chemistry*.[18] During that period many aspects of organoselenium chemistry have been covered in review articles[19–35] and in books completely devoted to different areas of selenium.[36–40] These reports highlight the current activities in selenium chemistry and stress the importance of selenium-containing molecules in different areas.

The physical properties of selenium-containing compounds and structural aspects of these molecules are described in various publications[6,41–44] and are beyond the coverage of this chapter. The various structures of organoselenium compounds are closely related to their sulfur analogs, but their properties are often quite different. Different bond lengths and bond strengths as well as differences in electronic behavior account for the difference in reactivity compared with homologous organochalcogen compounds. Sometimes reactions are possible which cannot be performed with organosulfur or organotellurium compounds. Certain features make selenium compounds therefore particularly valuable for organic chemists. Selenium forms weaker σ-bonds than sulfur and many reactions which involve the cleavage of such bonds are faster as with analogous sulfur compounds and proceed under milder reaction conditions. The selenoxide moiety is more strongly polarized than the corresponding sulfoxides; therefore, selenoxide eliminations are much faster and proceed at room temperature or below, whereas sulfoxide eliminations require elevated temperatures. Typically, the selenoxide elimination is faster than the elimination of the corresponding sulfoxides. Also sigmatropic rearrangements proceed at lower temperatures. Although the strength of the carbon–selenium double bond is comparable to the carbon–sulfur double bond, the relatively poor π-overlap in the C═Se bond makes these compounds more reactive.

Selenium electrophiles have relatively low-lying LUMOs and are therefore powerful reagents for the addition of the selenium moiety to alkenes together with another nucleophile. This process is advantageous when alkenes bearing internal nucleophiles are used, as the products of such selenocyclizations are very valuable building blocks in organic synthesis. The recent advances using this methodology are described in Section 9.11.2.1.

Selenium nucleophiles are usually less basic and more nucleophilic than the corresponding sulfur compounds. This unique property has been recognized in 1973 by K. B. Sharpless and used for the conversion of epoxides into allylic alcohols.[12] This publication can be regarded as another milestone in organoselenium chemistry. The potential for introducing selenium into a range of electrophilic substrates and applications in organic synthesis are highlighted in Section 9.11.2.2.

Besides the use of electrophilic or nucleophilic selenium reagents in synthesis, selenium has another advantage. It can stabilize adjacent carbanions or carbocations. While the deprotonation of selenides is difficult, the corresponding diselenoacetals can be used as efficient precursors through the cleavage of one of the carbon–selenium bonds. The chemistry of selenium-stabilized carbanions and carbocations is outlined in Section 9.11.2.3.

The homolytic cleavage of the carbon–selenium bond provides an easy access to radicals, which can undergo various subsequent reactions. The plethora of radical chemistry is accessible using selenium-containing compounds and examples of free-radical reactions are described in Section 9.11.2.4.

As already mentioned, the *syn*-elimination of selenoxides was discovered around 1970[10] and had a major impact on the development of organoselenium chemistry. This reaction is about three orders of magnitude more rapid than the elimination of the corresponding less polar and less basic sulfoxides. Sigmatropic rearrangements proceed at markedly lower temperatures. These reactions are discussed in detail in Section 9.11.2.5.

Selenium is more easily oxidized to selenium(IV), but the oxidation stage selenium(VI) is obtained with more difficulty than with the corresponding sulfur compounds. For example, selenuranes (tetravalent selenium compounds) are more easily obtained than the sulfur analogs. The synthesis as well as the chemistry of selected examples with selenium at higher oxidation stages is reviewed in Section 9.11.2.6.

The higher reactivity of organoselenium derivatives versus the corresponding sulfur or oxygen analogs can also be observed in the various reactions of compounds containing the selenocarbonyl unit. Interesting and versatile reactions are possible and highlights of this chemistry are summarized in Section 9.11.2.7. Organoselenium compounds have different electronic properties than the corresponding sulfur compounds. There is an increasing use of these compounds as ligands in metal-catalyzed reactions, but their use as catalysts in a variety of reactions is also under current investigation. This active area of research is summarized in Section 9.11.2.8.

9.11.2 Organoselenium Chemistry

The selenium atom in organoselenium compounds can be incorporated in various structures and the selenium atom can possess oxidation states from −2 to +6. Some representative structures are listed in Figure 1. The success of synthetic transformations involving organoselenium compounds is due to the high selectivities obtained with these molecules.

9.11.2.1 Electrophilic Selenium

Well before the wide use of organoselenium compounds in chemistry, it was discovered that electrophilic selenium compounds of the type RSeX add stereospecifically to alkenes.[45] Since that time this reaction has been an important tool in the portfolio of organic chemists and has been used even for the construction of complex molecules. Comprehensive reviews on this chemistry have appeared[46–49] and in recent times the synthesis of chiral selenium electrophiles and their application in asymmetric synthesis has emerged.[25,27,28,28a] As shown in Scheme 1, the addition reactions of selenium electrophiles to alkenes are stereospecific *anti* additions. They involve the initial formation of seleniranium ion intermediates **1** which are immediately opened in the presence of nucleophiles. External nucleophiles lead to the formation of addition products **2**. The addition to unsymmetrically substituted alkenes follows the thermodynamically favored Markovnikov orientation. The seleniranium ion intermediates of alkenes with internal nucleophiles such as **3** will be attacked intramolecularly to yield cyclic products **4** and **5** via either an *endo* or an *exo* pathway. Depending on the reaction conditions, the formation of the seleniranium ions can be reversible.

There are various ways to generate and synthesize selenium electrophiles and some of these compounds are commercially available. The addition reaction can also be dependent on the counterion X of these reagents and several protocols have been developed to exchange the counterions. The most commonly used electrophile is the phenylselenyl electrophile and compounds like phenylselenenyl chloride **6** and phenylselenenyl bromide **7** are commercially available. They can also be easily generated from diphenyl diselenide **8** by treatment with sulfuryl chloride or elementary chlorine or bromine, respectively. Diselenides in general are very versatile precursors for selenium electrophiles. For addition reactions using external nucleophiles the use of selenenyl halides can lead to complications, because chloride or bromide ions can also act as nucleophiles and lead to undesired side-products. An

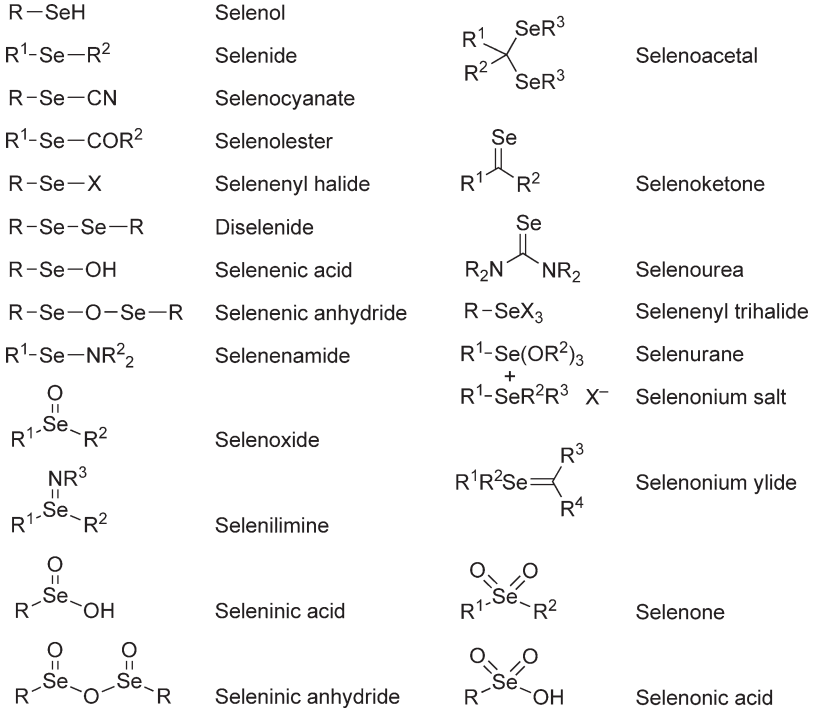
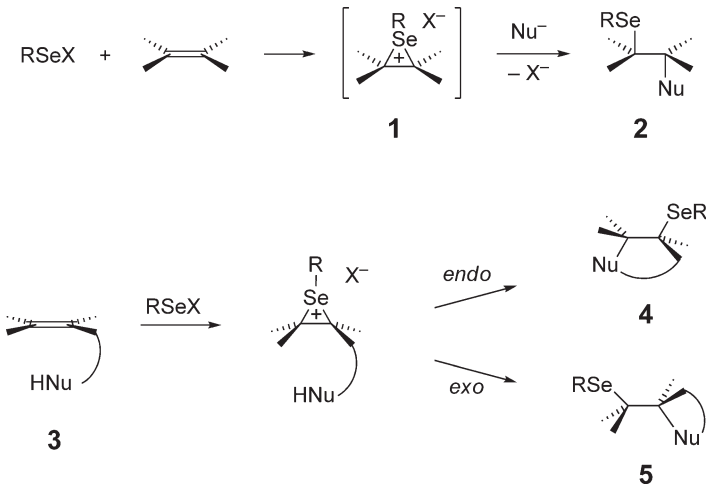


Figure 1 Different organoselenium compounds.



Scheme 1

exchange to less nucleophilic counterions is often necessary. Therefore, a range of different selenium electrophiles like *N*-(phenylseleno)phthalimide **9**,[50,51] phenylselenenyl tetrafluoroborate **10**, phenylselenenyl hexafluoroantimonate **11**,[52] phenylselenenyl hexafluorophosphate **12**,[52] phenylselenenyl triflate **13**,[53–55] phenylselenenyl sulfate **14**,[56,57] and phenylselenenyl tosylate **15**[58,59] have been synthesized and used successfully in many addition reactions to unsaturated systems (Figure 2). The choice of the reagent is dependent on the requirements of the particular transformation. Most widely used are the phenylselenenyl triflate **13** and the phenylselenenyl sulfate **14**, although the latter cannot be employed at very low temperatures (below −30 °C).

Diphenyl diselenide can also be used together with oxidizing reagents to generate selenium electrophiles. Several oxidants like potassium nitrate,[56,57,60] copper sulfate,[56,57] cerium ammonium nitrate (CAN),[56,57,61] manganese(III)acetate,[62] nitrogen dioxide,[63] 2-nitrobenzenesulfonyl peroxide,[64,65] (diacetoxy)iodobenzene,[66] and bis(trifluoroacetoxy) iodobenzene[67] have been used to generate phenylselenenylating reagents. Furthermore, the phenylselenyl cation can also be generated by photosensitized single electron transfer.[68–70] Several research groups are involved with the development of chiral, non-racemic selenium electrophiles. Some examples of optically active diselenides as precursors for the selenium electrophiles are shown in Figure 3.

The first stereoselective selenenylation reactions were reported using the binaphthyl-based diselenide **16** as the reagent precursor.[71–76] After that, several other diselenides have been prepared; initial attempts used quite long syntheses to obtain these compounds, for example, the C_2 symmetrical diselenides **17**[77–79] and **23**[80] and the mannose-derived diselenide **18**.[81–84] The ferrocenyl-based diselenide **19**[85–89] is using expensive starting materials and in 1995 more simple and easy accessible diselenides like **20** and **21** have been described in literature.[90–93] Camphor-based diselenides such as **22**[94–98] have been prepared and, based on the success of diselenides **20** and **21**, structural variants **24**[99,100] and diselenides with different coordinating heteroatoms such as sulfur and selenium **25**[101–108] and **26**[109] have been described recently.

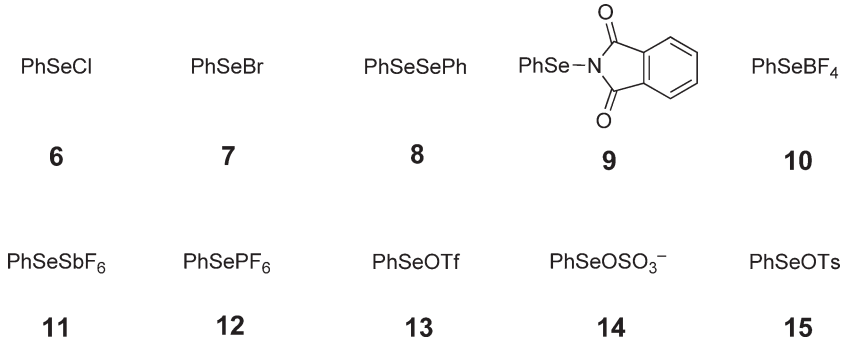


Figure 2 Various phenylselenyl electrophiles.

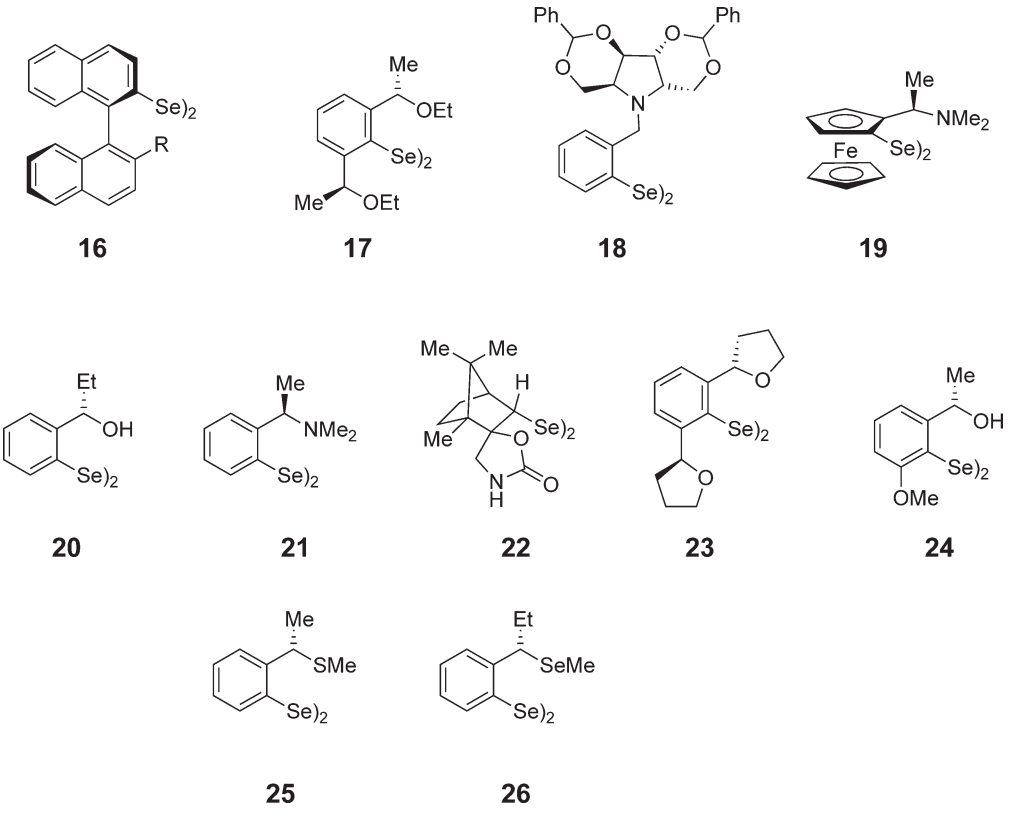
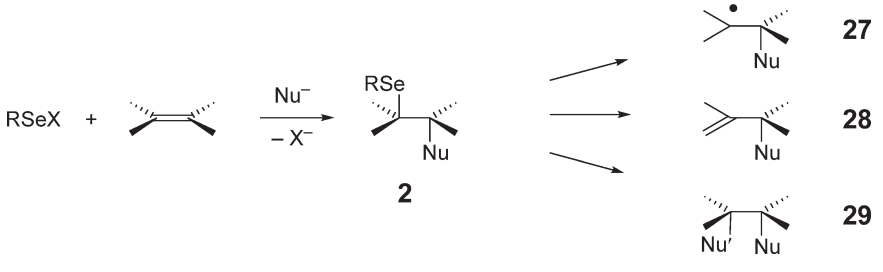


Figure 3 Selected chiral diselenides as precursors for the corresponding selenium electrophiles.

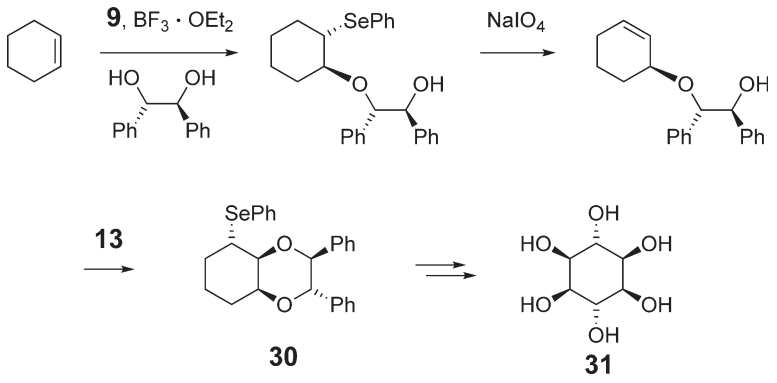
Additions of selenium electrophiles to double bonds have most frequently been used as part of a synthetic sequence, because the addition products are very versatile building blocks in synthesis. They can undergo a variety of subsequent transformations and can, therefore, serve as precursors for the generation of radicals **27** in radical reactions. Using a selenoxide elimination, new double bonds as shown in **28** can be generated. After oxidation of the selenide to the seleneone the selenium moiety can be replaced by a second nucleophile to generate compounds of type **29** (Scheme 2).

Various nucleophiles have been used in these addition reactions. Most prominent are oxygen nucleophiles and the stereospecific *anti*-addition of an organoselenium moiety and nucleophiles such as OH, OR, OCOR are very useful and this general reaction is covered in most of the reviews.[25,27,28,28a,38,39,41,46,47] An interesting application of an oxyselenenylation is the synthesis of biologically important cyclitols. The sequential use of two oxyselenenylations led to derivative **30**, which was converted to **31** in several steps using again the selenium-based elimination reaction to functionalize the remaining carbon atoms of the cyclohexyl moiety (Scheme 3).[110,111]

But due to the importance of nitrogen functional groups, the addition reactions of selenium electrophiles to alkenes using nitrogen nucleophiles represent another synthetically relevant process. Nitriles have been used as versatile



Scheme 2



Scheme 3

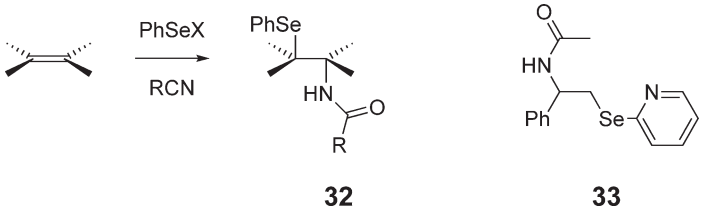
nucleophiles in this reaction which are, after hydrolytic workup, converted into the corresponding amides **32**.[112–114] But, other nitrogen-containing nucleophiles such as carbamates[115] or tosylamides[116] can be employed as well. In some cases, it was necessary to replace the phenylselenium electrophile with the more reactive 2-pyridylselenium electrophile in order to obtain reasonable yields of products such as **33** (using styrene and acetonitrile) in these reactions (Scheme 4).[117]

Azidoselenenylations are known as well; in these reactions, the azide ion serves as a nitrogen nucleophile.[118–120] The resulting azides can then be used for further transformations to modify the nitrogen functionality. Under certain reaction conditions, however, a radical reaction pathway is possible leading to non-stereospecific addition products.[121]

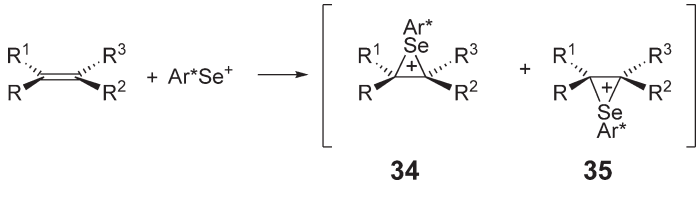
Carbon nucleophiles have been used with very limited success, but in the intramolecular version there are several examples of successful reactions.

All these reactions have also been performed using the selenium electrophiles generated from the optically active diselenides shown in Figure 3. These reactions typically proceed via the corresponding seleniranium ions resulting in an *anti*-addition of the selenium moiety and the nucleophile. The formation of the seleniranium ions is reversible, but at low temperatures the reaction is under kinetic control. The mechanistic course of the oxyselenenylation reaction with the chiral reagents **20** and **24** has been investigated in large detail.[122–124] The presence of a chiral moiety in these reagents results in a differentiation between the two faces of unsymmetrically substituted alkenes. Therefore, the attack of the alkene double bond from either the Re- or the Si-side is different from the steric and electronic point of view and the resulting seleniranium ions **34** and **35** are diastereomers (Scheme 5).

Experimentally, this was verified by the independent synthesis of the diastereomeric seleniranium ions **37** and **40**. The corresponding β-hydroxyselenides **36** and **39** were obtained by a reaction of the selenium anion with enantiomerically pure (*R*)- or (*S*)-styrene epoxide. These β-hydroxyselenides were then treated with trifluoromethane



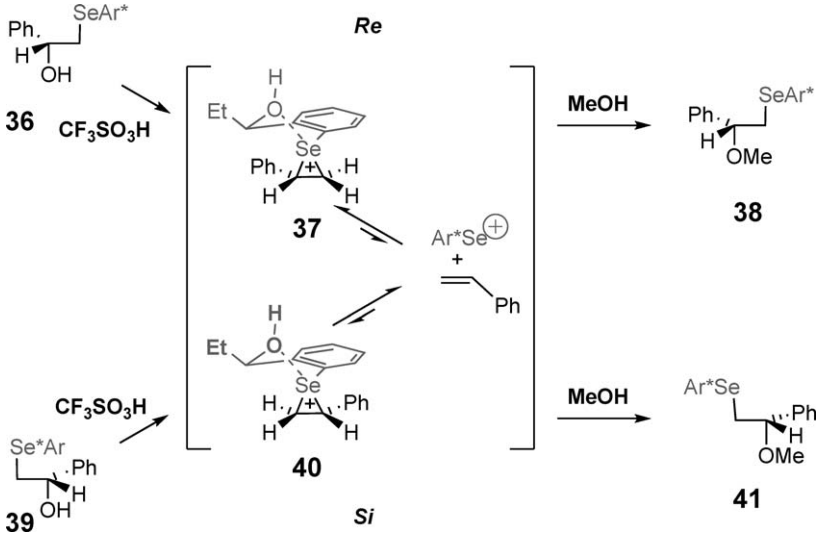
Scheme 4



Scheme 5

sulfonic acid to selectively generate the corresponding seleniranium ions via an intramolecular S_N2 displacement. In the case of β-hydroxyselenide **36**, it forms the more stable seleniranium ion **37** corresponding to a re-attack of the selenium electrophile to the styrene double bond. The subsequent reaction with methanol gave almost exclusively the addition product **38**. Using the β-hydroxyselenide **39** under identical reaction conditions, the less stable seleniranium ion **40** is formed initially. Via a decomplexation–complexation mechanism as indicated in Scheme 6 the more stable seleniranium ion **37** is generated as well and the ring-opened products **38** and **41** are obtained in a ratio of about 1 : 3. This decomplexation–complexation mechanism could be further verified as it was possible to trap the selenium electrophile by the addition of a different substituted alkene to the reaction mixture. Calculations of the seleniranium intermediates have been performed and the computational results on an *ab initio* level support the experimental findings.[122]

For a better comparison of the different chiral reagents shown in Figure 2, the methoxyselenenylation of (*E*)-1-phenylpropene leading to addition products **42** is shown as a representative example in Table 1. After oxidative elimination, ether **43** can be obtained; the absolute configuration of **43** is given in Table 1 as well (Scheme 7).

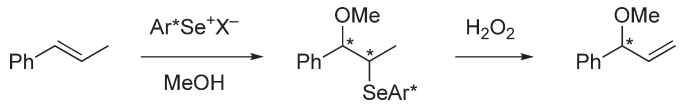


Scheme 6

Table 1 Asymmetric methoxyselenenylations of β-methylstyrene **42**

$(Ar^*Se)_2$	$Ar^*SeX : X^-$	*Reaction conditions*	**42** de (%)	**42** *Yield* (%)	*Configuration of* **43**	*References*
16[a]	Br^-	MeOH, 25 °C	24	49	[c]	74
16[b]	Br^-	MeOH, 25 °C	79	87	(*R*)	74,76
17	TfO^-	Et_2O, −78 °C	86	82	(*S*)	77
18	Br^-	CH_2Cl_2, −78 °C	52	85	(*R*)	84
18	ClO_4^-	CH_2Cl_2, −78 °C	80	47	(*R*)	84
18	TfO^-	CH_2Cl_2, −78 °C	89	68	(*R*)	84
18	BF_4^-	CH_2Cl_2, −78 °C	90	67	(*R*)	84
18	SbF_6^-	CH_2Cl_2, −78 °C	94	64	(*R*)	84
18	PF_6^-	CH_2Cl_2, −78 °C	95	58	(*R*)	84
19	TfO^-	CH_2Cl_2, −78 °C	96	99	(*S*)	88
20	TfO^-	Et_2O, −100 °C	80	45	(*S*)	25
23	TfO^-	Et_2O, −78 °C	98	81	(*S*)	80
24	TfO^-	Et_2O, −100 °C	85	51	(*S*)	99
25	TfO^-	CH_2Cl_2, −78 °C	92	78	(*S*)	101

[a]R = H.
[b]R = 1-(2,4-dinitrophenyl)-pyrrolidin-2-yl-carboxamide.
[c]Configuration not determined.



42 43

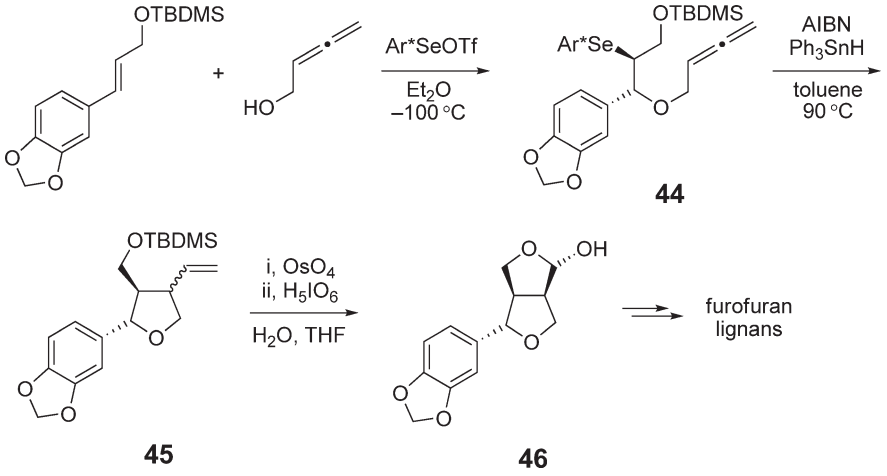
Scheme 7

Not only the reaction conditions of such selenenylations, but also the counterion to the selenium electrophile plays an important, although not yet completely understood, role. This is highlighted in the entries for diselenide **18** in Table 1. Based on these results it was suggested that a decreased nucleophilicity of the counterion leads to an increased electrophilicity of the selenium electrophile and hence to an increased selectivity which is reflected in higher diasteromeric ratios.[84] Similar observations were also made by other researchers[125] and recently, counterion effects together with coordinating additives have been investigated in cyclization reactions.[126,127]

Applications of asymmetric alkoxyselenenylations in natural product synthesis have been reported as well. It was found that even functionalized nucleophiles could be used in these reactions allowing a subsequent radical cyclization. This reaction sequence was applied to the synthesis of furofuran lignans as shown in Scheme 8. After stereoselective selenenylations using selenium electrophile derived from diselenide **20** and an allenylalcohol as nucleophile, addition products of type **44** can be obtained in good yields and diastereoselectivities. The favored 5-*exo-trig* radical cyclization of the major isomer yielded the cyclized product **45**. The vinylic side chain of the tetrahydrofurane derivative **45** is cleaved by oxidation and subsequent deprotection of the primary hydroxy group gives a fast access to furofuranes of type **46**, versatile building blocks for the synthesis of various lignans.[128,129]

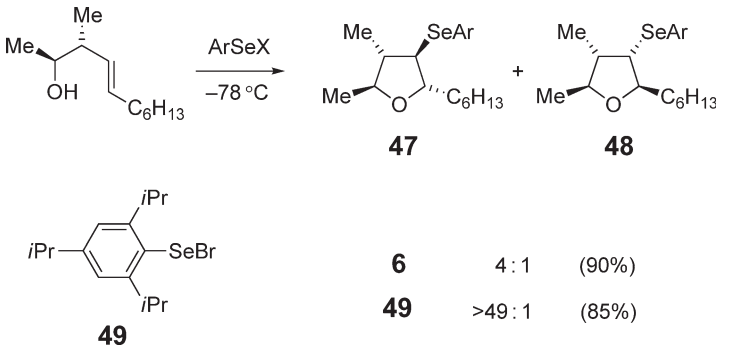
As already highlighted in Scheme 1, the potential of electrophilic reagents for cyclization reactions is enormous.[130] The great importance of heterocyclic compounds as final products or as reaction intermediates, and their occurrence in many natural products and in biologically active compounds has led to intensive research in this area. The increasing popularity gained by selenium reagents for cyclizations is due to the (i) easy availability of the reagents, (ii) numerous possible manipulations of the selenium moiety before or during its removal, and (iii) mild reaction conditions required in the various steps. Selenium-promoted cyclization reactions thus provide an easy access to a wide variety of heterocyclic compounds having various ring sizes.

The seleniranium ion intermediates in the cyclization reactions can be either generated from the corresponding β-hydroxyselenides as shown in Scheme 6 or from suitably substituted alkenes. Depending on the alkene and on the selenium electrophile, cyclizations can be performed with high selectivities. The size of the electrophilic reagent has



44 45 46

Scheme 8



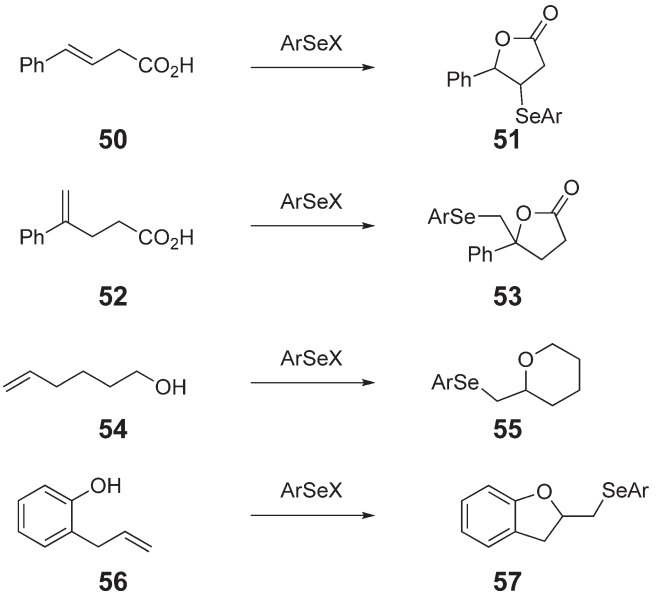
Scheme 9

a significant influence, increasing the ratio for the diastereomers **47** and **48** from 4 : 1[131] using phenylselenenyl chloride **6** to >49 : 1 with the triisoproyl derivative **49** as shown in Scheme 9.[132]

Many of the chiral selenium electrophiles have also been employed in cyclization reactions. Various internal nucleophiles can be used and access to different heterocycles is possible. Not only oxygen nucleophiles can be used for the synthesis of heterocyclic compounds, but also nitrogen nucleophiles are widely employed and even carbon nucleophiles can be used for the synthesis of carbacycles with new stereogenic centers. Oxygen nucleophiles have been widely used and some selected examples of selenolactonizations of unsaturated acids **50** and **52** and seleno-etherifications of unsaturated alcohols **54** and **56** are shown in Scheme 10.

These reactions have also been performed using enantiomerically pure selenium electrophiles to access heterocyclic compounds with stereogenic centers. The yields and selectivities obtained using some selected chiral electrophiles generated from the diselenides are given in Table 2.

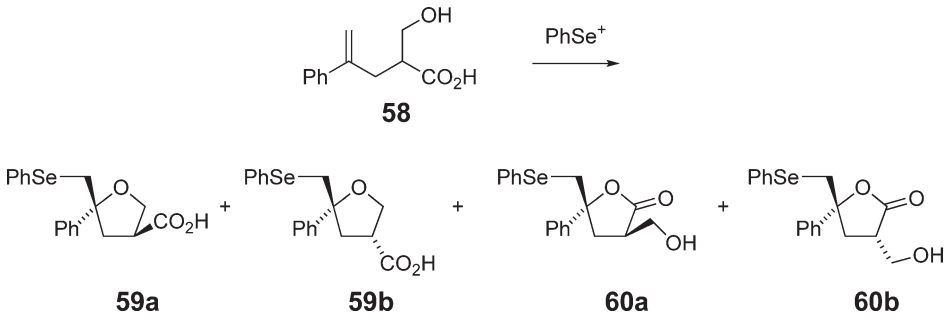
As already mentioned, the nature of the selenium electrophile, the counter ion, solvents, and external additives coordinating to the electrophilic species influence the course of such cyclizations. They can also be used to control such processes with high degrees of efficiency. This has recently been demonstrated by the selective cyclization of substrate **58**, which contains an alcohol and a carboxylic acid functionality as internal nucleophiles. Depending on the cyclizing nucleophile, electrophilic 5-*exo*-cyclizations of alkene **58** can lead to two different



Scheme 10

Table 2 Stereoselective selenocyclizations with different electrophiles

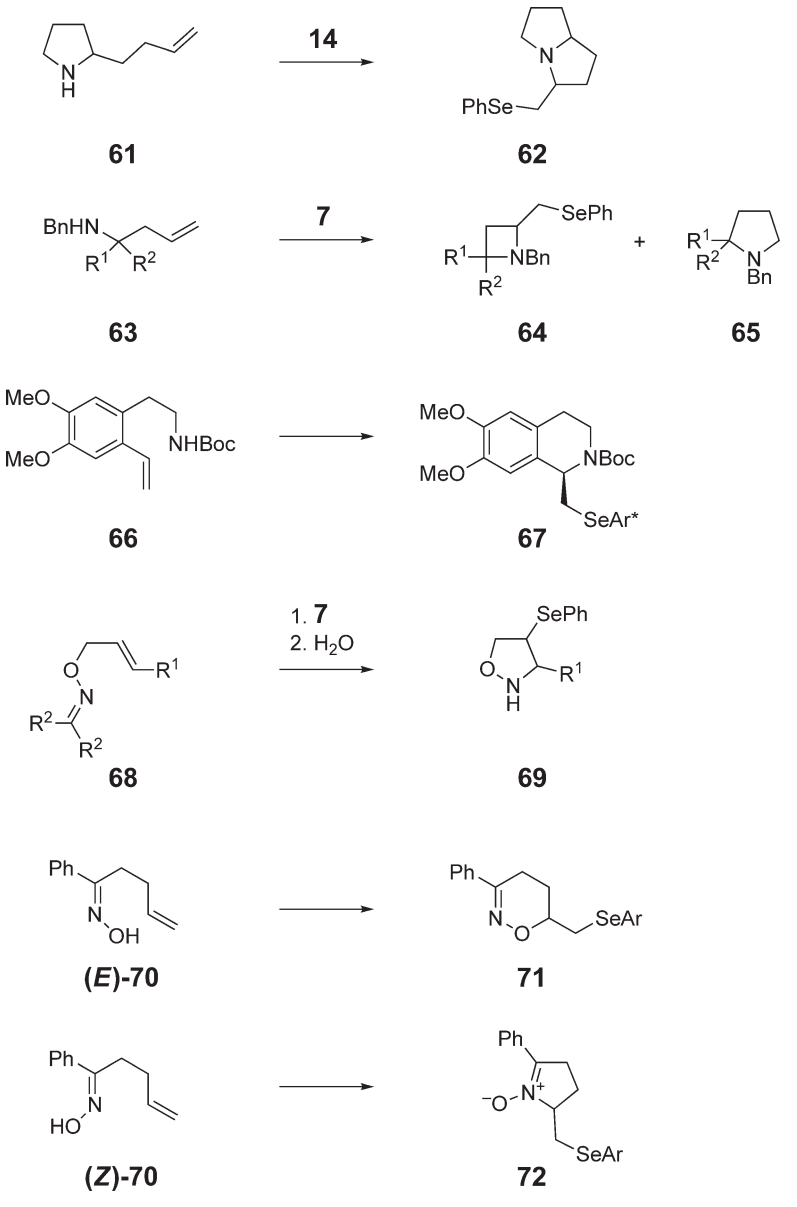
$(Ar^*Se)_2$	$Ar^*SeX: X^-$	*Starting material*	*Product*	*Yield* (%)	de (%)	*References*
18	PF_6^-	**50**	**51**	87	92	82,84
20	TfO^-	**50**	**51**	41	72	133
23	TfO^-	**50**	**51**	62	99	78,80
25	TfO^-	**50**	**51**	75	90	102
20	TfO^-	**52**	**53**	58	85	133
25	TfO^-	**52**	**53**	95	78	102
18	PF_6^-	**54**	**55**	80	59	82,84
22	Cl^-	**54**	**55**	96	74	96,98
18	PF_6^-	**56**	**57**	83	13	82,84
19	Br^-	**56**	**57**	20	95	86
22	Cl^-	**56**	**57**	93	84	96,98
25	TfO^-	**56**	**57**	60	40	102



Scheme 11

heterocycles: tetrahydrofurans or lactones. It has been reported how different interactions with selenium electrophiles can be used to direct these cyclizations either towards tetrahydrofurans **59a/59b** or towards lactones **60a/60b** (Scheme 11).[126,127] For example, electrophile **13** with 10 equiv. of acetic acid leads exclusively to the formation of compounds **59**, whereas with electrophile **12** and 10 equiv. of methanol as external additive only lactones **60** are formed.

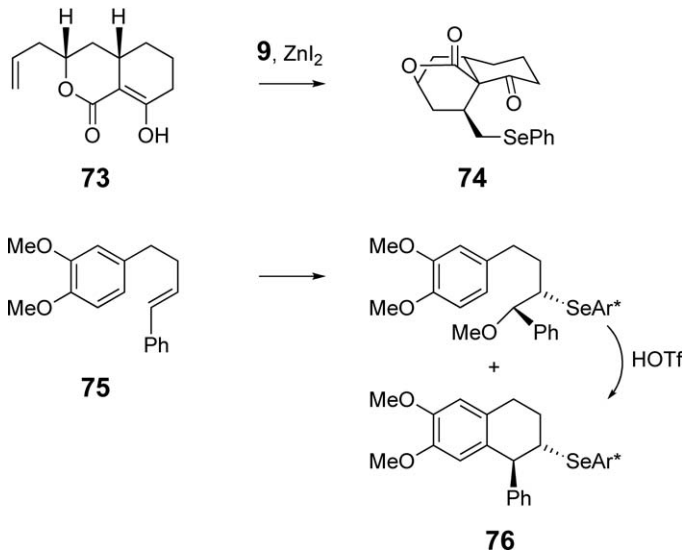
A wide range of nitrogen heterocycles is accessible by aminoselenenylations. Some selected examples are shown in Scheme 12. Pyrrolidine derivative **61** was cyclized to form the pyrrolizidine moiety **62**,[49] whereas homoallylamines of type **63** have been cyclized to afford azetidines **64** via a 4-*exo-trig* cyclization. Compounds **64** are favored according to Baldwins rules over the 5-*endo-trig* pathway, which leads to pyrrolidines **65**. Certain reaction conditions can lead to the exclusive formation of **64**.[134] An aminocyclization was further used as the key reaction for the synthesis of isoquinoline alkaloids. Cyclization of the styrene derivative **66** with different chiral selenium electrophiles yielded the cyclized product **67** in up to 85% de. After deselenylation and cleavage of the Boc-protecting group salsolidine was synthesized.[135] Also *O*-allyl oximes such as **68** can be cyclized; after an aqueous workup isoxazolidines **69** can be obtained.[136,137] Recently, also chiral selenium electrophiles have been employed in this reaction to yield enantiomerically enriched isoxazolidines (up to 88% de).[103] Those compounds can be used as versatile building blocks for various syntheses. The reaction products in the cyclization of oximes depend on their configuration. Compound (*E*)-**70** cyclizes to the corresponding 1,2-oxazine **71**, whereas the (*Z*)-derivative cyclizes via the nitrogen atom to yield the cyclic nitrone **72**.[104] Cyclizations of compounds with two different nitrogen atoms and their competition in cyclization reactions has been studied as well.[138,139] Carbon nucleophiles can also be employed in selenocyclization reactions. Cyclizations of β-dicarbonyl compounds have



Scheme 12

been investigated earlier;[140–143] recently, it was shown that this reaction can be used for the preparation of tricyclic compounds such as **74** from precursor **73**.[144] Even aromatic carbon atoms of electron-rich benzene derivatives can be used for such cyclizations. Chiral selenium electrophiles have been used in the synthesis of tetrahydronaphthalene compounds **76** from the starting material **75** (Scheme 13).[145] Such reactions can also be performed in an intermolecular fashion and chiral selenium electrophiles have been used as well for a stereoselective version of carboselenenylations.[146,147]

All these transformations need stoichiometric amounts of selenium-containing reagents. The addition or cyclization products are usually intermediates in synthetic sequences. Most target compounds do not contain a selenium moiety and there is the need for deselenenylation at some stage. Often this can be combined with a subsequent functionalization like substitution or elimination. Combinations of addition and deselenenylation reactions with only catalytic amounts of a selenium reagent are described in Section 9.11.2.8.2.



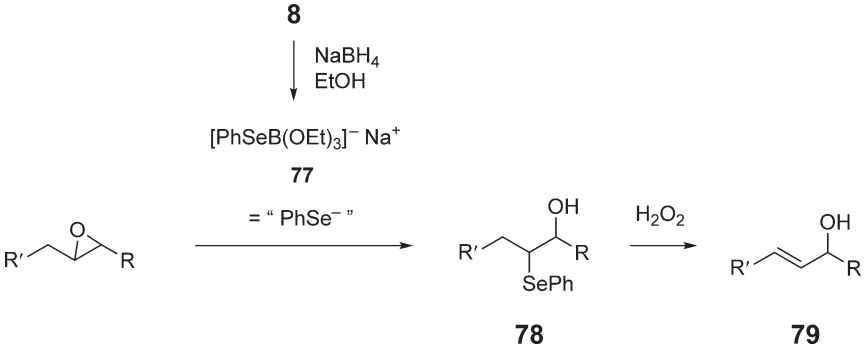
Scheme 13

9.11.2.2 Nucleophilic Selenium

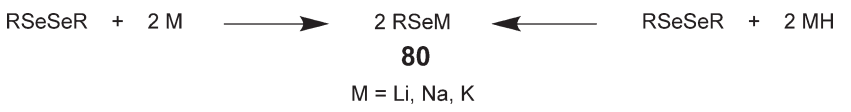
A wide range of selenium-containing molecules is accessible by using nucleophilic selenium reagents. Usually selenides or functionalized selenides are synthesized by this method. The high reactivity and selectivity of selenolates are advantageous in these transformations.[148] The nucleophilicity of selenolates is significantly higher than the nucleophilicity of the corresponding thiolates. Their reactivity depends on the method used for their preparation and on the additives present in the reaction mixture. In general, these nucleophilic selenium species are highly reactive and cannot be isolated. Only recently a series of more stable reagents, in which the selenium is bound to a main group element, has been developed. The chemistry of selenolates was pioneered in 1973 by Sharpless, who used selenolates for the nucleophilic ring opening of various epoxides.[12] Sodium borohydride was used as the reducing agent to generate the selenolate **77** from diphenyl diselenide. The β-hydroxyselenides **78** obtained in this reaction have been used for the formation of allylic alcohols **79** in a subsequent oxidative elimination reaction (Scheme 14).

Various reducing agents have been used for the generation of selenolates from diselenides or selenocyanates. Alkali metals M (M = Li, Na, K)[149,150] or alkali hydrides MH (M = Li, Na, K)[151,152] can generate the corresponding selenolate anions such as **80**; these are more reactive than the borane complexes of type **77** (Scheme 15). Diaryl diselenides are easier reduced than dialkyl diselenides, but the mechanism for the reduction of selenocyanates is complex and can lead to either diselenides or selenolates.[153,154]

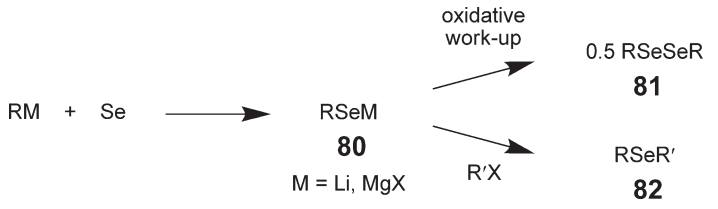
Hydrazine[155,156] or samarium diiodide[157–162] are other useful reagents for the synthesis of selenolates, but electrochemical methods[163,164] have also been employed for their selective synthesis from diselenides. Starting from elemental selenium, selenolates **80** can easily be prepared by insertion reactions of selenium into organolithium



Scheme 14



Scheme 15



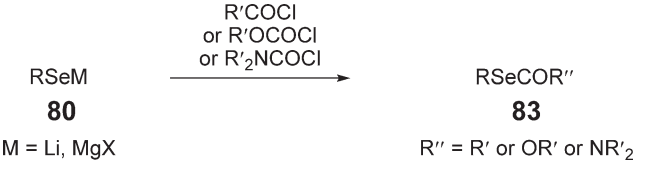
Scheme 16

or Grignard reagents. This route can be followed for the synthesis of diselenides **81** using an oxidative workup (Scheme 16). Detailed investigations on the mechanism of this procedure have been reported recently.[165]

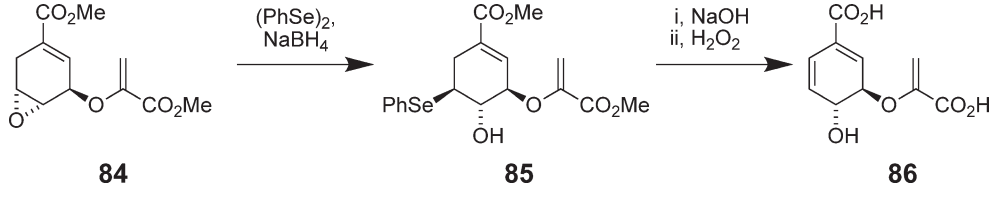
The most common reaction of selenolates is the nucleophilic substitution of halide compounds. For the synthesis of selenides **82** the selenolates **80** can be reacted with halides. Nucleophilic selenium species can also be reacted with a variety of other electrophilic compounds. The reaction with acid chlorides, chloroformates, or carbamoyl chlorides leads to the corresponding selenoesters **83** (R″ = R′), selenocarbonates **83** (R″ = OR′), or selenoamides **83** (R″ = NR'_2), respectively (Scheme 17).[166]

The ring opening of epoxides or of other cyclic ethers can be smoothly performed with a variety of selenium nucleophiles. As already mentioned in Scheme 14, a subsequent oxidative elimination can be used for the synthesis of allylic alcohols. This reaction sequence has been used in various natural product syntheses, for example, in the synthesis of chorismic acid **86**.[167,168] The epoxide **84**, prepared by epoxidation of the corresponding alkene with mCPBA, was treated with the phenylselenolate generated from diphenyl diselenide and sodium borohydride and underwent regiospecific ring opening to compound **85**. After ester hydrolysis, the oxidative elimination to chorismic acid was performed with hydrogen peroxide in 65% yield (Scheme 18).[168]

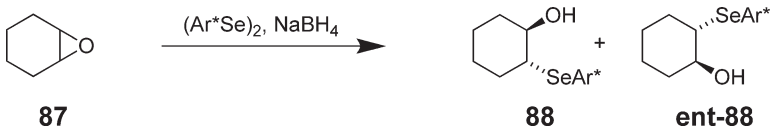
Enantioselective ring opening of *meso*-epoxides was one of the first reactions which was investigated using chiral selenium nucleophiles and is an important reaction in stereoselective synthesis.[169] Tomoda *et al.* reported the first reaction of this kind using the selenolate generated from diselenides **16** in the ring-opening reaction of cyclohexene oxide **87**.[73] Diastereoselectivities of up to 50% in the product **88** were obtained. Similar reactions were performed with the selenolate generated from diselenide **19**, which was used for the ring opening of different *meso*-epoxides yielding diastereoselectivities of up to 69% (Scheme 19).[170]



Scheme 17



Scheme 18



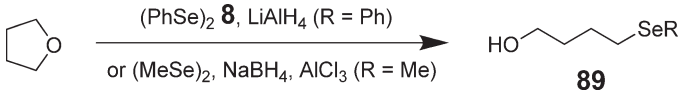
Scheme 19

Ring opening of larger cyclic ethers such as tetrahydrofuran does not normally proceed with selenolates of type **77** generated from diselenides and sodium borohydride in alcohols. If diselenides are reduced with lithium aluminum hydride in tetrahydrofuran,[171] or with sodium borohydride in the presence of aluminum trichloride,[172] ring-opened products **89** are obtained (Scheme 20).

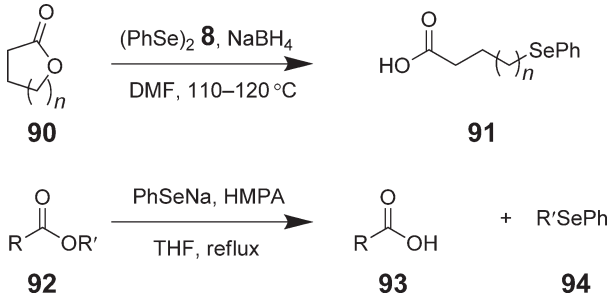
Selenolate **77**, prepared from diselenides with sodium borohydride, is also not reactive enough for reactions with esters or lactones. Only under higher reaction temperatures, lactones **90** can be ring opened with selenolates to the corresponding carboxylic acids **91**.[173,174] The selenium moiety can then be used for further manipulations. Using similar reaction conditions, esters **92** can be converted to the corresponding carboxylic acids **93** and selenides **94** (Scheme 21).[149]

Michael reactions of α,β-unsaturated carbonyl compounds **95** using selenium nucleophiles afford β-seleno carbonyl derivatives **96** usually in good yields.[175] This reaction has been used as a protection strategy for the α,β-unsaturated double bond, because an oxidative elimination of the selenium moiety in **96** leads to the regeneration of the double bond.[176] Such reactions have also been applied to natural product synthesis[177] and in asymmetric versions of Michael additions in the presence of alkaloids as chiral ligands (Scheme 22).[178]

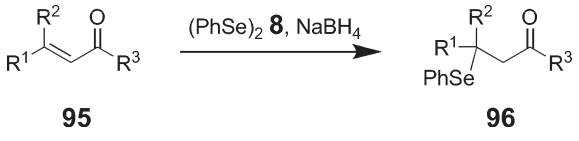
The concept of nucleophilic selenium reagents has also been applied to solid-phase synthesis. Polymer-supported selenium reagents have attracted the interest of synthetic chemists because of their facile handling without the formation of toxic and odorous by-products. The polystyrene-bound selenium-containing reagent



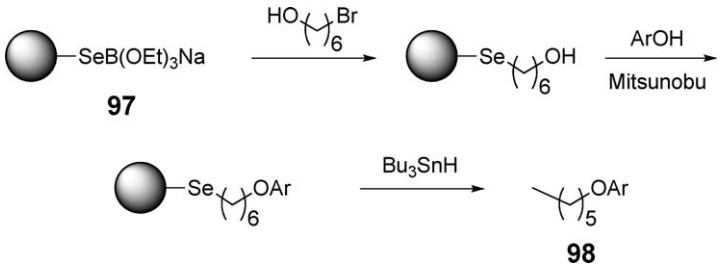
Scheme 20



Scheme 21



Scheme 22



Scheme 23

97 was applied in the traceless solid-phase synthesis of a library of aryl alkyl ethers by the reaction of **97** with 6-bromohexanol, etherification, and radical cleavage reaction of **98** from the polymer (Scheme 23).[179] But other research groups also used polymer-bound nucleophilic selenium reagents in synthetic transformations.[180,181]

The interest of selenium-containing compounds with the selenium moiety bound to other main group elements has attracted considerable interest, because these compounds are stable alternatives often to labile selenium nucleophiles. Group 13 elements can be used to prepare the corresponding selenium derivatives. Boron trihalides can react with selenolates to give the tri(organoseleno)boranes **99**.[182] Dimethylaluminum methylselenolate **100** is prepared by reaction of trimethylaluminum with elemental selenium,[183] but also diselenides can be reduced with diisobutylaluminum hydride (DIBALH) to generate diisobutylaluminum arylselenolates **101**.[184] Selenylations can also be performed in the presence of elemental indium, but the corresponding organoindium derivatives have not yet been characterized.[185–187] Compounds **99–101** can be employed in the various reactions using selenium nucleophiles (Figure 4).

Also widely employed are organoselenium compounds containing group 14 elements. Phenyl trimethylsilyl selenide **102** can be easily prepared from diphenyl diselenide **8** and is a good source for selenium nucleophiles (Scheme 24).[188,189] In the presence of methanol selenols are generated for use in Michael reactions[189] or in ring-opening reactions of lactones as mentioned above.[190] Organostannyl selenides **103** undergo almost similar reactions to the corresponding organostannyl selenides, but due to favorable orbital interactions between tin and selenium these compounds are more stable than organosilyl selenides (Scheme 24).[191] Compounds **103** can react with fluoride anions to generate nucleophilic selenium species.[192,193] This has also been applied to the regeneration protocol of chiral, polymer-supported selenium reagents.[194]

Although nucleophilic selenium species have already demonstrated their potential as versatile reagents in organic synthesis, their scope as useful reagents is still expanding as shown in applications towards stereoselective synthesis and synthesis on solid supports.

Figure 4 Versatile selenium nucleophiles for organic synthesis.

Scheme 24

9.11.2.3 Selenium-stabilized Carbanions and Carbocations

Selenium-stabilized carbanions are recognized as important intermediates in organic synthesis. Their formation and reactivity as nucleophilic reagents were studied some time ago and general aspects are decribed in earlier reviews.[46,47] More detailed descriptions and reactions of α-selanylalkyl lithiums and potassium analogs were presented in other reviews.[195]

Selenium-stabilized carbanions can be generated in different ways. One major route for their synthesis is the deprotonation of selenides **104** with sufficient acidic protons in the α-position. LDA (lithium diisopropylamide) is often used for compounds such as **104** but stronger bases, such as KDA (potassium diisopropylamide), are preferred for the deprotonation of selenides with structures of type **105**. The second general method for their preparation is the alkyllithium cleavage of one carbon–selenium bond of selenoacetals **106** or *ortho*-triselenoesters **107**. But the lithium–bromine exchange of α-bromoselenides or alkyllithium additions to vinyl phenyl selenides are also the methods used for the generation of selenium-stabilized carbanions (Figure 5).

Various applications of selenium-stabilized carbanions in synthesis have been reported. The mixed acetal **108** derived from benzaldehyde was efficiently metalated by KDA in THF. The α-methoxy-α-methylselanyl benzylpotassium compound **109** is stable at low temperatures (−78 °C) and reacted with a variety of electrophiles. The reaction products **110**, still mixed acetals, are obtained in good yields as shown in Table 3 (Scheme 25).[196]

The addition of a selenium-stabilized carbanion to an electrophile can be followed by another reaction as selenones are good leaving groups. α-Selenonylalkyl compounds **111** can be deprotonated using potassium *tert*-butoxide. Reactions with α,β-unsaturated *tert*-butyl esters lead to cyclopropane derivatives **112** in good yields (Scheme 26).[197]

α-Selanylalkyl lithium compounds are easily prepared by the reaction of selenoacetals **106** or **107** by treatment with alkyllithiums. The efficiency of such a selenium–lithium exchange reaction is strongly dependent not only of the structure of the selenoacetal, but also of the alkyllithium reagent and the solvent.[198] All compounds which can stabilize the carbanionic center will favor an exchange reaction and will allow the use of a less reactive organolithium reagent. The selenium–lithium exchange of the bis(phenylseleno) compound **113** (R = Ph) is more readily achieved

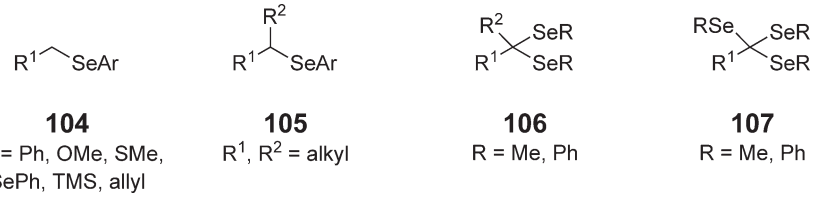
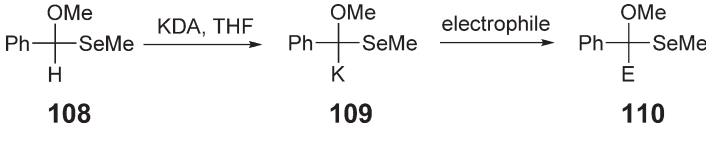


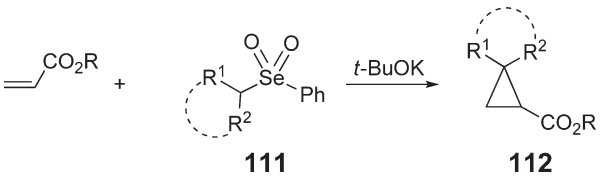
Figure 5 Precursors for the synthesis of selenium-stabilized carbanions from **123**.

Table 3 Reaction of anion **109** with different electrophiles

Electrophile	*E*	**110** *Yield* (%)	*References*
Me_3Si-Cl	$SiMe_3$	88	196
Propene oxide	$CH_2CH(OH)Me$	72	196
$Me(CH_2)_4Br$	$(CH_2)_4Me$	77	196
Me_2CHI	$CHMe_2$	98	196
$PhCH_2Cl$	CH_2Ph	98	196
$H_2C{=}CHCH_2I$	$CH_2CH{=}CH_2$	73	196

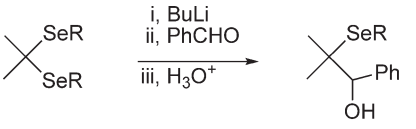


Scheme 25



111 112

Scheme 26



113 114

R = Ph: 94%
R = Me: 75%

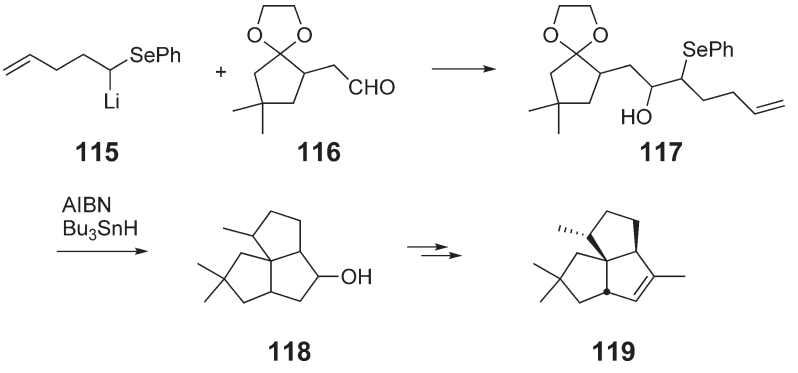
Scheme 27

than that of the corresponding bis(methylseleno) compound **113** (R = Me) leading to lower yields of product **114** in the subsequent reaction with benzaldehyde (Scheme 27).[198]

The formation of β-hydroxyselenides through the reaction of a selenium-stabilized carbanion with carbonyl compounds has been extensively used also in the context of natural product synthesis. The phenylselenoalkyllithium compound **115** was reacted with aldehyde **116** to afford β-hydroxyselenide **117**. In a radical cyclization cascade the tricyclic molecule **118** was generated in good yields and subsequent transformations led to the synthesis of pentalenene **119** (Scheme 28).[199] Also other natural products like zizaene and khusimone have been synthesized via a similar route.[200]

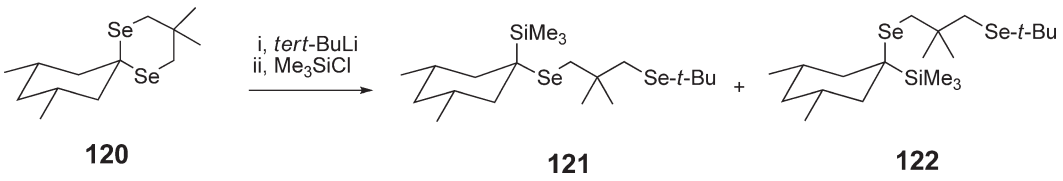
Mixed selenium and sulfur acetals have been invesigated in similar reactions[201] and other organolithium compounds such as lithium di-*tert*-butylbiphenyl (LiDBB) have been found to be efficient for the selenium–lithium exchange reaction even of bis(methylseleno) acetals.[202] Reich *et al.* have shown that the equatorial carbon–selenium bond of the 1,3-diselenane **120** can be cleaved kinetically using *tert*-butyllithium. The resulting carbanion was trapped by chlorotrimethylsilane to yield compounds **121** and **122** in high stereoselectivity (**121** : **122** 3 : 97), which was reversed in a sequential experiment with the addition of chlorotrimethylsilane after 1 h (Scheme 29). The axial/equatorial isomerization occurred at −78 °C leading to a 4 : 96 ratio of **121** : **122** in favor of the alkylselanyl group in equatorial position with the half-life time estimated to be 7 min.[203]

The lithiated compound derived from **120** and also other α-phenylselanylcyclohexyllithium compounds are configurationally labile even at low temperatures.[203,204] The diastereoselection in the selenium–lithium exchange



115 116 117 118 119

Scheme 28



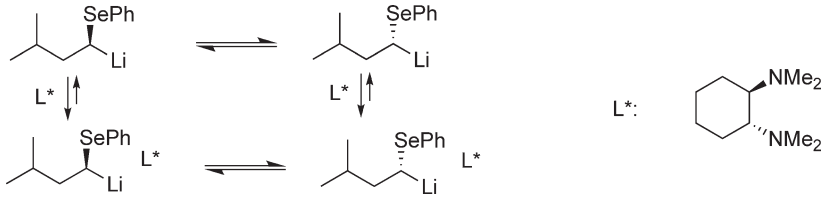
120 **121** **122**

Scheme 29

reaction has also been studied by trapping lithiated intermediate with ketones or aldehydes.[205,206] The complexation of α-selanylalkyllithium compounds with enantiomerically pure diamines led to complexed intermediates which reacted with aldehydes more rapidly than the uncomplexed forms. Equilibration occurred without dissociation and was followed by ^{77}Se NMR spectroscopy.[206,207] When a selenium–lithium exchange is followed by a second transmetallation with magnesium salts, selenenylated Grignard reagents are generated which are more stable than the lithium derivatives (Scheme 30).[209]

When α-selanylalkyllithium compound **123** is reacted with double bonds of type **124**, a methaneselenolate displacement generates functionalized arylcyclopropane derivatives **125**.[210] Depending on the substituents R^1 and R^2, the ratio of **125a** : **125b** can vary from 97 : 3 to 0 : 100 as shown in Table 4 (Scheme 31).

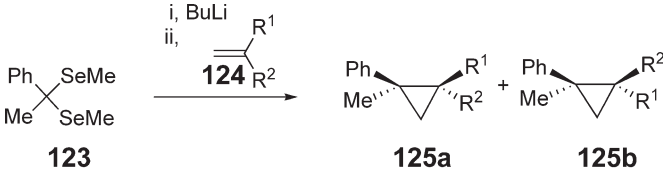
The deprotonation of α-phenylselanyl ketones, esters, or lactones is much easier and can be performed with LDA at low temperatures. The enolates formed by the deprotonation are relatively stable and can be used in a variety of



Scheme 30

Table 4 Cyclopropanation using α-selanyl alkyllithium compound derived

R^1 **124**	R^2 **124**	**125a**:**125b**	**125** *Yield* (%)	*References*
H	H		50	210
Ph	H	97 : 3	69	210
CH=CH$_2$	H	3 : 97	70	210
SiMe$_3$	H	15 : 85	81	210
SPh	H	0 : 100	59	210
Ph	Me	0 : 100	72	210
Ph	SeMe	0 : 100	96	210



123 **125a** **125b**

R^1 = H, Ph, CH_2=CH, Me_3Si, PhS

R^2 = H, Me, MeSe

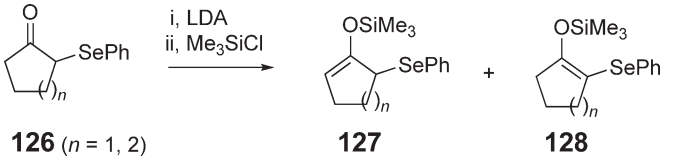
Scheme 31

subsequent reactions. The enolates can also be transformed into the corresponding β-selanyl enoxysilane derivatives for use in next reaction steps.[211] The formation of the β-selanyl enoxysilane derivatives is not regioselective, despite the higher acidity of the selenium-bearing carbon atom.[211] Enolates **127** and **128** are formed from ketones **126** independent of the ring size ($n = 1, 2$) in a ratio of about 1 : 1 (Scheme 32).

Enolates derived from 2-phenylselanyl esters can react with various electrophiles. The Michael addition of the enolate formed from *t*-butyl 2-phenylselanyl propanoate **129** to furanone **130** followed by iodination afforded the key intermediate **131** for the total synthesis of (−)-avenaciolide **132** (Scheme 33).[213]

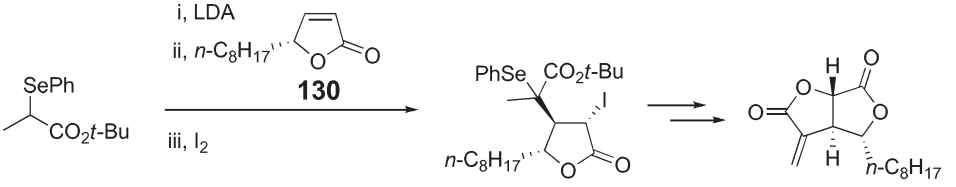
Selenium-stabilized carbanions can be also generated by 1,4-addition of nucleophilic reagents to α-selanyl α,β-unsaturated carbonyl compounds. The conjugate addition of trialkylsilyllithium compounds to **133**, followed by reaction with allyl iodide, afforded the addition products **134** with good *cis*-stereoselectivity (R = Me: dr 86 : 14; R = Ph: dr 94 : 6) (Scheme 34).[214] The addition of lithium dialkylcuprates to 2-phenylselanylcycloalk-2-enones has also been used for the synthesis of natural products.[215,216]

Also other functionalities can be present in selenium-stabilized carbanions. The choice of base for the deprotonation of compounds **135** is crucial and sometimes side-products are formed. α-Cyano substituted compounds **135a** (R = CN) are known;[217] α-phosphono compounds **135b** (R = P(O)(OEt)$_2$)[218] and also α-arenesulfanyl componds **135c** (R = SO_2Ar)[219,220] have been used in the synthesis of selenium-stabilized carbanions (Figure 6).



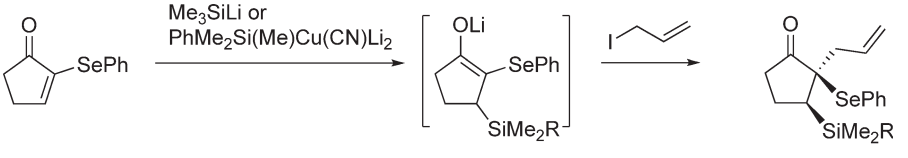
126 (n = 1, 2) **127** **128**

Scheme 32



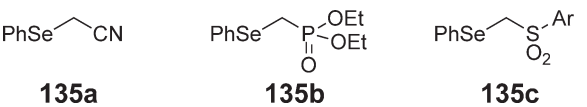
129 **131** **132**

Scheme 33



133 **134** (R = Me, Ph)

Scheme 34



135a **135b** **135c**

Figure 6 Precursor molecules for selenium stabilized carbanions.

By deprotonation of vinyl aryl selenides at the α-position the corresponding α-selanylvinylmetal derivatives can be prepared.[195] But also the cleavage of ketene selenoacetals or the bromine–lithium exchange of α-bromovinyl selenides can be used to access such compounds.[221,222] Again, the success of the deprotonation strategy is strongly dependent on substituents. The deprotonation of vinyl phenyl selenide can be carried out using either LDA or KDA at low temperatures in THF.[195] Another method for the generation of α-selanylvinylmetal derivatives is either the cuprate addition to acetylenic selenides[223–226] or a hydrometallation such as hydrostannylation[227–230] or hydrozirconation[231–235] of the triple bond in acetylenic selenides.

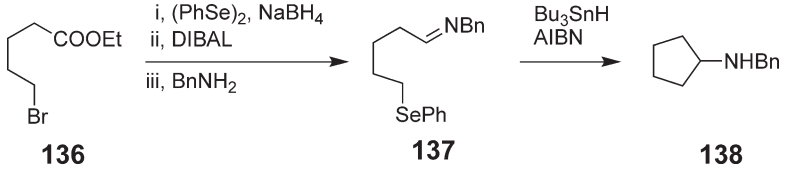
9.11.2.4 Radical Reactions Using Selenium Precursors

Organoselenium compounds play an improtant role as precursors for radicals and several reviews of free-radical reactions of selenium compounds have been published.[236,237] The homolytic cleavage of the carbon–selenium bond is a relatively easy process, which can be initiated either photochemically or thermally. AIBN is a common initiator for thermal processes, typically used in amounts of 5–10 mol%. Many radical reactions involving selenium compounds are of general synthetic utility, particularly when combined with other, non-radical selenium-based transformations. Radical substitution at selenium is very efficient with stannyl and silyl radicals and radical chain processes are easily performed using selenium-containing substrates. Selenium-containing compounds are routinely applied as attractive precursor molecules in radical chemistry. Apart from the chemical context, radical reactions involving selenium are also of importance in biologic systems.[238,239] Various selenoproteins are known and some of them like glutathione peroxidase are believed to act as antioxidants by suppressing cell damage by free-radical processes.

Simple phenyl selenides are often used as alkyl radical precursors. They can be prepared using either nucleophilic or electrophilic selenium reagents. Although halides are also versatile radical precursors, it is sometimes necessary to convert them into the corresponding selenides, especially when side-reactions with nucleophilic reagents can take place. Bromide **136** was converted into the corresponding selenide, which is stable to the following reduction and imine formation, so that a subsequent radical cyclization of **137** led to cyclopentylamine **138** in good yield (Scheme 35).[240]

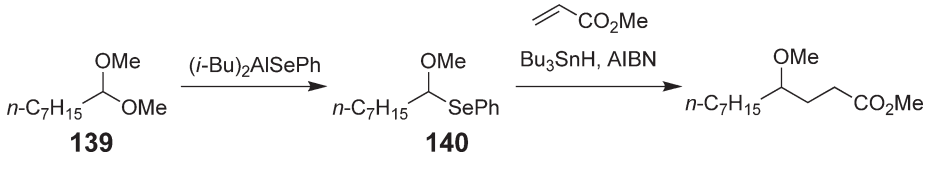
Other methods for the preparation of selenium-containing molecules for radical reactions have been used as well. In Scheme 8 the radical cyclization of compound **44** to the tetrahydrofuran derivative **45** is shown as a crucial step in natural product syntheses. Mixed acetal can also be used for the generation of radicals. 1-Alkoxy and 1-aminoalkyl radicals can be generated from O,Se- and N,Se-acetals in a direct way. The corresponding O,Hal- or N,Hal-mixed acetals are instable and this approach is rarely used. But the selenium-containing mixed acetals can be isolated and purified and are excellent radical precursors.[241] For example, acetals such as **139** can be converted into the mixed O,Se-acetals by reaction with diisobutylaluminum phenyl selenide. The mixed acetal **140** is then used under radical reaction conditions for the efficient formation of new carbon–carbon bonds (Scheme 36).[242]

Even the use of Se,N-acetals with stereogenic centers led to the corresponding products without racemization. The N,Se-acetal **141** was prepared from lactaldehyde without racemization. The subsequent radical allylation afforded product **142** in good yields (Scheme 37).[243]



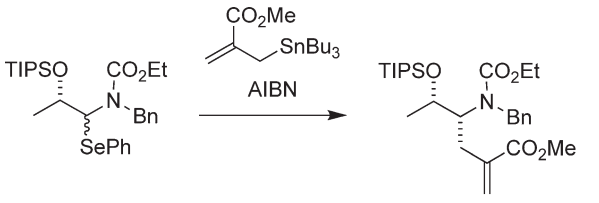
136 **137** **138**

Scheme 35



139 **140**

Scheme 36



141 **142** (*syn* : *anti* 68 : 32)

Scheme 37

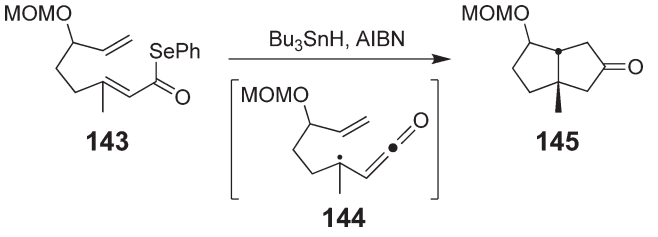
Another important application of mixed O,Se-acetals is the generation from radicals at the anomeric center in carbohydrate chemistry.[244–248]

The synthesis of acyl radicals can also be easily performed using selenium precursors. They can be prepared from the corresponding carboxylic acids, esters, or lacones.[249] Because the corresponding acyl halides are highly electrophilic reagents, they cannot be used as radical precursors. Especially acyl phenyl selenides are used frequently; they have found various applications in tandem radical reactions to alkenes in an inter-[250,251] as well as intramolecular[252] fashion. For example, the selenide **143** is the precursor for the corresponding acyl radical. It could react via the radical in the α-position of the ketene form **144** to give the bicyclic compound **145** in a very straightforward one-pot process (Scheme 38).[253]

Radical reactions with acyl radicals sometimes involve decarbonylation as side-reactions, especially when stabilized secondary or tertiary radicals can be formed. These side-reactions can be suppressed using low-temperature reaction conditions together with different reducing agents such as tris(trimethylsilyl)silane.[254]

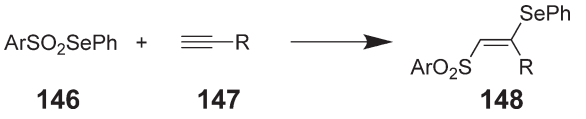
Selenium-containing molecules have also been used as precursors for radical seleno group transfer reactions. This is a very powerful method for radical additions to alkenes and alkynes; it is especially interesting from an atom economy point of view since all atoms remain in the product molecule. The free-radical addition of selenosulfonates **146** can be initiated either photochemically or thermally using AIBN. The addition of **146** not only to alkynes **147**,[255–257] but also to alkenes[258–261] or allenes,[261] has been reported and the products such as **148** are versatile building blocks for subsequent reactions (Scheme 39). For example, vinyl selenides **148** can be easily transformed into allenes.

The radical addition of selenomalonate **149** or the corresponding malononitriles are excellent substrates for phenylseleno group transfer reactions to alkenes and alkynes.[263] Malononitrile **150** can be used for annulation and cyclization reactions (Scheme 40).[264,265]



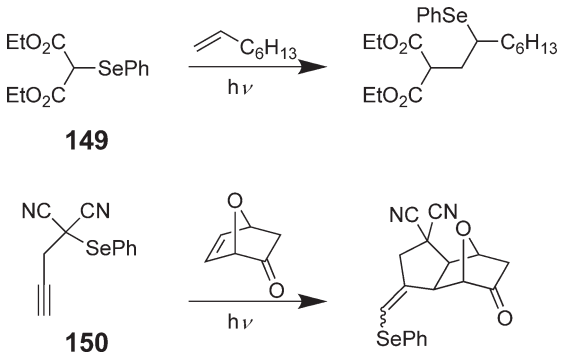
143 **144** **145**

Scheme 38



146 **147** **148**

Scheme 39



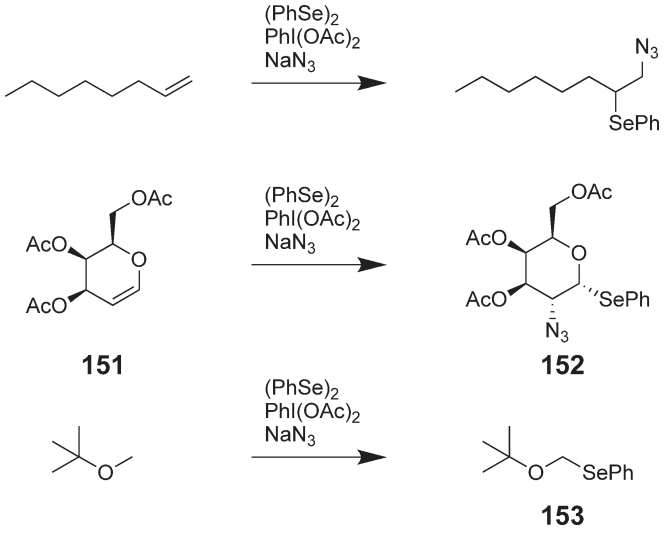
Scheme 40

A photosensitized activation of carbon–selenium bonds was also used for performing phenylseleno group transfer reactions. This process involves a photosensitized electron transfer (PET) as the initial step in the reaction sequence. Fragmentation affords a radical and phenylselenolate, which is oxidized to diphenyl diselenide in the presence of oxygen. The cyclized radical is then trapped by diphenyl diselenide to afford the final product. This process is quite general for intramolecular radical reactions.[70,266]

Although phenylsenenyl radicals can be generated easily by irradiation of diphenyl diselenide, their low reactivity toward unactivated alkenes and alkynes has prevented their extensive use in synthesis.[267,268] But diphenyl diselenide can be used as an efficient trap for alkyl radicals. The products are alkyl phenyl selenides. This trapping reaction has found application to different radical reactions and the selenides obtained by this reaction can be used in subsequent reactions.

The radical azidoselenenylation of alkenes can be achieved by reacting diphenyl diselenide with (diacetoxy)iodobenzene in the presence of sodium azide.[121,269,270] The unusual regiochemistry of this reaction is due to the radical process and the azide functionality is introduced at the least hindered substituted position. This reaction has found an interesting application for the synthesis of heterocycles after reduction of the azide moiety and in the area of carbohydrate chemistry.[271,272] The azidoselenenylation of glucals such as **151** leads to compounds **152** as precursor molecules for aminosugars (Scheme 41).

The reagent combination described for the azidoselenenylation can also be used for other reactions involving selenyl radicals. Aldehydes can be transformed into selenoesters by hydrogen atom abstraction and also methyl



Scheme 41

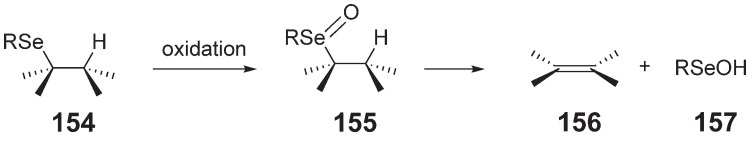
ethers react under hydrogen atom abstraction to generate O,Se mixed acetals such as **153**.[273] Various other reactions have been developed and radical substitutions at selenium atoms can be performed, especially when the leaving radical is stabilized;[274,275] fragmentation reactions by using tetravalent selenium reagents are also possible.[276,277]

9.11.2.5 Selenoxide Eliminations and Rearrangements

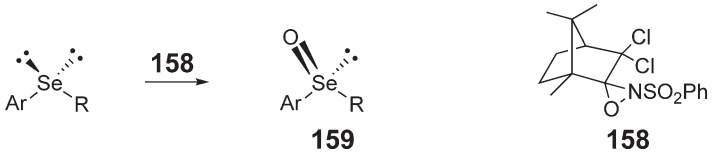
9.11.2.5.1 Selenoxides

Organic selenides **154** can be easily oxidized to the corresponding selenoxides **155**. When these selenoxides **155** bear a β-hydrogen atom, *syn*-elimination is an easy process which usually takes place under very mild conditions to yield alkenes **156** together with a selenenic acid derivative **157** as by-product (Scheme 42). This is a process which has proven to be widely applicable to a variety of substrates and its power for organic synthesis was recognized very early.[10–16] In comparison to the corresponding sulfur compounds, the activation energy for the elimination of sulfoxides is much higher and the elimination of selenoxides usually already proceeds at room temperature. Therefore, stereoselective versions of this reaction should have a high potential for asymmetric synthesis. Optically active organosulfur compounds are known in stereoselective reactions, but the corresponding organoselenium compounds have been used only recently for these purposes.

The preparation of optically active selenoxides will be essential for asymmetric reactions. Their chemistry has been neglected for a long time and their preparation was first described in the early 1980s.[278] The chemistry of optically active sulfoxides has been studied for a much longer time and these compounds now play an important role in asymmetric synthesis. The difficulty of preparing optically enriched selenoxides is their configurational lability. It was shown that selenoxides can racemize quickly in the presence of water and/or acid as they form achiral hydrates as intermediates.[279] Bulky substituents can slow down the reaction rate of hydrate formation and subsequent studies revealed that the rate-determining step is the protonation of the oxygen atom of the selenoxide.[280] This knowledge then allowed the preparation of configurationally stable enantiomerically enriched selenoxides with bulky substituents in the absence of water and acid and the absolute configuration was determined by X-ray crystallographic analysis. Optically active selenoxides can be synthesized by different routes. Racemic resolution of selenoxides is by complexation with optically active binaphthol[281] or by oxidation of the corresponding selenides. The oxidation can be performed in an enantioselective way by employing chiral oxidants in such a process, or in a diastereoselective fashion by using a selenide bearing a chiral substituent. The first case has been achieved by using the Davies-oxidant **158** in the asymmetric oxidation of prochiral selenides to the corresponding selenoxides **159**.[282] Compound **159** with Ar = Ph and R = Me has been obtained in selectivities >98 : 2 dr (Scheme 43). The Sharpless oxidant, a combination of *tert*-butylhydroperoxide and titanium(IV)alkoxide afforded the corresponding selenoxides only in low stereoselectivities.[283,284] The first diastereoselective synthesis of chiral selenoxides has been achieved by the oxidation of [2.2]paracyclophane-substituted selenides with *meta*-chloroperbenzoic acid.[285]



Scheme 42



Scheme 43

9.11.2.5.2 Eliminations

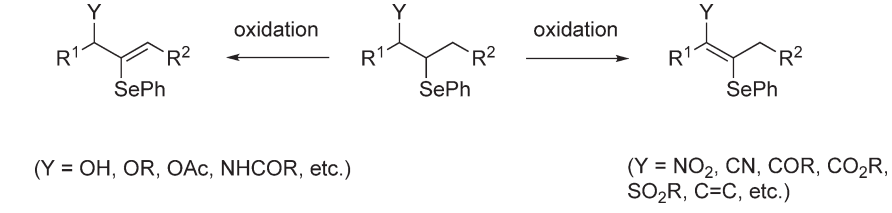
As shown in Scheme 42, selenoxides are crucial intermediates in the selenoxide elimination reactions. These are *syn*-eliminations which proceed via an intramolecular mechanism to yield alkenes as reaction products. The regioselectivities of these eliminations are dependent on the nature of the substituent Y in the β-position as shown in Scheme 44.[286] The mild reaction conditions for these elimination reactions make them highly useful in organic synthesis and theoretical studies on this reaction have been carried out as well.[286]

The elimination of optically active selenoxides can produce optically active alkenes and this asymmetric elimination methodology has been used in stereoselective synthesis. Optically active allenes and α,β-unsaturated carbonyl compounds have been prepared by using this method. Vinyl selenides of type **148** have been used for the preparation of allenes. Different oxidants and reaction conditions have been investigated in this transformation. After an initial isomerization of the double bond, which proceeds with very high *Z*-selectivity to give the compounds **160** in good yields, the oxidation to the selenoxide and the subsequent elimination produces allenes **161** in moderate yields (Scheme 45). Best results (59% yield, 38% ee) of *R*-**161** have been obtained using the Sharpless oxidation conditions with a substrate having Ar = 2-NO_2-C_6H_4 and R = *n*-C_3H_7.[287,288] The Davies reagent **158** did result in only 28% ee (41% yield) of product *R*-**161** using the same substrate.

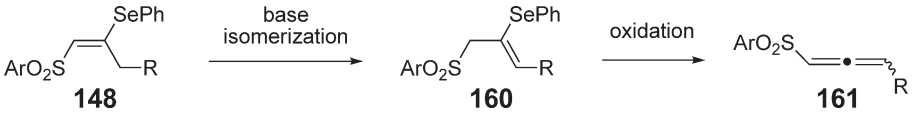
Another class of substrates investigated in this reaction are the cyclohexane derivatives **162**. The stereoselective oxidation of the selenide followed by an elimination provided a novel useful method for the synthesis of chiral cyclohexylidenemethyl ketones **163** (Scheme 46).[289]

Cyclohexyl selenides **162** can be prepared from the 4-substituted cyclohexanones via the selenoketals and upon oxidation with chiral oxidants, compounds **163** were obtained in high yields and with excellent stereoselectivities. Some representative examples are summarized in Table 5 and it is obvious that only the Davies oxidant **158** is leading to high enantiomeric excesses in the product **163** whereas under Sharpless oxidation conditions no selectivity is obtained. The titanium complex formed in the Sharpless oxidant may promote the racemization of the intermediate selenoxide by acting as a Lewis acid catalyst, while the aprotic nature of the Davies oxidant **158** slows down racemization dramatically.

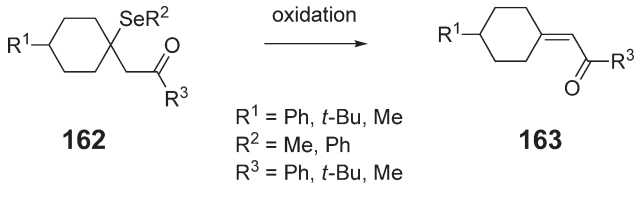
Similar reactions were also achieved by the formation of diastereomeric optically active selenoxides as intermediates in the elimination reaction. Optically active ferrocenyl diselenide **19** was used in selenenylations of alkynes generating vinyl selenides of type **164**. Oxidation of the selenides was performed with mCPBA under various reaction conditions which afforded the corresponding chiral selenoxides, which, after elimination, afforded axial chiral allenecarboxylic ester derivatives **165** in high enantioselectivities (R = Me: 89% ee, R = Et: 82% ee, R = C_3H_7: 85% ee) (Scheme 47).[85,87]



Scheme 44



Scheme 45

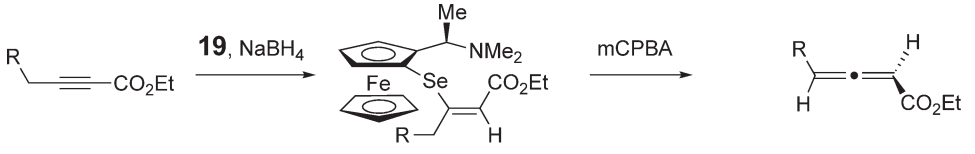


Scheme 46

Table 5 Stereoselective selenoxide formation and elimination

R^1	R^2	R^3	*Oxidant*	**163** *Yield* (%)	**163** ee (%) (*Configuration*)	*References*
Ph	Me	Ph	**158**	92%	74 (*R*)	289
t-Bu	Me	Ph	**158**	96%	83 (*R*)	289
t-Bu	Me	*t*-Bu	**158**	70%	82 (*R*)	289
t-Bu	Me	Me	**158**	97%	74 (*S*)	289
t-Bu	Ph	Ph	**158**	66%	7 (*R*)	289
Me	Me	Ph	**158**	91%	81 (*R*)	289
t-Bu	Me	Ph	Sharpless[a]	100%	2	289
t-Bu	Ph	Ph	Sharpless[a]	64%	0	289

[a]Ti(*i*-PrO)$_4$, (+)-DIPT, *t*-BuOOH.



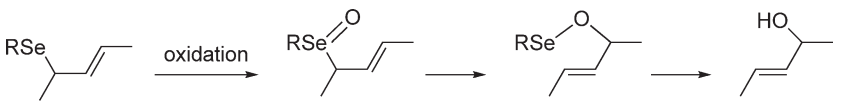
164 **165**

Scheme 47

9.11.2.5.3 Rearrangements

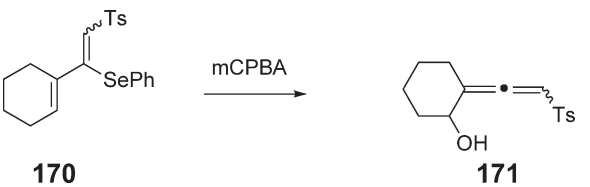
The use of allylic selenides **166** in oxidation reaction leads to intermediate selenoxides **167**, which can undergo [2,3]sigmatropic rearrangements to the corresponding allylic selenenates **168**. These componds will lead to allylic alcohols **169** after hydrolysis (Scheme 48). This is also a versatile procedure for the synthesis of optically active allylic alcohols, provided that either an asymmetric oxidation or an optically active selenide is used for the rearrangement. Detailed kinetic and thermodynamic studies of [2,3]sigmatropic rearrangements of allylic selenoxides have also been reported.[290–294]

The [2,3]sigmatropic rearrangement of allylic selenides has proven to be a useful method for the preparation of allenic alcohols. Selenide **170** was obtained by a free-radical selenosulfonation of the corresponding enyne. Oxidation with mCPBA afforded the allenic alcohol **171** in 89% yield via an intermediate selenoxide (Scheme 49).[295]



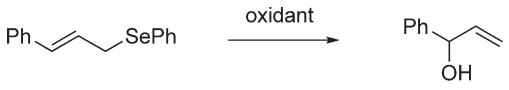
166 **167** **168** **169**

Scheme 48



170 **171**

Scheme 49



172 **173**

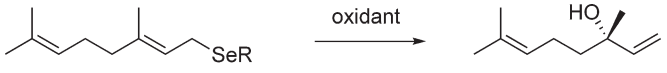
Scheme 50

Asymmetric [2,3]sigmatropic rearrangements can proceed via optically active selenoxides. It has been shown that the Davis oxidant **158** can be used for the oxidation of selenides such as **172**. The reaction product, after oxidation and rearrangement, is the allylic alcohol **173** formed with 35% ee (Scheme 50).[279,282] Also Sharpless conditions (Ti(*i*-PrO)$_4$, (+)-DIPT, *t*-BuOOH) have been applied to this reaction and the product has been obtained in 69% ee. When, however, the phenyl selenide moiety in **172** is replaced with an *ortho*-nitrophenyl selenide, the selectivity is increased to 92% ee in the allylic alcohol **173** using Sharpless conditions.[296] Other selenides such as 2′-pyridyl or ferrocenyl selenides gave much lower selectivities.

There is again the potential of performing asymmetric [2,3]sigmatropic rearrangements by the diastereoselective oxidation of optically active selenides. Compounds **174** with optically active substituents R have been employed, a [2.2]paracyclophane derivative led to linalool **175** in 67% ee via [2,3]sigmatropic rearrangement of the corresponding selenoxide.[285] Other chiral moieties like the ferrocenyl derivative synthesized from **19** yielded **175** in 83% ee,[87] while with nitrogen-containing moieties such as the selenide derived from **18** only 35% ee has been obtained (Scheme 51).[297] Also selenuranes (tetrasubstituted selenium(IV) compounds) have been prepared and used in asymmetric [2,3]sigmatropic rearrangements.[298,299]

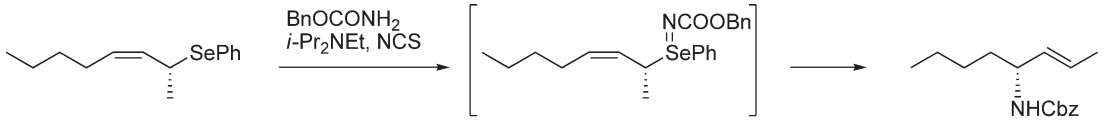
The nitrogen analogs of the selenoxides are the selenimides. They can be prepared by reacting selenides with, for example, Chloramine-T (TsNClNa).[300] Because Chloramine-T can decompose rapidly if heated above 130 °C, a mixture of *N*-chlorosuccinimide (NCS) and an amine can also be used.[301] If allylic selenides such as **176** are employed in these reactions, a subsequent [2,3]sigmatropic rearrangement produces allylamines **178** as products. In the example shown in Scheme 52 a chiral selenide is used and the product **178** is then an optically active allylic amine.[301,302] Optically active allylic amines are very useful building blocks in organic synthesis although procedures for the synthesis of such compounds are still quite limited.[303]

Other convenient reagents for the imidation of sulfides and selenides are imidoiodanes such as *N*-(*p*-tolylsulfonyl)-imino(phenyl)iodane (PhI=NTs).[304] Unfortunately, these reagents are sometimes difficult to prepare due to their thermal sensitivity and some have even been claimed to be explosive.[305] Selenimides are tricoordinate tetravalent compounds and can be isolated in optically active forms. They can be prepared from optically active selenoxides, a reaction which was shown to occur with an overall retention of stereochemistry.[306] They can also be obtained by optical resolution of a diastereomeric selenimide and stereochemical issues including kinetics of epimerization by pyramidal inversion were studied in detail.[307] Also the enantioselective imidation of prochiral selenides of type **179** is possible by using a combination of *N*-(*p*-tolylsulfonyl)imino(phenyl)iodane (PhI=NTs) and a catalytic amount of



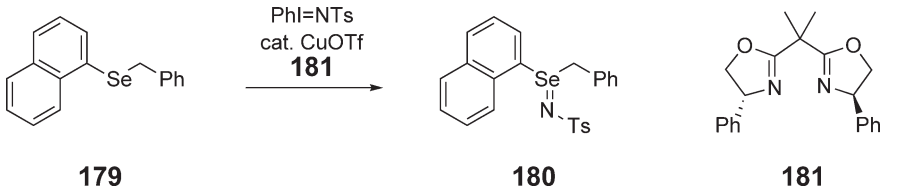
174 **175**

Scheme 51



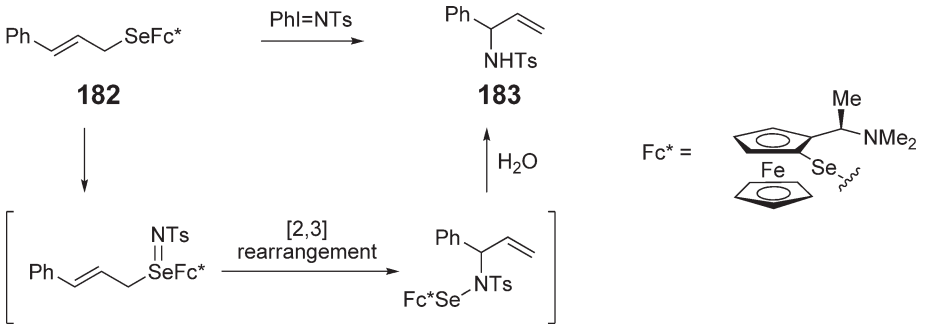
176 **177** **178**

Scheme 52



179 180 181

Scheme 53



Scheme 54

copper triflate together with a chiral bis(oxazoline) ligand such as **181**. Although the selectivities obtained are low, this direct catalytic imidation of selenides is potentially useful for the synthesis of optically active selenimides. Compound **180** was obtained in 64% yield with 36% ee (Scheme 53).[308]

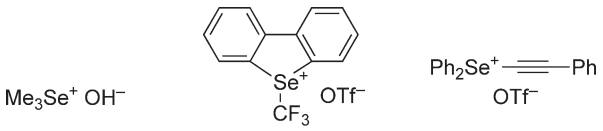
Similar reaction conditions can be applied to the imidation of allylic selenides. When the reaction conditions described in Scheme 53 are used for the imidation of **172**, the corresponding allylic amine is obtained with 20% ee.[308] Also diastereoselective [2,3]sigmatropic rearrangements of the corresponding selenimides have been investigated. The imidation of **182** with PhI═NTs has been proven to be more efficient than with Chloramine T in both product selectivity and enantioselectivity of the resulting secondary amine **183** (Scheme 54). Enantioselectivities of up to 87% have been obtained depending on the reaction conditions, which indicates that the initial imidation proceeds with high diastereoselectivity and the chirality transfer in the [2,3]sigmatropic rearrangement occurs with almost no loss of optical purity.[309]

9.11.2.6 Selenium at Higher Oxidation States

Compounds containing a selenium atom at a higher oxidation state have, apart from selenium dioxide, found only limited use in preparative organic chemistry. But in recent times it has been shown that these reagents also have a high potential for organic transformations and they often allow very selective reactions in the presence of other functional groups. At present, a large number of different selenium-containing compounds have been prepared and isolated with a formal oxidation state of the selenium atom between 2 and 6 and with 1 to 6 ligands attached to it. Divalent selenium compounds can be either monocoordinated such as selenocarbonyl compounds (these derivatives are covered separately in Section 9.11.2.7) or dicoordinated such as selenides (these compounds are covered in several other chapters and will not be mentioned here).

9.11.2.6.1 Trivalent derivatives

Trivalent selenium compounds such as seleniranium derivatives of type **34** and **35** are intermediates which are frequently used in organic synthesis, although these intermediates are usually instable and cannot be isolated. There are only very few tricoordinated compounds which have been isolated and reported. The parent member of this class of compounds, trimethylselenium hydroxide **184**, was found to be a strong methylating reagent to a wide range of nucleophilic substrates.[310] Similar properties were reported from compound **185**, which is used as a trifluoromethylating reagent for nucleophilic substrates.[311] Acyclic selenonium salts such as **186** have also been prepared and employed in various subsequent reactions (Figure 7).[312]

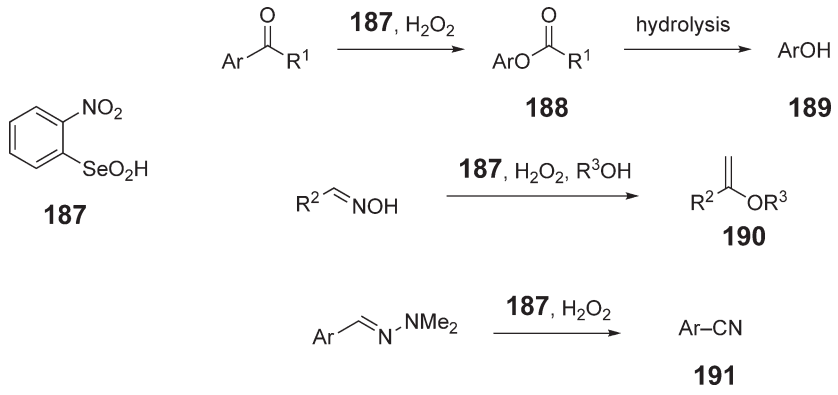


184 185 186

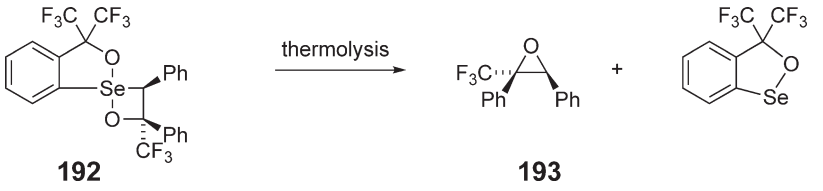
Figure 7 Trivalent selenium compounds.

9.11.2.6.2 Tetravalent derivatives

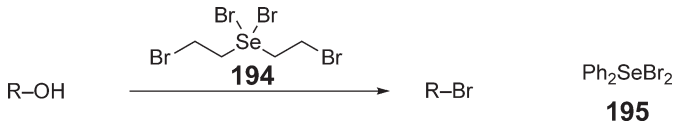
Within the class of tetravalent compounds, there are only two important dicoordinated derivatives: selenium dioxide (O═Se═O) and diimidoselenium (R—N═Se═N—R) reagents. The introduction of a carbonyl functionality at activated positions is one of the early synthetic applications of selenium dioxide.[9] The hydroxylation of allylic or propargylic positions or oxidative bond cleavage reactions belong to transformations, which are well explored and covered in several reviews. The oxidation of alkenes in allylic position is an important transformation in organic synthesis. The combination of selenium dioxide and formic acid in dioxane was found to be an efficient combination for the allylic oxidation of sterically hindered alkenes.[313] Other oxidations with hydrogen peroxide catalyzed by selenium dioxide have been performed. Aldehydes or ketones have been converted into esters or carboxylic acids[314–317] and sulfides have been oxidized to sulfoxides or sulfones.[318,319] The same reagent combination can be used for the cleavage of carbon–carbon double bonds.[320] The synthesis of selenoxides as very important representative compounds for tetravalent, tricoordinated selenium derivatives is covered in Section 9.11.2.5.1. Selenoxides can also be used as oxidants; this was demonstrated first by the oxidation of organophosphorus derivatives to the corresponding phosphoryl analogs.[321] Also novel methods for their preparation have been published, for example, potassium superoxide in the presence of a sulfonylchloride allows the clean synthesis of selenoxides from their selenide precursors.[322] However, in addition, seleninic acids (R—SeO_2H) or the corresponding anhydrides (R—Se(O)—O—Se(O)—R) have been used in oxidation reactions. Early reports focus on the oxidation of phenols,[323–325] whereas the selenenic acids can also be used for the introduction of hydroxy moieties or carbonyl functionalities into various substrates. In combination with hydrogen peroxide, seleninic acids are known to catalyze different oxidative processes.[326–328] The intermediate formation of the corresponding perseleninic acids (R—SeO_3H) is responsible for efficient Baeyer–Villiger reactions, oxidation of sulfides, or epoxidations of alkenes. The seleninic acid **187** can be used together with hydrogen peroxide to perform Baeyer–Villiger reactions to yield esters **188** (R^1 = Me) or aryl formates **188** (R^1 = H), which can then be hydrolyzed to the corresponding phenols **189** in good yields.[329] Seleninic acid **187** also shows remarkable reactivity in the hydrogen peroxide oxidation of alkenes such as styrene.[330] Aldoximes can be oxidized in the presence of alcohols to esters **190**,[331] while aromatic hydrazones can be oxidized to nitriles **191** in moderate to good yields (Scheme 55).[317]



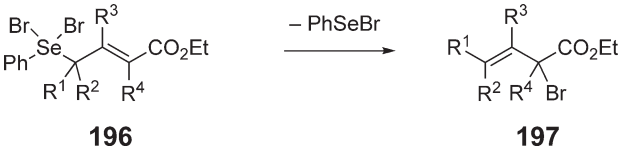
Scheme 55



Scheme 56



Scheme 57



Scheme 58

In contrast to thionyl chloride, which is used frequently as a reagent in synthesis, the applications of seleninyl chloride ($SeOCl_2$) are very limited. It can be used to synthesize selenium-bridged chromanones[332] or in the synthesis of novel selenium-containing heterocycles.[333,334]

Tetravalent selenium compounds which are tetracoordinated have one lone pair and are also called selenuranes. Some of these compounds have already been mentioned earlier as these compounds can be used in rearrangement reactions. Their chemistry is still not much explored although some stable compounds have been synthesized. The dialkoxyselenurane **192** was found to give oxiranes **193** by thermolysis (Scheme 56).[335]

Dichloroselenuranes or dibromoselenuranes such as **194** can be used for the conversion of alcohols into the corresponding halides.[336] Diphenyldibromoselenurane **195** has been found to be an efficient source for bromine cations (Scheme 57).[337]

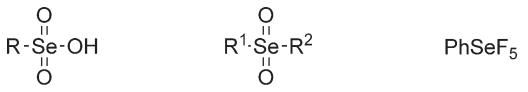
Dibromoselenuranes **196** can be prepared from the corresponding selenides by reaction with elemental bromine. The α,β-unsaturated ester **196** is converted into the α-bromo-β,γ-unsaturated ester **197** by elimination of phenylselenenyl bromide (Scheme 58).[338] Dibromoselenuranes from propargylic selenides undergo similar reactions leading to either allenes or propargylic bromides.[339]

Trichloroselenuranes ($RSeCl_3$) have been used as reagents in organic synthesis, either to introduce chlorine[340,341] or a selenyl moiety.[342,343]

9.11.2.6.3 Hexavalent derivatives

There are only few hexavalent selenium compounds of interest to synthetic chemists. Selenonic acids **198** and selenones **199** have found several synthetic applications, whereas the organic synthesis of perselenuranes such as phenylselenenyl pentafluoride **200** still remains unexplored. (Figure 8).[344]

The synthetic application of selenones **199** is due to the fact that these groups have excellent leaving group abilities. Substitution reactions can be used to replace a selenone moiety with almost any kind of nucleophile.[197,345–348] Internal nucleophiles will lead to cyclizations, this approach has been successfully used in the synthesis of various nitrogen-containing heterocycles of different size.[349] The selenones are usually obtained by oxidation of the corresponding selenides with *meta*-chloroperbenzoic acid. This methodology has also been used in nucleoside chemistry to synthesize a variety of biologically active compounds.[350–353]



198 199 200

Figure 8 Hexavalent selenium compounds.

9.11.2.7 Compounds with Selenium–Carbon Double Bonds

Selenocarbonyl compounds are the selenium analogs of carbonyl compounds having a carbon–selenium double bond. They have been found to be very versatile compounds for many reasons; they generally show a reasonable stability combined with high reactivity to allow unique reactions to be carried out. Their electrophilicity is usually higher due to a lower LUMO and their nucleophilicity is also enhanced because of a higher HOMO in these compounds. As the carbonyl group is one of the most important functionalities in organic chemistry, the replacement of the oxygen atom with a heavier atom such as sulfur or selenium has attracted lots of interest. Almost all functionalities with a carbon–oxygen double bond have been prepared with a carbon–selenium double bond instead. Selenoaldehydes and selenoketones, and a big variety of selenoesters and selenoamides together with selenoureas, selenocarbamates, and selenocarbonates have been prepared by various routes and several excellent reviews covering these classes of compounds have been published.[354–356]

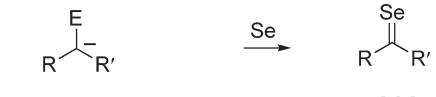
Selenoaldehydes and selenoketones are selenocarbonyl compounds which are usually unstable. Only the attachment of bulky groups next to the selenocarbonyl moiety has enabled their isolation, and selenoaldehydes[357] as well as selenoketones[358–360] have been described recently. More stable are selenoesters and selenoamides, and different methods for their preparation have been reported. Selenoureas, selenocarbamates, and selenocarbonates are the most stable selenocarbonyl compounds and the basic principles for their synthesis are known for a long time. But improved methods have been reported recently as well.

9.11.2.7.1 Synthesis of selenocarbonyl compounds

Different reagents are known to directly convert carbonyl functionalities of esters, aldehydes, amides, and ketones into the corresponding selenocarbonyl compounds. The treatment of carbonyl compounds with bis[1,5-cyclooctanediylboryl] selenide is an efficient synthesis of selenocarbonyl compounds.[361,362] A range of other reagents has also been developed to convert carbonyl compounds into selenocarbonyl compounds. Lewis-acidic selenium reagents such as $(Me_3Si)_2Se/n$-BuLi catalyst,[363] $(Me_2Al)_2Se$,[364–370] $(Me_3Si)_2Se/BF_3{\cdot}Et_2O$[371–373] have been developed. In the reaction with $(Me_2Al)_2Se$ acetals and orthoesters can be transformed into selenoaldehydes, selenoketones, and selenoesters with high efficiency.[368] The generation of α,β-unsaturated selenoaldehydes and selenoketones is also successful with $(Me_2Al)_2Se$.[367,370] Not only ketones can be converted to the corresponding selenoketones, but also esters and amides can be transformed into their selenium analogs albeit with lower yields.

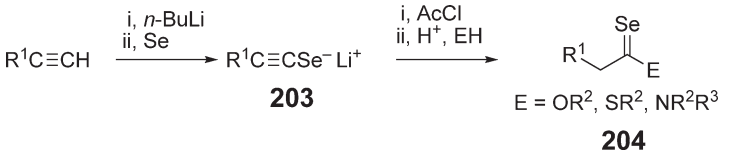
The ability of carbanions to react with elemental selenium can be advantageously used for the synthesis of selenocarbonyl compounds. For example, sulfur ylides **201** ($E = {}^{+}SMe_2$) have been reacted with elemental selenium to generate the corresponding selenocarbonyl compounds **202** (Scheme 59).[374,375] But Staudinger selenylation also has been applied to the synthesis of selenoketones **202** from phosphorus ylides **201** ($E = {}^{+}PPh_3$), which have been trapped by dienes in hetero-Diels–Alder reactions.[376–383]

Alkynyl anions can be reacted with elemental selenium to form alkynylselenolates **203**. These alkynylselenolates **203** have been used as key intermediates for the synthesis of a variety of selenocarbonyl compounds. First reactions have already been carried out earlier,[384] and some later improvements widened the scope of this reaction including the synthesis of selenoesters, selenothioesters, and selenoamides of type **204** (Scheme 60).[385,386] Even a direct

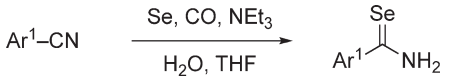


$E = {}^{+}SMe_2,\ {}^{+}PPh_3$ **201** **202**

Scheme 59



Scheme 60



Scheme 61

reaction of the alkynylselenolates **203** with amines[387] or thiols[388,389] is possible, whereas reactions with alcohols only yielded dimerized products. The selenoketene intermediates can also be trapped by propargyl bromides or allylic bromides to afford unsaturated selenoamides.[390–392]

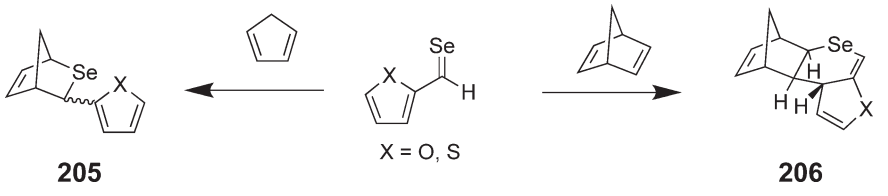
Also nucleophilic selenium species can be used for the synthesis of selenocarbonyls. These precursor compounds are ususally prepared by the reduction of elemental selenium. The addition of hydrogen selenide (H_2Se) or sodium hydrogen selenide (NaHSe) to imines or iminonium salts or silyl keteneacetals can be used for the preparation of selenoamides,[393] selenocarbonates,[394,395] or selenoesters.[396] The addition to nitriles leads directly to primary selenoamides in quite high yields. The first report described the synthesis of benzeneselenoamide from benzonitrile and hydrogen selenide.[397] To avoid the use of toxic hydrogen selenide, other methods have been developed for the conversion of nitriles into selenoamides. Carbon monoxide and water can be used for the *in situ* reduction of elemental selenium in the presence of triethylamine (Scheme 61). Various nitriles have been converted to the corresponding selenoamides.[398,399] A subsequent treatment of either the isolated products or the reaction mixture with a primary amine allows the efficient synthesis of substituted selenoamides.[400]

9.11.2.7.2 Reactions with selenocarbonyl compounds

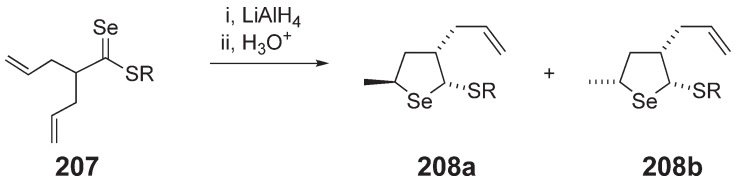
As already mentioned, the reactivity of selenocarbonyl compounds is usually higher than the corresponding sulfur and oxygen analogs, but their reactivity also strongly depends on their substitution pattern. Selenoaldehydes and selenoketones are generated usually only *in situ* due to their instability. They can be trapped by a variety of dienes in hetero-Diels–Alder reactions to give *endo*-adducts as major products. The regioselectivity with unsymmetrical dienes is high. α,β-Unsaturated selenoaldehydes can react both as dienes and as dienophiles to afford adducts such as **205** or **206** (Scheme 62).[370]

Also very common are reactions of selenocarbonyl compounds with nucleophiles. Reduction of selenoketones[401,402] or selenoesters[403] is known to produce the corresponding selenides. The reduction of selenothioic acid *S*-ester **207** is easily performed using lithium aluminum hydride and a subsequent cyclization affords tetrahydroselenophene derivative **208** with high stereoselectivities (R = Bu: **208a** : **208b** = 91 : 9) (Scheme 63).[404]

Wittig-type olefinations can also be performed using selenoaldehydes. Phosphorus ylides initially attack the carbon atom of the selenocarbonyl functionality.[405] Aromatic selenoketones undergo reductive dimerization with organolithium reagents probably via an electron transfer mechanism.[406] Also the addition of organolithium reagents takes



Scheme 62



Scheme 63

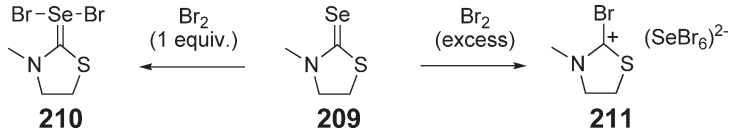
place at the carbon atom of selenocarbonyl group of selenoesters[407] and selenoamides.[408] With selenoesters a small amount of the products derived from an attack to the selenium atom of the selenocarbonyl moiety was also observed.

The reactions of selenocarbonyl compounds with electrophiles are also well-established procedures. Alkylations or acylations of the selenium atom of selenoamides[409] or selenoureas[410] are known. Selenonium salts are formed initially; they can then be converted into diselenides, selenazoles, or cyclic selenides depending on their structure. Reactions of selenocarbonyls with bromine and iodine have also been widely exploited. Selenocarbonates, selenothiocarbonates,[411–415] and selenoureas[416–418] can be employed, the reaction of **209** with 1 equiv. bromine led to the hypervalent 10-Se-3 complex **210**, whereas an excess of bromine gave rise to a cleavage of the carbon–selenium double bond and formation of product **211** (Scheme 64).

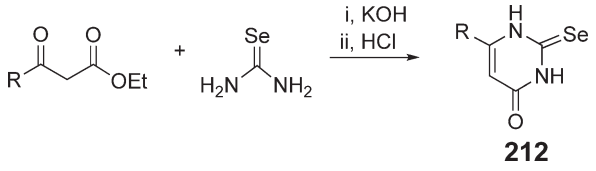
Reactions of selenoamides and selenoureas with aldehydes or ketones proceed via a nucleophilic attack of the selenium atom and lead to the formation of selenium- and nitrogen-containing heterocycles.[419–424] The reaction of selenourea with 1,3-dicarbonyl compounds in the presence of potassium hydroxide leads to the formation of selenouracil **212**;[425] its biological activity has also been tested (Scheme 65).[426]

The selenium counterparts of enolates, eneselenolate ions, can be generated by deprotonation of the corresponding selenocarbonyl compounds such as selenoamides[427,428] or selenoesters.[403,429] They can either be trapped with trimethylsilyl chloride or react with a variety of substrates to form a range of different products.

Selenocarbonyl compounds can form different metal complexes and some general structures are shown in Figure 9.



Scheme 64



Scheme 65

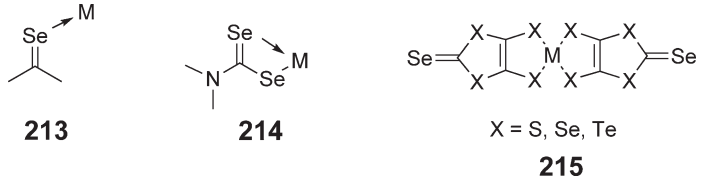
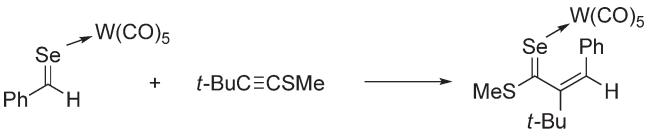


Figure 9 Metal complexes with selenocarbonyl compounds.



216 **217**

Scheme 66

The synthesis of metal complexes of type **213** can be performed by reacting metal–carbene complexes with selenium sources such as alkyneselenolates **203**.[430] Also the stability of unstable selenocarbonyl compounds such as selenoaldehydes can be enhanced by coordination to metal carbonyls and the reactivity of such complexes has been studied. Complex **216** can react with methylthiohexyne and the product is a different complex **217** with the selenium atom still coordinating to the metal carbonyl fragment (Scheme 66).[431]

Various other complexes have been formed by reacting selenourea or selenoamides with the corresponding metal halides or metal carbonyl compounds, such as Cu,[432] Ag, Au,[433,434] Zn, Cd,[435,436] Co,[437] and Cr, Mo, W.[438] Metal complexes of type **214** are also quite well known and such complexes have been characterized by various analytical techniques.[439,440] The electric conductivity of complexes **215** is especially interesting and many of these compounds have been prepared and their properties studied.[441,442]

During the last decade, many novel synthetic procedures for the synthesis of selenocarbonyl componds have been established avoiding the use of toxic hydrogen selenide. The utilization of selenocarbonyl compounds in biological chemistry as well as in the development of new synthetic reactions based on chiral selenocarbonyl compounds has been rather unexplored despite the fact that slight modifications of the structures of selenocarbonyl compounds are expected to highly attenuate the reactivity and sensitivity of these compounds.

9.11.2.8 Selenium-containing Compounds as Ligands and Catalysts

The synthesis of optically active selenium-containing reagents as well as their application to stereoselective synthesis is of high current interest. Several products also contain a selenium functionality and their use as chiral ligands and catalysts in asymmetric reaction is promising. Various reactions of this type are known and some recent developments in this novel area are summarized here.

9.11.2.8.1 Selenium-containing compounds as ligands

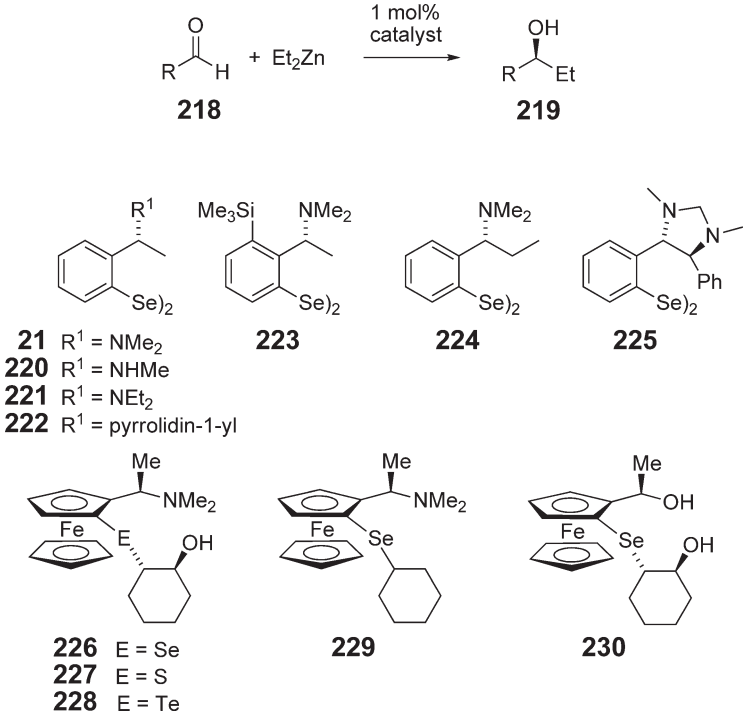
Asymmetric addition reactions of diorganozinc reagents to aldehydes can be catalyzed by a broad range of optically active ligands – most prominent compounds are aminoalcohols for these reactions[443–446] and detailed mechanistic studies have been reported.[447,448] But sulfur-containing amines also can catalyze such reactions efficiently.[449,450] Several research groups have reported the use of selenium-containing compounds for stereoselective dialkylzinc additions to aldehydes and a range of catalysts has been explored. It was found that diselenides are efficient procatalysts for these reactions as the dialkylzinc reagent rapidly cleaves the selenium–selenium bond to leave back a catalytically active zinc selenolate.[92] Various aldehydes **218** have been reacted with diethylzinc in the presence of diselenides **220–225** to yield the corresponding secondary alcohols **219**; some results are given in Table 6. Interestingly, only slight variations in the structure of the catalysts such as selenide **229** or selenoalcohols **230** led to the completely racemic alcohol **219** (Scheme 67).

Ferrocenyl-based diselenides can also be used efficiently as asymmetric ligands for hydrosilylation reactions of ketones and imines which are mechanistically considered to be transfer hydrogenations. The transition metal-catalyzed hydrosilylation of ketones is a widely studied reaction and recently nitrogen-containing compounds have been employed frequently as ligands in such transformations.[454–456] Several organoselenium compounds having a chiral ferrocenyl moiety have been prepared and used as efficient ligands in the Rh(I)-catalyzed hydrosilylation of acetophenone with diphenylsilane. The substituent on the ferrocenyl moiety has a remarkable effect on the reaction and influences the selectivity of the alcohol **231** obtained in this reaction (Scheme 68, Table 7).

Compared to the rhodium-catalyzed stereoselective reactions, studies on the iridium-catalyzed reactions have been limited until recently. Usually lower selectivities have been observed in the Ir(I)-catalyzed reactions.[459,460] The asymmetric hydrosilylation of imines affords optically active secondary amines. These are very valuable compounds, but the studies on that reaction are quite limited.[461] Close examinations of these reactions revealed that they proceed via a transfer hydrogenation. Other conditions such as the 2-propanol/base system in the presence of an appropriate metal complex have been employed as well, but only low selectivities were obtained.[462]

Table 6 Diethylzinc additions to aldehydes

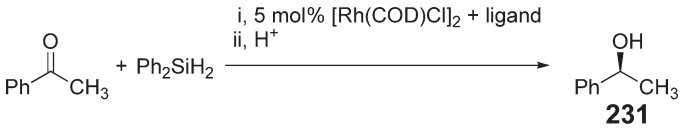
Catalyst	*R—CHO*	**219** *Yield* (%)	**219** ee (%)	*References*
21	Ph	87	92	91,92
220	Ph	48	82	92
221	Ph	57	91	91,92
222	Ph	91	97	91,92
222	4-CF_3-C_6H_4	98	98	92
222	4-*t*-Bu-C_6H_4	67	98	92
222	3,5-$(CF_3)_2$-C_6H_3	90	98	92
222	2,3,4,5-F_4-C_6H	95	97	92
223	Ph	98	96	451
224	Ph	95	91	451
225	Ph	89	97	452
226	Ph	98	94	453
226	4-MeO-C_6H_4	95	99	453
227	Ph	90	52	453
228	Ph	90	46	453
229	Ph	57	0	453
230	Ph	7	0	453

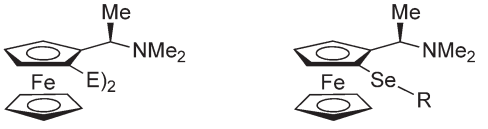


Scheme 67

9.11.2.8.2 Selenium-containing compounds as catalysts

Selenium-containing reagents can also be used as catalysts in various reactions. A well-known reagent is selenium dioxide, which is used as an oxidizing reagent for alkenes, carbonyl compounds, or other substrates. Selenium dioxide can introduce an oxygen moiety at the allylic position of alkenes. Depending on the reaction conditions, the products are either allylic alcohols **237** or the corresponding α,β-unsaturated carbonyl compounds **238** (Scheme 69). The mechanism of this reaction has been investigated extensively and also catalytic amounts of selenium dioxide together with *tert*-butyl hydroperoxide as oxidant can be used efficiently for the allylic oxidation of alkenes.[463] Sometimes the catalytic reaction gives higher yields than a stoichiometric use of selenium dioxide.





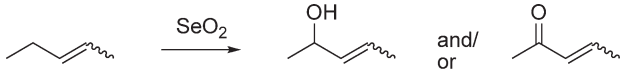
19 E = Se
232 E = S
233 E = Te

234 R = Ph
235 R = *n*-Pr
236 R = allyl

Scheme 68

Table 7 Hydrosilylations of acetophenone with different catalysts

Catalyst	**231** *Yield* (%)	**231** ee (%)	*References*
19	31	85	457,458
232	46	31	457,458
233	67	50	457,458
234	26	40	457,458
235	81	16	457,458
236	25	35	457,458
229	81	16	457,458

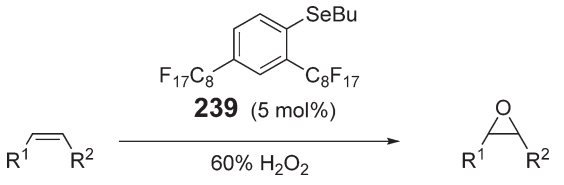


237 **238**

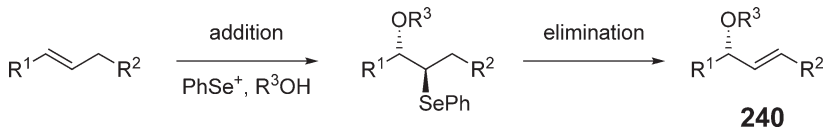
Scheme 69

Peroxyseleninic acids (RCO_3H) can be obtained by oxidation of seleninic acid derivatives and are efficient reagents for the epoxidation of alkenes. Such reactions can also be performed with catalytic amounts in the presence of a stoichiometric oxidant such as hydrogen peroxide.[327,464] To avoid issues concerning the toxicity of organoselenium derivatives, polymer-supported reagents have been developed and used in this transformation.[465] Related epoxidations have been reported in a biphasic reaction system. Selenide **239** bearing perfluoroalkyl substituents can be used as an efficient catalyst in a fluorous biphasic system to epoxidize alkenes with hydrogen peroxide as the stoichiometric oxidant (Scheme 70). The catalyst is selectively soluble in perfluorinated solvents and can, therefore, be easily recovered after the reaction and can be reused several times without a decrease of efficiency.[466]

It is possible to perform selenenylation–deselenenylation sequences with only catalytic amounts of selenium species. This reaction sequence provides double bond transpositioned allylic ethers, allylic esters, or allylic alcohols **240** from the corresponding alkenes (Scheme 71). This sequence can be performed electrochemically, and the selenium electrophile is generated from catalytic amounts of diphenyl diselenide.[467,468] It has been shown that the electrophilic selenium species can also be generated using diselenides and peroxosulfates together with copper (II)



Scheme 70



240

Scheme 71

nitrate. Moderate yields of the allylic ethers or esters **240** have been obtained (Scheme 71).[468,469] Other reactions also rely on the formation of the selenenyl sulfates from diselenides with peroxodisulfates as electrophilic reagents for the initial addition reaction to alkenes. The addition products are then oxidized by an excess peroxodisulfate and the subsequent elimination reaction yields allylic compounds.[56] Good yields are obtained in cases when R^2 is an electron acceptor substituent leading to α,β-unsaturated compounds of type **240**. Under similar experimental conditions, intramolecular versions of such catalytic transformations led to butenolides in good yields.[470,471] Different chiral diselenides have been employed in this reaction and after careful optimization of the reaction conditions, enantioselectivities up to 75% (R^1 = Ph, R^2 = H, R^3 = Me in **240**) have been obtained.[81,88,125,472] However, the turnover numbers are still small and further work is needed to improve the catalytic oxyselenenylation–elimination sequence.

9.11.3 Conclusions and Outlook

Various important aspects of organoselenium chemistry are summarized in this chapter. Major developments during the last 10 years are highlighted, but older work is also critically discussed. Improved and new selenium-containing reagents will surely be developed in the future to gain further profit from the usually very mild conditions in these reactions. This will lead to enhanced stereoselectivities in known reactions, new selenium-based transformations and methods, as well as new applications of this chemistry. The conceptual presentation of main principles will allow the reader to identify some future research directions and should allow also the non-specialist reader to understand the significant advantages of organoselenium chemistry.

References

1. Berzelius, J. J. *Afhandl. Fys. Kem. Min.* **1818**, *6*, 24.
2. Wöhler, F.; Siemens, C. *Ann. Chem.* **1847**, *61*, 360.
3. Kacer, F. Ger. Pat. 557,249, 1933 *Chem. Abstr.* **1933**, *27*, 304.
4. Flohé, L.; Gunzler, W. A.; Schock, H. H. *FEBS Lett.* **1973**, *32*, 132.
5. Rotruck, J. T.; Pope, A. L.; Ganther, H. E.; Swanson, A. B.; Hafeman, D. G.; Hoekstra, W. G. *Science* **1973**, *179*, 588.
6. Klayman, D. L.; Günther, W. H. H., Eds.; *Organic Selenium Compounds: Their Chemistry and Biology*; Wiley: New York, 1973.
7. Krief, A. Selenium. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11, pp 515–569, references 32–45.
8. Zybill, C. E. Selenium and its Compounds. In *Synthetic Methods of Organometallic and Inorganic Chemistry*; Herrmann, W. A., Ed.; Thieme: Stuttgart, 1997; Vol. 4, pp 124–175.
9. Woggon, W. D. Formation of C–O Bonds by Allylic Oxidation with Selenium(IV) Oxide. In *Houben-Weyl*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1996; Vol. E21, pp 4947–4956.
10. Jones, D. N.; Mundy, D.; Whitehouse, R. D. *Chem. Commun.* **1970**, 86–87.
11. Walter, R.; Roy, J. *J. Org. Chem.* **1971**, *36*, 2561–2563.
12. Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697–2699.
13. Sharpless, K. B.; Lauer, R. F.; Teranishi, A. Y. *J. Am. Chem. Soc.* **1973**, *95*, 6137–6139.
14. Sharpless, K. B.; Young, M. W.; Lauer, R. F. *Tetrahedron Lett.* **1973**, 1979–1982.
15. Reich, H. J.; Reich, I. L.; Renga, J. M. *J. Am. Chem. Soc.* **1973**, *95*, 5813–5815.
16. Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1973**, 695–696.
17. Okamoto, Y., Günther, W. H. H., Eds. *Ann. NY Acad. Sci.* **1972**; 192.
18. Krief, A. Selenium. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11, pp 515–569.
19. Wang, Z.; Ma, W.; Zhang, C. *Huaxue Shiji* **1993**, *15*, 25–30.
20. Xu, C. *Huaxue Shiji* **1993**, *15*, 155–161.
21. Warnke, Z.; Gleich, E. *Pol. J. Chem.* **1993**, *67*, 1527–1538.
22. Duddeck, H. *Prog. NMR Spectrosc.* **1995**, *27*, 1–323.
23. Fujita, K. *Yuki Gosei Kagaku Kyokaishi* **1996**, *54*, 166–175.
24. Murai, T. *Yuki Gosei Kagaku Kyokaishi* **1997**, *55*, 1092–1100.
25. Wirth, T. *Liebigs Ann. Recl.* **1997**, 2189–2196.
26. Block, E. *Phytochemistry* **1998**, 129–141.
27. Wirth, T. *Tetrahedron* **1999**, *55*, 1–28.

28. Wirth, T. *Angew. Chem.* **2000**, *112*, 3890–3900.
28a. Wirth, T. Angew. *Chem. Int. Ed.* **2000**, *39*, 3740–3749.
29. Mugesh, G.; Singh, H. B. *Chem. Soc. Rev.* **2000**, *29*, 347–357.
30. Mugesh, G.; du Mont, W. W.; Sies, H. *Chem. Rev.* **2001**, *101*, 2125–2179.
31. Arteel, G. E.; Sies, H. *Environ. Toxicol. Pharmacol.* **2001**, *10*, 153–158.
32. Abe, H. *Yakugaku Zasshi* **2003**, *123*, 423–430.
33. Mlochowski, J.; Brzaszcz, M.; Giurg, M.; Palus, J.; Wojtowicz, H. *Eur. J. Org. Chem.* **2003**, 4329–4339.
34. Potapov, V. A.; Amosova, S. V. *Russ. J. Org. Chem.* **2003**, *39*, 1373–1380.
35. Soriano-García, M. *Curr. Med. Chem.* **2004**, *11*, 1657–1669.
36. Klapötke, T. M.; Broschag, M. *Compilation of reported ^{77}Se NMR Chemical Shifts;* Wiley: Chichester, 1996.
37. Schrauzer, G. N. *Selen*, 3rd ed.; Barth: Heidelberg, 1998.
38. Back, T. G., Ed. *Organoselenium Chemistry: A Practical Approach*; Oxford University Press: Oxford, 1999.
39. Wirth, T., Ed. *Organoselenium Chemistry: Modern Developments in Organic Synthesis*; Topics in Current Chemistry 208, Springer: Berlin, 2000.
40. Hatfield, D. L., Ed. *Selenium: Its Molecular Biology and Role in Human Health*; Kluwer: Boston, 2001.
41. Krief, A.; Hevesi, L. *Organoselenium Chemistry I – Functional Group Transformations*; Springer: Heidelberg, 1988.
42. Jensen, K. A.; Kjaer, A. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1986; Vol. 1, pp 1–20.
43. Poirier, R. A.; Csizmadia, I. G. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1986; Vol. 1, pp 21–62.
44. Hargittai, I.; Rozsondai, B. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1986; Vol. 1, p 63.
45. Hölzle, G.; Jenny, W. *Helv. Chim. Acta* **1958**, *41*, 593–603.
46. Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis;* Pergamon: Oxford, 1986.
47. Liotta, D., Ed. *Organoselenium Chemistry*; Wiley: New York, 1987.
48. Beaulieu, P. L.; Déziel, R. In *Organoselenium Chemistry: A Practical Approach*; Back, T. G., Ed. Oxford University Press: Oxford, 1999; pp 35–66.
49. Tiecco, M. In *Organoselenium Chemistry: Modern Developments in Organic Synthesis*; Wirth, T., Ed.; Topics in Current Chemistry 208, Springer: Berlin, 2000; pp 7–54.
50. Nicolaou, K. C.; Petatis, N. A.; Claremon, D. A. *Tetrahedron* **1985**, *41*, 4835–4841.
51. Tomoda, S.; Usuki, Y.; Fujita, K. I.; Iwaoka, M. *Rev. Heteroatom. Chem.* **1991**, *4*, 249–262.
52. Jackson, W. P.; Ley, S. V.; Whittle, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1173–1174.
53. Murata, S.; Suzuki, T. *Chem. Lett.* **1987**, 849–852.
54. Murata, S.; Suzuki, T. *Tetrahedron Lett.* **1987**, *28*, 4297–4298.
55. Murata, S.; Suzuki, T. *Tetrahedron Lett.* **1987**, *28*, 4415–4416.
56. Tiecco, M.; Testaferri, L.; Tingoli, M.; Bartoli, D. *Tetrahedron Lett.* **1989**, *30*, 1417–1420.
57. Tiecco, M.; Testaferri, L.; Tingoli, M.; Bartoli, D.; Marini, F. *J. Chem. Soc., Perkin. Trans. 1* **1993**, 1989–1993.
58. Back, T. G.; Muralidharan, K. R. *Tetrahedron Lett.* **1990**, *31*, 1653–1656.
59. Back, T. G.; Muralidharan, K. R. *J. Org. Chem.* **1991**, *56*, 2781–2787.
60. Tiecco, M.; Testaferri, L.; Tingoli, M.; Chianelli, D.; Bartoli, D. *Tetrahedron* **1988**, *44*, 2273–2282.
61. Bosman, C.; D'Annibale, A.; Resta, S.; Trogolo, C. *Tetrahedron Lett.* **1994**, *35*, 6525–6528.
62. Lee, D. H.; Kim, Y. H. *Synlett* **1995**, 349–350.
63. Han, L. B.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1996**, 475–476.
64. Yoshida, M.; Satoh, N.; Kamigata, N. *Chem. Lett.* **1989**, 1433–1436.
65. Yoshida, M.; Sasage, S.; Kawamura, K.; Suzuki, T.; Kamigata, N. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 416–422.
66. Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A. *Synth. Commun.* **1998**, *28*, 1769–1778.
67. Roh, K. R.; Chang, H. K.; Kim, Y. H. *Heterocycles* **1998**, *48*, 437–441.
68. Pandey, G.; Rao, V. J.; Bhalerao, U. T. *J. Chem. Soc., Chem. Commun.* **1989**, 416–417.
69. Pandey, G.; Sekhar, B. B. V. S. *J. Chem. Soc., Chem. Commun.* **1993**, 780–782.
70. Pandey, G.; Gadre, S. R. *Acc. Chem. Res.* **2004**, *37*, 201–210.
71. Tomoda, S.; Iwaoka, M. *Chem. Lett.* **1988**, 1895–1898.
72. Tomoda, S.; Iwaoka, M.; Yakushi, K.; Kawamoto, A.; Tanaka, J. *J. Phys. Org. Chem.* **1988**, *1*, 179–184.
73. Tomoda, S.; Iwaoka, M. *J. Chem. Soc., Chem. Commun.* **1988**, 1283–1284.
74. Tomoda, S.; Fujita, K.; Iwaoka, M. *J. Chem. Soc., Chem. Commun.* **1990**, 129–131.
75. Tomoda, S.; Fujita, K.; Iwaoka, M. *Chem. Lett.* **1992**, 1123–1124.
76. Tomoda, S.; Fujita, K.; Iwaoka, M. *Phosphorus Sulfur* **1992**, *67*, 247–252.
77. Déziel, R.; Goulet, S.; Grenier, L.; Bordeleau, J.; Bernier, J. *J. Org. Chem.* **1993**, *58*, 3619–3621.
78. Déziel, R.; Malenfant, E. *J. Org. Chem.* **1995**, *60*, 4660–4662.
79. Déziel, R.; Malenfant, E.; Bélanger, G. *J. Org. Chem.* **1996**, *61*, 1875–1876.
80. Déziel, R.; Malenfant, E.; Thibault, C.; Fréchette, S.; Gravel, M. *Tetrahedron Lett.* **1997**, *38*, 4753–4756.
81. Fujita, K.; Iwaoka, M.; Tomoda, S. *Chem. Lett.* **1994**, 923–926.
82. Fujita, K.; Murata, K.; Iwaoka, M.; Tomoda, S. *J. Chem. Soc., Chem. Commun.* **1995**, 1641–1642.
83. Fujita, K.; Murata, K.; Iwaoka, M.; Tomoda, S. *Tetrahedron Lett.* **1995**, *36*, 5219–5222.
84. Fujita, K.; Murata, K.; Iwaoka, M.; Tomoda, S. *Tetrahedron* **1997**, *53*, 2029–2048.
85. Nishibayashi, Y.; Singh, J. D.; Uemura, S.; Fukuzawa, S. *Tetrahedron Lett.* **1994**, *35*, 3115–3118.
86. Nishibayashi, Y.; Srivastava, S. K.; Takada, H.; Fukuzawa, S.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, 2321–2322.
87. Nishibayashi, Y.; Singh, J. D.; Fukuzawa, S.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 4114–4120.
88. Fukuzawa, S.; Takahashi, K.; Kato, H.; Yamazaki, H. *J. Org. Chem.* **1997**, *62*, 7711–7716.
89. Uemura, S. *Phosphorus Sulfur* **1998**, *136–138*, 219–234.
90. Wirth, T. *Angew. Chem.* **1995**, *107*, 1872–1873.
90a. Wirth, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1726–1728.
91. Wirth, T. *Tetrahedron Lett.* **1995**, *36*, 7849–7852.

92. Wirth, T.; Kulicke, K. J.; Fragale, G. *Helv. Chim. Acta* **1996**, *79*, 1957–1966.
93. Wirth, T.; Fragale, G. *Chem. Eur. J.* **1997**, *3*, 1894–1902.
94. Back, T. G.; Dyck, B. P.; Parvez, M. *J. Chem. Soc., Chem. Commun.* **1994**, 515–516.
95. Back, T. G.; Dyck, B. P.; Parvez, M. *J. Org. Chem.* **1995**, *60*, 703–710.
96. Back, T. G.; Dyck, B. P. *Chem. Commun.* **1996**, 2567–2568.
97. Back, T. G.; Nan, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3123–3124.
98. Back, T. G.; Dyck, B. P.; Nan, S. *Tetrahedron* **1999**, *55*, 3191–3208.
99. Fragale, G.; Neuburger, M.; Wirth, T. *Chem. Commun.* **1998**, 1867–1868.
100. Uehlin, L.; Fragale, G.; Wirth, T. *Chem. Eur. J.* **2002**, *8*, 1125–1133.
101. Tiecco, M.; Testaferri, L.; Bagnoli, L.; Marini, F.; Temperini, A.; Tomassini, C.; Santi, C. *Tetrahedron Lett.* **2000**, *41*, 3241–3245.
102. Tiecco, M.; Testaferri, L.; Marini, F.; Sternativo, S.; Bagnoli, L.; Santi, C.; Temperini, A. *Tetrahedron: Asymmetry* **2001**, *12*, 1493–1502.
103. Tiecco, M.; Testaferri, L.; Marini, F.; Sternativo, S.; Santi, C.; Bagnoli, L.; Temperini, A. *Tetrahedron: Asymmetry* **2001**, *12*, 3053–3059.
104. Tiecco, M.; Testaferri, L.; Bagnoli, L.; Purgatorio, V.; Temperini, A.; Marini, F.; Santi, C. *Tetrahedron: Asymmetry* **2001**, *12*, 3297–3304.
105. Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Chem. Eur. J.* **2002**, *8*, 1118–1124.
106. Tiecco, M.; Testaferri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Angew. Chem. Int. Ed.* **2003**, *42*, 3131–3133.
107. Tiecco, M.; Testaferri, L.; Bagnoli, L.; Purgatorio, V.; Temperini, A.; Marini, F.; Santi, C. *Tetrahedron: Asymmetry* **2004**, *15*, 405–412.
108. Santi, C.; Tiecco, M.; Testaferri, L.; Tomassini, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Phosphorus Sulfur* **2005**, *180*, 1071–1075.
109. Cox, M.; Wirth, T. *Phosphorus Sulfur* **2005**, *180*, 659–666.
110. Kim, K. S.; Park, J. I.; Moon, H. K.; Yi, H. *J. Chem. Soc., Chem. Commun.* **1998**, 1945–1946.
111. Kim, K. S.; Park, J. I.; Ding, P. *Tetrahedron Lett.* **1998**, *39*, 6471–6474.
112. Toshimitsu, A.; Aoai, T.; Uemura, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1980**, 1041–1042.
113. Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *J. Org. Chem.* **1981**, *46*, 4727–4733.
114. Toshimitsu, A.; Hayashi, G.; Terao, K.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1986**, 343–347.
115. Francisco, C. G.; Hernandez, R.; Leon, E. I.; Salazar, J. A.; Suarez, E. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2417–2427.
116. Toshimitsu, A.; Kusumoto, T.; Oida, T.; Tanimoto, S. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2148–2152.
117. Toshimitsu, A.; Hayashi, G.; Terao, K.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2113–2117.
118. Hassner, A.; Amarasekara, A. *Tetrahedron Lett.* **1987**, *28*, 5185–5188.
119. Giuliano, R. M.; Duarte, F. *Synlett* **1992**, 419–421.
120. Tiecco, M.; Testaferri, L.; Temperini, A.; Bagnoli, L.; Marini, F.; Santi, C. *Synth. Commun.* **1998**, *28*, 2167–2179.
121. Tingoli, M.; Tiecco, M.; Chianelli, D.; Balducci, R.; Temperini, A. *J. Org. Chem.* **1991**, *56*, 6809–6813.
122. Wirth, T.; Fragale, G.; Spichty, M. *J. Am. Chem. Soc.* **1998**, *120*, 3376–3381.
123. Wang, X.; Houk, K. N.; Spichty, M.; Wirth, T. *J. Am. Chem. Soc.* **1999**, *121*, 8567–8576.
124. Spichty, M.; Fragale, G.; Wirth, T. *J. Am. Chem. Soc.* **2000**, *122*, 10914–10916.
125. Tiecco, M.; Testaferri, L.; Santi, C.; Marini, F.; Bagnoli, L.; Temperini, A. *Tetrahedron Lett.* **1998**, *39*, 2809–2812.
126. Khokhar, S. S.; Wirth, T. *Angew. Chem. Int. Ed.* **2004**, *43*, 631–633.
127. Khokhar, S. S.; Wirth, T. *Eur. J. Org. Chem.* **2004**, 4567–4581.
128. Wirth, T.; Kulicke, K. J.; Fragale, G. *J. Org. Chem.* **1996**, *61*, 2686–2689.
129. Wirth, T. *Liebigs Ann. Recl.* **1997**, 1155–1158.
130. Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321–3408.
131. Mihelich, E. D.; Hite, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 7318–7319.
132. Lipshutz, B. H.; Gross, T. *J. Org. Chem.* **1995**, *60*, 3572–3573.
133. Fragale, G.; Wirth, T. *Eur. J. Org. Chem.* **1998**, 1361–1369.
134. Paulmier, C.; Berthe, B.; Outurquin, F. *Tetrahedron Lett.* **1997**, *38*, 1393–1396.
135. Wirth, T.; Fragale, G. *Synthesis* **1998**, 162–166.
136. Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L. *J. Chem. Soc., Chem. Commun.* **1995**, 235–236.
137. Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Santi, C. *Tetrahedron* **1995**, *51*, 1277–1284.
138. Tiecco, M.; Testaferri, L.; Marini, F.; Santi, C.; Bagnoli, L.; Temperini, A. *Tetrahedron* **1997**, *53*, 7311–7318.
139. Tiecco, M.; Testaferri, L.; Marini, F.; Santi, C.; Bagnoli, L.; Temperini, A. *Tetrahedron* **1997**, *53*, 10591–10602.
140. Jackson, W. P.; Ley, S. V.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1980**, 1028–1029.
141. Jackson, W. P.; Ley, S. V.; Whittle, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1173–1174.
142. Jackson, W. P.; Ley, S. V.; Morton, J. A. *Tetrahedron Lett.* **1981**, *22*, 2601–2604.
143. Ley, S. V.; Lygo, B.; Molines, H.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1982**, 1251–1252.
144. Cuñat, A. C.; Diez-Martin, D.; Ley, S. V.; Montgomery, F. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 611–620.
145. Déziel, R.; Malenfant, E.; Thibault, C. *Tetrahedron Lett.* **1998**, *39*, 5493–5496.
146. Okamoto, K.; Nishibayashi, Y.; Uemura, S.; Toshimitsu, A. *Tetrahedron Lett.* **2004**, *45*, 6137–6139.
147. Toshimitsu, A. *Phosphorus Sulfur* **2005**, *180*, 935–937.
148. Iwaoka, M.; Tomoda, S. In *Organoselenium Chemistry: Modern Developments in Organic Synthesis*; Wirth, T., Ed.; Topics in Current Chemistry 208; Springer: Berlin, 2000; pp 55–80.
149. Liotta, D.; Markiewicz, W.; Santiesteban, H. *Tetrahedron Lett.* **1977**, *18*, 4365–4367.
150. Ley, S. V.; O'Neil, I. A.; Low, C. M. R. *Tetrahedron* **1986**, *42*, 5363–5368.
151. Krief, A.; Trabelsi, M.; Dumont, W. *Synthesis* **1992**, 933–935.
152. Dowd, P.; Kennedy, P. *Synth. Commun.* **1981**, *11*, 935–941.
153. Krief, A.; Delmotte, C.; Dumont, W. *Tetrahedron Lett.* **1997**, *38*, 3079–3080.
154. Krief, A.; Delmotte, C.; Dumont, W. *Tetrahedron* **1997**, *53*, 12147–12158.
155. Syper, L.; Mlochowski, J. *Synthesis* **1984**, 439–442.
156. Hu, X.; Tian, Z.; Lu, X.; Chen, Y. *Synth. Commun.* **1997**, *27*, 553–557.
157. Sekiguchi, M.; Tanaka, H.; Takami, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *Heteroatom. Chem.* **1991**, *2*, 427–430.
158. Bao, W. L.; Zhang, Y. M. *Synth. Commun.* **1995**, *25*, 143–148.
159. Lu, G.; Zhang, Y. *Synth. Commun.* **1998**, *28*, 4501–4506.
160. Fukuzawa, S.; Fujinami, T.; Sakai, S. *Chem. Lett.* **1990**, 927–930.

161. Wang, L.; Zhang, Y. *J. Chem. Res. (S)* **1998**, 598–599.
162. Zhou, L. H.; Zhang, Y. M. *J. Chem. Res. (S)* **1999**, 28–29.
163. Inokuchi, T.; Kusumoto, M.; Torii, S. *J. Org. Chem.* **1990**, *55*, 1548–1553.
164. Inokuchi, T.; Kusumoto, M.; Sugimoto, T.; Tanaka, H.; Torii, S. *Phosphorus Sulfur* **1992**, *67*, 271–276.
165. Krief, A.; Derock, M. *Synlett* **2005**, 1012–1014.
166. Reinerth, W. A.; Tour, J. M. *J. Org. Chem.* **1998**, *63*, 2397–2400.
167. McGowan, D. A.; Berchtold, G. A. *J. Am. Chem. Soc.* **1982**, *104*, 1153–1154.
168. Hoare, J. H.; Policastro, P. P.; Berchtold, G. A. *J. Am. Chem. Soc.* **1983**, *105*, 6264–6267.
169. Oguni, N.; Miyagi, Y.; Itoh, K. *Tetrahedron Lett.* **1998**, *39*, 9023–9026.
170. Nishibayashi, Y.; Singh, J. D.; Fukuzawa, S.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2871–2876.
171. Haraguchi, K.; Tanaka, H.; Miyasaka, T. *Synthesis* **1989**, 434–435.
172. Takanohashi, Y.; Funakoshi, H.; Akabori, S. *Synth. Commun.* **1994**, *24*, 2733–2741.
173. Scarborough, R. M.; Smith, A. B. *Tetrahedron Lett.* **1977**, *18*, 4361–4364.
174. Liotta, D.; Santiesteban, H. *Tetrahedron Lett.* **1977**, *18*, 4369–4372.
175. Miyashita, M.; Yoshikoshi, A. *Synthesis* **1980**, 664–666.
176. Grieco, P. A.; Miyashita, M. *Tetrahedron Lett.* **1974**, *15*, 1869–1871.
177. Mori, K. *Tetrahedron* **1976**, *32*, 1101–1106.
178. Pluim, H.; Wynberg, H. *Tetrahedron Lett.* **1979**, *20*, 1251–1254.
179. Ruhland, T.; Andersen, K.; Pedersen, H. *J. Org. Chem.* **1998**, *63*, 9204–9211.
180. Nicolaou, K. C.; Pastor, J.; Barluenga, S.; Winssinger, N. *Chem. Commun.* **1998**, 1947–1948.
181. Yanada, K.; Fujita, T.; Yanada, R. *Synlett* **1998**, 971–972.
182. Schmidt, M.; Block, H. D. *J. Organomet. Chem.* **1970**, *25*, 17–21.
183. Kozikowski, A. P.; Ames, A. *J. Org. Chem.* **1978**, *43*, 2735–2737.
184. Maruoka, K.; Miyazaki, T.; Ando, M.; Matsumura, Y.; Sakane, S.; Hattori, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1983**, *105*, 2831–2843.
185. Bao, W.; Zheng, Y.; Zhang, Y.; Zhou, J. *Tetrahedron Lett.* **1996**, *37*, 9333–9334.
186. Zheng, Y.; Bao, W.; Zhang, Y. *Synth. Commun.* **1997**, *27*, 79–83.
187. Bao, W.; Zhang, Y. *Synlett* **1996**, 1187–1188.
188. Detty, M. R. *Tetrahedron Lett.* **1978**, *19*, 5087–5090.
189. Miyoshi, N.; Ishii, H.; Kondo, K.; Murai, S.; Sonoda, N. *Synthesis* **1979**, 300.
190. Miyoshi, N.; Ishii, H.; Murai, S.; Sonoda, N. *Chem. Lett.* **1979**, 873–876.
191. Harpp, D. N.; Gingras, M. *J. Am. Chem. Soc.* **1988**, *110*, 7737–7745.
192. Schultz, E. K. V.; Harpp, D. N. *Synthesis* **1998**, 1137–1140.
193. Krief, A.; Badaoui, E.; Dumont, W. *Tetrahedron Lett.* **1993**, *34*, 8521–8522.
194. Uehlin, L.; Wirth, T. *Org. Lett.* **2001**, *3*, 2931–2933.
195. Krief, A. In *The Chemistry of Organic Selenium and Tellurium Compounds*. Synthesis of Selenium and Tellurium Ylides and Carbanions: Application to Organic Synthesis; Patai, S., Ed. Wiley, 1987; Vol 2, chap 17, p 684.
196. Krief, A.; Bousbaa, J. *Tetrahedron Lett.* **1997**, *38*, 6289–6290.
197. Krief, A.; Dumont, W.; De Mahieu, A. F. *Tetrahedron Lett.* **1988**, *29*, 3269–3272.
198. Krief, A.; Dumont, W.; Clarembeau, M.; Bernard, G.; Badaoui, E. *Tetrahedron* **1989**, *45*, 2005–2022.
199. Kim, S.; Cheong, J. H.; Yoo, J. *Synlett* **1998**, 981–982.
200. Kim, S.; Cheong, J. H. *Synlett* **1997**, 947–949.
201. Krief, A.; Dumont, W.; Clarembeau, M.; Badaoui, E. *Tetrahedron* **1989**, *45*, 2023–2030.
202. Krief, A.; Nazih, A. *Tetrahedron Lett.* **1995**, *36*, 8115–8118.
203. Reich, H. J.; Bowe, M. D. *J. Am. Chem. Soc.* **1990**, *112*, 8994–8995.
204. Krief, A.; Evrard, G.; Badaoui, E.; De Beys, V.; Dieden, R. *Tetrahedron Lett.* **1989**, *30*, 5635–5638.
205. Hoffmann, R. W.; Bewersdorf, M. *Liebigs Ann. Chem.* **1992**, 643–653.
206. Hoffmann, R. W.; Julius, M.; Chemla, F.; Ruhland, T.; Frenzen, G. *Tetrahedron* **1994**, *50*, 6049–6060.
207. Klute, W.; Dress, R.; Hoffmann, R. W. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1409–1411.
208. Hoffmann, R. W.; Klute, W.; Dress, R. K.; Wenzel, A. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1721–1726.
209. Klute, W.; Krüger, M.; Hoffmann, R. W. *Chem. Ber.* **1996**, *129*, 633–638.
210. Krief, A.; Barbeaux, P.; Guittet, E. *Synlett* **1990**, 509–510.
211. Ponthieux, S.; Outurquin, F.; Paulmier, C. *Tetrahedron Lett.* **1998**, *39*, 4017–4020.
212. Ponthieux, S.; Outurquin, F.; Paulmier, C. *Tetrahedron* **1995**, *51*, 9569–9580.
213. Tsuboi, S.; Sakamoto, J.; Sakai, T.; Utaka, M. *Chem. Lett.* **1989**, 1427–1428.
214. Kusuda, S.; Ueno, Y.; Hagiwara, T.; Toru, T. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1981–1988.
215. Kolb, H. C.; Hoffmann, M. H. R. *Tetrahedron: Asymmetry* **1990**, *1*, 237–250.
216. Toru, T.; Yamada, Y.; Ueno, T.; Maekawa, E.; Ueno, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4815–4817.
217. Jahn, U.; Curran, D. P. *Synlett* **1997**, 565–567.
218. Coutrot, P.; Grison, C.; Tabrizi, Y. *Synthesis* **1987**, 169–170.
219. Simpkins, N. S. *Tetrahedron* **1991**, *47*, 323–332.
220. Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, *112*, 5609–5617.
221. Braga, A. L.; Zeni, G.; De Andrade, L. H.; Silveira, C. C. *Synlett* **1997**, 595–596.
222. Comasseto, J. V.; Menezes, P. H.; Stefani, H. A.; Zeni, G.; Braga, A. L. *Tetrahedron* **1996**, *52*, 9687–9702.
223. Chapdelaine, M. J.; Hulce, M. *Org. React.* **1990**, *38*, 225–653.
224. Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135–631.
225. Back, T. G.; Bethell, R. J.; Parvez, M.; Wehrli, D. *J. Org. Chem.* **1998**, *63*, 7908–7919.
226. Back, T. G.; Wehrli, D. *Tetrahedron Lett.* **1995**, *36*, 4737–4740.
227. Ma, Y.; Huang, X. *Synth. Commun.* **1997**, *27*, 225–229.
228. Huang, X.; Ma, Y. *Synthesis* **1997**, 417–419.
229. Ma, Y.; Huang, X. *Synth. Commun.* **1997**, *27*, 3441–3447.

230. Ma, Y.; Huang, X. *J. Chem. Res. (S)* **1998**, 312–313.
231. Zhu, L. S.; Huang, Z. Z.; Huang, X. *J. Chem. Res. (S)* **1996**, 112–113.
232. Huang, X.; Zhu, L. S. *J. Organomet. Chem.* **1996**, *523*, 9–11.
233. Zhu, L. S.; Huang, Z. Z.; Huang, X. *Tetrahedron* **1996**, *52*, 9819–9822.
234. Dabdoub, M. J.; Begnini, M. L.; Guerrero, P. G., Jr. *Tetrahedron* **1998**, *54*, 2371–2400.
235. Sun, A. M.; Huang, X. *J. Chem. Res. (S)* **1998**, 616–617.
236. Back, T. G. In *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley: New York, 1987; pp 325–364.
237. Castle, L.; Perkins, M. J. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1987; Vol. 2, Chapter 16.
238. Mugesh, G.; du Mont, W.-W.; Sies, H. *Chem. Rev.* **2001**, *101*, 2125–2180.
239. Birringer, M.; Pilawa, S.; Flohé, L. *Nat. Prod. Rep.* **2002**, *19*, 693–718.
240. Bowman, W. R.; Stephenson, P. T.; Terrett, N. K.; Young, A. R. *Tetrahedron* **1995**, *51*, 7959–7980.
241. Keck, G. E.; Tafesh, A. M. *Synlett* **1990**, 257–258.
242. Nishiyama, Y.; Yamamoto, H.; Nakata, S.; Ishii, Y. *Chem. Lett.* **1993**, 841–844.
243. Stojanovic, A.; Renaud, P. *Helv. Chim. Acta* **1998**, *81*, 353–373.
244. Giese, B.; Erdmann, P.; Giraud, L.; Göbel, T.; Petretta, M.; Schäfer, T.; Von Raumer, M. *Tetrahedron Lett.* **1994**, *35*, 2683–2686.
245. Shuto, S.; Kanazaki, M.; Ichikawa, S.; Minakawa, N.; Matsuda, A. *J. Org. Chem.* **1998**, *63*, 746–754.
246. Zhang, J.; Clive, D. L. J. *J. Org. Chem.* **1999**, *64*, 770–779.
247. Fairbanks, A. J.; Perrin, E.; Sinaÿ, P. *Synlett* **1996**, 679–681.
248. Mallet, A.; Mallet, J. M.; Sinaÿ, P. *Tetrahedron: Asymmetry* **1994**, *5*, 2593–2608.
249. Ogawa, A.; Sonoda, N. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 6, pp 461–484.
250. Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4003–4007.
251. Boger, D. L.; Mathvink, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4008–4011.
252. Pattenden, G.; Roberts, L.; Blake, A. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 863–868.
253. Hayes, C. J.; Pattenden, G. *Tetrahedron Lett.* **1996**, *37*, 271–274.
254. Lenz, R.; Giese, B. *J. Am. Chem. Soc.* **1997**, *119*, 2784–2794.
255. Back, T. G.; Collins, S.; Kerr, R. G. *J. Org. Chem.* **1983**, *48*, 3077–3084.
256. Back, T. G.; Collins, S.; Gokhale, U.; Law, K.-W. *J. Org. Chem.* **1983**, *48*, 4776–4779.
257. Miura, T.; Kobayashi, M. *J. Chem. Soc., Chem. Commun.* **1982**, 438–439.
258. Back, T. G.; Collins, S. *Tetrahedron Lett.* **1980**, *21*, 2215–2218.
259. Back, T. G.; Collins, S. *J. Org. Chem.* **1981**, *46*, 3249–3256.
260. Gancarz, R. A.; Kice, J. L. *J. Org. Chem.* **1981**, *46*, 4899–4906.
261. Kang, Y.-H.; Kice, J. L. *J. Org. Chem.* **1984**, *49*, 1507–1511.
262. Kice, J. L.; Kang, Y.-H. *Tetrahedron* **1985**, *41*, 4739–4746.
263. Byers, J. H.; Lane, G. C. *J. Org. Chem.* **1993**, *58*, 3355–3360.
264. Curran, D. P.; Shu, M. *Bull. Soc. Chim. Fr.* **1993**, *130*, 314–322.
265. Vionnet, J. P.; Schenk, K.; Renaud, P. *Helv. Chim. Acta* **1993**, *76*, 2490–2499.
266. Pandey, G.; Rao, K. S. S. P.; Rao, K. V. N. *J. Org. Chem.* **1996**, *61*, 6799–6804.
267. Ito, O. *J. Am. Chem. Soc.* **1983**, *105*, 850–853.
268. Ogawa, A.; Yokoyama, H.; Yokoyama, K.; Masawaki, T.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 5721–5723.
269. Tiecco, M.; Tingoli, M.; Testaferri, L. *Pure Appl. Chem.* **1993**, *65*, 715–722.
270. Tingoli, M.; Tiecco, M.; Testaferri, L.; Andrenacci, R.; Balducci, R. *J. Org. Chem.* **1993**, *58*, 6097–6102.
271. Czernecki, S.; Ayadi, E.; Randriamandimby, D. *J. Org. Chem.* **1994**, *59*, 8256–8260.
272. Czernecki, S.; Ayadi, E. *Can. J. Chem.* **1995**, *73*, 343–350.
273. Tingoli, M.; Temperini, A.; Testaferri, L.; Tiecco, M. *Synlett* **1995**, 1129–1130.
274. Schiesser, C. H.; Wild, L. M. *J. Org. Chem.* **1999**, *64*, 1131–1139.
275. Lyons, J. E.; Schiesser, C. H.; Sutej, K. *J. Org. Chem.* **1993**, *58*, 5632–5638.
276. Dorta, R. L.; Francisco, C. G.; Suarez, E. *Tetrahedron Lett.* **1994**, *35*, 1083–1086.
277. Francisco, C. G.; Martin, C. G.; Suarez, E. *J. Org. Chem.* **1998**, *63*, 2099–2109.
278. Davis, F. A.; Billmers, J. M.; Stringer, O. D. *Tetrahedron Lett.* **1983**, *24*, 3191–3194.
279. Davis, F. A.; Stringer, O. D.; McCauley, J. P. *Tetrahedron* **1985**, *41*, 4747–4757.
280. Shimizu, T.; Yoshida, M.; Kamigata, N. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3761–3763.
281. Toda, F.; Mori, K. J. *Chem. Soc., Chem. Commun.* **1986**, 1357–1358.
282. Davis, F. A.; Reddy, R. T. *J. Org. Chem.* **1992**, *57*, 2599–2606.
283. Tiecco, M.; Tingoli, M.; Testaferri, L.; Bartoli, D. *Tetrahedron Lett.* **1987**, *28*, 3849–3852.
284. Shimizu, T.; Kobayashi, M.; Kamigata, N. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2099–2101.
285. Reich, H. J.; Yelm, K. E. *J. Org. Chem.* **1991**, *56*, 5672–5679.
286. Kondo, N.; Fueno, H.; Fujimoto, H.; Makino, M.; Nakaoka, H.; Aoki, I.; Uemura, S. *J. Org. Chem.* **1994**, *59*, 5254–5263.
287. Komatsu, N.; Nishibayashi, Y.; Sugita, T.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1992**, 46–47.
288. Komatsu, N.; Murakami, T.; Nishibayashi, Y.; Sugita, T.; Uemura, S. *J. Org. Chem.* **1993**, *58*, 3697–3702.
289. Komatsu, N.; Matsunaga, S.; Sugita, T.; Uemura, S. *J. Am. Chem. Soc.* **1993**, *115*, 5847–5848.
290. Reich, H. J.; Reich, I. L.; Wollowitz, S. *J. Am. Chem. Soc.* **1978**, *100*, 5981–5982.
291. Reich, H. J.; Shah, S. K.; Gold, P. M.; Olson, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 3112–3120.
292. Reich, I. L.; Reich, H. J. *J. Org. Chem.* **1981**, *46*, 3721–3727.
293. Reich, H. J.; Wollowitz, S. *J. Am. Chem. Soc.* **1982**, *104*, 7051–7059.
294. Reich, H. J.; Yelm, K. E.; Wollowitz, S. *J. Am. Chem. Soc.* **1983**, *105*, 2503–2504.
295. Back, T. G.; Lai, E. K.; Muralidharan, K. M. *J. Org. Chem.* **1990**, *55*, 4595–4602.
296. Komatsu, N.; Nishibayashi, Y.; Uemura, S. *Tetrahedron Lett.* **1993**, *34*, 2339–2342.
297. Fujita, K.; Kanakubo, M.; Ushijima, H.; Oishi, A.; Ikeda, Y.; Taguchi, Y. *Synlett* **1998**, 987–988.
298. Takahashi, T.; Kurose, N.; Kawanami, S.; Arai, Y.; Koizumi, T.; Shiro, M. *J. Org. Chem.* **1994**, *59*, 3262–3264.

299. Kurose, N.; Takahashi, T.; Koizumi, T. *Tetrahedron* **1997**, *53*, 12115–12129.
300. Fankhauser, J. E.; Peevey, R. M.; Hopkins, P. B. *Tetrahedron Lett.* **1984**, *25*, 15–18.
301. Shea, R. G.; Fitzner, J. N.; Fankhauser, J. E.; Hopkins, P. B. *J. Org. Chem.* **1984**, *49*, 3647–3650.
302. Shea, R. G.; Fitzner, J. N.; Fankhauser, J. E.; Spaltenstein, A.; Carpino, P. A.; Peevey, R. M.; Pratt, D. V.; Tenge, B. J.; Hopkins, P. B. *J. Org. Chem.* **1986**, *51*, 5243–5252.
303. Johannsen, M.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689–1708.
304. Dauban, P.; Dodd, R. H. *Synlett* **2003**, 1571–1586.
305. Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123–1178.
306. Shimizu, T.; Seki, N.; Taka, H.; Kamigata, N. *J. Org. Chem.* **1996**, *61*, 6013–6014.
307. Kamigata, N.; Taka, H.; Matsuhisa, A.; Matsuyama, H.; Shimizu, T. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2257–2264.
308. Takada, H.; Oda, M.; Miyake, Y.; Ohe, K.; Uemura, S. *Chem. Commun.* **1998**, 1557–1558.
309. Nishibayashi, Y.; Chiba, T.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1995**, 1243–1244.
310. Yamauchi, K.; Nakamura, K.; Kinoshita, M. *Tetrahedron Lett.* **1979**, 1787–1790.
311. Uenemoto, T.; Ishihara, S. *J. Am. Chem. Soc.* **1993**, *115*, 2156–2164.
312. Kataoka, T.; Banno, Y.; Watanabe, S.; Iwamura, S.; Shimizu, H. *Tetrahedron Lett.* **1997**, *38*, 1809–1812.
313. Shibuya, K. *Synth. Commun.* **1994**, *24*, 2923–2941.
314. Mlochowski, J. *Phosphorus Sulfur* **1998**, *136–138*, 191–204.
315. Guzman, J. A.; Mendoza, V.; Garcia, E.; Garibay, C. F.; Olivarez, L. Z.; Maldonado, L. A. *Synth. Commun.* **1995**, *25*, 2121–2133.
316. Bird, C. W.; Cooper, R. *Org. Prep. Proced. Int.* **1993**, *25*, 237–240.
317. Said, S. B.; Skarzewski, J.; Mlochowski, J. *Synthesis* **1989**, 223–224.
318. Drabowicz, J.; Lyzwa, P.; Mikolajczyk, M. *Phosphorus Sulfur* **1983**, *17*, 169–172.
319. Kudzin, Z. H.; Andrijewski, G.; Drabowicz, J. *Heteroatom. Chem.* **1994**, *5*, 1–6.
320. Naota, T.; Sasao, S.; Tanaka, K.; Yamamoto, H.; Murahashi, S. I. *Tetrahedron Lett.* **1993**, *34*, 4843–4846.
321. Mikolajczyk, M.; Luczak, J. *J. Org. Chem.* **1978**, *43*, 2132–2138.
322. Tiecco, M.; Testaferri, L.; Temperini, A.; Terlizzi, R.; Bagnoli, L.; Marini, F.; Santi, C. *Tetrahedron Lett.* **2005**, *46*, 5165–5168.
323. Barton, D. H. R.; Magnus, P. D.; Rosenfeld, M. N. *J. Chem. Soc., Chem. Commun.* **1975**, 301.
324. Barton, D. H. R.; Brewster, A. G.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1976**, 985–986.
325. Barton, D. H. R.; Ley, S. V.; Magnus, P. D.; Rosenfeld, M. N. *J. Chem. Soc., Perkin Trans. 1* **1977**, 567–571.
326. Grieco, P. A.; Yokoyama, Y.; Gilman, S.; Nishizama, N. *J. Org. Chem.* **1977**, *42*, 2034–2036.
327. Hori, T.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 1689–1697.
328. Reich, H. J.; Chow, F.; Peake, S. L. *Synthesis* **1978**, 299–301.
329. Syper, L. *Synthesis* **1989**, 167–172.
330. Kubicz, E.; Mlochowski, J.; Syper, L. *J. Prakt. Chem.* **1991**, *333*, 243–247.
331. Said, S. B.; Skarzewski, J.; Mlochowski, J. *Synth. Commun.* **1992**, *22*, 1851–1862.
332. Lowe, W.; Rutjes, T. *J. Heterocycl. Chem.* **1995**, *32*, 43–48.
333. Ogawa, S.; Kikuchi, T.; Sasaki, A.; Chida, S. I.; Sato, R. *Tetrahedron Lett.* **1994**, *35*, 5469–5472.
334. Beer, L.; Brusso, J. L.; Haddon, R. C.; Itkis, M. E.; Leitch, A. A.; Oakley, R. T.; Reed, R. W.; Richardson, J. F. *Chem. Commun.* **2005**, 1543–1545.
335. Kawashima, T.; Ohno, F.; Okazaki, R. *Phosphorus Sulfur* **1998**, *136–138*, 501–504.
336. Akabori, S.; Takanohashi, Y. *Bull. Soc. Chem. Jpn.* **1991**, *64*, 3482–3484.
337. Leonard, K. A.; Zhou, F.; Detty, M. R. *Organometallics* **1996**, *15*, 4285–4292.
338. Duclos, J. F.; Outurquin, F.; Paulmier, C. *Tetrahedron Lett.* **1993**, *34*, 7417–7420.
339. Duclos, J. F.; Outurquin, F.; Paulmier, C. *Tetrahedron Lett.* **1995**, *36*, 2627–2630.
340. Stuhr-Hansen, N.; Henriksen, L.; Kodra, J. T. *Synth. Commun.* **1996**, *26*, 3345–3350.
341. Ali, H.; van Lier, J. E. *Tetrahedron Lett.* **1991**, *32*, 5015–5019.
342. Houllemare, D.; Ponthieux, S.; Outurquin, F.; Paulmier, C. *Synthesis* **1997**, 101–106.
343. Chivers, T.; Doxsee, D. D.; Fait, J. F.; Parvez, M. *Inorg. Chem.* **1993**, *32*, 2243–2248.
344. Lermontov, S. A.; Zavorin, S. I.; Bakhtin, I. V.; Zefirov, N. S.; Stang, P. J. *Phosphorus Sulfur* **1995**, *102*, 283–286.
345. Shimizu, M.; Kuwajima, I. *J. Org. Chem.* **1980**, *45*, 4063–4065.
346. Tiecco, M.; Chianelli, D.; Testaferri, L.; Tingoli, M.; Bartoli, D. *Tetrahedron* **1986**, *42*, 4889–4896.
347. Uemura, S.; Ohe, K.; Sugita, N. *J. Chem. Soc., Chem. Commun.* **1988**, 111–112.
348. Shimizu, M.; Ando, R.; Kuwajima, I. *J. Org. Chem.* **1984**, *49*, 1230–1238.
349. Toshimitsu, A.; Hirosawa, C.; Tanimoto, S.; Uemura, S. *Tetrahedron Lett.* **1992**, *33*, 4017–4020.
350. Wu, J. C.; Chattopadhyaya, J. *Tetrahedron* **1989**, *45*, 4507–4522.
351. Wu, J. C.; Chattopadhyaya, J. *Tetrahedron* **1990**, *46*, 2587–1592.
352. Tong, W.; Wu, J. C.; Sandstrom, A.; Chattopadhyaya, J. *Tetrahedron* **1990**, *46*, 3037–3060.
353. Tong, W.; Xi, Z.; Gioeli, C.; Chattopadhyaya, J. *Tetrahedron* **1991**, *47*, 3431–3438.
354. Wirth, T. *Sci. Synth.* **2005**, *22*, 181–212.
355. Okazaki, R. *J. Synth. Org. Chem. Jpn.* **1988**, *46*, 1149–1163.
356. Kato, S., Ed.; In *Chalcogenocarboxylic Acid Derivatives;* Topics in Current Chemistry 251; Springer: Berlin, 2005.
357. Okazaki, R.; Kumon, N.; Inamoto, N. *J. Am. Chem. Soc.* **1989**, *111*, 5949–5951.
358. Takeda, N.; Tokitoh, N.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 660–662.
359. Takeda, N.; Tokitoh, N.; Okazaki, R. *Tetrahedron* **1997**, *53*, 12167–12182.
360. Takeda, N.; Tokitoh, N.; Okazaki, R. *Phosphorus Sulfur* **1998**, *136–138*, 633–636.
361. Shimada, K.; Jin, N.; Fujimura, M.; Nagano, Y.; Kudoh, E.; Takikawa, Y. *Chem. Lett.* **1992**, 1843–1846.
362. Shimada, K.; Jin, N.; Kawaguchi, M.; Dobashi, K.; Nagano, Y.; Fujimura, M.; Kudoh, E.; Kai, T.; Saito, N., Masuda, J., *et al. Bull. Chem. Soc. Jpn.* **1997**, *70*, 197–206.
363. Segi, M.; Nakajima, T.; Suga, S.; Murai, S.; Ryu, I.; Ogawa, A.; Sonoda, N. *J. Am. Chem. Soc.* **1988**, *110*, 1976–1978.
364. Segi, M.; Koyama, T.; Nakajima, T.; Suga, S.; Murai, S.; Sonoda, N. *Tetrahedron Lett.* **1989**, *30*, 2095–2098.
365. Segi, M.; Kojima, A.; Nakajima, T.; Suga, S. *Synlett* **1991**, 105–106.

366. Segi, M.; Takahashi, T.; Ichinose, H.; Li, G. M.; Nakajima, T. *Tetrahedron Lett.* **1992**, *33*, 7865–7868.
367. Li, G. M.; Segi, M.; Nakajima, T. *Tetrahedron Lett.* **1992**, *33*, 3515–3518.
368. Segi, M.; Nakajima, T. *J. Synth. Org. Jpn.* **1995**, *53*, 678–686.
369. Segi, M.; Yamamoto, H.; Hori, T.; Nakajima, T. *Phosphorus Sulfur* **1998**, *136–138*, 599–602.
370. Li, G. M.; Niu, S.; Segi, M.; Zingaro, R. A.; Yamamoto, H.; Watanabe, K.; Nakajima, T.; Hall, M. B. *J. Org. Chem.* **1999**, *64*, 1565–1575.
371. Takikawa, Y.; Uwano, A.; Watanabe, H.; Asanuma, M.; Shimada, K. *Tetrahedron Lett.* **1989**, *30*, 6047–6050.
372. Shimada, K.; Hikage, S.; Takeishi, Y.; Takikawa, Y. *Chem. Lett.* **1990**, 1403–1406.
373. Takikawa, Y.; Watanabe, H.; Sasaki, R.; Shimada, K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 876–878.
374. Nakayama, J.; Akimoto, K.; Niijima, J.; Hoshino, M. *Tetrahedron Lett.* **1987**, *28*, 4423–4426.
375. Nakayama, J.; Akimoto, K.; Hoshino, M. *J. Phys. Org. Chem.* **1988**, *1*, 53–57.
376. Erker, G.; Hock, R.; Nolte, R. *J. Am. Chem. Soc.* **1988**, *110*, 624–625.
377. Erker, G.; Hock, R.; Krüger, C.; Werner, S.; Klärner, F. G.; Artschwager–Perl, U. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1067–1068.
378. Hock, R.; Hillenbrand, S.; Erker, G.; Krüger, C.; Werner, S. *Chem. Ber.* **1993**, *126*, 1895–1903.
379. Okuma, K.; Sakata, J.; Tachibana, Y.; Honda, T.; Ohta, H. *Tetrahedron Lett.* **1987**, *52*, 6649–6652.
380. Okuma, K.; Komiya, Y.; Kaneko, I.; Tachibana, Y.; Iwata, E.; Ohta, H. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1653–1657.
381. Okuma, K.; Kaneko, I.; Ohta, H.; Yokomori, Y. *Heterocycles* **1990**, *31*, 2107–2110.
382. Okuma, K.; Kojima, K.; Kaneko, I.; Ohta, H. *Chem. Lett.* **1991**, 1053–1056.
383. Okuma, K. *J. Synth. Org. Chem. Jpn.* **1995**, *53*, 218–225.
384. Sukhai, R. S.; de Jond, R.; Brandsma, L. *Synthesis* **1977**, 888–889.
385. Ishihara, H.; Yoshimi, M.; Hara, N.; Ando, H.; Kato, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 835–841.
386. Kato, S.; Komuro, T.; Kanda, T.; Ishihara, H.; Murai, T. *J. Am. Chem. Soc.* **1993**, *115*, 3000–3001.
387. Murai, T.; Ezaka, T.; Niwa, N.; Kanda, T.; Kato, S. *Synlett* **1996**, 865–866.
388. Murai, T.; Hayashi, A.; Kanda, T.; Kato, S. *Chem. Lett.* **1993**, 1469–1472.
389. Murai, T.; Kakami, K.; Hayashi, A.; Komuro, T.; Takada, H.; Fujii, M.; Kanda, T.; Kato, S. *J. Am. Chem. Soc.* **1997**, *119*, 8592–8597.
390. Shimada, K.; Akimoto, S.; Itoh, H.; Nakamura, H.; Takikawa, Y. *Chem. Lett.* **1994**, 1743–1746.
391. Murai, T.; Ezaka, T.; Kanda, T.; Kato, S. *J. Chem. Soc., Chem. Commun.* **1996**, 1809–1810.
392. Murai, T.; Ezaka, T.; Kato, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1193–1200.
393. Nivorozhkin, A. L.; Nivorozhkin, L. E.; Konstantinovsky, L. E.; Minkin, V. I. *Mendeleev Commun.* **1991**, 78–79.
394. Copeland, C. M.; Ghosh, J.; McAdam, D. P.; Skelton, B. W.; Stick, R. V.; White, A. H. *Aust. J. Chem.* **1988**, *41*, 549–561.
395. Zmitrovich, N. I.; Petrov, M. L. *Russ. J. Org. Chem.* **1996**, *32*, 1870–1874.
396. Wright, S. W. *Tetrahedron Lett.* **1994**, *35*, 1331–1334.
397. Dechend, F. *Chem. Ber.* **1874**, *7*, 1273–1274.
398. Sonoda, N.; Kondo, K.; Nagano, K.; Kambe, N.; Morimoto, F. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 308–309.
399. Ogawa, A.; Miyake, J.; Karasaki, Y.; Murai, S.; Sonoda, N. *J. Org. Chem.* **1985**, *50*, 384–386.
400. Ogawa, A.; Miyake, J.; Kambe, N.; Murai, S.; Sonoda, N. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1448–1451.
401. Back, T. G.; Barton, D. H. R.; Britten-Kelly, M. R.; Guziec, F. S., Jr., *J. Chem. Soc., Perkin Trans. 1* **1976**, 2079–2089.
402. Mckinnon, B. J.; De Mayo, P.; Payne, N. C.; Ruge, B. *Nouv. J. Chim.* **1978**, *2*, 91–94.
403. Barton, D. H. R.; Hanse, P. E.; Picker, K. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1723–1730.
404. Murai, T.; Maeda, M.; Matsuoka, F.; Kanda, T.; Kato, S. *J. Chem. Soc., Chem. Commun.* **1996**, 1461–1462.
405. Li, G. M.; Kamogawa, T.; Segi, M.; Nakajima, T. *Chem. Express* **1993**, *8*, 53–56.
406. Okuma, K.; Koda, G.; Okumura, S.; Ohno, A. *Chem. Lett.* **1996**, 609–610.
407. Okazaki, R.; Ishii, A.; Inamoto, N. *J. Chem. Soc., Chem. Commun.* **1986**, 71–72.
408. Murai, T.; Ezaka, T.; Kato, S. *Tetrahedron Lett.* **1998**, *39*, 4329–4332.
409. Koketsu, M.; Hiramatsu, S.; Ishihara, H. *Chem. Lett.* **1999**, 485–486.
410. Nizar, P. N. H.; Parkash, S.; Chauhan, S. M. S. *J. Indian Chem. Soc.* **1997**, *74*, 161–162.
411. Cristiani, F.; Demartin, F.; Devillanova, F. A.; Isaia, F.; Lippolis, V.; Verani, G. *Inorg. Chem.* **1994**, *33*, 6315–6324.
412. Cristiani, F.; Devillanova, F. A.; Isaia, F.; Lippolis, V.; Verani, G.; Demartin, F. *Polyhedron* **1995**, *14*, 2937–2943.
413. Demartin, F.; Devillanova, F. A.; Isaia, F.; Lippolis, V.; Verani, G. *Phosphorus Sulfur* **1998**, *136–138*, 283–286.
414. Devillanova, F. A.; Deplano, P.; Isaia, F.; Lippolis, V.; Mercuri, M. L.; Piludu, S.; Verani, G.; Demartin, F. *Polyhedron* **1998**, *17*, 305–312.
415. Arca, M.; Demartin, F.; Devillanova, F. A.; Garau, A.; Isaia, F.; Lippolis, V.; Piludu, S.; Verani, G. *Polyhedron* **1998**, *17*, 3111–3119.
416. Bigoli, F.; Deplano, P.; Devillanova, F. A.; Lippolis, V.; Mercuri, M. L.; Pellinghelli, M. A.; Trogu, E. F. *Eur. J. Inorg. Chem.* **1998**, 137–141.
417. Kuhn, N.; Fawzi, R.; Kratz, T.; Steimann, M. *Phosphorus Sulfur* **1996**, *108*, 107–119.
418. Kuhn, N.; Kotowski, H.; Kratz, T.; Henkel, G. *Phosphorus Sulfur* **1998**, *136–138*, 517–520.
419. Bochu, C.; Couture, A.; Grandclaudon, D. *J. Org. Chem.* **1988**, *53*, 4852–4855.
420. Sekiguchi, M.; Ogawa, A.; Fujiwara, S.; Ryu, I.; Kambe, N.; Sonoda, N. *Chem. Lett.* **1990**, 913–916.
421. Moriarty, R. M.; Vaid, B. K.; Duncan, M. P.; Levy, S. G.; Prakash, O.; Goyal, S. *Synthesis* **1992**, 845–846.
422. Bo, L.; Caiding, X.; Xunjun, Z. *Huaxue Shiji* **1993**, *15*, 334–335.
422a. Bo, L.; Caiding, X.; Xunjun, Z. *Chem. Abstr.* **1993**, *121*, 57594.
423. Shafiee, A.; Rezayazdi, M. *J. Heterocycl. Chem.* **1995**, *32*, 177–178.
424. Koketsu, M.; Senda, T.; Yoshimura, K.; Ishihara, H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 453–456.
425. Hu, W. X.; Guziec, F. S., Jr. *OPPI Briefs* **1994**, *26*, 682.
426. Taurog, A.; Dorris, M. L.; Hu, W. X.; Guziec, F. S., Jr. *Biochem. Pharm.* **1995**, *49*, 701–709.
427. Sukhai, R. S.; Brandsma, L. *Synthesis* **1979**, 455–457.
428. Murai, T.; Ezaka, T.; Ichimiya, T.; Kato, S. *Synlett* **1997**, 775–776.
429. Kanda, T.; Ezaka, T.; Murai, T.; Kato, S. *Tetrahedron Lett.* **1995**, *36*, 2807–2810.
430. Raubenheimer, H. G.; Kruger, G. J.; Linford, L.; Marais, C. F.; Otte, R.; Hattingh, J. T. Z.; Lombard, A. *J. Chem. Soc., Dalton Trans.* **1989**, 1565–1577.
431. Fischer, H.; Treier, K.; Troll, C. *Chem. Ber.* **1995**, *128*, 1149–1156.
432. Devillanova, F. A.; Diaz, A.; Isaia, F.; Verani, G. *Transition Met. Chem.* **1989**, *14*, 153–154.
433. Jones, P. G.; Thöne, C. *Chem. Ber.* **1991**, *124*, 2725–2729.

434. Eikens, W.; Jones, P. G.; Lautner, J.; Thöne, C. *Z. Naturforsch. B* **1994**, *49*, 21–26.
435. Bensch, W.; Schuster, M. *Z. Anorg. Allg. Chem.* **1993**, *619*, 786–790.
436. Bensch, W.; Schuster, M. *Z. Anorg. Allg. Chem.* **1993**, *619*, 791–795.
437. Williams, D. J.; Jones, T. A.; Rice, E. D.; Davis, K. J.; Ritchie, J. A.; Pennington, W. T.; Schimek, G. L. *Acta Cryst. C* **1997**, *53*, 837–838.
438. Li, G. M.; Reibenspies, J. H.; Zingaro, R. A. *Heteroatom. Chem.* **1998**, *9*, 57–64.
439. Mazaki, Y.; Kobayashi, K. *Tetrahedron Lett.* **1989**, *30*, 2813–2816.
440. Saluschke, S.; Pink, M.; Dietzsch, P. W.; Kirmse, R.; Law, N. *Z. Anorg. Allg. Chem.* **1993**, *619*, 1862–1868.
441. Kato, R.; Liu, Y. L.; Sawa, H.; Aonuma, S.; Ichikawa, A.; Takahashi, H.; Mori, N. *Solid State Commun.* **1995**, *94*, 973–977.
442. Kobayashi, A.; Sato, A.; Naito, T.; Kobayashi, H. *Mol. Cryst. Liq. Cryst.* **1996**, *284*, 85–96.
443. Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–69.
444. Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833–856.
445. Oguni, N.; Omi, T. *Tetrahedron Lett.* **1984**, *25*, 2823–2824.
446. Kitamura, M.; Suga, S.; Kawai, K.; Noyori, N. *J. Am. Chem. Soc.* **1986**, *108*, 6071–6072.
447. Kitamura, M.; Suga, S.; Oka, M.; Noyori, N. *J. Am. Chem. Soc.* **1998**, *120*, 9800–9809.
448. Yamakawa, M.; Noyori, R. *Organometallics* **1999**, *18*, 128–133.
449. Kang, J.; Lee, J. W.; Kim, J. I. *J. Chem. Soc., Chem. Commun.* **1994**, 2009–2010.
450. Gibson, C. L. *Chem. Commun.* **1996**, 645–646.
451. Santi, C.; Wirth, T. *Tetrahedron: Asymmetry* **1999**, *10*, 1019–1023.
452. Santi, C.; Fragale, G.; Wirth, T. *Tetrahedron: Asymmetry* **1998**, *9*, 3625–3628.
453. Fukuzawa, S.; Tsudzuki, K. *Tetrahedron: Asymmetry* **1995**, *6*, 1039–1042.
454. Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 497–526.
455. Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97–102.
456. Britovsek, G. J. P.; Gibson, V. C.; Wass, D. F. *Angew. Chem., Int. Ed. Eng.* **1999**, *38*, 428–447.
457. Nishibayashi, Y.; Singh, J. D.; Segawa, K.; Fukuzawa, S.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1375–1376.
458. Nishibayashi, Y.; Segawa, K.; Singh, J. D.; Fukuzawa, S.; Ohe, K.; Uemura, S. *Organometallics* **1996**, *15*, 370–379.
459. Nishibayashi, Y.; Segawa, K.; Ohe, K.; Uemura, S. *Organometallics* **1995**, *14*, 5486–5487.
460. Nishibayashi, Y.; Segawa, K.; Takada, H.; Ohe, K.; Uemura, S. *Chem. Commun.* **1996**, 847–848.
461. Takei, I.; Nishibayashi, Y.; Arikawa, Y.; Uemura, S.; Hidai, M. *Organometallics* **1999**, *18*, 2271–2274.
462. Nishibayashi, Y.; Singh, J. D.; Arikawa, Y.; Uemura, S.; Hidai, M. *J. Organomet. Chem.* **1997**, *531*, 13–18.
463. Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526–5528.
464. Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelborn, D. F. *J. Org. Chem.* **1978**, *43*, 1697–1705.
465. Taylor, R. T.; Flood, L. A. *J. Org. Chem.* **1983**, *48*, 5160–5164.
466. Betzemeier, B.; Lhermitte, F.; Knochel, P. *Synlett* **1999**, 489–491.
467. Torii, S.; Uneyama, K.; Ono, M. *Tetrahedron Lett.* **1980**, *21*, 2653–2654.
468. Torii, S.; Uneyama, K.; Ono, M.; Bannou, T. *J. Am. Chem. Soc.* **1981**, *103*, 4606–4608.
469. Iwaoka, M.; Tomoda, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1165–1166.
470. Tiecco, M.; Testaferri, L.; Tingoli, M.; Bagnoli, L.; Santi, C. *Synlett* **1993**, 798–800.
471. Tiecco, M.; Testaferri, L.; Santi, C. *Eur. J. Org. Chem.* **1999**, 797–803.
472. Wirth, T.; Häuptli, S.; Leuenberger, M. *Tetrahedron: Asymmetry* **1998**, *9*, 547–550.

9.12
Copper, Silver, and Gold

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9.12.1 Introduction

Whereas structural aspects of organometallic compounds of copper, silver, and gold (the coin metals) have been highlighted extensively in COMC (1995),[1,2] the coverage of preparative applications has been restricted to organocopper reagents.[3] Indeed, copper is probably the most frequently used transition metal in preparative organic chemistry if one considers both stoichiometric and catalytic applications. The rich chemistry made possible with these reagents (in particular with organocuprates) renders the task of providing a "comprehensive" overview hopeless. Rather, in this chapter we will concentrate on selected aspects of organocopper chemistry (e.g., transmetallation reactions, application of heterocuprates, stereoselective addition and substitution reactions, and applications in natural product synthesis) with contributions dating from 1994 to 2004.

In contrast to preparative organocopper chemistry which is characterized by the careful preparation of well-defined reagents and their subsequent reaction with an organic molecule, organosilver and organogold compounds usually occur in preparative organic chemistry as a transient species formed by the treatment of (often unsaturated) substrates with Lewis-acidic silver or gold promotors, or precatalysts. Here, the transition metal serves to activate carbonyl compounds, alkenes, alkynes, and other electron-rich molecules for a subsequent nucleophilic attack. Furthermore, gold salts are also capable of undergoing C–H insertion of certain aromatic and C–H acidic substrates, providing a second activation mode. Thus, silver and gold catalysis very nicely supplements the tremendous utility of organocopper reagents for the formation of C–H, C–C, and C–heteroatom bonds.

9.12.2 Copper

Applications of organocopper reagents in preparative organic chemistry over the last decade (1994–2004) have been the subject of numerous reviews[4–20] and several books.[21–23] Most of these transformations still belong to the three "classical" reaction types of organocopper chemistry, that is, conjugate addition and substitution reactions, as well as the carbocupration of non-activated C–C multiple bonds. Besides the development of new types of organocopper reagents (e.g., heterocuprates) and methods for their preparation (e.g., transmetallation of "uncommon" precursors), the focus has been on the introduction of novel copper catalysts for stereoselective transformations and on the widening of the substrate scope (e.g., to extended multiple bond systems). A much better understanding of mechanistic features of organocopper chemistry has contributed tremendously to the progress made. Of course, the real value of a synthetic method becomes evident when it is applied in the synthesis of complex target molecules, and this is certainly true for many of the new reagents and transformations covered in this chapter. As already mentioned before, a comprehensive coverage of all developments made in the last decade is impossible, and we will therefore concentrate on the most innovative and promising contributions (according to our subjective, hence imperfect, judgement). Here, we have chosen to classify the contributions according to reaction types (not reagent types) with stoichiometric or catalytic applications of copper as the highest criterion.

9.12.2.1 Stoichiometric Applications

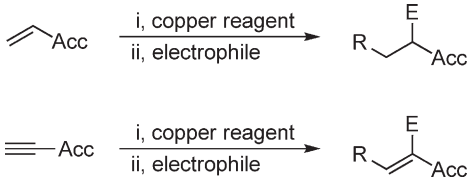
9.12.2.1.1 Conjugate addition reactions

The prototype of copper-mediated conjugate addition reactions is the transformation of acceptor-substituted alkenes and alkynes into the corresponding adducts (Scheme 1). Whereas full control of the regio- and chemoselectivity in these Michael additions has been possible for a long time,[3] the emphasis of the last decade has been put on the use of new copper reagents, the broadening of the substrate scope, and the control of the stereoselectivity of the conjugate addition.

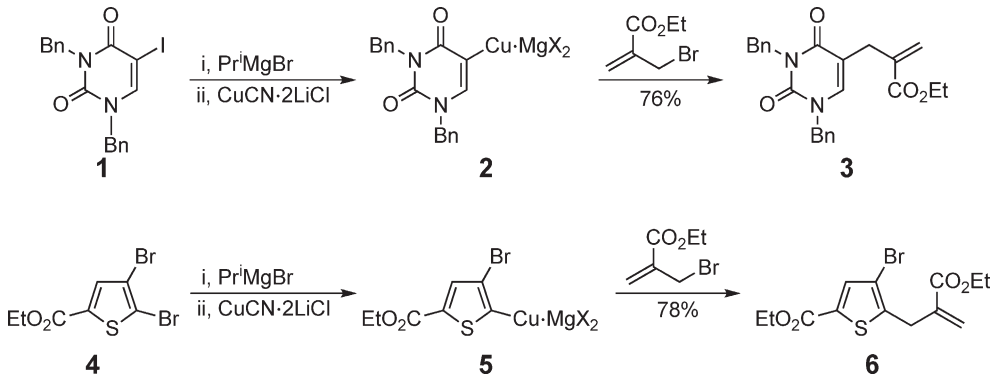
9.12.2.1.1.(i) Copper reagents

Organocopper reagents and organocuprates are usually prepared by classical transmetallation of organolithium reagents with copper salts, a method introduced by Gilman *et al.*[24,24a] more than 50 years ago. This procedure affords reagents with high reactivity and selectivity which can be further modulated by variation of the copper salt, for example, the use of copper cyanide (CuCN).[3–6,18] However, it is hardly possible to introduce functional groups with interesting reactivities by this method. Recent advances in the synthesis of functionalized organocopper reagents and their application in conjugate additions and other transformations take advantage of the fact that organometallic compounds with less electronegative metals, compared to copper, or weaker carbon–metal bonds, are in principle amenable to transmetallation to the corresponding (functionalized or unfunctionalized) organocopper reagents. In this respect, organomagnesium, -boron, and -zinc reagents have been exploited particularly in recent years, complemented by many less frequently used metals.[25]

The halogen–magnesium exchange reaction has proved to be particularly prolific for the generation of functionalized Grignard reagents which can then be transmetallated to the corresponding organocopper reagents.[25] Knochel and coworkers[26,26a–26d] could demonstrate that many functional groups are tolerated in this sequence if appropriate conditions for the halogen–magnesium exchange are chosen. In many cases, catalytic amounts of copper are sufficient to utilize these functionalized Grignard reagents in Michael additions (see Section 9.12.2.2.1). Recent examples for the use of stoichiometric, functionalized organocopper reagents in this sequence comprise the formation of heteroaromatic copper reagents (e.g., **2**, **5**) by treatment of the corresponding electron-deficient heteroaryl iodides **1**, bromides **4** or even chlorides with Pr^iMgBr, and the soluble copper salt CuCN·2LiCl; the subsequent trapping in a 1,4-addition–elimination with ethyl (2-bromomethyl)acrylate afforded the products **3** and **6** with good yield (Scheme 2).[27,28]



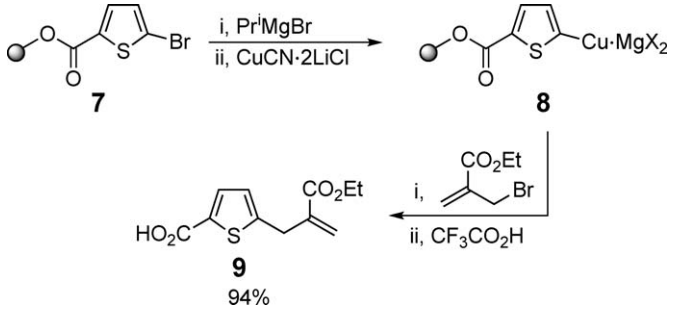
Scheme 1



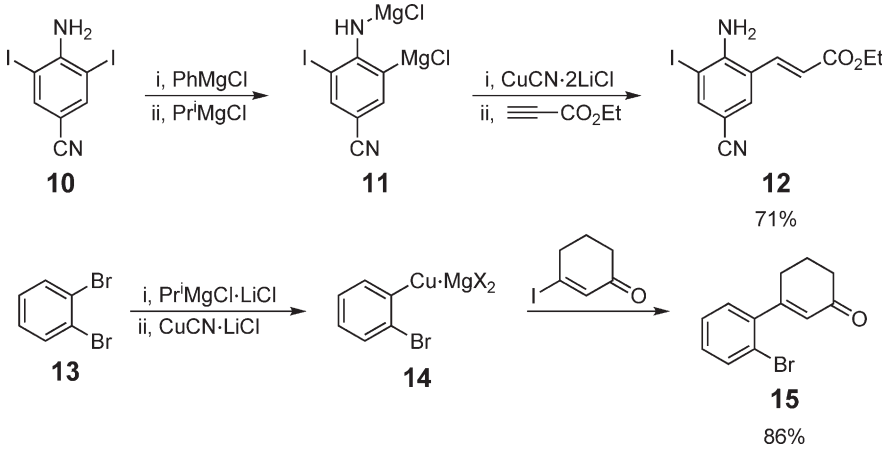
Scheme 2

The method has been extended successfully to the solid phase (Scheme 3).[28] Thus, the Wang resin-attached bromothiophene **7** was converted with the sequence mentioned above into the copper reagent **8** which was transformed into the adduct **9** by 1,4-addition–elimination and acidic cleavage from the resin.

The sequence halogen–magnesium exchange—transmetallation—electrophilic capture can also be applied to certain carbocyclic aromatics. Thus, successive addition of PhMgCl and Pr^iMgCl to functionalized iodoanilines (e.g., **10**) gives rise to the formation of the arylmagnesium compound of type **11** which, after transmetallation with CuCN·2LiCl, undergoes a smooth 1,4-addition to ethyl propiolate to afford adduct **12** (Scheme 4).[29] The



Scheme 3



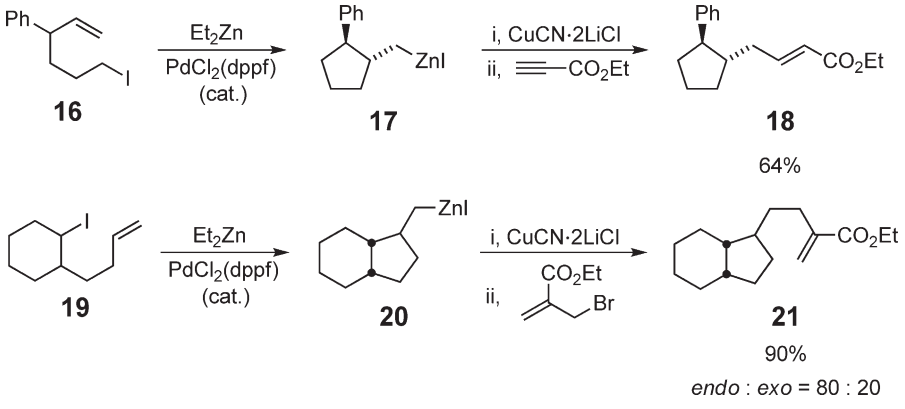
Scheme 4

corresponding halogen–magnesium exchange of aryl bromides requires the presence of a lithium salt, that is, the reagent $Pr^iMgCl{\cdot}LiCl$. For example, treatment of 1,2-dibromobenzene **13** with this reagent, CuCN·LiCl, and 3-iodocyclohex-2-enone provides the desired Michael adduct **15** via the arylcopper species **14**.[30,30a]

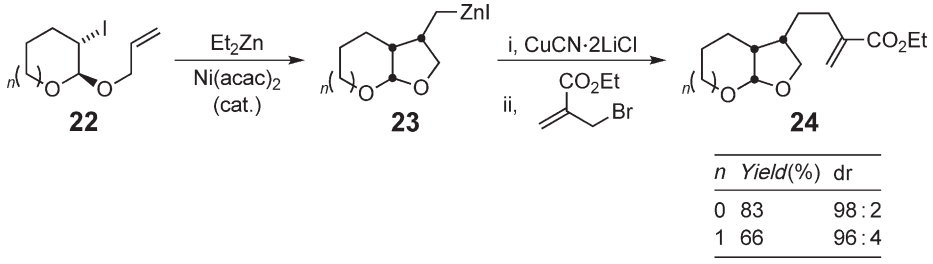
Besides Grignard reagents, organozinc compounds are the most useful precursors of functionalized organocopper reagents. The low reactivity of organozinc nucleophiles allows the incorporation of many functional groups, and highly efficient transmetallation protocols have been developed and reviewed extensively by Knochel and co-workers.[3,25,31,31a] More recent applications of this chemistry involve the palladium-catalyzed iodine–zinc exchange reaction of unsaturated substrates of type **16** and **19** (Scheme 5) which occurs with radical ring closure to the organozinc species **17** and **20**, respectively. Subsequent transmetallation with CuCN·2LiCl enabled the use of the copper reagents formed in Michael additions to provide the products **18** and **21** with good to high stereoselectivity.[32]

The extension of this method to heterocyclic products took advantage of nickel catalysis for the iodine–zinc exchange, for example, of iodoacetals **22**, and the organozinc intermediates **23** formed by radical cyclization were again transmetallated to the corresponding copper species which could be reacted with the usual Michael acceptors to afford the products **24** with high diastereoselectivity (Scheme 6).[33,33a]

A breakthrough in the development of new routes toward organocopper compounds by transmetallation was the rediscovery of the boron–zinc exchange reaction by Knochel and co-workers.[31,31a] Since a wide range of organoboranes is accessible by hydroboration, this method allows the use of olefins as a precursor for organocopper reagents. Many reactive functional groups are tolerated in this process, as exemplified by the hydroboration of the nitroolefin **25** with diethylborane, followed by successive transmetallation of the borane **26** with diethylzinc and CuCN·2LiCl. The resulting organocopper species **27** could be trapped with the typical electrophiles, for example, with diethyl benzylidenemalonate, giving the product **28** with 62% yield over four steps (Scheme 7).[34,34a] Application of this method to 1,2-disubstituted alkenes (e.g., norbornene **29**) revealed that the boron–zinc exchange takes place with loss of stereoselectivity, so that trapping of the copper reagent **30** affords the product **31** as a mixture of stereoisomers.[34,34a]

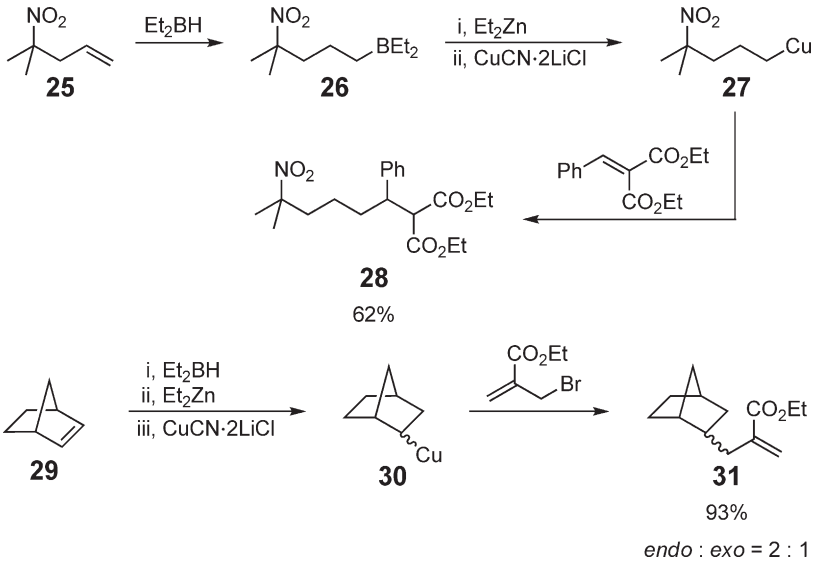


Scheme 5

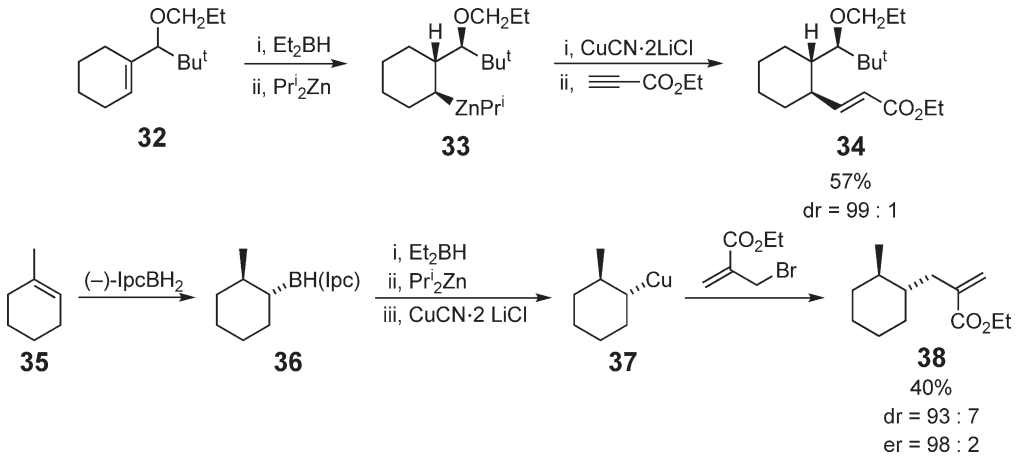


n	*Yield*(%)	dr
0	83	98 : 2
1	66	96 : 4

Scheme 6



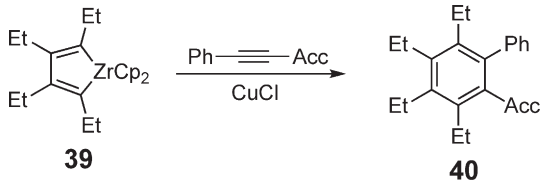
Scheme 7



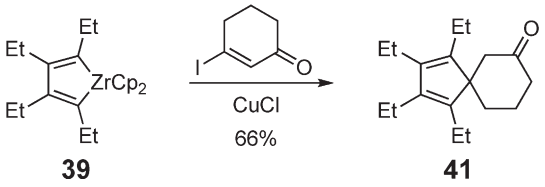
Scheme 8

By using diisopropylzinc instead of diethylzinc, the boron–zinc exchange could be accelerated dramatically, so that the stereochemical information gained in the hydroboration is no longer lost. This effect has been used in the diastereoselective construction of stereotriads by hydroboration of chiral endocyclic olefins of the type **32**, followed by the usual twofold transmetallation and final electrophilic capture of the resulting copper intermediate (Scheme 8).[35,35a] The analogous enantioselective procedure started with the hydroboration of prochiral alkenes (e.g., **35**) with isopinocampheylborane ($IpcBH_2$), followed by three transmetallation steps which all took place with the retention of configuration. The trapping reaction of copper species **37** with ethyl (2-bromomethyl)acrylate afforded the desired product **38** with moderate chemical yield, but excellent diastereo- and enantioselectivity.[36]

Like alkenes, terminal alkynes can also be employed as precursors for organocopper reagents. In this case, hydrozirconation opens up a regio- and stereoselective access to alkenylzirconium intermediates which can be transmetallated to the corresponding copper reagents without difficulty. For applications in conjugate addition reactions, catalytic amounts of copper salts are usually sufficient for the transmetallation (see Section 9.12.2.2.1).[37] Recent examples involving the stoichiometric formation of organocopper compounds from cyclic organozirconium compounds were reported by Takahashi and co-workers. For instance, treatment of zirconacyclopentadiene **39** with an excess of CuCl and various acetylenic Michael acceptors leads to the smooth formation of hexasubstituted benzenes **40** with moderate to good chemical yields (Scheme 9).[38,38a] Since the zirconacyclopentadiene is formed



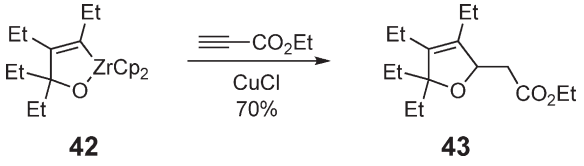
Acc	*Yield*(%)
CO_2Et	58
CN	70
$CONMe_2$	55



Scheme 9

from 2 equiv. of hex-3-yne and zirconocene dichloride, the aromatic products of type **40** can also be obtained in a one-pot reaction from two or three different alkynes. The reaction probably proceeds by transmetallation of the organic moiety of **39** to copper, followed by a Michael addition and ring closure. If 3-iodocyclohex-2-enone is used as a Michael acceptor, 1,4-addition–elimination is followed by a second conjugate addition to afford spirobicyclic cyclopentadienes of the type **41**.[39]

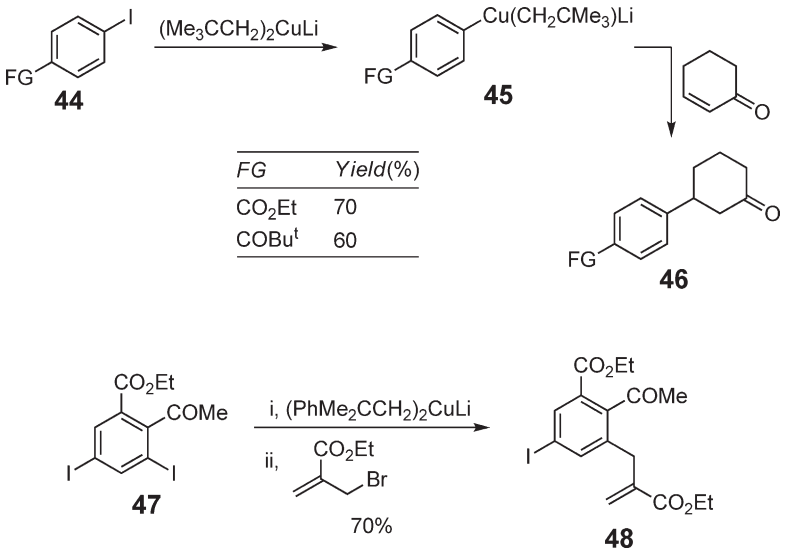
Takahashi *et al.* have also extended the method to oxazirconacyclopentenes (e.g., **42**). Here, transmetallation with CuCl and treatment with ethyl propiolate provides 2,5-dihydrofuran **43** with 70% isolated yield (Equation (1)).[40] Deuterium-labeling experiments indicate that Michael addition of the copper intermediate is followed by an intramolecular conjugate addition of the hydroxy group to the acrylate moiety introduced in the first step.



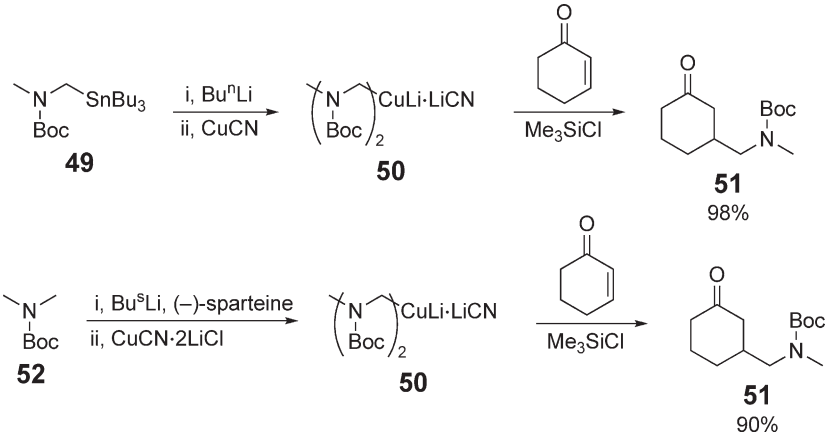
(1)

Although the various and highly elaborate transmetallation protocols reported so far open up an efficient access to many types of functionalized organocopper reagents, the most economic way would be to perform a direct halogen–copper exchange of an organic halide with a suitable copper compound. An efficient protocol for this fundamental transformation has recently been described by Knochel and Piazza.[41,41a–41c] By employing the sterically hindered lithium dineopentylcuprate, $(Me_3CCH_2)_2CuLi$, or lithium dineophylcuprate, $(PhMe_2CCH_2)_2CuLi$, the halogen–copper exchange of aromatic bromides or iodides (e.g., **44**) takes place without competing cross-coupling, and the arylcopper reagents **45** thus obtained can be trapped with various electrophiles, including enones (Scheme 10). Interestingly, the starting material can also contain aldehyde or keto groups, that is, functional groups which are usually not compatible with a halogen–magnesium exchange. The method has also been used for the selective functionalization of polyhalogenated aromatic substrates, as exemplified by the iodine–copper exchange reaction of **47** with lithium dineophylcuprate and 1,4-addition–elimination of the mixed cuprate with ethyl (2-bromomethyl)-acrylate to afford product **48** with 70% yield.[42] This reaction once again demonstrates the tremendous functional group tolerance of the halogen–copper exchange.

Among various heteroatom-substituted organocopper reagents, α-heteroatomalkylcuprates have been studied extensively since introduction of these moieties into an electrophile, for example, by conjugate addition, opens up a straightforward and convenient access to many natural or unnatural target molecules.[43] Recently, α-aminoalkylcuprates, which are readily accessible from the corresponding stannanes by a tin to lithium to copper transmetallation sequence (or by deprotonation of a suitable protected amine with a lithium base, followed by cuprate formation), have proved to be particularly useful for this purpose. For example, Sn–Li exchange of the stannylcarbamate **49** with Bu^nLi and transmetallation with CuCN afforded the cuprate **50** which underwent the 1,4-addition to cyclohex-2-enone to the desired product **51** with excellent 98% yield (Scheme 11).[43,44,44a] Due to the moderate reactivity of the α-aminoalkylcuprate, activation of the reactants with chlorotrimethylsilane was necessary to achieve this result. Alternatively, the cuprate can be obtained by direct deprotonation of the carbamate **52** (in the presence of



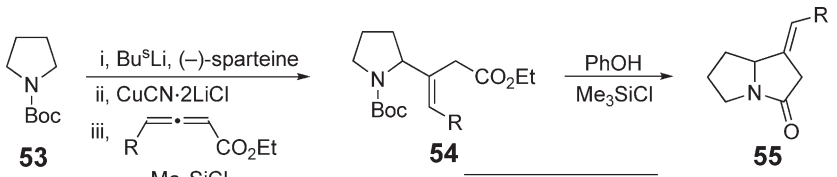
Scheme 10



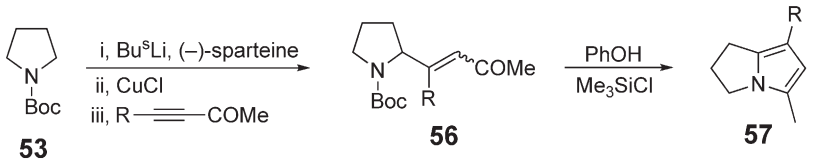
Scheme 11

TMEDA or sparteine) and transmetallation with CuCN·2LiCl, providing the adduct **51** with 90% yield. Enantioselective 1,4-additions of chiral, non-racemic α-aminoalkylcuprates (formed from the corresponding stannylcarbamates by transmetallation, or by enantioselective deprotonation) have also been described recently.[45,45a–45c]

Besides simple enones and enals, less reactive Michael acceptors like β,β-disubstituted enones, as well as α,β-unsaturated esters, thioesters, and nitriles, can also be transformed into the 1,4-addition products by this procedure.[44,44a,46,46a] The conjugate addition of α-aminoalkylcuprates to allenic or acetylenic Michael acceptors has been utilized extensively in the synthesis of heterocyclic products.[46–49] For instance, addition of the cuprate, formed from cyclic carbamate **53** by deprotonation and transmetallation, to alkyl-substituted allenic esters proceeded with high stereoselectivity to afford the adducts **54** with good yield (Scheme 12).[46,46a,47] Treatment with phenol and chlorotrimethylsilane effected a smooth Boc deprotection and lactam formation. In contrast, the corresponding reaction with acetylenic esters[46,46a] or ketones[48] invariably produced an *E*/*Z*-mixture of addition products **56**. This poor stereoselectivity could be circumvented by the use of (*E*)- or (*Z*)-3-iodo-2-enoates instead of acetylenic esters,[49] but turned out to be irrelevant for the subsequent deprotection/cyclization to the pyrroles **57** since this step took place with concomitant *E*/*Z*-isomerization.



	Yield(%)	
R	54	55
Me	85	60
Pr^i	77	67



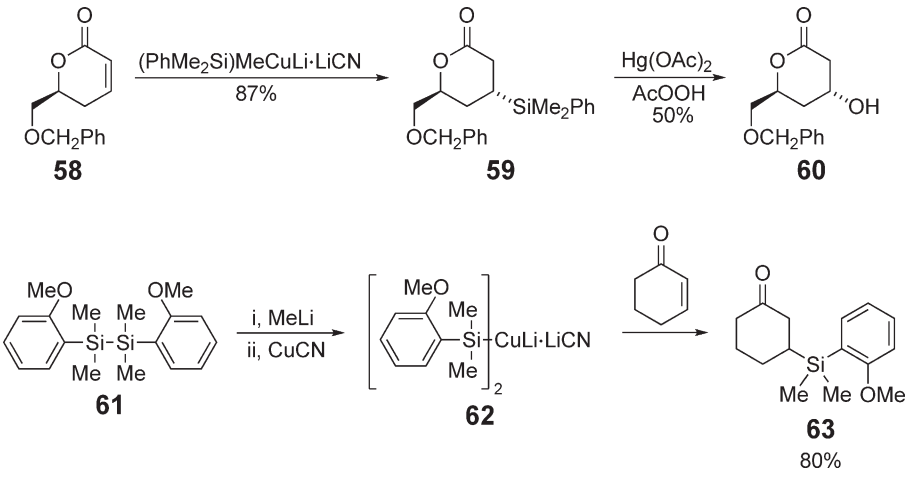
	Yield(%)	
R	56	57
Bu^n	81	81
Ph	69	85

Scheme 12

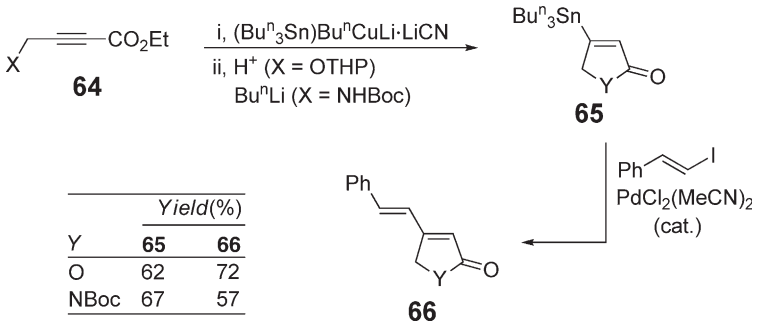
Nitrogen, oxygen, or sulfur ligands bound to copper via the heteroatom usually serve as non-transferable, residual "dummy ligands" and have been used extensively in mixed cuprates of the composition $R^1Cu(XR^2)Li$ for the economic transfer of a "valuable" carbon nucleophile R^1 to an electrophile.[3,4] This strategy has been particularly useful in the so-called "chiral cuprates" wherein a chiral, non-transferable heteroatom ligand controls the enantioselectivity of the transfer of an achiral carbon group to a prochiral substrate.[50,50a,50b] Nowadays, however, this strategy is no longer used since highly efficient copper catalysts for the catalytic enantioselective conjugate addition have been developed in recent years (see Section 9.12.2.2.1).

In contrast to these heterocuprates, silylcuprates and stannylcuprates readily transfer their hetero ligand to many electrophiles and have therefore found wide applications in organic synthesis, exploiting the hetero group for further transformations.[43,51,52] Like their carbon counterparts, silylcopper and stannylcopper compounds are usually prepared by transmetallation of the corresponding silyl- or stannyllithium reagents with copper(I) salts. Interestingly, mixed cuprates of the stoichiometry $(R_3M)CuRLi$ (M = Si, Sn; accessible from lithium dialkylcuprates R_2CuLi by ligand exchange with R_3SiSnR_3, R_3SnSnR_3, etc.,) preferentially transfer the heteroatom group to an electrophile.[43,51] As their carbon analogs, silylcopper and stannylcopper reagents readily undergo conjugate addition reactions to various Michael acceptors. One of the major advantages of the use of silylcopper reagents is the subsequent transformation of the C–Si bond into a C–OH bond by Tamao–Fleming oxidation.[43,51,53,53a,53b] Recent examples for this well-established synthetic strategy comprise the stereoselective formation of the lactone moiety **60** of the enzyme-inhibiting natural products (+)-compactin, (+) mevinolin, and (+)-pravastatin by diastereoselective 1,4-addition of the mixed cyanocuprate $(PhMe_2Si)MeCuLi{\cdot}LiCN$ to the chiral enone **58**, followed by stereospecific oxidation of adduct **59** with mercuric acetate and peracetic acid (Scheme 13).[54] In a similar fashion, various target molecules were synthesized by Fleming and co-workers,[55] including the Prelog–Djerassi lactone[56] and the terpene lavandulol.[57] Lee and Corey[58,58a] introduced the use of the (2-methoxyphenyl)dimethylsilylcuprate **62** (obtained by treatment of disilane **61** with methyllithium and copper cyanide) which underwent substitution and addition reactions with various substrates, for example, cyclohex-2-enone. The advantage of this procedure is a cleavage of the aryl silicon bond of adducts of type **63** under much milder conditions (N-bromosuccinimide or trifluoroacetic acid) than those usually employed for the Tamao–Fleming oxidation of $PhMe_2Si$ groups (H_2O_2/KF).[52]

The corresponding 1,4-addition products of stannylcuprates can be also used for further elaboration, for example, by Stille-coupling.[43,51] For example, treatment of the acetylenic esters **64** bearing a protected hydroxy or amino group with the mixed stannylcuprate ($Bu^n{}_3Sn$) $Bu^n{}_3CuLi{\cdot}LiCN$ afforded, after cyclization, the heterocycles **65** which underwent a smooth Stille-coupling with β-iodostyrene to the expected products **66** (Scheme 14).[59] Stereoselective variations of this chemistry took advantage of the use of the Garner aldehyde as a precursor for the chiral Michael



Scheme 13



	Yield(%)	
Y	**65**	**66**
O	62	72
NBoc	67	57

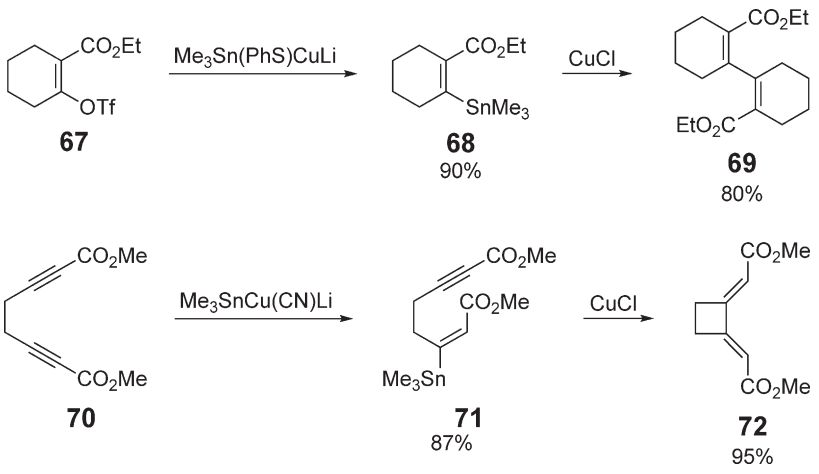
Scheme 14

acceptor.[60,60a,60b] The high *cis*-selectivity of the stannylcuprate addition to many acetylenic Michael acceptors was also utilized in retinoid synthesis.[61,61a]

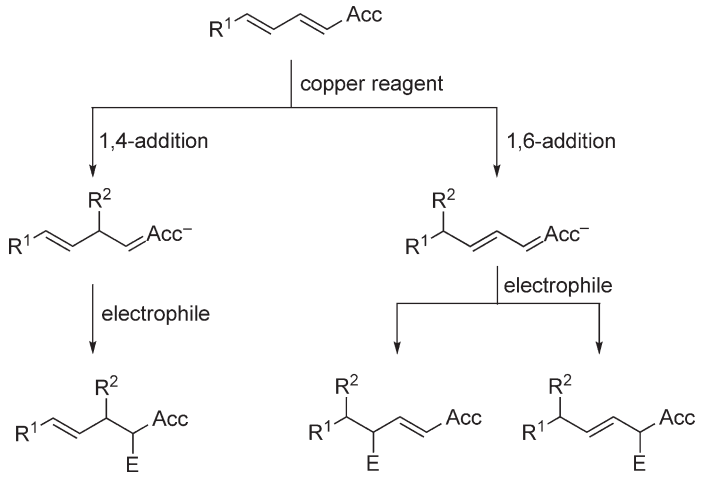
A different coupling strategy for the stannylcuprate 1,4-addition products was developed by Piers and coworkers.[62,62a] Michael addition–elimination reaction of the enol triflate **67** with another type of a mixed stannylcuprate, $Me_3Sn(PhS)CuLi$, gave the β-stannylester **68** with high yield, and subsequent treatment with an excess of CuCl lead to the formation of the dimerization product **69** (Scheme 15). This transformation probably occurs via tin–copper exchange[63] and oxidative coupling of the vinylcopper species formed to produce **69** and metallic copper. Performing the sequence in an intramolecular fashion (e.g., with substrate **70**) opens up an efficient access to interesting dienes, for example, bis(methylene)cyclobutane **72**.[62,62a] In this case, however, the vinylcopper intermediate formed from **71** by Sn–Cu exchange undergoes a 1,4-addition to the second acetylenic Michael acceptor.

9.12.2.1.1.(ii) Substrate scope

The examples summarized in the previous section prove that numerous, highly sophisticated organocopper reagents (and protocols for their application) have been developed in the last decade. In terms of the substrates, however, simple enones, enoates, and acceptor-substituted alkynes are still predominating. Only recently, Michael additions of ambident acceptors with extended multiple bond systems (i.e., with two or more reactive positions) have received attention.[7,7a,14,64,65] In the simplest system, an acceptor-substituted diene, three regioisomeric products might be formed, originating from different regioselectivities of the nucleophilic attack (1,4- vs. 1,6-addition) and of the electrophilic capture of the ambident enolate formed in the latter case (Scheme 16). Moreover, each of these products can be generated as *E*/*Z* isomers, and basic conditions may give rise to an isomerization of the initially formed



Scheme 15



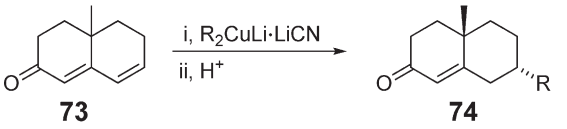
Scheme 16

β,γ-unsaturated carbonyl compound to the thermodynamically more stable conjugated isomer. Fortunately, organocuprates usually react with high regioselectivities in favor of the 1,6-addition product.[64,65]

The method has been applied frequently in natural product synthesis, in particular in the generation of steroid hormones by 1,6-cuprate addition to $\Delta^{4,6}$-steroids.[14,64,65] A more recent example involves the bicyclic tetrahydro-3*H*-naphthalen-2-one **73** as Michael acceptor which undergoes 1,6-addition reactions of cyano-Gilman reagents $R_2CuLi{\cdot}LiCN$ to afford the products **74** with high *trans*-selectivity (Scheme 17).[66] NMR spectroscopic investigations revealed the formation of cuprate-π-complexes at the double bond adjacent to the carbonyl groups as reactive intermediates en route to the adducts **74**.

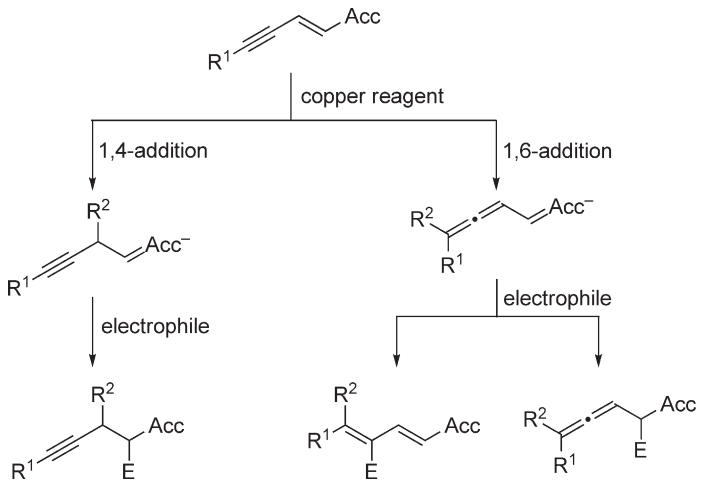
Even more interesting, both from the preparative and the mechanistic point of view, are conjugate addition reactions to Michael acceptors containing at least one triple bond besides one or several double bonds.[7,7a,14,64,65] Whereas conjugated enynes bearing an acceptor substituent at the triple bond react with organocuprates exclusively by 1,4-addition,[64,67] the corresponding addition reactions to enynes bearing the acceptor group at the double bond can result in the formation of several regioisomeric products (Scheme 18).

Similar to the addition reactions of acceptor-substituted dienes (Scheme 16), the outcome of the transformation depends on the regioselectivity of the nucleophilic attack of the organocopper reagent (1,4- vs. 1,6-addition) and of the electrophilic capture of the enolate formed. The allenyl enolate obtained by 1,6-addition can afford either a conjugated diene or an allene upon reaction with a soft electrophile, and thus opens up the possibility to create axial chirality. The first copper-mediated addition reactions to Michael acceptors of this type, for example, 3-alkynyl-2-cyclopentenone **75**,

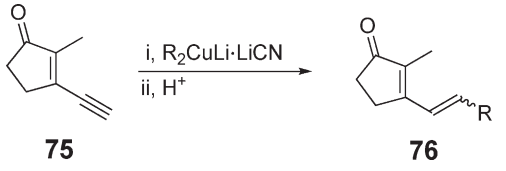


R	Yield(%)	trans : cis
Me	79	98 : 2
Bu^n	54	97 : 3
Ph	81	96 : 4

Scheme 17



Scheme 18



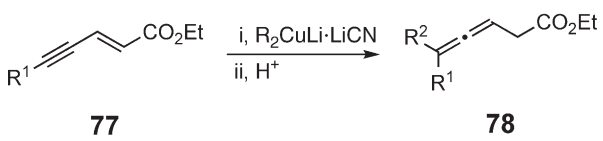
R	Yield(%)	E : Z
Me	91	29 : 71
Bu^t	93	3 : 97
Ph	88	14 : 86

Scheme 19

uniformly provided *E*/*Z*-mixtures of conjugated dienes **76** formed by 1,6-addition and protonation of the allenyl enolate at C4 (Scheme 19).[9] The use of other electrophiles gave similar results. Interestingly, substrates of the type **75** can also undergo successive 1,6- and 5,6-addition reactions, indicating that the allenyl enolate formed in the first step is sufficiently nucleophilic to react with another organometallic reagent in a carbometallation of the allenic double bond distal to the enolate moiety.[9]

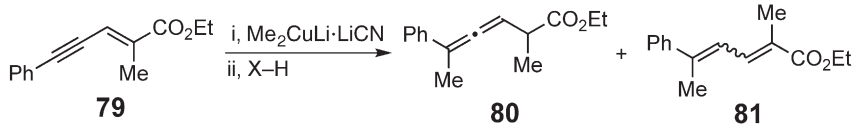
By using acyclic enynes and different acceptor groups, in particular esters, the regioselectivity of the protonation of the allenyl enolates obtained by cuprate 1,6-addition could be shifted towards the formation of allenes.[7,7a,14,64,65,68] Thus, the reaction of various substituted 2-en-4-ynoates **77** with the Gilman cuprate $Me_2CuLi{\cdot}LiI$ or the cyano-Gilman reagents $R_2CuLi{\cdot}LiCN$ ($R \neq Me$) afforded, after protonation with dilute sulfuric acid, the β-allenic esters **78** with moderate to good chemical yield (Scheme 20). The regioselectivity of the protonation was found to depend not only on the electronic, but also on the steric properties of the substrate: whereas sterically demanding groups at C5 block the attack of a proton at C4 and therefore favor the formation of allenes, the presence of a substituent at C2 of the enolate disfavors protonation at this position, so that mixtures of allenes and conjugated dienes are formed. For example, treatment of enynoate **79** with lithium dimethylcuprate and dilute sulfuric acid affords a 1 : 1 mixture of allene **80** and diene **81** (mixture of *E*/*Z* isomers). The former can be easily isomerized to the thermodynamically more stable product **81** with weak base; if, however, the allene **80** is the desired product, the protonation should be carried out with weak organic acid, in particular pivalic acid (2,2-dimethylpropionic acid) at low temperature which gives rise to the exclusive formation of the allene.

In contrast to the protonation, the regioselectivity of reactions between other electrophiles and allenyl enolates derived from 2-en-4-ynoates is independent of the steric and electronic properties of the reaction partners.[7,7a]



77 **78**

R^1	R^2	*Yield*(%)
Ph	Me	79
Ph	Bu^t	81
Bu^n	Ph	62
Me_3Si	Me	57



79 **80** **81**

X–H	*Temp.*	**80 : 81**
2N H_2SO_4	25 °C	50 : 50
Bu^tCO_2H	–80 °C	>99 : <1

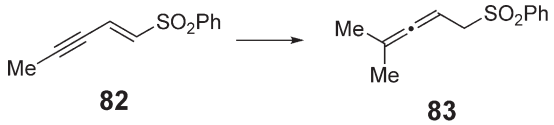
Scheme 20

As expected according to the HSAB principle, hard electrophiles such as silyl halides and triflates react at the enolate oxygen atom to form allenyl ketene acetals, while soft electrophiles such as carbonyl compounds attack at C2. Only allylic and propargylic halides react regioselectively at C4 of the allenyl enolate to give substituted conjugated dienes.

The nature of the acceptor substituent exerts hardly any influence on the regioselectivity of the cuprate addition to acceptor-substituted enynes. Enynes variously incorporating thioester, lactone, dioxanone, keto, sulfonyl, sulfinyl, cyano, and oxazolidino groups, all react in a 1,6-manner to furnish functionalized allenes.[68] In contrast, 1-nitro-1-en-3-ynes are attacked at the C=C double bond, with the formation of the corresponding 1,4-adducts. The differences in reactivity can be described qualitatively by the following reactivity scale: acceptor (Acc) = NO_2 > COR, CO_2R, COSR > CN, SO_3R, oxazolidino > SO_2R > SOR ≫ $CONR_2$. Remarkably, the regioselectivity of the cuprate addition to acceptor-substituted enynes is also insensitive to the steric properties of the substrate. Thus, enynes with *t*-butyl substituents at the triple bond undergo 1,6-additions even when the cuprate itself is sterically demanding, making the method highly useful for the preparation of sterically encumbered allenes.[7,7a]

In order to achieve acceptable chemical yields with less reactive Michael acceptors, such as sulfones and sulfoxides, it is often necessary to use more reactive organocopper reagents or to activate the substrate by Lewis acids. Thus, treatment of enyne sulfone **82** with 5 equiv. of the Gilman cuprate Me_2CuLi alone gave no trace of the addition product, whereas the analogous reaction with the higher-order cuprate Me_3CuLi_2 provided the desired allene **83** with a disappointing 16% yield (Scheme 21).[68] With 2 equiv. of Me_2CuLi in the presence of 1 equiv. of Me_3SiI, however, the yield was increased to 45%, although with Me_3SiOTf as additive the allene **83** was isolated in only 29% yield. Unfortunately, enyne amides completely fail to form 1,6-addition products even under these conditions.

Unlike the substrate, the organocuprate component has a pronounced influence on the regiochemical course of the addition to acceptor-substituted enynes. The Gilman cuprate $Me_2CuLi{\cdot}LiI$ as well as cyano-Gilman reagents $R_2CuLi{\cdot}LiCN$ ($R \neq Me$) readily afford 1,6-addition products, and the same regioselectivity is observed when the reaction is carried out with organolithium reagents and catalytic amounts of the cuprate or copper (2-dimethylaminomethyl)thiophenolate.[7,7a] In contrast to this, the Yamamoto reagents $RCu{\cdot}BF_3$ and organocopper compounds RCu activated by Me_3SiI both afford 1,4-adducts.[7,7a] In some cases, even 1,4- and 1,6-reduction products are observed; these may be the result of electron transfer from the cuprate to the substrate or of hydrolysis of a stable copper(III) intermediate.[7,7a] Lower-order cyanocuprates RCu(CN)Li again show a different behavior; although these

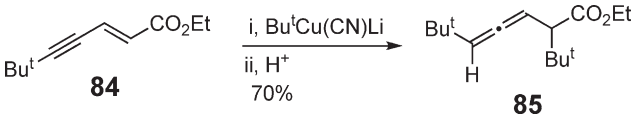


82 **83**

Cuprate	*Additive*	*Yield*(%)
$Me_2CuLi{\cdot}LiI$		0
$Me_3CuLi_2{\cdot}LiI$		16
$Me_2CuLi{\cdot}LiI$	Me_3SiI	45
$Me_2CuLi{\cdot}LiI$	Me_3SioTf	29

Scheme 21

do not usually react with acceptor-substituted enynes, the cuprate $Bu^tCu(CN)Li$ nevertheless undergoes anti-Michael additions with 2-en-4-ynoates and nitriles. For example, reaction of this cuprate with enynoate **84** afforded the allene **85** with 70% yield (Equation (2)).[69]

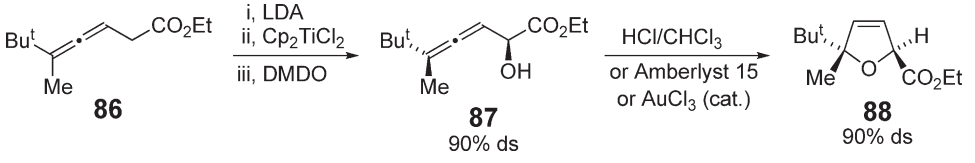


(2)

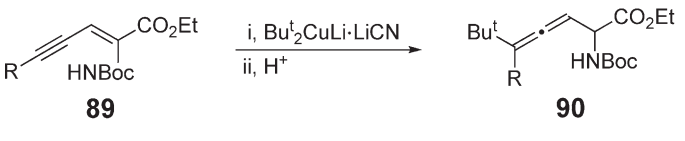
Preparative applications of the 1,6-cuprate addition to acceptor-substituted enynes comprise the synthesis of natural products, for example, (±)-sterpurene, as well as the use of the vinylallenes in Diels–Alder reactions,[70] aldol reactions of allenyl enolates,[71] and Ireland–Claisen rearrangements of silyl allenylketene acetals.[72] In these transformations, the axial chirality of the allene is transferred to one or several newly formed stereogenic centers. Another example for this type of chirality transfer is the oxidation of titanium allenyl enolates (formed by deprotonation of β-allenylcarboxylates of type **86** and transmetallation with titanocene dichloride) with dimethyl dioxirane (DMDO) which was found to proceed regioselectively at C2. In this way, depending on the steric demand of the substituents at the allenic moiety, the corresponding 2-hydroxy-3,4-dienoates (e.g., **87**) were obtained diastereoselectively with up to 90% ds (Scheme 22).[73,74] α-Hydroxyallenes of this type are synthetically valuable precursors for 2,5-dihydrofurans, found not only in several natural products but also in biologically active compounds. The cyclization of allene **87** to heterocycle **88** takes place with complete axis-to-center chirality transfer, being easily achieved by treatment with HCl gas in chloroform,[73] acidic ion exchange resins such as Amberlyst 15,[74] or with catalytic amounts of gold(III) chloride (see Section 9.12.4.3).[74,75]

Allenic amino acid derivatives **90**, which are of special interest as selective vitamin B_6 decarboxylase inhibitors, represent another type of heterosubstituted allene which is accessible through 1,6-cuprate addition to 2-amino-substituted enynes **89** (Scheme 23).[74] However, because of the low reactivity of these particular Michael acceptors, the reaction succeeds only with the most reactive cuprate: the *t*-butyl cyano-Gilman reagent $Bu^t_2CuLi{\cdot}LiCN$. Nevertheless, the addition products are obtained with good chemical yields, and selective deprotection of either the ester or the amino functionality under acidic conditions provides the desired target molecules.

In contrast to nucleophilic addition reactions to activated dienes, the mechanism of 1,6-cuprate additions to acceptor-substituted enynes is quite well understood, largely thanks to kinetic and NMR spectroscopic investigations. ^{13}C NMR spectroscopic studies have revealed that these transformations proceed through π-complexes, with an interaction between the π-system of the C═C double bond and the nucleophilic copper atom (a soft–soft interaction in terms of the HSAB principle), together with a second interaction between the hard lithium ion of the cuprate and the hard carbonyl oxygen atom.[76] In particular, the use of ^{13}C-labeled substrates has shed light on the structure of the metal-containing part of these π-complexes, indicating, for example, that the cuprate does not interact with the triple bond.[76,77] Furthermore, the experimental determination and theoretical calculation of ^{13}C kinetic isotope effects has



Scheme 22

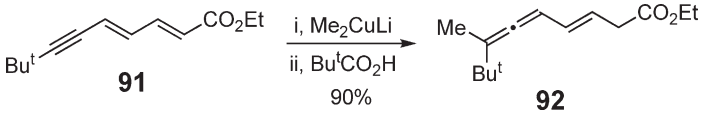


R	*Yield*(%)
Ph	54
Bu^t	71
Me_3Si	68
	63

Scheme 23

proved that bond formation between C5 of the acceptor-substituted enyne and the cuprate occurs in the rate-determining step.[78,78a] With the aid of kinetic measurements with a variety of different substrates, even activation parameters for these transformations have been determined experimentally.[79,79a]

In view of the high regioselectivity observed in the addition of organocuprates to acceptor-substituted enynes, it seemed interesting to determine whether the preference of these reagents for triple bonds persists even when the distance between the acceptor group and the triple bond is increased by the introduction of further C=C double bonds. Of course, the number of possible regioisomeric products rises with increasing length of the Michael acceptor. The 2,4-dien-6-ynoate **91**, for example, can be attacked by an organocopper reagent at C3, C5, or C7, the latter possibility producing a vinylogous allenyl enolate possessing four reactive positions (enolate oxygen, C2, C4, C6). The high regioselectivity of the reaction between **91** and lithium dimethylcuprate is therefore striking; the cuprate attacks the triple bond exclusively, and protonation with pivalic acid occurred at C2 of the enolate, giving the 1,8-addition product **92** as the only isolable regioisomer in 90% yield (Equation (3)).[70]



91 **92** (3)

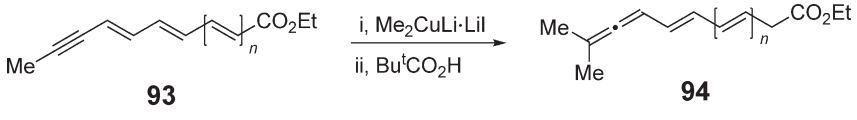
In an analogous manner, the trienynoate **93** ($n = 1$) reacted in a 1,10-addition to give the 3,5,7,8-tetraenoate **94** ($n = 1$), and it was even possible to obtain the 1,12-adduct from the Michael acceptor **93** ($n = 2$) containing four double bonds between the triple bond and the acceptor substituent (Scheme 24). In the latter case, however, the yield was only 26%; this is probably due to the reduced thermal stabilities of the starting material and the addition product (the 1,12-adduct was the only isolable reaction product apart from polymeric compounds).[70]

These transformations and those summarized previously indicate that Michael acceptors containing any combination of double and triple bonds undergo highly regioselective copper-mediated addition reactions. The following rule holds: "Michael acceptors with any given arrangement of conjugated double and triple bonds react regioselectively with organocuprates at the triple bond closest to the acceptor substituent."

9.12.2.1.1.(iii) Stereoselectivity

Stereoselective Michael additions of stoichiometric copper reagents comprise enantioselective 1,4-additions of so-called "chiral cuprates" RCu(L*)Li, bearing a chiral ligand L*, as well as diastereoselective cuprate additions to chiral Michael acceptors. Whereas the former strategy has examined extensively in the 1980s and early 1990s,[50,50a,50b] it has now been completely replaced by the use of highly efficient chiral copper catalysts for catalytic enantioselective conjugate additions (see Section 9.12.2.2.1). In contrast to this, diastereoselective 1,4-additions of organocuprates to chiral enones and other Michael acceptors, which often occur with high levels of stereoselectivity, had a major impact in the total synthesis of prostaglandins, steroids, and other natural products,[3,4,5,8] and are still extensively examined.[80]

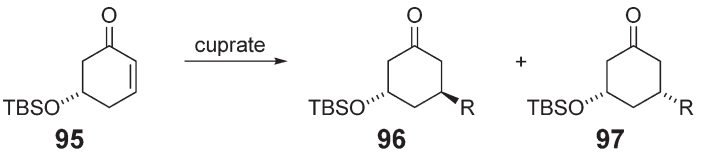
Generally, diastereoselective conjugate addition reactions take place via passive or active substrate control. In certain cases, the choice of the organocopper reagents makes it possible to switch between these direction modes. For example, treatment of the 5-TBSO-substituted enone **95** with cyano-Gilman reagents $R_2CuLi{\cdot}LiCN$ affords the *trans*-adducts **96** originating from shielding of the back side of the enone by the substituent at C5 (Scheme 25).[81,81a–81c] In contrast to this, lower-order cyanocuprates RCu(CN)Li precoordinate to the oxygen atom of the silyloxy substituent and therefore provide the *cis*-adducts **97** with very high diastereofacial selectivity. A similar behavior was also observed in 6-amino-substituted cycloheptenones.[82]



93 **94**

n	*Yield*(%)
1	68
2	26

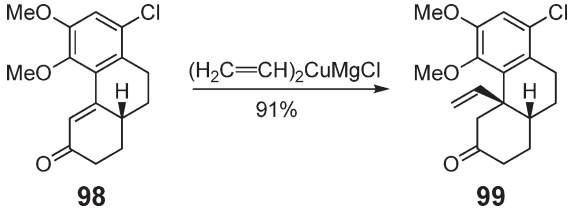
Scheme 24



Cuprate	**96 : 97**	*Yield*(%)
$Me_2CuLi \cdot LiCN$	97 : 3	83
MeCu(CN)Li	<1 : 99	77
$Bu^n{}_2CuLi \cdot LiCN$	98 : 2	92
$Bu^nCu(CN)Li$	<1 : 99	91

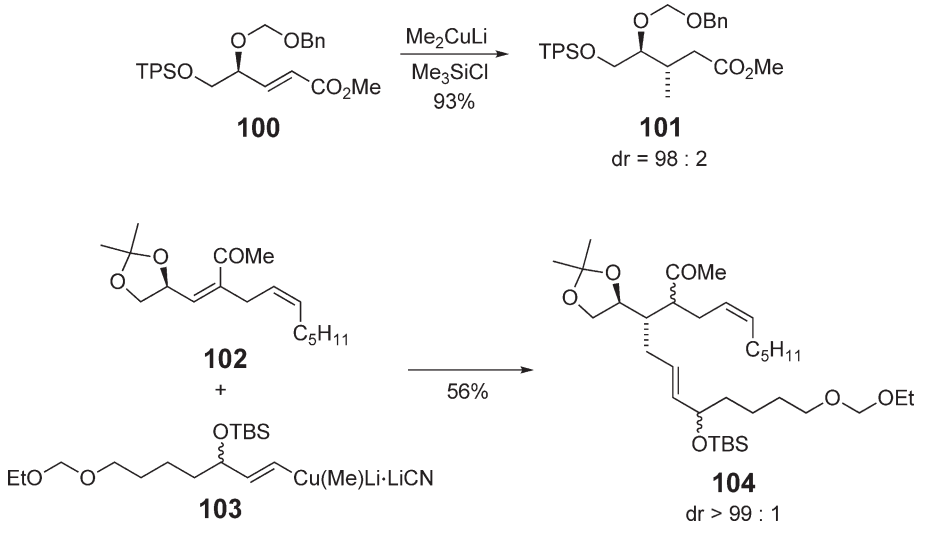
Scheme 25

Among various recent applications of diastereoselective cuprate addition reactions to cyclic enones in target-oriented synthesis,[81,81a–81c,83–87] the synthesis of (−)-dihydrocodeinone and (−)-morphine by Mulzer and co-workers[88,88a–88c] deserves special mention. In the key step, a quarternary benzylic stereocenter was constructed by highly diastereoselective conjugate addition of the vinylmagnesiumcuprate $(H_2C{=}CH)_2CuMgCl$ to the chiral enone **98**, affording the desired adduct **99** with 91% yield (Equation (4)). Here, several other organocopper reagents gave only dismal yields of the addition product **99** besides a dimeric by-product which indicates a single electron transfer (SET) mechanism.



(4)

Due to their high conformational flexibility, chiral acyclic Michael acceptors often display low diastereofacial selectivities in copper-mediated conjugate addition reactions.[80] Nevertheless, acceptable levels of diastereoselection can be obtained, in particular with heteroatom-substituted Michael acceptors. For example, treatment of the γ-benzyloxymethyl-substituted enoate **100** with lithium dimethylcuprate in the presence of chlorotrimethylsilane gives the anti-adduct **101** with excellent diastereoselectivity (Scheme 26).[89,89a] Products of this type can be easily



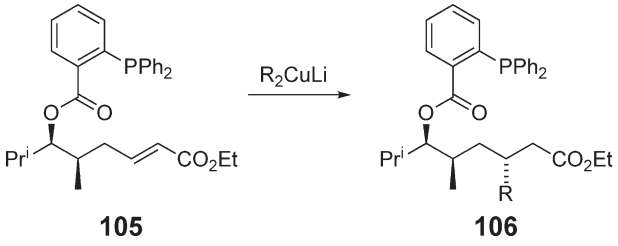
Scheme 26

functionalized in the α-position, for example, by enolate oxidation, which makes the method highly useful for the stereocontrolled synthesis of polypropionate chains. Hanessian and co-workers have applied this strategy to the synthesis of the macrolide antibiotics rifamycin S[90,90a,90b] and bafilomycin A_1.[91]

In a similar fashion, diastereoselective addition of the vinylcuprate **103** to the glyceraldehyde-derived enone **102** was used for the construction of the precursor **104** of iso[7]-levuglandin D_2.[92] Besides enones and enoates, heteroatom-substituted nitroolefins and α,β-unsaturated phosphine oxides also participate in diastereoselective copper-mediated 1,4-addition reactions.[93,93a,93b]

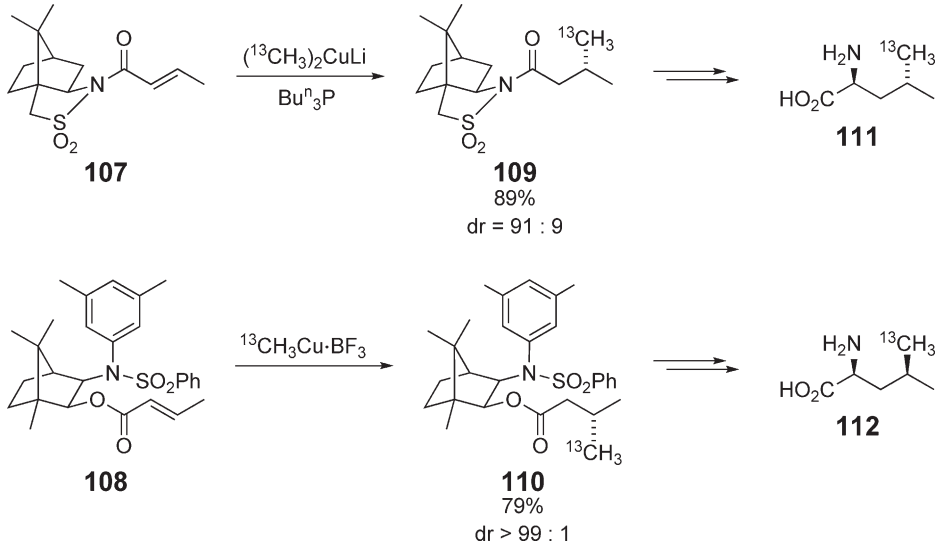
A highly efficient method for the directed diastereoselective conjugate cuprate addition to acyclic enoates was recently introduced by Breit.[94,94a–94c] Additions to the *ortho*-diphenylphosphinobenzoyl-substituted enoate **105** took place with precoordination of the cuprate to the phosphino group to afford the *anti*-adducts **106** with high diastereofacial selectivity (Scheme 27). The corresponding phosphine oxide did not react with cuprates, indicating that the phosphine in substrates of the type **105** acts both as an activating and reagent-directing group.

Chiral Michael acceptors bearing a removable auxiliary have been used extensively for the synthesis of enantiomerically enriched or pure products via diastereomeric 1,4-addition products.[50,50a,50b,80] Recent applications of this successful strategy include the use of chiral oxazolidinones,[95] imidazolidinones,[96] and glucopyranoside derivatives,[97] as well as the introduction of organometallic fragments into chiral auxiliaries for conjugate cuprate addition reactions.[98,98a] An interesting application was recently described by Fletcher and co-workers[99] who used the chiral enamide **107** or ester **108** as starting material for conjugate addition reactions of ^{13}C-labeled organocopper reagents (Scheme 28). The adducts **109** and **110** were subjected to hydrolysis and further elaboration to the L-leucine derivatives **111** and **112** which are selectively labeled at the two diastereotopic methyl groups.

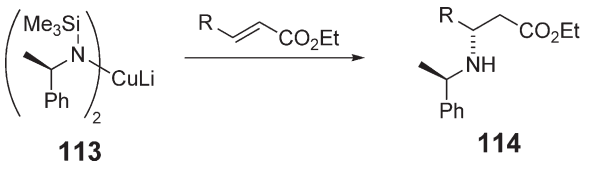


R	*Yield*(%)	dr
Me	93	95 : 5
Bu^n	68	95 : 5
CH=CH_2	61	80 : 20

Scheme 27

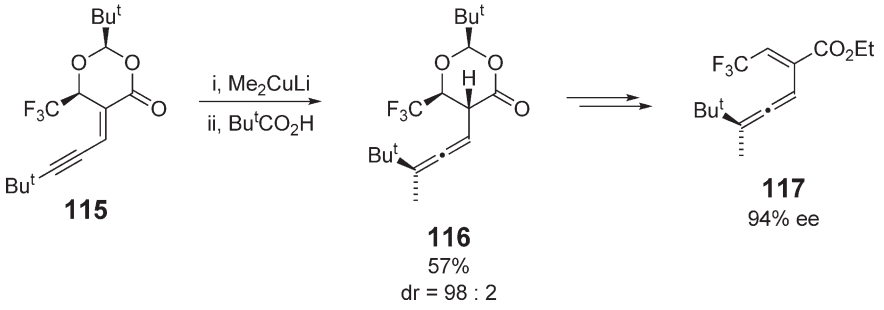


Scheme 28



R	*Yield*(%)	dr
Me	54	80 : 20
Et	46	>99 : 1
Pr^i	50	99 : 1

Scheme 29



Scheme 30

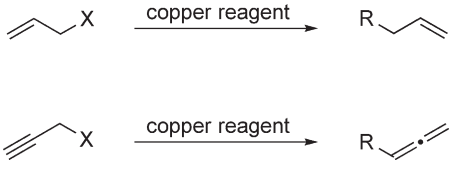
Products of this type are of interest for protein NMR studies, as well as for the investigation of metabolic reactions.

Diastereoselective conjugate cuprate additions can also be used for the stereoselective formation of carbon–nitrogen bonds. Although lithium amides are often used directly for 1,4-addition to enoates, Sewald *et al.*[100,100a] also employed the corresponding amidocuprates for this purpose. For example, reaction of the homochiral amidocuprate **113** with various enoates gave the β-amino acid derivatives **114** with good to excellent diastereoselectivities (Scheme 29). After transmetallation of the lithium/copper enolate to the corresponding titanium enolate, stereoselective trapping reactions with carbon electrophiles were also possible. The method was applied to the synthesis of both diastereomers of β-homothreonine and precursors of 3-amino-substituted carbohydrates.[100,100a]

Diastereoselective 1,6-cuprate addition reactions to chiral dienones[66] (Scheme 17) and acceptor-substituted enynes were reported recently. Due to an efficient shielding of the top face of the enyne moiety by the trifluoromethyl residue of the chiral 5-alkynylidene-1,3-dioxan-4-ones **115**, the addition of lithium dimethylcuprate occurs preferentially at the underside to provide allene **116** with high diastereoselectivity after protonation with pivalic acid (Scheme 30).[7,7a] The stereochemical information generated in this step remained intact during the conversion into the chiral vinylallene **117**.

9.12.2.1.2 Substitution reactions

Organocopper reagents undergo substitution reactions with various electrophiles. Historically, the direct S_N2 substitution of saturated halides, as well as of vinyl and aryl halides, belongs to the oldest and most intensely studied reactions of organocopper compounds[3–5,25] and is still used routinely in the synthesis of complex natural products since it can be superior to other methods, for example, palladium-catalyzed coupling reactions.[101] In contrast to this, the S_N2'-substitution of allylic or propargylic substrates is still studied extensively (Scheme 31). Similar to conjugate addition reactions, the emphasis of the last decade has been the control of regio- and stereoselectivity,[80] as well as the use of new, unusual copper reagents and substrates.



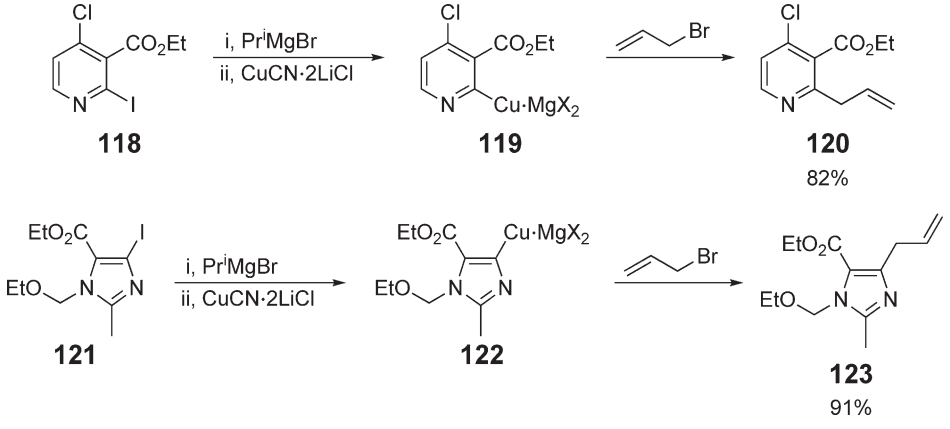
Scheme 31

9.12.2.1.2.(i) Allylic substrates

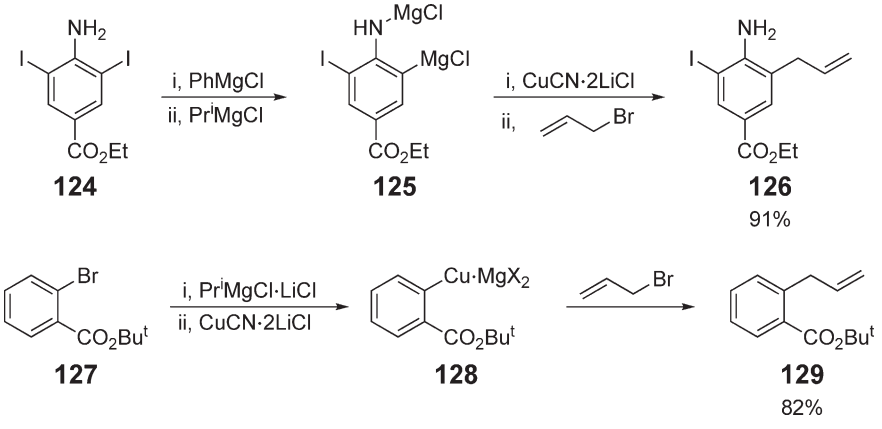
The functionalized organocopper reagents prepared from various precursors by the methods developed by Knochel and co-workers[25,26,26a–26d] (Section 9.12.2.1.1) were often applied in S_N2'-substitution reactions, allowing a rapid access to complex target molecules in a one-pot reaction. Often, catalytic amounts of copper salts are sufficient to achieve the desired substitution with high yield (see Section 9.12.2.2.2). Examples for the use of stoichiometric, functionalized organocopper reagents formed by halogen–magnesium exchange and transmetallation include the formation of the heteroaromatic copper reagents **119** and **122** by treatment of the corresponding electron-deficient heteroaryl iodides **118** and **121** with Pr^iMgBr, transmetallation of the Grignard reagent with CuCN·2LiCl, and trapping with allyl bromide to afford the products **120** and **123** with high yield (Scheme 32).[28,102]

The successful application of the reaction sequence halogen–magnesium exchange—transmetallation—allylation to carbocyclic aromatics was also reported. For instance, formation of the arylmagnesium compound **125** by successive addition of PhMgCl and Pr^iMgCl to the functionalized iodoaniline **124**, transmetallation with CuCN·2LiCl, and trapping with allyl bromide furnished the product **126** with high yield (Scheme 33).[29] The corresponding halogen–magnesium exchange of aryl bromides requires the presence of a lithium salt, that is, the reagent $Pr^iMgCl{\cdot}LiCl$. For example, treatment of *t*-butyl 2-bromobenzoate **127** with this reagent, CuCN·2LiCl, and allyl bromide provided the substitution product **129** via the arylcopper species **128**.[30,30a]

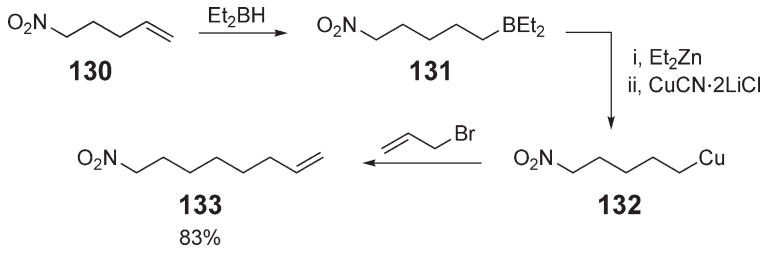
An example for the use of the boron–zinc exchange reaction for copper-mediated S_N2'-substitutions of allylic electrophiles is the hydroboration of nitroolefin **130** with diethylborane, followed by successive transmetallation of the borane **131** with diethylzinc and CuCN·2LiCl, and final trapping with allyl bromide to give the product **133** with 83% yield over four steps (Scheme 34).[34,34a] This transformation again demonstrates the tolerance of the method towards functional groups and acidic hydrogen atoms.



Scheme 32



Scheme 33

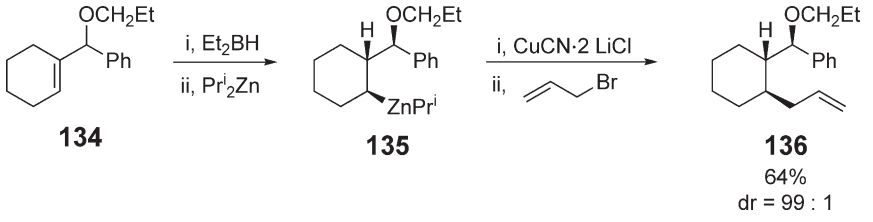


Scheme 34

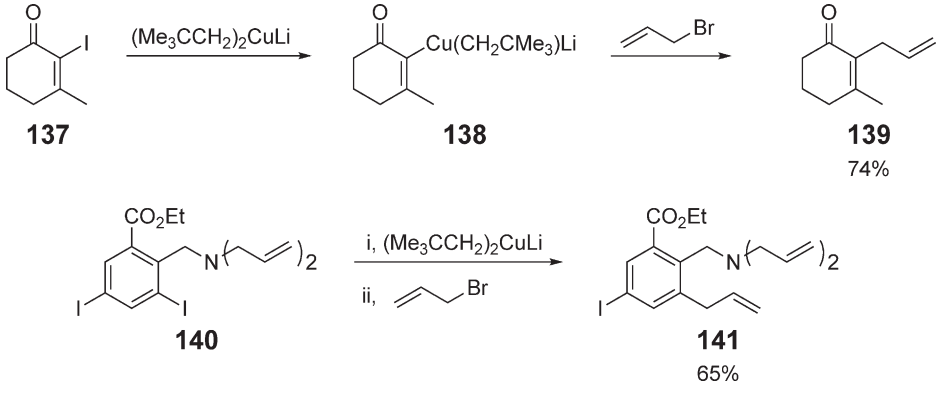
As mentioned in Section 9.12.2.1.1, the boron–zinc exchange can be performed stereoselectively if diisopropylzinc instead of diethylzinc is used. For example, hydroboration of the chiral, racemic endocyclic olefin **134** with diethylzinc, followed by twofold transmetallation and electrophilic capture of the resulting copper intermediate with allyl bromide was used for the highly diastereoselective formation of the stereotriad in product **136** (Scheme 35).[35,35a,103] Corresponding enantioselective transformations were carried out with chiral boranes and catalytic amounts of copper salts (see Section 9.12.2.2.2).[36]

The direct halogen–copper exchange of organic iodides with lithium dineopentylcuprate, $(Me_3CCH_2)_2CuLi$, or lithium dineophylcuprate, $(PhMe_2CCH_2)_2CuLi$ also lends itself nicely to the formation of functionalized organocopper compounds that undergo S_N2'-substitutions with allyl bromide. The transformation of the substrates **137** and **140** into the products **139** and **141** (Scheme 36) are exemplary.[41,41a–41c,42] The stability of the iodoenone **137** under the reaction conditions is particularly remarkable.

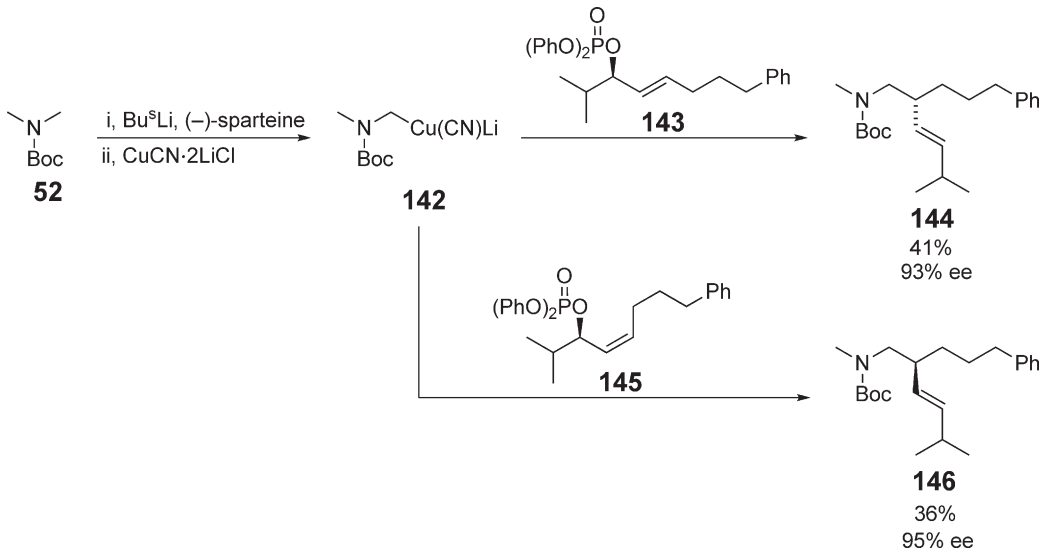
α-Aminoalkylcuprates prepared by the methods described in Section 9.12.2.1.1 undergo substitution reactions with allylic halides only with modest regiocontrol.[43,104] In contrast, the regioselectivity of the reaction with allyl phosphates is governed by steric factors in both the cuprate and electrophile and can be designed to afford either the S_N2- or S_N2'-substitution product.[105] For example, reaction of the lower-order cyanocuprate **142** (formed from carbamate



Scheme 35



Scheme 36



Scheme 37

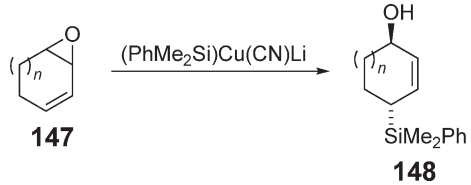
52 by treatment with 1 equiv. each of *s*-butyllithium and CuCN·2LiCl in the presence of (−)-sparteine) with the allylic phosphates **143** and **145** furnished the S_N2'-substitution products **144** and **146** with complete regioselectivity, as well as high enantioselectivities (Scheme 37).[105] The chemical yield of these transformations, however, was only moderate.

Like their carbon counterparts, silylcuprates and stannylcuprates readily participate in S_N2'-substitution reaction with allylic electrophiles.[43,51] For example, *anti*-diastereoselective allylic substitution of the vinyl oxiranes **147** with the lower-order cyanocuprate (PhMe$_2$Si)Cu(CN)Li cleanly affords the allylsilanes **148** (Scheme 38).[106] Products of this type can be converted into the corresponding diols with retention of configuration by Tamao–Fleming oxidation.[53,53a,53b,107]

Several applications of the method in natural product chemistry were reported by the Fleming group,[55] including a synthesis of the Prelog–Djerassi lactone[56] as well as of prostaglandins[108] and carbacyclins.[109] In their synthesis of the (±)-dihydronepetalactone **153**,[110] reaction of the allylic acetate **149** with (PhMe$_2$Si)$_2$CuLi·LiCN afforded two *anti*-S_N2'-substitution products **150** and **151** which were both converted into the allylic alcohol **152** by epoxidation and treatment with tetra-*n*-butylammonium fluoride (Scheme 39). An oxy-Cope rearrangement of **152** and further elaboration of the functional groups furnished the target molecule **153**.

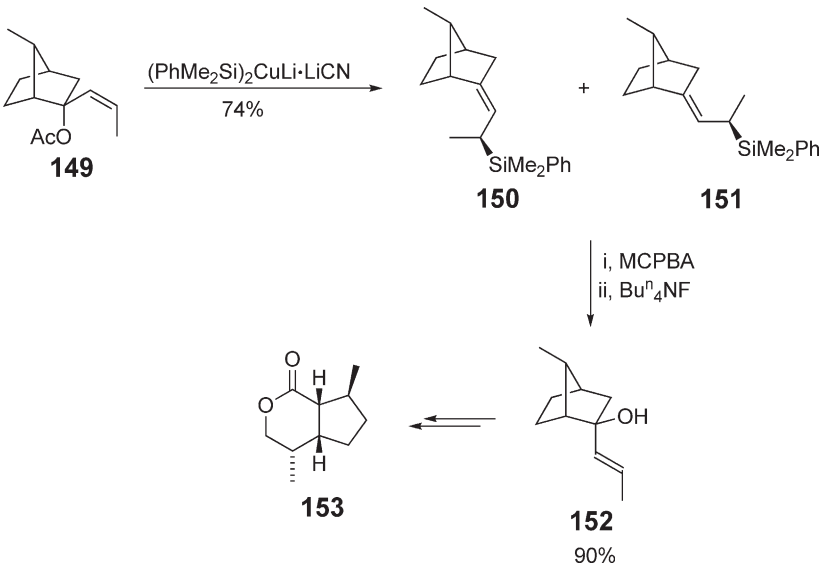
An interesting application of a stannylcuprate S_N2'-substitution was reported by Echavarren and co-workers.[111] Highly regioselective reaction at the sterically less hindered double bond of the bisallylacetate **154** with the mixed cuprate (Bu$_3^n$Sn)(Bu^n)CuLi·LiCN provided the allylstannane **155** with high yield, which was then submitted to a palladium-catalyzed carbocyclization reaction (Scheme 40). The product **156** was easily transformed into the natural product (±)-10-*epi*-elemol **157**.

The previous examples have amply demonstrated the high levels of *anti*-stereoselectivity that are usually encountered in copper-mediated S_N2'-substitution reactions.[3–5,16,16a,80] Several new approaches to influence the stereochemical course of these transformations and to utilize them for target-oriented synthesis have been reported in the

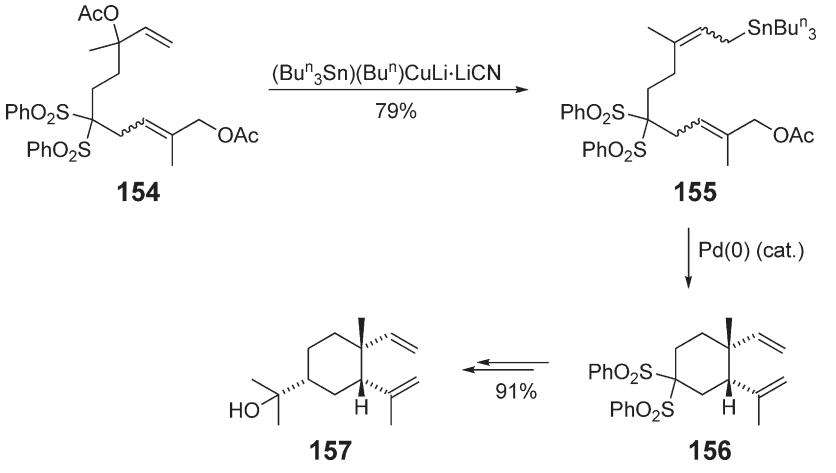


n	*Yield*	*anti* : *syn*
0	72%	85 : 15
1	70%	>99 : 1

Scheme 38



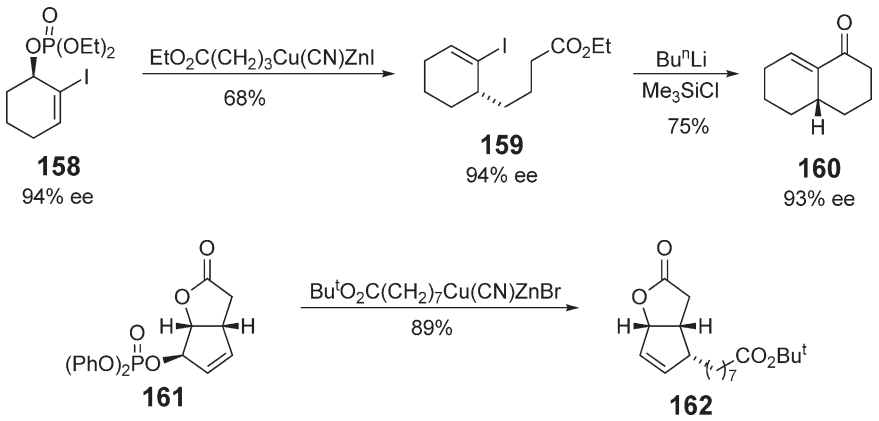
Scheme 39



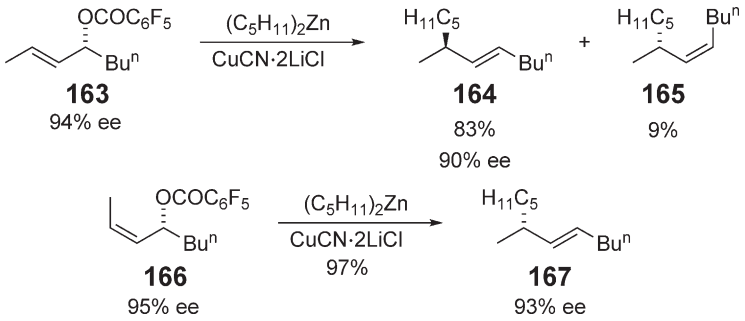
Scheme 40

last decade. For example, the use of allylic phosphates, which has been advantageous in the S_N2'-substitutions of α-aminoalkylcuprates (Scheme 37), has turned out to afford particularly high stereoselectivities in several other cases as well.[112–115,115a] Thus, Knochel and co-workers[113] employed 2-iodocycloalk-2-enyl phosphates of the type **158** for stereospecific allylic substitution reactions of various functionalized organocopper reagents, providing iodoalkenes (e.g., **159**) which were further transformed into bicyclic products, for instance, **160** (Scheme 41). Several chiral α-ionone derivatives were synthesized in a similar manner.[114] A key step in the enantioselective synthesis of various jasmonoids as reported by Helmchen *et al.*[115,115a] was the transformation of chiral allylic bromides or phosphates, for example, **161**, into bicyclic products of the type **162** by highly regio- and stereoselective S_N2'-substitution with zinc cyanocuprates.

Another highly useful leaving group for copper-mediated allylic substitutions is the pentafluorobenzoyl group. In contrast to allylic acetates or benzoates, allylic pentafluorobenzoates undergo smooth S_N2'-substitutions with less reactive organocopper reagents, for example, zinc cuprates.[116,116a] Thus, reaction of the substrate **163** with the cuprate formed from dipentylzinc and CuCN·2LiCl afforded the expected *anti*-S_N2' product **164**, contaminated by



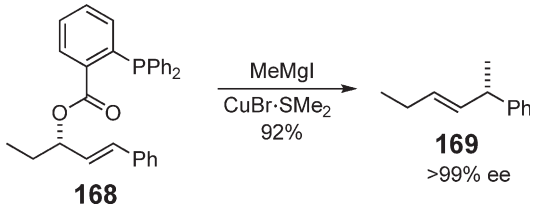
Scheme 41



Scheme 42

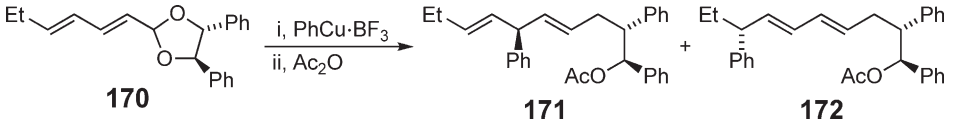
small amounts of the olefin **165** originating from the attack of the cuprate at a minor conformer of **163** (Scheme 42). If the (*Z*)-olefin **166** is employed as the substrate, however, the minor conformer is strongly disfavored because of its high allylic strain, so that the reaction with the zinc cuprate leads to the exclusive formation of the *anti*-substitution product **167**. Not unexpectedly, allylic substitutions of pentafluorobenzoates of the type **166** can also be carried out efficiently with various functionalized zinc cuprates.[116,116a]

Further unusual allylic electrophiles that have been utilized recently in *anti*-stereoselective copper-mediated S_N2'-substitution comprise chiral aziridines,[117,117a–117c] carbonates,[118,118a–118c] and iron complexes.[119] The concept of a reagent-directing group that had already been employed successfully for diastereoselective conjugate cuprate additions (Scheme 27) was recently extended by Breit *et al.*[120,120a–120e] to allylic substitution reactions. By using an achiral *ortho*-diphenylphosphinobenzoate (e.g., substrate, **168**) or a planar chiral *ortho*-diphenylphosphinoferrocene carboxylate as the reagent-directing leaving group, highly *syn*-selective allylic substitution reactions with magnesium cuprates were achieved (Equation (5)). These transformations also proceed smoothly with catalytic amounts of copper salts, as do reagent-controlled enantioselective S_N2'-substitutions of prochiral allylic electrophiles (see Section 9.12.2.2.2).



(5)

Few investigations have been reported so far on copper-mediated substitution reactions of extended allylic electrophiles. In the case of dienyl electrophiles, three possible regioisomers (i.e., α-, γ-, and ε-alkylated product) can be formed, and the regioselectivity can be controlled by the choice of the organocopper nucleophile.[12,64] Substitution reactions of chiral dienyl electrophiles can also be carried out diastereo- and enantioselectively. For example, S_N2'-substitutions of dienyl carbonates were reported to proceed with high *anti*-selectivity.[121] An interesting diverging behavior was observed in the reaction of the chiral dienyl acetal **170** with the Yamamoto reagent $PhCu{\cdot}BF_3$ which leads to a 1 : 3 mixture of the substitution products **171** and **172** (Equation (6)); whereas the former is the result of an *anti*-S_N2'-substitution, the S_N2''-(1,5)-substitution which leads to **172** takes place with *syn*-stereoselectivity.[122] A mechanistic rationalization of this surprising result has not yet been put forward.

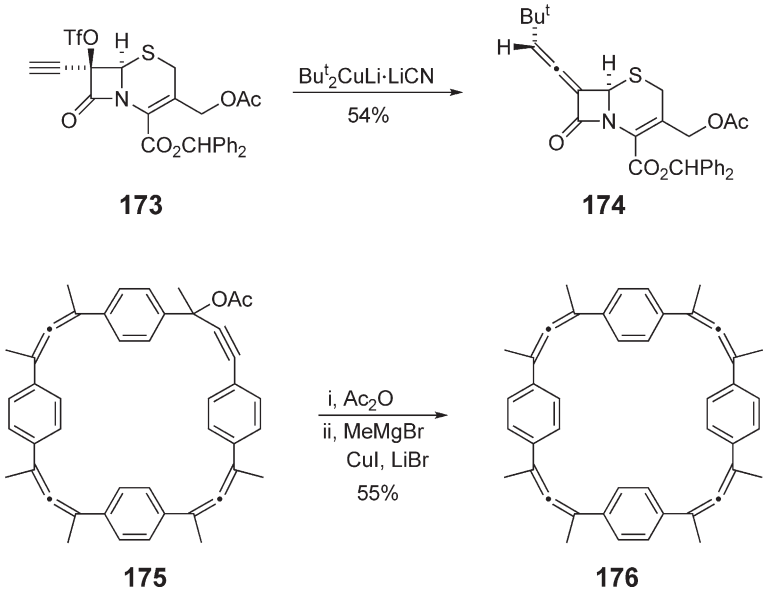


170 **171** **172** (6)

9.12.2.1.2.(ii) Propargylic substrates

The copper-mediated S_N2'-substitution of propargylic electrophiles is one of the most powerful methods for the synthesis of allenes.[65,123] One reason for its popularity is that many combinations of organocopper reagents and leaving groups result in clean conversions of the propargylic electrophiles into the desired allenes, which are often isolated in high chemical yield. Thus, besides acetates, benzoates and carbonates,[65,124] propargylic sulfonates,[125,125a,125b] ethers and acetals, halides,[126] oxiranes,[74,127,128] and even aziridines[127,129,129a] have been successfully employed as the substrates. With regard to the copper reagents, simple lithium diorganocuprates have been complemented by magnesium cuprates of different compositions,[130] as well as by functionalized cuprates derived from the corresponding Grignard or organozinc reagents.[45,45a–45c,131,131a–131f]

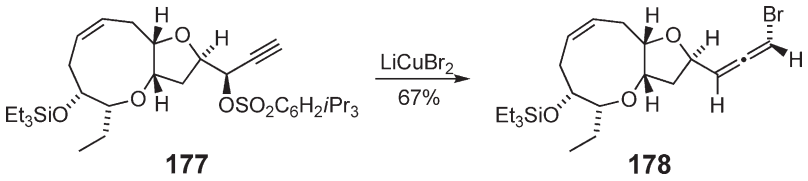
Several applications of the method in the synthesis of allenic natural products and pharmacologically active compounds have been documented.[132,132a,132b] For example, the 7-alkylidenecephalosporin **174** was efficiently formed by *anti*-S_N2'-substitution reaction of the corresponding propargylic triflate **173** with lithium di-*t*-butylcyanocuprate (Scheme 43).[133,133a] In the area of allenic non-natural product chemistry, the synthesis of the [3$_4$]allenophane **176** is particularly noteworthy, with all its four allenic bridges being formed through subsequent S_N2'-substitution reactions of propargylic acetates with a methylmagnesium cuprate.[134,134a]



173 **174** **175** **176**

Scheme 43

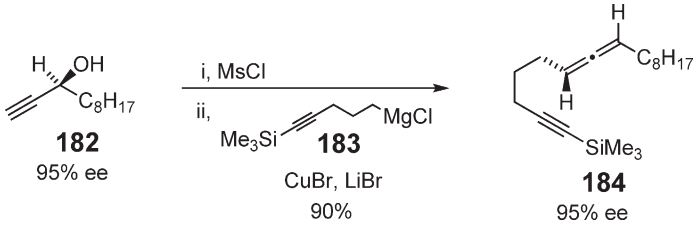
The copper-mediated S_N2'-substitution of propargylic electrophiles is not restricted to carbon–carbon bond formation, as can be seen from the synthesis of silylallenes,[135,135a–135d] stannylallenes, and bromoallenes[136,136a–136g] using propargylic electrophiles and the corresponding heterocuprates. The resulting allenes are often used as intermediates in target-oriented synthesis, for example, in cyclization and reduction reactions.[135,135a–135d,136,136a–136g] In particular, the S_N2'-substitution of propargylic acetates with $LiCuBr_2$ has proved to be valuable for the synthesis of naturally occurring bromoallenes.[132,132a,132b] In one example, treatment of the chiral propargyl sulfonate **177** with lithium dibromocuprate afforded the bicyclic bromoallene **178**, a precursor of the natural product isolaurallene (Equation (7)),[137,137a] and an analogous protocol was recently used in a synthesis of laurallene.[138]



177 **178** (7)

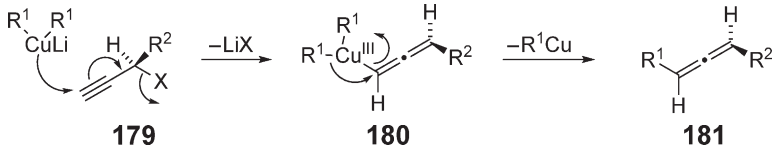
Many of these applications take advantage of the fact that the copper-promoted S_N2'-substitution of propargylic electrophiles (in particular sulfonates) often proceeds with high *anti*-stereoselectivity (see Scheme 43, Equation (7)).[123,139,139a] This efficient center-to-axis chirality transfer is rationalized by an interaction of a copper-centered *d*-orbital with the σ and π^* orbitals of the substrate **179**. This leads to the formation of a σ-copper(III) species **180**, which finally undergoes a reductive elimination of an alkylcopper compound to furnish the *anti*-substitution product **181** (Scheme 44). Unfortunately, theoretical calculations, which have been highly useful for the mechanistic understanding of other copper-mediated transformations,[16,16a,140] have not yet been carried out for the S_N2'-substitution of propargylic electrophiles.

Due to its reliability, the S_N2'-substitution is often used in applications which require the highly enantioselective formation of the allene. For instance, Brummond *et al.*[139a] have prepared the yneallene **184** (a starting material for intramolecular allenic Pauson–Khand cycloadditions) through the *anti*-selective S_N2'-substitution of the chiral propargylic mesylate obtained from alcohol **182** with a suitable magnesium cuprate prepared from the Grignard reagent **183** (Equation (8)).



182 95% ee **183** **184** 95% ee (8)

For several reasons, propargyl oxiranes belong to the most interesting propargylic electrophiles among the many different kinds which can be employed in these transformations. Thus, the α-hydroxyallenes formed in the S_N2'-substitution reaction contain not only one, but two functionalities which are highly useful for further synthetic manipulations and, due to the availability of enantiomerically pure or enriched oxiranes[141] by Katsuki–Sharpless,[142] Jacobsen,[143] or Shi epoxidation,[144] the corresponding α-hydroxyallenes can also be obtained easily in a stereochemically defined form. Furthermore, a particularly deep insight into the details of the reaction mechanism has been gained for this class of compounds.[74,127] For example, deviations from the preferred *anti*-selectivity can occur with certain substrates and organocopper reagents, which are probably due to a racemization of the allene entity by the cuprate itself or by other reactive copper species present in the reaction mixture.[74,145,145a] Such racemizations of



179 **180** **181**

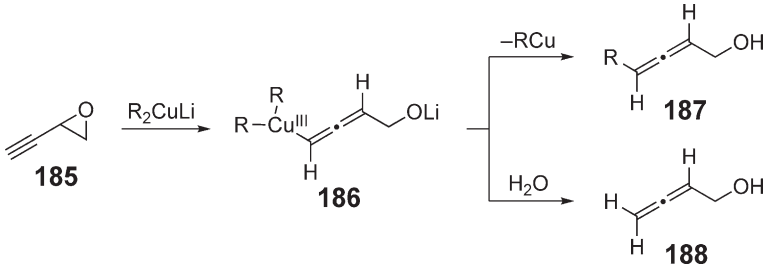
Scheme 44

allenes have frequently been observed in copper-promoted substitution reactions of propargylic electrophiles and probably occur via SET steps, even at rather low temperatures. The racemization can be suppressed by addition of sulfides, phosphines, or phosphites, probably by formation of stabilized copper species which are less prone to undergo electron transfer processes.[74,145,145a]

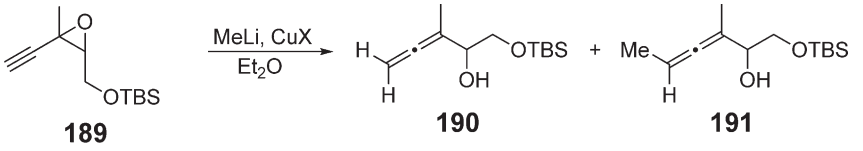
These additives also serve to suppress the formation of a common side-product, that is, an allene containing a hydrogen atom instead of the carbon substituent which should have been delivered by the cuprate. The occurrence of such reduction products is also in accordance with the generally accepted mechanistic model (Scheme 44), in which the copper(III) intermediate **186** resulting from the epoxide **185** may be sufficiently stable to "survive" until work-up of the reaction mixture (or undergo reductive elimination of R–R to give an allenic copper(I) compound), so that protonation leads to the reduction product **188**, besides the desired substitution product **187** (Scheme 45).[65,74]

The beneficial effect of added phosphine on the chemo- and stereoselectivity of the S_N2'-substitution of propargyl oxiranes is demonstrated in the reaction of the substrate **189** with lithium dimethylcyanocuprate in diethyl ether (Scheme 46). In the absence of the phosphine ligand, reduction of the substrate prevailed, and attempts to shift the product ratio in favor of **191** by the addition of methyl iodide (which should alkylate the presumable intermediate **186**) had almost no effect. In contrast to this observation, the desired substitution product **191** was formed with good chemo- and *anti*-stereoselectivity when tri-*n*-butylphosphine was present in the reaction mixture.[74] Interestingly, this effect is strongly solvent dependent, since a complex product mixture was formed when THF was used instead of diethyl ether. With sulfur-containing copper sources such as the copper bromide–dimethyl sulfide complex or copper 2-thiophenecarboxylate, however, the addition of the phosphine caused the opposite effect, that is, exclusive formation of the reduced allene **190**. Thus, the course and outcome of the S_N2'-substitution show a rather complex dependence on the reaction partners and conditions which needs to be further elucidated.

Whereas the S_N2'-substitution of propargyl epoxides of the type **189** with lithium diorganocuprates proved to be rather capricious, the corresponding transformations with magnesium cuprates proceed in a more predictable manner (the use of Grignard reagents and catalytic amounts of copper salts leads to direct nucleophilic attack at the oxirane ring). Thus, treatment of the epoxide **189** in THF with the cuprates formed from 2 equiv. of a Grignard reagent and 1 equiv. of CuCN in the presence of 1 equiv. of tri-*n*-butylphosphine or triethylphosphite consistently led to the exclusive formation of the desired S_N2'-substitution products **192** with good chemical yields and high *anti*-diastereoselectivity (Scheme 47).[74] Most

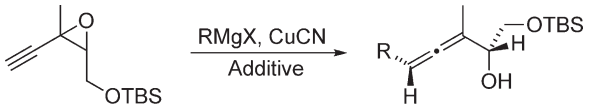


Scheme 45



CuX	**190 : 191**
CuCN	80 : 20
CuCN/Bu^n_3P	4 : 96
CuBr·SMe_2	68 : 32
CuBr·SMe_2/Bu^n_3P	>99 : 1

Scheme 46



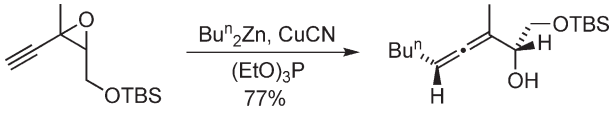
189 **192**

RMgX	*Additive*	*Yield*(%)	ds
MeMgBr	$Bu^n{}_3P$	71	94 : 6
$C_6H_{13}MgBr$	$(EtO)_3P$	95	>95 : 5
Pr^iMgCl	$(EtO)_3P$	76	>95 : 5
Bu^tMgCl	$(EtO)_3P$	82	>95 : 5
PhMgBr	$Bu^n{}_3P$	84	95 : 5
2-FC_6H_4MgCl	$Bu^n{}_3P$	99	85 : 15
4-$MeO_2CC_6H_4MgCl$	$Bu^n{}_3P$	85	85 : 15

Scheme 47

gratifyingly, these conditions are also applicable to Knochel's functionalized Grignard reagents,[26,26a–26d] as demonstrated by the formation of the aromaric α-hydroxyallenes bearing an ester, nitrile, or fluoro substituent.[65]

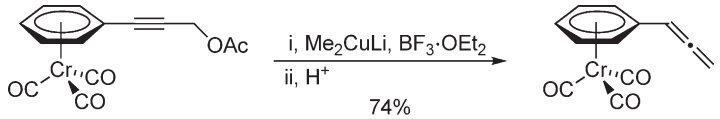
The related zinc cuprates formed from diorganozinc reagents and copper(I) cyanide also undergo smooth S_N2'-substitution reactions with propargylic oxiranes in the presence of phosphines or phosphites (Equation (9)).[65] These transformations can also be performed with catalytic amounts of the copper salt, since no direct reaction between the organozinc reagent and the substrate interferes, and should therefore be applicable to functionalized organozinc compounds as well.



189 **193**

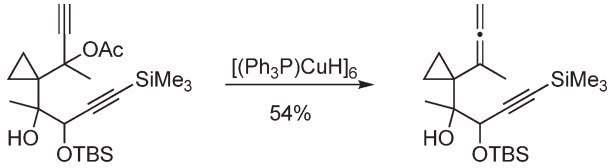
ds >95 : 5 (9)

The occurrence of reduction products in S_N2'-substitution reactions of propargylic electrophiles with organocuprates is not limited to oxiranes and can even be controlled in such a way that the reduced allenes are formed (almost) exclusively (see Scheme 46). The method has also been used in target-oriented synthesis, for instance, in the preparation of allenic prostaglandin analogs.[132,132a,132b] A recent example is the transformation of the chromotricarbonyl-complexed propargyl acetate **194** into the corresponding allene **195** (Equation (10)).[146] Here, the addition of boron trifluoride etherate improved the yield of **195** from 37% to 74%.

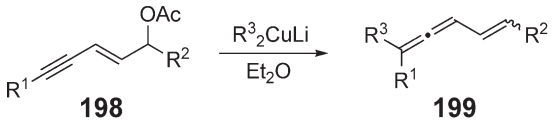


194 **195** (10)

Another, albeit less-frequently employed option for a copper-mediated reduction of propargylic electrophiles to allenes relies upon the use of a copper hydride, for example, Stryker's reagent $[(Ph_3P)CuH]_6$. This reagent was applied by Brummond and Lu[147] to the synthesis of the structurally complex precursor **197** for a potent antitumor agent, (±)-hydroxymethylacylfulvalene, from propargyl acetate **196** (Equation (11)).



196 **197** (11)

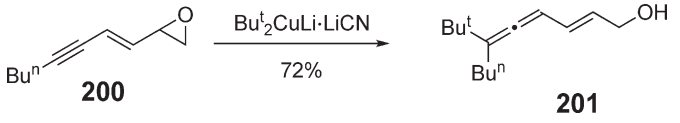


R^1	R^2	R^3	*Yield*(%)	*E* : *Z*
Me	Me	Bu^n	90	67 : 33
Me	Me	Bu^t	93	25 : 75
Me_3Si	Me	Bu^t	96	40 : 60
Bu^n	Bu^t	Me	92	>99 : 1

Scheme 48

The introduction of a double bond between the triple bond and the leaving group of a propargyl electrophile leads to enyne electrophiles (e.g., **198**) which would give access to vinylallenes **199** if the attack of the nucleophile takes place at the triple bond in an S_N2'' (1,5)-substitution reaction (Scheme 48). Besides the regioselectivity, two types of stereoselectivity have to be considered in this transformation, that is, the configuration of the olefinic double bond of the vinylallene and the (relative or absolute) configuration of the allenic chirality axis. In the event, the reaction of enyne acetates **198** with various lithium cuprates proceeds smoothly and regioselectively in diethyl ether, affording exclusively vinylallenes **199** with variable substituent patterns.[148]

Although the resulting vinylallenes **199** were usually obtained as mixtures of the (*E*)-and (*Z*)-isomers, complete stereoselection with regard to the vinylic double bond was achieved in some cases. Besides enyne acetates, the corresponding oxiranes (e.g., **200**) also participate in the 1,5-substitution (Equation (12)) and are transformed into synthetically interesting hydroxy-substituted vinylallenes (e.g., **201**).[148] Moreover, these transformations can also be conducted under copper catalysis by simultaneous addition of the organolithium compound and the substrate to catalytic amounts of the cuprate.

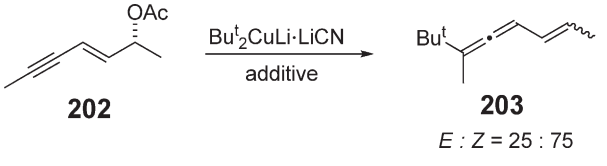


(12)

Initial attempts to perform the 1,5-substitution enantioselectively with chiral enyne acetates proceeded disappointingly. For example, treatment of the enantiomerically pure substrate **202** with the cyano-Gilman cuprate $Bu^t_2CuLi{\cdot}LiCN$ at −90 °C provided the vinylallene **203** as a 1 : 3 mixture of *E*/*Z* isomers with 20% and 74% ee, respectively (Scheme 49).[145,145a] As previously described for the corresponding S_N2'-substitution of propargylic electrophiles, this unsatisfactory stereoselection may be attributed to a racemization of the allene by the cuprate or other organometallic species present in the reaction mixture. Fortunately, the use of phosphines or phosphites as additive served, again, to improve the enantioselectivity up to a preparatively useful level (92%/93% ee in the case of **203**).[145,145a] Due to the distance between the stereogenic center and the position of the nucleophilic attack, the enantioselective 1,5-substitution of chiral enyne acetates constitutes one of the rare cases of "remote stereocontrol" in organocopper chemistry. Moreover, the method is not limited to the substrate **202**, but can also be applied to the synthesis of enantiomerically enriched or pure vinylallenes with variable substituent patterns.[145,145a]

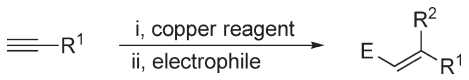
9.12.2.1.3 Carbocupration and related reactions

The carbocupration of alkynes, that is, the addition to a non-activated C–C triple bond, is another classical reaction of organocopper compounds. Due to the high regioselectivity and *cis*-stereoselectivity usually observed in



Additive	ee(%) (*E*)	ee(%) (*Z*)
	20	74
$Bu^n{}_3P$	92	93

Scheme 49

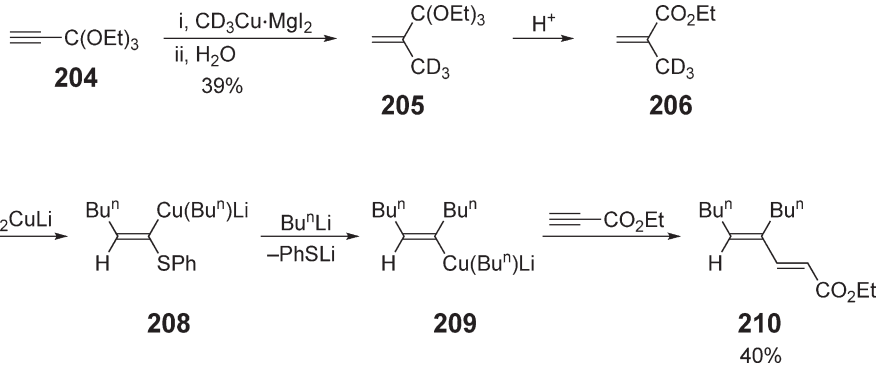


Scheme 50

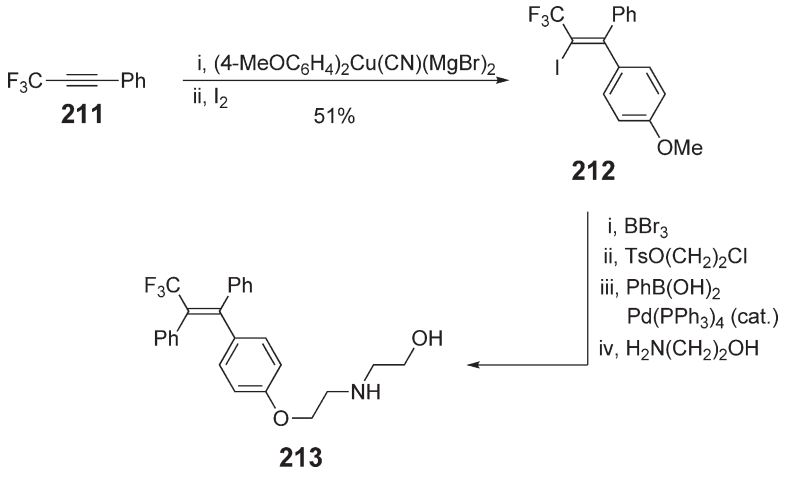
this transformation, the method has been frequently employed in the stereocontrolled synthesis of alkenes and polyenes (Scheme 50).[3,149].

Various functionalized alkynes can be submitted to carbocupration reactions, such as alkoxyalkynes,[150] alkynyl carbamates,[151] acetylenic orthoesters,[152] and thioalkynes.[153] The carbocupration of orthoesters, for example, **204**, has been used to prepare α-substituted esters of the type **206** by acidic hydrolysis of the adduct **205** (Scheme 51).[152] This allows the formation of regioisomers that are not accessible by copper-mediated addition to acetylenic esters. A stereoselective synthesis of trisubstituted alkenes has been described by Normant *et al.*[153] starting from phenylthioacetylene **207**. Carbocupration with lithium di-*n*-butylcuprate affords the intermediate **208** which, upon addition of *n*-butyllithium, undergoes a 1,2-metalate rearrangement to the vinylcuprate **209**. The latter can be trapped with various electrophiles, for example, ethyl propiolate, providing product **210** with complete regio- and stereocontrol.

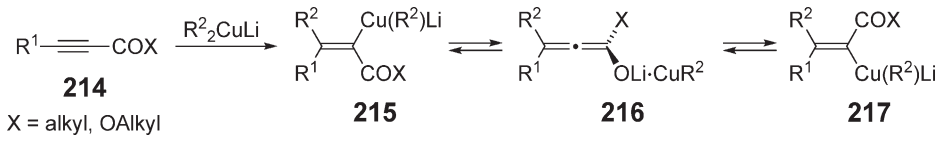
The highly regio- and stereoselective carbocupration of the trifluoromethyl-substituted alkyne **211** was recently used by Konno and co-workers[154] in a short synthesis of the antiestrogenic drug panomifene **213**. The initial product **212** was transformed into the target molecule by Suzuki coupling and elaboration of the side chain (Scheme 52).



Scheme 51



Scheme 52



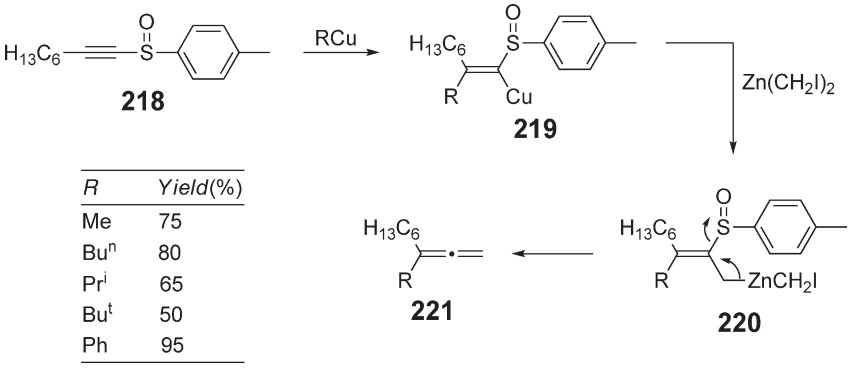
Scheme 53

The reaction of various acceptor-substituted alkynes also proceeds as a carbocupration rather than a conjugate addition.[155,155a,156,156a,156b] Thus, detailed NMR spectroscopic investigations,[156,156a,156b] as well as theoretical calculations,[157,157a] have revealed that the addition of organocuprates to acetylenic ketones and esters **214** gives a π-complex as primary intermediate, which is then converted into the *cis*-alkenylcuprate **215** by regio- and stereoselective carbocupration of the alkyne. Isomerization to the *trans*-alkenylcuprate **217** takes place via the lithium allenolate **216** and can be prevented by removal of the lithium ions or their complexation by solvents like THF (Scheme 53). For some combinations of substrate and cuprate (e.g., lithium dimethylcuprate and acetylenic ketones) the allenolate **216** is the thermodynamically most stable intermediate.[156,156a,156b]

These mechanistic features are of prime importance for the control and understanding of the stereoselectivity of the electrophilic trapping, for example, by protonation.[155,155a,156,156a,156b] It has been known for a long time that the protonation of organocuprate adducts to acetylenic esters prepared in THF results in very high *cis*-selectivities, whereas diethyl ether as the solvent and/or higher temperatures lead to reduced selectivities. In contrast, it is difficult to control the stereoselectivity of protonation of the adducts formed from acetylenic ketones and organocuprates under any reaction conditions. The protonation of the alkenylcuprates **215**/**217** proceeds rapidly and stereoselectively to give the corresponding alkenes, so that the *cis*/*trans* ratio of the isolated products reflects the *cis*/*trans* ratio of the alkenylcopper intermediates. On the contrary, the stereoselectivity of the protonation of the allenolate **216** is difficult to control since it may depend on the acidity of the proton source and can take place via the corresponding allenol. Thus, reaction conditions that favor the formation of alkenylcuprates rather than allenolates are required for optimal stereoselectivities.

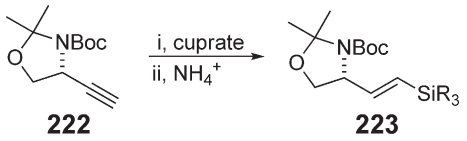
An interesting application of the carbocupration of acetylenic sulfoxides for the synthesis of allenes was recently reported by Marek and co-workers.[158,158a,158b] The alkenylsulfoxides **219** obtained from substrate **218** and various organocopper reagents were submitted to a homologation with the zinc carbenoid $Zn(CH_2I)_2$, followed by a spontaneous β-elimination to afford the allenes **221** in high yield (Scheme 54). Notably, the method can also be applied to functionalized organocopper reagents formed by halogen–magnesium exchange and transmetallation.

Like the carbocupration, the silylcupration and stannylcupration of non-activated C–C double and triple bonds is a well-established synthetic method and has been reviewed extensively.[20,43,51,159] Recent applications of this transformation include the introduction of the sterically hindered reagent $(PhMe_2Si)_2CuLi{\cdot}LiCN$ for the silylcupration of simple alkynes,[160] as well as the use of propargyl amines[161,161a] and of alkynes bearing an additional electrophilic group[162] as the substrate. For example, reaction of the ethynylglycine derivative **222** with various silylcuprates afforded the vinylsilanes **223** with high yield, which could be easily elaborated into unnatural amino acid building



R	*Yield*(%)
Me	75
Bu^n	80
Pr^i	65
Bu^t	50
Ph	95

Scheme 54



222 **223**

Cuprate	*Yield*(%)
$(Me_3Si)_2CuLi{\cdot}LiCN$	79
$PhMe_2Si(Me)CuLi{\cdot}LiCN$	67
$(Ph_2Bu^tSi)_2CuLi{\cdot}LiCN$	80

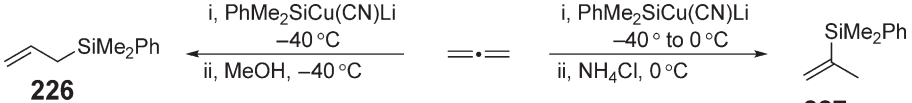
224 **225** (83%)

Scheme 55

blocks for peptide synthesis (Scheme 55).[161,161a] An example for a cyclization induced by silylcupration is the transformation of the acetylenic oxirane **224** into the cyclopentene derivative **225**.[162]

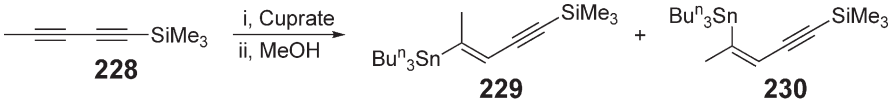
Pulido and co-workers[20,159,163] have used allenes as substrate for various transformations involving silylcupration. The silylcupration of propadiene has turned out to be reversible, so that the regioselectivity is temperature dependent (Scheme 56); whereas treatment with the lower-order cyanocuprate $PhMe_2SiCu(CN)Li$ at −40 °C and protonation with methanol at this temperature delivers the allylsilane **226** as the kinetic product, the thermodynamically more stable vinylsilane **227** is obtained after warming of the reaction mixture to 0 °C (or by using the more reactive cyano-Gilman reagent $(PhMe_2Si)_2CuLi{\cdot}LiCN$).[20,159] The organocopper intermediates have been trapped with numerous electrophiles besides protons, allowing an access to cyclopentanes,[163] 1,4-dienes,[164] and other complex target molecules. The analogous silylcupration reactions of styrenes[165] and conjugated dienes[166] have recently been reported by Liepins and Bäckvall.

The stannylcupration of alkynes occurs in a similar fashion as the silylcupration.[43,51,159] Recent investigations on regio- and stereoselective stannylcuprations were carried out with propargylic alcohols and enynes,[167,167a–167d] propargylic amines,[168,168a] and acetylenic ketones[169] as the substrate. Due to its reliability, the method has been routinely applied in the synthesis of polyene target molecules (e.g., retinoids[170,170a,170b] and other pharmacologically active compounds).[171,171a,172] In their landmark synthesis of the immunosuppressant (−)-rapamycin, Smith III and co-workers[173] utilized the highly regio- and stereoselective stannylcupration of the conjugated diyne **228** for the formation of either the (*E*)-enyne **229** or its (*Z*)-stereoisomer **230**, both of which were key precursors for the triene subunit of the target molecule (Scheme 57).



226 **227**

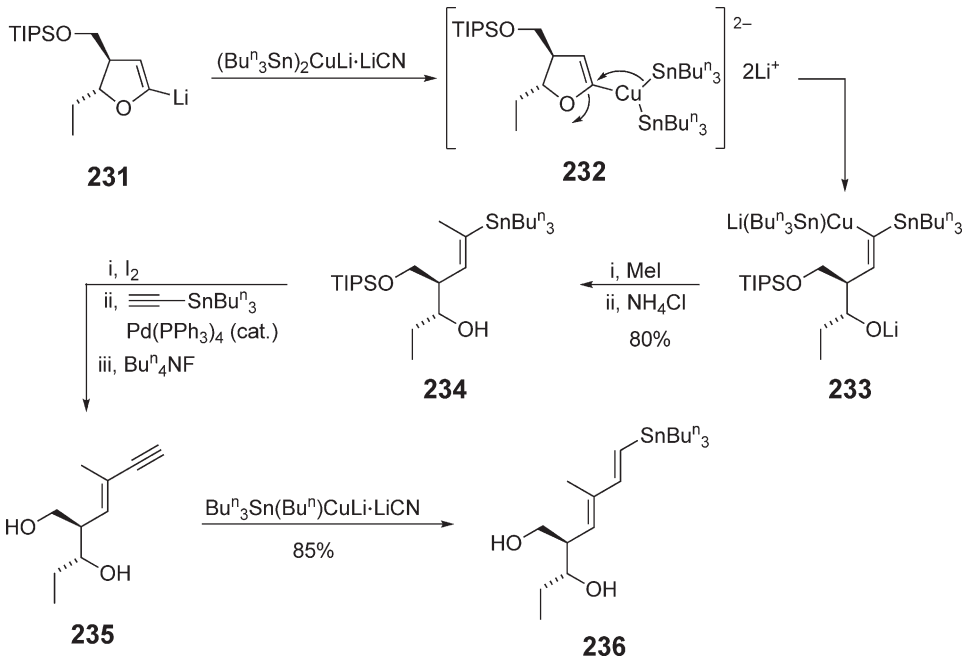
Scheme 56



228 **229** **230**

Cuprate	*Temperature*	**229 : 230**	*Yield*(%)
$Bu^n_3Sn(Bu^n)CuLi{\cdot}LiCN$	−78 °C	94 : 6	79
$Bu^n_3Sn(Me)CuLi{\cdot}LiCN$	−78 ° to −20 °C	4 : 96	99

Scheme 57



Scheme 58

The stannylcupration in connection with a 1,2-metalate rearrangement[174] has been applied several times in natural product synthesis.[175,175a,175b,176] In their synthesis of a building block for the aglycon of tylosin, Ardisson *et al.*[175,175a,175b] treated the lithiated dihydrofuran **231** with the stannylcuprate (Bu$^n_3$Sn)$_2$CuLi·LiCN and obtained the vinylstannane **234** with high yield, probably via the higher-order cuprate **232** and a stereoselective 1,2-metalate rearrangement of the latter to intermediate **233** which was then trapped with methyl iodide (Scheme 58). The product **234** was transformed into the enyne **235** by iodolysis of the tin–carbon bond, subsequent Stille coupling and deprotection, and the final regio- and stereoselective stannylcupration afforded the target molecule **236** with excellent yield.

The biaryl synthesis by Ullmann coupling, as well as a large number of related coupling reactions, constitutes another type of copper-mediated or -catalyzed reaction used extensively for the formation of carbon–carbon and carbon–heteroatom bonds. These transformations have been reviewed recently[17,177,177a,177b] and will not be discussed in detail here.

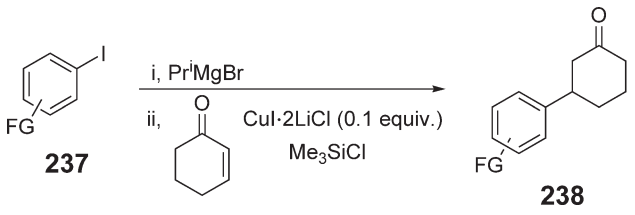
9.12.2.2 Catalytic Applications

Many of the copper-mediated transformations summarized in the previous sections of this chapter can also be performed efficiently with catalytic amounts of copper salts or reagents. Indeed, some of the copper-catalyzed reactions have been discovered before the development of stoichiometric organocopper reagents. The focus of the last decade has been put on new copper-catalyzed transformations (e.g., conjugate reductions) and in particular on the discovery of chiral copper catalysts for highly enantioselective 1,4-addition and S_N2'-substitution reactions of prochiral substrates.

9.12.2.2.1 Conjugate addition reactions

9.12.2.2.1.(i) Copper catalysts

The copper-catalyzed 1,4-addition of Grignard reagents to enones has been described by Kharasch in 1941, that is, one decade before the discovery of Gilman cuprates (1952) and more than two decades before the first use of organocuprates in conjugate addition reactions. Consequently, numerous variations and applications of the method have been reported over the years.[3–5,7,7a,23] Not surprisingly, several of the advances made in the last decade with



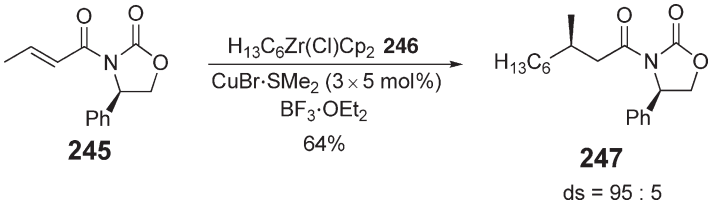
FG	Yield(%)
3-CO_2Et	74
4-CONBn_2	89
4-CN	72

Scheme 59

stoichiometric organocopper reagents have also found application to copper-catalyzed Michael additions. Thus, Knochel and co-workers showed that functionalized arylmagnesium reagents obtained from precursors **237** by iodine–magnesium exchange (see Section 9.12.2.1.1) readily undergo 1,4-addition reactions to enones to afford the products **238** with high yield in the presence of chlorotrimethylsilane and catalytic amounts of copper(I) salts (Scheme 59).[25,178,178a]

The transmetallation of organozirconium compounds to organocopper reagents has also been applied frequently for copper-catalyzed Michael additions.[8] Lipshutz and Wood[8,179] have devised a one-pot three-component coupling sequence involving four different metals for the synthesis of prostaglandins and related products that starts out with the hydrozirconation of a terminal alkyne (e.g., **239**) with Schwartz' reagent (Scheme 60). The alkenylzirconocene **240** is then submitted to a methylation with MeLi and a zirconium–zinc exchange to afford the zincate **241** which undergoes a diastereoselective 1,4-addition to the enone **242** in the presence of 0.2 equiv. of the cyano-Gilman cuprate $Me_2CuLi{\cdot}LiCN$. The copper or lithium enolate thus formed is notoriously unreactive towards electrophiles; however, another transmetallation step with **241** leads to the corresponding zinc enolate that reacts smoothly with aldehyde **243** to provide the prostaglandin E_1 derivative **244** with high yield.

The direct transmetallation of alkenyl,[180] acyl,[181] and alkylzirconocenes[182] to a copper catalyst and subsequent conjugate addition is also possible without a detour via another metal like zinc. For example, Wipf and Takahashi[182] reported the highly diastereoselective 1,4-addition of *in situ*-prepared alkylzirconocenes (e.g., **246**) to chiral N-acyl oxazolidinone **245** and similar substrates in the presence of $BF_3{\cdot}OEt_2$ and catalytic amount of $CuBr{\cdot}SMe_2$, giving adducts of the type **247** with moderate to good yield (Equation (13)).



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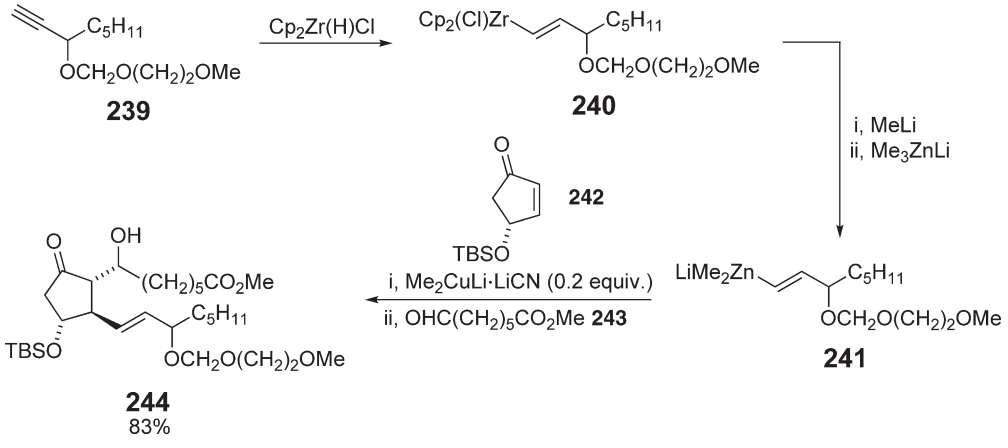
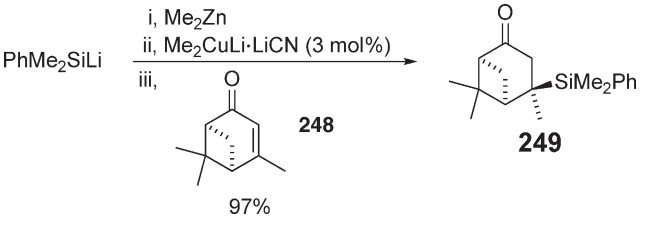


Scheme 60

Several catalytic protocols have been developed for the 1,4-addition of silylcopper reagents to enones and other Michael acceptors. Lipshutz *et al.*[183] treated phenyldimethylsilyllithium with dimethylzinc and used the silylzinc reagent $PhMe_2SiZnMe_2Li$ thus formed as the nucleophile in copper-catalyzed 1,4-additions to various enones and enals, for instance, verbenone **248** which afforded the desired product **249** in almost quantitative yield (Equation (14)). Interestingly, the rather slow addition reaction is strongly accelerated by catalytic amounts of scandium triflate. Recently, the disilylzinc reagent $(PhMe_2Si)_2Zn$ has also been used for copper-catalyzed Michael additions to enones.[184]

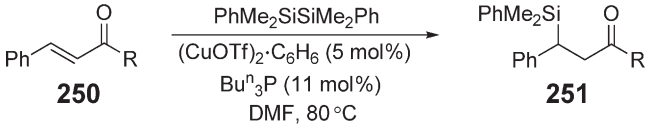


(14)

A different approach that even obviates the use of a preformed silyllithium reagent takes advantage of the cleavage of the Si–Si bond of a disilane by a copper salt. Hosomi and co-workers[185] have reported on the reaction of various enones or enals **250** with hexamethyldisilane or 1,1,2,2-tetramethyl-1,2-diphenyldisilane, catalyzed by copper(I) triflate–benzene complex (Scheme 61). The transformation requires heating to 80–100 °C in DMF or DMI and the presence of tri-*n*-butylphosphine in order to stabilize the copper catalyst under these harsh conditions. The addition products **251** were obtained with high yield after acidic work-up. The application of the method to alkylidene malonates as the Michael acceptor was recently disclosed.[186]

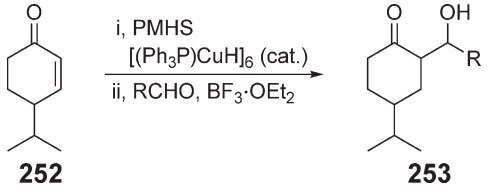
A number of efficient copper catalysts for reductive conjugate addition reaction have been developed in recent years. Stryker's reagent $[(Ph_3P)CuH]_6$ is the most commonly used stoichiometric or catalytic copper reagent for hydride delivery to various electrophiles (see Equation (11)).[187,188] Thus, exposure of enones or enals to tin or silyl hydrides in the presence of catalytic amounts of Stryker's reagent induced a smooth formation of the conjugate reduction products without direct hydride delivery to the carbonyl group.[189] In the presence of Lewis acids, the silyl enol ether initially formed readily undergoes an aldol reaction; for example, treatment of enone **252** with polymethylhydrosiloxane (PMHS), catalytic amounts of $[(Ph_3P)CuH]_6$, and various aldehydes in the presence of $BF_3{\cdot}OEt_2$ gave the three-component coupling products **253** with good yield (Scheme 62).[190,190a] High levels of stereocontrol in the electrophilic trapping reaction can also be achieved by transmetallation of the silyl enol ether to the corresponding boron enolate.[191,191a]

Intramolecular aldol reactions of copper enolates generated by conjugate reduction of enediones allow for the stereoselective construction of complex carbocycles, but require stoichiometric amounts of Stryker's reagent.[192,192a,192b] A catalytic version of this transformation has recently been disclosed by Chiu and Leung[193] who treated alkynediones of the type **254** with PMHS and catalytic amounts of $[(Ph_3P)CuH]_6$ to obtain bicyclic



R	*Yield*(%)
H	79
Me	95
Ph	92

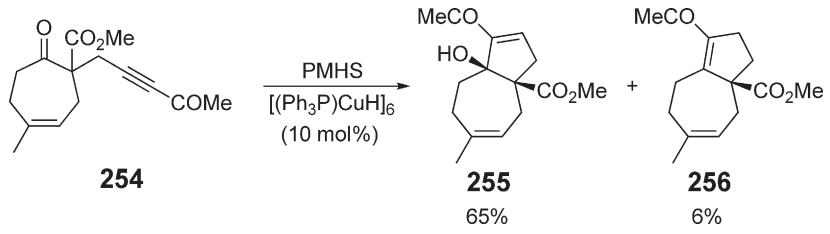
Scheme 61



R	*Yield*(%)
CH_2CHMe_2	89
$CH_2O(CH_2)_2Cl$	87
$CH{=}C(Me)SnBu^n_3$	76

Scheme 62

products (e.g., **255**) with moderate to good yield besides small amounts of over-reduction and dehydration products like **256** (Equation (15)).



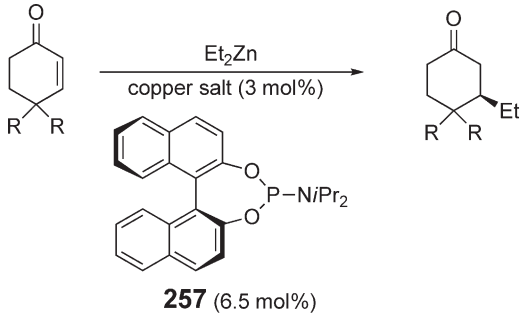
(15)

9.12.2.2.1.(ii) Enantioselectivity

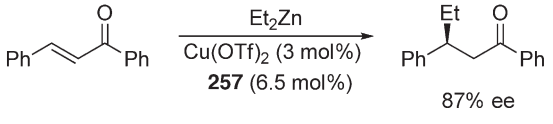
One of the most powerful and frequently used transformations in recent organocopper chemistry is the copper-catalyzed enantioselective Michael addition. Traditional tools for stereocontrolled copper-mediated conjugate addition reactions (which have been the state of the art up to the end of the last century) comprise diastereoselective additions to chiral Michael acceptors bearing removable chiral auxiliaries (see Scheme 28), as well as enantioselective additions of the so-called "chiral cuprates" wherein a chiral, non-transferable heteroatom ligand controls the enantioselectivity of the transfer of an achiral carbon group to a prochiral substrate.[50,50a,50b,80] Although both strategies have proved to be successful in terms of high stereoselectivities, stoichiometric amounts of the copper salt and the chiral ligand or auxiliary are required. Another drawback is a high substrate specificity, that is, a certain chirally modified reagent often gives high stereoselectivities with only one or very few Michael acceptors.

The development of enantioselective copper-catalyzed Michael additions has been hampered for a long time due to the lack of highly reactive catalysts that allow suppression of the uncatalyzed, non-stereoselective background reaction of the nucleophile with the substrate. The breakthrough achieved in the last decade has been made possible mainly by the use of organozinc reagents such as the stoichiometric nucleophile, and the development of chiral binaphthalene-, TADDOL- and oxazoline-derived ligands that allow the copper-catalyzed conjugate addition to take place with strong ligand acceleration. The impact of these developments is evident from the fact that one[17] of the many reviews on the subject[10,10a,194–197,197a,197b] has been the world's most cited chemistry paper in November 2002.

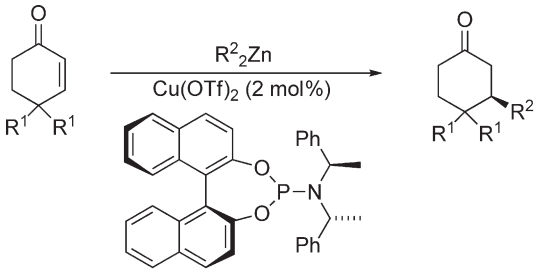
In 1996, Feringa *et al.*[198,198a] reported the use of monodentate phosphoramidites of type **257** in Michael additions of diethylzinc to several enones (Scheme 63). These reactions are catalyzed by copper(I) salts and also by copper(II) triflate; when cyclohex-2-enone was used as substrate, stereoselectivities of 60% ee (with CuOTf) and 63% ee (with $Cu(OTf)_2$) were obtained, whereas a much higher value of 81% ee resulted with 4,4-dimethylcyclohex-2-enone in the



R	*Copper salt*	ee(%)
H	CuOTf	60
H	$Cu(OTf)_2$	63
Me	$Cu(OTf)_2$	81



Scheme 63



R^1	R^2	ee(%)
H	Me	>98
H	Et	>98
H	Pr^i	94
H	Ph	94
Ph	Et	>98

Scheme 64

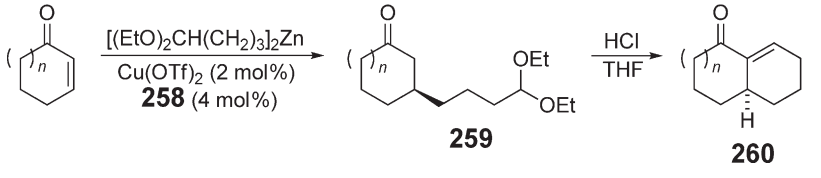
presence of **257** and $Cu(OTf)_2$. Similarly, an enantiomeric excess of 85% ee was realized by Zhang and Chan[199] in the corresponding reaction of cyclohex-2-enone using an analog of **257** with a partly hydrogenated H_8-binaphthalene moiety. Even when $Cu(OTf)_2$ is employed, the actual chiral catalyst is probably a copper(I) species which is formed by *in situ* reduction of the copper(II) complex. Notably, this was also the first catalytic system which gave reasonably high enantioselectivities with acyclic Michael acceptors, for example, 87% ee for the addition product of diethylzinc to chalcone. In all these cases, the regioselectivities (1,4- vs. 1,2-addition) and chemical yields of the adducts were acceptable or good.

By combining the C_2-symmetrical axially chiral binaphthol with the likewise C_2-symmetrical bis(1-phenylethyl)-amine through a phosphorus center, Feringa and co-workers[200,200a] then obtained the phosphoramidite **258** which, to date, represents the most versatile and generally applicable monodentate chiral ligand for enantioselective copper-catalyzed Michael additions of diorganozinc reagents (Scheme 64).[201,201a] Most importantly, the steric properties of the substrate and the reagent are negligible since the transfer of methyl, ethyl, and isopropyl groups to cyclohex-2-enone took place with high enantioselectivities and good chemical yields (72–95%), as did the transfer of an ethyl group to 4,4-diphenylcyclohex-2-enone. Even diphenylzinc can be added with a very high enantioselectivity of 94% ee to cyclohex-2-enone if the reaction is carried out at very low temperature (−60 °C).[201a]

Not surprisingly, the enantiomeric excess of the addition product strongly depends on the configuration of the BINOL and diamine parts of phosphorus amidite **258**. Whereas the (*S*)-addition product of diethylzinc to cyclohex-2-enone was obtained with >98% ee when using (S_a,*R*,*R*)-**258**, the diastereomeric catalyst with (S_a,*S*,*S*) configuration gave rise to the formation of the same enantiomer with only 75% ee.[200,200a] These findings indicate that the BINOL moiety exerts a stronger influence on the enantiodiscrimination than the diamine.

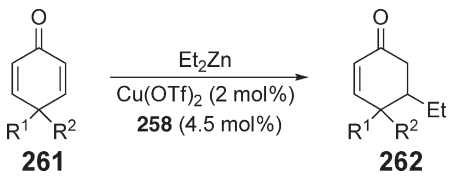
Organozinc compounds are ideal reagents for copper-catalyzed enantioselective Michael additions because of their low reactivity toward the substrate in the absence of a copper catalyst; moreover, they allow the introduction of functional groups into the addition product.[200,200a,202] Thus, the functionalized zinc reagent $[(EtO)_2CH(CH_2)_3]_2Zn$, prepared by hydroboration of the corresponding alkene and subsequent transmetallation, was added smoothly to six- to eight-membered cyclic enones in the presence of $Cu(OTf)_2$ and **258**. Hydrolysis of the acetals **259** followed by spontaneous aldol cyclization finally afforded the annulated products **260** with at least 96% ee (Scheme 65).[202] An alternative approach to chiral bicycles took advantage of ring-closing metathesis for the formation of the second ring.[203] These transformations confirm that this catalytic system can be applied confidently to cyclic enones of different ring size.

Recently, copper-catalyzed enantioselective addition reactions in the presence of phosphorus amidite **258** have also been applied to different Michael acceptors. Thus, both symmetrical and unsymmetrical 4,4-disubstituted cyclohexa-2,5-dienones **261** were found to add diethylzinc with moderate to high enantioselectivities and good



n	ee(%)
1	97
2	96
3	>98

Scheme 65



R^1	R^2	ds	ee(%)
OMe	OMe		97
CH_2CH_2			92
OMe	CH_2Ph	97 : 3	93
$OCH_2(CH_2)_2$		99 : 1	65

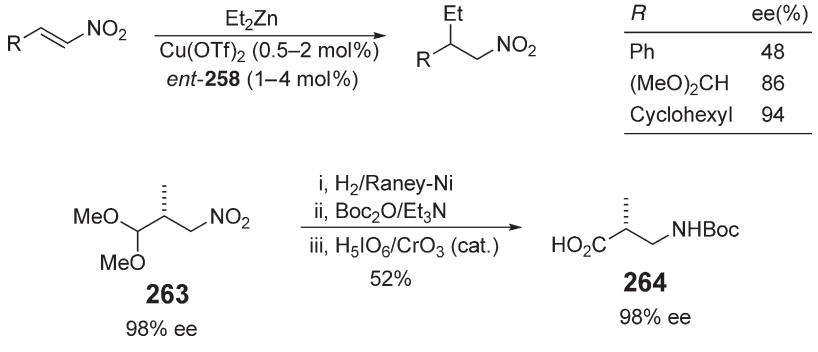
Scheme 66

chemical yields, with the latter affording the products **262** with high diastereoselectivities (Scheme 66).[204] In the case of unsymmetrical substrates, the nucleophilic attack occurred preferably *cis* to the alkoxy moiety, indicating a precoordination of the catalytically active species at this group. Sequential catalytic 1,4-additions to both enone moieties of substrates **261** was used to selectively access tetrasubstituted *cis*- or *trans*-3,4,4,5-cyclohexanones.[205]

Other substrates that have been used successfully in copper-catalyzed conjugate additions of organozinc reagents in the presence of chiral phophoramidites of the type **258** include unsaturated malonates[206] and lactams,[207] as well as nitroolefins.[208] The latter belong to the most reactive Michael acceptors, making it particularly difficult to suppress the uncatalyzed background reaction. On the other hand, the addition products are particularly useful for further transformations. Sewald and Wendisch[209] were the first to report on copper-catalyzed conjugate additions to nitroolefins in the presence of the enantiomer of phosphoramidite **258**, observing an enantiomeric excess of 48% ee in the conjugate addition of diethylzinc to β-nitrostyrene and of 86% ee to the corresponding substrate bearing an acetal functionality (Scheme 67). By using the same ligand, Alexakis and Benhaim[210] realized an enantioselectivity of 94% ee for the cyclohexyl-substituted addition product. Feringa and co-workers employed 3-nitrocoumarins[211] as well as various acyclic nitroolefins[212] as substrates and obtained similar results. An example for a typical subsequent transformation of the addition products is the stereospecific conversion of **263** into the β-amino acid derivative **264** by reduction of the nitro group and hydrolysis/oxidation of the acetal function.[213,213a]

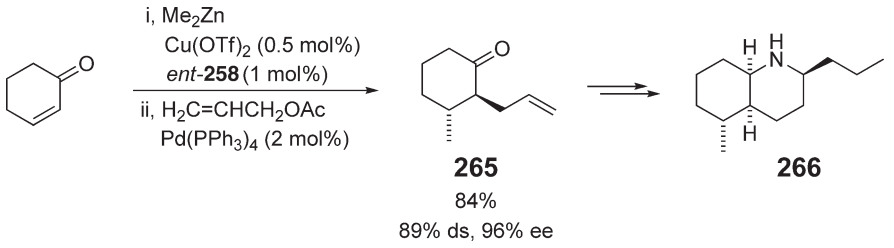
Recent advances in the use of phosphoramidites of the type **258** in copper-catalyzed enantioselective 1,4-additions comprise the development of bidentate ligands with two phosphoramidite units linked with a diamine bridge,[214] as well as the introduction of an insoluble polymer-bound ligand using a Merrifield resin.[215] The method has also been applied in natural product synthesis, that is, for the preparation of (−)-prostaglandin E_1 methyl ester[216,216a] and of (−)-pumiliotoxin C **266**,[217] taking advantage of stereoselective electrophilic trapping reactions of the zinc enolate formed in the conjugate addition.[218,218a] The latter synthesis starts out with the copper-catalyzed enantioselective 1,4-addition of dimethylzinc to cyclohex-2-enone, followed by the palladium-catalyzed allylation of the zinc enolate which afforded the adduct **265** with high diastereo- and enantioselectivity (Scheme 68). Further steps en route to the target molecule include the diastereoselective reduction of the keto group of **265**, introduction of the nitrogen functionality by Mitsunobu reaction, and a tandem Heck-allylic substitution reaction. Thus, three of the four stereogenic centers of the natural product were controlled via the copper-catalyzed enantioselective Michael addition and subsequent diastereoselective steps.[217]

Several other groups developed alternative BINOL-derived phosphoramidite ligands for highly enantioselective copper-catalyzed Michael additions.[219–221,221a–221d] Whereas Waldmann *et al.*[220,220a] included a bicyclic bispidine in



R	ee(%)
Ph	48
$(MeO)_2CH$	86
Cyclohexyl	94

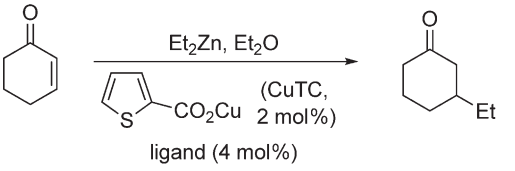
Scheme 67



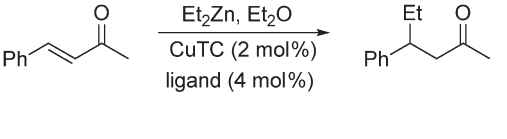
Scheme 68

their ligand system and achieved moderate to good enantioselectivities in copper-catalyzed 1,4-additions, Alexakis and co-workers[221,221a–221d] took advantage of the fact that the binaphthol unit of ligands of the type **258** dictates the absolute configuration of the addition product (see above). Knowing that the atropisomerism of the binaphthol is of prime importance, they developed a series of phosphoramidites (e.g., **267–269**) bearing a flexible biphenol moiety where the chiral amine induces the atropisomerism. Whereas the traditional reaction conditions, that is, use of copper(II)–triflate in an apolar solvent like toluene, afforded the conjugate addition products of dialkylzinc reagents to cyclic enones with high enantioselectivity (e.g., 98% ee for cyclohex-2-enone), only moderate stereoselectivities were attained with acyclic enones and nitroolefins.[221,221a–221d] In contrast to this, replacement of $Cu(OTf)_2$ by much cheaper copper carboxylates allowed the addition to be carried out with high enantioselectivities in coordinating solvents like diethyl ether (Scheme 69).[222] For example, treatment of cyclohex-2-enone with diethylzinc in diethyl ether in the presence of catalytic amounts of copper thiophene-2-carboxylate (CuTC) and ligand **267**, **268**, or **269** furnished the addition product with enantioselectivities of 96–99.1% ee, and up to 91% ee were obtained for the corresponding reaction of benzylidene acetone. Similar stereoselectivities could also be achieved for various nitroolefins.[221–223]

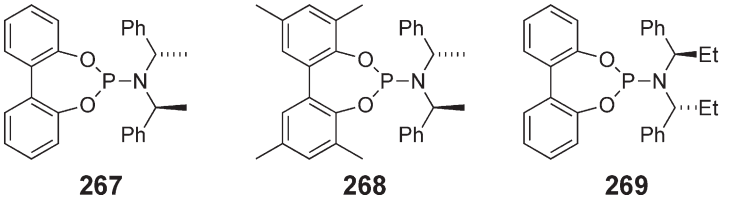
Once again, the zinc enolates generated in the conjugate addition can be trapped with various electrophiles besides protons.[224,225] For example, reaction of the enolate **270** obtained by treating cyclohex-2-enone with dimethylzinc in the presence of $Cu(OTf)_2$ and phosphoramidite **269** with trimethylsilyl triflate and diiodomethane provided the cyclopropanation product **271** with good diastereoselectivity and high enantiomeric excess and chemical yield



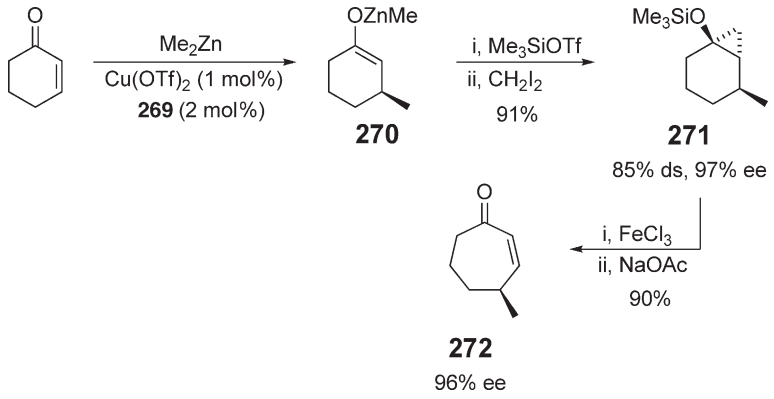
Ligand	ee(%)
267	96
268	99.0
269	99.1



Ligand	ee
267	80
268	91
269	70



Scheme 69

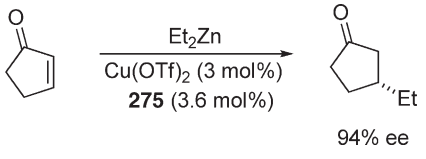


Scheme 70

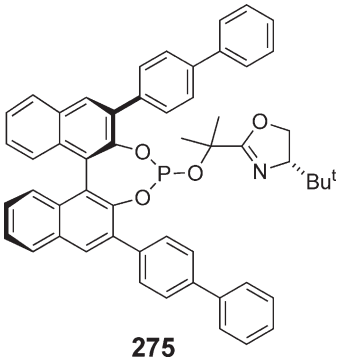
(Scheme 70). Several different ring-opening protocols lead to monocyclic ketones, for instance, the precursor **272** of the sesquiterpenes (−)-clavukerin A and (+)-isoclavukerin.[225]

Many other binaphthalene-derived phosphoramidites were used as chiral ligands in copper-catalyzed Michael additions as well. Whereas 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene (BINAP) gave unsatisfactory stereoselectivities in $Cu(OTf)_2$-catalyzed 1,4-additions of diethylzinc to enones,[226] BINOL oxazoline phosphites obtained by Pfaltz *et al.*[227,227a,227b] turned out to be remarkably versatile and in some cases complementary to phosphoramidite **258** (Scheme 71). Thus, reaction of cyclohex-2-enone with Et_2Zn catalyzed by copper(II) triflate and **273** gave the conjugate addition product with 54% ee. This selectivity was improved dramatically to 90% ee by using the 3,3′-dimethyl-substituted ligand **274**. The corresponding addition of dimethylzinc in the presence of **274** furnished the adduct with 96% ee.

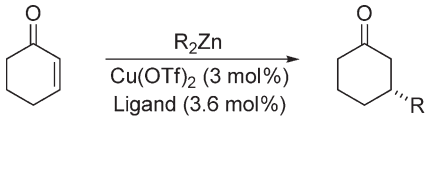
Extensive screening provided efficient ligands of type **273**/**274** for other enones as well.[227b] Even for one of the most challenging Michael acceptors, cyclopent-2-enone, high enantioselectivities were achieved for the first time with oxazoline phosphites. This substrate not only gave notoriously low stereoselectivities with other ligands, for example, phosphoramidites **257** and **258**, but the chemical yields were also low due to extensive addition/condensation reactions of the enolate formed during the 1,4-addition. Indeed, by using the biphenyl-substituted ligand **275**, the adduct of diethylzinc was isolated with an extraordinarily high enantiomeric excess of 94% ee, whereas the chemical yield of 41% still requires improvement (Equation (16)). The side-reactions can be avoided by *in situ* trapping of the enolate with an aldehyde.[214,216,216a] Chiral phosphites **273**–**275** also enabled Michael additions of functionalized organozinc reagents to cyclic enones with moderate to good levels of enantioselection.[227b]



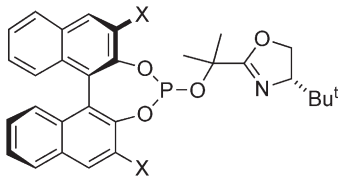
(16)



275



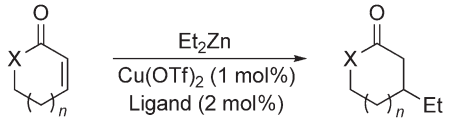
R	*Ligand*	ee(%)
Et	**273**	54
Et	**274**	90
Me	**274**	96



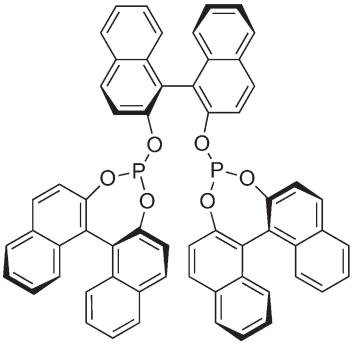
273 (X = H)
274 (X = Me)

Scheme 71

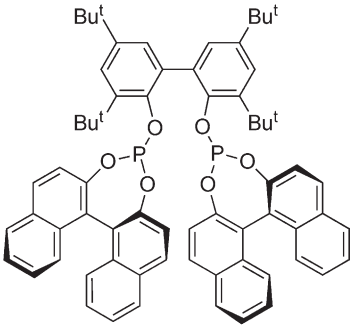
Another efficient class of chiral ligands, aryl diphosphites consisting of two or three BINOL units and two phosphorus bridges, was described by Chan *et al.*[228,228a–228g] Also, these ligands enabled $Cu(OTf)_2$-catalyzed Michael additions of diethylzinc to different cyclic enones with moderate to high enantioselectivities (Scheme 72). Particularly noteworthy is the reaction of cyclopent-2-enone which took place in the presence of **276** with 77% ee and a comparatively high chemical yield of 71%. Interestingly, this product has the opposite absolute configuration than the adduct obtained with 90% ee from cyclohex-2-enone with the same catalyst; this reversal of the enantiofacial selectivity has been observed previously in conjugate additions of the chirally modified cuprates $RCu(L^*)Li$.[50,50a,50b] In contrast to the cyclic enones, the highest selectivity for the corresponding transformation of chalcone was only 16% ee. Again, improved enantiodiscrimination was realized by screening of several ligands of this type.[228,228a–228g] For instance, enantiomeric excesses of 90% and 89% ee were observed for the copper-catalyzed 1,4-addition of diethylzinc to cyclohex-2-enone and cyclopent-2-enone, respectively, when the biphenyl-bridged diphosphite **277** was used. Here, in contrast to ligand **276**, both products have the same absolute configuration. With ligand **277**, Michael additions to unsaturated lactones (e.g., 5,6-dihydropyran-2-one) also proceeded with high enantioselectivity.



X	*n*	*Ligand*	ee(%)
CH_2	1	**276**	90
CH_2	1	**277**	90
CH_2	0	**276**	77
CH_2	0	**277**	89
O	1	**277**	92

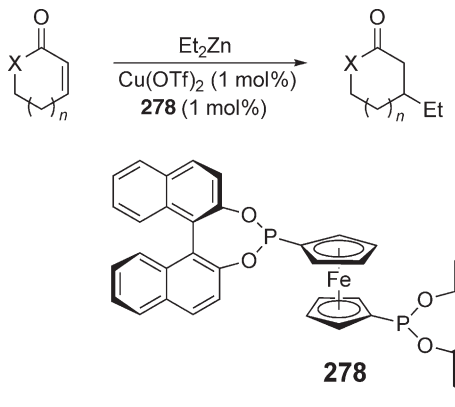


276



277

Scheme 72



X	n	ee(%)
CH_2	1	96
CH_2	2	93
O	1	98

278

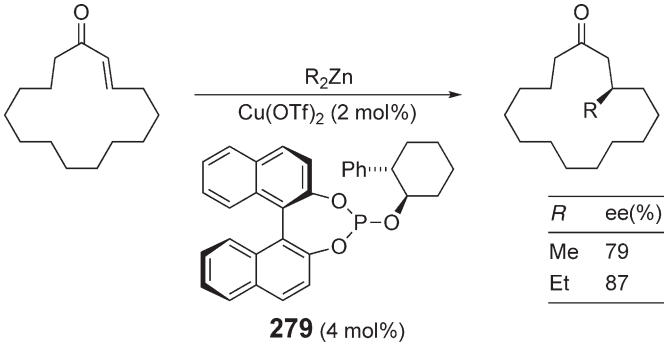
Scheme 73

A similar bidentate ligand containing a ferrocenyl bridge between two BINOL moieties was described by Reetz and co-workers.[229,229a,229b] Copper-catalyzed 1,4-addition reactions of diethylzinc to cyclohex-2-enone and cyclohept-2-enone in the presence of diphosphonate **278** provided the addition products with 96% and 93% ee, respectively (Scheme 73). Notably, an extraordinary high stereoselectivity of 98% ee was achieved with 5,6-dihydropyran-2-one as the substrate. In contrast to this, a somewhat lower value of 77% ee was observed in the corresponding reaction of chalcone. A variety of chiral monodentate BINOL-derived phosphonates was used by Feringa *et al.*[230] in copper-catalyzed conjugate addition reactions.

Alexakis *et al.*[231] reported copper-catalyzed enantioselective Michael additions in the presence of various 2-arylcyclohexyl-substituted phosphites. Ligand **279** turned out to be particularly efficient for the 1,4-addition of organozinc reagents to cyclopentadec-2-enone. Whereas Et_2Zn gave the addition product with 87% ee, the corresponding reaction of dimethylzinc furnished (*R*)-(−)-muscone with an enantiomeric excess of 79% ee (Scheme 74).

In an extensive study of sulfur-containing BINOL derivatives, Woodward *et al.*[232,232a–232d] identified several suitable ligands for copper-catalyzed 1,4-addition reactions of diethylzinc and trimethylaluminum to acyclic enones with up to 79% ee. Another very selective class of ligands, the pyridine-containing binaphthalene derivative **280** and its desmethyl analog, were synthesized by Zhang *et al.*[233,233a–233e] from 2-amino-2′-hydroxybinaphthalene (NOBIN). Both cyclohex-2-enone and acyclic enones like chalcone and benzylideneacetone underwent highly enantioselective copper-catalyzed Michael additions of diethylzinc in the presence of **280**, giving rise to the formation of the addition products with at least 90% ee (Scheme 75). Thus, this catalyst is one of the very few that affords high stereoselectivities for both cyclic and acyclic enones. A similar but less selective quinoline-based ligand system was reported by Faraone and co-workers,[234] whereas Müller *et al.*[235] used a phosphoramidite derived from 1,1′-binaphthalene-8,8′-diol.

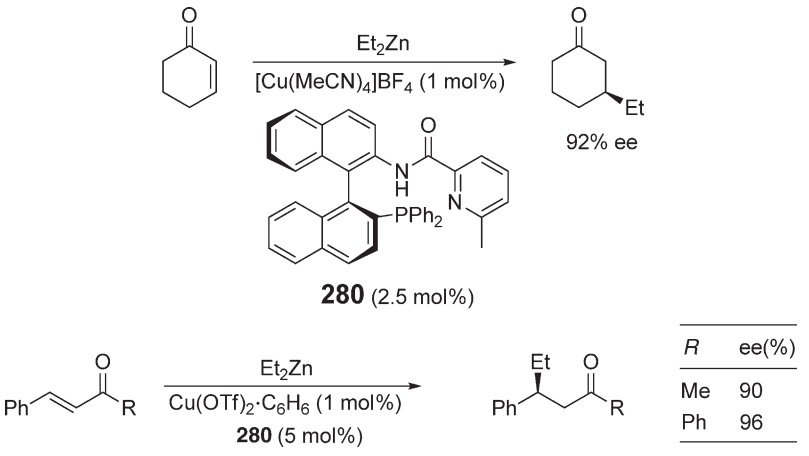
It is evident from the previous examples that most copper catalysts have been applied only to simple, unsubstituted Michael acceptors so far. Only very recently, chiral, substituted cyclohex-2-enones were used as substrates for copper-catalyzed enantioselective 1,4-additions with phosphoramidites as the chiral ligand. Thus, highly enantioselective kinetic resolutions of several 4- or 5-substituted cyclohex-2-enones were reported by Feringa and co-workers.[236,236a] In contrast to these Michael acceptors, the corresponding 6-substituted cyclohex-2-enones possess a stereogenic center which can be



R	ee(%)
Me	79
Et	87

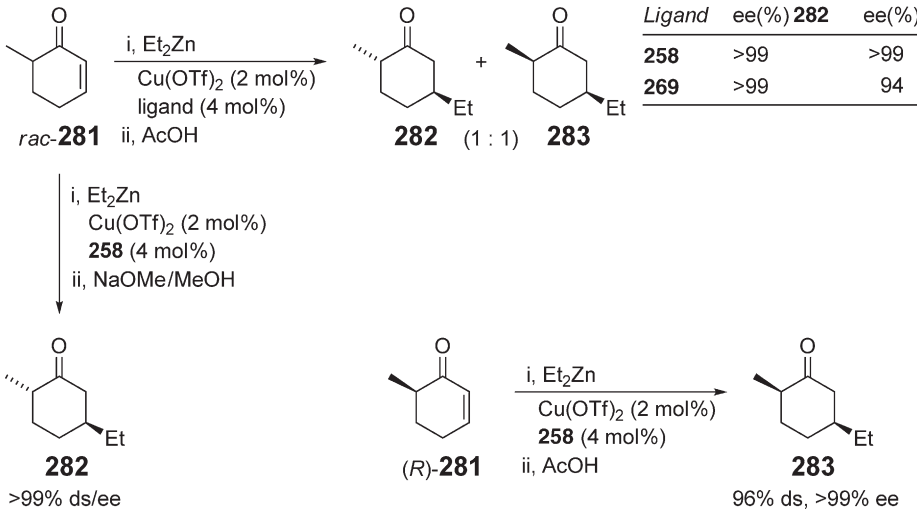
279 (4 mol%)

Scheme 74



R	ee(%)
Me	90
Ph	96

Scheme 75



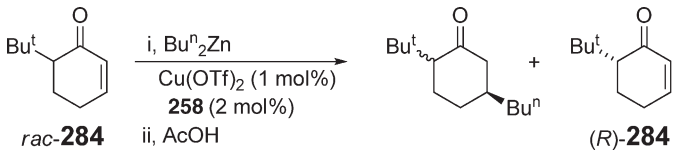
Ligand	ee(%) 282	ee(%) 283
258	>99	>99
269	>99	94

Scheme 76

epimerized by enolate formation. For example, treatment of racemic 6-methylcyclohex-2-enone (*rac*-**281**) with diethylzinc in the presence of catalytic amounts of copper(II)–triflate and phosphoramidite **258** or **269**, followed by protonation of the enolate with acetic acid gave a 1 : 1 mixture of the enantiomerically pure or enriched ketones **282** and **283** (Scheme 76).[237] Thus, a completely reagent-controlled enantioselective Michael addition (without any influence of the stereogenic center of **281**) took place, and an epimerization of the product is avoided under the mild protonation conditions. In contrast to this, strong acidic or basic work-up conditions induce an epimerization to the thermodynamically more stable *trans*-isomer **282**.

Since both enantiomers of the substrate are reacting with virtually the same rate, a kinetic resolution is not possible. Rather, any stereoisomeric adduct can be prepared deliberately by starting either from racemic or enantiomerically pure enone and by conducting the reaction with or without epimerization at C6. For example, treatment of *rac*-**281** under the previous conditions, but with basic epimerization in the presence of sodium methanolate furnished the diastereo- and enantiomerically pure *trans*-disubstituted ketone **282**, whereas the same sequence with enantiomerically pure enone (*R*)-**281** as the substrate, but without epimerization, afforded the *cis*-disubstituted ketone **283**. The enantiomers of **282** and **283** are available by using the enantiomeric ligand with *rac*-**281** or (*S*)-**281** as the substrate under the appropriate reaction conditions.[237]

In contrast to enone **281**, the enantiomers of the corresponding *t*-butyl-substituted Michael acceptor **284** show different rates and enantioselectivities in their reaction with organozinc reagents and chiral copper catalysts. In all



Conversion (%)	ee(%)	**284**
45	84	
78	>99	

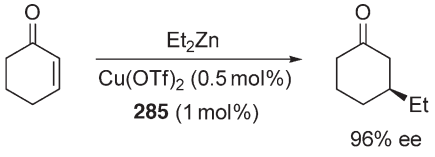
Scheme 77

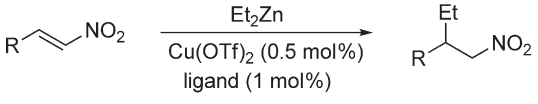
cases examined, the (*S*)-enantiomer is more reactive, so that enantiomerically enriched (*R*)-**284** can be obtained by kinetic resolution. For example, treatment of the racemic enone with di-*n*-butylzinc and catalytic amounts of $Cu(OTf)_2$, and ligand **258** led to a recovery of unreacted (*R*)-**284** with 84% ee at 45% conversion, and with >99% ee at 78% conversion (Scheme 77).[237]

$\alpha,\alpha,\alpha',\alpha'$-Tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs) represent another type of chiral building blocks for ligands that have been used successfully in copper-catalyzed conjugate addition reactions. The first examples were reported by Seebach and co-workers,[238,238a,238b] who observed stereoselectivities of up to 82% ee in the reaction of cyclic enones with Bu^{n}MgCl. In extensive investigations of several TADDOL-derived phosphorus ligands, Alexakis *et al.*[239,239a] identified phosphite **285** as particularly selective in the copper-catalyzed 1,4-addition of diethylzinc to cyclohex-2-enone, giving the adduct with 96% ee (Scheme 78). The diastereomeric ligand gave only the racemic addition product. Unfortunately, ligands of this type display only low enantioselectivities in the corresponding addition reactions to acyclic enones.[231]

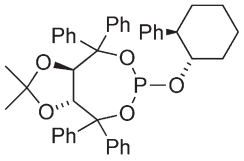
The corresponding TADDOL-derived phosphoramidites and phosphonates (e.g., **286**) afford inferior stereoselectivities in copper-catalyzed Michael additions to enones.[239,239a,240] So far, it has also been difficult to attain high stereoselectivities with alkylidene malonates as the substrate.[241] In contrast to this, highly enantioselective Michael additions to nitroolefins can be achieved with TADDOL-phosphonate **286**.[210] For instance, copper-catalyzed 1,4-addition of diethylzinc to aromatic nitroalkenes furnished the adducts with 81% and 86% ee, respectively (Scheme 78). In these cases, phosphite **285** gave the enantiomeric products with somewhat lower selectivities (64/56% ee). In contrast to these TADDOL ligands, phosphites containing an unmodified diethyltartrate moiety are not suitable for efficient enantioselective copper-catalyzed Michael additions.[30,30a]

Chiral oxazolines represent the third important chiral building block for chiral ligands used in enantioselective copper-catalyzed conjugate addition reactions. Early examples include the BINOL oxazolines **273**/**274**[227,227a,227b] (see Scheme 71), as well as an oxazoline-substituted copper thiophenolate which gave enantiomeric excesses of up to 87% ee in 1,4-addition reactions of Grignard reagents to cyclic enones.[243,243a] On the contrary, simple aryl-substituted oxazolines afforded inferior stereoselectivities (up to 68% ee) in addition reactions of trimethylaluminum with cyclohexa-2,5-dienones.[244,244a,244b] Stangeland and Sammakia[245,245a] obtained much better results by





R	*Ligand*	ee(%)
Ph	**285**	64
Ph	**286**	81
4-MeC$_6$H$_4$	**285**	56
4-MeC$_6$H$_4$	**286**	86



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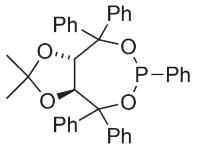
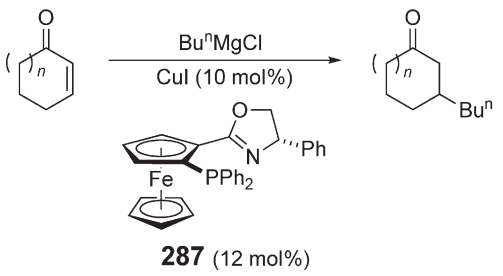


286

Scheme 78



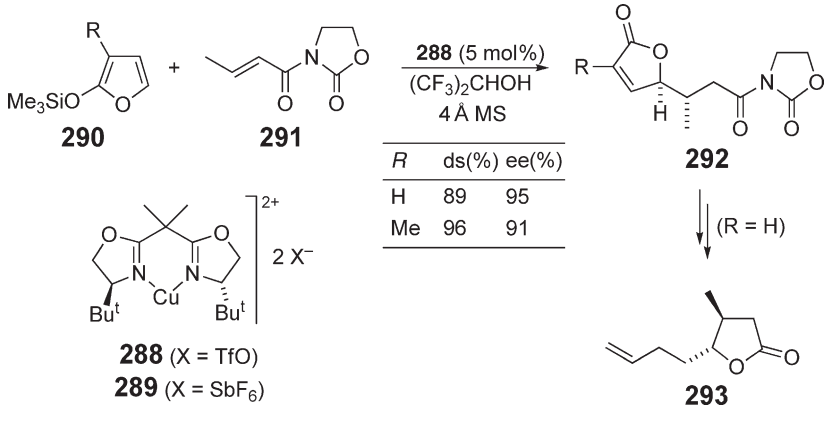
n	ee(%)
0	65
1	83
2	92

Scheme 79

employing the chiral ferrocenyl oxazoline phosphine **287** and the corresponding valine-derived isopropyl-substituted ligand in CuI-catalyzed Michael additions of Bu^{n}MgCl to various enones (Scheme 79). As has already been observed frequently with other ligands, the enantioselectivity rose with increasing ring size, and the adduct formed from cyclopent-2-enone has the opposite absolute configuration than the products obtained from the larger cycloenones with the same catalyst (cf. **276**, Scheme 72). Interestingly, ligand **287** is one of the few which gives similar stereoselectivities for cyclic and acyclic enones, as is exemplified by the formation of the addition product of Bu^{n}MgCl to benzylidene acetone (81% ee).

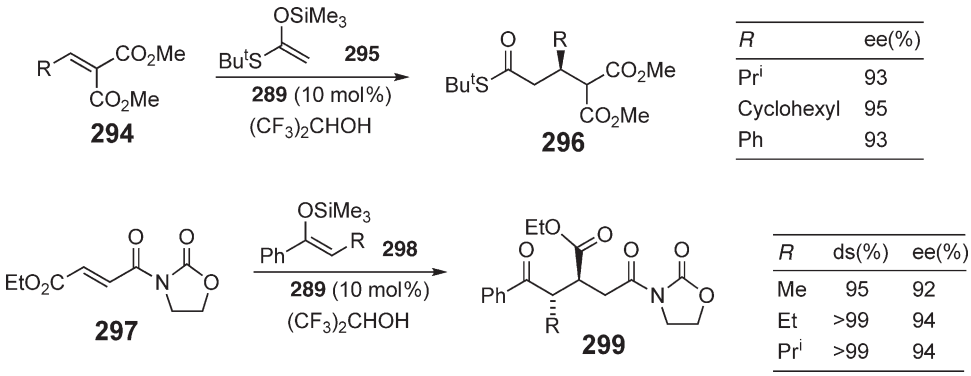
The bisoxazoline copper(II) complex **288** and the corresponding hexafluoroantimonate **289** are highly versatile catalysts for enantioselective Michael additions. These chiral Lewis acids have been introduced by Evans *et al.*[246,246a] for Diels–Alder reactions and various other transformations; the first use of complexes of this type for enantioselective conjugate additions, however, was reported by Scolastico *et al.*,[247] who observed enantiomeric excesses of up to 66% ee in Mukaiyama–Michael additions of silyl ketene acetals to 2-methoxycarbonylcyclopent-2-enone. Preparative useful levels of stereodiscrimination were later achieved by Katsuki *et al.*[248] in addition reactions of trimethylsilyloxyfurans **290** to unsaturated oxazolidinone **291** catalyzed by **288** (Scheme 80). In the presence of molecular sieves and hexafluoroisopropanol (which prevents undesired Dieckmann condensations of zwitterionic intermediates), products **292** were obtained with high enantiomeric excesses and *anti*-diastereoselectivities. The adduct **292** (R = H) was converted into the diastereo- and enantiomerically pure *trans*-whiskey lactone **293**.[249]

The chiral Lewis acids **288**/**289** were also employed extensively by Evans and co-workers[246,246a,250a–250d] in enantioselective Michael additions to alkylidene malonates and fumaroyl oxazolidinones. Thus, treatment of alkylidene malonates **294** with silyl ketene acetal **295** in the presence of **289** gave the desired adducts **296** with at least 93% ee and high chemical yields (Scheme 81). Again, hexafluoroisopropanol served to prevent undesired Dieckmann condensations. Likewise, the corresponding additions of silyl enol ethers **298** to fumaroyl oxazolidinone **297** furnished products **299** with high degrees of diastereo- and enantioselection. In a similar fashion, Jørgensen *et al.*[251] realized enantioselectivities of up to 92% ee in 1,4-addition reactions of 4-hydroxycoumarins to 2-oxo-3-butenoates, catalyzed by bisoxazoline copper(II) complex **288**.

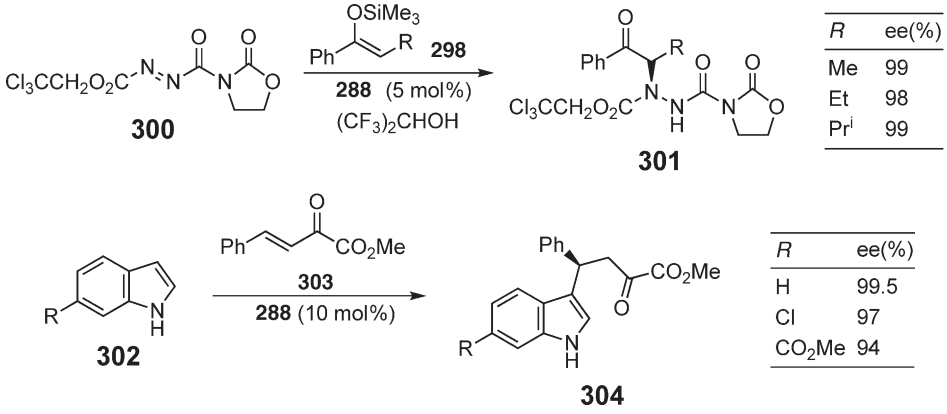


R	ds(%)	ee(%)
H	89	95
Me	96	91

Scheme 80



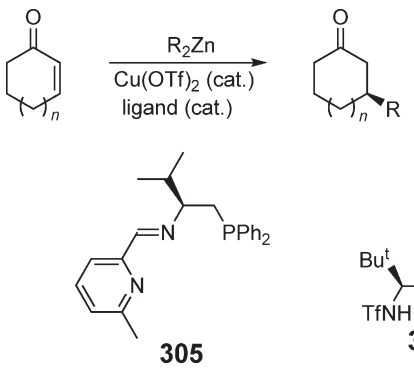
Scheme 81



Scheme 82

The extension of this method to the amination of azodicarboxylate **300** was successful with triflate **288** as Lewis-acidic catalyst, giving rise to the formation of hydrazines **301** with extraordinary high enantiomeric excesses (Scheme 82).[250b] Jørgensen *et al.*[252,252a,252b] used α- or β-ketoesters as the nucleophile and the corresponding phenyl-substituted bisoxazoline copper(II) triflate to obtain amination products of azodicarboxylates, also with very high enantioselectivity. Another important application of the copper catalysts **288**/**289** is the enantioselective Friedel–Crafts alkylation of aromatic or heteroaromatic compounds with Michael acceptors.[253] Whereas the reaction of various indoles **302** with 2-oxobutenoate **303** afforded the products **304** with very high enantioselectivities in the presence of catalytic amounts of **288**,[254,254a] inferior stereoselectivities were observed with alkylidene malonates as the Michael acceptor.[255,255a] In contrast to this, attempts to utilize chiral bisoxazoline copper catalysts for enantioselective, 1,4-additions of organozinc reagents to enones have been unsatisfactory so far.[256]

A large number of chiral ligands without a binaphthalene, TADDOL, or bisoxazoline motif have also been developed for copper-catalyzed enantioselective Michael additions in the last decade.[17] Copper catalysts derived from chiral amines,[257,257a] aminophosphines,[258,258a–258g] aminothiols,[259,259a] carbohydrates,[260,260a–260e] and N-heterocyclic carbenes[261,261a] mainly afford unsatisfactory enantioselectivities or require high catalyst loading. A class of chiral aminophosphines that does provide high enantioselection in copper-catalyzed 1,4-additions of diorganozinc reagents to enones was introduced by Morimoto *et al.*[262] as well as by Leighton and co-workers (Scheme 83).[263,263a] The valinol-derived aminophosphine **305** induced an enantioselectivity of 91% ee in the copper-catalyzed conjugate addition of diethylzinc to cyclohex-2-enone,[262] and an even higher selectivity of 97% ee was realized with the related *t*-leucine-derived ligand **306**.[263,263a] The latter turned out to be fairly general, as good to excellent stereoselectivities were observed with a variety of cyclic enones and dialkylzinc reagents. A related ligand system bearing two amino functionalities and a stereogenic phosphorus atom was recently applied in highly enantioselective copper-catalyzed 1,4-additions of organozinc reagents to acyclic enones.[264]

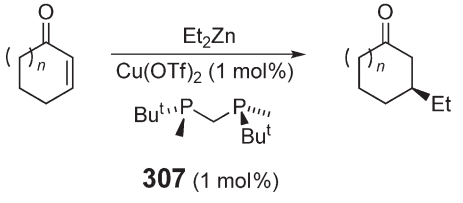


R	n	Ligand	ee(%)
Et	1	**305**	91
Et	1	**306**	97
Pr^i	1	**306**	96
Pr^i	0	**306**	86
Et	2	**306**	97

Scheme 83

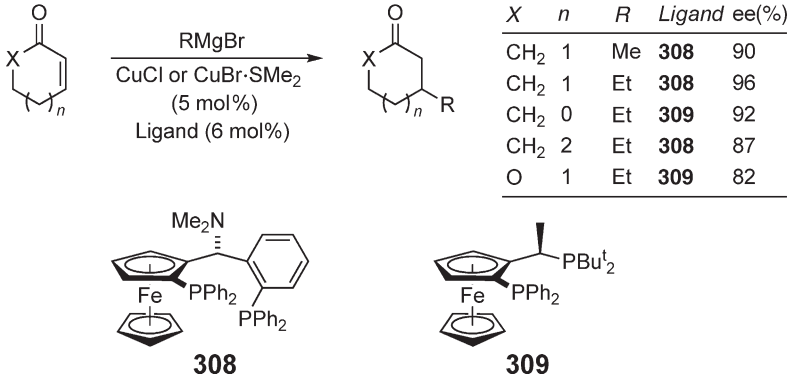
The first example for the use of a diphosphine bearing stereogenic phosphorus atoms as a ligand in copper-catalyzed Michael additions has been reported by Inamoto and co-workers,[265,265a] who showed that the reaction of cyclohex-2-enone and the corresponding seven-membered enone with diethylzinc in the presence of $Cu(OTf)_2$ and **307** (abbreviated as MiniPHOS) gave rise to the formation of the addition products with 70% and 97% ee, respectively (Scheme 84). The corresponding transformation of chalcone proceeded with 71% ee. Other simple diphosphines, however, displayed only moderate enantioselectivities in copper-catalyzed Michael additions.[226]

Very recently, Feringa and co-workers[266] reported a ligand system that affords exceptionally high enantioselectivities in copper-catalyzed 1,4-additions of Grignard reagents. In the presence of a copper salt and the ferrocenyl diphosphines **308**/**309** (which combine central and planar chirality), the Michael addition of various Grignard reagents to five-, six-, or seven-membered cyclic enones, as well as 5,6-dihydropyran-2-one, proceeds with high to excellent enantioselectivity (Scheme 85). Remarkably, the reactivity of this catalytic system is so high that uncatalyzed side-reactions leading to the racemic conjugate addition product (or the 1,2-adduct) are efficiently suppressed. Similar results were also obtained for acyclic enones.[267]



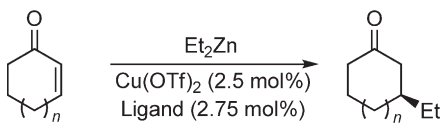
n	ee(%)
1	70
2	97

Scheme 84

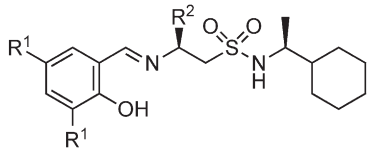


X	n	R	Ligand	ee(%)
CH_2	1	Me	**308**	90
CH_2	1	Et	**308**	96
CH_2	0	Et	**309**	92
CH_2	2	Et	**308**	87
O	1	Et	**309**	82

Scheme 85



n	*Ligand*	ee(%)
1	**310**	90
2	**310**	85
0	**311**	80



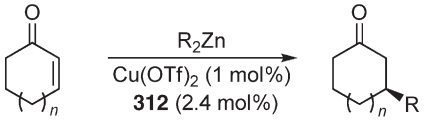
310 (R^1 = Cl, R^2 = Pr^i)
311 (R^1 = Bu^t, R^2 = Bu^i)

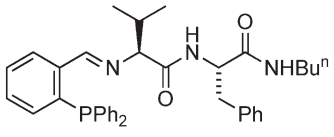
Scheme 86

A combinatorial approach for the evaluation of chiral ligands for copper-catalyzed enantioselective 1,4-additions was described by Gennari *et al.*[268,268a,268b] A library of 100 imines was subjected to a high-throughput screening for the $Cu(OTf)_2$-catalyzed conjugate addition of diethylzinc to cyclohex-2-enone and cyclohept-2-enone, revealing ligand **310** as the most selective one for these substrates (Scheme 86). After optimization of the reaction conditions, the addition products were obtained with 90% and 85% ee, respectively, and high chemical yields. The most selective ligand of this library for the more challenging addition to cyclopent-2-enone turned out to be **311** which provided the addition product with 80% ee (but a disappointingly low chemical yield of only 25%). The method was also applied to phosphorus ligands[269] and to nitroolefins as the substrate.[270]

In an analogous manner, Hoveyda and co-workers[271] prepared a large number of small peptidic phosphines and screened them in copper-catalyzed enantioselective conjugate additions and several other reactions. This highly efficient and successful strategy was first applied to cyclic enones[272,272a,272b] and then expanded to acyclic enones,[273], N-acyl oxazolidinones,[274,274a] and nitroolefins.[275,275a] For example, treatment of cyclic enones with various diorganozinc reagents in the presence of catalytic amounts of copper(II)–triflate and peptide-based phosphine **312** afforded the conjugate addition products with excellent enantioselectivities, even for cyclopent-2-enone as the substrate (Scheme 87).[272,272a,272b] The method is applicable to functionalized organozinc reagents as well, and the highly enantioselective addition of bulky nucleophiles succeeds after slight variation of the ligand structure.[271]

Several applications of the method in target-oriented synthesis have been reported.[271] Particularly remarkable is the first enantioselective synthesis of the antimycobacterial agent erogorgiaene **319** since the copper-catalyzed enantioselective Michael addition was employed twice with high efficiency (Scheme 88).[276] Thus, reaction of the enone **313** with dimethylzine in the presence of $Cu(OTf)_2$ and ligand **314** leads to the enantiomerically pure product **315** with excellent yield, which was converted over several steps into the dienone **316**. At this point, phosphine **317** was used for the second conjugate addition of Me_2Zn which took place not only with excellent diastereoselectivity

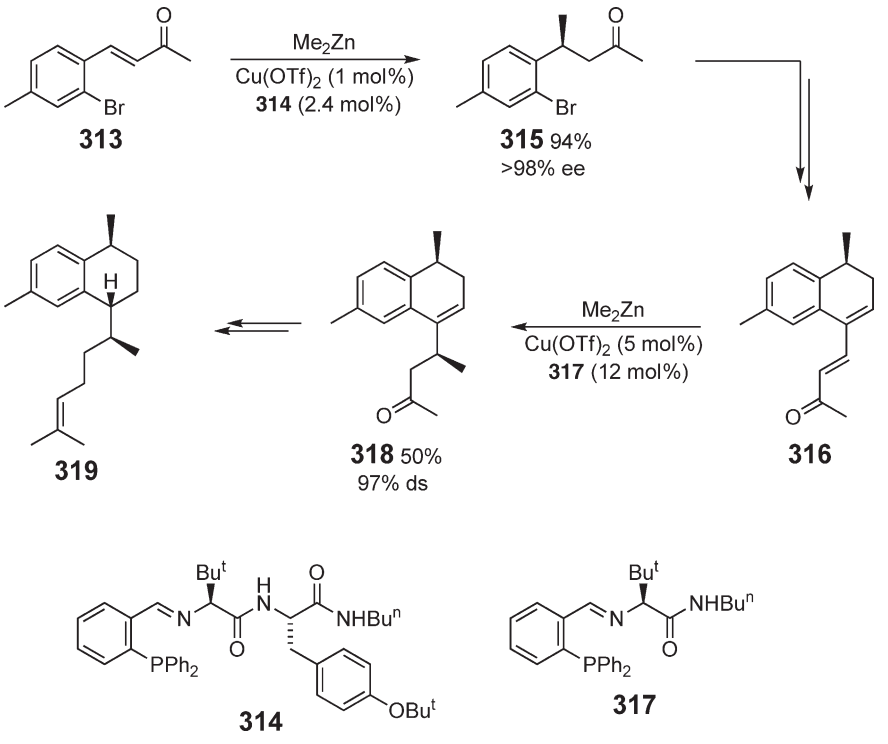




312

R	*n*	*ee*(%)
Et	0	97
$(CH_2)_4OAc$	0	>98
Me	1	>98
Et	1	98
Me	2	>98
Bu^n	2	95

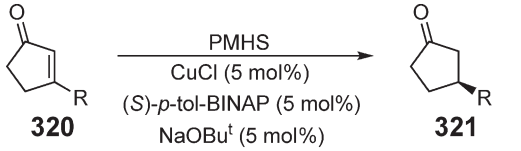
Scheme 87



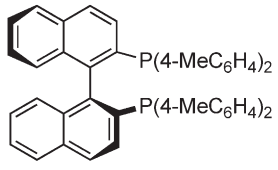
Scheme 88

(97% ds), but also with high regioselectivity in favor of product **318** (1,4- : 1,6-addition = 9 : 1). Overall, two of the three stereogenic centers of the hydrocarbon **319** were generated by enantioselective copper catalysis.

A common feature of all enantioselective copper catalysts mentioned so far is that they were used exclusively for the formation of carbon–carbon bonds. Recently, a substantial number of highly efficient and selective catalysts for the corresponding C–H bond formation by conjugate reduction have been disclosed. Thus, Buchwald *et al.* used 2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphthalene (*p*-tol-BINAP) as chiral ligand in the copper-catalyzed reduction of various Michael acceptors. Whereas the method can be applied to α,β-unsaturated esters to give the reduction products with up to 99% ee,[277,277a] the favorite substrates are cyclic enones, as well as unsaturated lactones and lactams. For instance, treatment of 3-substituted cyclopent-2-enones **320** with polymethylhydrosiloxane (PMHS) in the presence of catalytic amounts of CuCl, (*S*)-*p*-tol-BINAP, and sodium *t*-butoxide gave rise to the formation of the conjugate reduction products **321** with high yield and excellent enantioselectivities (Scheme 89).[278] Similar results were obtained with the corresponding six- and seven-membered enones. The method tolerates various functional

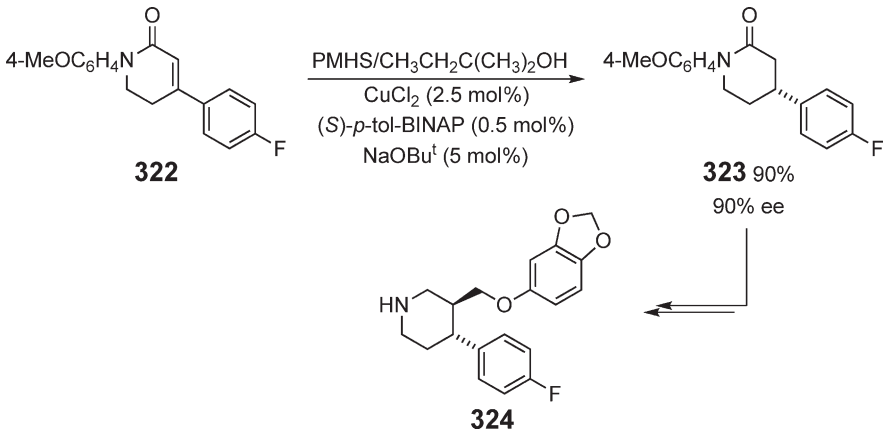


R	ee(%)
Me	94
Pr^i	94
CH_2Ph	96
$(CH_2)_4OBn$	94
$(CH_2)_2CO_2Me$	92



(*S*)-*p*-tol-BINAP

Scheme 89



Scheme 90

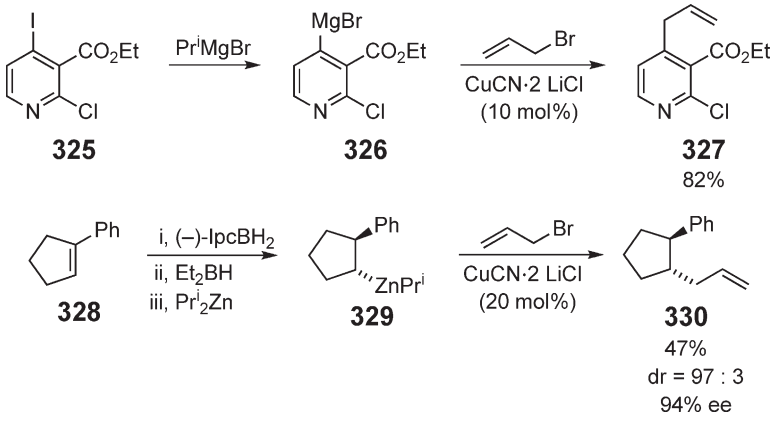
groups present in the substrate and can be combined with an alkylation or palladium-catalyzed arylation of the intermediate silyl enol ethers in a one-pot procedure.[279,279a] Likewise, the conjugate reduction of racemic 3,5-disubstituted cyclopent-2-enones can be performed as a highly selective kinetic resolution or dynamic kinetic resolution.[280] Thus, the copper-catalyzed enantioselective conjugate reduction is highly competitive with respect to the corresponding Michael addition of carbon nucleophiles.

The analogous reaction of unsaturated lactones and lactams is strongly accelerated in the presence of alcohols which protonate the copper enolate formed in the conjugate reduction.[281] This protocol was used in an enantioselective synthesis of the antidepressant (−)-paroxetine **324**. Here, the key step was the conjugate reduction of the lactam **322** by PMHS in the presence of *t*-amylalcohol and catalytic amounts of $CuCl_2$, (*S*)-*p*-tol-BINAP, and sodium *t*-butoxide, giving the product **323** with 90% yield and 90% ee (Scheme 90).[281] The second chirality center was installed by diastereoselective alkylation of **323**.

In a similar manner, Lipshutz and co-workers[282,282a–282c] used chiral ferrocenyl phosphines like JOSIPHOS and biphenyl phosphines (e.g., SEGPHOS) in highly enantioselective copper-catalyzed conjugate reductions of enones and α,β-unsaturated esters, whereas Czekelius and Carreira[283,283a,283b] reported the corresponding transformation of nitroolefins. The chiral nitroalkanes obtained in the latter case are valuable precursors for chiral amines.

9.12.2.2.2 Substitution reactions

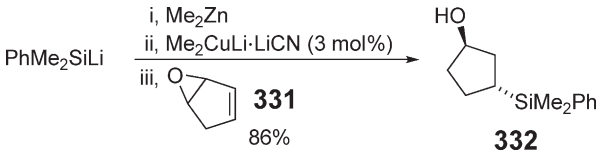
The copper-catalyzed S_N2'-substitution reaction of allylic or propargylic electrophiles with carbon nucleophiles is a well-developed synthetic method.[3–5,25] Not surprisingly, several methodological advances made in the last decade have also found application for this transformation. Thus, various functionalized Grignard or organozinc reagents were found to react smoothly with allyl bromide in the presence of catalytic amounts of copper salts (Scheme 91).[25,36,284,284a,284b] For



Scheme 91

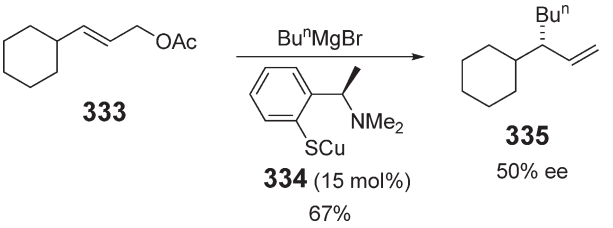
example, the presence of 10 mol.% of the copper salt CuCN·2LiCl is sufficient to promote an efficient allylation of the highly functionalized pyridylmagnesium reagent **326** which was obtained as usual by halogen–magnesium exchange of aryl iodide **325** with Pr^iMgBr (cf. Section 9.12.2.1.2).[284,284a,284b] Likewise, the product **330** was obtained with high stereoselectivity by copper-catalyzed allylation of the chiral organozinc intermediate **329** (formed by hydroboration of olefin **328** with isopinocampheylborane, $IpcBH_2$, and boron zinc exchange).[36]

Heteronucleophiles can also be transferred to electrophiles in copper-catalyzed S_N2'-substitution reactions. The silylzinc reagent $PhMe_2SiZnMe_2Li$ formed by treating phenyldimethylsilyllithium with dimethylzinc undergoes substitutions with vinyl oxiranes (e.g., **331**) to afford products of the type **332** with high yield and *anti*-stereoselectivity (Equation (17)).[183]



(17)

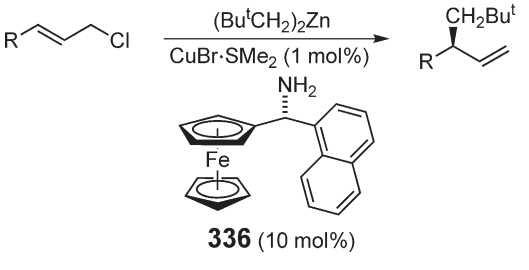
Similar to the conjugate addition, the focus of the last decade has been put on the development of chiral copper catalysts for enantioselective S_N2'-substitutions of prochiral substrates.[197,197a,197b,271,285] These represent a useful alternative for the preparation of those substitution products which cannot be obtained by *anti*-stereoselective copper-promoted or -catalyzed S_N2'-substitution of chiral substrates (see Section 9.12.2.1.2). The first reported example for such a transformation is the reaction of the allyl acetate **333** with *n*-butylmagnesium bromide in the presence of 15 mol.% of the copper arenethiolate **334** which gave the substitution product **335** with exclusive γ-selectivity and 50% ee (Equation (18)).[286,286a]



(18)

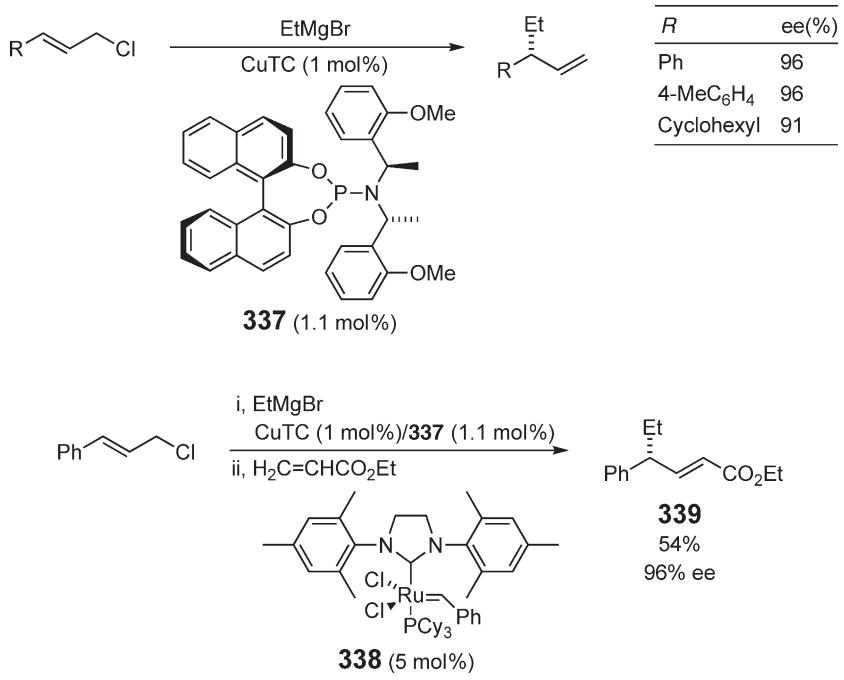
Various alternative ligand systems have been introduced subsequently with superior results. Whereas Dübner and Knochel[287,287a–287c] observed enantioselectivities of up to 87% ee in the copper-catalyzed S_N2'-substitution of allyl chlorides with dineopentylzinc in the presence of catalytic amounts of the ferrocenylamine **336**, substantially lower stereoselectivities were attained with less bulky nucleophiles (Scheme 92). Similar levels of enantioselectivity were reached by Feringa *et al.*[288] using BINOL-phosphoramidites of the type **258**, as well as by Alexakis and co-workers[289,289a,289b] with TADDOL-derived phosphites and phosphoramidite **267**.

Very recently, Alexakis *et al.*[290,290a,290b] reached preparatively useful levels of enantioselection in the copper-catalyzed S_N2'-substitution of allyl halides by slight variation of the phosphoramidite structure. The installation of two methoxy groups in the amine part of ligand **258** led to the new phosphoramidite **337** which afforded extraordinarily high enantioselectivities in the copper thiophene-2-carboxylate-(CuTC)-catalyzed reaction of various allyl chlorides or bromides with Grignard reagents or diorganozinc compounds (Scheme 93). Furthermore, the substitution reaction can be combined with a ruthenium-catalyzed olefin metathesis in a one-pot procedure, as is exemplified by



R	ee(%)
Ph	82
4-$CF_3C_6H_4$	87
Cyclohexyl	76

Scheme 92



R	ee(%)
Ph	96
4-MeC_6H_4	96
Cyclohexyl	91

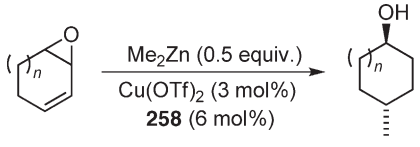
Scheme 93

the formation of the chiral ester **339** with good yield and high enantiomeric excess by copper-catalyzed allylic substitution and subsequent cross-metathesis with ethyl acrylate in the presence of the Grubbs-II catalyst **338**.[290,290a,290b]

Extensive studies on copper- and phosphoramidite-catalyzed enantioselective allylic substitution reactions of vinyl oxiranes were reported in recent years by Pineschi and co-workers.[291] Thus, the reaction of cyclic vinyl oxiranes with dialkylzinc reagents under kinetic resolution conditions, that is, with 0.5 equiv. of the nucleophile in the presence of catalytic amounts of $Cu(OTf)_2$ and ligand **258** gave the *anti*-S_N2'-substitution products with moderate ($n = 0$) to excellent ($n = 1, 2$) enantioselectivities (Scheme 94).[292,292a] Since both enantiomers of the chiral ligand are readily available, this procedure opens up a flexible access to valuable chiral allylic alcohols. The method has been extended subsequently to the catalytic kinetic resolution of vinyloxiranes with an exocyclic double bond[293] and of vinylaziridines,[294] as well as to the desymmetrization of divinyloxiranes and other *meso*-compounds.[295,295a–295d] Even propargylic oxiranes can be converted into the corresponding α-hydroxyallenes under these conditions, albeit with unsatisfactory enantioselectivities of up to 38% ee.[296]

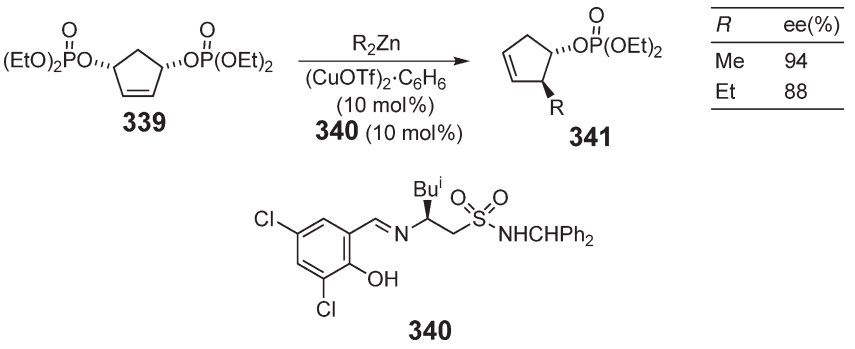
Of the many other ligand types that have been used successfully in copper-catalyzed enantioselective conjugate addition reactions (Section 9.12.2.2.1), the imines of the type **310**/**311** have turned out to be prolific for the corresponding S_N2'-substitutions as well. Gennari and co-workers[297,297a,297b] used their combinatorial approach to identify ligand **340** as the most selective one of a library of 125 imines for the copper-catalyzed desymmetrization of bisphosphate **339** with dimethyl- or diethylzinc, affording the *anti*-substitution products **341** with high enantioselectivity (Scheme 95). Unfortunately, the corresponding six- and seven-membered substrates gave much lower selectivities; here the phosphoramidite **258** turned out to be the ligand of choice.[295d]

Very similar ligands were used by Hoveyda *et al.*[298,298a,298b] for the enantioselective copper-catalyzed S_N2'-substitution of allyl phosphates, allowing the highly enantioselective formation of tertiary und quarternary



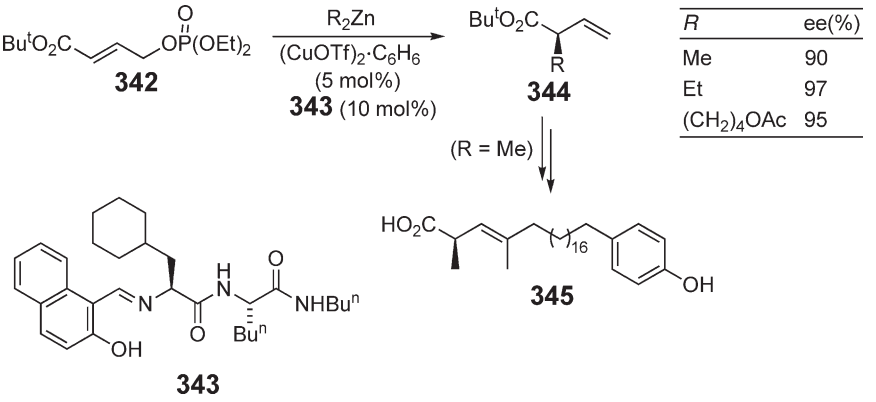
n	ee(%)
0	50
1	92
2	96

Scheme 94



R	ee(%)
Me	94
Et	88

Scheme 95



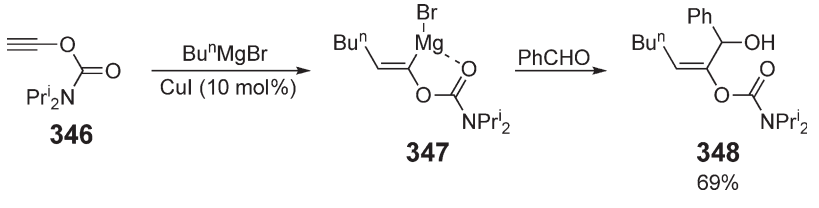
R	ee(%)
Me	90
Et	97
$(CH_2)_4OAc$	95

Scheme 96

stereogenic centers. For example, treatment of the ester-substituted allyl phosphate **342** with various functionalized or unfunctionalized organozinc reagents in the presence of catalytic amounts of copper(I)–triflate–benzene complex and dipeptide **343** provided the substitution products **344** with excellent regio- and stereoselectivity (Scheme 96). The product formed with dimethylzinc was transformed into the enzyme inhibitor (*R*)-(−)-elenic acid **345** by ruthenium-catalyzed cross-metathesis.[299]

9.12.2.2.3 Carbometallation and other reactions

A number of examples for the copper-catalyzed carbometallation[151,300,300a] or stannylmetallation[61,61a] of C–C double or triple bonds have been described in recent years. For example, reaction of ethynyl carbamate **346** with *n*-butylmagnesium bromide in the presence of 10 mol.% of copper(I)–iodide induced a smooth regio- and stereoselective carbomagnesiation to afford the vinylmagnesium intermediate **347** which can be trapped with benzaldehyde to the allyl alcohol **348** (Scheme 97).[151]



Scheme 97

Various other copper-catalyzed transformations have been studied extensively, but cannot be discussed in detail here. Thus, bisoxazoline copper(II) complexes of the type **288**/**289**,[246,246a,301,301a] as well as analogous complexes of pyridin-2,6-bisoxazolines[302] and 2,2′-bipyridines,[303] have been utilized as highly stereoselective catalysts for cycloadditions, carbonyl–ene reactions, aldol additions, cyclopropanations,[304] aziridinations, allylic oxidations,[304,305,305a–305c] and Claisen rearrangements.[306,306a,306b] Furthermore, copper salts are indispensable catalysts for coupling reactions of aryl or vinyl electrophiles with carbon or heteroatom nucleophiles, prominent examples being the palladium- and copper-catalyzed coupling with terminal alkynes (Sonogashira coupling),[307,307a–307c] as well as the copper-catalyzed amination of aryl halides.[308,308a]

9.12.3 Silver

Silver salts or reagents have received much attention in preparative organic chemistry because they are useful catalysts for various transformations involving C–C and C–heteroatom bond formation.[309] Especially, the silver(I)/BINAP (2,2′-bis(diphenylphosphino)-1,1′-binaphthalene) system is a very effective catalyst for a variety of enantioselective reactions, including aldol, nitroso aldol, allylation, Mannich, and ene reactions. Moreover, silver salts are known to efficiently catalyze cycloisomerization and cycloaddition reactions of various unsaturated substrates. Recently, new directions in silver catalysis were opened by the development of unique silver complexes that catalyze aza-Diels–Alder reactions, as well as carbene insertions into C–H bonds.

In this chapter, we concentrate on the applications of silver catalysts in preparative organic chemistry over the last decade (1994–2004). The use of stoichiometric amounts of silver reagents lies beyond the scope of this chapter.

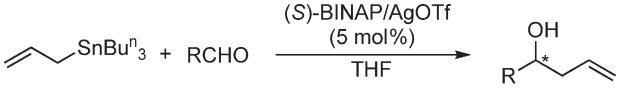
9.12.3.1 Allylation and Aldol Reactions

Yamamoto and co-workers have developed an enantioselective allylation reaction of aldehydes catalyzed by the BINAP/AgOTf complex (Scheme 98).[310] The reaction gave homoallyl alcohols in high yields and enantioselectivities with aromatic and α,β-unsaturated aldehydes, whereas aliphatic aldehydes afforded lower yields or stereoselectivities. Among various catalysts examined, such as $PdCl_2$, $PtCl_2$, $SnCl_4$, $InCl_3$, silver catalysts, that is, $AgNO_3$, $AgClO_4$, and especially AgOTf gave the best results. The reaction mechanism is not clear, but the BINAP/AgOTf system is thought to act as a chiral Lewis acid rather than to generate an allylsilver reagent by tin–silver transmetallation.

Furthermore, the enantioselective addition of substituted allyl groups to aldehydes is also catalyzed by the BINAP/Ag(I) complex (Scheme 99).[311] Thus, the reaction of methallyltin or crotyltin reagents **349** with various aldehydes in the presence of BINAP/AgOTf afforded the corresponding homoallyl alcohols **350** with good yields and high enantioselectivities. In the case of the crotyltin reagent, a highly γ- and *anti*-selective allylation of the aldehyde was observed for both the (*Z*)- and the (*E*)-nucleophile.

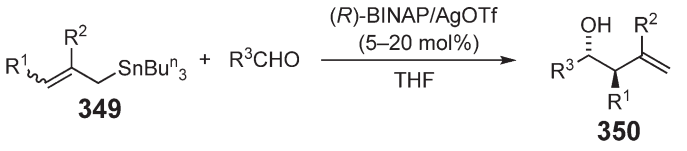
The regio- and enantioselective pentadienylation of aldehydes is also catalyzed by the BINAP/silver complex.[312] The reaction of dienylstannanes **351** with various aldehydes takes place in the γ-position exclusively to afford the products **352** with good to high enantioselectivities (Scheme 100). The reaction was proposed to occur either via a Lewis acid mechanism (transition state **353**) or by transmetallation (transition state **354**).

The enantioselective allylation of aldehydes can also be carried out by using allylsilanes as the nucleophile. For example, Yamamoto and co-workers[313,313a] employed allyltrimethoxysilane for the allylation of various aldehydes in



R	*Yield*(%)	ee(%)
Ph	88	96
(*E*)-PhCH=CH	83	88
$PhCH_2CH_2$	47	88

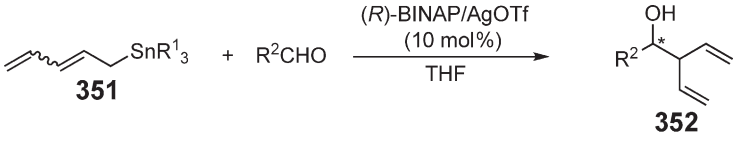
Scheme 98



349 350

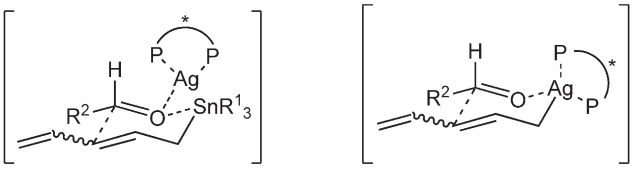
R^1	R^2	$E:Z$	R^3	*Yield*(%)	ee
H	Me		Ph	75	92%
H	Me		(*E*)-PhCH=CH	62	91%
Me	H	95 : 5	Ph	56	*anti* 85 (94%) : *syn* 15 (64%)
Me	H	2 : 98	Ph	72	*anti* 85 (91%) : *syn* 15 (50%)

Scheme 99



351 352

$SnR^1{}_3$	R^2	*Yield*(%)	ee(%)
$SnBu^n{}_3$	Ph	61	90
$SnBu^n{}_3$	(*E*)-PhCH=CH	73	58
$SnBu^n{}_3$	$PhCH_2CH_2$	52	71
$SnMe_3$	Ph	68	89

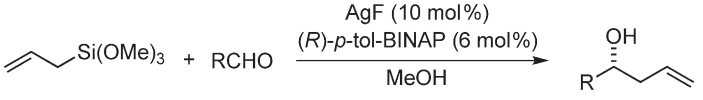


353 354

Scheme 100

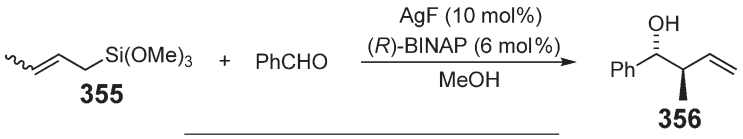
the presence of *p*-tol-BINAP/AgF (Scheme 101). The yields and enantioselectivities are similar to those obtained with allylstannanes.

The same catalytic system brings about the enantioselective addition of the corresponding crotylsilyl reagent **355** to aldehydes (Scheme 102).[313,313a] Both the (*E*)- and (*Z*)-isomer reacted with benzaldehyde in the presence of AgF/BINAP to afford preferentially the *anti*-homoallyl alcohols **356** with high yields and excellent enantioselectivities.



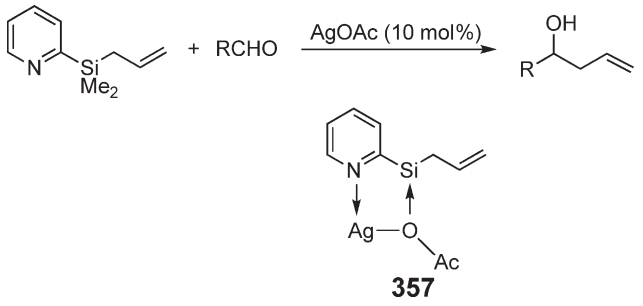
R	*Yield*(%)	ee(%)
Ph	80	94
(*E*)-PhCH=CH	93	78
4-BrC_6H_4	90	93

Scheme 101



E : *Z*	*Yield*(%)	*anti* (ee) : *syn* (ee)
83 : 17	77	92 (96%) : 8 (62%)
<1 : 99	82	94 (94%) : 6 (60%)
45 : 55	99	93 (94%) : 7 (60%)

Scheme 102



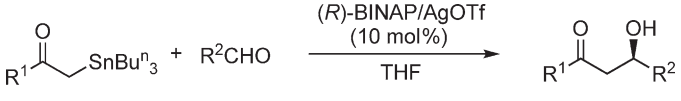
R	*Yield*(%)
Ph	85
4-MeC_6H_4	45
4-ClC_6H_4	59

Scheme 103

Yoshida and co-workers have examined the silver(I)-catalyzed allylation of aldehydes using allyldimethyl (2-pyridyl)silane (Scheme 103).[314] Treatment of various aldehydes with this reagent in the presence of silver acetate in toluene afforded the corresponding homoallyl alcohols in moderate to good yields. Various other silver salts such as AgF, AgO, Ag_2O, Ag_2S, AgOTs, AgOTf, and $AgBF_4$ were less efficient in this reaction. The silver catalyst may promote the allylation by acting both as a Lewis acid and base (see intermediate **357**), that is, the interaction of the Lewis-acidic silver with the pyridine nitrogen atom may be accompanied by a second interaction of the Lewis-basic acetate oxygen with the silicon atom.

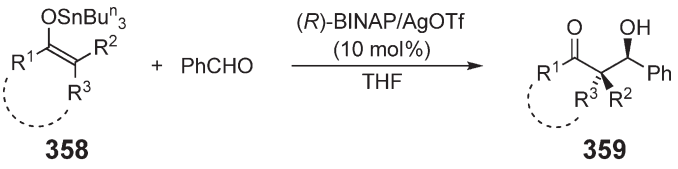
Besides allylation reactions, the BINAP/AgOTF complex effectively catalyzes the enantioselective aldol reaction of tin enolates with various aldehydes.[315] Under these conditions, a wide range of aldol products were smoothly formed with good to high yields and enantioselectivities (Scheme 104).

In the case of cyclic or α-substituted tin enolates **358**, it was found that *E*-enolates provide *anti*-products **359**, whereas the corresponding *Z*-tin enolates give *syn*-aldols (Scheme 105).[315] Thus, the reaction seems to follow the classical Zimmerman–Traxler transition states **360**/**361** whereby the chiral silver catalyst activates the aldehyde. A possible alternative is a tin–silver exchange and formation of an analogous transition state of the silver enolate.



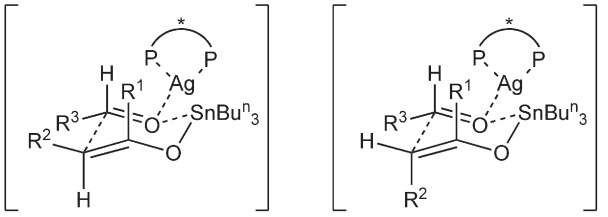
R^1	R^2	*Yield*(%)	ee(%)
Me	Ph	73	77
Me	(*E*)-PhCH=CH	83	53
Bu^t	$PhCH_2CH_2$	75	94
Ph	Ph	57	71

Scheme 104



358 **359**

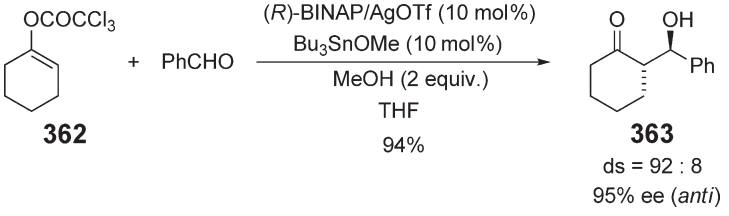
Tin enolate		*Yield*(%)	*anti* : *syn*	ee(%)
OSnBu$^n_3$	n = 1	92	89 : 11	92
	n = 2	94	92 : 8	93
	n = 3	90	85 : 15	96
OSnBu$^n_3$ Bu^t		81	<1 : 99	95



360 (→ *anti*) **361** (→ *syn*)

Scheme 105

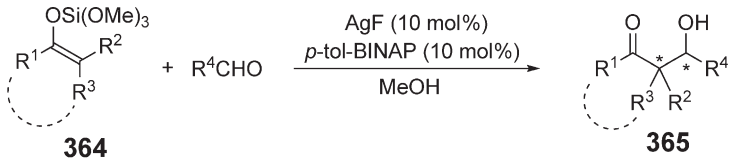
Yamamoto and co-workers[316] have also reported the first example of an enantioselective aldol reaction using catalytic amounts of both the tin enolate and the BINAP/silver complex. Treatment of the enol trichloroacetate **362** with benzaldehyde and methanol in the presence of catalytic amounts of tri-*n*-butyltin methoxide and (*R*)-BINAP/AgOTf in THF solution afforded preferentially the *anti*-aldol adduct **363** with high yield and enantioselectivity (Equation (19)). The catalytic amount of the tin enolate was generated *in situ* by an exchange reaction of the trichloroacetyl group with the tributylstannyl residue of the tin alkoxide. Interestingly, also diketene can be employed as a precursor for a catalytic tin enolate.[316]



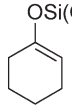
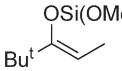
362 **363**
ds = 92 : 8
95% ee (*anti*)

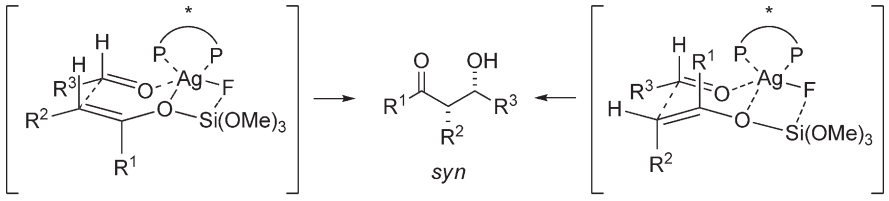
(19)

The AgF/*p*-tol-BINAP system is an efficient catalyst for enantioselective Mukaiyama aldol reactions of trimethyoxysilyl enol ethers **364** with aldehydes (Scheme 106).[317] The *syn*-aldols **365** were obtained from both (*E*)- and (*Z*)-silyl enol ethers with excellent enantioselectivities. The reaction gave good yields with aryl- and α,β-unsaturated aldehydes, whereas aliphatic aldehydes afforded only low yields of the desired aldol products. Again, the silver/BINAP complex is believed to act as a chiral Lewis acid, and the *syn*-selectivity is rationalized by a boat transition state **366** for the (*E*)-enol ether, and by a chair transition state **367** for the (*Z*)-enol ether. In both cases, the six-membered transition state may be stabilized by an additional four-membered ring formed by AgF and the silyl ether. In a closely related study, Yamagishi *et al.*[318] have examined Mukaiyama aldol reactions catalyzed by BINAP/silver(I) complexes and found that BINAP/$AgPF_6$ gives much higher enantioselectivities than the BINAP/AgOAc precatalyst. Based on low-temperature NMR studies, the authors suggest a six-membered transition state for the aldol reaction catalyzed by BINAP/$AgPF_6$, whereas the corresponding reaction catalyzed by BINAP/AgOAc may proceed via an acyclic transition state by attack of a silver enolate on the aldehyde.



364 **365**

Silyl enol ether	R^4	*Yield*(%)	*syn* : *anti*	ee(%)
	Ph	78	84 : 16	87
	p-$MeOC_6H_4$	86	75 : 25	92
	Ph	84	>99 : 1	97
	(*E*)-PhCH=CH	56	>99 : 1	85

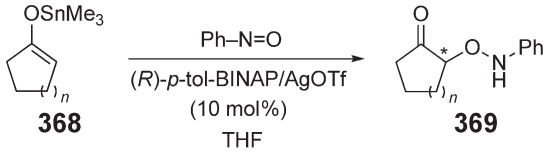


366 **367**

Scheme 106

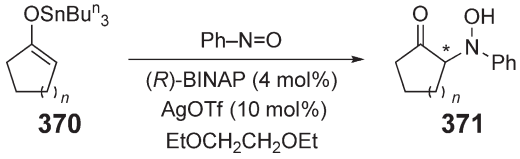
The enantioselective *O*- and *N*-nitroso aldol reaction of tin enolates with nitrosobenzene in the presence of a BINAP/AgX complex was achieved by Yamamoto and co-workers.[319,319a,319b] Thus, the 1 : 1 complex BINAP/AgX or *p*-tol-BINAP/AgX (X = OTf, ClO_4) efficiently catalyzes the formation of the *O*-nitroso aldol products **369** from trimethylstannyl enolates **368** (or the corresponding tri-*n*-butylstannyl enolates) and nitrosobenzene (Scheme 107). The N–O bond of the products can be cleaved by treatment with $CuSO_4$ to afford the corresponding α-hydroxyketones without erosion of the enantiomeric excess. In contrast to this, the *N*-adducts **371** are obtained selectively with a 1 : 2 complex formed from (*R*)-BINAP and silver triflate as the catalyst. The study includes a careful investigation of the precatalyst structure using low-temperature NMR studies and X-ray analysis.

The peptidic phosphine ligands that had been introduced by Hoveyda and co-workers[271] for enantioselective copper-catalyzed Michael additions (see Section 9.12.2.2.1) were also employed successfully in silver-catalyzed asymmetric Mannich reactions.[320] Thus, the aryl-substituted imines **372** reacted with various silyl enol ethers in the presence of stoichiometric amounts of isopropanol, as well as catalytic amounts of silver acetate and ligand **373** to



368 **369**

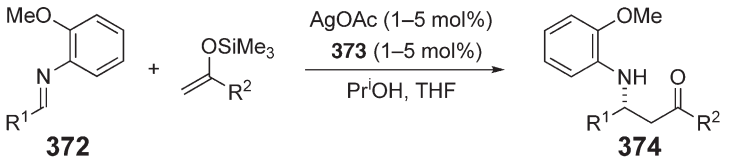
n	*Yield*(%)	ee(%)
1	93	92
2	95	97
3	95	82

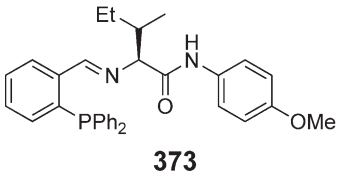


370 **371**

n	*Yield*(%)	ee(%)
1	87	86
2	91	>99
3	96	97

Scheme 107





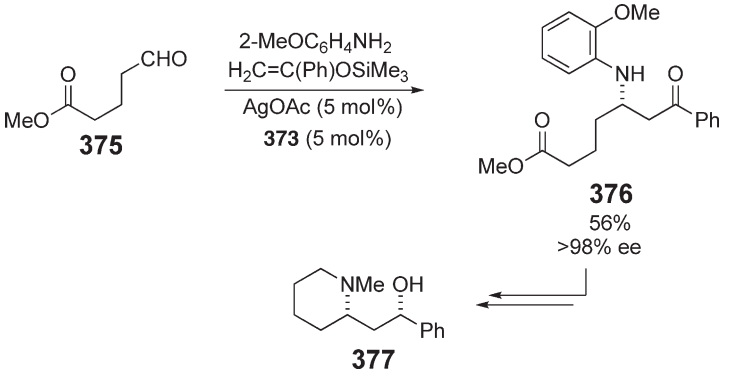
R^1	R^2	*Yield*(%)	ee(%)
Ph	Me	65	92
2-Naphthyl	Ph	88	98
(*E*)-PhCH=CH	Me	77	89
PhC≡C	Ph	93	92

Scheme 108

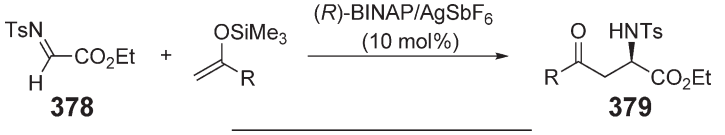
afford the β-amino ketones **374** with good to excellent yields and enantioselectivities (Scheme 108). Interestingly, the reaction proceeds smoothly even in undistilled THF without exclusion of oxygen.

Under these reaction conditions, adducts of the type **374** can also be obtained by three-component coupling reaction of 2-methoxyaniline with an aldehyde and a silyl enol ether. This method was utilized in a short total synthesis of enantiomerically pure (−)-sedamine **377** from aldehyde **375** via the adduct **376** (Scheme 109).[320]

In a similar fashion, Lectka *et al.*[321] have developed the silver-catalyzed enantioselective alkylation of α-imino ester **378** by treatment with silyl enol ethers in the presence of $AgSbF_6$ and (*R*)-BINAP, giving the amino acid derivatives **379** in good to high yields and enantioselectivities (Scheme 110). The analogous ene reaction of substrate **378** with 2-phenyl-propene afforded the corresponding unsaturated amino ester with 71% ee.[322]



Scheme 109



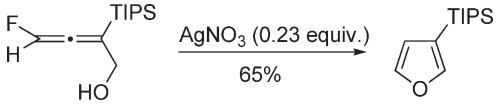
R	*Yield*(%)	ee(%)
Ph	95	90
4-MeOC$_6$H$_4$	94	86
Bu^t	70	75

Scheme 110

9.12.3.2 Cycloisomerizations and Rearrangements

The prototype of a silver-catalyzed cycloisomerization reaction is the conversion of α-hydroxyallenes into 2,5-dihydrofurans in the presence of $AgNO_3$ or $AgBF_4$ which was disclosed by Olsson and Claesson in 1979.[323,324] These authors also reported the first example for the corresponding cyclization of β-hydroxyallenes to 5,6-dihydro-2*H*-pyrans. In the last decade, Marshall and co-workers used the method for the transformation of various α-allenic alcohols **380** bearing additional reactive groups, such as silyl, MOM, and benzyl ethers, into the corresponding 2,5-dihydrofurans **381** which were obtained with good to high yields and complete axis-to-center chirality transfer (Scheme 111).[325,325a] The use of silver nitrate on silica gel led to particularly fast cyclization reactions, although this system is still considerably less reactive than gold catalysts (see Section 9.12.4.3).

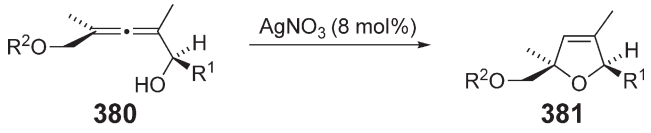
The analogous treatment of the α-hydroxyallene **382** bearing a leaving group (fluorine) at the terminal allenic carbon atom afforded the furan **383** in good yield via cyclization and dehydrofluorination (Equation (20)).[326]



382 **383** (20)

The same products are accessible by silver-catalyzed cycloisomerization of allenic ketones. Marshall and Bartley[327] used $AgNO_3$/silica gel in hexane to convert the allenic ketones **384** into the furans **386** with excellent yields (Scheme 112). Deuterium labeling experiments were interpreted in terms of the intermediate **385** which seems to arise from the coordination of silver catalyst to the allenic double bond distal to the carbonyl group. Again, gold precatalysts can be used with much lower catalyst loadings than their silver counterparts (see Section 9.12.4.3).

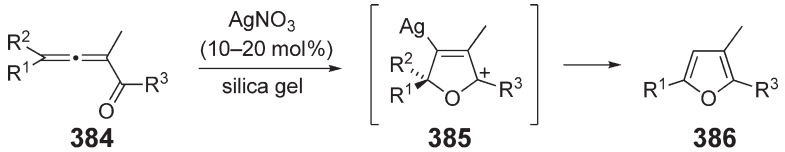
Various applications of the method have been reported[324,325,325a] and include the efficient formation of the functionalized furan **388**, a precursor of the agylcon **389** of the naturally occurring antibiotic eleutherobin, from the allenic ketone **387** (Scheme 113).[328]



380 **381**

R^1	R^2	*Yield*(%)
CH_2OMOM	TBS	86
CH_2OBn	TBS	91
Me	TIPS	90

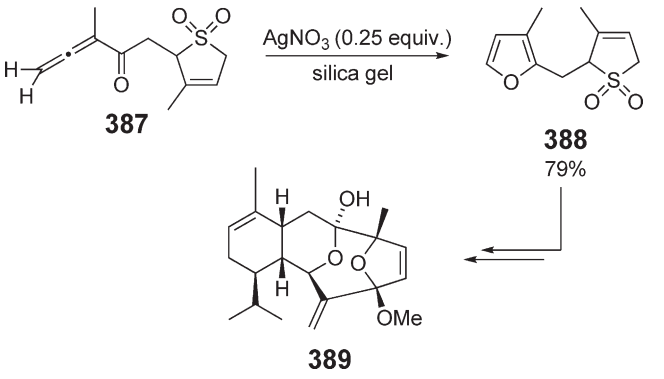
Scheme 111



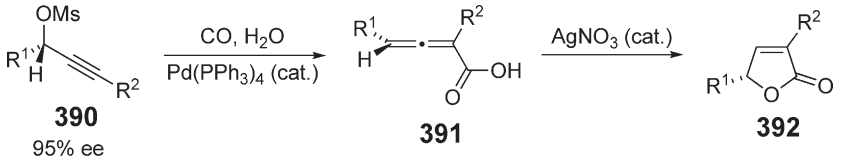
384 **385** **386**

R^1	R^2	R^3	*Yield*(%)
$^nC_7H_{15}$	H	$^nC_6H_{13}$	99
Bu^n	D	$^nC_6H_{13}$	92

Scheme 112



Scheme 113



R^1	R^2	*Yield*(%)	ee(%)
Me	$^nC_7H_{15}$	62	90
$^nC_5H_{11}$	H	91	60

Scheme 114

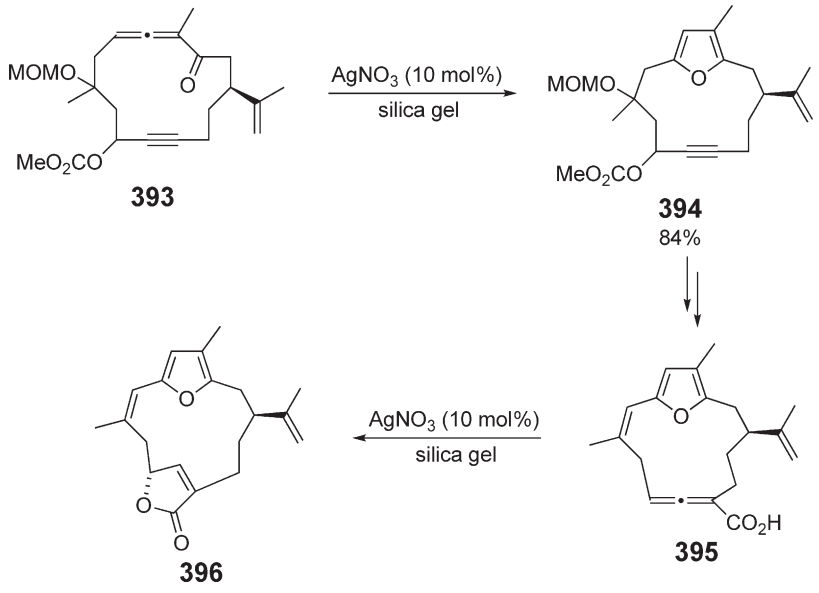
The silver-catalyzed cycloisomerization of allenic carboxylic acids to butenolides was also reported by Marshall and co-workers.[329] Starting from the enantiomerically enriched propargyl mesylate **390**, palladium-catalyzed hydroxycarbonylation led to the chiral allenecarboxylates **391** which afforded the butenolides **392** upon treatment with silver nitrate (Scheme 114). Unfortunately, partial racemization could not be avoided in this two-step sequence. In a related study, Ma and Shi[330] have shown that the combination of $Pd(PPh_3)_4$ and Ag_2CO_3 promotes the cyclization of allenecarboxylates to the corresponding butenolides, accompanied by the introduction of aryl or alkenyl groups at C3.

Silver-catalyzed cyclization reactions of allenic carbonyl compounds were applied for the total synthesis of various natural products, including rubifolide,[331] kallolide A and B,[332,332a] and deoxypukalide.[333] In their total synthesis of the enantiomer of rubifolide **396**, Marshall and Sehon[331] took advantage of the silver-catalyzed cycloisomerization of the allenic ketone **393** to the furan **394**, as well as of the analogous reaction of the allenic carboxylate **395** to the target molecule **396** (Scheme 115).

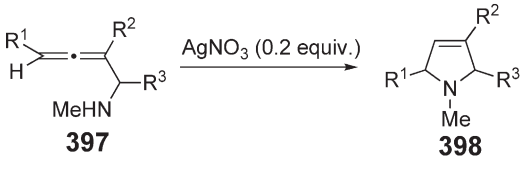
The corresponding nitrogen-containing heterocycles are accessible by silver-catalyzed cyclization of allenic amines, amides, or oximes.[334] Thus, Dieter and Yu[335] have reported the efficient transformation of various α-aminoallenes **397** or **399** into mono- or bicyclic 3-pyrrolines **398** or **400** in the presence of $AgNO_3$ (Scheme 116). Unfortunately, a rather high catalyst loading was required.

A key step in the synthesis of the natural products clavepictine A and B **403** was the silver(I)-promoted isomerization of the δ-aminoallene **401** to the quinolizidine **402** which was obtained as a 7 : 1 mixture of diastereomers with regard to the newly formed stereogenic center (Scheme 117).[336,336a]

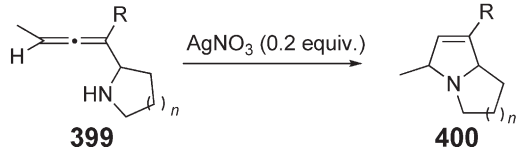
Like their unprotected counterparts, α-allenic sulfonamides of the type **404**, which are easily accessible by lithiated methoxyallene to N-tosylimines, can be cyclized to the corresponding 3-pyrrolines (e.g., **405**) in the presence of substoichiometric amounts of silver nitrate (Equation (21)).[337,337a] The method can be applied to the synthesis of mono- or bicyclic products which were obtained with moderate to good yields. The analogous cycloisomerization of β-allenic sulfonamides to tetrahydropyridins was developed by Ibuka and co-workers.[338]



Scheme 115

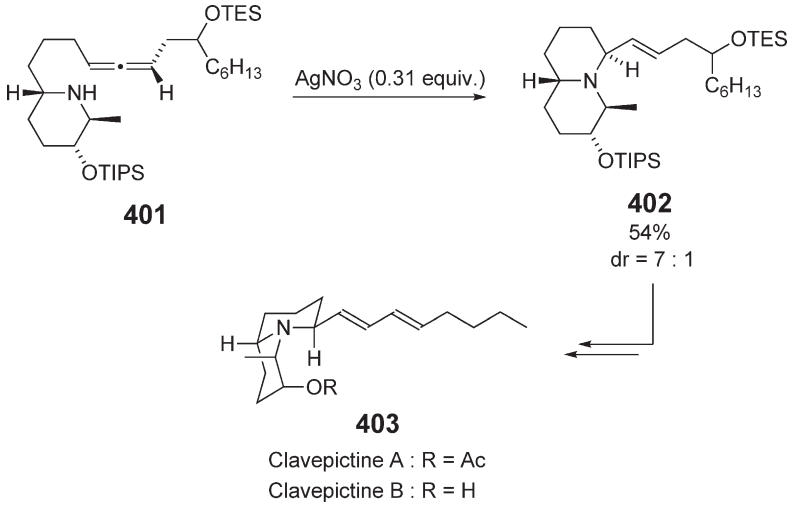


R^1	R^2	R^3	*Yield*(%)
Pr^i	Ph	H	70
Me	Bu^n	H	82
Me	Bu^n	Ph	75



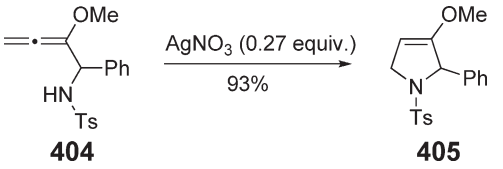
R	*n*	*Yield*(%)
Bu^n	1	90
Bu^n	2	67
Ph	1	67

Scheme 116



Scheme 117

An interesting and truly catalytic cycloisomerization reaction of α-allenic amides was also reported recently which, however, afforded mixtures of 2-(5*H*)-furanylidenamines and 1,5-dihydro-2*H*-pyrrol-2-ones in most cases.[339,339a]

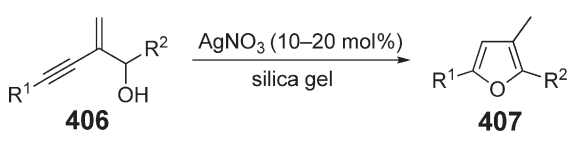


404 **405** (21)

Most of the cycloisomerizations described so far in this chapter can also be carried out with acetylenic instead of allenic substrates. A major difference is of course that the alkynes are not chiral and thus do not lend themselves for the stereoselective formation of chiral heterocycles as nicely as allenes do. This is of no consequence for the transformation of β-alkynyl allylic alcohols **406** into the (achiral) furans **407** which were obtained in good to excellent yields by treatment with silver nitrate on silica gel (Scheme 118).[325a] Although various precatalysts such as AgOTf, $AgBF_4$, and AgO_2CCF_3 also afford furans **407** in high yields (86–97%), the $AgNO_3$/silica gel system is superior in terms of lower catalyst loadings and shorter reaction times, and it can even be reused twice. The method can also be applied to macrocyclic substrates of the type **408** which gave the bicyclic furan **409** with 86% yield.[325a]

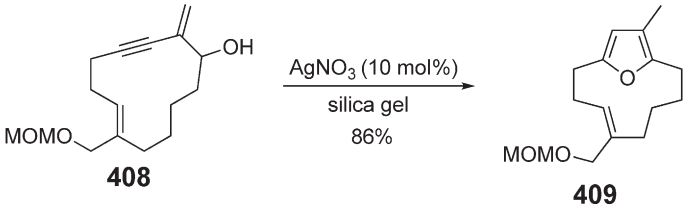
Pale and Dalla[340] have shown that 4-alkyn-1-ols **410** can be converted into 2-methylene oxolanes **411** in the presence of 10 mol% of Ag_2CO_3 (Scheme 119). Under these conditions, a wide range of functional groups such as hydroxy, alkyl ether, and silyl ether groups are tolerated. Even 2,3-epoxy-4-alkyn-1-ols can be converted into the corresponding 3,4-epoxy-2-methylene oxolanes without competing reactions affecting the oxirane ring.[341] Methylene oxolanes represent a common structural feature of various natural products with biological activities such as plant metabolites or mycalisines.

Under the same conditions, pent-4-ynoic acids **412** afford γ-methylenefuranones **413** in excellent yields (Scheme 120).[340,342] Whereas the reaction proceeds rather slowly in the absence of an additional alcohol group ($R^1 = H$), substrates bearing a hydroxy function are smoothly cyclized within a few minutes. The first total synthesis of the naturally occurring *cis*-2-hexadecyl-3-hydroxy-4-methylenefuranone was achieved in four steps with an overall yield of 64% by this procedure. The corresponding 3-ynoic acids **414** are cleanly converted into the labile enol lactones **415** in the presence of 0.2 equiv. of $AgNO_3$.[329]



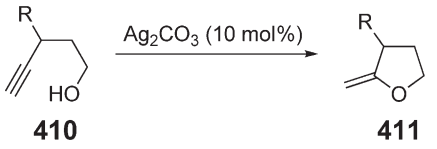
406 **407**

R^1	R^2	*Yield*(%)
C_7H_{15}	C_5H_{11}	96
$MOMO(CH_2)_4$	Et	99
$MOMO(CH_2)_4$	H	89



408 **409**

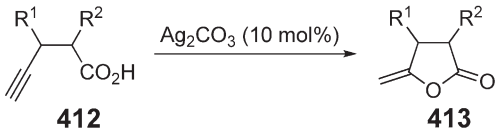
Scheme 118



410 **411**

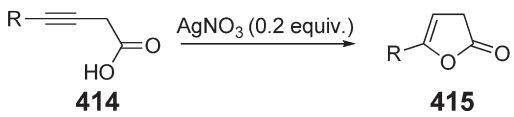
R	*Yield*(%)
OH	99
OMOM	99
OTPS	99

Scheme 119



412 **413**

R^1	R^2	*Yield*(%)
H	H	99
OH	$C_{16}H_{33}$	99
OH	(*Z*)-$C_6H_{13}CH{=}CH$	99

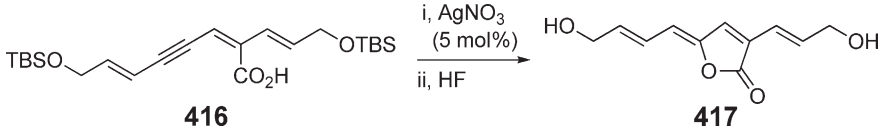


414 **415**

R	*Yield*(%)
$^nC_5H_{11}$	95
$CH_2{=}CH(CH_2)_7$	95

Scheme 120

Silver nitrate is also an efficient precatalyst for the transformation of 2-en-4-ynoic acids into γ-alkylidenebutenolides.[343] The method was used by Negishi and Xu in the total synthesis of the antibiotic lissoclinolide **417** which is active against both Gram-negative and Gram-positive bacteria (Equation (22)). The γ-alkylidenebutenolide ring of the target molecule was easily prepared by treatment of substrate **416** with 5 mol% of $AgNO_3$ in methanol. The same authors also examined the silver-catalyzed cycloisomerization of (*Z*)-2-en-4-ynoic acids and obtained mixtures of (*Z*)-5-alkylidenefuran-2-(5*H*)-ones and 2*H*-pyran-2-ones, the product ratio being a function of the counterion of the silver precatalyst and the solvent.[344] A total synthesis of ligustilide, which has remarkably wide-ranging biological activities such as anticholinertic, antispasmodic, and smooth muscle relaxing activities, took advantage of this transformation for the construction of a bicyclic γ-alkylidenebutenolide.[345]

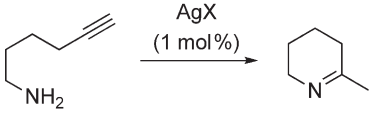


416 **417** (22)

Various nitrogen heterocycles are accessible by silver-catalyzed cyclization of acetylenic precursors as well. The intramolecular hydroamination of aminoalkynes catalyzed by late transition metals was described by Müller and Pleier.[346,346a] They investigated the reaction using various late transition metals such as Ru, Co, Rh, Pd, Cu, Ag, and reported that $AgBF_4$ or [Ag(triphos)]BF_4 in CH_2Cl_2 or toluene solution can promote the intramolecular hydroamidation of 6-aminohex-1-yne to 2,3,4,5-tetrahydro-6-methylpyridine, albeit with moderate yield and conversion (Scheme 121). The highest catalytic activity in this reaction was observed for $[Cu(CH_3CN)_4]PF_6$.[346,346a]

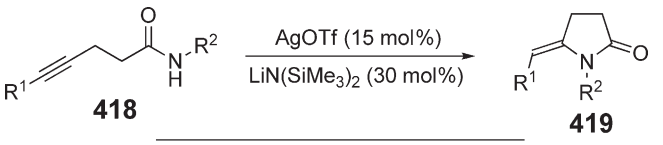
For the corresponding cyclization of acetylenic amides **418**, Nagasaka *et al.*[347,347a] used a mixture of silver(I) triflate and lithium hexamethyldisilazide as the precatalyst. The process is probably initiated by the coordination of $AgN(SiMe_3)_2$ (generated *in situ* from AgOTf and LHMDS) to the triple bond, followed by nucleophilic attack of the lithium amide at the activated alkyne which affords (*Z*)-γ-alkylidene-γ-butyrolactams **419** in high yields (Scheme 122).

The rather unusual precatalyst silver(I) isocyanate was found to efficiently catalyze the cyclization of propargyl carbamates **420** to 4-alkylideneoxazolidin-2-ones **421** in good to high yields (Scheme 123).[348] The presence of a base such as potassium *t*-butoxide or triethylamine is required for formation of the amide nucleophile which undergoes a stereoselective intramolecular attack at the activated triple bond (*trans*-aminometallation) to afford the (*Z*)-stereoisomer **421** exclusively. Likewise, homopropargyl carbamates are converted into six-membered (*Z*)-4-alkylidene-1,3-oxazinane-2-ones under the same conditions.



AgX	*Yield*(%)	*Conversion*(%)
$AgBF_4$	56	44
[Ag(Triphos)]BF_4	75	26

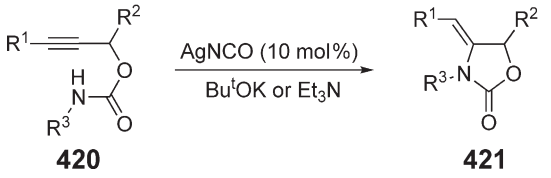
Scheme 121



418 419

R^1	R^2	*Yield*(%)
Me	3-$MeOC_6H_4CH_2$	89
Me	$MeOCH_2(Ph)CH$	88
$^nC_{12}H_{25}$	3-$MeOC_6H_4CH_2$	89

Scheme 122



420 421

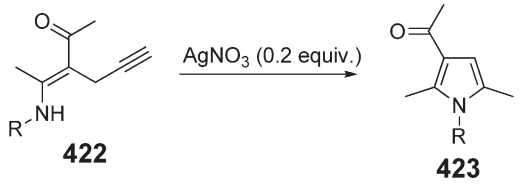
R^1	R^2	R^3	*Yield*(%)
H	Et	COPh	90
CH_2=CMe	H	Ts	66
$THPOCH_2$	H	Ts	66

Scheme 123

Aromatic heterocycles can be obtained by silver-catalyzed cyclization of acetylenic enamines or imines. Robinson and co-workers[349,349a] have shown that enamines of the type **422** are smoothly converted into pyrroles **423** in the presence of 0.2 equiv. of $AgNO_3$ (Scheme 124). Only 5 mol% of silver nitrate is required for the synthesis of a wide range of isoquinolines and 1,6-naphthyridines **425** starting out from acetylenic imines **424**.[350] Among various electrophiles such as I_2, ICl, PhSeCl, and CuI used for this reaction, $AgNO_3$ was the most effective precatalyst.

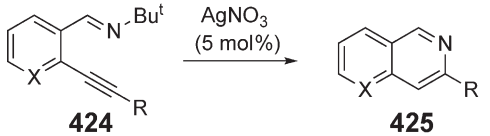
Silver carboxylates are well known to promote the Wolff rearrangement of diazoketones to generate ketene intermediates.[351] The subsequent trapping reaction of the latter depends on the presence of additional functionalities in the substrate, as well as on the reaction conditions, making the method highly prolific for the preparation of natural products and biologically active target molecules. Wang and Hou[352] have reported the cyclization of ketene intermediates **427** derived from diazo ketones **426** by silver-catalyzed Wolff rearrangement to produce pyrrolidinones **428** in high yields (Scheme 125). This transformation showed a strong solvent dependence, the heterocycles **428** being the sole reaction product in THF, whereas the use of methanol caused the formation of acyclic γ-amino esters.

Silver benzoate in methanol is also the catalyst of choice for the classical homologation of α-amino acids (and peptides) to the corresponding β-amino esters by Wolff rearrangement.[353] An interesting application in natural



422 423

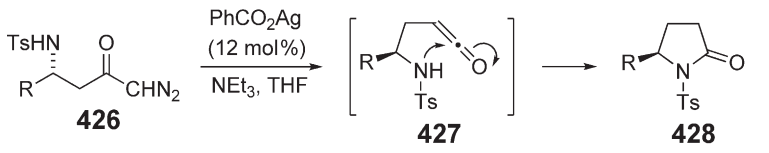
R	*Yield*(%)
Me	93
Bu^n	95
Ph	75



424 425

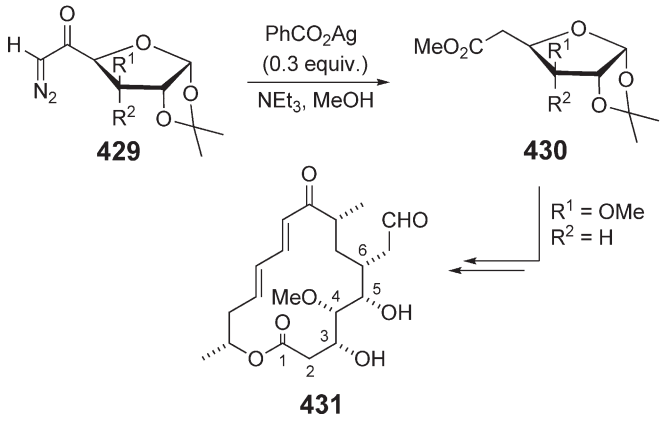
R	*X*	*Yield*(%)
Ph	CH	82
Cy	CH	75
CH_2CH_2OTHP	CH	62
Ph	N	92

Scheme 124



R	*Yield*(%)
H	93
Me	85
$PhCH_2$	86

Scheme 125



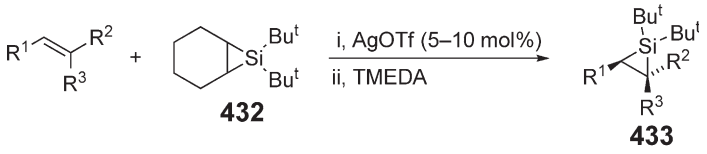
R^1	R^2	*Yield*(%)
OMe	H	78
OBn	H	66
H	OBn	70

Scheme 126

product synthesis is the transformation of the carbohydrate-derived diazo ketones **429** into the esters **430** which, however, required large amounts (0.3 equiv.) of silver benzoate (Scheme 126).[354] The method was used in the synthesis of the C1–C6 segment of carbonolide B **431**, the aglycone of the 16-membered macrolide antibiotic carbomycin B.

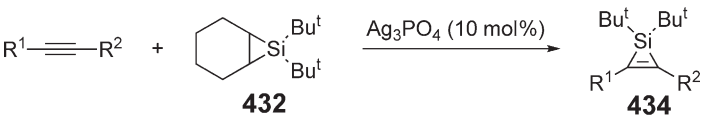
9.12.3.3 Cycloadditions

Silver compounds are versatile catalysts for various cycloaddition reactions, including [2 + 1]-, [2 + 2]-, [3 + 2]-, and [4 + 2]-cycloadditions. An example for the silver-catalyzed formation of three-membered rings by [2 + 1]-cycloaddition is the silacyclopropanation reaction of mono- and disubstituted alkenes by silylene transfer from the cyclohexene silacyclopropane **432** that was reported recently by Woerpel *et al.*[355,355a] (Scheme 127). The reaction tolerates a number of functionalities in the substrate (OBn, $OSiR_3$, Bu^tCO_2, etc.,) and is stereospecific with regard to the *cis*/*trans*



R^1	R^2	R^3	*Yield*(%)
Pr^i	H	H	99
$PhCH_2$	H	H	90
$BnOCH_2CH_2$	H	H	71
Me	Me	H	99
Me	H	Me	92

Scheme 127



R^1	R^2	*Yield*(%)
Ph	Me	91
$BnMeNCH_2$	H	97
$TIPSOCH_2$	Me	94

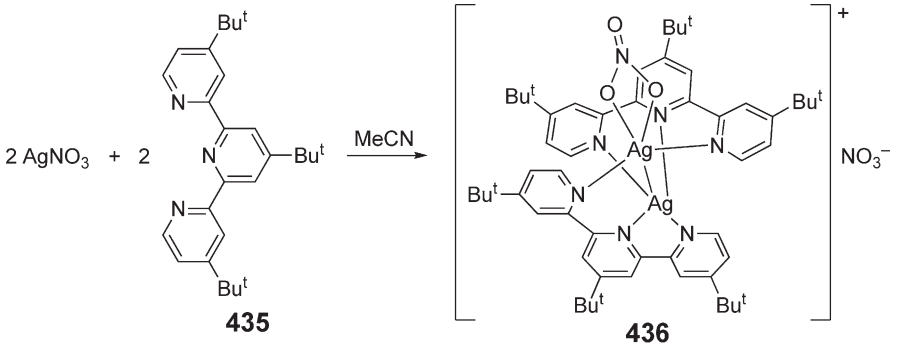
Scheme 128

configuration of the starting olefin and the silacyclopropane **433** formed. After complete transfer, TMEDA was added in order to sequester the catalyst and to prevent further reactions; alternatively, addition of zinc bromide and methyl formate induced a regioselective insertion of the latter into the silacyclopropane to afford oxasilacyclopentanes.

The analogous silacyclopropenation of alkynes with silylene transfer reagent **432** is catalyzed by Ag_3PO_4 (Scheme 128).[356] Again, the reaction is not affected by the presence of coordinating groups in the substrate. Addition of a copper salt and an aldehyde or ketone to the reaction mixture causes a regioselective carbonyl insertion into the more substituted C–Si bond of the silacyclopropene **434**.

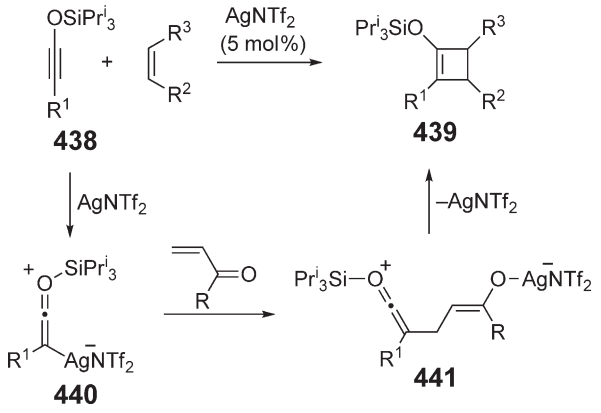
The aziridination of olefins with PhI = NTs as nitrene source was found to be smoothly catalyzed by a novel and unique disilver(I) complex $[Ag_2(Bu^t{}_3tpy)_2(NO_3)](NO_3)$ **436**.[357] This complex is easily prepared in good yield as pale yellow crystals by mixing equimolar amount of $AgNO_3$ and tri-*t*-butylterpyridine ($Bu^t{}_3tpy$, **435**) in CH_3CN solution and leaving the mixture at room temperature for 3 days (Scheme 129). The disilver(I) core is stabilized by the two Bu^t_3tpy ligands in different ways: one silver center is coordinated by four nitrogen atoms whereas the other is coordinated by two nitrogen atoms of the ligand and two nitrate oxygen atoms. The rather short Ag–Ag distance of 2.842 Å suggests a strong bonding interaction between the two metal ions. In the presence of complex **436**, a wide range of aziridines **437** was formed in good to high yields from mono- or disubstituted alkenes and PhI = NTs. Other silver salts such as AgOTf, $AgClO_4$, or $AgBF_4$ gave similar results. The mechanistic course of the reaction is not clear at present, but is believed to involve high-valent silver species as reactive intermediates. Very recently, complex **436** was found to catalyze the intramolecular amidation of C–H bonds as well.[358,358a]

An example for a silver-catalyzed [2 + 2]-cycloaddition was reported by Kozmin and co-workers.[359] Treatment of siloxyalkynes **438** with acceptor-substituted alkenes in the presence of 5 mol% of $AgNTf_2$ afforded the cyclobutenes **439** in good yields (Scheme 130). The use of cyclohex-2-enone allowed the preparation of the corresponding



R^1	R^2	*Yield*(%)
Bu^n	H	71
Ph	H	91
Ph	Me	90

Scheme 129



R^1	R^2	R^3	*Yield*(%)
Bu^n	H	COPh	90
Bu^n	H	CO_2Me	78
Bu^n	H	CN	69
Bn	$(CH_2)_3CO$		68
Ph	H	COMe	76

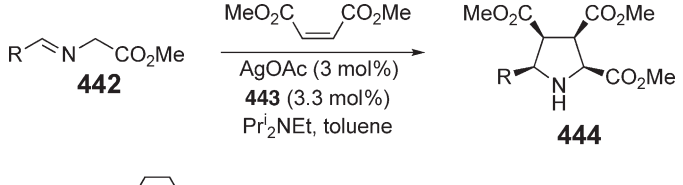
Scheme 130

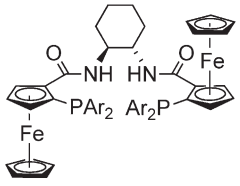
bicyclo[4.2.0]octene. Mechanistic studies by low-temperature NMR spectroscopy suggest an activation of the siloxyalkyne by the silver catalyst to produce a silver ketenium intermediate **440** that undergoes a 1,4-addition to the enone, followed by ring closure of the zwitterionic intermediate **441**.

In the area of [3 + 2]-cycloadditions (1,3-dipolar cycloadditions), chiral silver catalysts have been utilized extensively for the enantioselective formation of five-membered rings from prochiral substrates. For example, Zhang and co-workers[360] have reported the highly enantioselective Ag(I)-catalyzed [3 + 2]-cycloaddition of azomethine ylides to electron-deficient alkenes. Thus, reaction of α-imino esters **442** with dimethyl maleate in the presence of catalytic amounts of silver(I) acetate and the chiral bisferrocenyl amide phosphine **443** provided the chiral pyrrolidines **444** with high stereoselectivities and chemical yields (Scheme 131). Only the *endo*-products were isolated in all cases.

Related asymmetric [3 + 2]-cycloaddition reactions of azomethine ylides were developed by Schreiber *et al.*[361] as well as by Carreira and co-workers.[362,362a] Treatment of α-imino esters **445** with *t*-butyl acrylate in the presence of 3–10 mol% of AgOAc and (*S*)-QUINAP as chiral ligand afforded the corresponding pyrrolidines **446** in high yields and excellent levels of both enantio- and diastereoselectivity (Scheme 132).[361] This is the first general catalytic enantioselective [3 + 2]-cycloaddition that generates quaternary centers at the C2 position of the pyrrolidine ring. Other dipolarophiles reacted with reduced stereoselectivities. The analogous transformations with PINAP as chiral ligand gave similar results.[362,362a] Azlactones were also used as precursor for azomethine ylides in silver-catalyzed [3 + 2]-cycloadditions to acceptor-substituted alkenes,[363] but no enantioselective version of this transformation has been reported so far.

In the field of [4 + 2]-cycloadditions, silver catalysts have been used mainly for aza-Diels–Alder reactions of Danishefsky's diene **447** with various imines. Kobayashi and co-workers[364] have recently shown that this transformation can be carried out with catalytic amounts of silver(I) triflate in water (Scheme 133). Various aryl- or alkenyl-substituted pyridone derivatives **448** were obtained in high yields. A survey of other silver catalysts revealed that

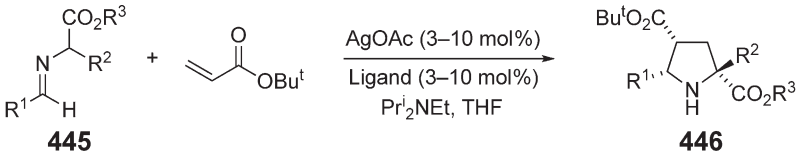


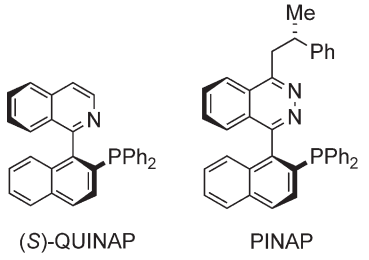


443 (Ar = 3,5-$Me_2C_6H_4$)

R	*Yield* (%)	ee(%)
Ph	87	87
3-Pyridyl	98	84
Pr^i	82	70

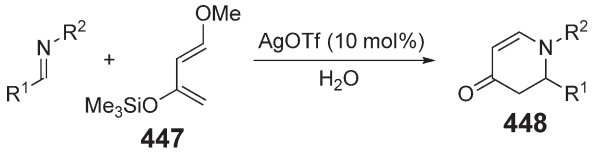
Scheme 131



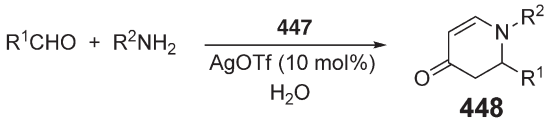


R^1	R^2	R^3	*Ligand* (%)	*Yield*(%)	ee(%)
4-$MeOC_6H_4$	H	Me	(S)-QUINAP	93	95
2-Naphtyl	H	Me	(S)-QUINAP	89	94
Ph	Me	Me	(S)-QUINAP	98	80
Ph	Bn	Me	(S)-QUINAP	93	77
4-NCC_6H_4	H	Et	PINAP	94	95
4-$MeOC_6H_4$	H	Et	PINAP	88	92

Scheme 132



R^1	R^2	*Yield*(%)
Ph	Ph	83
(*E*)-PhCH=CH–	Ph	92
Ph	4-BrC_6H_4	83



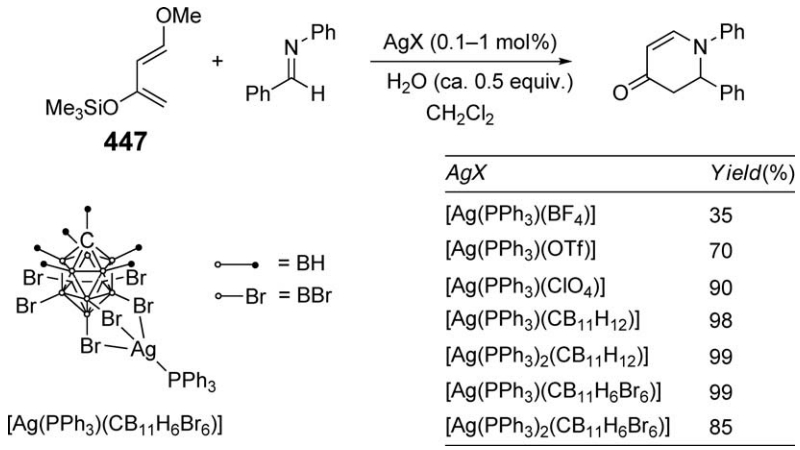
R^1	R^2	*Yield*(%)
Ph	4-BrC_6H_4	90
Cyclohexyl	Ph	70
Me_2CHCH_2	Ph	72

Scheme 133

$AgClO_4$ gives similar results, whereas $AgNO_3$, $AgSbF_6$, and $AgBF_4$ afforded lower yields of **448**, and Ag_2CO_3 as well as AgOAc gave no product at all. In addition, they have developed an efficient silver-catalyzed three-component aza-Diels–Alder reaction in water by starting out from an aldehyde and an amine that form the imine *in situ* in the presence of the diene **447**. This procedure is not only simpler, but also allows the preparation of pyridones **448** from unstable imines, for example, those derived from aliphatic aldehydes.

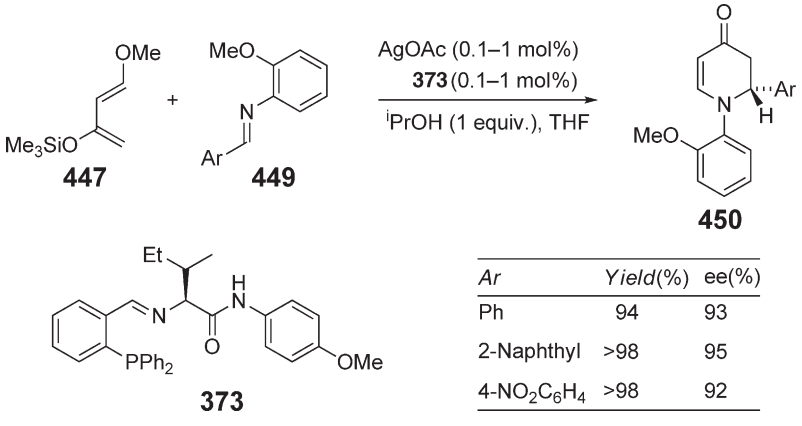
Silver catalysts with an extraordinarily high activity in the aza-Diels–Alder reaction of Danishefsky's diene with imines were recently reported by Weller and co-workers.[365] Reaction of silver salts with very weakly nucleophilic carborane anions and triphenylphosphine afforded the air-stable silver complexes $[Ag(PPh_3)_n(CB_{11}H_{12})]$ or $[Ag(PPh_3)_n(CB_{11}H_6Br_6)]$ ($n = 1, 2$)[366] that catalyze the aza-Diels–Alder reaction of N-benzylideneaniline with **447** with catalyst loadings of only 0.1–1 mol.% (Scheme 134). The most active of the silver catalysts examined is $[Ag(PPh_3)(CB_{11}H_6Br_6)]$ which gave a yield of 99% in less than 30 minutes with a loading of only 0.1 mol.%, indicating a turnover rate of $>2000\ h^{-1}$.

Enantioselective silver-catalyzed aza-Diels–Alder reactions have also been described. Whereas the use of BINAP as the chiral ligand gave only unsatisfactory enantioselectivities,[367,367a] Hoveyda *et al.*[368] used the peptidic phosphine **373** which has already been used for silver-catalyzed asymmetric Mannich reactions (see Scheme 108) in the efficient Ag(I)-catalyzed cycloaddition of arylimines **449** with Danishefsky's diene (Scheme 135). After acidic work-up, the chiral pyridones **450** were obtained with excellent yields and enantioselectivities. The presence of isopropanol as a proton source is essential for obtaining high conversions and stereoselectivities. Similar to the Mannich reactions, the cycloaddition is not affected by the presence of air or the use of undistilled THF.



AgX	*Yield*(%)
$[Ag(PPh_3)(BF_4)]$	35
$[Ag(PPh_3)(OTf)]$	70
$[Ag(PPh_3)(ClO_4)]$	90
$[Ag(PPh_3)(CB_{11}H_{12})]$	98
$[Ag(PPh_3)_2(CB_{11}H_{12})]$	99
$[Ag(PPh_3)(CB_{11}H_6Br_6)]$	99
$[Ag(PPh_3)_2(CB_{11}H_6Br_6)]$	85

Scheme 134



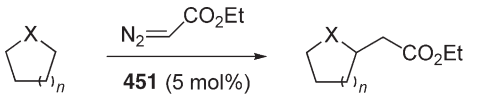
Ar	*Yield*(%)	ee(%)
Ph	94	93
2-Naphthyl	>98	95
$4\text{-}NO_2C_6H_4$	>98	92

Scheme 135

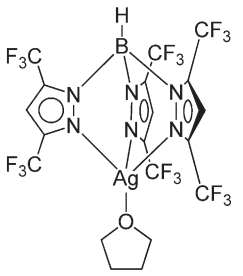
9.12.3.4 Other Reactions

In a series of papers, Dias, Lovey and co-workers have shown that the silver(I) complex $[HB(3,5\text{-}\{CF_3\}_2Pz)_3]Ag(THF)$ **451** is an efficient catalyst for the carbene insertion into C–H and C–C bonds of various substrates. The silver center in **451** is stabilized by the coordination of three nitrogen atoms of the tris(pyrazolyl)borate ligands and the THF oxygen atom. It is easily prepared from $[HB(3,5\text{-}\{CF_3\}_2Pz)_3]Na$ and AgOTf in THF solution[369,369a] and shows a good solubility in common organic solvents. Whereas the carbene insertion into C–H bonds of alkyl halides with ethyl diazoacetate as carbene source[370] is of limited interest since the products can be obtained easily by conventional methods, the corresponding C–H insertion of cyclic or acyclic hydrocarbons or heterocycles[371] might also be of use in target-oriented synthesis. For example, reaction of cyclopentane or cyclohexane with ethyl diazoacetate in the presence of 5 mol.% of **451** furnished the corresponding ethyl cycloalkylacetates with good yields (Scheme 136). In the case of heterocyclic substrates like tetrahydrofuran, however, the yields were relatively low. In a related study, Sulikowski *et al.*[372,372a] investigated an intramolecular stereoselective carbene C–H insertion in the presence of $AgSbF_6$ and chiral bisoxazolines. The first example of a silver-catalyzed enantioselective carbene insertion reaction into N–H bonds was recently reported by Jørgensen and co-workers,[373] giving the insertion product of aniline and ethyl diazoacetate with up to 48% ee, but only 5% chemical yield.

Li and co-workers[374,374a] reported the three-component coupling reaction of an aldehyde, an amine, and a terminal alkyne catalyzed by a silver salt in water. Of various precatalysts examined, water-insoluble silver iodide gave the highest yields of the propargyl amines **452** (Scheme 137). The reaction probably proceeds via attack of a silver acetylide, generated *in situ* from the silver salt and the alkyne, to the iminium ion derived from the aldehyde and the

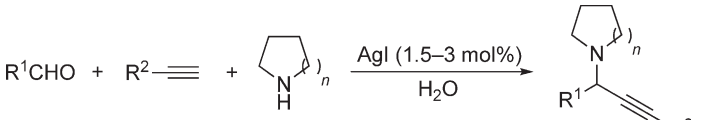


X	n	Yield(%)
CH_2	1	88
CH_2	2	88
O	2	41



451

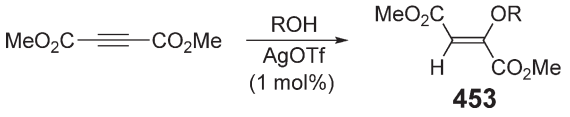
Scheme 136



452

R^1	R^2	n	Yield(%)
Cyclohexyl	Ph	1	99
Cyclohexyl	Ph	3	96
Cyclohexyl	Et_3Si	2	64
$^nC_{10}H_{21}$	Ph	2	79

Scheme 137



453

ROH	Yield
MeOH	Quant.
Pr^iOH	87%
$PhCH_2OH$	86%

Scheme 138

amine. Gold precatalysts have also been used successfully in this transformation (see Section 9.12.4.1). In an analogous fashion, Chan *et al.*[375] obtained various acetylenic α-amino acid derivatives by AgOTf-catalyzed addition of terminal alkynes to α-imino esters.

Tani and co-workers[376] have reported the use of catalytic amounts of silver(I) triflate for the activation of electron-deficient alkynes (e.g., dimethyl acetylenedicarboxylate) toward a nucleophilic attack of alcohols, affording the *trans*-addition products **453** with high yields (Scheme 138). Other silver salts ($AgPF_6$, $AgBF_4$, $AgClO_4$, and $AgNO_3$) gave similar results whereas AgCl and Ag_2CO_3 were ineffective. The corresponding reaction of methyl tridec-2-ynoate with methanol furnished a mixture of the mono- and bisaddition product. Gold precatalysts have also been used for the activation of alkynes (see Section 9.12.4.2).

9.12.4 Gold

Unlike the other coin metals, gold is still rarely used in preparative organic chemistry. Applications of gold and gold salts in heterogeneous catalysis evolved at the beginning of the last century, and nowadays they belong to the most active catalysts for diverse reactions such as the low-temperature oxidation of carbon monoxide and the hydrochlorination of ethyne.[377,377a–377c] In contrast, the benefits of gold as a homogeneous catalyst for the synthesis of fine chemicals have emerged only in the last 5 years.[378–381] The major virtue of gold salts in homogeneous catalysis is

their unique ability to activate C–C multiple bonds as soft, carbophilic Lewis acids, allowing the formation of new C–C, C–O, C–N, and C–S bonds by nucleophilic attack at these activated substrates. Furthermore, gold is an excellent catalyst for the activation of C–H bonds, for example, of aromatic compounds, thereby opening again an unprecedented pathway for carbon–carbon bond formation. In many cases, both Au(I) and Au(III) salts can be used as precatalysts for the same transformation, and it is not clear what the oxidation state of the catalytically active species might be. The fact that gold compounds are easily reduced but hard to oxidize makes it tempting to assume that gold(I) catalysts are operative in most transformations, even if a gold(III) precatalyst is used.

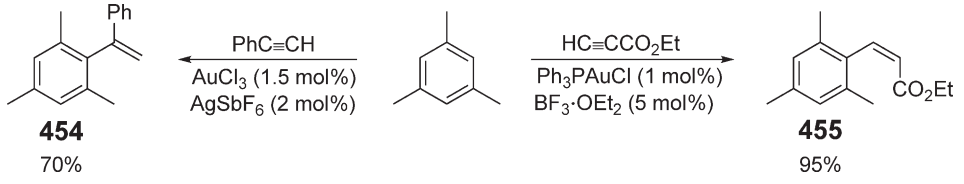
9.12.4.1 C–H Bond Activation

Gold(I) and gold(III) salts are able to activate C–H bonds of terminal alkynes, arenes, and β-dicarbonyl compounds, thus forming nucleophiles which can react with various electrophiles. The latter can also be activated by the Lewis-acidic gold catalyst which therefore might play a dual role in these transformations.[378–381] A typical example is the hydroarylation of alkynes reported by Reetz and Sommer[382] (Scheme 139). Whereas gold(III) chloride is the most active precatalyst for the reaction of mesitylene and other benzene derivatives with electron-rich acetylenes, the gold(I) complex Ph_3PAuCl is preferable for the hydroarylation of electron-poor alkynes. In both cases, the presence of silver salts or boron trifluoride etherate as a co-catalyst is required in order to achieve good yields, probably by inducing cationization of the gold precatalyst.

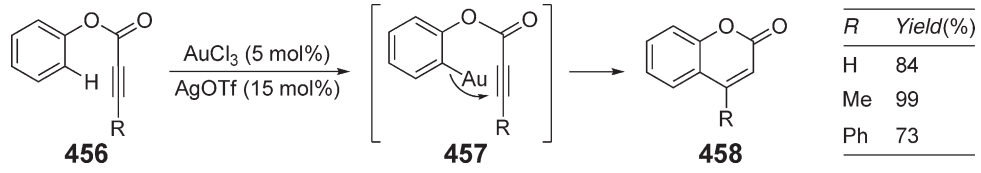
Interestingly, phenylacetylene and other terminal, electron-rich alkynes provide 1,1-disubstituted olefins of the type **454** exclusively, whereas the inverse regioselectivity in favor of product **455** is observed for ethyl propiolate. Although these authors doubt the involvement of arene auration as part of the hydroarylation process, spectroscopic and isotope-labeling experiments carried out by Shi and He[383] indicate the presence of an arenegold intermediate of the type **457**, and the addition to the alkyne could be aided by Lewis acid-activation of the triple bond (see Section 9.12.4.3). Intramolecular hydroarylations of substrates of the type **456**, catalyzed by $AuCl_3$ and AgOTf, leading to coumarins **458** have also been reported (Scheme 140).

Besides substituted benzenes, indoles also undergo gold-catalyzed C–H bond activation with subsequent addition of the aurated heterocycles to enones.[384] Moreover, imines and oxiranes can be used instead of alkenes and alkynes as reaction partners for the arenegold intermediates (Scheme 141). Thus, treatment of (phenoxymethyl)oxiranes (e.g., **459**) with gold(III) chloride and silver triflate induced a cycloalkylation to give 3-chromanols of the type **460** with high yield,[385,385a] whereas benzylamines (e.g., **462**) are formed under the same conditions by addition of arenes of the type **461** to imines.[386] Again, the gold catalyst might also act as a Lewis-acidic activator of the electrophile.

Further examples involving the C–H bond activation of substrates other than arenes were recently reported by Wei and Li[387] (Scheme 142). Thus, the three-component coupling of an aldehyde, a secondary amine, and a terminal alkyne (e.g., phenylacetylene) to furnish propargyl amines **463** (cf. Scheme 137) proved to be equally well catalyzed by gold(I) and gold(III) halides in water, indicating that Au(I) is the catalytically active species even if a gold(III) salt is used as the precatalyst. In contrast to this, the well-established bimetallic system $AuCl_3$/AgOTf was found to

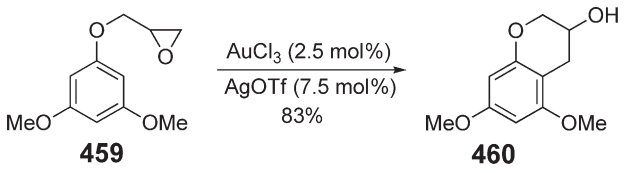


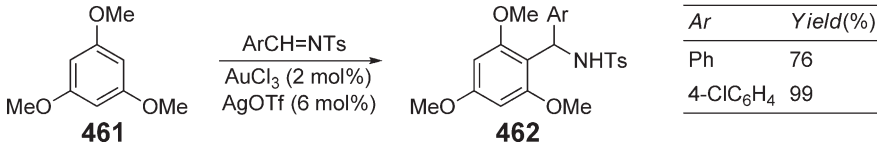
Scheme 139



R	*Yield*(%)
H	84
Me	99
Ph	73

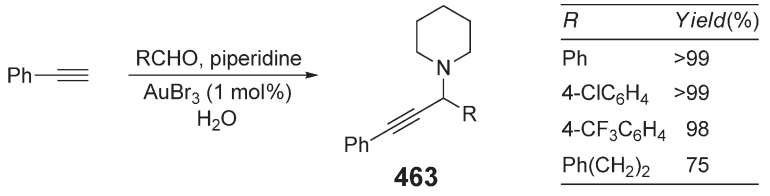
Scheme 140



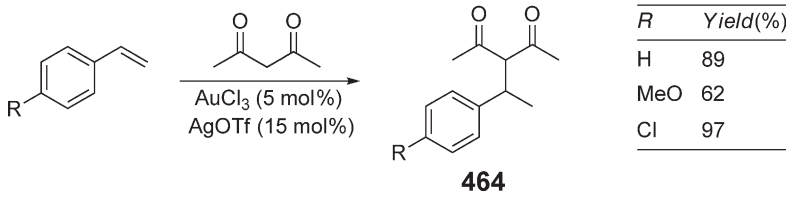


Ar	*Yield*(%)
Ph	76
4-ClC_6H_4	99

Scheme 141



R	*Yield*(%)
Ph	>99
4-ClC_6H_4	>99
4-$CF_3C_6H_4$	98
$Ph(CH_2)_2$	75



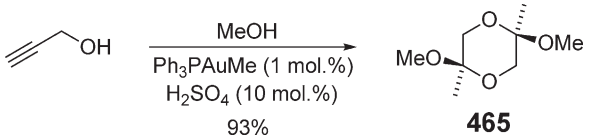
R	*Yield*(%)
H	89
MeO	62
Cl	97

Scheme 142

efficiently promote the regioselective addition of various β-diketones to styrenes, leading to 1,1-disubstituted ethanes **464** in good to excellent yield.[388]

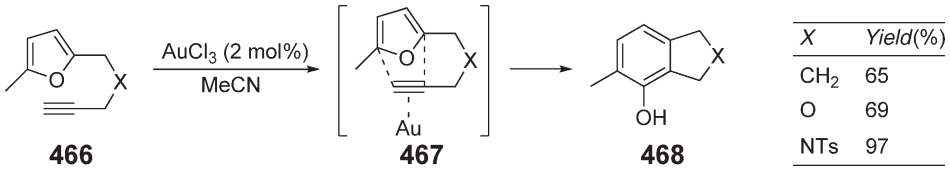
9.12.4.2 Activation of Alkynes

The activation of alkynes with carbophilic, Lewis-acidic gold salts is the most widespread application of homogeneous gold catalysis. In their seminal paper that had been crucial for the recognition of gold catalysis as a tool for organic synthesis, Teles and co-workers[389,389a–389d] showed that cationic gold(I) catalysts are highly efficient catalysts for the nucleophilic addition of alcohols to alkynes. These catalysts are obtained by treating methyl gold complexes LAuMe (L = phosphine, phosphite, or arsine) with mineral acids, or by reacting gold halide complexes LAuX with silver salts or boron trifluoride etherate. In contrast to the corresponding silver-catalyzed transformation which is only applicable to electron-deficient alkynes (see Scheme 138), electron-rich mono- or dialkyl-substituted alkynes are converted into acetals with high turnover numbers and frequencies in the presence of these cationic gold catalysts. Likewise, treatment of propargyl alcohol with methanol under these conditions affords the cyclic bisacetal **465** with 93% yield in the presence of just 1 mol.% of Ph_3PAuMe (Equation (23)).



(23)

The activation of alkynes by gold catalysts is also utilized for the preparation of aromatic, as well as heterocyclic, target molecules. For example, Hashmi *et al.*[390,390a–390d] have shown that various furans **466** can be isomerized to



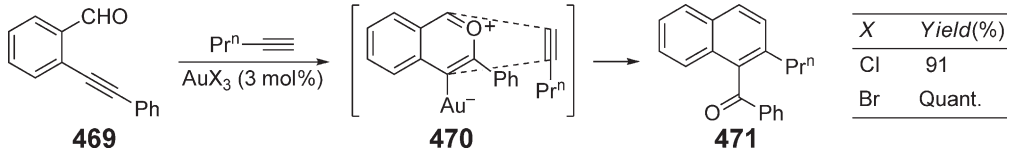
X	Yield(%)
CH_2	65
O	69
NTs	97

Scheme 143

phenols **468** in the presence of catalytic amounts of gold(III) chloride in acetonitrile (Scheme 143). The reaction is probably initiated by the coordination of the gold catalyst to the triple bond to give intermediate **467**, thus providing by electrophilic activation the driving force required for an intramolecular Diels–Alder reaction and subsequent C–O bond cleavage. Among several applications of this method,[390,390a–390d] the synthesis of the sesquiterpenes junganiol and *epi*-junganiol should be noted.[391]

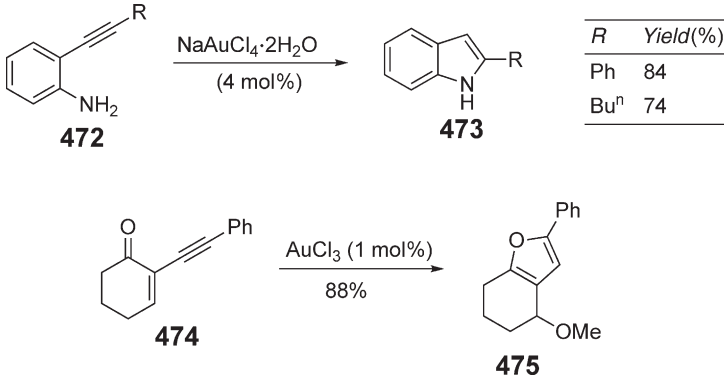
A related benzannulation process was recently reported by Asao, Yamamoto, and co-workers[392,392a,392b] who transformed 2-alkynylbenzaldehydes of the type **469** into naphthalene derivatives (e.g., **471**) by gold-catalyzed intermolecular [4 + 2]-cycloaddition with an alkyne (Scheme 144). Again, activation of the triple bond of the substrate **469** by the gold catalyst is believed to be essential for the subsequent intramolecular attack of the aldehyde oxygen atom; the zwitterionic intermediate **470** thus formed may then act as the diene component in a Diels–Alder reaction with the external alkyne. Interestingly, $AuBr_3$ is slightly more efficient than $AuCl_3$ in this transformation. The authors also reported several variations of the method,[393,393a] including the use of enols as the dienophile in the cycloaddition.

The gold-mediated activation of alkynes is very prolific for the synthesis of heterocycles as well.[394–397] For example, Arcadi *et al.* have reported several examples for the gold-catalyzed preparation of N-heterocycles,[394,394a,394b] including the cycloisomerization of 2-alkynylanilines **472** to indoles **473** (Scheme 145).[395] Here, sodium tetrachloroaurate and gold(I) chloride are much more effective than palladium, platinum, and copper precatalysts. A gold-catalyzed nucleophilic addition/cyclization sequence of 2-alkynyl-2-enones (e.g., **474**) to furans of the type **475** was recently reported by Larock and co-workers.[396] Although it is not yet clear whether this transformation proceeds via a Michael addition and subsequent cyclization or vice versa, the electrophilic activation of the triple bond by the carbophilic gold catalyst seems to be the crucial step, once again. Gratifyingly, many different, highly functionalized enones and nucleophiles can be employed in this process, including carbon



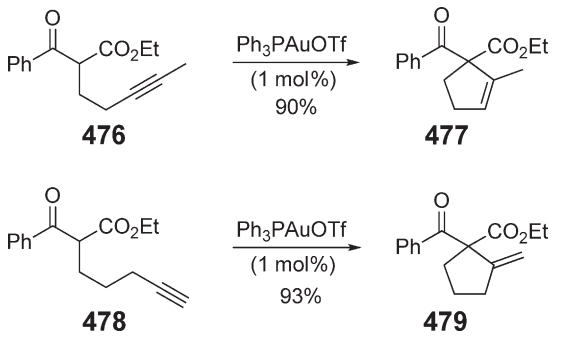
X	Yield(%)
Cl	91
Br	Quant.

Scheme 144



R	Yield(%)
Ph	84
Bu^n	74

Scheme 145



Scheme 146

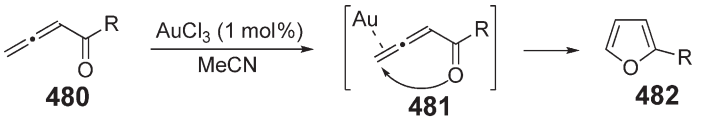
nucleophiles like N,N-dimethylaniline or indole. In a similar fashion, propargyl oxiranes can be isomerized to furans with catalytic amounts of $AuCl_3$.[397]

Gold(I) complexes are also the catalysts of choice for carbocyclization reactions of alkynes (Scheme 146). Thus, treatment of the acetylenic β-ketoester **476** with catalytic amounts of Ph_3PAuCl induced a 5-*endo-dig* cyclization to the cyclopentene derivative **477**, whereas the isomeric substrate **478** furnished the 5-*exo-dig* cyclization product **479**.[398,398a–398c] Isotopic labeling experiments again favor a mechanistic model involving activation of the triple bond by the Lewis-acidic gold catalyst. In a similar fashion, gold(I) salts catalyze various cyclization reactions of enynes.[399,399a–399e]

9.12.4.3 Activation of Allenes

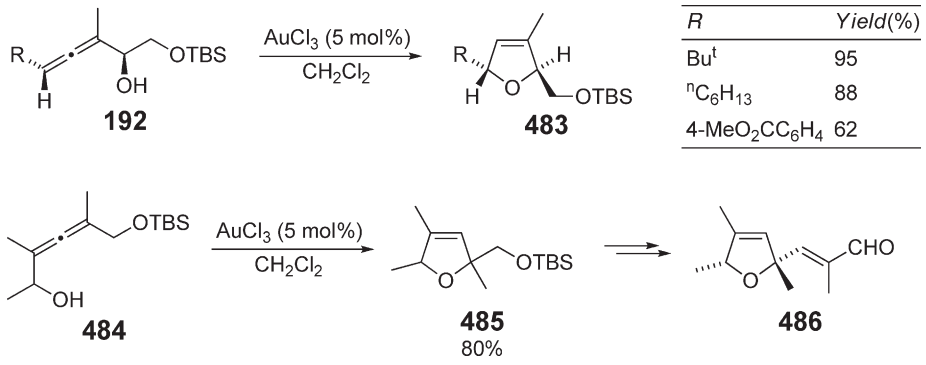
The activation of allenes is a rather new, but particularly promising area of gold catalysis.[381,400] The first example for such a transformation is the cycloisomerization of allenic ketones **480** to furans **482** which probably occurs via intermediate **481** (Scheme 147). Hashmi *et al.*[401,401a] showed that this reaction proceeds much faster when gold(III) chloride in acetonitrile is employed as the precatalyst instead of the traditionally used silver salts (cf. Section 9.12.3.2). The products are usually contaminated by substituted furans originating from a Michael addition of aurated **482** to the substrates **480**, thereby indicating that the gold catalyst is also capable to activate C–H bonds of furans.

As most applications of homogeneous gold catalysis described so far, this reaction provides achiral products and therefore does not take advantage of the inherent chirality of the substrate. However, the use of chiral allenes has recently opened a third dimension to gold catalysis, for example, by employing α-hydroxyallenes **192** (cf. Scheme 47) as substrates for the gold-catalyzed cycloisomerization to 2,5-dihydrofurans **483** (Scheme 148).[74,75] Similar to the corresponding cyclization of allenic ketones **480**, the use of the gold catalyst results in much higher reaction rates than those achievable with silver salts (see Section 9.12.3.2). Since this transformation takes place with complete axis-to-center chirality transfer, it is ideally suited for application in target-oriented stereoselective synthesis. For example, the gold chloride-catalyzed cycloisomerization of the α-hydroxyallene **484** readily



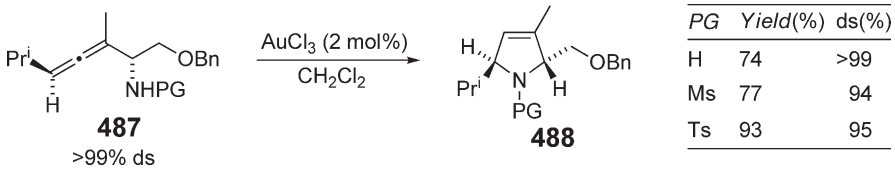
R	*Yield*(%)
Me	47
4-$O_2NC_6H_4$	88
4-$MeOC_6H_4CH_2$	60

Scheme 147



R	*Yield*(%)
Bu^t	95
$^nC_6H_{13}$	88
4-$MeO_2CC_6H_4$	62

Scheme 148



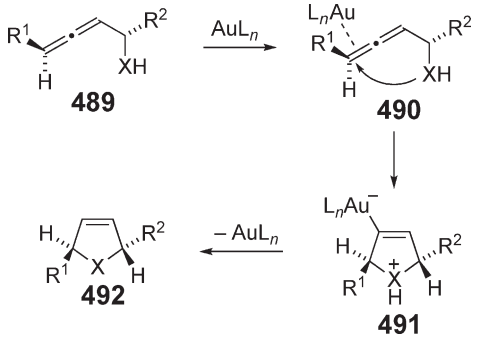
PG	*Yield*(%)	ds(%)
H	74	>99
Ms	77	94
Ts	93	95

Scheme 149

provides the dihydrofuran **485** which can be converted into citreoviral **486**, a metabolite and synthetic precursor of the mycotoxin citreoviridin.[74]

Gratifyingly, the method is not limited to α-hydroxyallenes, since the corresponding α-aminoallenes **487** can also be cyclized smoothly to 3-pyrrolines **488** in the presence of catalytic amounts of $AuCl_3$ (Scheme 149).[402] In this case, however, the reactivity and degree of chirality transfer strongly depend upon the N-protecting group, and only the unprotected aminoallene afforded the diastereomerically pure 3-pyrroline. Since this structural element is frequently found in the natural products of various biological activities, new avenues in natural product chemistry are opened with the gold-catalyzed cycloisomerization.

What is the mechanistic origin of the high reactivity and stereoselectivity observed in these transformations? Although it is not clear at present whether the catalytically active species is a gold(I) or a gold(III) intermediate, it seems reasonable to assume that the key is once again the ability of the gold catalyst to act as soft, carbophilic Lewis acid which enables it to coordinate to an allenic double bond of the substrate **489** and to form a π-complex **490** (Scheme 150). As a consequence of the increased electrophilicity, cyclization via an S_N2 type transition state and subsequent protodemetallation of the σ-gold species **491** produces the heterocyclic product **492** with complete axis-to-center chirality transfer, releasing the gold catalyst into the catalytic cycle.[381]



Scheme 150

References

1. Grohmann, A.; Schmidbaur, H. Gold. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 3, pp 1–56.
2. Van Koten, G.; James, S. L.; Jastrzebski, J. T. B. H. Copper and Silver. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 3, pp 57–133.
3. Lipshutz, B. H. Transition Metal Alkyl Complexes from RLi and CuX. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 12, pp 59–130.
4. Lipshutz, B. H. Synthetic Procedures Involving Organocopper Reagents. In *Organometallics in Synthesis*; Schlosser, M., Ed.; Wiley: Chichester, 1994; pp 283–382.
5. Lipshutz, B. H.; Bhandari, A.; Lindsey, C.; Keil, R.; Wood, M. R. *Pure Appl. Chem.* **1994**, *66*, 1493–1500.
6. Lipshutz, B. H. Recent Progress in Higher Order Cyanocuprate Chemistry. In *Advances in Metal-organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, 1995; Vol. 4, pp 1–64.
7. Krause, N.; Gerold, A. *Angew. Chem.* **1997**, *109*, 194–213.

7a. Krause, N.; Gerold, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 186–204.

8. Lipshutz, B. H. *Acc. Chem. Res.* **1997**, *30*, 277–282.
9. Fredrick, M. A.; Hulce, M. *Tetrahedron* **1997**, *53*, 10197–10227.
10. Krause, N. *Angew. Chem.* **1998**, *110*, 295–297.

10a. Krause, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 283–285.

11. Krause, N. *Angew. Chem.* **1999**, *111*, 83–85.

11a. Krause, N. *Angew. Chem. Int. Ed.* **1999**, *38*, 79–81.

12. Krause, N.; Thorand, S. *Inorg. Chim. Acta* **1999**, *296*, 1–11.
13. Woodward, S. *Chem. Soc. Rev.* **2000**, *29*, 393–401.
14. Krause, N.; Zelder, C. Nucleophilic Additions to Dienes, Enynes and Polyenes. In *The Chemistry of Dienes and Polyenes*; Rappoport, Z., Ed.; Wiley: New York, 2000; Vol. 2, pp 645–691.
15. Krause, N. (Ed.) *Organocopper Chemistry II (Tetrahedron Symposium-in-Print Number 78), Tetrahedron* **2000**, *56*, 2727–2903.
16. Nakamura, E.; Mori, S. *Angew. Chem.* **2000**, *112*, 3902–3924.

16a. Nakamura, E.; Mori, S. *Angew. Chem. Int. Ed.* **2000**, *39*, 3750–3771.

17. Krause, N.; Hoffmann-Röder, A. *Synthesis* **2001**, 171–196.
18. Lipshutz, B. H. Organocopper Chemistry. In *Organometallics in Synthesis. A Manual*; Schlosser, M., Ed.; Wiley: Chichester, 2002; pp 665–815.
19. Ley, S. V.; Thomas, A. W. *Angew. Chem.* **2003**, *115*, 5558–5607.
20. Barbero, A.; Pulido, F. J. *Acc. Chem. Res.* **2004**, *37*, 817–825.
21. Taylor, R. J. K., Ed., *Organocopper Reagents: A Practical Approach*, Oxford University Press: Oxford, 1994.
22. Ibuka, T. *Organocopper Reagents in Organic Synthesis;* Camellia and Rose Press: Osaka, **2000**.
23. Krause, N., Ed., *Modern Organocopper Chemistry*, Wiley-VCH: Weinheim, 2002.
24. Gilman, H.; Straley, J. M. *Recl. Trav. Chim. Pays-Bas* **1936**, *55*, 821–834.

24a. Gilman, H.; Jones, R. G.; Woods, L. A. *J. Org. Chem.* **1952**, *17*, 1630–1634.

25. Knochel, P.; Betzemeier, B. Transmetalation Reactions Producing Organocopper Reagents. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 45–78.
26. Rottländer, M.; Boymond, L.; Bérillon, L.; Lepretre, A.; Varchi, G.; Avolio, S.; Laaziri, H.; Quéguiner, G.; Ricci, A.; Cahiez, G.; Knochel, P. *Chem. Eur. J.* **2000**, *6*, 767–770.

26a. Boudier, A.; Bromm, L. A.; Lotz, M.; Knochel, P. *Angew. Chem.* **2000**, *112*, 4584–4606.

26b. Boudier, A.; Bromm, L. A.; Lotz, M.; Knochel, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 4414–4435.

26c. Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem.* **2003**, *115*, 4438–4456.

26d. Knochel, P.; Dohle, W.; Gommermann, N.; Kneisel, F.; Kopp, F.; Korn, T.; Sapountzis, I.; Vu, V. A. *Angew. Chem. Int. Ed.* **2003**, *42*, 4302–4320.

27. Abarbri, M.; Dehmel, F.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 7499–7453.
28. Abarbri, M.; Thibonnet, J.; Berillon, L.; Dehmel, F.; Rottländer, M.; Knochel, P. *J. Org. Chem.* **2000**, *65*, 4618–4634.
29. Varchi, G.; Kofink, C.; Lindsay, D. M.; Ricci, A.; Knochel, P. *Chem. Commun.* **2003**, 396–397.
30. Krasovskiy, A.; Knochel, P. *Angew. Chem.* **2004**, *116*, 3396–3399.

30a. Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 3333–3336.

31. Knochel, P. *Synlett* **1995**, 393–403.

31a. Knochel, P.; Almena Perea, J. J.; Jones, P. *Tetrahedron* **1998**, 8275–8317.

32. Stadtmüller, H.; Vaupel, A.; Tucker, C. E.; Stüdemann, T.; Knochel, P. *Chem. Eur. J.* **1996**, *2*, 1204–1220.
33. Vaupel, A.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 8349–8352.

33a. Vaupel, A.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 5743–5753.

34. Langer, F.; Devasagayaraj, A.; Chavant, P.-Y.; Knochel, P. *Synlett* **1994**, 410–412.

34a. Langer, F.; Schwink, L.; Devasagayaraj, A.; Chavant, P.-Y.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 8229–8243.

35. Boudier, A.; Hupe, E.; Knochel, P. *Angew. Chem.* **2000**, *112*, 2396–2399.

35a. Boudier, A.; Hupe, E.; Knochel, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 2294–2297.

36. Boudier, A.; Flachsmann, F.; Knochel, P. *Synlett* **1998**, 1438–1440.
37. Wipf, P.; Jahn, H. *Tetrahedron* **1996**, *52*, 12853–12910.
38. Takahashi, T.; Kotora, M.; Xi, Z. *Chem. Commun.* **1995**, 361–362.

38a. Takahashi, T.; Xi, Z.; Yamazaki, A.; Liu, Y.; Nakajima, K.; Kotora, M. *J. Am. Chem. Soc.* **1998**, *120*, 1672–1680.

39. Xi, C.; Kotora, M.; Nakajima, K.; Takahashi, T. *J. Org. Chem.* **2000**, *65*, 945–950.
40. Xi, C.; Kotora, M.; Takahashi, T. *Tetrahedron Lett.* **1999**, *40*, 2375–2378.
41. Piazza, C.; Knochel, P. *Angew. Chem.* **2002**, *114*, 3397–3399.

41a. Piazza, C.; Knochel, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 3263–3265.

41b. Kondo, Y.; Matsudaira, T.; Sato, J.; Murata, N.; Sakamoto, T. *Angew. Chem.* **1996**, *108*, 818–820.

41c. Kondo, Y.; Matsudaira, T.; Sato, J.; Murata, N.; Sakamoto, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 736–738.

42. Yang, X.; Rotter, T.; Piazza, C.; Knochel, P. *Org. Lett.* **2003**, *5*, 1229–1231.
43. Dieter, R. K. Heteroatomcuprates and α-Heteroatomalkylcuprates in Organic Synthesis. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 79–144.
44. Dieter, R. K.; Alexander, C. W.; Nice, L. E. *Tetrahedron* **2000**, *56*, 2767–2778.
44a. Dieter, R. K.; Topping, C. M.; Nice, L. E. *J. Org. Chem.* **2001**, *66*, 2302–2311.
45. Tomoyasu, T.; Tomooka, K.; Nakai, T. *Tetrahedron Lett.* **2000**, *41*, 345–349.
45a. Dieter, R. K.; Topping, C. M.; Chandupatla, K. R.; Lu, K. *J. Am. Chem. Soc.* **2001**, *123*, 5132–5133.
45b. Dieter, R. K.; Oba, G.; Chandupatla, K. R.; Topping, C. M.; Lu, K.; Watson, R. T. *J. Org. Chem.* **2004**, *69*, 3076–3086.
45c. Dieter, R. K.; Watson, R. T.; Goswami, R. *Org. Lett.* **2004**, *6*, 253–256.
46. Dieter, R. K.; Velu, S. E. *J. Org. Chem.* **1997**, *62*, 3798–3799.
46a. Dieter, R. K.; Lu, K.; Velu, S. E. *J. Org. Chem.* **2000**, *65*, 8715–8724.
47. Dieter, R. K.; Lu, K. *Tetrahedron Lett.* **1999**, *40*, 4011–4014.
48. Dieter, R. K.; Yu, H. *Org. Lett.* **2000**, *2*, 2283–2286.
49. Dieter, R. K.; Lu, K. *J. Org. Chem.* **2002**, *67*, 847–855.
50. Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771–806.
50a. Alexakis, A. Asymmetric Conjugate Addition. In *Organocopper Reagents: A Practical Approach*; Taylor, R. J. K., Ed.; Oxford University Press: Oxford, 1994; pp 159–183.
50b. Leonard, J.; Diez-Barra, E.; Merino, S. *Eur. J. Org. Chem.* **1998**, 2051–2061.
51. Fleming, I. Synthetic Application of Silylcuprates and Stannylcuprates. In *Organocopper Reagents: A Practical Approach*; Taylor, R. J. K., Ed.; Oxford University Press: Oxford, 1994; pp 257–292.
52. Dambacher, J.; Bergdahl, M. *Chem. Commun.* **2003**, 144–145.
53. Fleming, I.; Henning, R.; Parker, D. C.; Plaut, H. E.; Sanderson, P. E. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 317–337.
53a. Fleming, I. *Chemtracts, Org. Chem.* **1996**, *9*, 1–64.
53b. Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662.
54. Schabbert, S.; Tiedemann, R.; Schaumann, E. *Liebigs Ann. Recl.* **1997**, 879–880.
55. Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063–2192.
56. Chow, H.-F.; Fleming, I. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2651–2662.
57. Fleming, I.; Lee, D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2701–2709.
58. Lee, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2001**, *123*, 1872–1877.
58a. Lee, T. W.; Corey, E. J. *Org. Lett.* **2001**, *3*, 3337–3339.
59. Reginato, G.; Capperucci, A.; Degl'Innocenti, A.; Mordini, A.; Pecchi, S. *Tetrahedron* **1995**, *51*, 2129–2136.
60. Reginato, G.; Mordini, A.; Degl'Innocenti, A.; Manganiello, S.; Capperucci, A.; Poli, G. *Tetrahedron* **1998**, *54*, 10227–10238.
60a. Krief, A.; Provins, L.; Dumont, W. *Angew. Chem.* **1999**, *111*, 2123–2126.
60b. Krief, A.; Provins, L.; Dumont, W. *Angew. Chem. Int. Ed.* **1999**, *38*, 1946–1948.
61. Thibonnet, J.; Launay, V.; Abarbri, M.; Duchene, A.; Parrain, J.-L. *Tetrahedron Lett.* **1998**, *39*, 4277–4280.
61a. Thibonnet, J.; Abarbri, M.; Duchene, A.; Parrain, J.-L. *Synlett* **1999**, 141–143.
62. Piers, E.; McEachern, E. J.; Romero, M. A.; Gladstone, P. L. *Can. J. Chem.* **1997**, *75*, 694–701.
62a. Piers, E.; Boehringer, E. M.; Yee, J. G. K. *J. Org. Chem.* **1998**, *63*, 8642–8643.
63. Piers, E.; McEachern, E. J.; Burns, P. A. *Tetrahedron* **2000**, *56*, 2753–2765.
64. Krause, N.; Hoffmann-Röder, A. Copper-mediated Addition and Substitution Reactions of Extended Multiple Bond Systems. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 145–166.
65. Krause, N.; Hoffmann-Röder, A. *Tetrahedron* **2004**, *60*, 11671–11694.
66. Uerdingen, M.; Krause, N. *Tetrahedron* **2000**, *56*, 2799–2804.
67. Bennani, Y. *J. Org. Chem.* **1996**, *61*, 3542–3544.
68. Hohmann, M.; Krause, N. *Chem. Ber.* **1995**, *128*, 851–860.
69. Gerold, A.; Krause, N. *Chem. Ber.* **1994**, *127*, 1547–1549.
70. Koop, U.; Handke, G.; Krause, N. *Liebigs Ann.* **1996**, 1487–1499.
71. Laux, M.; Krause, N.; Koop, U. *Synlett* **1996**, 87–88.
72. Becker, M.; Krause, N. *Liebigs Ann. Recl.* **1997**, 725–728.
73. Krause, N.; Laux, M.; Hoffmann-Röder, A. *Tetrahedron Lett.* **2000**, *41*, 9613–9616.
74. Krause, N.; Hoffmann-Röder, A.; Canisius, J. *Synthesis* **2002**, 1759–1774.
75. Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537–2538.
76. Krause, N.; Wagner, R.; Gerold, A. *J. Am. Chem. Soc.* **1994**, *116*, 381–382.
77. Canisius, J.; Mobley, T. A.; Berger, S.; Krause, N. *Chem. Eur. J.* **2001**, *7*, 2671–2675.
78. Mori, S.; Uerdingen, M.; Krause, N.; Morokuma, K. *Angew. Chem.* **2005**, *117*, 4795–4798.
78a. Mori, S.; Uerdingen, M.; Krause, N.; Morokuma, K. *Angew. Chem. Int. Ed.* **2005**, *44*, 4715–4719.
79. Canisius, J.; Gerold, A.; Krause, N. *Angew. Chem.* **1999**, *111*, 1727–1730.
79a. Canisius, J.; Gerold, A.; Krause, N. *Angew. Chem. Int. Ed.* **1999**, *38*, 1644–1646.
80. Breit, B.; Demel, P. Copper-mediated Diastereoselective Conjugate Addition and Allylic Substitution Reactions. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 188–223.
81. Hareau-Vittini, G.; Hikichi, S.; Sato, F. *Angew. Chem.* **1998**, *110*, 2221–2223.
81a. Hareau-Vittini, G.; Hikichi, S.; Safo, F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2099–2101.
81b. Hareau, G. P.-J.; Koiwa, M.; Hikichi, S.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 3640–3650.
81c. Hanazawa, T.; Koiwa, M.; Hareau, G.; Sato, F. *Tetrahedron Lett.* **2000**, *41*, 2659–2662.
82. Koiwa, M.; Hareau, G. P.-J.; Morizono, D.; Sato, F. *Tetrahedron Lett.* **1999**, *40*, 4199–4202.
83. Weinmann, H.; Winterfeldt, E. *Synthesis* **1995**, 1097–1101.
84. Kuramochi, T.; Asaoka, M.; Ohkubo, T.; Takei, H. *Tetrahedron Lett.* **1996**, *37*, 7075–7078.
85. Ireland, R. E.; Gleason, J. L.; Gegnas, L. D.; Highsmith, T. K. *J. Org. Chem.* **1996**, *61*, 6856–6872.
85a. Ireland, R. E.; Liu, L.; Roper, T. D. *Tetrahedron* **1997**, *53*, 13221–13256.
86. Hareau, G.; Koiwa, M.; Hanazawa, T.; Sato, F. *Tetrahedron Lett.* **1999**, *40*, 7493–7496.

87. Ebert, S.; Krause, N. *Eur. J. Org. Chem.* **2001**, 3831–3835.
88. Mulzer, J.; Dürner, G.; Trauner, D. *Angew. Chem.* **1996**, *108*, 3046–3048.
88a. Mulzer, J.; Dürner, G.; Trauner, D. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2830–2832.
88b. Trauner, D.; Bats, J. W.; Werner, A.; Mulzer, J. *J. Org. Chem.* **1998**, *63*, 5908–5918.
88c. Mulzer, J.; Trauner, D. *Chirality* **1999**, *11*, 475–482.
89. Hanessian, S.; Gai, Y.; Wang, W. *Tetrahedron Lett.* **1996**, *37*, 7473–7476.
89a. Hanessian, S.; Wang, W.; Gai, Y. *Tetrahedron Lett.* **1996**, *37*, 7477–7480.
90. Hanessian, S.; Wang, W.; Gai, Y.; Oliver, E. *J. Am. Chem. Soc.* **1997**, *119*, 10034–10041.
90a. Hanessian, S.; Ma, J.; Wang, W. *Tetrahedron Lett.* **1999**, *40*, 4627–4630.
90b. Hanessian, S.; Ma, J.; Wang, W. *Tetrahedron Lett.* **1999**, *40*, 4631–4634.
91. Hanessian, S.; Ma, J.; Wang, W. *J. Am. Chem. Soc.* **2001**, *123*, 10200–10206.
92. Roy, S. C.; Nagarajan, L.; Salomon, R. G. *J. Org. Chem.* **1999**, *64*, 1218–1224.
93. Ayerbe, M.; Morao, I.; Arrieta, A.; Linden, A.; Cossio, F. P. *Tetrahedron Lett.* **1996**, *37*, 3055–3058.
93a. Galley, G.; Hübner, J.; Anklam, S.; Jones, P. G.; Pätzel, M. *Tetrahedron Lett.* **1996**, *37*, 6307–6310.
93b. Clayden, J.; Nelson, A.; Warren, S. *Tetrahedron Lett.* **1997**, *38*, 3471–3474.
94. Breit, B. *Angew. Chem.* **1998**, *110*, 535–538.
94a. Breit, B. *Angew. Chem. Int. Ed.* **1998**, *37*, 525–527.
94b. Breit, B.; Demel, P. *Tetrahedron* **2000**, *56*, 2833–2846.
94c. Breit, B. *Chem. Eur. J.* **2000**, *6*, 1519–1524.
95. Williams, D. R.; Kissel, W. S.; Li, J. J. *Tetrahedron Lett.* **1998**, *39*, 8593–8596.
96. Van Heerden, P. S.; Bezuidenhoudt, B. C. B.; Ferreira, D. *Tetrahedron Lett.* **1997**, *38*, 1821–1824.
97. Totani, K.; Nagatsura, T.; Tarao, K.; Ohba, S.; Tadano, K. *Org. Lett.* **1999**, *1*, 1447–1450.
98. Hudson, R. D. A.; Osborne, S. A.; Roberts, E.; Stephenson, G. R. *Tetrahedron Lett.* **1996**, *37*, 9009–9012.
98a. Mandai, S.; Sarkar, A. *J. Org. Chem.* **1999**, *64*, 2454–2458.
99. Fletcher, M. D.; Harding, J. R.; Hughes, R. A.; Kelly, N. M.; Schmalz, H.; Sutherland, A.; Willis, C. L. *J. Chem. Soc., Perkin Trans. 1* **2000**, 43–52.
100. Sewald, N.; Hiller, K. D.; Helmreich, B. *Liebigs Ann. Chem.* **1995**, 925–928.
100a. Sewald, N.; Hiller, K. D.; Körner, M.; Findeisen, M. *J. Org. Chem.* **1998**, *63*, 7263–7274.
101. Chounan, Y.; Yamamoto, Y. Copper-mediated Synthesis of Natural and Unnatural Products. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 289–314.
102. Dehmel, F.; Abarbri, M.; Knochel, P. *Synlett* **2000**, 345–346.
103. Darcel, C.; Flachsmann, F.; Knochel, P. *Chem. Commun.* **1998**, 205–206.
104. Dieter, R. K.; Velu, S. E.; Nice, L. E. *Synlett* **1997**, 1114–1116.
105. Dieter, R. K.; Gore, V. K.; Chen, N. Y. *Org. Lett.* **2004**, *6*, 763–766.
106. Clive, D. L. J.; Zhang, C.; Zhou, Y.; Tao, Y. *J. Organomet. Chem.* **1995**, *489*, C35–C37.
107. Tamao, K.; Kawachi, A.; Tanaka, Y.; Ohtani, H. *Tetrahedron* **1996**, *52*, 5765–5772.
108. Fleming, I.; Winter, S. B. D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2687–2700.
109. Fleming, I.; Higgins, D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2673–2678.
110. Fleming, I.; Tarrett, N. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2645–2649.
111. Cuerva, J. M.; Gomez-Bengoa, E.; Mendez, M.; Echavarren, A. M. *J. Org. Chem.* **1997**, *62*, 7540–7541.
112. Belelie, J. L.; Chong, J. M. *J. Org. Chem.* **2001**, *66*, 5552–5555.
113. Calaza, M. I.; Hupe, E.; Knochel, P. *Org. Lett.* **2003**, *5*, 1059–1061.
114. Soorukram, D.; Knochel, P. *Org. Lett.* **2004**, *6*, 2409–2412.
115. Ernst, M.; Helmchen, G. *Angew. Chem.* **2002**, *114*, 4231–4234.
115a. Ernst, M.; Helmchen, G. *Angew. Chem. Int. Ed.* **2002**, *41*, 4054–4056.
116. Harrington-Frost, N.; Leuser, H.; Calaza, M. I.; Kneisel, F. F.; Knochel, P. *Org. Lett.* **2003**, *5*, 2111–2114.
116a. Calaza, M. I.; Yang, X.; Soorukram, D.; Knochel, P. *Org. Lett.* **2004**, *6*, 529–531.
117. Ibuka, T.; Nakai, K.; Habashita, H.; Hotta, Y.; Fujii, N.; Mimura, N.; Miwa, Y.; Taga, T.; Yamamoto, Y. *Angew. Chem.* **1994**, *106*, 693–695.
117a. Ibuka, T.; Nakai, K.; Habashita, H.; Hotta, Y.; Fujii, N.; Mimura, N.; Miwa, Y.; Taga, T.; Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 652–694.
117b. Aoyama, H.; Mimura, N.; Ohno, H.; Ishii, K.; Toda, A.; Tamamura, H.; Otaka, A.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1997**, *38*, 7383–7386.
117c. Toda, A.; Aoyama, H.; Mimura, N.; Ohno, H.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1998**, *63*, 7053–7061.
118. Spino, C.; Beaulieu, C. *J. Am. Chem. Soc.* **1998**, *120*, 11832–11833.
118a. Beaulieu, C.; Spino, C. *Tetrahedron Lett.* **1999**, *40*, 1637–1640.
118b. Spino, C.; Beaulieu, C. *Angew. Chem.* **2000**, *112*, 2006–2008.
118c. Spino, C.; Beaulieu, C. *Angew. Chem. Int. Ed.* **2000**, *39*, 1930–1932.
119. Enders, D.; Von Berg, S.; Jandeleit, B. *Synlett* **1996**, 18–20.
120. Breit, B.; Demel, P. *Adv. Synth. Catal.* **2001**, *343*, 429–432.
120a. Breit, B.; Demel, P.; Studte, C. *Angew. Chem.* **2004**, *116*, 3874–3877.
120b. Breit, B.; Demel, P.; Studte, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 3786–3789.
120c. Breit, B.; Herber, C. *Angew. Chem.* **2004**, *116*, 3878–3880.
120d. Breit, B.; Herber, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 3790–3792.
120e. Breit, B.; Breuninger, D. *Synthesis* **2005**, 147–157.
121. Kang, S.-K.; Cho, D.-G.; Chung, J.-U.; Kim, D.-Y. *Tetrahedron: Asymmetry* **1994**, *5*, 21–22.
122. Rakotoarisoa, H.; Perez, R. G.; Mangeney, P.; Alexakis, A. *Organometallics* **1996**, *8*, 1957–1959.
123. Krause, N., Hashmi, A. S. K., Eds.; *Modern Allene Chemistry*, Wiley-VCH: Weinheim, 2004.
124. Spino, C.; Thibault, C.; Gingras, S. *J. Org. Chem.* **1998**, *63*, 5283–5287.
125. Gridnev, I.; Kanai, G.; Miyaura, N.; Suzuki, A. *J. Organomet. Chem.* **1994**, *481*, C4–C7.
125a. Agami, C.; Couty, F.; Evano, G.; Mathieu, H. *Tetrahedron* **2000**, *56*, 367–376.
125b. Ohno, H.; Anzai, M.; Toda, A.; Ohishi, S.; Fujii, N.; Tamaka, T.; Takemoto, Y.; Ibuka, T. *J. Org. Chem.* **2001**, *66*, 4904–4914.

126. Yus, M.; Gomis, J. *Eur. J. Org. Chem.* **2003**, 2043–2048.
127. Chemla, F.; Ferreira, F. *Curr. Org. Chem.* **2002**, *6*, 539–570.
128. Spino, C.; Frechette, S. *Tetrahedron Lett.* **2000**, *41*, 8033–8036.
129. Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1999**, *40*, 349–352.
129a. Ohno, H.; Toda, A.; Fujii, N.; Takemoto, Y.; Tanaka, T.; Ibuka, T. *Tetrahedron* **2000**, *56*, 2811–2820.
130. Jansen, A.; Krause, N. *Synthesis* **2002**, 1987–1992, and references cited.
131. Dunn, M. J.; Jackson, R. F. W.; Pietruszka, J.; Turner, D. *J. Org. Chem.* **1995**, *60*, 2210–2215.
131a. Dunn, M. J.; Jackson, R. F. W. *Tetrahedron* **1997**, *53*, 13905–13914.
131b. Jackson, R. F. W.; Fraser, J. L.; Wishart, N.; Porter, B.; Wythes, M. J. *J. Chem. Soc., Chem. Commun.* **1998**, 1903–1912.
131c. Dieter, R. K.; Nice, L. E. *Tetrahedron Lett.* **1999**, *40*, 4293–4296.
131d. Parsons, P. J.; Gold, H.; Semple, G.; Montagnon, T. *Synlett* **2000**, 1184–1186.
131e. Yokomatsu, T.; Ichimura, A.; Kato, J.; Shibuya, S. *Synlett* **2001**, 287–289.
131f. Papillon, J. P. N.; Taylor, R. J. K. *Org. Lett.* **2002**, *4*, 119–122.
132. Krause, N.; Hoffmann-Röder, A. Allenic Natural Products and Pharmaceuticals. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; pp 997–1040.
132a. Hoffmann-Röder, A.; Krause, N. *Angew. Chem.* **2004**, *116*, 1216–1236.
132b. Hoffmann-Röder, A.; Krause, N. *Angew. Chem. Int. Ed.* **2004**, *43*, 1196–1216.
133. Buynak, J. D.; Khasnis, D.; Bachmann, B.; Wu, K.; Lamb, G. *J. Am. Chem. Soc.* **1994**, *116*, 10955–10965.
133a. Buynak, J. D.; Rao, A. S.; Ford, G. P.; Carver, C.; Adam, G.; Geng, B.; Bachmann, B.; Shobassy, S.; Lackey, S. *J. Med. Chem.* **1997**, *40*, 3423–3433.
134. Thorand, S.; Vögtle, F.; Krause, N. *Angew. Chem.* **1999**, *111*, 3929–3931.
134a. Thorand, S.; Vögtle, F.; Krause, N. *Angew. Chem. Int. Ed.* **1999**, *38*, 3721–3723.
135. Borzilleri, R. M.; Weinreb, S. M.; Parvez, M. *J. Am. Chem. Soc.* **1994**, *116*, 9789–9790.
135a. Borzilleri, R. M.; Weinreb, S. M.; Parvez, M. *J. Am. Chem. Soc.* **1995**, *117*, 10905–10913.
135b. Jin, J.; Weinreb, S. M. *J. Am. Chem. Soc.* **1997**, *119*, 5773–5784.
135c. Weinreb, S. M.; Smith, D. T.; Jin, J. *Synthesis* **1998**, 509–521.
135d. Aoyagi, S.; Hirashima, S.; Saito, K.; Kibiyashi, C. *J. Org. Chem.* **2002**, *67*, 5517–5526.
136. D'Aniello, F.; Mann, A.; Taddei, M.; Wermuth, C.-G. *Tetrahedron Lett.* **1994**, *35*, 7775–7778.
136a. D'Aniello, F.; Schoenfelder, A.; Mann, A.; Taddei, M. *J. Org. Chem.* **1996**, *61*, 9631–9634.
136b. Bernard, N.; Chemla, F.; Normant, J. F. *Tetrahedron Lett.* **1998**, *39*, 8837–8840.
136c. Chemla, F.; Bernard, N.; Normant, J. F. *Eur. J. Org. Chem.* **1999**, 2067–2078.
136d. Wan, Z.; Nelson, S. G. *J. Am. Chem. Soc.* **2000**, *122*, 10470–10471.
136e. Löfstedt, J.; Franzén, J.; Bäckvall, J.-E. *J. Org. Chem.* **2001**, *66*, 8015–8020.
136f. Ohno, H.; Hamaguchi, H.; Tanaka, T. *Org. Lett.* **2001**, *3*, 2269–2271.
136g. Ohno, H.; Ando, K.; Hamaguchi, H.; Takeoka, Y.; Tanaka, T. *J. Am. Chem. Soc.* **2002**, *124*, 15255–15266.
137. Crimmins, M. T.; Emmitte, K. A. *J. Am. Chem. Soc.* **2001**, *123*, 1533–1534.
137a. Crimmins, M. T.; Emmitte, K. A.; Choy, A. L. *Tetrahedron* **2002**, *58*, 1817–1834.
138. Saitoh, T.; Suzuki, T.; Sugimoto, M.; Hagiwara, H.; Hoshi, T. *Tetrahedron Lett.* **2003**, *44*, 3175–3178.
139. Myers, A. G.; Condroski, K. R. *J. Am. Chem. Soc.* **1995**, *117*, 3057–3083.
139a. Brummond, K. M.; Kerekes, A. D.; Wan, H. *J. Org. Chem.* **2002**, *67*, 5156–5163.
140. Mori, S.; Nakamura, E. Mechanisms of Copper-mediated Addition and Substitution Reactions. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 315–346.
141. Bonini, C.; Righi, G. *Tetrahedron* **2002**, *58*, 4981–5021.
142. Katsuki, T.; Martin, V. S. *Org. React.* **1996**, *48*, 1–300, and references cited therein.
143. Jacobsen, E. N. Transition Metal-catalyzed Oxidations: Asymmetric Epoxidation. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 12, pp 1097–1136, and references cited therein.
144. Tian, H.; She, X.; Yu, H.; Shu, L.; Shi, Y. *J. Org. Chem.* **2002**, *67*, 2435–2446, and references cited therein.
145. Krause, N.; Purpura, M. *Angew. Chem.* **2000**, *112*, 4512–4514.
145a. Krause, N.; Purpura, M. *Angew. Chem. Int. Ed.* **2000**, *39*, 4355–4356.
146. Ansorge, M.; Polborn, K.; Müller, T. J. J. *J. Organomet. Chem.* **2001**, *630*, 198–204.
147. Brummond, K. M.; Lu, J. *J. Am. Chem. Soc.* **1999**, *121*, 5087–5088.
148. Purpura, M.; Krause, N. *Eur. J. Org. Chem.* **1999**, 267–275.
149. Normant, J.-F. Alkyne Carbocupration and Polyene Synthesis. In *Organocopper Reagents: A Practical Approach*; Taylor, R. J. K., Ed.; Oxford University Press: Oxford, 1994; pp 237–256.
150. Kato, N.; Miyaura, N. *Tetrahedron* **1996**, *52*, 13347–13354.
151. Chechik-Lankin, H.; Marek, I. *Org. Lett.* **2003**, *5*, 5087–5089.
152. Shattuck, J. C.; Svatos, A.; Blazey, C. M.; Meinwald, J. *Tetrahedron Lett.* **1997**, *38*, 6803–6806.
153. Creton, I.; Marek, I.; Brasseur, D.; Jestin, J.-L.; Normant, J.-F. *Tetrahedron Lett.* **1994**, *35*, 6873–6876.
154. Konno, T.; Daitoh, T.; Noiri, A.; Chae, J.; Ishihara, T.; Yamanaka, H. *Org. Lett.* **2004**, *6*, 933–936.
155. Gil, J.-M.; Oh, D.-Y. *J. Org. Chem.* **1999**, *64*, 2950–2953.
155a. Huang, X.; Wu, Z. *Synthesis* **2004**, 2445–2448.
156. Nilsson, K.; Ullenius, C.; Krause, N. *J. Am. Chem. Soc.* **1996**, *118*, 4194–4195.
156a. Nilsson, K.; Andersson, T.; Ullenius, C.; Gerold, A.; Krause, N. *Chem. Eur. J.* **1998**, *4*, 2051–2058.
156b. Jennings, M. P.; Sawant, K. B. *Eur. J. Org. Chem.* **2004**, 3201–3204.
157. Nakamura, E.; Mori, S.; Nakamura, M.; Morokuma, K. *J. Am. Chem. Soc.* **1997**, *119*, 4887–4899.
157a. Mori, S.; Nakamura, E.; Morokuma, K. *Organometallics* **2004**, *23*, 1081–1088.
158. Varghese, J. P.; Knochel, P.; Marek, I. *Org. Lett.* **2000**, *2*, 2849–2852.
158a. Varghese, J. P.; Zouev, I.; Aufauvre, L.; Knochel, P.; Marek, I. *Eur. J. Org. Chem.* **2002**, 4151–4158.
158b. Sklute, G.; Amsallem, D.; Shabli, A.; Varghese, J. P.; Marek, I. *J. Am. Chem. Soc.* **2003**, *125*, 11776–11777.
159. Barbero, A.; Pulido, F. J. *Rec. Res. Devel. Synth. Org. Chem.* **1999**, *2*, 1–22.

160. Barbero, A.; Cuadrado, P.; Fleming, I.; Gonzalez, A. M.; Pulido, F. J.; Sanchez, A. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1525–1532.
161. Reginato, G.; Mordini, A.; Valacchi, M.; Grandini, E. *J. Org. Chem.* **1999**, *64*, 9211–9216.
161a. Ricci, A.; Blart, E.; Comes-Franchini, G.; Reginato, G.; Zani, P. *Pure Appl. Chem.* **1996**, *68*, 679–682.
162. Fleming, I.; Martinez de Marigorta, E. *J. Chem. Soc., Perkin Trans. 1* **1999**, 889–900.
163. Barbero, A.; Garcia, C.; Pulido, F. J. *Tetrahedron* **2000**, *56*, 2739–2751.
164. Liepins, V.; Karlström, A. S. E.; Bäckvall, J.-E. *Org. Lett.* **2000**, *2*, 1237–1239.
165. Liepins, V.; Bäckvall, J.-E. *Chem. Commun.* **2001**, 265–266.
166. Liepins, V.; Bäckvall, J.-E. *Org. Lett.* **2001**, *3*, 1861–1864.
167. Betzer, J.-F.; Ardisson, J.; Lallemand, J.-Y.; Pancrazi, A. *Tetrahedron Lett.* **1997**, *38*, 2279–2282.
167a. Betzer, J.-F.; Delaloge, F.; Muller, B.; Pancrazi, A.; Prunet, J. *J. Org. Chem.* **1997**, *62*, 7768–7780.
167b. Betzer, J.-F.; Pancrazi, A. *Synlett* **1998**, 1129–1131.
167c. Betzer, J.-F.; Pancrazi, A. *Synthesis* **1999**, 629–634.
167d. Suzenet, F.; Blart, E.; Quintard, J.-P. *Synlett* **1998**, 879–881.
168. Reginato, G.; Mordini, A.; Messina, F.; Degl'Innocenti, A.; Poli, G. *Tetrahedron* **1996**, *52*, 10985–10996.
168a. Reginato, G.; Mordini, A. *J. Org. Chem.* **1997**, *62*, 6187–6192.
169. Nielsen, T. E.; Cubillo de Dios, M. A.; Tanner, D. *J. Org. Chem.* **2002**, *67*, 7309–7313.
170. Thibonnet, J.; Prie, G.; Abarbi, M.; Duchene, A.; Parrain, J.-L. *Tetrahedron Lett.* **1999**, *40*, 3151–3154.
170a. Prie, G.; Abarbi, M.; Thibonnet, J.; Parrain, J.-L.; Duchene, A. *New J. Chem.* **2003**, *27*, 432–441.
170b. Alvarez, R.; Iglesias, B.; Lopez, S.; De Lera, A. R. *Tetrahedron Lett.* **1998**, *39*, 5659–5662.
171. Andrus, M. B.; Lepore, S. D. *J. Am. Chem. Soc.* **1997**, *119*, 2327–2328.
171a. Andrus, M. B.; Lepore, S. D.; Turner, T. M. *J. Am. Chem. Soc.* **1997**, *119*, 12159–12169.
172. Carig, D.; Payne, A. H.; Warner, P. *Synlett* **1998**, 1264–1266.
173. Smith, A. B., III; Condon, S. M.; McCauley, J. A.; Leazen, J. I., Jr.; Leahy, J. W.; Maleczka, R. E., Jr., *J. Am. Chem. Soc.* **1997**, *119*, 962–973.
174. Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, *62*, 1933–1940.
175. Le Menez, P.; Fargeas, V.; Berque, I.; Poisson, J.; Ardisson, J.; Lallemand, J.-Y.; Pancrazi, A. *J. Org. Chem.* **1995**, *60*, 3592–3599.
175a. Fargeas, V.; Menez, P. L.; Berque, I.; Ardisson, J.; Pancrazi, A. *Tetrahedron* **1996**, *52*, 6613–6634.
175b. Le Menez, P.; Brion, J.-D.; Lensen, N.; Chelain, E.; Pancrazi, A.; Ardisson, J. *Synthesis* **2003**, 2530–2534.
176. Pommier, A.; Kocienski, P. *Chem. Commun.* **1997**, 1139–1140.
177. Hassan, J.; Sevingnon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1469.
177a. Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, 2428–2439.
177b. Nelson, T. D.; Crouch, R. D. *Org. React.* **2004**, *63*, 265–555.
178. Varchi, G.; Ricci, A.; Cahiez, G.; Knochel, P. *Tetrahedron* **2000**, *56*, 2727–2731.
178a. Kneisel, F. F.; Knochel, P. *Synlett* **2002**, 1799–1802.
179. Lipshutz, B. H.; Wood, M. R. *J. Am. Chem. Soc.* **1994**, *116*, 11689–11702.
180. El-Batta, A.; Hage, T. R.; Plotkin, S.; Bergdahl, M. *Org. Lett.* **2004**, *6*, 107–110.
181. Hanzawa, Y.; Narita, K.; Yabe, M.; Taguchi, T. *Tetrahedron* **2002**, *58*, 10429–10435.
182. Wipf, P.; Takahashi, H. *Chem. Commun.* **1996**, 2675–2676.
183. Lipshutz, B. H.; Sclafani, J. A.; Takanami, T. *J. Am. Chem. Soc.* **1998**, *120*, 4021–4022.
184. Oestreich, M.; Weiner, B. *Synlett* **2004**, 2139–2142.
185. Ito, H.; Ishizuka, T.; Tateiwa, J.; Sonoda, M.; Hosomi, A. *J. Am. Chem. Soc.* **1998**, *120*, 11196–11197.
186. Clark, C. T.; Lake, J. F.; Scheidt, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 84–85.
187. Lipshutz, B. H. Copper(I)-mediated 1,2- and 1,4-Reductions. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 167–187.
188. Chiu, P. *Synthesis* **2004**, 2210–2215.
189. Lipshutz, B. H.; Keith, J.; Papa, P.; Vivian, R. W. *Tetrahedron Lett.* **1998**, *39*, 4627–4630.
190. Lipshutz, B. H.; Chrisman, W.; Noson, K.; Papa, P.; Sclafani, J. A.; Vivian, R. W.; Keith, J. M. *Tetrahedron* **2000**, *56*, 2779–2788.
190a. Chen, J.-X.; Daeuble, J. F.; Stryker, J. M. *Tetrahedron* **2000**, *56*, 2789–2798.
191. Lipshutz, B. H.; Papa, P. *Angew. Chem.* **2002**, *114*, 4762–4764.
191a. Lipshutz, B. H.; Papa, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 4580–4582.
192. Chiu, P.; Chen, B.; Cheng, K. F. *Tetrahedron Lett.* **1998**, *39*, 9229–9232.
192a. Chiu, P.; Szeto, C. P.; Geng, Z.; Cheng, K. F. *Org. Lett.* **2001**, *3*, 1901–1903.
192b. Kamanecka, T. M.; Overman, L. E.; Sakata, S. K. L. *Org. Lett.* **2002**, *4*, 79–82.
193. Chiu, P.; Leung, S. K. *Chem. Commun.* **2004**, 2308–2309.
194. Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033–8061.
195. Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346–353.
196. Feringa, B. L.; Naasz, R.; Imbos, R.; Arnold, L. A. Copper-catalyzed Enantioselective Conjugate Addition Reactions of Organozinc Reagents. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 224–258.
197. Alexakis, A. *Pure Appl. Chem.* **2002**, *74*, 37–42.
197a. Alexakis, A.; Benhaim, C. *Eur J. Org. Chem.* **2002**, 3221–3236.
197b. Alexakis, A. Asymmetric Organocopper Chemistry: Cu-catalyzed Conjugate Addition and Allylic Substitution. In *Methodologies in Asymmetric Catalysis*; Malhotra, S. V., Ed.; ACS Symposium Series 880; American Chemical Society: Washington, 2004; pp 43–59.
198. De Vries, A. H. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem.* **1996**, *108*, 2526–2528.
198a. De Vries, A. H. M.; Meetsma, A.; Feringa, B. L. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2374–2376.
199. Zhang, F.-Y.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1998**, *9*, 1179–1182.
200. Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; De Vries, A. H. M. *Angew. Chem.* **1997**, *109*, 2733–2736.
200a. Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; De Vries, A. H. M. *Angew. Chem. Int. Ed. Ed. Engl.* **1997**, *36*, 2620–2623.
201. Arnold, A.; Imbos, R.; Mandoli, A.; De Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865–2878.
201a. Pena, D.; Lopez, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2004**, 1836–1837.
202. Naasz, R.; Arnold, L. A.; Pineschi, M.; Keller, E.; Feringa, B. L. *J. Am. Chem. Soc.* **1999**, *121*, 1104–1105.
203. Naasz, R.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2001**, 735–736.

204. Imbos, R.; Brilman, M. H. G.; Pineschi, M.; Feringa, B. L. *Org. Lett.* **1999**, *1*, 623–625.
205. Imbos, R.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron* **2001**, *57*, 2485–2489.
206. Schuppan, J.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2004**, 792–793.
207. Pineschi, M.; Del Moro, F.; Gini, F.; Minnaard, A. J.; Feringa, B. L. *Chem. Commun.* **2004**, 1244–1245.
208. Rimkus, A.; Sewald, N. *Synthesis* **2004**, 135–146.
209. Sewald, N.; Wendisch, V. *Tetrahedron: Asymmetry* **1998**, *9*, 1341–1344.
210. Alexakis, A.; Benhaim, C. *Org. Lett.* **2000**, *2*, 2579–2581.
211. Versleijen, J. P. G.; Van Leusen, A. M.; Feringa, B. L. *Tetrahedron Lett.* **1999**, *40*, 5803–5806.
212. Duursma, A.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron* **2002**, *58*, 5773–5778.
213. Rimkus, A.; Sewald, N. *Org. Lett.* **2003**, *5*, 79–80.
213a. Duursma, A.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2003**, *125*, 3700–3701.
214. Mandoli, A.; Arnold, L. A.; De Vries, A. H. M.; Salvadori, P.; Feringa, B. L. *Tetrahedron: Asymmetry* **2001**, *12*, 1929–1937.
215. Mandoli, A.; Calamante, M.; Feringa, B. L.; Salvadori, P. *Tetrahedron: Asymmetry* **2003**, *14*, 3647–3650.
216. Arnold, L. A.; Naasz, R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2001**, *123*, 5841–5842.
216a. Arnold, L. A.; Naasz, R.; Minnaard, A. J.; Feringa, B. L. *J. Org. Chem.* **2002**, *67*, 7244–7254.
217. Dijk, E. W.; Panella, L.; Pinho, P.; Naasz, R.; Meetsma, A.; Minnaard, A. J.; Feringa, B. L. *Tetrahedron* **2004**, *60*, 9687–9693.
218. Alexakis, A.; Trevitt, G. P.; Bernardinelli, G. *J. Am. Chem. Soc.* **2001**, *123*, 4358–4359.
218a. Agapiou, K.; Cauble, D. F.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 4528–4529.
219. Choi, Y. H.; Choi, J. Y.; Yang, H. Y.; Kim, Y. H. *Tetrahedron: Asymmetry* **2002**, *13*, 801–804.
219a. For spiro phosphoramidites see Zhou, H.; Wang, W.-H.; Fu, Y.; Xie, J.-H.; Shi, W.-J.; Wang, L.-X.; Zhou, Q.-L. *J. Org. Chem.* **2003**, *68*, 1582–1584.
220. Huttenloch, O.; Laxman, E.; Waldmann, H. *Chem. Commun.* **2002**, 673–675.
220a. Huttenloch, O.; Laxman, E.; Waldmann, H. *Chem. Eur. J.* **2002**, *8*, 4767–4780.
221. Alexakis, A.; Rosset, S.; Allamand, J.; March, S.; Guillen, F.; Benhaim, C. *Synlett* **2001**, 1375–1378.
221a. Alexakis, A.; Polet, D.; Benhaim, C.; Rosset, S. *Tetrahedron: Asymmetry* **2004**, *15*, 2199–2203.
221b. Alexakis, A.; Polet, D.; Rosset, S.; March, S. *J. Org. Chem.* **2004**, *69*, 5660–5667.
221c. Dieguez, M.; Deerenberg, S.; Pamies, O.; Claver, C.; van Leeuwen, P. W. N. M.; Kamer, P. *Tetrahedron: Asymmetry* **2000**, *11*, 3161–3166.
221d. Arena, C. G.; Casilli, V.; Faraone, F. *Tetrahedron: Asymmetry* **2003**, *14*, 2127–2131.
222. Alexakis, A.; Benhaim, C.; Rosset, S.; Humam, M. *J. Am. Chem. Soc.* **2002**, *124*, 5262–5263.
223. Choi, H.; Hua, Z.; Ojima, I. *Org. Lett.* **2004**, *6*, 2689–2691.
224. Knopff, O.; Alexakis, A. *Org. Lett.* **2002**, *4*, 3835–3837.
225. Alexakis, A.; March, S. *J. Org. Chem.* **2002**, *67*, 8753–8757.
226. Alexakis, A.; Burton, J.; Vastra, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *8*, 3987–3990.
227. Knöbel, A. K. H.; Escher, I.; Pfaltz, A. *Synlett* **1997**, 1429–1431.
227a. Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336–345.
227b. Escher, I.; Pfaltz, A. *Tetrahedron* **2000**, *56*, 2879–2888.
228. Yan, M.; Yang, L.-W.; Wong, K.-Y.; Chan, A. S. C. *Chem. Commun.* **1999**, 11–12.
228a. Yan, M.; Chan, A. S. C. *Tetrahdron Lett.* **1999**, *40*, 6645–6648.
228b. Yan, M.; Zhou, Z.-Y.; Chan, A. S. C. *Chem. Commun.* **2000**, 115–116.
228c. Liang, L.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2002**, *13*, 1393–1396.
228d. Liang, L.; Au-Yeung, T. T.-L.; Chan, A. S. C. *Org. Lett.* **2002**, *4*, 3799–3801.
228e. Liang, L.; Su, L.; Li, X.; Chan, A. S. C. *Tetrahedron Lett.* **2003**, *44*, 7217–7220.
228f. Wang, L.; Li, Y.-M.; Yip, C.-W.; Qiu, L.; Zhou, Z.; Chan, A. S. C. *Adv. Synth. Catal.* **2004**, *346*, 947–953.
228g. Liang, L.; Yan, M.; Li, Y.-M.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2004**, *15*, 2575–2578.
229. Reetz, M. T. *Pure Appl. Chem.* **1999**, *71*, 1503–1509.
229a. Reetz, M. T.; Gosberg, A.; Moulin, D. *Tetrahedron Lett.* **2002**, *43*, 1189–1191.
229b. Reetz, M. T.; Maiwald, P. *C.R. Chimie* **2002**, *5*, 341–344.
230. Martorell, A.; Naasz, R.; Feringa, B. L.; Pringle, P. G. *Tetrahedron: Asymmetry* **2001**, *12*, 2497–2499.
231. Alexakis, A.; Benhaim, C.; Fournioux, X.; Van der Heuvel, A.; Leveque, J.-M.; March, S.; Rosset, S. *Synlett* **1999**, 1811–1813.
232. Bennett, S. M. W.; Brown, S. M.; Muxworthy, J. P.; Woodward, S. *Tetrahedron Lett.* **1999**, *40*, 1767–1770.
232a. Bennett, S. M. W.; Brown, S. M.; Conole, G.; Dennis, M. R.; Fraser, P. K.; Radojevic, S.; McPartlin, M.; Topping, C. M.; Woodward, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3127–3132.
232b. Bennett, S. M. W.; Brown, S. M.; Cunningham, A.; Dennis, M. R.; Muxworthy, J. P.; Oakley, M. A.; Woodward, S. *Tetrahedron* **2000**, *56*, 2847–2855.
232c. Börner, C.; König, W. A.; Woodward, S. *Tetrahedron Lett.* **2001**, *42*, 327–329.
232d. Börner, C.; Dennis, M. R.; Sinn, E.; Woodward, S. *Eur. J. Org. Chem.* **2001**, 2435–2446.
233. Hu, X.; Chen, H.; Zhang, X. *Angew, Chem.* **1999**, *111*, 3720–3723.
233a. Hu, X.; Chen, H.; Zhang, X. *Angew. Chem. Int. Ed.* **1999**, *38*, 3518–3521.
233b. Hu, Y.; Liang, X.; Wang, J.; Zheng, Z.; Hu, X. *J. Org. Chem.* **2003**, *68*, 4542–4545.
233c. Wan, H.; Hu, Y.; Liang, Y.; Gao, S.; Wang, J.; Zheng, Z.; Hu, X. *J. Org. Chem.* **2003**, *68*, 8277–8280.
233d. Morimoto, T.; Mochizuki, N.; Suzuki, M. *Tetrahedron Lett.* **2004**, *45*, 5717–5722.
233e. Shi, M.; Wang, C.-J.; Zhang, W. *Chem. Eur. J.* **2004**, *10*, 5507–5516.
234. Arena, C. G.; Calabro, G.; Francio, G.; Faraone, F. *Tetrahedron: Asymmetry* **2000**, *11*, 2387–2392.
235. Müller, P.; Nury, P.; Bernardinelli, G. *Helv. Chim. Acta* **2000**, *83*, 843–854.
236. Naasz, R.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Angew. Chem.* **2001**, *113*, 953–956.
236a. Naasz, R.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Angew. Chem. Int. Ed.* **2001**, *40*, 927–930.
237. Mediavilla Urbaneja, L.; Alexakis, A.; Krause, N. *Tetrahedron Lett.* **2002**, *43*, 7887–7890.
238. Seebach, D.; Jaeschke, G.; Pichota, A.; Audergon, L. *Helv. Chim. Acta* **1997**, *80*, 2515–2519.
238a. Pichota, A.; Pregosin, P. S.; Valentini, M.; Wörle, M.; Seebach, D. *Angew. Chem.* **2000**, *112*, 157–160.
238b. Pichota, A.; Pregosin, P. S.; Valentini, M.; Wörle, M.; Seebach, D. *Angew. Chem. Int. Ed.* **2000**, *39*, 153–156.

239. Alexakis, A.; Vastra, J.; Burton, J.; Benhaim, C.; Mangeney, P. *Tetrahedron Lett.* **1998**, *39*, 7869–7872.
239a. Alexakis, A.; Burton, J.; Vastra, J.; Benheim, C.; Fournioux, X.; van den Heuvel, A.; Leveque, J.-M.; Mazé, F.; Rosset, S. *Eur. J. Org. Chem.* **2000**, 4011–4027.
240. Keller, E.; Maurer, J.; Naasz, R.; Schader, T.; Meetsma, A.; Feringa, B. L. *Tetrahedron: Asymmetry* **1998**, *9*, 2409–2413.
241. Alexakis, A.; Benhaim, C. *Tetrahedron: Asymmetry* **2001**, *12*, 1151–1157.
242. Alexakis, A.; Vastra, J.; Burton, J.; Mangeney, P. *Tetrahedron: Asymmetry* **1997**, *8*, 3193–3196.
243. Zhou, Q.-L.; Pfaltz, A. *Tetrahedron* **1994**, *50*, 4467–4478.
243a. De Vries, A. H. M.; Hof, R. P.; Staal, D.; Kellogg, R. M.; Feringa, B. L. *Tetrahedron: Asymmetry* **1997**, *8*, 1539–1543.
244. Takemoto, Y.; Kuraoka, S.; Hamaue, N.; Iwata, C. *Tetrahedron: Asymmetry* **1996**, *7*, 993–996.
244a. Takemoto, Y.; Kuraoka, S.; Hamaue, N.; Aoe, K.; Hiramatsu, H.; Iwata, C. *Tetrahedron* **1996**, *52*, 14177–14188.
244b. Takemoto, Y.; Kuraoka, S.; Ohra, T.; Yonetoku, Y.; Iwata, C. *Chem. Commun.* **1996**, 1655–1656.
245. Stangeland, E. L.; Sammakia, T. *Tetrahedron* **1997**, *53*, 16503–16510.
245a. Shintani, R.; Fu, G. C. *Org. Lett.* **2002**, *4*, 3699–3702.
246. Evans, D. A.; Rovis, T.; Johnson, J. S. *Pure Appl. Chem.* **1999**, *71*, 1407–1415.
246a. Johnson, J. S.; Evans, D. A. *Acc. Chem. Res.* **2000**, *33*, 325–335.
247. Bernardi, A.; Colombo, G.; Scolastico, C. *Tetrahedron Lett.* **1996**, *37*, 8921–8924.
248. Kitajima, H.; Ito, K.; Katsuki, T. *Tetrahedron* **1997**, *53*, 17015–17028.
249. Nishikori, H.; Ito, K.; Katsuki, T. *Tetrahedron: Asymmetry* **1998**, *9*, 1165–1170.
250. Evans, D. A.; Rovis, T.; Kozlowski, M. C.; Tedrow, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 1994–1995.
250a. Evans, D. A.; Willis, M. C.; Johnston, J. N. *Org. Lett.* **1999**, *1*, 865–868.
250b. Evans, D. A.; Johnson, D. S. *Org. Lett.* **1999**, *1*, 595–598.
250c. Evans, D. A.; Rovis, T.; Kozlowski, M. C.; Downey, C. W.; Tedrow, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 9134–9142.
250d. Evans, D. A.; Scheidt, K. A.; Johnston, J. N.; Willis, M. C. *J. Am. Chem. Soc.* **2001**, *123*, 4480–4491.
251. Halland, N.; Velgaard, T.; Jørgensen, K. A. *J. Org. Chem.* **2003**, *68*, 5067–5074.
252. Juhl, K.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 2420–2421.
252a. Marigo, M.; Juhl, K.; Jørgensen, K. A. *Angew. Chem.* **2003**, *115*, 1405–1407.
252b. Marigo, M.; Juhl, K.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2003**, *42*, 1367–1369.
253. Jørgensen, K. A. *Synthesis* **2003**, 1117–1125.
254. Jensen, K. B.; Thorhauge, J.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem.* **2001**, *113*, 164–167.
254a. Jensen, K. B.; Thorhauge, J.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2001**, *40*, 160–163.
255. Zhuang, W.; Hansen, T.; Jørgensen, K. A. *Chem. Commun.* **2001**, 347–348.
255a. Zhou, J.; Ye, M.-C.; Huang, Z.-Z.; Tang, Y. *J. Org. Chem.* **2004**, *69*, 1309–1320.
256. Arai, M. A.; Arai, T.; Sasai, H. *Org. Lett.* **1999**, *1*, 1795–1797.
257. Desimoni, G.; Dusi, G.; Faita, G.; Quadrelli, P.; Righetti, P. R. *Tetrahedron* **1995**, *51*, 4131–4144.
257a. Wendisch, U.; Sewald, N. *Tetrahedron: Asymmetry* **1997**, *8*, 1253–1257.
258. Kanai, M.; Tomioka, K. *Tetrahedron Lett.* **1995**, *36*, 4275–4278.
258a. Nakagawa, Y.; Kanai, M.; Nagaoka, Y.; Tomioka, K. *Tetrahedron* **1998**, *54*, 10295–10307.
258b. Kanai, M.; Nakagawa, Y.; Tomioka, K. *Tetrahedron* **1999**, *55*, 3843–3854.
258c. Tomioka, K.; Nakagawa, Y. *Heterocycles* **2000**, *52*, 95–97.
258d. Nakagawa, Y.; Matsumoto, K.; Tomioka, K. *Tetrahedron* **2000**, *56*, 2857–2863.
258e. Mori, T.; Kosaka, K.; Nakagawa, Y.; Nagaoka, Y.; Tomioka, K. *Tetrahedron: Asymmetry* **1998**, *9*, 3175–3178.
258f. Delapierre, G.; Canstantieux, T.; Brunel, J. M.; Buono, G. *Eur. J. Org. Chem.* **2000**, 2507–2511.
258g. Shi, M.; Zhang, W. *Tetrahedron: Asymmetry* **2004**, *15*, 167–176.
259. Van Koten, G. *Pure Appl. Chem.* **1994**, *66*, 1455–1462.
259a. Van Klaveren, M.; Lambert, F.; Eijkelkamp, D. J. F. M.; Grove, D. M.; Van Koten, G. *Tetrahedron Lett.* **1994**, *35*, 6135–6138.
260. Pamies, O.; Net, G.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **1999**, *10*, 2007–2014.
260a. Pamies, O.; Net, G.; Ruiz, A.; Claver, C.; Woodward, S. *Tetrahedron: Asymmetry* **2000**, *11*, 871–877.
260b. Pamies, O.; Diéguez, M.; Net, G.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **2000**, *11*, 4377–4383.
260c. Dieguez, M.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **2001**, *12*, 2861–2866.
260d. Dieguez, M.; Ruiz, A.; Claver, C. *Tetrahedron: Asymmetry* **2001**, *12*, 2895–2900.
260e. Dieguez, M.; Pamies, O.; Net, G.; Ruiz, A.; Claver, C. *J. Mol. Catal. A* **2002**, *185*, 11–16.
261. Guillen, F.; Winn, C. L.; Alexakis, A. *Tetrahedron: Asymmetry* **2001**, *12*, 2083–2086.
261a. Alexakis, A.; Winn, C. L.; Guillen, F.; Pytkowicz, J.; Roland, S.; Mangeney, P. *Adv. Synth. Catal.* **2003**, *345*, 345–348.
262. Morimoto, T.; Yamaguchi, Y.; Suzuki, M.; Saitoh, A. *Tetrahedron Lett.* **2000**, *41*, 10025–10029.
263. Krauss, I. J.; Leighton, J. L. *Org. Lett.* **2003**, *5*, 3201–3203.
263a. Malkov, A. V.; Hand, J. B.; Kocovsky, P. *Chem. Commun.* **2003**, 1948–1949.
264. Duncan, A. P.; Leighton, J. L. *Org. Lett.* **2004**, *6*, 4117–4119.
265. Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1999**, *64*, 2988–2989.
265a. Taira, S.; Crepy, K. V. L.; Imamoto, T. *Chirality* **2002**, *14*, 386–392.
266. Feringa, B. L.; Badorrey, R.; Pena, D.; Harutyunyan, S. R.; Minnaard, A. J. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5834–5838.
267. Lopez, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2004**, *126*, 12784–12785.
268. Chataigner, I.; Gennari, C.; Piarulli, U.; Ceccarelli, S. *Angew. Chem.* **2000**, *112*, 953–956.
268a. Chataigner, I.; Gennari, C.; Piarulli, U.; Ceccarelli, S. *Angew. Chem. Int. Ed.* **2000**, *39*, 916–918.
268b. Chataigner, I.; Gennari, C.; Ongeri, S.; Piarulli, U.; Ceccarelli, S. *Chem. Eur. J.* **2001**, *7*, 2628–2634.
269. Monti, C.; Gennari, C.; Steele, R. M.; Piarulli, U. *Eur. J. Org. Chem.* **2004**, 3557–3565.
270. Ongeri, S.; Piarulli, U.; Jackson, R. F. W.; Gennari, C. *Eur. J. Org. Chem.* **2001**, 803–807.
271. Hoveyda, A. H.; Hird, A. W.; Kacprzynski, M. A. *Chem. Commun.* **2004**, 1779–1785.
272. Degrado, S. J.; Mizutani, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2001**, *123*, 755–756.
272a. Degrado, S. J.; Mizutani, H.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 13362–13363.
272b. Breit, B.; Laungani, A. C. *Tetrahedron: Asymmetry* **2003**, *14*, 3823–3826.

273. Mizutani, H.; Degrado, S. J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 779–781.
274. Hird, A. W.; Hoveyda, A. H. *Angew. Chem.* **2003**, *115*, 1314–1317.
274a. Hird, A. W.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2003**, *42*, 1276–1279.
275. Luchaco-Cullis, C. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2002**, *124*, 8192–8193.
275a. Mampreian, D. M.; Hoveyda, A. H. *Org. Lett.* **2004**, *6*, 2829–2832.
276. Cesati, R. R., III; De Armas, J.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 96–101.
277. Appella, D. H.; Moritani, Y.; Shintani, R.; Ferreira, E. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9473–9474.
277a. Rainka, M. P.; Aye, S.; Buchwald, S. L. *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5821–5823.
278. Moritani, Y.; Appella, D. H.; Jurkauskas, V.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 6797–6798.
279. Yun, J. S.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 1129–1131.
279a. Chae, J. H.; Yun, J. S.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 4809–4812.
280. Jurkauskas, V.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 2892–2893.
281. Hughes, G.; Kimura, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 11253–11258.
282. Lipshutz, B. H.; Servesko, J. M. *Angew. Chem.* **2003**, *115*, 4937–4940.
282a. Lipshutz, B. H.; Servesko, J. M. *Angew. Chem. Int. Ed.* **2003**, *42*, 4789–4792.
282b. Lipshutz, B. H.; Servesko, J. M.; Petersen, T. B.; Papa, P.; Lover, A. *Org. Lett.* **2004**, *6*, 1273–1275.
282c. Lipshutz, B. H.; Servesko, J. M.; Taft, B. R. *J. Am. Chem. Soc.* **2004**, *126*, 8352–8353.
283. Czekelius, C.; Carreira, E. M. *Angew. Chem.* **2003**, *115*, 4941–4943.
283a. Czekelius, C.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2003**, *42*, 4793–4795.
283b. Czekelius, C.; Carreira, E. M. *Org. Lett.* **2004**, *6*, 4575–4577.
284. Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem.* **1998**, *110*, 1801–1803.
284a. Boymond, L.; Rottländer, M.; Cahiez, G.; Knochel, P. *Angew. Chem. Int. Ed.* **1998**, *37*, 1701–1703.
284b. Berillon, L.; Lepretre, A.; Turck, A.; Ple, N.; Queguiner, G.; Cahiez, G.; Knochel, P. *Synlett* **1998**, 1359–1360.
285. Karlström, A. S. E.; Bäckvall, J.-E. Copper-mediated Enantioselective Substitution Reactions. In *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, 2002; pp 259–288.
286. Van Klaveren, M.; Persson, E. S. M.; Del Villar, A.; Grove, D. M.; Bäckvall, J.-E.; Van Koten, G. *Tetrahedron Lett.* **1995**, *36*, 3059–3062.
286a. Meuzelaar, G. J.; Karlström, A. S. E.; Van Klaveren, M.; Persson, E. S. M.; Del Villar, A.; Van Koten, G.; Bäckvall, J.-E. *Tetrahedron* **2000**, *56*, 2895–2903.
287. Dübner, F.; Knochel, P. *Angew. Chem.* **1999**, *111*, 391–393.
287a. Dübner, F.; Knochel, P. *Angew. Chem. Int. Ed.* **1999**, *38*, 379–381.
287b. Dübner, F.; Knochel, P. *Tetrahedron Lett.* **2000**, *41*, 9233–9237.
287c. Karlström, A. S. E.; Huerta, F. F.; Meuzelaar, G. J.; Bäckvall, J.-E. *Synlett* **2001**, 923–926.
288. Malda, H.; Van Zijl, A. W.; Arnold, L. A.; Feringa, B. L. *Org. Lett.* **2001**, *3*, 1169–1171.
289. Alexakis, A.; Malan, C.; Lea, L.; Benhaim, C.; Fournioux, X. *Synlett* **2001**, 927–930.
289a. Alexakis, A.; Croset, K. *Org. Lett.* **2002**, *4*, 4147–4149.
289b. Shi, W.-J.; Wang, L.-X.; Fu, Y.; Zhu, S.-F.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2003**, *14*, 3867–3872.
290. Tissot-Croset, K.; Polet, D.; Alexakis, A. *Angew. Chem.* **2004**, *116*, 2480–2482.
290a. Tissot-Croset, K.; Polet, D.; Alexakis, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 2426–2428.
290b. Tissot-Croset, K.; Polet, D.; Gille, S.; Hawner, C.; Alexakis, A. *Synthesis* **2004**, 2586–2590.
291. Pineschi, M. *New J. Chem.* **2004**, *28*, 657–665.
292. Badalassi, F.; Crotti, P.; Macchia, F.; Pineschi, M.; Arnold, A.; Feringa, B. L. *Tetrahedron Lett.* **1998**, *39*, 7795–7798.
292a. Bertozzi, F.; Crotti, P.; Feringa, B. L.; Macchia, F.; Pineschi, M. *Synthesis* **2001**, 483–486.
293. Bertozzi, F.; Crotti, P.; Macchia, F.; Pineschi, M.; Arnold, A.; Feringa, B. L. *Org. Lett.* **2000**, *2*, 933–936.
294. Gini, F.; Del Moro, F.; Macchia, F.; Pineschi, M. *Tetrahedron Lett.* **2003**, *44*, 8559–8562.
295. Bertozzi, F.; Crotti, P.; Macchia, F.; Pineschi, M.; Feringa, B. L. *Angew. Chem.* **2001**, *113*, 956–958.
295a. Bertozzi, F.; Crotti, P.; Macchia, F.; Pineschi, M.; Feringa, B. L. *Angew. Chem. Int. Ed.* **2001**, *40*, 930–932.
295b. Bertozzi, F.; Pineschi, M.; Macchia, F.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2002**, *4*, 2703–2705.
295c. Del Moro, F.; Crotti, P.; Di Bussolo, V.; Macchia, F.; Pineschi, M. *Org. Lett.* **2003**, *5*, 1971–1974.
295d. Piarulli, U.; Claverie, C.; Daubos, P.; Gennari, C.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2003**, *5*, 4493–4496.
296. Bertozzi, F.; Crotti, P.; Macchia, F.; Pineschi, M.; Arnold, A.; Feringa, B. L. *Tetrahedron Lett.* **1999**, *40*, 4893–4896.
297. Ongeri, S.; Piarulli, U.; Roux, M.; Monti, C.; Gennari, C. *Helv. Chim. Acta* **2002**, *85*, 3388–3399.
297a. Piarulli, U.; Daubos, P.; Claverie, C.; Roux, M.; Gennari, C. *Angew. Chem.* **2003**, *115*, 244–246.
297b. Piarulli, U.; Daubos, P.; Claverie, C.; Roux, M.; Gennari, C. *Angew. Chem. Int. Ed.* **2003**, *42*, 234–236.
298. Luchaco-Cullis, C. A.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem.* **2001**, *113*, 1504–1508.
298a. Luchaco-Cullis, C. A.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2001**, *40*, 1456–1460.
298b. Kacprzynski, M. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 10676–10681.
299. Murphy, K. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 4690–4691.
300. Barluenga, J.; Sanz, R.; Granados, A.; Fananas, F. J. *J. Am. Chem. Soc.* **1998**, *120*, 4865–4866.
300a. Bouyssi, D.; Monteiro, N.; Balme, G. *Tetrahedron Lett.* **1999**, *40*, 1297–1300.
301. Jorgensen, K. A.; Johannsen, M.; Yao, S. L.; Audrain, H.; Thorhauge, J. *Acc. Chem. Res.* **1999**, *32*, 605–613.
301a. Rechavi, D.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 3467–3493.
302. Desimoni, G.; Faita, G.; Quadrelli, P. *Chem. Rev.* **2003**, *103*, 3119–3154.
303. Chelucci, G.; Thummel, R. P. *Chem. Rev.* **2002**, *102*, 3129–3170.
304. Pfaltz, A. Cyclopropanation and C–H Insertion with Cu. In *Comprehensive Asymmetric Catalysis I–III*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; pp 513–538.
305. Eames, J.; Watkinson, M. *Angew. Chem.* **2001**, *113*, 3679–3683.
305a. Eames, J.; Watkinson, M. *Angew. Chem. Int. Ed.* **2001**, *40*, 3567–3571.
305b. Murahashi, S.; Komiya, N.; Hayashi, Y.; Kumano, T. *Pure Appl. Chem.* **2001**, *73*, 311–314.
305c. Andrus, M. B.; Lashley, J. C. *Tetrahedron* **2002**, *58*, 845–866.
306. Abraham, L.; Czerwonka, R.; Hiersemann, M. *Angew. Chem.* **2001**, *113*, 4835–4837.

306a. Abraham, L.; Czerwonka, R.; Hiersemann, M. *Angew. Chem. Int. Ed.* **2001**, *40*, 4700–4703.
306b. Hiersemann, M.; Abraham, L. *Eur. J. Org. Chem.* **2002**, 1461–1471.
307. Sonogashira, K. Palladium-catalyzed Alkynylation. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I., De Meijere, A., Eds.; Wiley: New York, 2002; pp 493–529.
307a. Sonogashira, K. J. *Organomet. Chem.* **2002**, *653*, 46–49.
307b. Tykwinsky, R. R. *Angew. Chem.* **2003**, *115*, 1604–1606.
307c. Tykwinsky, R. R. *Angew. Chem. Int. Ed.* **2003**, *42*, 1566–1568.
308. Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 7727–7729.
308a. Kwong, F. Y.; Buchwald, S. L. *Org. Lett.* **2003**, *6*, 793–796.
309. Yanagisawa, A. Ag(I), Au(I) Lewis Acids. In *Lewis Acids in Organic Synthesis*; Yamamoto, H., Ed.; Wiley-VCH: Weinheim, 2000; pp 575–596.
310. Yanagisawa, A.; Nakashima, H.; Ishiba, A.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 4723–4724.
311. Yanagisawa, A.; Ishiba, A.; Nakashima, H.; Yamamoto, H. *Synlett.* **1997**, 88–90.
312. Yanagisawa, A.; Nakatsuka, Y.; Nakashima, H.; Yamamoto, H. *Synlett.* **1997**, 933–934.
313. Yanagisawa, A.; Kageyama, H.; Nakatsuka, Y.; Asakawa, K.; Matsumoto, Y.; Yamamoto, H. *Angew. Chem.* **1999**, *111*, 3916–3919.
313a. Yanagisawa, A.; Kageyama, H.; Nakatsuka, Y.; Asakawa, K.; Matsumoto, Y.; Yamamoto, H. *Angew. Chem. Int. Ed.* **1999**, *38*, 3701–3703.
314. Itami, K.; Kamei, T.; Mineno, M.; Yoshida, J. *Chem. Lett.* **2002**, 1084–1085.
315. Yanagisawa, A.; Matsumoto, Y.; Nakashima, H.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1997**, *119*, 9319–9320.
316. Yanagisawa, A.; Matsumoto, Y.; Asakawa, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1999**, *121*, 892–893.
317. Yanagisawa, A.; Nakatsuka, Y.; Asakawa, K.; Kageyama, H.; Yamamoto, H. *Synlett* **2001**, 69–72.
318. Ohkouchi, M.; Masui, D.; Yamaguchi, T. *J. Mol. Catal. A: Chem.* **2001**, *170*, 1–15.
319. Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2003**, *125*, 6038–6039.
319a. Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2004**, *126*, 5360–5361.
319b. Yamamoto, Y.; Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2004**, *126*, 5962–5963.
320. Josephsohn, N. S.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 3734–3735.
321. Ferraris, D.; Young, B.; Dudding, T.; Lectka, T. *J. Am. Chem. Soc.* **1998**, *120*, 4548–4549.
322. Drury, W. J., III; Ferraris, D.; Cox, C.; Young, B.; Lectka, T. *J. Am. Chem. Soc.* **1998**, *120*, 11006–11007.
323. Olsson, L.-I.; Claesson, A. *Synthesis* **1979**, *3*, 743–745.
324. Hashmi, A. S. K. Transition Metal-catalyzed Cycloisomerizations of Allenes. In *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004; pp 877–923.
325. Marshall, J. A.; Pinney, K. G. *J. Org. Chem.* **1993**, *58*, 7180–7184.
325a. Marshall, J. A.; Sehon, C. A. *J. Org. Chem.* **1995**, *60*, 5966–5968.
326. Lan, Y.; Hammond, G. B. *Org. Lett.* **2002**, *4*, 2437–2439.
327. Marshall, J. A.; Bartley, G. S. *J. Org. Chem.* **1994**, *59*, 7169–7171.
328. Winkler, J. D.; Quinn, K. J.; MacKinnon, C. H.; Hiscock, S. D.; McLaughlin, E. C. *Org. Lett.* **2003**, *5*, 1805–1808.
329. Marshall, J. A.; Wolf, M. A.; Wallace, E. M. *J. Org. Chem.* **1997**, *62*, 367–371.
330. Ma, S.; Shi, Z. *J. Org. Chem.* **1998**, *63*, 6387–6389.
331. Marshall, J. A.; Sehon, C. A. *J. Org. Chem.* **1997**, *62*, 4313–4320.
332. Marshall, J. A.; Liao, J. *J. Org. Chem.* **1998**, *63*, 5962–5970.
332a. Marshall, J. A.; Bartley, G. S.; Wallace, E. M. *J. Org. Chem.* **1996**, *61*, 5729–5735.
333. Marshall, J. A.; Devender, E. A. V. *J. Org. Chem.* **2001**, *66*, 8037–8041.
334. Shaw, R. W.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3549–3555.
335. Dieter, R. K.; Yu, H. *Org. Lett.* **2001**, *3*, 3855–3858.
336. Ha, J. D.; Lee, D.; Cha, J. K. *J. Org. Chem.* **1997**, *62*, 4550–4551.
336a. Ha, J. D.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 10012–10020.
337. Amombo, M. O.; Hausherr, A.; Reissig, H.-U. *Synlett* **1999**, 1871–1874.
337a. Flögel, O.; Amombo, M. O.; Reissig, H.-U.; Zahn, G.; Brüdgam, I.; Hartl, H. *Chem. Eur. J.* **2003**, *9*, 1405–1415.
338. Anzai, M.; Toda, A.; Ohno, H.; Takemoto, Y.; Fujii, N.; Ibuka, T. *Tetrahedron Lett.* **1999**, *40*, 7393–7397.
339. Nedolya, N. A.; Brandsma, L.; Schlyakhtina, N. I.; Albanov, A. I. *Chem. Heterocycl. Compd.* **2001**, *37*, 1173–1174.
339a. Nedolya, N. A.; Schlyakhtina, N. I.; Zinov'eva, V. P.; Albanov, A. I.; Brandsma, L. *Tetrahedron Lett.* **2002**, *43*, 1569–1571.
340. Dalla, V.; Pale, P. *New J. Chem.* **1999**, *23*, 803–805.
341. Pale, P.; Chuche, J. *Eur. J. Org. Chem.* **2000**, 1019–1025.
342. Dalla, V.; Pale, P. *Tetrahedron Lett.* **1994**, *35*, 3525–3528.
343. Xu, C.; Negishi, E. *Tetrahedron Lett.* **1999**, *40*, 431–434.
344. Anastasia, L.; Xu, C.; Negishi, E. *Tetrahedron Lett.* **2002**, *43*, 5673–5676.
345. Ogawa, Y.; Maruno, M.; Wakamatsu, T. *Synlett* **1995**, 871–872.
346. Müller, T. E. *Tetrahedron Lett.* **1998**, *39*, 5961–5962.
346a. Müller, T. E.; Pleier, A.-K. *J. Chem. Soc., Dalton Trans.* **1999**, 583–587.
347. Koseki, Y.; Kusamo, S.; Nagasaka, T. *Tetrahedron Lett.* **1998**, *39*, 3517–3520.
347a. Koseki, Y.; Omino, K.; Anzai, S.; Nagasaka, T. *Tetrahedron Lett.* **2000**, *41*, 2377–2380.
348. Tamaru, Y.; Kimura, M.; Tanaka, S.; Kure, S.; Yoshida, Z. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2838–2849.
349. Robinson, R. S.; Dovey, M. C.; Gravestock, D. *Tetrahedron Lett.* **2004**, *45*, 6787–6789.
349a. Harrison, T. J.; Dake, G. R. *Org. Lett.* **2004**, *6*, 5023–5026.
350. Huang, Q.; Hunter, J. A.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 3437–3444.
351. Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091–1160.
352. Wang, J.; Hou, Y. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1919–1923.
353. Darkins, P.; McCarthy, N.; McKervey, M. A.; O'Donnell, K.; Ye, T.; Walker, B. *Tetrahedron: Asymmetry* **1994**, *5*, 195–198.
354. Tilekar, J. N.; Patil, N. T.; Dhavale, D. D. *Synthesis* **2000**, 395–398.
355. Cirakovic, J.; Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 9370–9371.
355a. Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9993–10002.
356. Clark, T. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9522–9523.

357. Cui, Y.; He, C. *J. Am. Chem. Soc.* **2003**, *125*, 16202–16203.
358. Cui, Y.; He, C. *Angew. Chem.* **2004**, *116*, 4306–4308.
358a. Cui, Y.; He, C. *Angew. Chem. Int. Ed.* **2004**, *43*, 4210–4212.
359. Sweis, R. F.; Schramm, M. P.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 7442–7443.
360. Longmire, J. M.; Wang, B.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 13400–13401.
361. Chen, C.; Li, X.; Schreiber, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 10174–10175.
362. Knöpfel, T. F.; Aschwanden, P.; Ichikawa, T.; Watanabe, T.; Carreira, E. M. *Angew. Chem.* **2004**, *116*, 6097–6099.
362a. Knöpfel, T. F.; Aschwanden, P.; Ichikawa, T.; Watanabe, T.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 5971–5973.
363. Peddibhotla, S.; Tepe, J. J. *J. Am. Chem. Soc.* **2004**, *126*, 12776–12777.
364. Loncaric, C.; Manabe, K.; Kobayashi, S. *Adv. Synth. Catal.* **2003**, *345*, 475–477.
365. Patmore, N. J.; Hague, C.; Cotgreave, J. H.; Mahon, M. F.; Frost, C. G.; Weller, A. S. *Chem. Eur. J.* **2002**, *8*, 2088–2098.
366. Xie, Z.; Jelínek, T.; Bau, R.; Reed, C. A. *J. Am. Chem. Soc.* **1994**, *116*, 1907–1913.
367. Yao, S.; Johannsen, M.; Hazell, R. G.; Jøgensen, K. A. *Angew. Chem.* **1998**, *110*, 3318–3321.
367a. Yao, S.; Johannsen, M.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem. Int. Ed.* **1998**, *37*, 3121–3124.
368. Josephsohn, N. S.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2003**, *125*, 4018–4019.
369. Dias, H. V. R.; Jin, W. *Inorg. Chem.* **1996**, *35*, 267–268.
369a. Dias, H. V. R.; Wang, Z.; Jin, W. *Inorg. Chem.* **1997**, *36*, 6205–6215.
370. Dias, H. V. R.; Browning, R. G.; Polach, S. A.; Diyabalanage, H. V. K.; Lovely, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9270–9271.
371. Dias, H. V. R.; Browning, R. G.; Richey, S. A.; Lovely, C. J. *Organometallics* **2004**, *23*, 1200–1202.
372. Burgess, K.; Lim, H.-J.; Porte, A. M.; Sulikowski, G. A. *Angew. Chem.* **1996**, *108*, 192–194.
372a. Burgess, K.; Lim, H.-J.; Porte, A. M.; Sulikowski, G. A. *Angew. Chem. Int. Ed.* **1996**, *35*, 220–222.
373. Bachmann, S.; Fielenbach, D.; Jørgensen, K. A. *Org. Biomol. Chem.* **2004**, *2*, 3044–3049.
374. Wei, C.; Li, Z.; Li, C.-J. *Org. Lett.* **2003**, *5*, 4473–4475.
374a. Li, Z.; Wei, C.; Chen, L.; Varma, R. S.; Li, C.-J. *Tetrahedron Lett.* **2004**, *45*, 2443–2446.
375. Ji, J.-X.; Au-Yeung, T. T.-L.; Wu, J.; Yip, C. W.; Chan, A. S. C. *Adv. Synth. Catal.* **2004**, *346*, 42–44.
376. Kataoka, Y.; Matsumoto, O.; Tani, K. *Chem. Lett.* **1996**, 727–728.
377. Thompson, D. *Gold Bull.* **1998**, *31*, 111–118.
377a. Thompson, D. *Gold Bull.* **1999**, *32*, 12–19.
377b. Bond, G. C. *Catal. Today* **2002**, *72*, 5–9.
377c. Hutchings, G. J. *Catal. Today* **2005**, *100*, 55–61.
378. Dyker, G. *Angew. Chem.* **2000**, *112*, 4407–4409.
378a. Dyker, G. *Angew. Chem. Int. Ed.* **2000**, *39*, 4237–4239.
379. Hashmi, A. S. K. *Angew. Chem.* **2000**, *112*, 3737–3740.
379a. Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2000**, *39*, 3590–3593.
379b. Hashmi, A. S. K. *Gold Bull.* **2003**, *36*, 3–9.
379c. Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51–65.
380. Arcadi, A.; Di Giuseppe, S. *Curr. Org. Chem.* **2004**, *8*, 795–812.
381. Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, *3*, 387–391.
382. Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485–3496.
383. Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669–3671.
384. Arcadi, A.; Bianchi, G.; Chiarini, M.; D'Anniballe, G.; Marinelli, F. *Synlett* **2004**, 944–950.
385. Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 5964–5965.
385a. Shi, Z.; He, C. *J. Am. Chem. Soc.* **2004**, *126*, 13596–13597.
386. Luo, Y.; Li, C.-J. *Chem. Commun.* **2004**, 1930–1931.
387. Wei, C.; Li, C.-J. *J. Am. Chem. Soc.* **2003**, *125*, 9584–9585.
388. Yao, X.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 6884–6885.
389. Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem.* **1998**, *110*, 1475–1478.
389a. Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 1415–1418.
389b. Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem.* **2002**, *114*, 4745–4747.
389c. Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 4563–4565.
389d. Casado, R.; Contel, M.; Laguna, M.; Romero, P.; Sanz, S. *J. Am. Chem. Soc.* **2003**, *125*, 11925–11935.
390. Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11553–11554.
390a. Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Org. Lett.* **2001**, *3*, 3769–3771.
390b. Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *Catal. Today* **2002**, *72*, 19–27.
390c. Hashmi, A. S. K.; Weyrauch, J. P.; Rudolph, M.; Kurpejovic, E. *Angew. Chem.* **2004**, *116*, 6707–6709.
390d. Hashmi, A. S. K.; Weyrauch, J. P.; Rudolph, M.; Kurpejovic, E. *Angew. Chem. Int. Ed.* **2004**, *43*, 6545–6547.
391. Hashmi, A. S. K.; Ding, L.; Bats, J. W.; Fischer, P.; Frey, W. *Chem. Eur. J.* **2003**, *9*, 4339–4345.
392. Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650–12651.
392a. Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921–10925.
392b. For a theoretical study, see: Straub, B. F. *Chem. Commun.* **2004**, 1726–1728.
393. Asao, N.; Sato, K.; Yamamoto, Y. *Tetrahedron Lett.* **2003**, *44*, 5675–5677.
393a. Asao, N.; Aikawa, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **2004**, *126*, 7458–7459.
394. Arcadi, A.; Di Giuseppe, S.; Marinelli, F.; Rossi, E. *Tetrahedron: Asymmetry* **2001**, *12*, 2715–2720.
394a. Arcadi, A.; Chiarini, M.; Di Giuseppe, S.; Marinelli, F. *Synlett* **2003**, 203–206.
394b. Abbiati, G.; Arcadi, A.; Bianchi, G.; Di Giuseppe, S.; Marinelli, F.; Rossi, E. *J. Org. Chem.* **2003**, *68*, 6959–6966.
395. Arcadi, A.; Bianchi, G.; Marinelli, F. *Synthesis* **2004**, 610–618.
396. Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164–11165.
397. Hashmi, A. S. K.; Sinha, P. *Adv. Synth. Catal.* **2004**, *346*, 432–438.
398. Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526–4527.
398a. Staben, S. T.; Kennedy-Smith, J. J.; Toste, F. D. *Angew. Chem.* **2004**, *116*, 5464–5466.

398b. Staben, S. T.; Kennedy-Smith, J. J.; Toste, F. D. *Angew. Chem. Int. Ed.* **2004**, *43*, 5350–5352.
398c. Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 15978–15979.
399. Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2003**, *9*, 2627–2635.
399a. Nieto-Oberhuber, C.; Munoz, M. P.; Bunuel, E.; Nevado, C.; Cardenas, D. J.; Echavarren, A. M. *Angew. Chem.* **2004**, *116*, 2456–2460.
399b. Nieto-Oberhuber, C.; Munoz, M. P.; Bunuel, E.; Nevado, C.; Cardenas, D.; Echavarsen, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402–2406.
399c. Fürstner, A.; Hannen, P. *Chem. Commun.* **2004**, 2546–2547.
399d. Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858–10859.
399e. Zhang, L.; Kozman, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806–11807.
400. Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12–21.
401. Hashmi, A. S. K.; Schwarz, L.; Choi, J.-K.; Frost, T. M. *Angew. Chem.* **2000**, *112*, 2382–2385.
401a. Hashmi, A. S. K.; Schwarz, L.; Choi, J.-K.; Frost, T. M. *Angew. Chem. Int. Ed.* **2000**, *39*, 2285–2288.
402. Morita, N.; Krause, N. *Org. Lett.* **2004**, *6*, 4121–4123.

9.13 Tellurium

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9.13.1 Introduction

The organic chemistry of tellurium has a long history. The first organic tellurium compound to be prepared was diethyl telluride, described by Wöhler in 1840.[1] Since its beginning, this branch of organic chemistry was the focus of negative comments. In one of the first reports on the organic chemistry of tellurium, Wöhler wrote about diethyl telluride: "... and because its highly obnoxious and persistent smell is connected with unpleasantness, which one wouldn't like to endure a second time...."[2] Shortly thereafter, Heeren also wrote: "the smell is so persistent, that one has to avoid social life for several months in order not to annoy other people."[3] These comments were probably responsible for the long hibernation of the organic chemistry of tellurium. Between 1910 and 1950, only about 50 papers on the subject were published. In the mid-1950s, Heinrich Rheinboldt published the first systematic and comprehensive account of the organic chemistry of tellurium, as a part of a chapter in Houben-Weyl.[4] In the 1960s, extensive studies of the reactivity of inorganic and organic compounds of tellurium toward organic substrates were undertaken by Petragnani, Rheinboldt's last student. These studies constituted the basis for further investigations of organic tellurium chemistry. After this period, the activity in this field became so intense that between 1950 and 1990, an average of 100 papers per year was published on the organic chemistry of tellurium. In 1990, a 1,000-page volume of Houben-Weyl was devoted exclusively to organic tellurium chemistry.[5] Throughout the last and the present decade, the field has continued to grow, and a number of review articles[6–10] and books[11,12] dealing with the applications of the organic and inorganic tellurium compounds in synthetic transformations have been published. Notwithstanding this impressive development of the field, the organic chemistry of tellurium continues to be studied by a rather restricted number of chemists, and very few applications of the discovered reactions were used by research groups dedicated to total synthesis, in spite of the advantages presented by some synthetic transformations using tellurium compounds over similar methodologies available in the literature. This fact is probably due to the negative comments found in the old and also recent literature on the bad smell and alleged toxicity of the organic tellurium compounds. About these concerns it is interesting to comment that already in the 1950s Rheinboldt's group had observed that several classes of organic tellurium compounds are solid and almost odorless, or present an odor not more unpleasant than most of the reagents commonly used in an organic chemistry laboratory. However, as far as we know, these observations were not explicitly commented on in the publications of the laboratories dedicated to the organic chemistry of tellurium, so the misconception concerning the bad smell of the organic tellurium compounds persisted and the negative comments can still be found in many recent papers. It must be emphasized that the original old-literature comments were effectively true, but only for the specific compounds under consideration, which were low molecular weight aliphatic tellurides and ditellurides containing no additional functional groups.

The stability of organic tellurium compounds is another controversial topic. Several publications mention the sensitivity of such compounds to sunlight and to the air as a rule. Indeed, some organic tellurium compounds are light and air-sensitive, like specific representatives of any class of organic compounds, but this is not an intrinsic characteristic of the compounds of this element. In our laboratory, flasks of specific organic tellurium compounds were kept on the benches for several months exposed to the ceiling light with no perceptible decomposition. From our experience with organic compounds of tellurium, we concluded that some recommendations found in the literature concerning the care to be taken in handling these compounds are overemphasized.

Another negative concern about tellurium compounds is their alleged toxicity. Few studies about this matter do exist, as was recently pointed out in a review article on the toxicology and pharmacology of organic selenium and organic tellurium compounds.[13] The few data available indicate that the studied compounds are indeed toxic for mammals, and therefore care must be taken in the manipulation of the inorganic and organic compounds of this element. Our long experience with organic compounds of tellurium showed that the improper handling of such compounds gave to the manipulator a strong garlic breath, which could persist for several days. This inconvenience, which has been pointed out by several authors, can be minimized or even totally eliminated by the appropriate use of disposable gloves and a well-ventilated hood whenever an inorganic or organic compound of this element is manipulated. Any contact with the skin or inhalation of such compounds must be avoided. The comments above are obvious precautions to be taken in the manipulation of any laboratory chemical. The experience of our group for more than two decades in this branch of organic chemistry has demonstrated that the organic compounds of tellurium can be handled safely with no need for special techniques.

This chapter is dedicated to describing the main routes to the most studied classes of organic compounds of tellurium and the useful synthetic transformations they can perform. As already mentioned, in the last two decades, a number of books and exhaustive review articles have been published on tellurium chemistry. Due to the enormous body of information available and to space limitations, we have selected the reactions which, in our point of view, present a greater synthetic potential and generality. In view of this fact, the text intends to be a comprehensive account rather than an exhaustive review. For a recent review with references to prior reviews and books, as well as recent advances in the tellurium chemistry not covered in this chapter, we recommend the reader to consult Ref: 10.

9.13.2 Main Classes of Organic Tellurium Compounds

A number of different classes of organic derivatives of tellurium are known.[5] In this chapter, only the classes most often used for synthetic purposes will be discussed (Figure 1).

Organotellurols **1**, the tellurium analogs of alcohols, constitute a class of organic tellurium compounds, which have to be prepared and used *in situ* due to their high succeptibility to oxidation. The participation of this class of compounds in several reactions has been proposed,[5–12] but their real existence has never been demonstrated in such processes. A few tellurols exhibiting special structural features could be isolated and characterized (e.g., compound **10**, Figure 2).[14]

Organotellurolates **2**, the tellurium analogs of alkoxides, are extremely air-sensitive compounds. Although these compounds have been isolated and characterized,[15] for synthetic purposes they are generated and used *in situ*.[5–12] Extreme care must be taken to avoid any contact with oxygen by using carefully deoxygenated inert atmosphere for their preparation. Usually, the solutions containing these compounds are colorless or pale yellow. Accidental introduction of oxygen in the reaction vessel makes the solution to turn red, due to the formation of

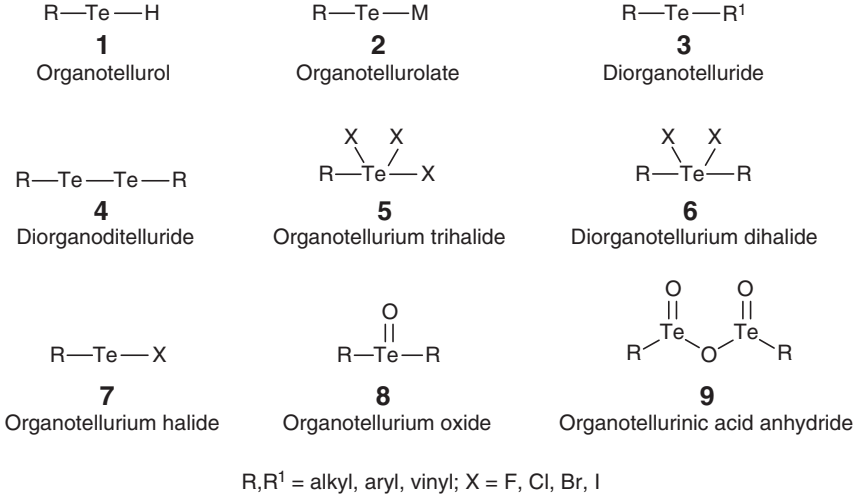
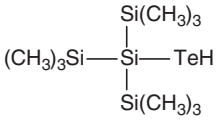


Figure 1 Most-often-used classes of organic tellurium compounds.



10

Figure 2 Structure of the isolated, stable sylilated tellurol.

diorganoditellurides **4**. However, the preparation of solutions containing organotellurolates **2** is nowadays a routine practice, and high yields of the products resulting from their interaction with organic substrates are obtained.

The low-weight diorganotellurides **3** are very bad-smelling yellow oils, which must be handled in a well-ventilated hood. Disposable gloves must be used to manipulate them, and all glassware used for their preparation must be immersed into a solution of sodium hypochlorite immediately after use. The presence of an additional functional group in the molecule usually attenuates the bad smell, and some of these diorganotellurides are not bad smelling at all. Some comparisons are made in Figure 3.

The diaryl or aryl alkyl tellurides are dense yellow oils or crystalline solids, which are easier to handle than the dialkyl tellurides of similar molecular weight. Some of the diaryl derivatives are almost odorless solids. The same comments are valid for the diorganoditellurides **4**, which are dark red oils (aliphatic derivatives) and dark red solids (aromatic derivatives). It is recommended that solutions of tellurides or ditellurides should not be kept in contact with air, since an amorphous white solid will form after some time. For some compounds, this reaction with oxygen is very fast. Aliphatic derivatives are more air sensitive than the aromatic ones. In view of this fact, it is recommended to bubble nitrogen into the solutions while a column or thin-layer chromatographic separation is performed. Evaporation of the solvent, however, minimizes the air oxidation. Pure liquids or solids can be handled in air with no need for special precautions, but prolonged exposure to air and to ambient light should be avoided.

Organic tellurium halides **7** are normally unstable and cannot be isolated. Attempts to isolate organotellurium halides lead to their disproportionation, giving a mixture of organotellurium trihalides **5** and the corresponding diorganoditellurides **4** (Equation (1)). In this way, they are generated and used *in situ*.[5,11,12]

7 **5** **4** (1)

An electron-donating group suitably positioned, able to coordinate with tellurium, stabilizes organotellurium halides, allowing their isolation (Figure 4).[5,11,12,16] Recently, compound **11** was isolated by careful crystallization.[17]

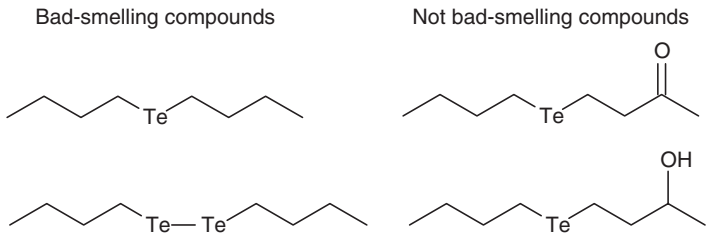


Figure 3 Examples of bad-smelling and not bad-smelling tellurium compounds.

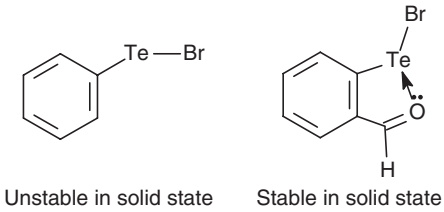


Figure 4 Intramolecular coordination with tellurium lead to stable organotellurium halides.

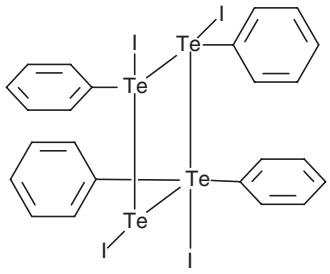


Figure 5 Molecular structure of phenyltellurium iodide **11** tetramer.[17]

An X-ray structure determination indicated that in the solid state, compound **11** exists as the tetrameric structure shown in Figure 5.

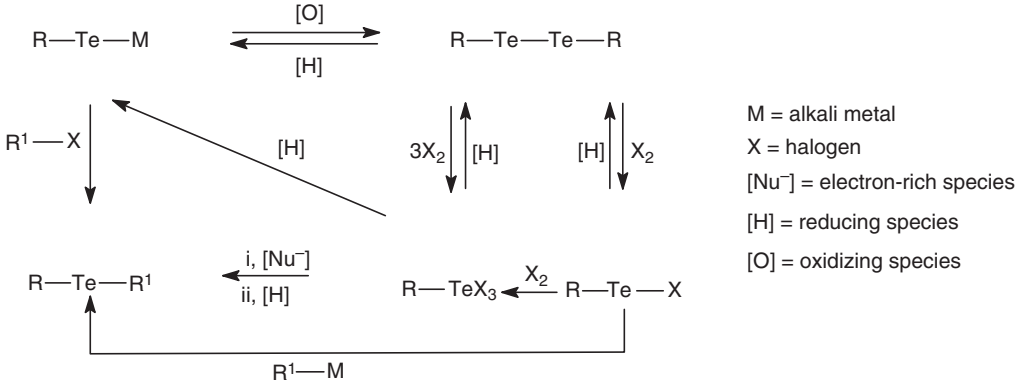
Aryltellurium trichlorides **5** (R = aryl, X = Cl) are usually yellow, very stable crystalline solids, with a slight odor of hydrochloric acid, which probably arises from the reaction of **5** with the air moisture. Contact of **5** with metallic spatulas, with moist solvents, or prolonged exposure to light must be avoided. These compounds, however, can be handled in the air with no risk of decomposition. Aryltellurium tribromides (**5**, R = aryl, X = Br) are yellow crystalline solids, and the triiodides (**5**, R = aryl, X = I) are dark red solids. The aryltellurium tribromides and triiodides were less explored for synthetic purposes, in contrast to the aryltellurium trichlorides, which were frequently used in several synthetic transformations. The aliphatic tellurium trihalides are less stable than the aromatic ones and were much less studied and used for preparative purposes.

Diorganotellurium dichlorides **6** (X = Cl) are odorless viscous oils or colorless crystalline solids. These compounds are more stable than the corresponding diorganotellurides **3**, and most of them are not moisture or air sensitive. The analogous diorganotellurium dibromides or diiodides are less common than the diorganotellurium dichlorides.

Diaryltellurium oxides **8** and aryltellurinic acid anhydrides **9** are white solids and find use as mild oxidizing agents in organic synthesis. These classes of organic tellurium compounds are quite stable and can be handled with no need for special care.

The classes of organic tellurium compounds mentioned above are prepared by interaction of nucleophilic or electrophilic tellurium species with different classes of organic compounds. Such species are generated from elemental tellurium or from diorganoditellurides **4**, as will be discussed in the following sections.

In addition, several classes of organic tellurium compounds can be interconverted, as shown in Scheme 1.[5,9,11,12] These interconversions will be discussed later.



Scheme 1 Interconversions of the main classes of organic tellurium compounds.

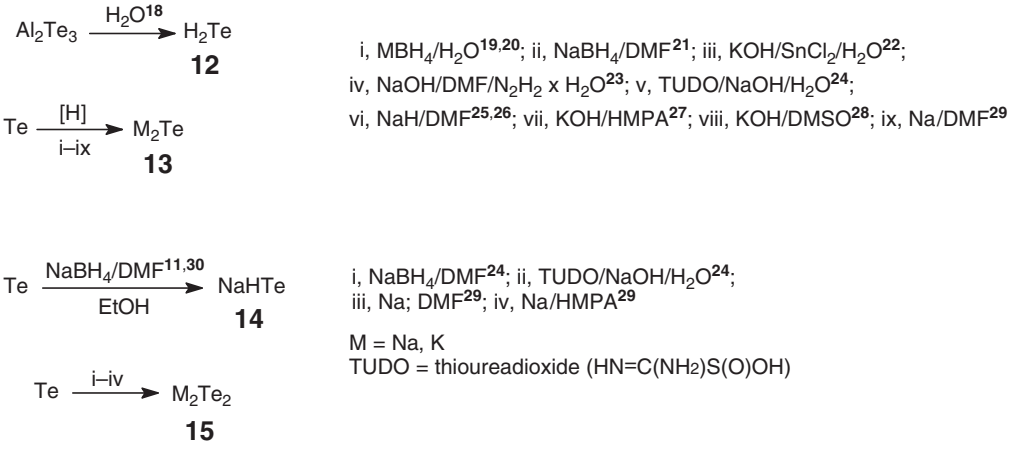
9.13.3 Preparation of Nucleophilic Tellurium Species

9.13.3.1 From Elemental Tellurium and Reducing Agents

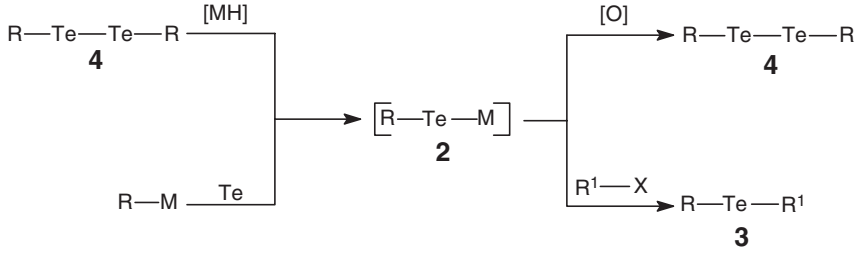
Hydrogen telluride **12** is prepared by hydrolysis of Al_2Te_3 and is an extremely toxic and malodorous gas. Its use must be avoided. Alkali tellurides **13** and **14**, and ditellurides **15** are prepared from elemental tellurium and reducing agents. These species are extremely sensitive toward oxygen and must be generated *in situ* in a carefully deoxygenated atmosphere. The solutions containing alkali tellurides must be used *in situ* immediately after their preparation for further synthetic transformations. Scheme 2[19–29] shows the most widely used methods to generate nucleophilic tellurium.[5,9,11,12]

9.13.3.2 From Elemental Tellurium and Organolithium and Grignard Reagents

Other nucleophilic tellurium species of synthetic interest are the organotellurolates **2**. These species can be prepared by reaction of elemental tellurium with a Grignard[31–35] or an organolithium reagent[36–40] (Scheme 3). The success of the reaction with Grignard reagents is highly dependent on the granule size of the tellurium used. Usually, tellurium powder of 200–300 mesh is appropriate.[35] The organotellurolates so obtained are also oxygen sensitive, and extreme care must be taken to deoxygenate the inert gas used as the reaction atmosphere to avoid the transformation of organotellurolates into diorganoditellurides **4**. In fact, the most practical method to prepare diorganoditellurides **4**



Scheme 2 Generation of the most important alkali tellurides used in organic synthesis.[5,11,12]



Scheme 3

consists in the insertion of elemental tellurium in a Grignard or organolithium reagent followed by air oxidation of the intermediate organotellurolate **2** (Section 9.13.4.4 and Scheme 3).[5,9,11,12]

One of the organotellurolates most widely used in organic synthesis in recent years is the lithium *n*-butyltellurolate, which is prepared by adding commercial ^{n}BuLi to a suspension of elemental tellurium in tetrahydrofuran at room temperature under deoxygenated nitrogen. At the beginning of the addition, a purple solution is formed. The reaction behaves as a titration. When the right amount of *n*-butyllithium is added, the purple color fades and a clear yellow color persists. At this point, the solution must be used immediately for further transformations.[41,42]

9.13.3.3 From Diorganoditellurides and Organotellurium Trihalides with Reducing Agents

Alternatively, organotellurolates can be prepared by reaction of preformed diorganoditellurides **4** with a reducing agent,[5,9,11,12] usually sodium borohydride[41,43–46] (Scheme 3). This reaction can be easily visualized, since the diorganoditellurides generate a deep red solution, usually in ethanol, which turns colorless by the slow addition of a solution of sodium borohydride in ethanol or water. The reaction occurs with gas evolution. When the red color of the solution fades, the reduction is complete. Besides the elemental tellurium insertion into Grignard or organolithium reagents, this is the most widely used method to generate organotellurolate anions. The organotellurolates prepared in this way must also be protected from oxygen, and are used immediately after being prepared.

Recently, it was found that sodium borohydride generates organotellurolate anions **2** also by reduction of organotellurium trihalides **5** (Equation (2)).[47,48]

$$\underset{\mathbf{5}}{R{-}TeCl_3} \xrightarrow[THF/EtOH,\ RT,\ N_2]{NaBH_4} \underset{\mathbf{2}}{[RTeM]} \qquad (2)$$

9.13.4 Preparation of Electrophilic Tellurium Species

9.13.4.1 Tellurium Tetrachloride

Tellurium tetrachloride **16** is the most commonly used tellurium tetrahalide. It is a very hygroscopic white solid, which decomposes immediately upon contact with metallic spatulas. Thus, porcelain spatulas must be used to manipulate this reagent. It reacts immediately with air moisture. When manipulated in contact with air, the operation must be performed as fast as possible.

Tellurium tetrachloride **16** was widely used in the past to introduce tellurium into organic substrates. It reacts with several functional groups giving organotellurium trichlorides **5** (X = Cl), which constitute an important class of tellurium electrophiles. Tellurium tetrachloride **16** is prepared by passing a stream of dry chlorine over elemental tellurium in an appropriate glass apparatus (Equation (3)).

$$Te + 2Cl_2 \longrightarrow \underset{\mathbf{16}}{TeCl_4} \qquad (3)$$

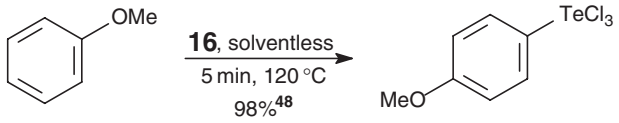
The reaction is exothermic and requires only initial heating. After completion of the reaction, the product is distilled with the aid of a Bunsen burner into glass ampules, which are sealed after **16** crystallizes. Using the procedure described in *Inorganic Synthesis*,[49] 1–2 mol batches are easily prepared in a few hours.

9.13.4.2 Organotellurium Trihalides

9.13.4.2.1 Reaction of aromatic substrates with tellurium tetrachloride

One of the most studied and used reactions of tellurium tetrachloride **16** is the electrophilic aromatic substitution with activated aromatic hydrocarbons.[5,9,11,12] Traditionally, the reaction is performed in carbon tetrachloride or chloroform under reflux.[50–54] The aryltellurium trichlorides **5** are insoluble in these solvents and precipitate as crystalline solids. Usually, the reaction gives high yields. The *para*-substituted aryltellurium trichlorides are formed. The reaction can take several hours under reflux to reach completion.[5] It can be performed also in the absence of

solvents. However, in this case, long heating must be avoided to prevent the formation of diaryltellurium dichlorides **6**.[55] Recently, it was observed that in most cases, the aryltellurium trichlorides were formed in high yields by heating equimolar amounts of tellurium tetrachloride **16** with the activated aromatic compound for 5 min at 120 °C in the absence of solvents (Equation (4)).[48] This procedure avoided the use of carbon tetrachloride and chloroform, as well as the need for long reaction times.



(4)

Non-activated aromatics react with tellurium tetrachloride in the presence of Lewis acids. However, mixtures of aryltellurium trichlorides **5** and diaryltellurium dichlorides **6** can be formed,[56] since **5** are also electrophiles and can react further with the aromatic substrate leading to **6**.

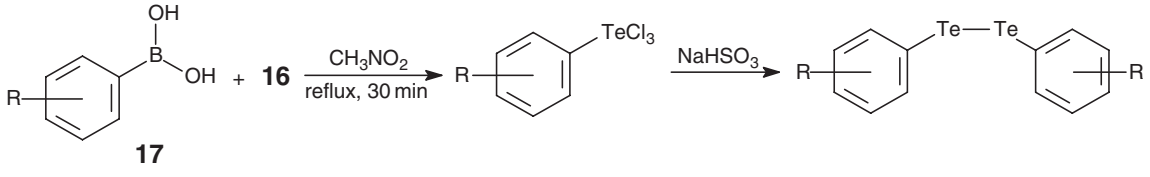
9.13.4.2.2 Reaction of arylmercurium and arylboronic acids with tellurium tetrachloride

An old method, which is no longer used to prepare aryltellurium trichlorides in view of the toxicity of the starting materials and the solvent used, consists in the reaction of tellurium tetrachloride **16** with arylmercurium chlorides[5] in dioxane.[53,57–59] Recently, a more attractive method employing arylboronic acids **17** instead of arylmercuric chlorides was developed to prepare aryltellurium trichlorides **5** using tellurium tetrachloride **16** as the tellurium source (Scheme 4).[60] The aryltellurium trichlorides **5** were not isolated, being reduced without purification to diaryl ditellurides **4**. The arylmercury[53,57–59] and arylboronic acid[60] methods allow the introduction of the tellurium atom into non-activated and deactivated aromatic rings by reaction with **16**.

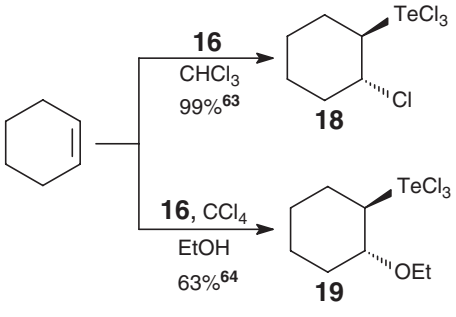
9.13.4.2.3 Addition of tellurium tetrachloride to alkenes and alkynes

Ketones react with **16** probably via the enol form to give α-trichlorotellurium ketones.[61,62] Reaction of alkenes with **16** in an inert solvent gives chloroalkyltellurium trichlorides (e.g., **18**).[63] When an alcohol is present in the reaction medium, an oxyalkyltellurium trichloride (e.g., **19**) is formed[64] (Scheme 5). In some cases, tellurium tetrachloride is generated *in situ* from TeO_2 and HCl.[65]

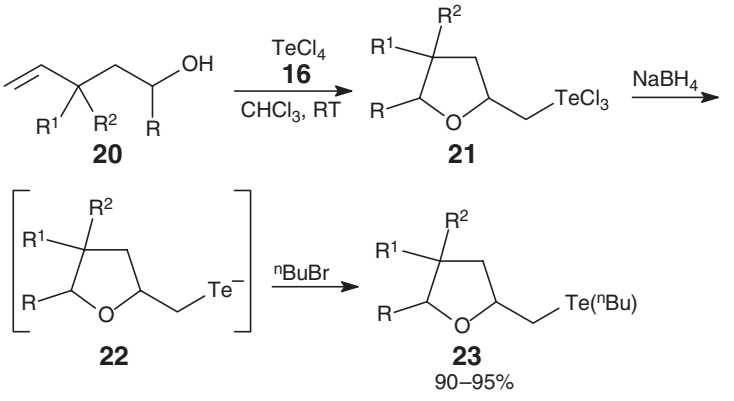
Reaction of tellurium tetrachloride with substrates bearing an internal nucleophile **20** gives rise to cyclic products.[66,67] In some cases, the organotellurium trichlorides **21** obtained in this way are reduced to the corresponding organotellurolates **22** followed by alkylation to give tellurides **23** (Scheme 6).[47]



Scheme 4



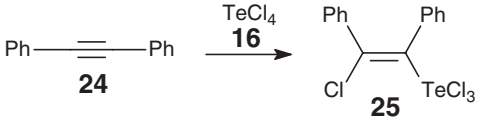
Scheme 5



Scheme 6

The reaction of tellurium tetrachloride with olefins as a route to organotellurium trichlorides is, however, not general. In some cases, the yields are very poor or unidentified products are formed.[5]

The reaction of alkynes with tellurium tetrachloride **16** was recently reinvestigated.[68] Aryl alkynes (e.g., **24**) react with **16** to give the (*Z*)-vinylic tellurium trichlorides (e.g., **25**) (Equation (5)),[47,68,69] whereas alkynes bearing a hydroxyl group at C_3 **26** give olefins of (*E*)-stereochemistry **28** or **29** that reflect the steric demand at C_3 (Scheme 7).[68,72]



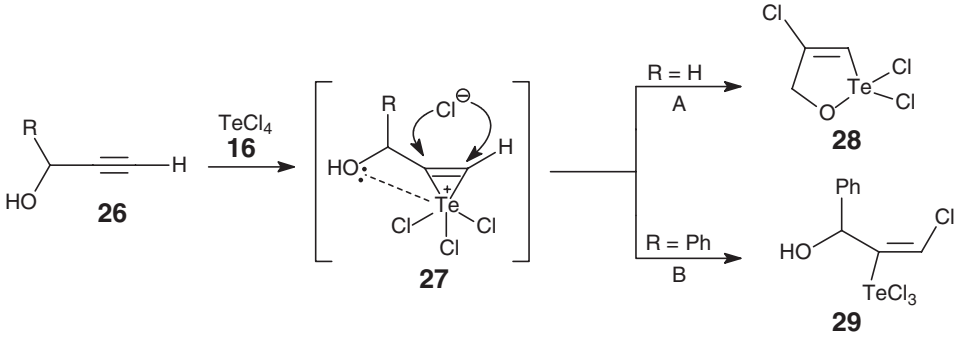
(5)

When R = H, no steric interaction between the chloride ion and the substituent at C_3 of the intermediate **27** occurs. The chloride ion attacks C_2 of the intermediate **27** reacting by route A to give the cyclic tellurane **28**.[72] When R = Ph, a steric interaction between the phenyl group and the chloride ion occurs, and the intermediate **27** is opened by route B to give the vinyltellurium trichloride **29**[68] (Scheme 7).

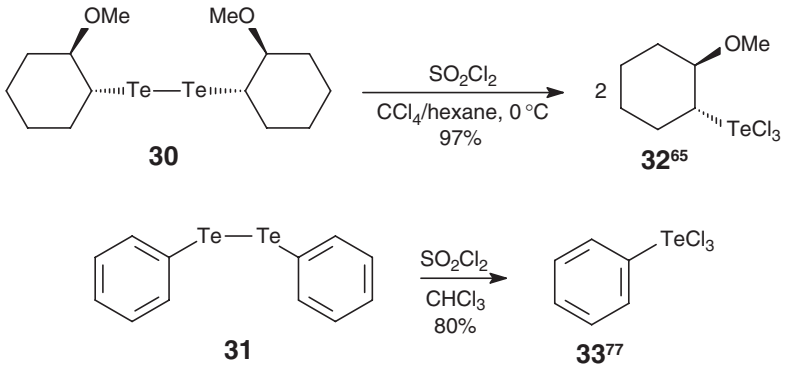
The reaction is highly dependent on the alkyne used. When structurally simple 3-hydroxy alkynes such as propargyl alcohol are used, acceptable yields of the addition products are obtained, whereas reactions with alkynes prone to carbocation formation and rearrangement, such as 1-ethynyl-cyclohexanol, give a complex mixture of products.[68,73]

9.13.4.2.4 Halogenolysis of diorganoditellurides

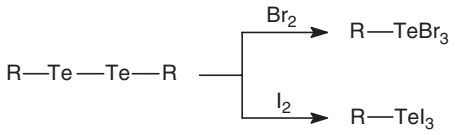
Dialkyl (e.g., **30**) and diaryl ditellurides (e.g., **31**) are transformed into the corresponding diorganotellurium trichlorides (e.g., **32** and **33**) by reaction with elemental chlorine,[74,75] with thionyl chloride,[4,76] or with sulphuryl chloride (Scheme 8).[65,77]



Scheme 7



Scheme 8



Scheme 9

Organotellurium tribromides or triiodides are prepared by halogenolysis of the corresponding diorganoditelluride (Scheme 9).[5,11,12,53]

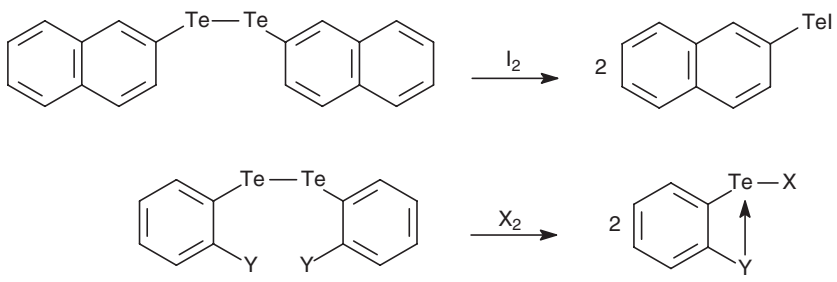
The halogenolysis of diorganoditellurides is very fast and the organotellurium trihalides precipitate immediately, usually as light yellow solids in the case of the chlorides, as yellow solids in the case of the bromides, and as red-brown solids in the case of iodides. Some trihalides, specially the aliphatic derivatives, precipitate as dense oils, which crystallize by addition of appropriate solvents.

9.13.4.3 Organotellurium Halides

This class of electrophilic organotellurium compounds is prepared by the controlled addition of a halogen to diorganoditellurides. For many years, naphthyltellurium iodide, prepared for the first time in 1959,[78] was the only stable organotellurium halide known in the solid state. Those containing an *ortho*-group able to coordinate with tellurium can be isolated (Scheme 10).[5,10,11,79]

When such groups are not present, the organotellurium halide cannot be isolated. In these cases, aryl, alkenyl, and alkyl tellurenyl halides, usually bromides and iodides, are prepared and used *in situ*.[5,10–12,80]

The discovery by Petragnani[80] that organotellurium halides can be generated and captured *in situ* by nucleophiles opened a new chapter in organic tellurium chemistry, as exemplified by the reactions described in Section 9.13.6.1.



Scheme 10

9.13.4.4 Diorganoditellurides

This class of organotellurium compounds is an important source of nucleophilic (Sections 9.13.3.1 and 9.13.3.2) or electrophilic (Sections 9.13.4.2.4 and 9.13.4.3) tellurium species. Diorganoditellurides can also behave as electrophiles, but in such cases normally one organotellurium group is lost. In this way, the corresponding organotellurium halides (Section 9.13.4.3) are prepared as source of electrophilic tellurium. In the past, the title compounds were prepared mainly by reduction of aryltellurium trihalides, in some cases under drastic reaction conditions[5,9,11,12] (Scheme 11).

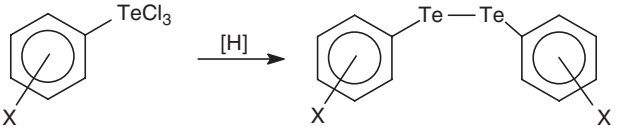
Recently, more practical and milder reducing agents and reaction conditions were used in the reduction of organotellurium trihalides to diorganoditellurides[10] (Scheme 12).[81]

Another general route to diorganoditellurides consists in the insertion of elemental tellurium into Grignard[31–35] or organolithium[36–40] reagents, followed by oxidation of the intermediate organotellurolate (Scheme 13). Usually, the oxidation is performed by the air oxygen.

Finally, dialkyl ditellurides **4** can be prepared by alkylation of alkali ditellurides **15** (Section 9.13.5.2.1).

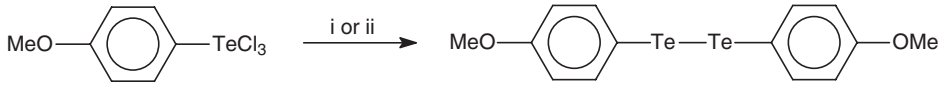
9.13.4.5 Aryltellurium Oxides and Aryltellurinic Acid Anhydrides

Diorganotellurium oxides **8** are prepared by oxidation of diorganotellurides. The dialkyl derivatives are prone to air oxidation specially when they are in solution. The diaryl tellurides **3** are more stable being oxidized to the corresponding tellurium oxides **8** by sodium periodate[32] or *N*-chlorosuccinimide followed by alkaline hydrolysis[82] (Scheme 14). Alternatively, diaryltellurium dichlorides **6**, prepared by electrophilic aromatic substitution (Section 9.13.6.2, Scheme 70), can be hydrolyzed in alkaline medium to the corresponding tellurium oxide **8**[83] (Scheme 14).



[H] = $Na_2S·9H_2O$; $KHSO_3$; $(H_2N)_2·H_2O$; $HN{=}C(NH_2)S(O)OH$

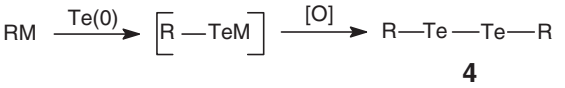
Scheme 11



5 **4**

i, Na ascorbate, $MeOH/H_2O$/acetone[81];
ii, $NaBH_4$, THF, H_2O, 0 °C, air[47]

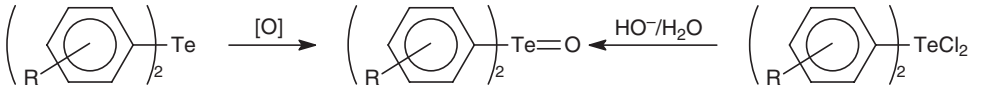
Scheme 12



4

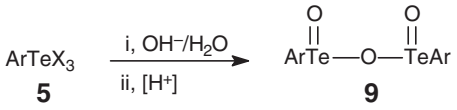
R = alkyl, Ph, vinyl
M = MgX, Li

Scheme 13

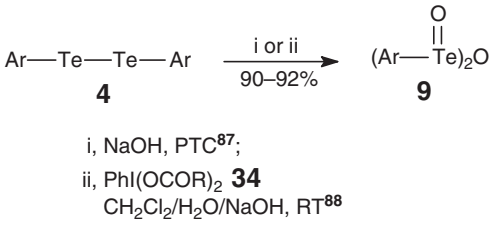


3 **8** **6**

Scheme 14



Scheme 15



Scheme 16

Aryltellurinic acid anhydrides **9** are prepared by alkaline hydrolysis of aryltellurium trihalides **5**, followed by acidification.[84–86] The anhydrides **9** precipitate as white solids in high yields (Scheme 15).

Alternatively, these compounds can be prepared in a two-phase system, by alkaline hydrolysis[87] of diaryl ditellurides **4** or by reaction of these precursors with phenyl iodine(III) dicarboxylates **34**[88] (Scheme 16).

9.13.5 Interaction of Nucleophilic Tellurium Species with Organic Substrates

9.13.5.1 Interaction of Nucleophilic Tellurium Species with Organic Substrates without Incorporation of Tellurium

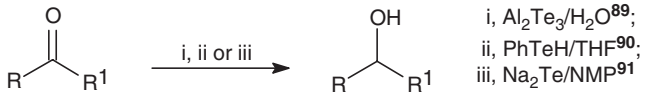
The nucleophilic species of tellurium presented in Section 3 interact with organic substrates promoting synthetically useful transformations. At the end of the reaction, the tellurium atom is not incorporated into the product. Some of these processes present advantages over the known methodologies for being milder, more selective, or catalytic on tellurium. These reactions have been extensively discussed already in preceding reviews.[6,7,10–12] In this section, we present just the most representative examples of the synthetic applications of some nucleophilic species of tellurium.

9.13.5.1.1 Reduction of functional groups

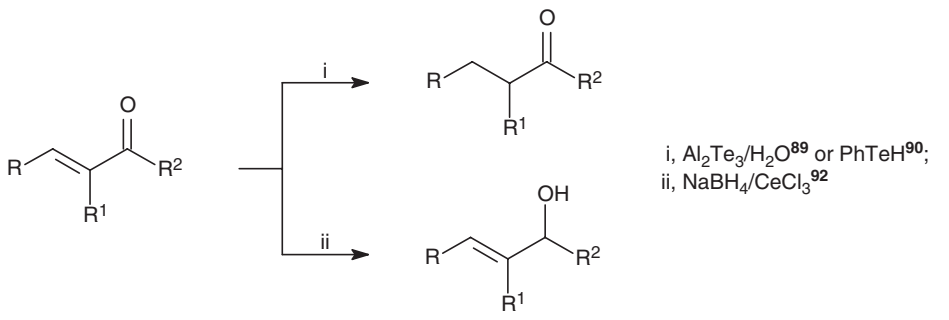
Aldehydes and ketones are reduced to the corresponding alcohols by hydrogen telluride[89] or phenyl tellurol.[90] In addition, aromatic aldehydes can be reduced to the respective alcohols by sodium telluride in *N*-methyl-2-pyrrolidinone (NMP)[91] (Scheme 17).

Under appropriate experimental conditions, hydrogen telluride, phenyl tellurol, and sodium hydrogen telluride perform the selective reduction of double bonds of α,β-unsaturated carbonyl systems.[89,90] This reaction with α,β-unsaturated ketones complements the cerium trichloride/sodium borohydride method, which reduces the carbonyl group, keeping the carbon–carbon double bond intact[92] (Scheme 18).

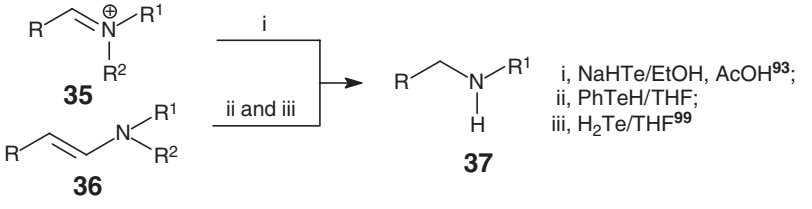
Similarly, iminium salts **35**[90,93] and enamines **36**[91,94] (Scheme 19) are reduced to the corresponding amines **37** by means of tellurium reagents.



Scheme 17



Scheme 18



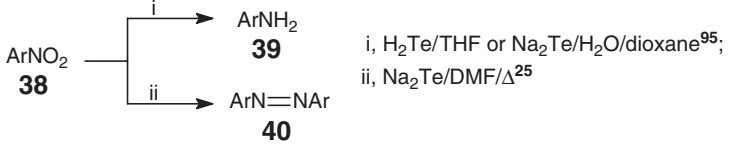
Scheme 19

The reduction of nitro compounds **38** by tellurium reagents depends on the structure of the substrate and on the solvent used. For example, phenyl tellurol[90] and sodium telluride[95] reduce nitroarenes to anilines **39** in protic solvents. When an aprotic solvent is used, sodium telluride converts the nitroarenes **38** into the respective azo compounds **40** (Scheme 20).[25]

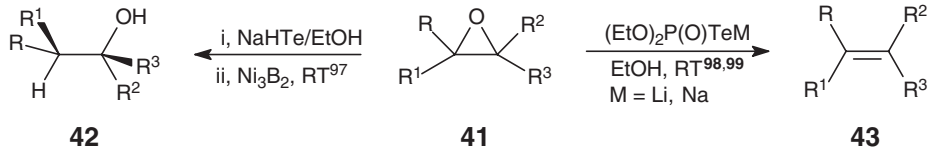
The reaction of nitroalkanes and dinitroalkanes with sodium hydrogen telluride gives nitrosoalkane dimers and olefins, respectively.[96] The reduction of other nitrogenated species such as hydroxylamines, azides, nitroso, azo, and azoxy compounds can also be performed by using tellurium reagents.[6,11,12]

9.13.5.1.2 Epoxides and aziridines ring openings

Sodium hydrogen telluride reacts with epoxides **41** by a S_N2 mechanism giving the respective telluroalcohols. These intermediates are easily converted into the corresponding alcohols **42** by treatment with nickel boride.[97] In contrast, epoxides suffer deoxygenation when treated with alkali *O,O*-dialkyl phosphorotellurolates, to give the corresponding olefins **43** (Scheme 21).[98,99]



Scheme 20



Scheme 21

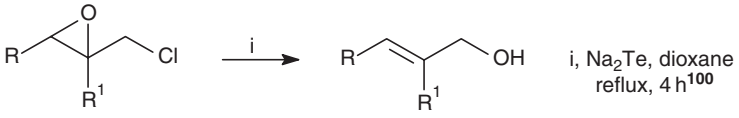
The reaction of sodium telluride with epoxides bearing a leaving group in a suitable position, such as in chloromethyl epoxides **44**, gives allylic alcohols **45**. This process has been performed under mild conditions due to the high nucleophilicity of the telluride ion (Scheme 22).[100]

The combination of the chemistry shown in Scheme 22,[100] with the Sharpless kinetic resolution (SKR) of secondary allylic alcohols **46**[101] provides a method for the conversion of racemic allylic alcohols **46** into a single enantiomer with 100% theoretical yield.[102] The reaction of sodium telluride with the mesylate **48** derived from **47** affords **46a**. In this way, a single enantiomer of the allylic alcohol **46** is obtained in high yield (Scheme 23).[102]

By a similar process, sodium telluride reacts with aziridine sulphonates **49** bearing a trityl or benzydryl group at the *N*-atom affording the corresponding allylic amines **50** (Scheme 24).[103]

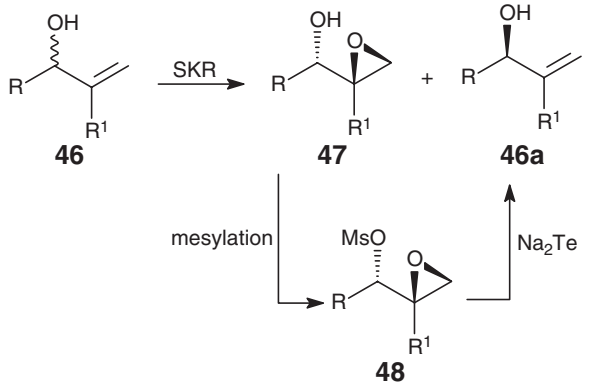
9.13.5.1.3 Heteroatoms removals

The dehalogenation of *vic*-dibromides by diaryl tellurides or diaryl ditellurides giving alkenes constitutes one of the first applications of tellurium reagents in organic synthesis.[6,9–12,104] This classic transformation has been reinvestigated and it was shown that *para*-$Me_2NC_6H_4$ and $(C_6H_{13})_2Te$, associated to different reducing agents, such as sodium ascorbate, are better debrominating systems than the previously employed $(para\text{-}MeOC_6H_4)_2Te$.[105,106] Besides *vic*-dibromides, other types of vicinal substituents such as ditosylates,[107] dimesylates,[107] and dinitro[96] groups are also removed by anionic tellurium species, leading to the corresponding olefins. The method allows the preparation of conjugated dienes as well (Scheme 25).[108]



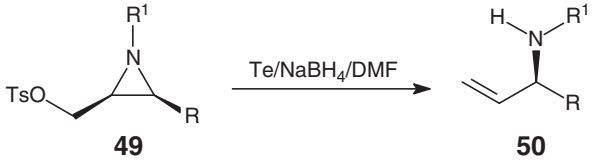
44 **45**

Scheme 22



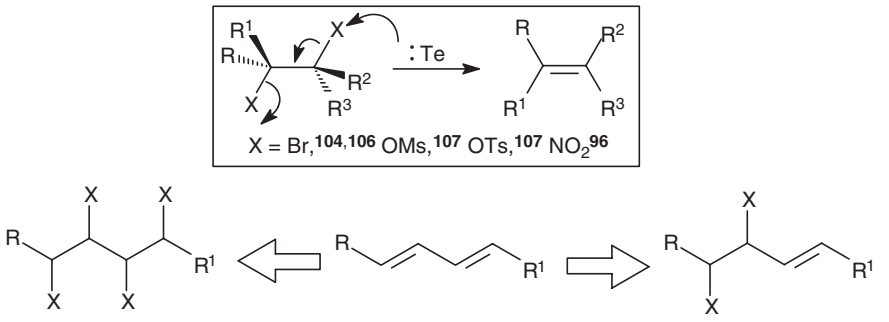
46 **47** **46a** **48**

Scheme 23

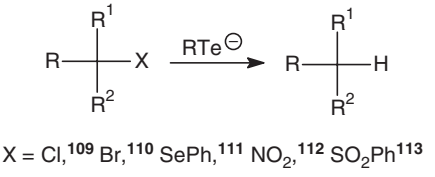


49 **50**

Scheme 24



Scheme 25



Scheme 26

Tellurium species are also useful to remove several different types of substituents from organic compounds. In some cases, variation of the experimental conditions allows the reductive removal of a substituent to be performed selectively in the presence of other functional groups. Scheme 26[109–113] shows the removal of different substituents mediated by nucleophilic tellurium species.[6,11,12]

9.13.5.1.4 Deprotection of functional groups

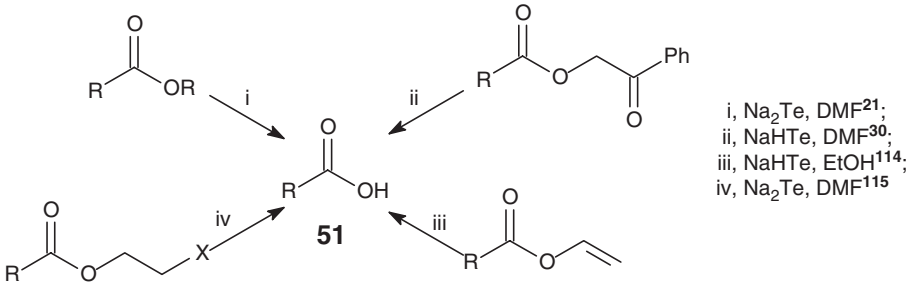
Some nucleophilic species of tellurium are used to regenerate a functional group from its protected form. For example, carboxylic acids **51** are regenerated in high yields from their alkyl and benzyl esters by using sodium hydrogen telluride or sodium telluride (Scheme 27).[21,30,114,115]

Similarly, the regeneration of phenols **52** from carboxylates **53**,[115] carbonates **54**,[116] or allyl ethers **55**[114] derivatives is performed with nucleophilic tellurium species (Scheme 28).

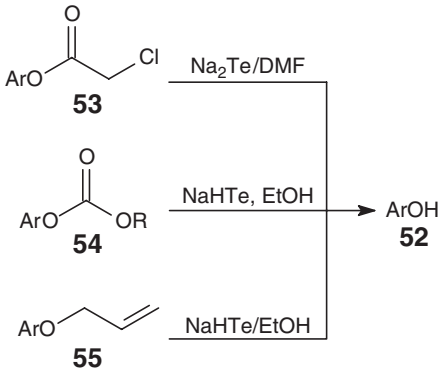
Amines **58** are recovered from trichloro-*t*-butyl carbamates **56** by reaction with sodium 2-thienyltellurolate **57**, which is regenerated in a catalytic process (Scheme 29).[117]

9.13.5.1.5 Carbon–carbon bond formation mediated by tellurium compounds

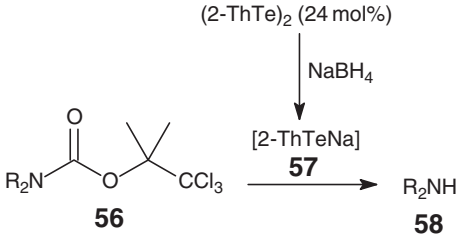
Some tellurium compounds can mediate the formation of anionic species and their reactions with electrophiles.[6,10–12,118] Some examples are given in the following.



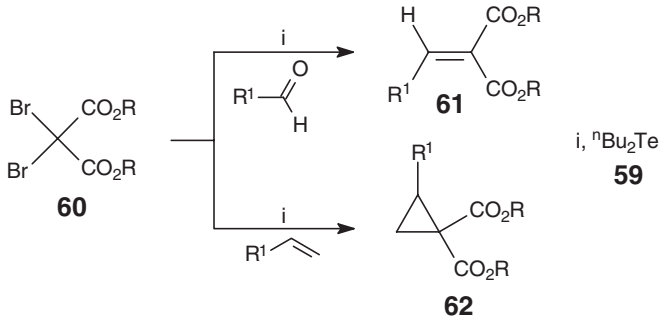
Scheme 27



Scheme 28



Scheme 29



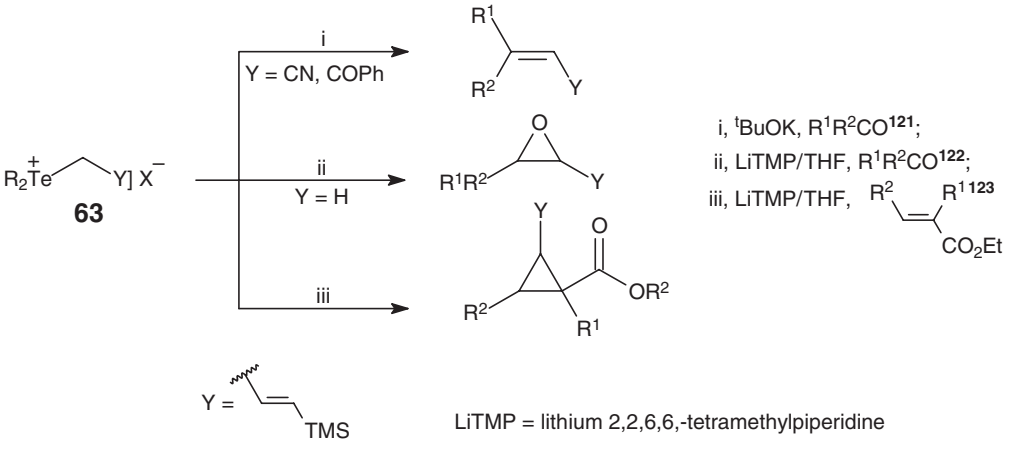
Scheme 30

Dibutyl telluride **59** reacts with iodomethyl triphenylphosphonium iodide to give triphenylmethylidene phosphorane, which reacts with aldehydes leading to the methylenation products in good yields.[119] The same reagent **59** also assists the reaction of dibromomalonates **60** with aldehydes and activated olefins affording alkylidene malonates **61** and cyclopropanes **62** derivatives, respectively (Scheme 30).[120]

Telluronium ylides,[118] derived from triorganotelluronium salts **63**, react with aldehydes, ketones, and α,β-unsaturated esters to give different products depending on the nature of the substituent at the α-carbon of the telluronium salt **63**. In Scheme 31,[121–123] examples of such transformations are given.

9.13.5.2 Interaction of Nucleophilic Tellurium with Organic Substrates with Incorporation of Tellurium

Nucleophilic species of tellurium can interact with organic substrates promoting functional groups and structural changes with incorporation of the tellurium atom into such substrates. Subsequent removal of tellurium from the resulting structures can give useful synthetic intermediates.



Scheme 31

9.13.5.2.1 Alkylation reactions

Alkali tellurides **13** and **14**, or ditellurides **15**, are potent nucleophiles and react rapidly with alkyl halides. Table 1 presents some representative examples of such reactions leading to dialkyl tellurides **3** and dialkyl ditellurides **4**. Alkali organotellurolates **2** are also potent nucleophiles and are used to prepare symmetrical and unsymmetrical tellurides (Table 2).

As the telluride or ditelluride anions and the organotellurolate anions are potent nucleophiles, the alkylation reaction is fast and occurs in a number of organic solvents. These are well-known reactions and deserve more comment. For specific examples, the interested reader should consult the exhaustive review works available.[4,5,11,12]

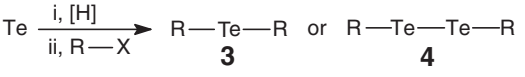
Diorganotellurides are themselves nucleophiles and react with alkyl halides to give triorganotelluronium salts.[118]

9.13.5.2.2 Arylation reactions

Although not widely used as a route to organic tellurium compounds, the arylation of nucleophilic tellurium species has been considered for this purpose.[5,11,12] In Scheme 32,[26,29,126,127] some illustrative examples of such methods are presented.

The drastic reaction conditions used in some cases and the low yields of specific examples limit the usefulness of this approach as a general method to introduce tellurium into organic substrates.

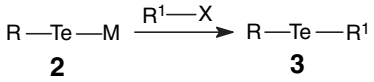
Table 1 Alkylations of nucleophilic tellurium species



[H]	*R–X (conditions)*	*Product*	*Yield (%)*	*References*
Na, NH_3 liq.	^{i}Pr	$(^{i}Pr)_2Te$	80	124
KBH_4, NaOH, Ar, reflux, 2 h	^{n}OctBr, MeOH, reflux, 1 h	$(^{n}Oct)_2Te$	78	20
TUDO, NaOH, H_2O, THF, CTAB	^{n}OctBr, THF, N_2, CTAB, reflux, 2 h	$(^{n}Oct)_2Te$	85	24
CTAB, THF, DMSO, TUDO, NaOH, reflux, 1 h	^{n}OctBr, NT, 1 h	$(^{n}OctTe)_2$	98	24

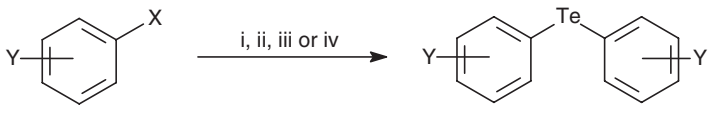
CTAB = cetyltrimethylammonium bromide; TUDO = thiourea dioxide (HN=C(NH_2)S(O)OH).

Table 2 Reaction of organotellurolates **2** as nucleophiles



[R–Te–M] (generation method)	*R–X (conditions)*	*Product*	*Yield (%)*	*References*
$(PhTe)_2/NaBH_4$, EtOH, N_2	$^nC_{12}H_{25}Br$, reflux, 3.5 h	$PhTe^nC_{12}H_{25}$	76	44
Te/(*E*)-PhCH=CHMgBr, THF, reflux	$^nC_4H_gBr$, RT, 0.5 h	(*E*)-$PhCH{=}CHTe^nC_4H_9$	79	34
(*para*-$CH_3OC_6H_4Te)_2$/TUDO, NaOH, THF, CTAB	$^nC_{12}H_{25}Br$, reflux, 6.0 h	*para*-$CH_3OC_6H_4Te^nC_{12}H_{25}$	96	125

CTAB = cetyltrimethylammonium bromide; TUDO = thiourea dioxide ($HN{=}C(NH_2)S(O)OH$).



i, Te + Na, solvent, 130–170 °C, 16–24 h[29];
ii, Te/$HOCH_2SO_2Na$, NaOH/H_2O, DMF, 60 °C, 10 h[26];
iii, Te/NaH/NMP, 50–100 °C[126];
iv, RTeNa, UV[127]

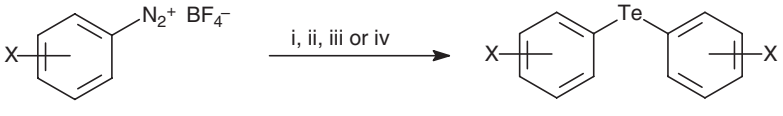
Scheme 32

Another approach to aryl tellurides involving nucleophilic tellurium species consists in the use of aryldiazonium salts as substrates. Arenediazonium tetrafluoroborates **64** react with sodium telluride,[128] potassium tellurocyanate **65**, sodium *O,O*-diethylphosphorotellurolate **66**, or aryl tellurolate **2** to give the corresponding diaryl tellurides **3** in moderate yields (Scheme 33).[129,130]

9.13.5.2.3 Hydrotelluration of alkynes

The hydrometallation of alkynes is one of the most widely used routes to vinyl organometallics,[131] which in turn are valuable in the construction of molecular structures containing carbon–carbon double bonds of defined stereochemistry.

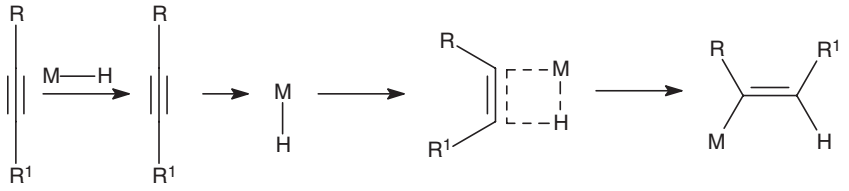
Usually, the reaction displays *cis*-stereoselectivity giving (*E*)-organometallics. However, isomerization occurs very often leading to mixtures of (*Z*)- and (*E*)-vinyl organometallics. The accepted general mechanism for the hydrometallation reaction involves the initial coordination of the alkyne to a vacant orbital of the metal, followed by insertion of the hydrogen–metal bond to a π-bond of the alkyne (Scheme 34).[132]



64 **3**

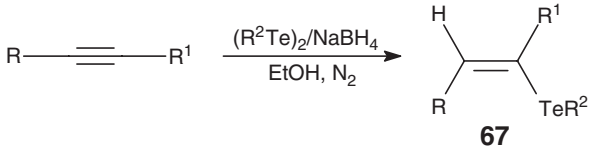
i, Na_2Te, DMF, 0–5 °C, 30 min[128];
ii, KTeCN **65**, DMSO, RT[129];
iii, $(EtO)_2P(O)TeNa$ **66**, DMF, RT[128];
iv, $(ArTe)_2/NaBH_4$ **2**, EtOH, THF, NaOH aq.[130]

Scheme 33



Scheme 34

Contrary to the *cis*-nature of the addition observed for all the other hydrometallation reactions, the hydrotelluration is *anti*, leading to (*Z*)-vinylic tellurides **67**,[5,8,9,11,12,41,132] which are stereochemically stable. No isomerization of the hydrotelluration products of alkynes was reported to date. Organotellurols are too unstable to be isolated (Section 2). In this way, the hydrotelluration of alkynes is performed using *in situ* generated organotellurols. The hydrotelluration system is prepared by reacting a diorganoditelluride with sodium borohydride in ethanol (9.13.6.1). The nature of the hydrotelluration agent was never determined and some authors represent it as RTeNa. In view of the protic nature of the solvent, an equilibrium between ionic species present in solution and the solvent can occur, giving rise to a tellurol. However, since the nature of the species present in the ethanolic solution was not yet determined, it seems to be more correct to indicate the hydrotelluration agent as $(R^2Te)_2/NaBH_4$ (Equation (6)).



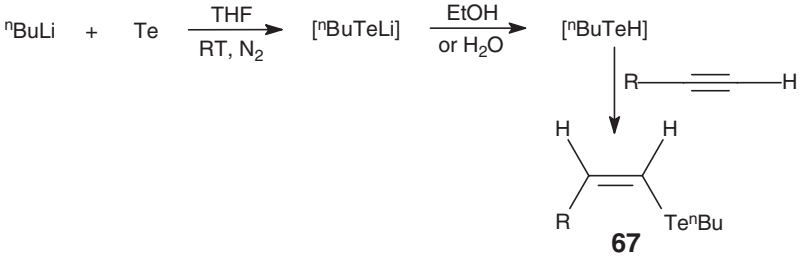
(6)

67

This is a very practical method to prepare vinylic tellurides in good yields when oxygen is excluded from the reaction medium, since oxygen rapidly transforms the hydrotellurating agent into diorganoditelluride that is indicated by the fast change of the color of the solution from colorless to dark red when air is accidentally introduced in the reaction flask.[133] The only serious drawback of the procedure is when dibutylditelluride is employed as the source of the tellurol, since dibutyl ditelluride is not commercially available and is a very bad smelling compound. A method to generate the hydrotellurating agent which circumvents this problem was developed.[42] This method consists of the insertion of elemental tellurium into a carbon–lithium bond, followed by addition of a proton source such as ethanol or water in stoichiometric amounts. The reaction is performed in deoxygenated tetrahydrofuran under a nitrogen atmosphere. Reaction with the appropriate alkyne gives the vinylic tellurides **67** with similar yields to the ones obtained by the ditelluride/sodium borohydride method (Scheme 35).[42]

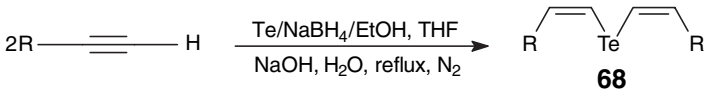
For practical reasons, this method should replace the traditional one involving the system diorganoditelluride/sodium borohydride.

Bis-vinylic tellurides **68** can be prepared by reacting monosubstituted alkynes with a hydrotelluration system prepared from elemental tellurium and sodium borohydride in a mixture of ethanol/aqueous sodium hydroxide.[133] The stereochemistry of the resulting vinylic tellurides is also *Z* (Equation (7)).



67

Scheme 35



68 (7)

Experimentally, this reaction is more troublesome than the hydrotelluration using organotellurium species, because a two-phase system is formed which makes it difficult to control the reaction time.

To date, a number of vinylic tellurides have been prepared by the methods described above. In the following sections we will comment on the influence of the substrate structure on the yields and regiochemistry of the product.

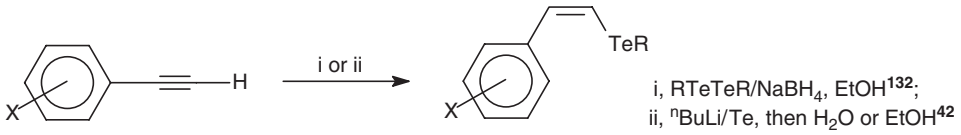
9.13.5.2.3.(i) Monosubstituted aryl alkynes

Several vinylic tellurides are prepared starting from monosubstituted aryl alkynes.[41,42,133–136] The yields are usually high and the reports in the literature mention that the stereochemistry of the product is 100% *Z*. In the same way, only the formation of 1,2-disubstituted vinylic tellurides is reported (Scheme 36).

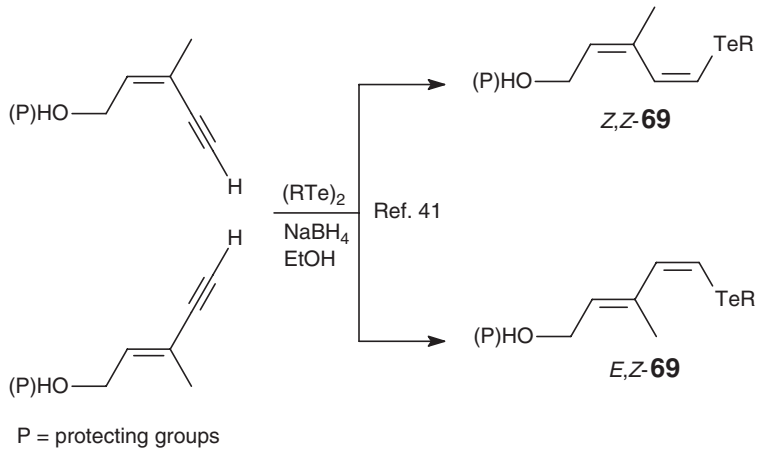
Most of the products are odorless, crystalline solids, or dense pale yellow oils, which can be manipulated for short periods in the presence of air and indoor light. In addition, these compounds can be recrystallized or chromatographed with no perceptible decomposition. After long standing under refrigeration in the dark, no decomposition or isomerization is observed. However, long exposure to indoor light leads to darkening of the products. Another precaution to avoid decomposition is to evaporate the solutions to dryness immediately after the isolation or chromatographic purification, since the compounds in solution are prone to air oxidation. In this way, it is advisable to keep vinylic tellurides protected from light and air. These general comments are valid for the other classes of vinylic tellurides discussed in the forthcoming sections.

9.13.5.2.3.(ii) Monosubstituted alkynes conjugated to a carbon–carbon double bond

Alkynes conjugated to double bonds are hydrotellurated in a similar way to aryl alkynes. The reaction with this class of alkynes is important, since it leads to conjugated double bonds of defined stereochemistry.[27,34,41,42,137] In view of the easy access to enynes of defined stereochemistry,[138] *Z,Z*-**69** or *E,Z*-**69**, vinylic tellurides can be obtained as illustrated in Scheme 37.



Scheme 36



Scheme 37

In view of the easy transformation of vinylic tellurides into reactive vinyl organometallics (see Section 9.13.8.2), the structures shown in Scheme 37 are valuable bifunctional synthons of conjugated olefins (Scheme 38).

9.13.5.2.3.(iii) Alkynes conjugated to triple bonds

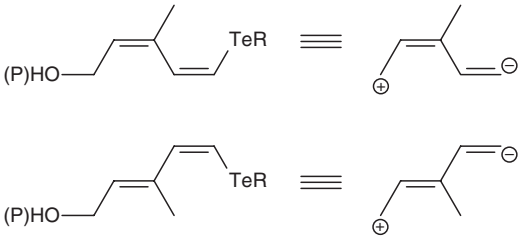
Alkynes conjugated to a triple bond are very reactive systems toward hydrotelluration. The reaction occurs in a shorter reaction time when compared to the reactions commented above. In this case, even disubstituted triple bonds give vinylic tellurides in good yields.[41,42,139,140] In the case of non-symmetrical diynes, an order of reactivity is established for the hydrotelluration of triple bonds of the enyne systems (terminal > propargylic > alkyl substituted > aryl substituted).[140] This order of reactivity is reflected in the preferential formation of the vinylic tellurides shown in Scheme 39.

9.13.5.2.3.(iv) Alkynes bearing electron-stabilizing groups

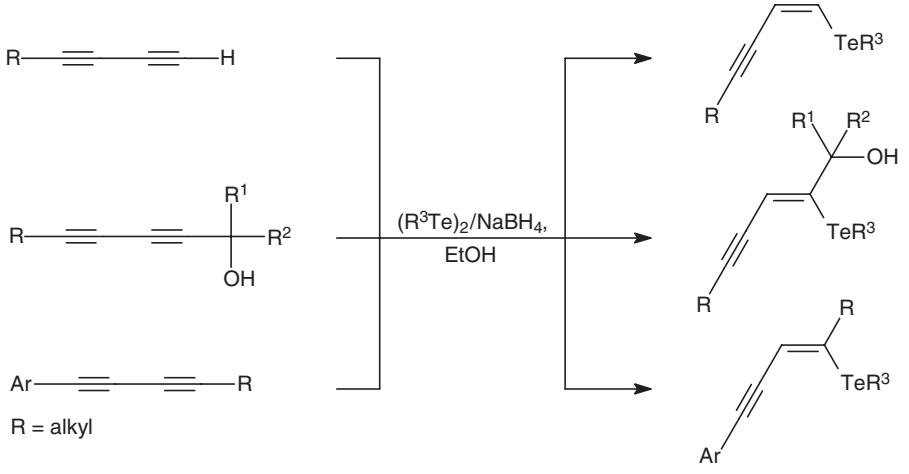
The hydrotelluration reaction of alkynes bearing keto or ester groups was among the first to be studied. Recently, a number of reports dealing with the hydrotelluration of alkynes bearing electron-stabilizing groups has appeared in the literature. All systems reported to date give the (*Z*)-vinylic telluride, with the tellurium moiety linked to the β-carbon. Several examples of the successful hydrotelluration of internal alkynes of this type have been reported (Scheme 40).[33,141–143,145–150]

Activated alkynes react with alkali, alkyl, or aryl tellurolates in non-protic solvents to give intermediate carbanions, which are trapped with electrophiles leading to tri- and tetrasubstituted olefins (Scheme 41).[151]

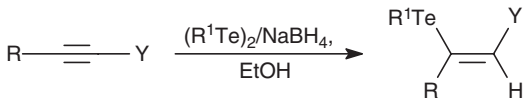
The products present the (*Z*)-stereochemistry preferentially, in view of the *trans*-addition of the tellurolate to the triple bond. In some cases, mixtures of (*Z*)- and (*E*)-olefins are obtained due to equilibration of the intermediate vinyl anion, as a consequence of the nature of the tellurolate or the electrophile.[151] By using alkynes **70** bearing an internal electrophile, the cyclic product **71** is formed (Scheme 42).



Scheme 38

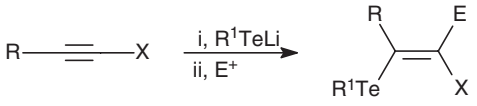


Scheme 39



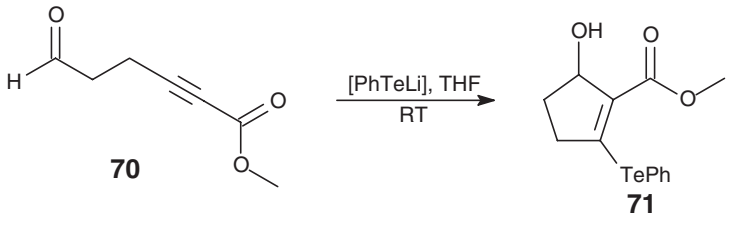
Y = CHO,[141,142] COR^1,[142] CO_2R^1,[33,142–146] $(EtO)_2P(O)$,[147,148] $PhSO_2$,[148,149] SPh[150]

Scheme 40



X = CO_2Me, PhSO, *p*-TolS, $PhSO_2$
E^+ = PhCHO, Ph_2CO, CH_3CHO, TMSCl

Scheme 41



Scheme 42

9.13.5.2.3.(v) Alkyl alkynes

Alkyl alkynes **72** are hydrotellurated, giving a mixture of regioisomers. The (*Z*)-1,2-disubstituted vinylic tellurides **73** predominate.[8,9,11,12] Internal alkynes of this type do not react. Alkyl alkynes substituted by an oxygen or nitrogen on carbon-3 **74** also give a mixture of regioisomers. In this case, the (*Z*)-1,2-disubstituted isomers **75** also predominate. On the other hand, secondary or tertiary propargyl alcohols are hydrotellurated to give predominantly (*Z*)-1,2-disubstituted vinylic tellurides.[135,145] Recently, it was observed that the propargyl alcohol protected by the *tert*-butyldimethylsilyl (TBDMS) **76** group gives almost exclusively the 1,2-disubstituted regioisomer **77** on hydrotelluration (Scheme 43).[152,153] The regioisomers can be separated by silica gel column chromatography. This is the less-studied class of alkynes toward hydrotelluration.

Enantiomerically pure propargyl alcohols **76** protected by TBDMS are hydrotellurated to give enantiomerically pure protected allylic alcohols (*R*)-**77** and (*S*)-**77** (Scheme 44).[153]

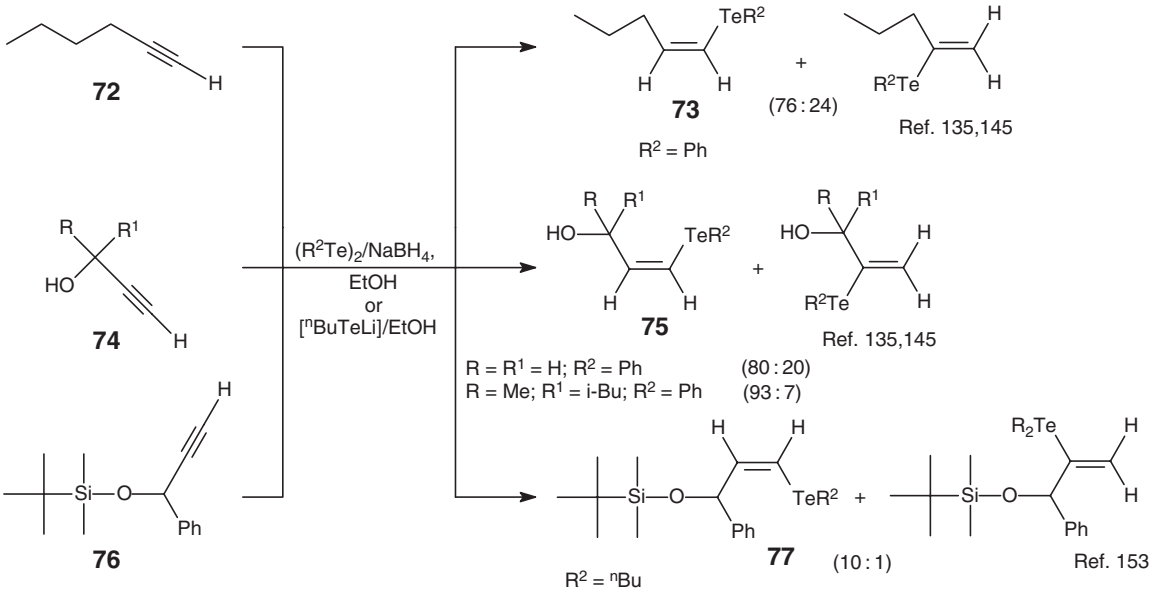
Another route to alkyl vinyl tellurides of (*Z*)-configuration recently developed is shown in Scheme 45.[154]

In this case, the hydrotelluration occurs rapidly due to the presence of the electron-attracting group linked to the alkynyl carbon. Then, the carbonyl group is reduced with sodium borohydride or with DIBAL-H to give the (*Z*)-vinylic tellurides **78** in high yields.[154]

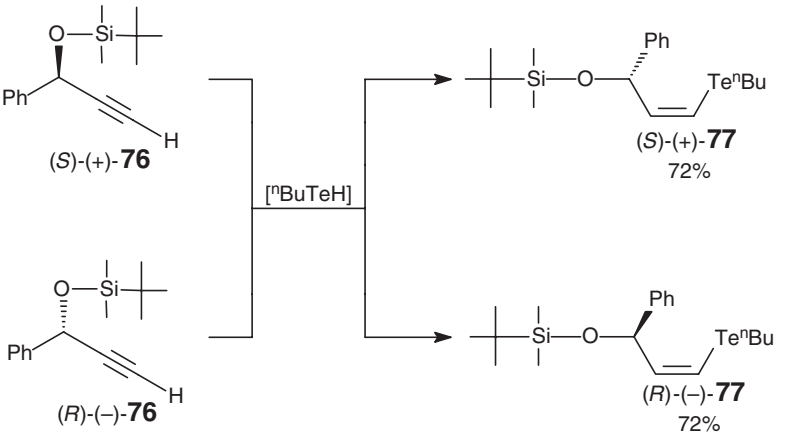
The hydrotelluration methods described in Equation (6) and in Scheme 35 are used to prepare tellurium-containing heterocycles by intramolecular hydrotelluration of alkynes. Depending on the structure of the starting alkynes, mixtures of *endo*-dig and *exo*-dig products (Scheme 46) are formed. In some cases, the exclusive formation of one of the possible isomers is observed.[155–166]

9.13.5.2.4 Hydrotelluration of alkenes

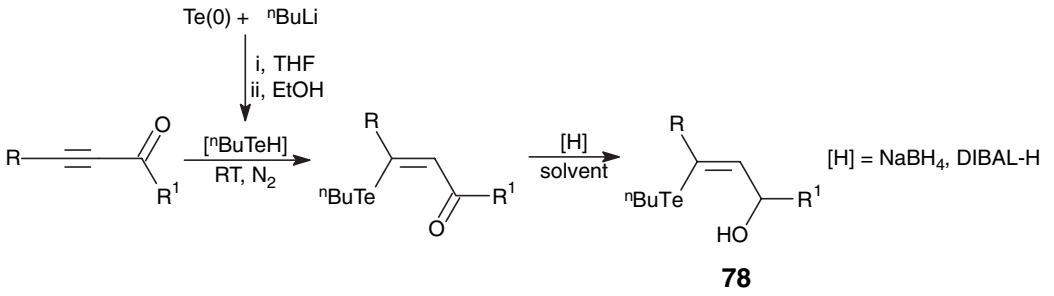
In contrast to the hydrotelluration of alkynes, the hydrotelluration of alkenes has been very little investigated. To date, only two papers dealing with this reaction have been published.[167,168] In the first one, the hydrotellurating system used is PhTeTePh/$NaBH_4$ (Scheme 47).[167]



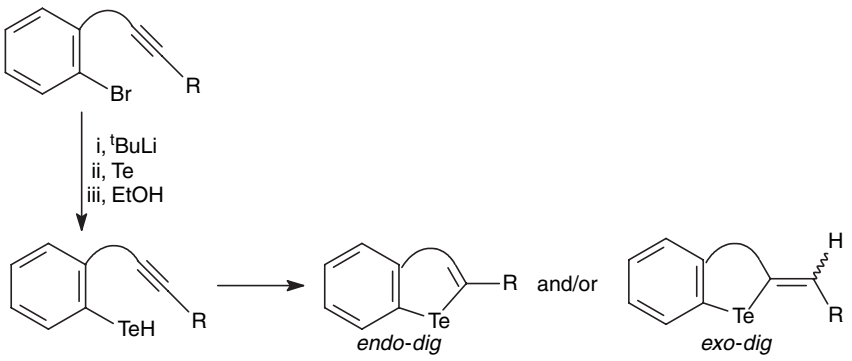
Scheme 43



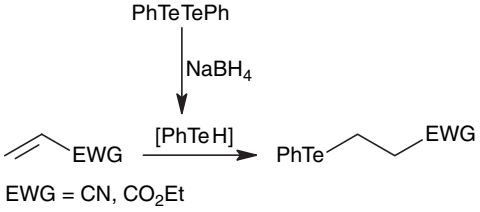
Scheme 44



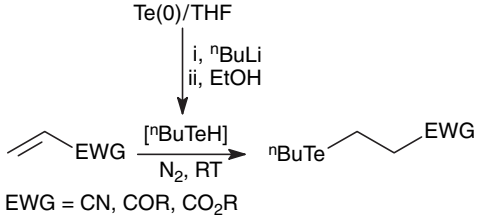
Scheme 45



Scheme 46



Scheme 47



Scheme 48

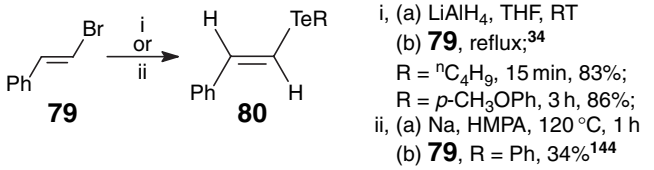
More recently, the hydrotelluration of similar alkenes has been performed under non-reducing conditions.[168] It is observed that only olefins containing electron-withdrawing groups (EWGs) can be hydrotellurated. Usually, the yields are good and the formed alkyl tellurides are not bad-smelling compounds, except the telluride-containing CN as the EWG, which has a penetrating odor (Scheme 48). This is a practical and attractive method to prepare functionalized alkyl tellurides, since the starting materials are easily available.

9.13.5.2.5 Vinylic substitution

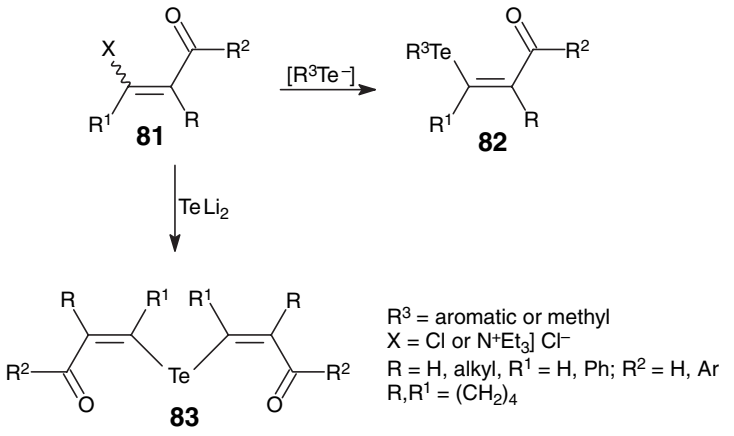
The vinylic substitution by tellurolate anions has not been extensively investigated. It is, however, an efficient method for synthesizing vinylic tellurides of defined stereochemistry. (*E*)-*β*-bromostyrene **79** reacts with organotellurolate anions to give (*E*)-vinylic tellurides **80** (Scheme 49).[34,144]

Reaction of *β*-haloenones **81** with organotellurolates gives the corresponding vinylic tellurides (*Z*)-**82** and (*Z*)-**83** (Scheme 50).[169]

Organotellurolates are generated by insertion of elemental tellurium into organolithiums or by reduction of diaryl ditellurides with lithium naphthalide.[169] Good results are also obtained when dibutyl ditelluride is transformed into *n*-butylaluminum tellurolate by reaction with DIBAL-H, followed by vinylic substitution with haloenones.[170] In all cases, the (*Z*)-vinylic tellurides are obtained, even starting from mixtures of (*Z*)- and (*E*)-haloenones. This result is surprising, since the vinylic substitution shown in Scheme 49 occurs with retention of the double-bond geometry.[171]



Scheme 49



Scheme 50

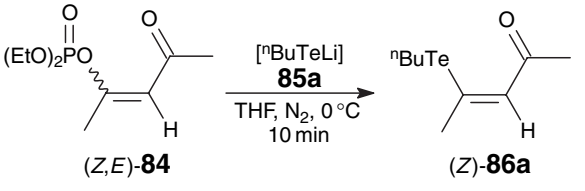
The preparation of the β-haloenones starting materials sometimes requires acidic reaction conditions. In view of the synthetic potential of the vinylic tellurides (Section 9.13.8.2) associated with the above-commented stereoselectivity, enol phosphates are employed instead as starting materials for the preparation of vinylic tellurides, since enol phosphates can be prepared under very mild basic conditions.

The reaction of enol phosphates **84** with lithium *n*-butyl tellurolate **85a**, generated by reaction of *n*-butyllithium with elemental tellurium, occurs rapidly to give the corresponding vinylic tellurides **86** (Scheme 51). Mixtures of (*Z*)- and (*E*)-enol phosphates afford the (*Z*)-vinylic telluride as the only product.[170,172]

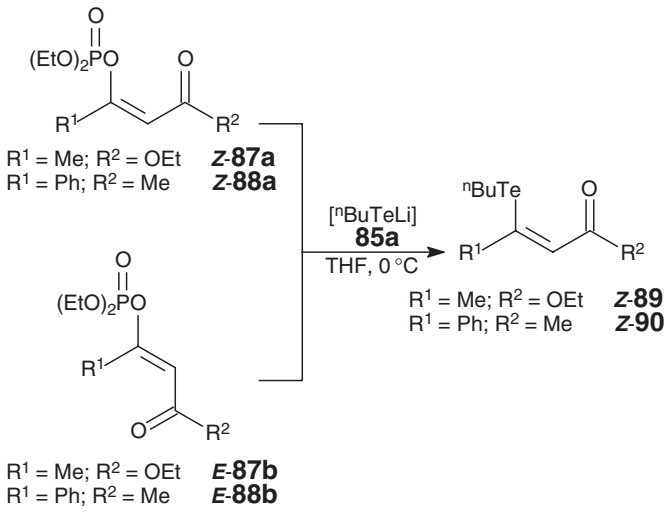
The stereoselectivity of the process is demonstrated by reacting the (*Z*)-**87a**, (*Z*)-**88a** and the (*E*)-**87b**, (*E*)-**88b** enol phosphates with lithium *n*-butyl tellurolate **85a**. The same products (*Z*)-**89** and (*Z*)-**90** are obtained in both cases (Scheme 52).[170]

The vinylic substitution was investigated with five different tellurolate anions, ^{n}BuTeLi **85a**, ^{s}BuTeLi **85b**, ^{t}BuTeLi **85c**, PhTeMgBr **85d**, and (2-Th)TeLi **85e**. These organotellurolates were reacted with the same enol phosphate **84**. In all cases, the stereochemistry of the products **86** was *Z*. Aryl tellurolates **85d** and **85e** reacted more slowly than the alkyl tellurolates **85a–85c** (Scheme 53).[170]

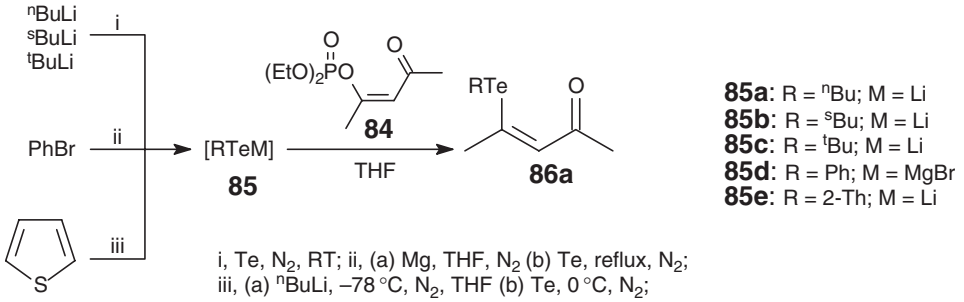
The leaving group had no significative influence on the reaction time as shown in Scheme 54. In all cases, only the (*Z*)-vinylic tellurides **86a** and **89** were obtained starting from mixtures of the enolic substrates **84, 87, 91–94** (Scheme 54).[170]



Scheme 51

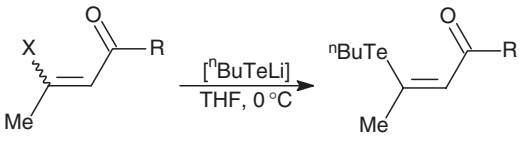


Scheme 52



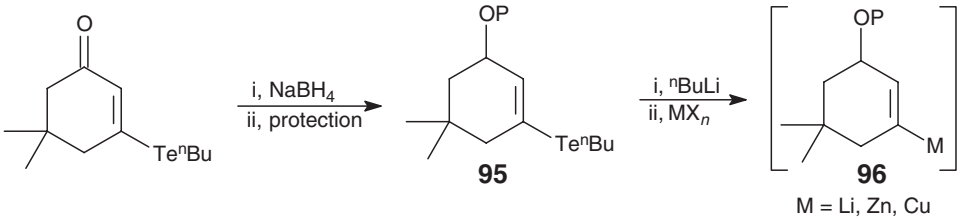
Telluralate canion	*Product*	*Yield* (%)	*Temperature* (°C)	*Reaction time* (min)
85a	**86a**	85	0	10
85b	**86b**	70	0	15
85c	**86c**	65	0	15
85d	**86d**	60	RT	300
85e	**86e**	70	RT	300

Scheme 53

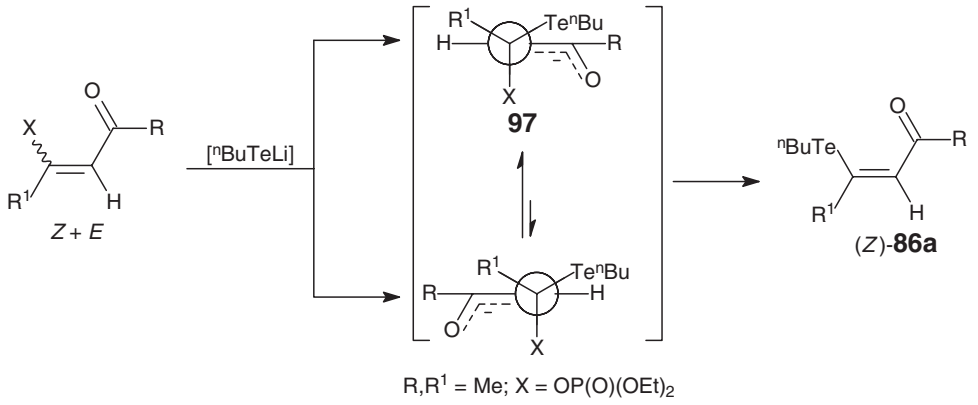


X,R	*Substrate*	*Product*	*Yield* (%)	*Reaction time* (min)
X = $(EtO)_2$ P(O)O; R = Me	(*Z*,*E*)-**84**	(*Z*)–**86a**	85	10
X = $(EtO)_2$ P(O)O; R = OEt	(*Z*,*E*)-**87**	(*Z*)–**89**	75	10
X = OTs; R = Me	(*Z*,*E*)-**91**	(*Z*)–**86a**	75	20
X = OTs; R = OEt	(*Z*,*E*)-**92**	(*Z*)–**89**	70	20
X = OTf; R = OEt	(*Z*,*E*)-**93**	(*Z*)–**89**	80	20
X = OAc; R = Me	(*Z*,*E*)-**94**	(*Z*)–**86a**	80	15

Scheme 54



Scheme 55



Scheme 56

The vinylic substitution allows the synthesis of allylic alcohols **95** bearing a vinyltellurium moiety that constitute synthons of the corresponding organometallics **96** (see Section 9.13.8.2) (Scheme 55).[154]

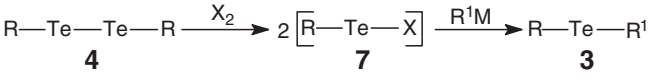
The substitution reaction probably occurs via an addition–elimination mechanism with the intermediate formation of an enolate. A through-space interaction of the carbonyl oxygen with the tellurium atom should favor rotamer **97**, which eliminates X^- to give only the (*Z*)-isomer **86a** (Scheme 56).[170]

9.13.6 Interaction of Electrophilic Tellurium Species with Organic Substrates

In this section, the reactions of electrophilic tellurium species will be considered. Among these species are tellurium tetrachloride **16**, organotellurium halides **7**, organotellurium trihalides **5**, and also diorganoditellurides **4**, since these species can be attacked by carbanions. Diorganotellurium oxides **8**, arenetellurinic acid anhydrides **9**, and other oxidizing agents will also be discussed in Section 9.13.6.3, since in these species the tellurium atom is electron deficient.

9.13.6.1 Reaction with Organometallics

The most synthetically useful reaction of nucleophilic tellurium consists in the reaction of organotellurium halides with organometallics. This reaction was systematically studied for the first time by Petragnani several years ago.[80] In recent years, it has been used to prepare a number of tellurium-containing organic substrates. The general route is shown in Scheme 57.



Scheme 57

In the following, the preparation of specific classes of organic tellurium compounds by means of this general route will be discussed.

9.13.6.1.1 Preparation of diaryl, arylalkyl, and arylalkynyl tellurides

The reaction of a Grignard reagent with an aryltellurium halide is of general character, leading to the title compounds in high yields. Normally, the aryltellurium halide is generated *in situ* by reaction of a diaryldittelluride with bromine or iodine in an inert solvent (Scheme 58).[5,9,11,12,80]

The alkynyl aryl tellurides are more conveniently prepared by means of the lithium acetylide,[173] although magnesium acetylides can be used as well[80] (Scheme 59).

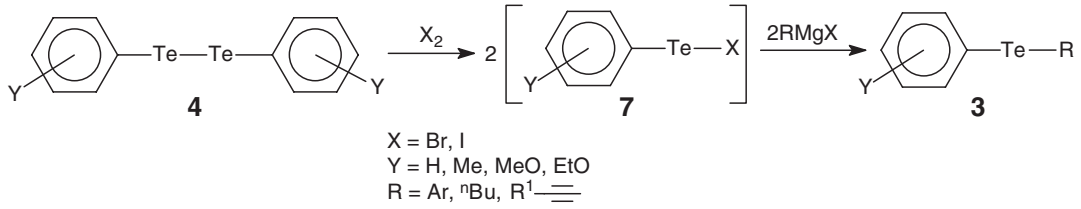
9.13.6.1.2 Preparation of vinylic tellurides

Vinylic tellurides bearing simple vinyl groups (e.g., CH_2═CH, PhCH═CH) can be prepared by reacting the corresponding lithium or Grignard reagents with organotellurium halides.[8,9,34,174]

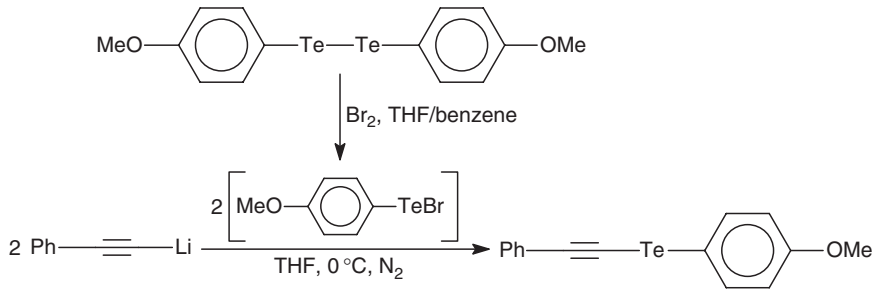
If unusual vinylic tellurides or vinylic tellurides of defined stereochemistry are required, other vinyl organometallics are employed. In recent years, a number of methods of preparing vinylic derivatives of tellurium using organotellurium halides have been developed.

In a recent example, diphenyl ditelluride is used instead of an aryltellurium halide as the tellurating agent (Scheme 60).[175]

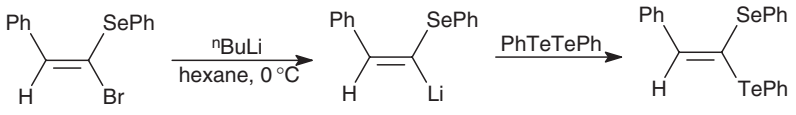
The hydrozirconation of alkynes is a well-established reaction, giving vinylic zirconium species of known regio- and stereochemistry.[176] These species react with aryltellurium halides leading to vinylic tellurides with the (*E*)-stereochemistry **98** (Scheme 61),[177,178] so complementing the other general routes to these compounds which give preferentially the (*Z*)-products (Sections 9.13.5.2.3, 9.13.5.2.5).



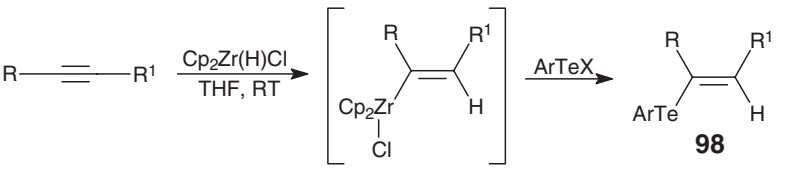
Scheme 58



Scheme 59



Scheme 60



Scheme 61

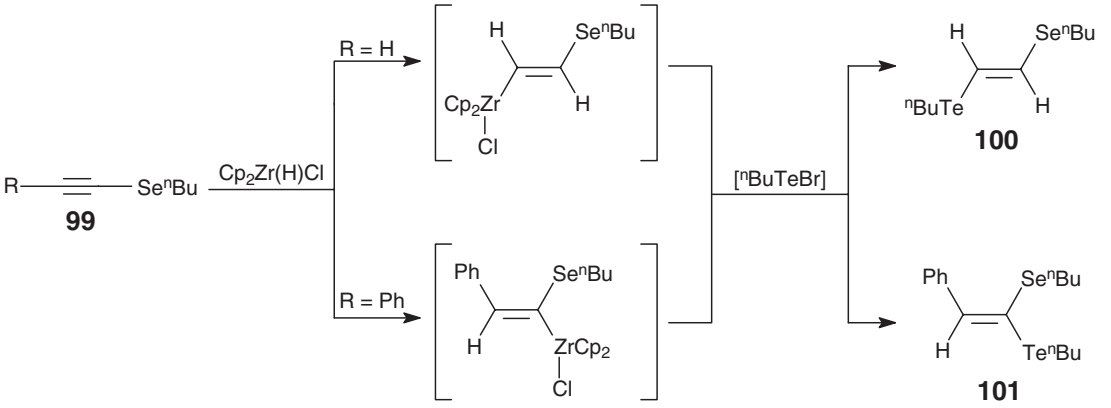
The hydrozirconation of alkynylselenides **99** has been applied to prepare mixed vinylic selenides and tellurides, (e.g., **100**) and selenotelluroketene acetals (e.g., **101**) (Scheme 62).[179]

Depending on the nature of the R groups of the alkynyl selenides **99**, vinylic species with different regio- and stereochemistry are obtained (Scheme 62). When R is an alkyl group, mixture of products of different regiochemistry is obtained,[179] which makes this method unsuitable for the preparation of this class of compounds. A solution for this problem consists in the use of lithium alkynyl selenolates **102** as precursors of the vinylzirconium species **103**, as shown in Scheme 63.[180]

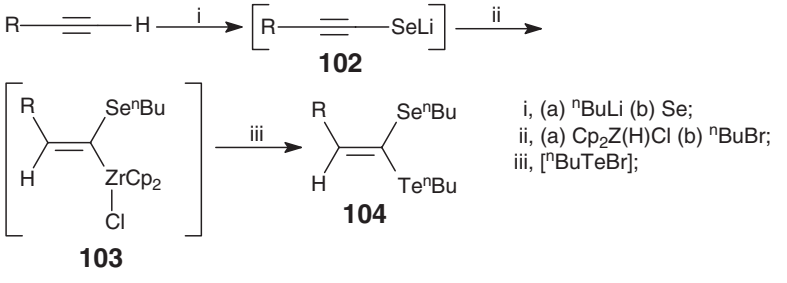
Under these conditions, the selenotelluroketene acetals **104** are the only products detected in good yields.[180]

When telluroalkynes **105** are submitted to the hydrozirconation, only the vinylzirconium intermediates **106** are formed.[179,181] These are captured with organotellurium halides to give bistelluroketene acetals **107** (Scheme 64).[179]

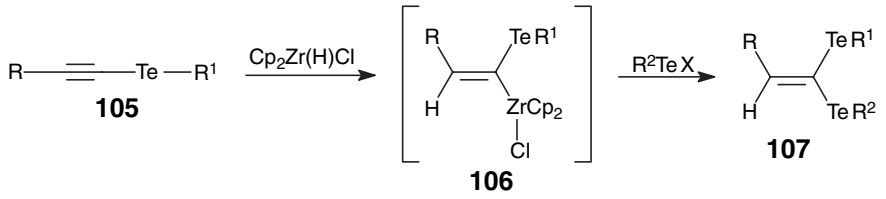
Similarly, hydrozirconation of stannyl acetylenes **108** followed by treatment of the intermediate vinylzirconium species **109** with *n*-butyltellurium bromide and then with sodium borohydride gives tintelluroketene acetals **110** (Scheme 65).[182]



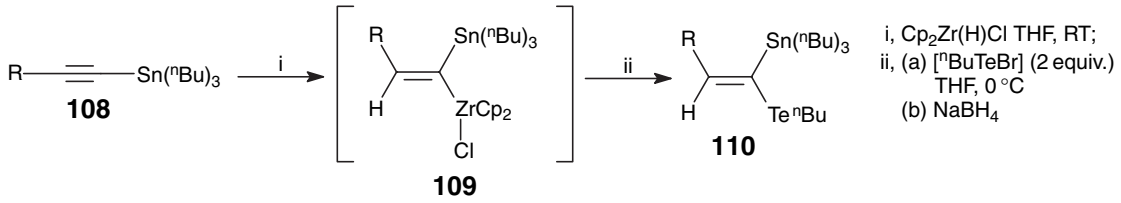
Scheme 62



Scheme 63



Scheme 64

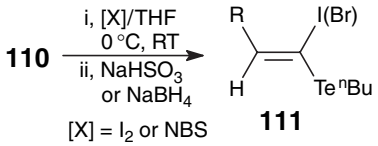


Scheme 65

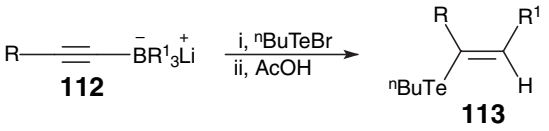
The tributyltin group of **110** can be replaced by bromine or iodine to give **111** with retention of configuration, as shown in Scheme 66.[182]

The reaction of *n*-butyl tellurium bromide with alkynyl borates **112** is used to prepare (*E*)-vinylic tellurides **113** as shown in Scheme 67.[183]

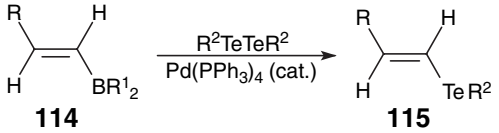
Diorganoditellurides are used as the tellurating agent in a catalytic process involving vinylic boranes **114** to prepare vinylic tellurides **115** (Scheme 68).[184]



Scheme 66



Scheme 67



Scheme 68

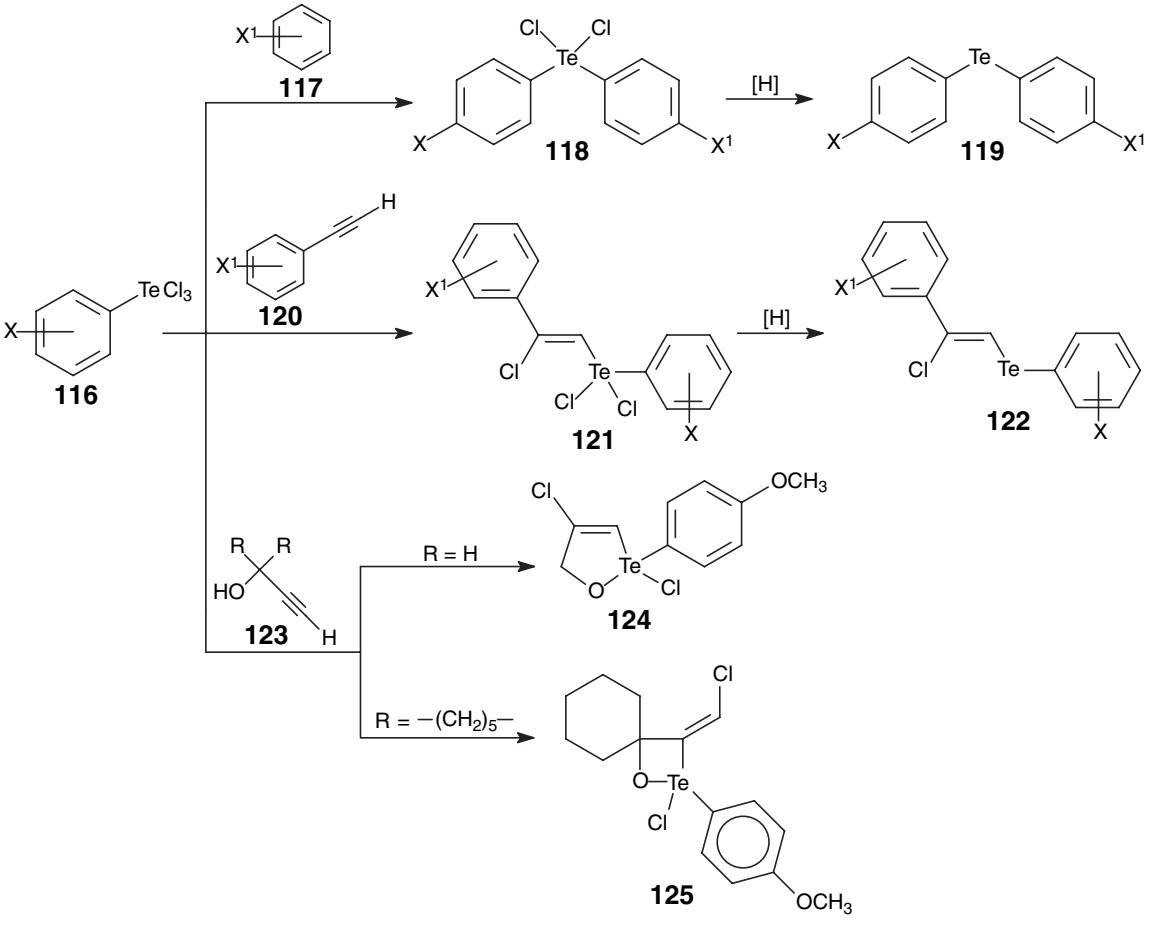
9.13.6.2 Reaction with Activated Aromatics, Alkenes, and Alkynes

The reactivity of aryltellurium trichlorides **116**, the most synthetically used organotellurium trihalides, toward activated aromatics, alkenes, and alkynes is similar to the reactivity of tellurium tetrachloride toward the same substrates (Section 9.13.4.2.3). In Scheme 69, the principal features of the reactions involving aryltellurium trichlorides are presented.

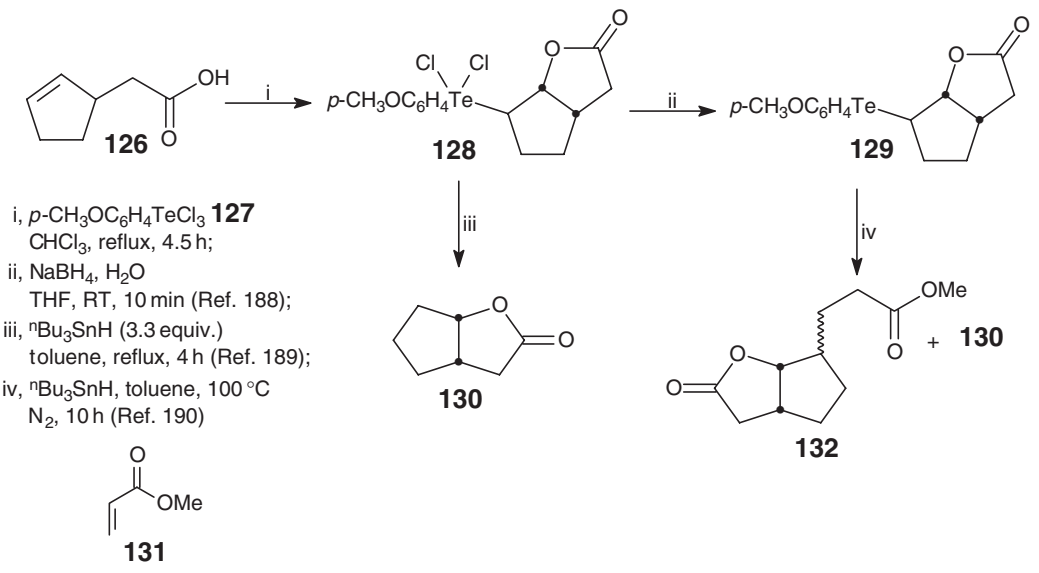
The reaction of aryltellurium trichlorides **116** with activated aromatics **117** gives the corresponding diaryltellurium dihalides **118**, which by reduction give the diaryl tellurides **119**.[5,11,12,55]

Reaction of **116** with monosubstituted aryl alkynes **120** gives the (*Z*)-vinylic aryltellurium dichlorides **121**, which are reduced to the (*Z*)-vinyl aryl tellurides **122** by reaction with sodium borohydride.[185] Alkynes bearing an OH at C_3 react with aryltellurium trichlorides **116** to give cyclic products **124** or **125** depending on the steric demand on C_3, in a similar way that was observed in the reaction with tellurium tetrachloride (Section 9.13.4.2.3).[186]

The reaction of aryltellurium trichlorides with olefins bearing an internal nucleophile also presents features similar to those observed in the reaction of such substrates with tellurium tetrachloride (Section 9.13.4.2.3). The cyclofunctionalizations with aryltellurium trichlorides were explored more than the $TeCl_4$-promoted reaction, in view of the greater stability of the aryltellurium trichlorides toward moisture. The first synthetic transformation of this type was described by Petragnani in 1959.[66,187] In view of the synthetic importance of the selenocyclization of unsaturated substrates, the corresponding tellurocyclization was also explored (Scheme 70). γ,δ-Unsaturated carboxylic acids (e.g., **126**) are transformed into lactones by reaction with electrophilic tellurium species (e.g., **127**).[187,188] The diorganotellurium dichlorides (e.g., **128**) formed are reduced to the corresponding tellurides (e.g., **129**) by reaction with a suitable reducing agent.[188] The detellurated lactone, (e.g., **130** or **132**) is obtained by reaction of **128** or **129** with



Scheme 69



Scheme 70

tri-*n*-butyltin hydride in toluene. The intermediate free radical can be captured by a suitable radical trapping agent (e.g., **131**) to give the chain-elongation product (e.g., **132**).[189] Substrates containing other functional groups such as alcohols and esters have also been used in cyclofunctionalization reactions.[10,190–194]

As can be observed in Scheme 70, these transformations have parallels with well-established selenium processes.[195] Contrary to the cyclofunctionalization using selenium reagents, the tellurium version does not tolerate the presence of amines to capture the HCl formed during the process, since amines react with organotellurium trichlorides.[5,196] In this way, although several cyclizations can be successfully performed using tellurium electrophiles, the selenium methodology continues to be the method of choice for this purpose in view of the milder cyclofunctionalization conditions and the easier removal of the heteroatom at the end of the process.

9.13.6.3 Oxidation of Functional Groups

Some tellurium compounds find use as mild and selective oxidizing reagents for several functionalities. Some examples of the oxidizing properties of dianisyl tellurium oxide (An_2TeO) **133**[83,197,198] are shown in Scheme 71.

Immobilization of **133** on a polymeric resin shows several advantages over the corresponding monomeric species.[199] Oxidation of **133** with sodium periodate affords the corresponding bis-(*para*-methoxyphenyl) tellurone (An_2TeO_2) **134**, which presents a peculiar reactivity.[198] For example, the tellurone **134** oxidizes benzyl alcohols to benzaldehydes in good yields (Scheme 72), and also converts hydrobenzoin in benzaldehyde in good yield.

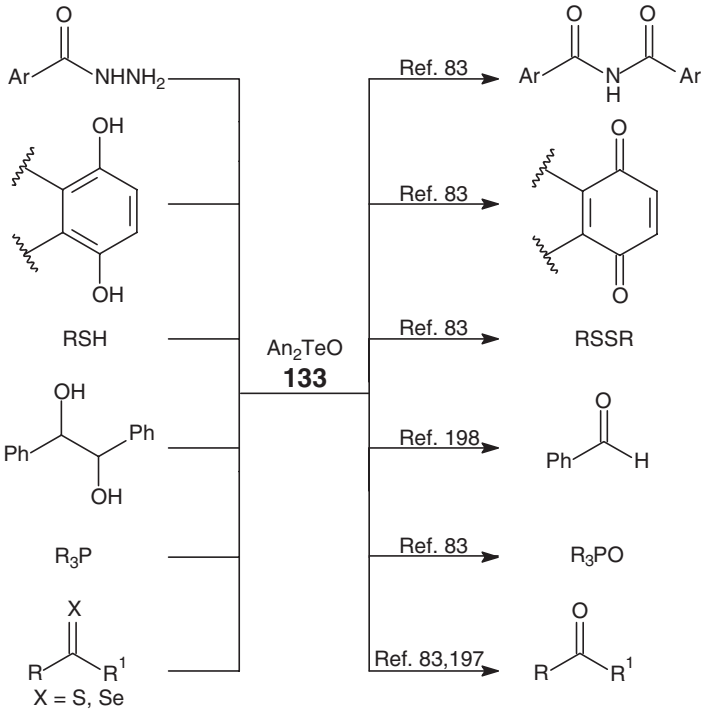
Aromatic, benzylic, and aliphatic thiols **135** are oxidized to the corresponding disulphides **136** by sodium tellurite under phase transfer conditions[200] (Scheme 73).

Arenetellurinic acid anhydrides **137** present similar reactivity to the diaryltellurium oxides shown in Scheme 71. However, oxidation of the *N*,*N*-diphenylthiourea **138** with **137** gives the unexpected *N*,*N*-diphenylcarbodimide **139** (Scheme 74).[201]

Oxidizing tellurium reagents react with olefins affording the products shown in Scheme 75.

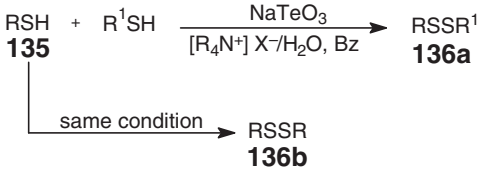
9.13.7 Free Radical Species

Organic tellurium compounds on heating, under light irradiation, or on reaction with radical initiators can originate free radicals, which interact with other molecules promoting transformations that can be of synthetic interest. Three main homolytic cleavage processes of organic tellurium compounds leading to free radicals can be mentioned: the homolytic cleavage of tellurium–tellurium or the tellurium–silicon bonds (process A, Scheme 76), the homolytic

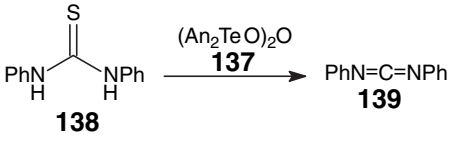


Scheme 71

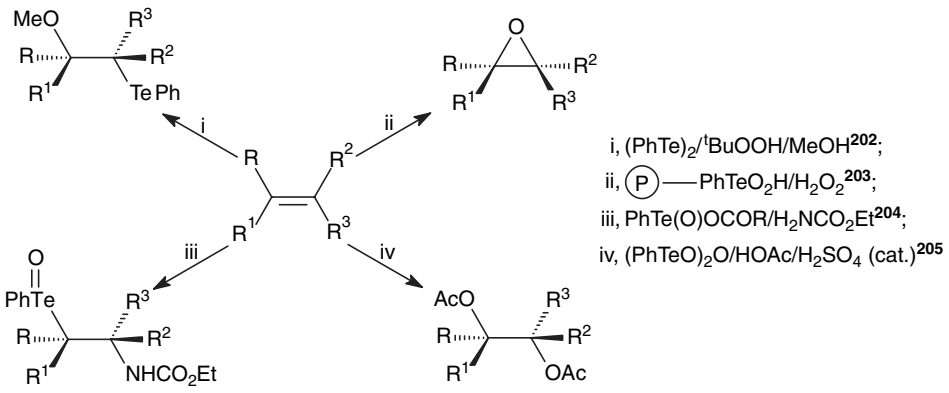
Scheme 72



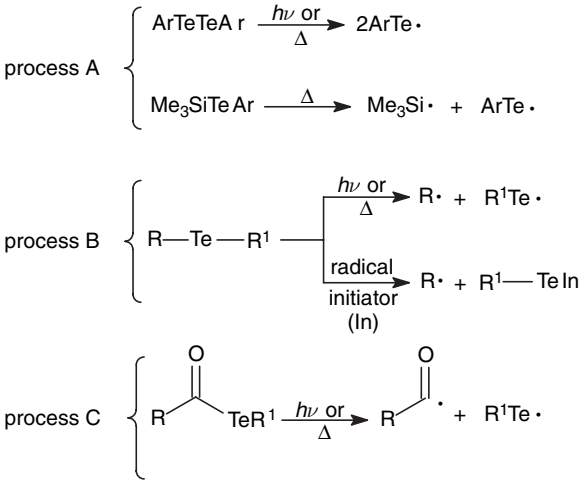
Scheme 73



Scheme 74



Scheme 75



Scheme 76

cleavage of sp^3-carbon–tellurium bonds of alkyl tellurides (process B, Scheme 76) and the sp^2-carbon–tellurium bond in acyl tellurides (process C, Scheme 76).

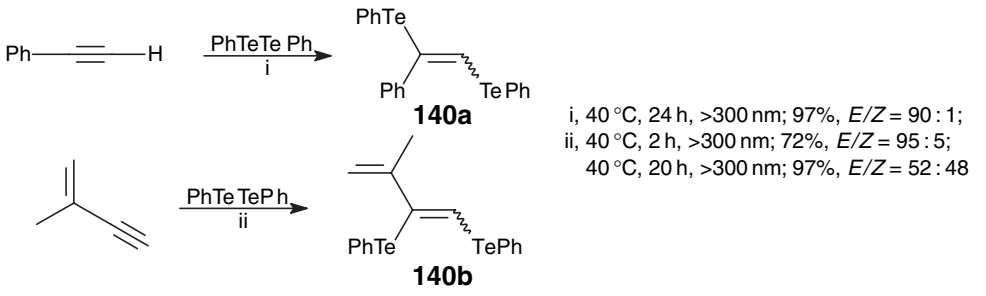
In the following, each process will be presented with the most general transformations they can perform in organic substrates.

9.13.7.1 Homolytic Cleavage of Tellurium–Tellurium or Tellurium–Silicon Bonds

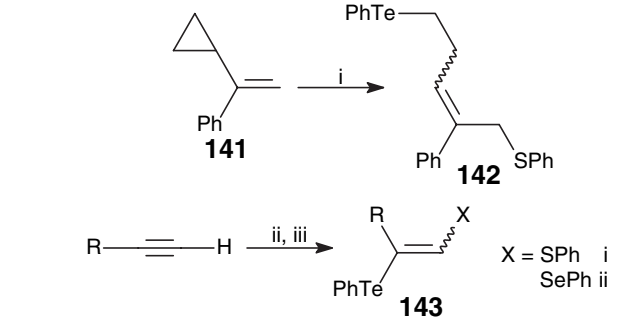
Irradiation of a mixture of diphenyl ditelluride and alkynes with a tungsten lamp in the absence of solvents gives 1,2-bis-(phenyltelluro)-alkenes **140** in variable yields. The *E*/*Z* ratio of the products is time dependent. Examples are given in Scheme 77.[206,207]

Irradiation of a mixture of diphenyl disulfide and diphenyl ditelluride in the presence of vinyl cyclopropane **141** with visible light gives the ring-opened thiatelluration product **142** as an *E*/*Z* mixture.[208] Similar reaction with alkynes gives the thiatelluration product **143**. The product stereochemistry depends on the nature of the alkyne.[208] A mixture of diphenyl diselenide and diphenyl ditelluride reacts with alkynes in a similar way (Scheme 78).[208] Similar reactions with allenes are less satisfactory.[209]

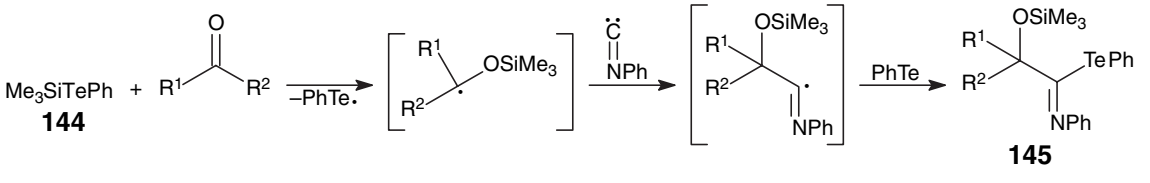
Reaction of phenyltellurotrimethylsilane **144** with aldehydes and ketones in the presence of phenylisocyanide gives tellurides **145** through the proposed mechanistic pathway shown in Scheme 79.[210]



Scheme 77



Scheme 78



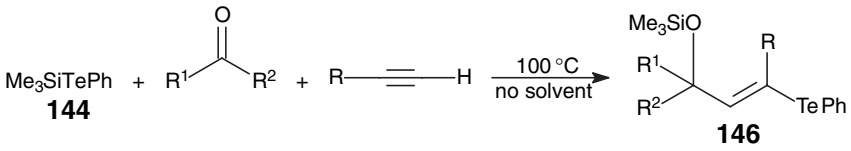
Scheme 79

By using an alkyne instead of the isocyanide, vinylic tellurides **146** are formed in good yields as a mixture of *Z*/*E*-isomers, predominating the (*E*)-olefin (Scheme 80).[211]

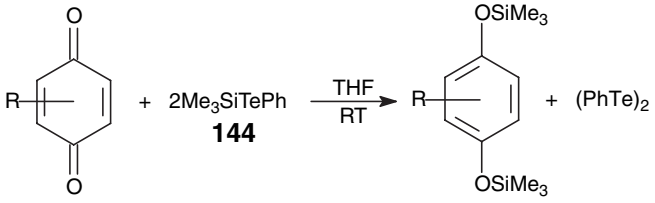
Compound **144** reduces quinones to the corresponding bis-silylated hydroquinones through a proposed free-radical mechanistic pathway (Scheme 81).[212]

9.13.7.2 Homolytic Cleavage of sp^3-Carbon–Tellurium Bonds

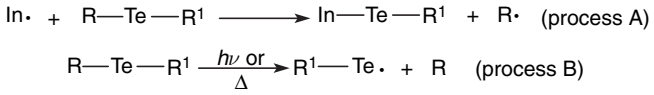
A sp^3-carbon–tellurium bond can be homolyticaly cleaved either by action of a radical initiator (process A) or by light irradiation or heat (process B) (Scheme 82). The radical species formed interact with organic substrates through radical mechanistic pathways leading to the products with or without incorporation of tellurium in the final structure.



Scheme 80



Scheme 81



Scheme 82

By process A, alkynes are carbotellurated[213] and cyclic products are formed.[214–218] In Scheme 83, representative examples of this process are given.

By process B, quinones are alkylated,[219,220] cyclic products are formed,[221] olefins are polymerized,[222,223] and glucosides are functionalized.[224–226] In Scheme 84, representative examples of such transformations are shown.

9.13.7.3 Homolytic Cleavage of sp^2-Carbon–Tellurium Bonds

Acyltellurides **147** on heating or photolysis are homolyticaly cleaved giving acyl radicals, which can be trapped inter- or intramolecularly.[227–232] In Schemes 85 and 86, representative examples of these processes are shown.

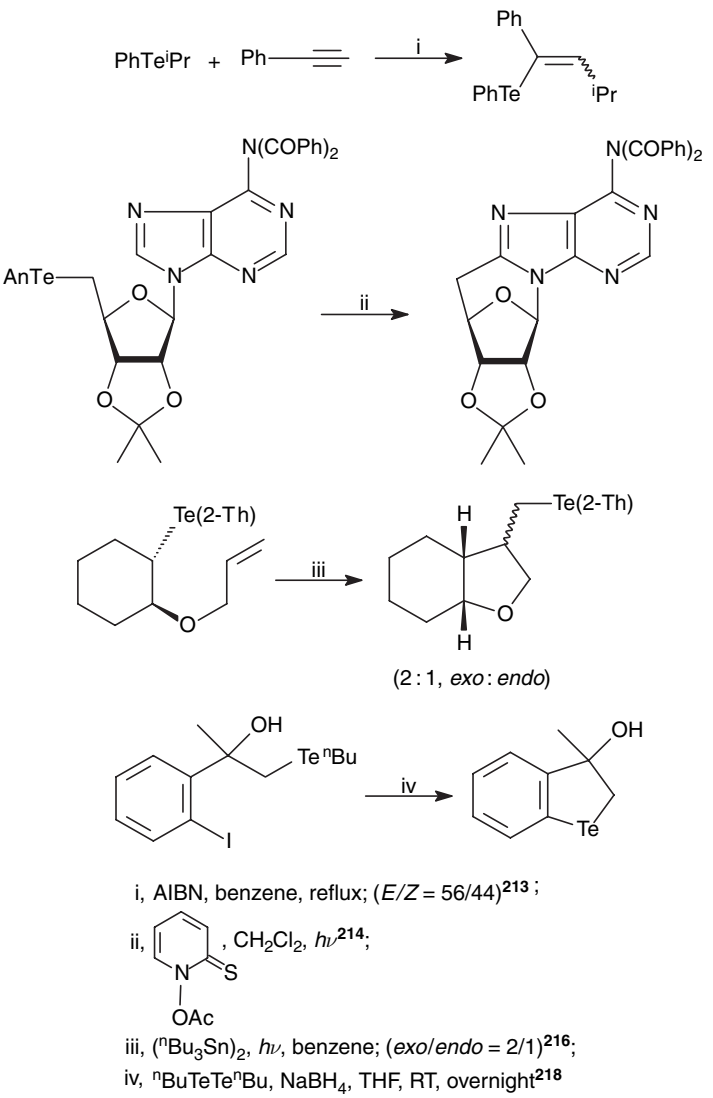
The radical reactions of organic tellurium compounds were recently reviewed.[233]

9.13.8 Tellurium Removal from Organic Substrates

The introduction of tellurium into an organic substrate promotes functional groups transformations or presents structural features that can be used for synthetic purposes, if suitable methods to remove tellurium from the resulting structures are available. To date, four main strategies have been explored for this end, namely, the telluroxide elimination, the tellurium/metal exchange, the coupling of tellurides with organometallic species and with alkynes, and the reductive removal via free radicals.

9.13.8.1 Telluroxide Elimination

The removal of tellurium from organic substrates through the oxidation of tellurides to tellurium oxides followed by elimination was first described by Sharpless.[234] However, soon it was observed that this reaction does not present the same attractiveness of the analogous selenoxide *syn*-elimination, since the tellurium version requires long heating or

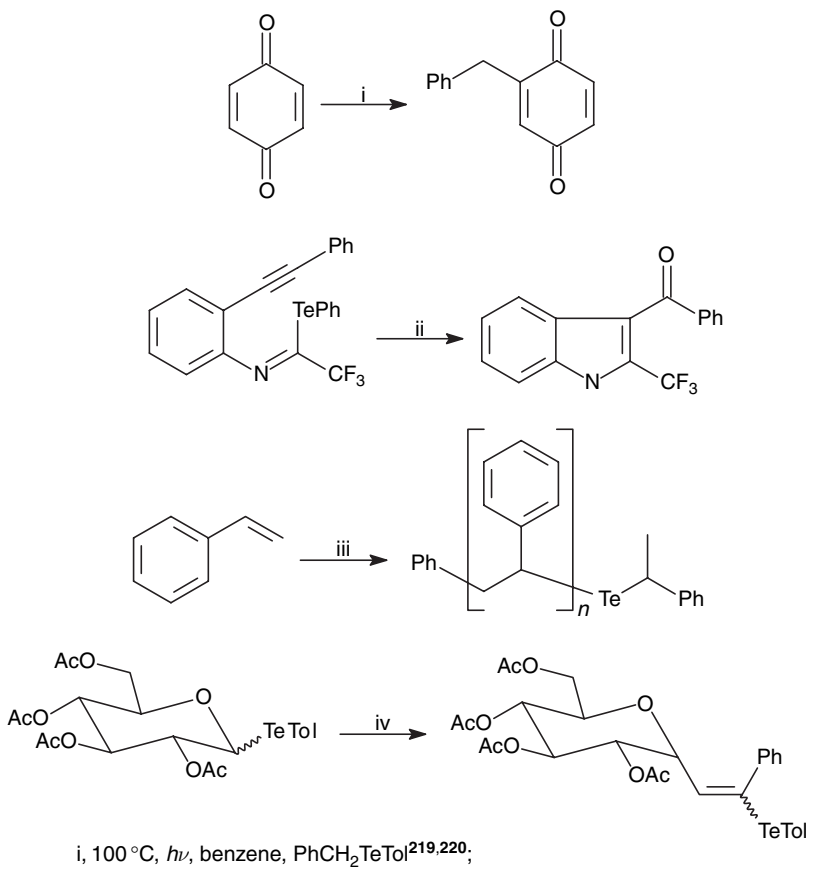


Scheme 83

high temperatures to occur.[11,12,46,235] In Scheme 87, the transformations of tellurides into olefins by telluroxide elimination[236] or sigmatropic rearrangement are shown.[237]

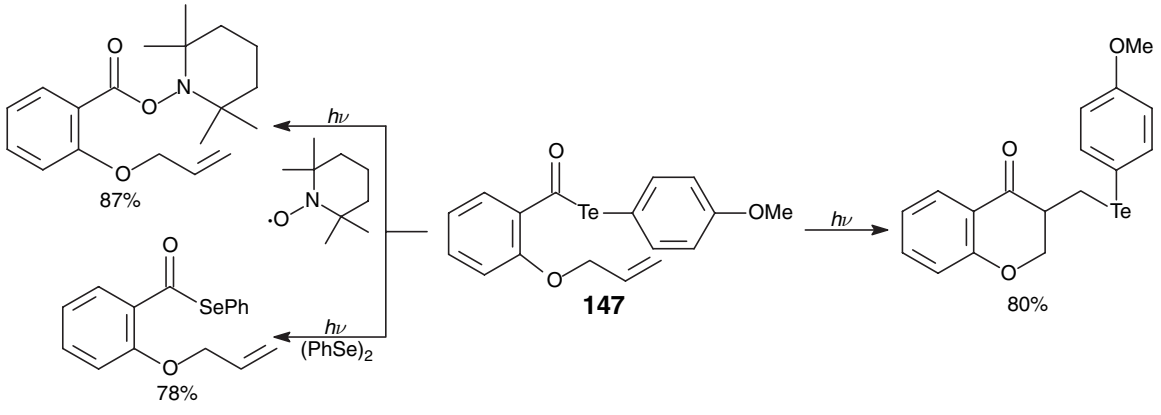
9.13.8.2 Tellurium–Metal Exchange

To date, the most promising synthetic transformation of organic tellurium compounds is their transformation into reactive organometallic compounds by reaction with commercially available alkyllithiums or with other easily prepared organometallic species. As mentioned in the preceding sections, the preparation of organic tellurium compounds is nowadays a routine practice, and compounds with defined stereochemistry can be easily obtained. Their transformation into reactive organometallics is a powerful synthetic tool that allows the formation of new carbon–carbon bonds in a stereoselective way. Considering the relative carbanion stability, an organometallic reagent attacks the tellurium atom of a diorganotelluride generating another organometallic, if the latter is more stable than the former. It is worth mentioning that this is a unique property of tellurides, when compared with similar compounds of the other members of the chalcogen family. Neither sulfides nor selenides suffer such an exchange reaction in a clean and mild way as the tellurides do.

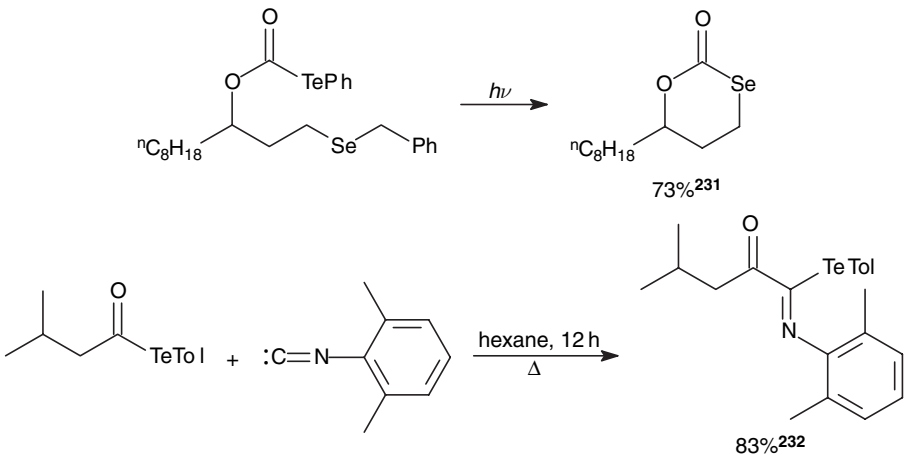


i, 100 °C, *hν*, benzene, $PhCH_2TeTol$[219,220];
ii, *hν*, THF/H_2O, RT[221];
iii, PhTe(Ph)CH, 105 °C, 16–18 h, N_2[223];
iv, Ph—≡—H, *hν*, 120 °C, 20 h, (α-*E*:α-*Z*:β-*E*:β-*Z* = 47:29:13:11)[225]

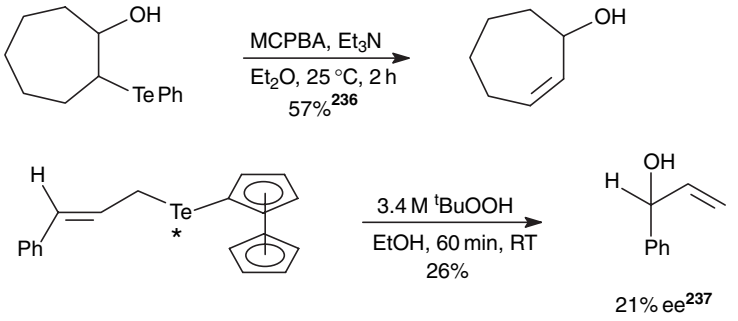
Scheme 84



Scheme 85[227]



Scheme 86



Scheme 87

9.13.8.2.1 Tellurium–lithium exchange

The tellurium–lithium exchange is one of the fastest lithium–metalloid exchange reactions.[238] Recently, NMR studies provided evidences that this exchange proceeds through an ate complex.[239]

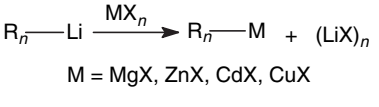
Having in mind the fact that lithium is the most electropositive metal among those with wide synthetic applications (Li, Mg, Zn, Cd, Cu), the preparation of an organolithium compound formally represents the access to any other of such classes of organometallic compounds by a transmetallation reaction (Scheme 88).[240]

Some of these transmetallations were already experimentally performed with organolithium species derived from tellurides and will be commented upon in the forthcoming sections.

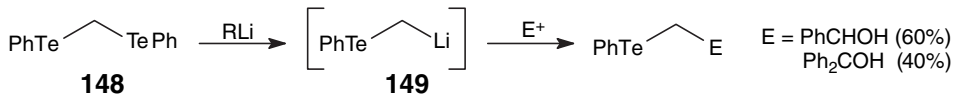
9.13.8.2.1.(i) Tellurium–lithium exchange of alkyl, alkynyl, aryl, and aroyl tellurides

Several years ago, Seebach described the tellurium–lithium exchange reaction of bis-(phenyltelluro)-methane **148** with an alkyllithium. The phenyltelluromethyllithium **149** formed was captured with electrophiles (Scheme 89).[241]

Later on, it was shown that tellurium is preferentially exchanged when phenylseleno(phenyltelluro)methane **150** is treated with *n*-butyllithium (entry 1, Table 3).[242] More recently, a number of organolithiums were prepared by



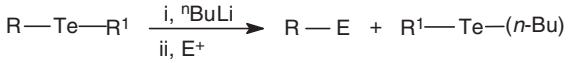
Scheme 88



148 **149**

Scheme 89

Table 3 Tellurium–lithium exchange reactions of organic tellurides



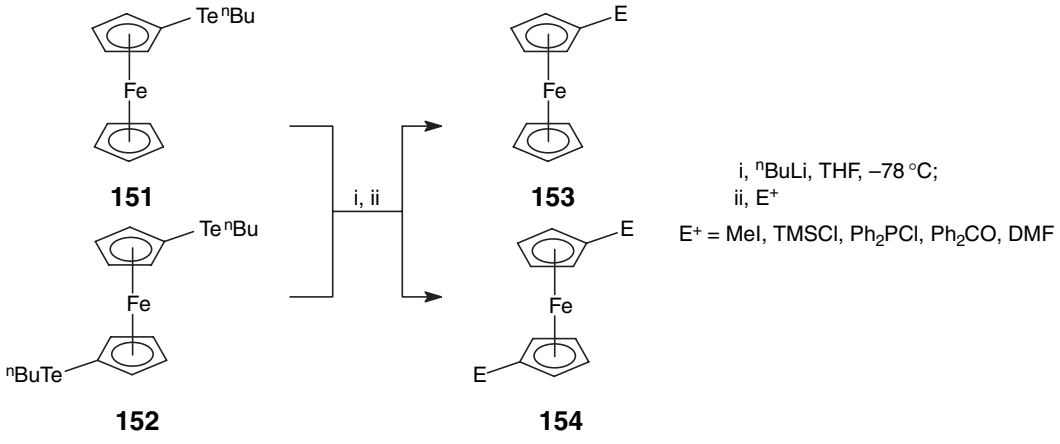
Entry	*R*	*R*^{1}	*E*$^+$	*Product*	*Yield (%)*	*References*
1	$PhSeCH_2$ **150**	Ph	H_3O^+	$PhSeCH_3$	90	242
2	$PhCH_2OCH_2$	^{n}Bu	PhCHO	$PhCH_2OCH_2CH(OH)Ph$	66	244
3	Me_2NCH_2	^{n}Bu	PhCHO	$Me_2NCH_2CH(OH)Ph$	73	244
4	Me_3SiCH_2	^{n}Bu	PhCHO	$Me_3SiCH_2CH(OH)Ph$	89	244
5	^{n}BuTeCH_2	^{n}Bu	PhCHO	^{n}BuTe$CH_2CH(OH)Ph$	81	244
6	PhC≡C	Ph	PhCHO	PhC≡CCH(OH)Ph	89	243
7	Ph	Ph	PhCHO	$Ph_2CH(OH)$	80	243
8	CH_2=CH—CH_2[a]	Ph	PhCHO	CH_2=CH—$CH_2CH(OH)Ph$	96	243
9	$CH_3CH_2CH_2$[a]	^{s}Bu	PhCHO	$CH_3CH_2CH_2CH(OH)Ph$	84	243
10	$PhCH_2$[a]	^{n}Bu	PhCHO	$PhCH_2CH(OH)Ph$	89	245

[a]The tellurides were generated *in situ* by reaction of allyl bromide, *n*-propyl iodide, or benzyl chloride with PhTeLi, ^{s}BuTeLi, or ^{n}BuLi, respectively. This was followed by reaction with ^{n}BuLi (entries 8 and 10) or ^{s}BuLi (entry 9) and benzaldeyde.

tellurium–lithium exchange using alkyl, aryl, ethynyl, allyl, benzyl, and vinyl tellurides.[243–245] Table 3 shows representative examples of such transformations; the tellurium–lithium exchange of vinylic tellurides will be discussed later in more detail in view of the synthetic potential of the resulting organometallics. In some cases, the telluride is generated *in situ* and the tellurium–lithium exchange occurs in a one-pot process (entries 8, 9 and 10, Table 3).[243,245]

Recently, substituted aromatic tellurides were submitted to the tellurium–lithium exchange reaction as a way to access substituted aryllithiums,[48] synthetic intermediates normally prepared by halogen–lithium exchange. Alkyltelluro heterocycles were also successfully transformed into lithium heteroaromatics.[246,247]

Telluroferrocenes **151** and **152** are prepared and used as source of lithium ferrocenes,[248] which are captured with electrophiles to give mono- **153** or disubstituted **154** ferrocenes in good yields (Scheme 90).



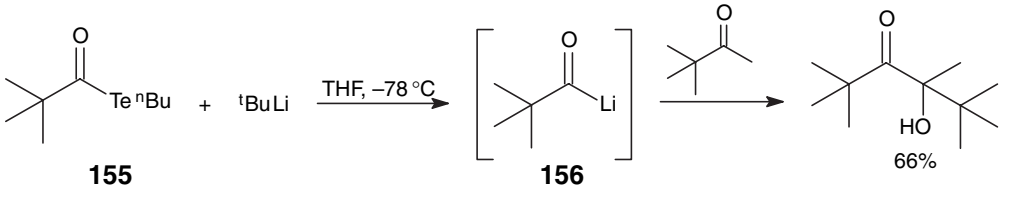
Scheme 90

Acyllithiums (e.g., **156**) can be obtained by reacting telluro esters (e.g., **155**) with alkyllithiums at low temperature (Scheme 91). The telluro esters (e.g., **155**) are obtained by reaction of acyl chlorides with organotellurolate anions.[249]

The tellurium–lithium exchange reaction of functionalized alkyl tellurides is described. A β-(butyltelluro)-ketal is prepared *in situ* and then reacted with *n*-butyllithium to give the corresponding functionalized alkyllithium **157**, which is captured with electrophiles (Scheme 92).[250]

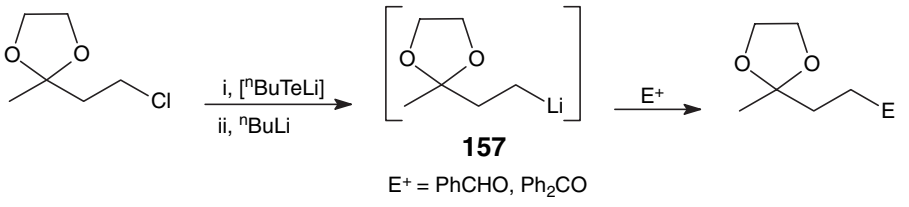
Recently, functionalized butyl tellurides (e.g., **159**) prepared by hydrotelluration of enones **158** (Section 9.13.5.2.4), were reacted with *t*-butyllithium to give the functionalized alkyllithiums (e.g., **160**) which were captured with benzaldehyde or transformed into functionalized alkylcyano cuprates by reaction with CuCN·2 LiCl. In both cases, the obtained organometallics reacted as expected (Scheme 93).[251]

From the reactions shown in Scheme 93, we can conclude that telluride **159** behaves as a homoenolate equivalent **160a** (Figure 6).

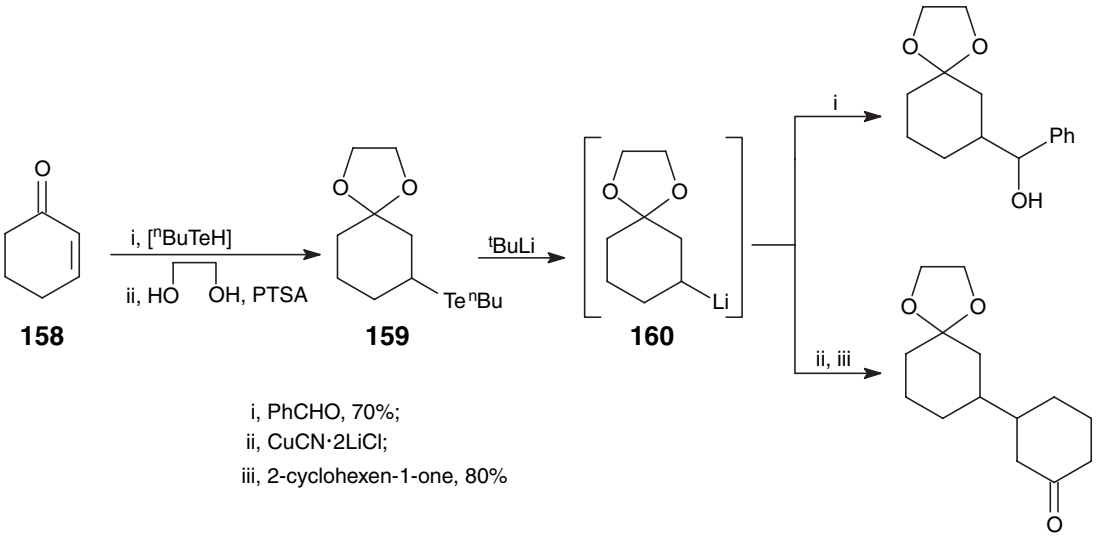


155 **156**

Scheme 91



Scheme 92



Scheme 93

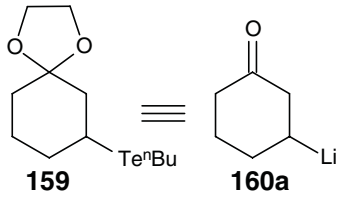


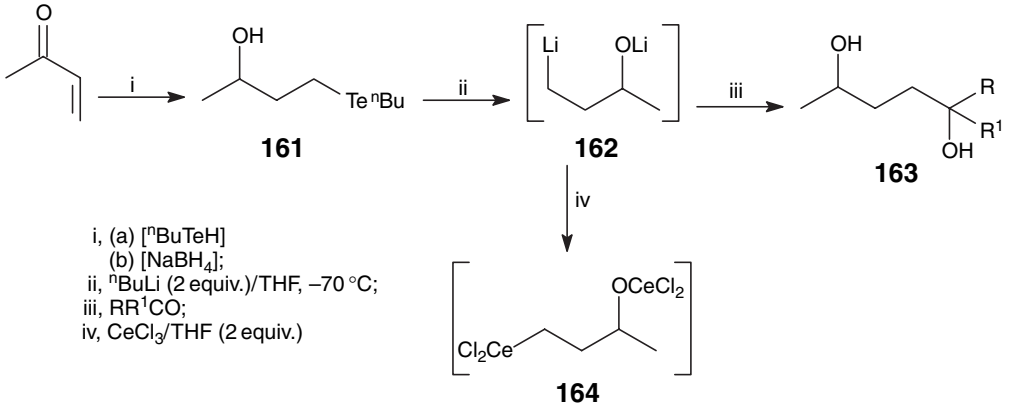
Figure 6 Functionalized tellurides as synthetic equivalents of homoenolates.

The γ-hydroxy telluride **161** is prepared by hydrotelluration of methyl vinyl ketone, followed by *in situ* reduction with sodium borohydride.[154] Treatment of **161** with 2 equiv. of ^{n}BuLi, followed by capture of the dianion **162** with electrophiles, gives the corresponding alcohols **163**.[252] Dianions like **162** can be transmetallated with $CeCl_3$, leading to organometallics of the type **164**, which on reaction with lactones give spiroketals (Scheme 94).[253]

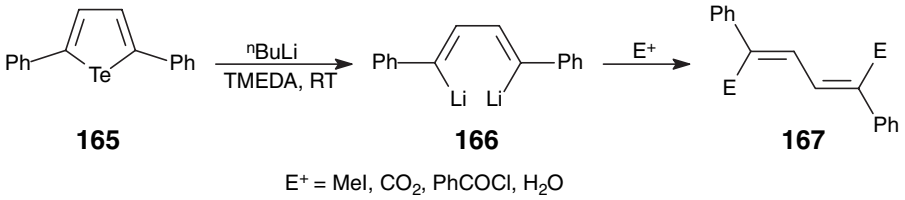
9.13.8.2.1.(ii) Tellurium–lithium exchange of vinylic tellurides

To our knowledge, the first example reported of a tellurium–lithium exchange reaction leading to a vinyllithium was the reaction of 2,5-diphenyltellurophene **165** with *n*-butyllithium, giving 1,4-dilithium-1,4-diphenylbuta-1,3-diene **166**, which was trapped with several electrophiles leading to the corresponding disubstituted dienes **167** with retention of configuration (Scheme 95).[254]

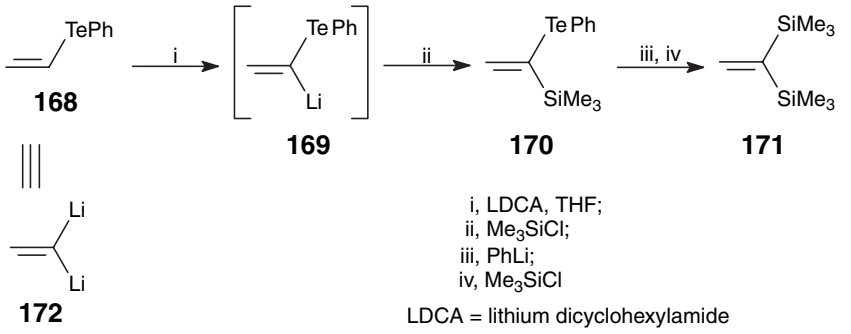
Kauffmann reported the first tellurium–lithium exchange reaction of a vinylic telluride with an organolithium compound.[255] Phenyl vinyl telluride **168** was deprotonated by lithium dicyclohexylamide (LDCA) in THF, and the resulting vinyl anion **169** was reacted with chlorotrimethylsilane to give telluride **170**. Vinylsilane telluroacetal **170** was then reacted with phenyllithium to give the corresponding vinyllithium, which was captured with chlorotrimethylsilane to give the bis-silylated ethane **171** (Scheme 96).[255]



Scheme 94



Scheme 95

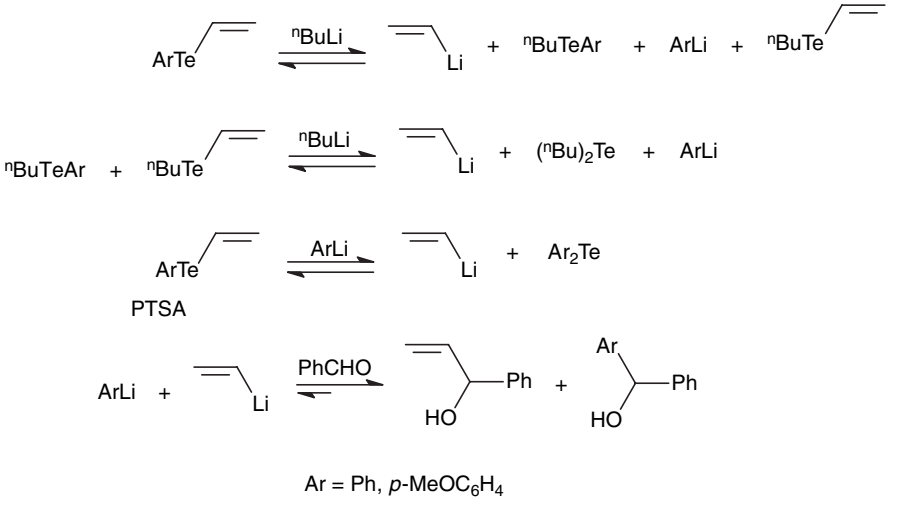


Scheme 96

This sequence of reactions showed that phenyl vinyl telluride **168** could be considered a synthetic equivalent of 1,1-dilithioethene **172**. This conclusion drew the attention of some laboratories to the synthetic potential of vinylic tellurides.

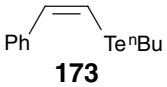
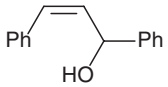
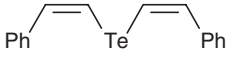
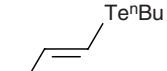
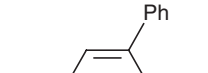
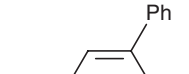
In 1987, Sonoda and co-workers reported that the tellurium–lithium exchange reaction of 1-(phenyltelluro)-2-phenylethene with *n*-butyllithium, followed by capture with benzaldehyde, gave the corresponding allylic alcohol with retention of the double-bond configuration.[243] It was observed that, depending on the length of time the reaction mixture of the aryl vinyl telluride and *n*-butyllithium was allowed to equilibrate prior to addition of the electrophile, a complex mixtures of products could be formed (Scheme 97).[256]

This problem was overcome by using butyl vinyl tellurides instead of aryl vinyl tellurides. At the time that the study of the tellurium–lithium exchange reactions of vinylic tellurides was initiated,[243,255,256] the use of alkyl groups linked to tellurium had not been considered by the tellurium chemists in view of the comments in the older literature about the low stability of the aliphatic tellurium compounds. However, as remarked at the beginning of this chapter, these compounds are relatively stable and can be handled without any need for special precautions. The tellurium–lithium exchange reaction using butyl vinyl tellurides (e.g., **173**) or bis(vinyl) tellurides (e.g., **174**) occurs rapidly in THF at −78 °C, and the vinyl anion is captured with a number of electrophiles, such as aldehydes, ketones, alkyl halides, carbon dioxide, and so on.[139,140,178] The reaction is stereospecific: starting from the (*Z*)-vinylic telluride, (e.g., **173**, **174**, and **175**), only the (*Z*)-olefins **177** and **179** are obtained. More recently, it has been shown that the tellurium–lithium exchange reaction of the (*E*)-vinylic tellurides (e.g., **176**) is also stereospecific and presents a general character leading to the *E*-detellurated olefins (e.g., **178**).[178]



Scheme 97

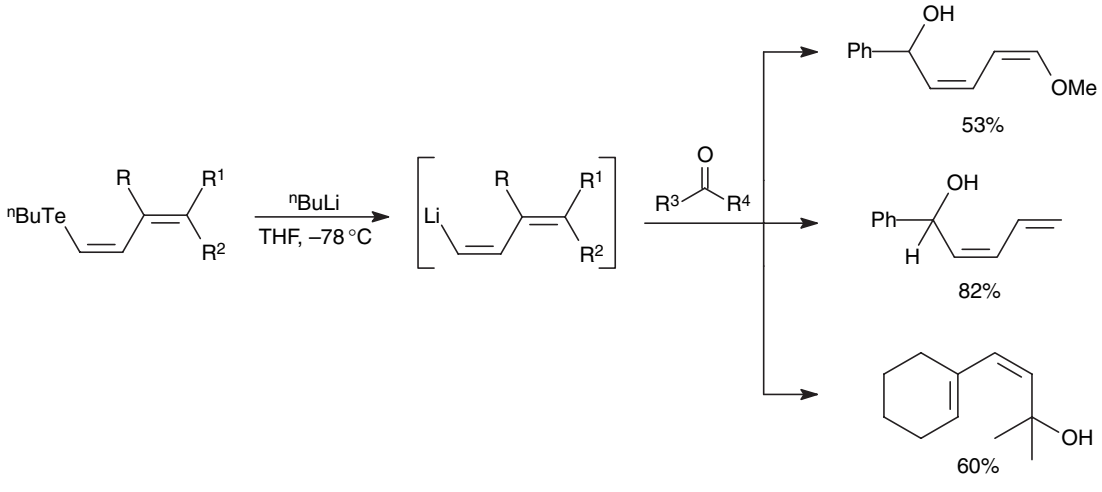
Table 4 Stereospecific tellurium–lithium exchange in vinylic tellurides[a]

Vinylic telluride	E^+	*Product*	*Yield (%)*	*References*
 **173**	PhCHO	 **177**	85	256
 **174**	PhCHO	**177**	80	256
 **175**	PhCHO	 **178**	79	256
 **176**	Me_2SO_4	 **179**	93	139

[a]Reaction conditions: i, ^{n}BuLi, THF, N_2, −78 °C; ii, E^+.

Representative examples of these reactions are shown in Table 4. For more details, see recent reviews.[8,10]

Recently, more complex unsaturated systems were subjected to the tellurium–lithium exchange reaction.[137,141] In Scheme 98, some examples of such a process are shown. In all cases, the (*Z*)-stereochemistry of the starting vinylic telluride was preserved.[137]



Scheme 98

The bis-telluro butadiene **180**, prepared by hydrotelluration of butadiyne, presents an unusual behavior, leading to the lithiated tellurophene **181**, which is captured with electrophiles (Scheme 99).[137]

A hydrotelluration reaction, followed by a tellurium–lithium exchange, was used in the first step of the total synthesis of Gymnodimine **182** (Scheme 100).[257]

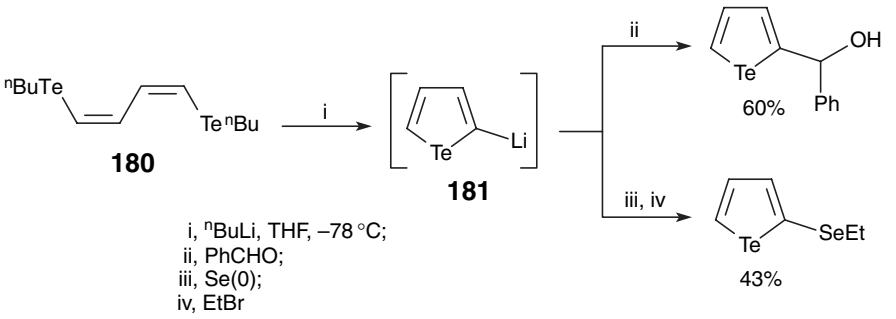
9.13.8.2.2 Tellurium–sodium, calcium, magnesium, and aluminum exchange

These tellurium–metal exchanges are also possible, but have received less attention due to the lesser utility of the resulting organometallics or to the less attractive reaction conditions when compared with tellurium–lithium exchange. In Scheme 101,[258,259] tellurium–metal exchange reactions involving the title elements are summarized.

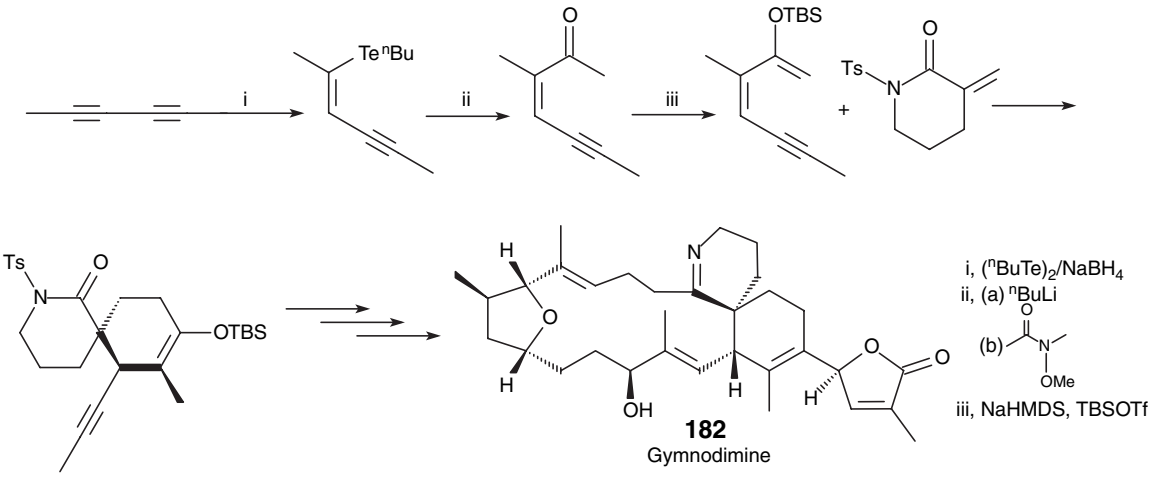
9.13.8.2.3 Tellurium–zinc exchange

In view of the synthetic significance of organozinc compounds,[260] this tellurium–metal exchange was studied in more detail. It is used to prepare arylzinc reagents from diaryl tellurides or ditellurides, which are captured by allyl halides (Scheme 102).[261]

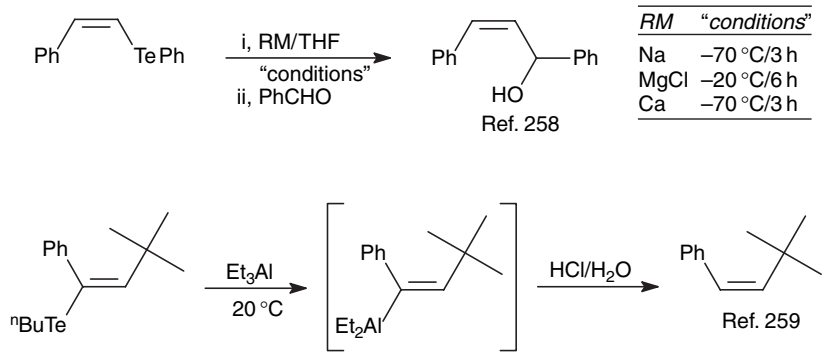
Vinylic tellurides (e.g., **183**) are reacted with diethylzinc to give the corresponding vinylzincs, which are captured with H_2O or D_2O to give the detellurated olefin (e.g., **184**) in variable isomeric ratios (Scheme 103).[262] In one case, the intermediate vinylzinc was coupled with *para*-MeC_6H_4I under $Pd(PPh_3)_4$ catalysis, leading to the trisubstituted olefin **185** in 72% yield with retention of the double-bond geometry (Scheme 103).[262]



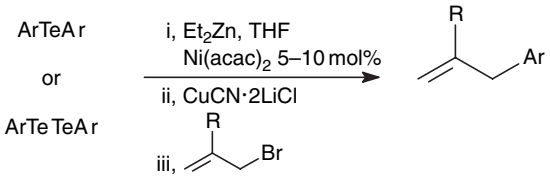
Scheme 99



Scheme 100



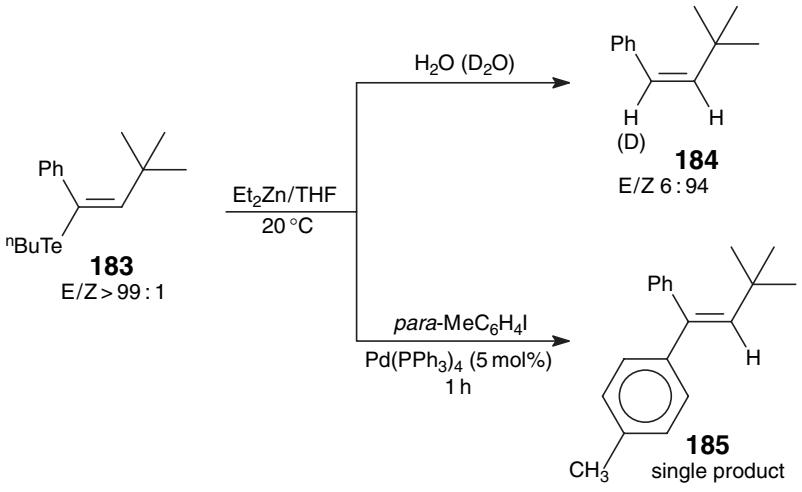
Scheme 101



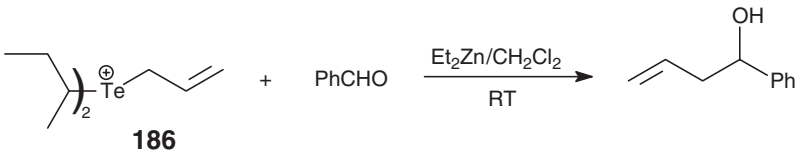
Scheme 102

Telluronium salts **186** react with diethylzinc leading to organozinc compounds, which are captured with electrophiles as exemplified in Scheme 104.[263]

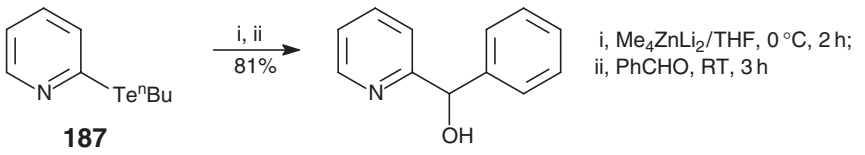
Butyl 2-pyridinyl telluride **187** is treated with Me_4ZnLi_2 and then with benzaldehyde to give phenyl-(2-pyridinyl)-methanol (Scheme 105).[264]



Scheme 103



Scheme 104



Scheme 105

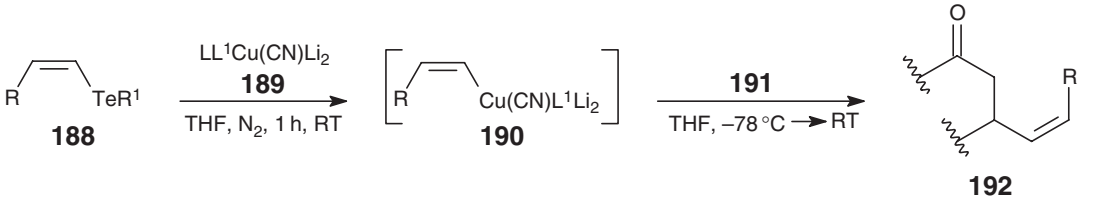
9.13.8.2.4 Tellurium–copper exchange

The tellurium–copper exchange with higher order lithium cyanocuprates **189** is the most versatile and promising exchange reaction of tellurides.[265,265a] Different non-transferable ligands have been used (Scheme 106, Table 5).[266,267] The reaction with vinylic tellurides (e.g., **188a–d**) occurs with retention of the double bond geometry. The (*Z*)-vinyl cyanocuprates **190** react with unhindered enones (e.g., **191a**) in the usual way. Hindered enones (e.g., **191b**) fail to react when the (*Z*)-vinyl cyanocuprate is generated in THF.[266] However, the reaction is successful when boron trifluoride is added to the reaction mixture (entries 3 and 4, Table 5).[267] A similar result is obtained by using diethyl ether as solvent, even in the absence of boron trifluoride. A useful variation of the exchange reaction involves the use of vinyl thienyl tellurides. Treatment of **188d** with dilithium dibutyl cyanocuprate **189d** generates in one step the vinyl cyanocuprate with the non-transferable 2-thienyl ligand **189d** (entry 4, Table 5).[41,266,267]

Enolates **193**, resulting from the 1,4 addition of (*Z*)-vinyl cyanocuprates **190** to enones (e.g., **191a**) can be captured by electrophiles, giving access to useful synthetic intermediates.[268] Among the most interesting, we mention enolphosphates **194**[268] and enol triflates **195** (Scheme 107).[269] As stated before (Section 9.13.5.2.5), enolphosphates are valuable starting materials for tri- and tetrasubstituted (*Z*)-vinylic tellurides.[172] Enol triflates (e.g., **195a**) give access to highly unsaturated systems (e.g., **197**) by palladium-catalyzed reaction with vinylzinc chlorides (e.g., **196**) (Scheme 108).[269]

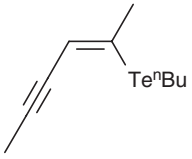
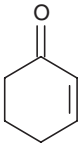
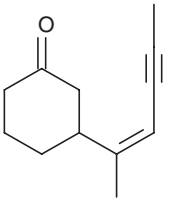
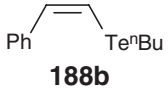
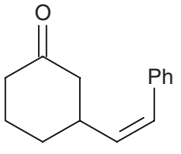
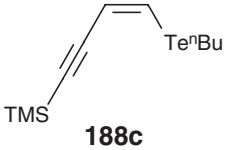
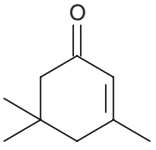
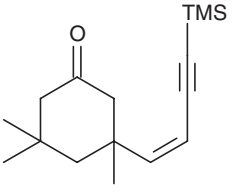
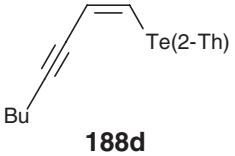
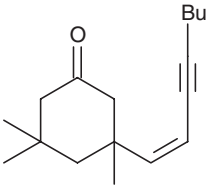
The (*Z*)-vinylic cyanocuprates also react with epoxides (e.g., **198**) giving the (*Z*)-homoallylic alcohols (e.g., **199**).[41,270] The reaction is stereospecific and offers the possibility of its application in enantioselective synthesis (Scheme 109).

Keeping in mind the easy access to vinylic tellurides (see Sections 5.2.3 and 5.2.5), and their fast transformation into widely-used reactive organometallics, we can consider this reaction sequence as a valid alternative to the known methods of generating vinyllithiums and, specially, vinyl cyanocuprates. In addition, the *anti*-hydrotelluration of alkynes is unique among the known, synthetically useful hydrometallations, since it allows the direct preparation of



Scheme 106

Table 5 Tellurium–copper exchange of vinylic tellurides with lithium cyanocuprates

Entry	*Vinylic telluride*	*LL*^{1}	*L*^{1}	*Enone*	*Product (Yield, %)*	*References*
1	 **188a**	(Me, Me) **189a**	Me **190a**	 **191a**	 **192a** (63)	41
2	 **188b**	(^{n}Bu, lmid) **189b**	lmid **190b**	**191a**	 **192b** (88)	41
3	 **188c**	(^{n}Bu, 2-Th) **189c**	2-Th **190c**	 **191b** ($BF_3{\cdot}Et_2O$)	 **192c** (81)	267
4	 **188d**	(^{n}Bu, ^{n}Bu) **189d**	2-Th **190d**	**191b** ($BF_3{\cdot}Et_2O$)	 **192d** (70)	267

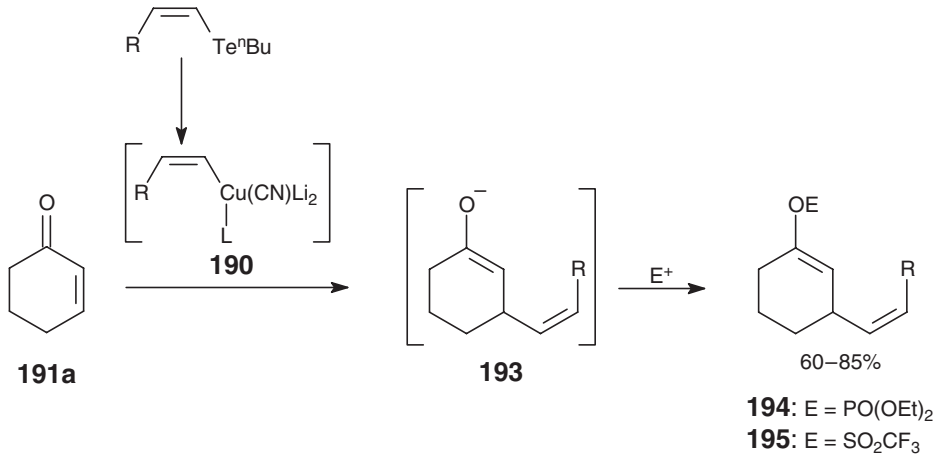
reactive (*Z*)-organometallics via tellurium–metal exchange reactions. This is not possible with the known processes, which give rise to the (*E*)-isomer preferentially (Scheme 110).[131,176]

Recently, this unique characteristic of vinylic tellurides was explored in the enantioselective synthesis of macrolactin A **205**, an antiviral macrolactone extracted from sea bacteria. The first step of the synthesis featured the chiral epoxide **203** opening by the vinyl cyanocuprate **202**, derived from a tellurium–copper exchange reaction using the vinylic telluride **201**, obtained by hydrotelluration of **200** (Scheme 111). Further manipulation of **204** led to macrolactin A **205**.[271]

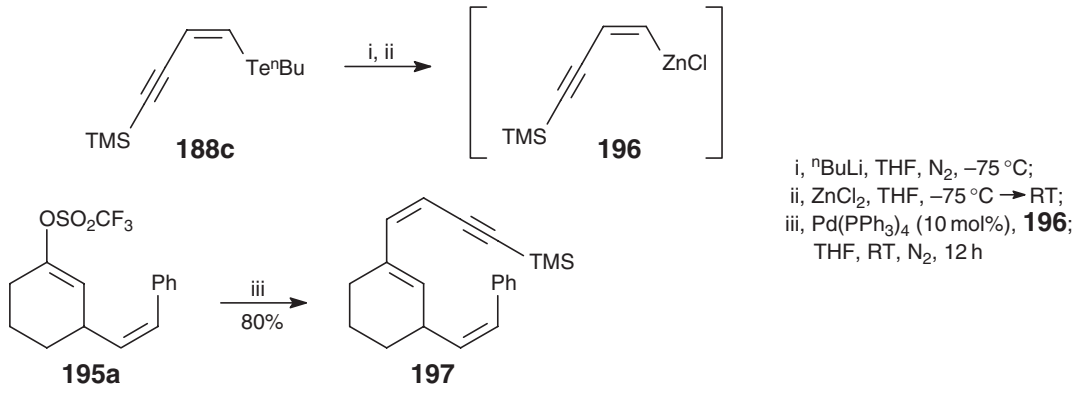
Recently, the direct transformation of allyl- **206**[272] and aryl tellurides **209**[273] into the corresponding organocopper species **207** and **210** by tellurium–copper exchange was described. The resulting allyl **207** or aryl cuprates **210** were captured by coupling with vinyl triflates **208**[272] or by 1,4-addition to enones **211**,[273] respectively (Scheme 112).

9.13.8.3 Coupling Reactions

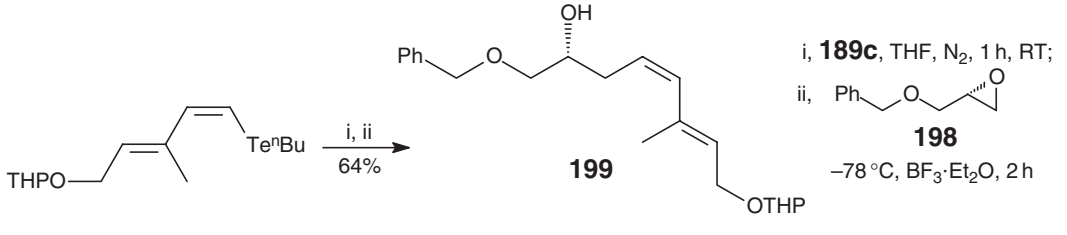
Coupling reactions play an important role in modern organic synthesis. Among the most synthetically important coupling reactions are Stille,[274] Sonogashira,[275] Heck,[276] and Suzuki[277] reactions. Taking advantage of the special



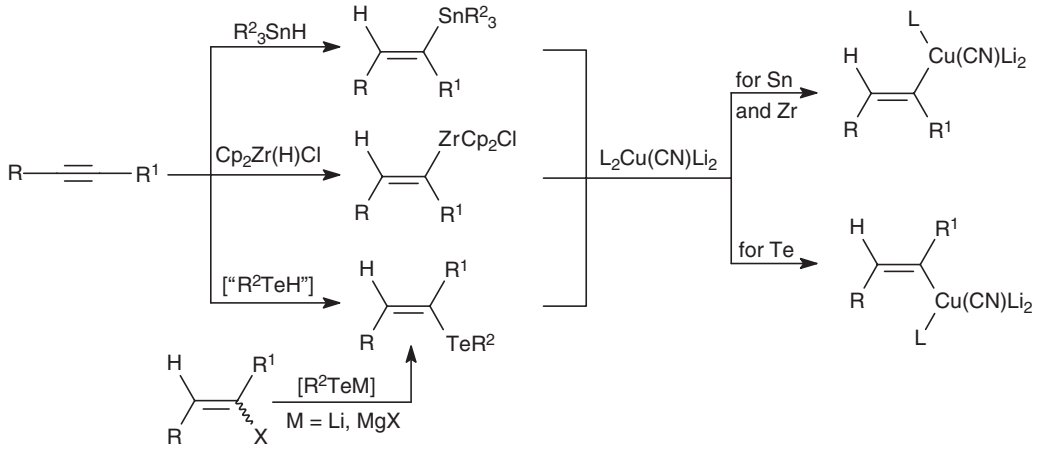
Scheme 107



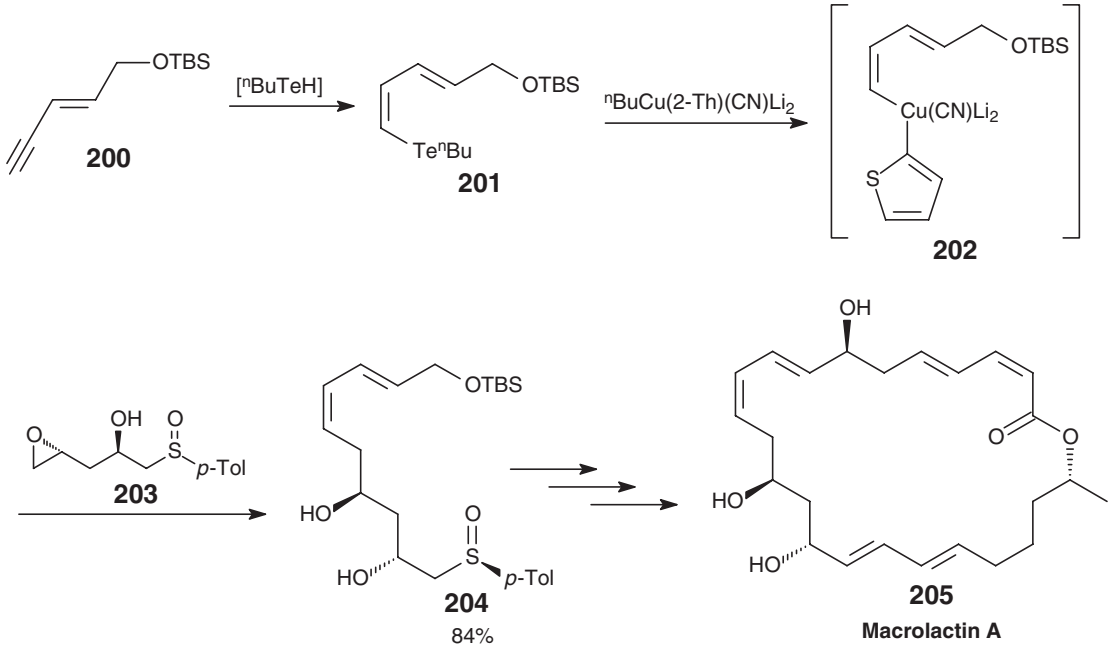
Scheme 108



Scheme 109



Scheme 110

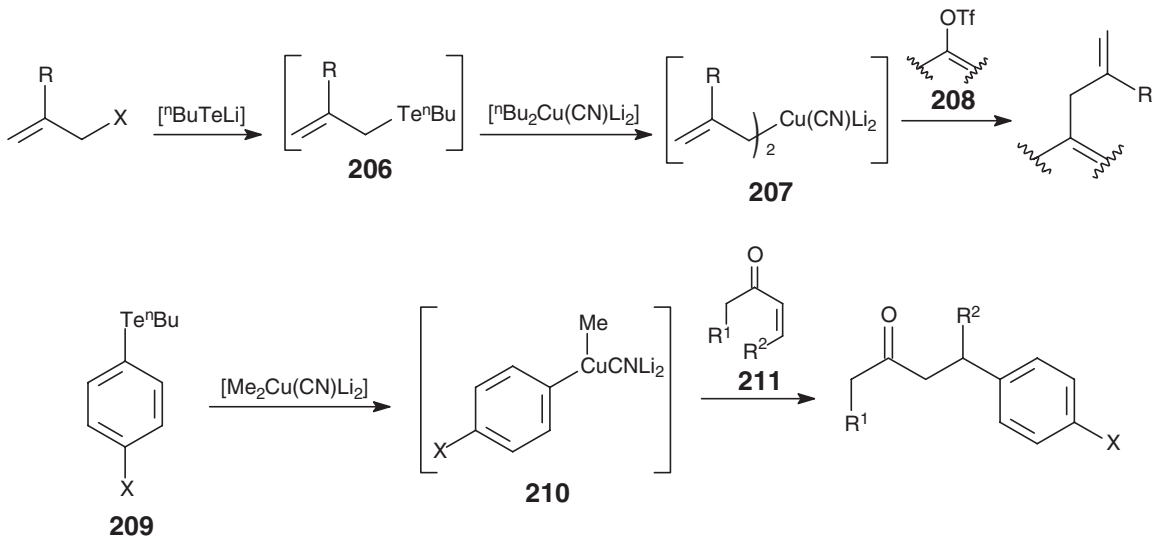


Scheme 111

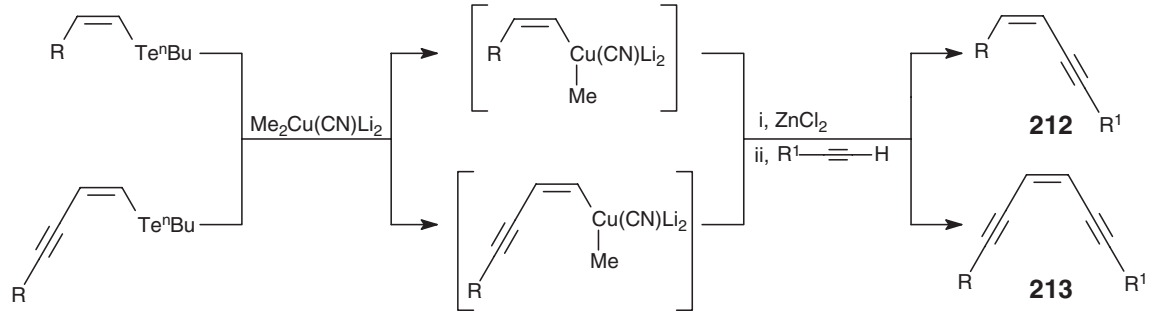
features of the tellurium chemistry described in the preceding sections, these coupling reactions, when applied to organic tellurium compounds, lead to useful synthetic intermediates, specially unsaturated systems with defined stereochemistry.

9.13.8.3.1 Copper-mediated couplings

(*Z*)-vinylic tellurides are the source of enynes **212** and enediynes **213** by transformation into vinylcopper species (Section 9.13.8.2.4), followed by reaction with haloalkynes (Scheme 113).[278,279] The transformation occurs with retention of the double-bond stereochemistry. This is an efficient and straightforward route to important unsaturated units present in natural products, specially in enediyne antibiotics.[280]



Scheme 112



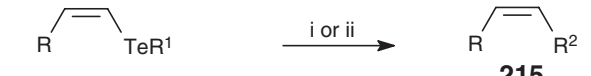
Scheme 113

Higher order alkyl cyanocuprates containing MgBr as the counter-ion **214** couple efficiently with (*Z*)-vinylic tellurides to give the corresponding tellurium-free olefins with retention of the (*Z*)-stereochemistry **215**.[281] By using lower-order cyanocuprates **216**, the coupling is efficient even with lithium as the counter-ion (Scheme 114).[282]

Gilman cuprates **217** also promote the coupling reaction with retention of the original geometry of the double bond (Scheme 115).[283]

The functionalized dienic (*Z*)-telluride **218** on reaction with magnesium cuprates **219** gives the (*E*)-olefins **220** (Scheme 116).[284]

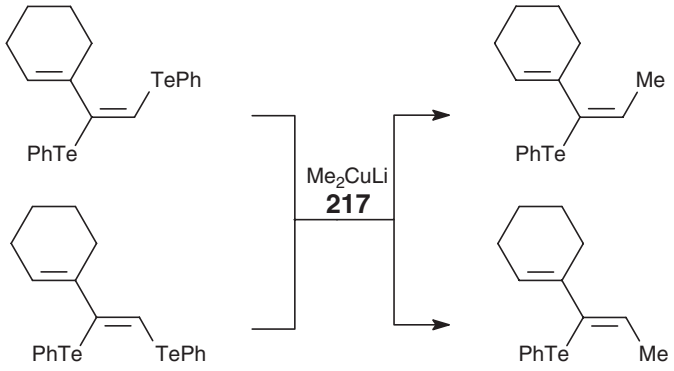
Recently, a more detailed study on the coupling reaction of vinylic tellurides with cuprates was published, showing that the stereochemistry of the coupled product depends on the reaction conditions.[285,286] When the reaction was performed at room temperature, the pure (*E*)-olefin or a mixture of (*Z*/*E*)-isomers was formed. At lower temperature, the (*Z*)-isomer was the main product (Scheme 117).[286]



214: M = Li, MgBr[281]
216: M = Li, MgBr[282]

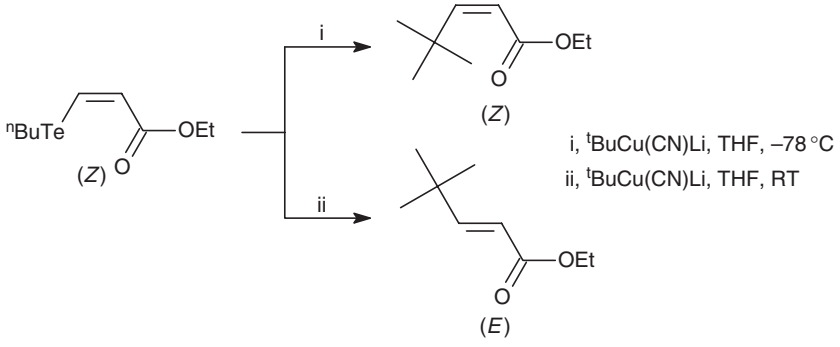
i, $R^2(L)Cu(CN)M_2$;
ii, $R^2Cu(CN)M$

Scheme 114



Scheme 115

Scheme 116



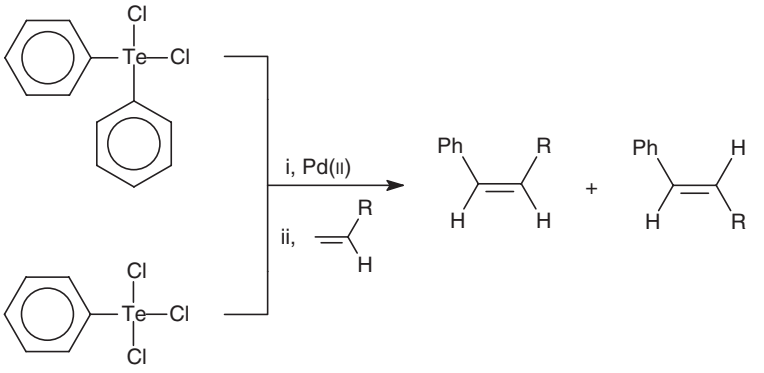
Scheme 117

In this way, simply by controlling the reaction temperature, (*Z*)- or (*E*)-enones or enoates could be prepared starting from the same (Z)-vinylic telluride.[286]

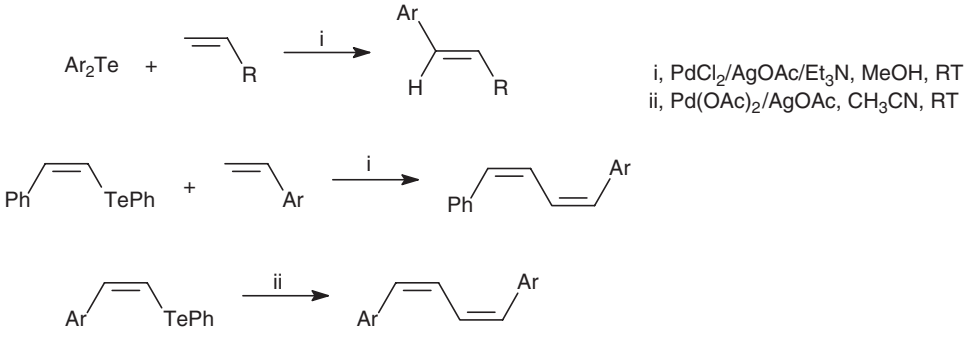
9.13.8.3.2 Palladium-mediated couplings

To our knowledge, the first report on a coupling reaction of an organic tellurium compound promoted by palladium was published in 1977.[287] Later on, Uemura reported that diphenyltellurium dichloride and phenyltellurium trichloride reacted with olefins under palladium catalysis to give stilbenes[288] (Scheme 118).

The same author reported the cross-coupling reactions of aryl tellurides with olefins[289] and the cross-coupling and homocoupling reactions promoted by palladium involving vinyl tellurides. Different solvents and reaction conditions, including a reoxidant, were used, leading to the products in variable yields. In Scheme 119, some of the obtained results are summarized.



Scheme 118



Scheme 119

Organotin **221**[290] and organoboron **222**[291] compounds and iodonium salts **223**[292] couple with diorganotellurium dichlorides under palladium catalysis to give tellurium-free products in good yields. In Scheme 120, representative examples of such transformations are given.

Vinylic tellurides with the (*Z*)-configuration couple with alkynes under $PdCl_2$ catalysis to give highly unsaturated systems **224** with retention of the (*Z*)-double-bond geometry.[293] In Scheme 121, representative examples of such systems are shown.

As can be observed in Scheme 121, the reaction conditions tolerate carboxyl and hydroxyl groups. This methodology was recently employed in the synthesis of biologically active polyacetylenic acids **225** and **226** (Scheme 122).[294]

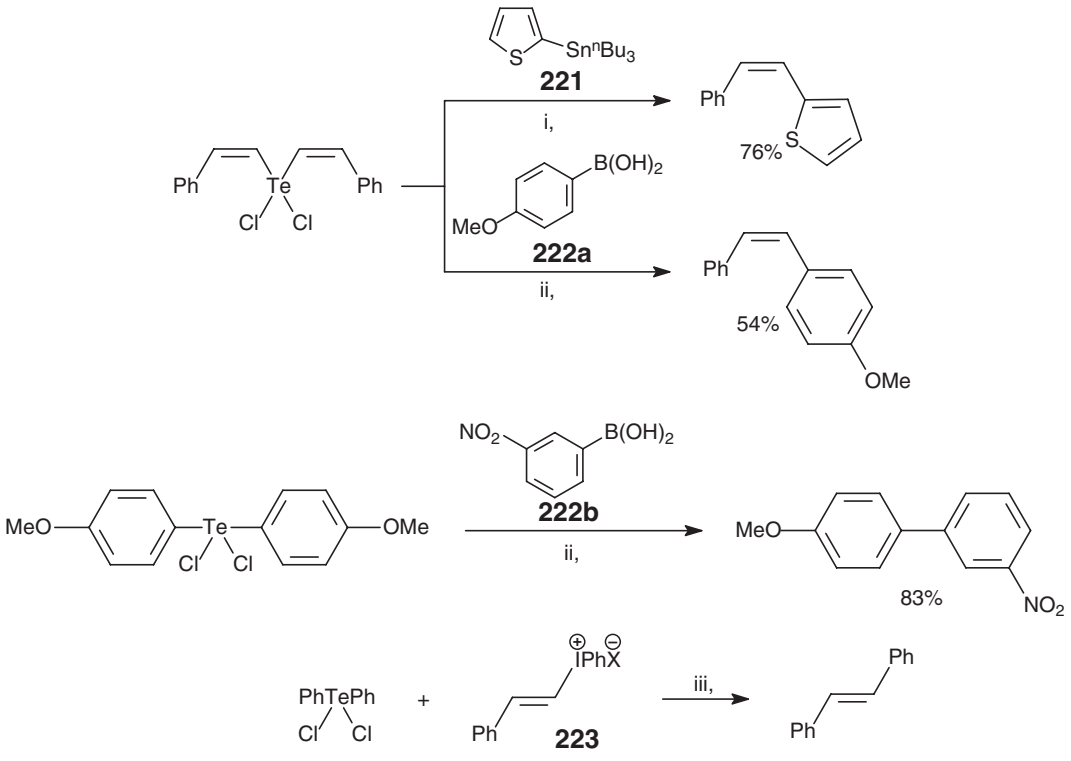
The reaction conditions shown in Scheme 121, but using variable amounts of $PdCl_2$, are used in the construction of a number of unsaturated systems, as shown in Scheme 123.[293–297] In all cases, the transformation occurs with retention of the double-bond stereochemistry.

The coupling reaction with alkynes was extended to other tellurium-containing unsaturated systems. In this case also, the reaction conditions were similar to the ones described in Scheme 121, using different amounts of $PdCl_2$ (Scheme 124).[298–300]

Bis-(butyltelluro)-thiophene **227** couples with the same (route A) or different (route B) alkynes to give the unsaturated systems **228** and **229** in good yields (Scheme 125).[301]

The use of alkynylzinc reagents instead of alkynes and the use of $Pd(PPh_3)_4$ as the catalyst also promotes the coupling reaction leading to enynes **230** and enediynes **231** in good yields and with retention of the double-bond configuration (Scheme 126).[302]

$Pd(acac)_2$ efficiently catalyzes the Suzuki-type reaction of potassium alkynyl trifluoroborates **232** with vinylic tellurides (Scheme 127).[303] This reaction presents the advantage of using compounds of the type **232**, which can be isolated and manipulated in the air.



i, $PdCl_2$ (10 mol%), $CsCO_3$, CH_3CN, RT, 3 h[290];
ii, $PdCl_2(PPh_3)_2$ (10 mol%), MeONa, DME/H_2O, 50 °C, 5 h[291];
iii, $PdCl_2$ (10 mol%), CH_3CN/MeOH, RT, 7 h[292]

Scheme 120

A catalytic cycle was recently proposed to account for the coupling reaction of alkynes with vinylic tellurides promoted by $PdCl_2$.[304]

The palladium-catalyzed coupling of tellurides bearing a sp^2-hybridized carbon linked to tellurium was recently reviewed.[305]

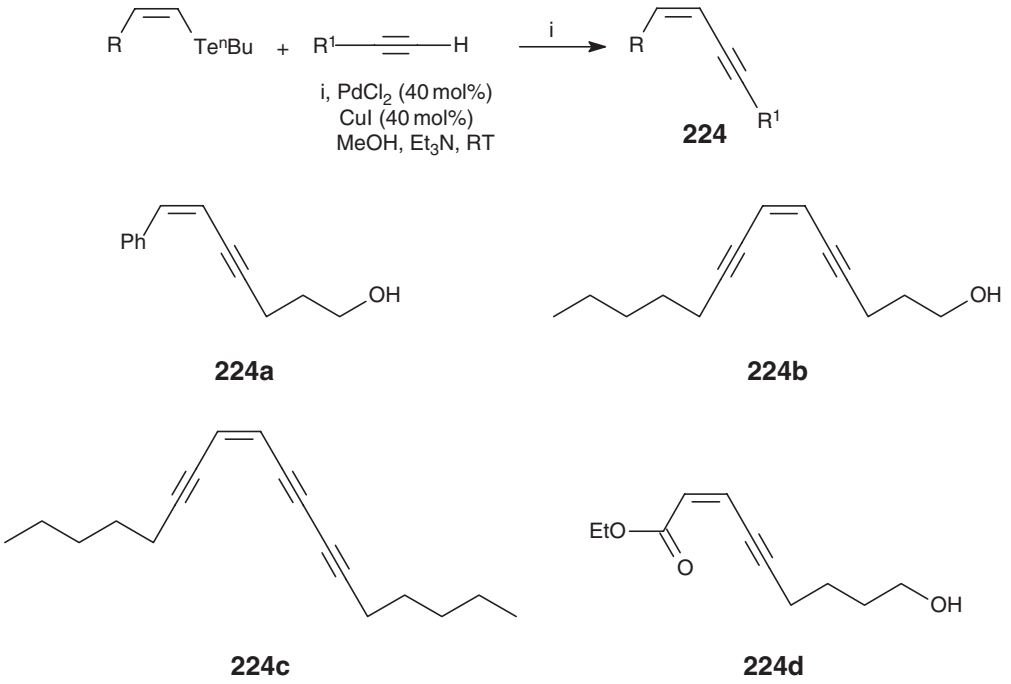
9.13.8.3.3 Nickel-mediated couplings

The coupling reaction of tellurides with Grignard reagents promoted by Ni(II) was described many years ago by Uemura.[143] Recently, bis-vinylic tellurides were reacted with alkynes in the presence of catalytic amounts of Ni(dppe)Cl_2 and CuI leading to enynes with retention of the (*Z*)-stereochemistry (Scheme 128).[306]

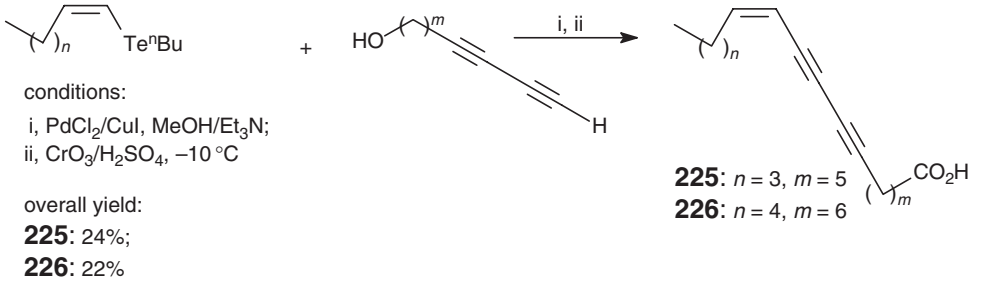
Under these conditions, vinyl butyl tellurides fail to give the coupling product. By using magnesium, lithium, or zinc alkynoates, the coupling reaction is successful, leading to enynes **233** or enediynes **234** in good yields and with retention of the double-bond configuration. Typical examples are given in Scheme 129.[307]

9.13.8.4 Free Radical Processes to Remove Tellurium from Organic Substrates

Triphenyl- and tributyltin hydrides react with organic tellurides, usually in toluene, promoting the reductive removal of the aryltellurium group.[11,12,44] If a radical trapping agent is present in the reaction medium, a chain-elongation product is formed[189] (see Section 9.13.6.2, Scheme 70). Usually, the yields are high and no radical initiators are necessary.



Scheme 121

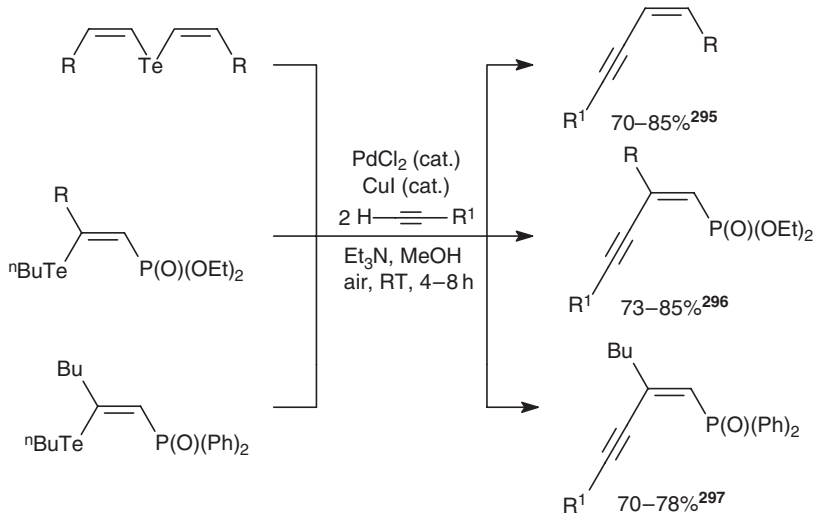


Scheme 122

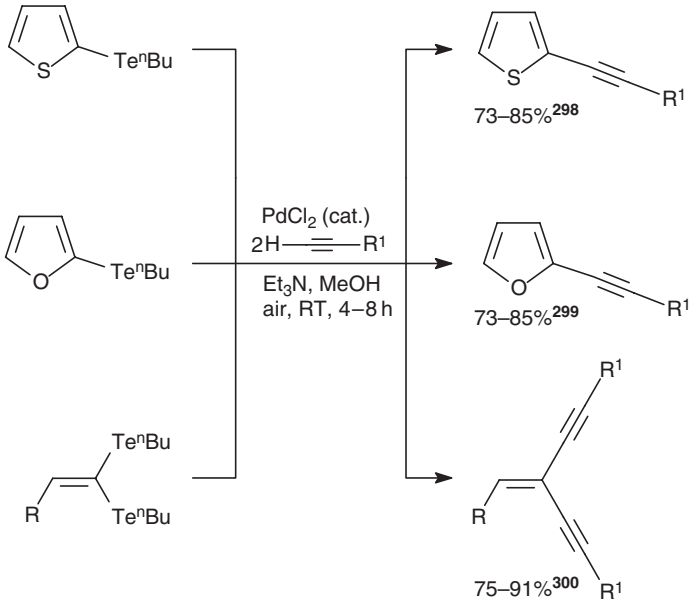
9.13.9 Conclusion

In the last two decades, the organic chemistry of tellurium has experienced great development, and, nowadays, many practical methods to introduce and to remove tellurium into and from organic substrates are available. The experience gained by the chemists dedicated to this branch of organic chemistry showed that many negative comments found in the old literature about the instability and the bad smell of the organotellurium compounds can not be considered a rule, and that these compounds can be prepared and manipulated safely in a conventional organic-synthesis laboratory. Practical methods to introduce tellurium into organic substrates with no need to manipulate malodorous starting materials have been developed. Most of these methods use elemental tellurium as the starting material.

Since the publication of the chapter *Tellurium* in the second edition of this encyclopedia,[12] a number of methods to transform organotellurium compounds into tellurium-free reactive organometallics and the use of such species in stereoselective carbon–carbon bond formation have been developed. Coupling reactions of organotellurium



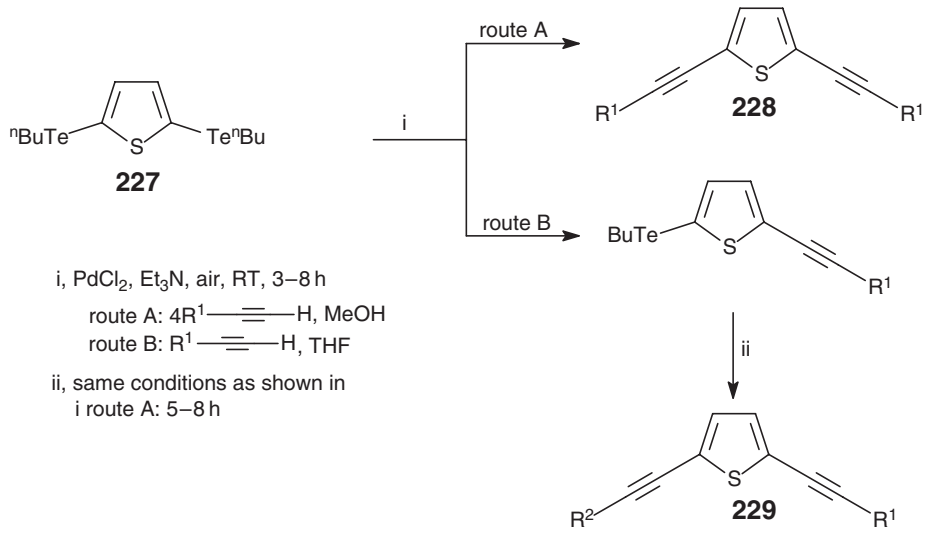
Scheme 123



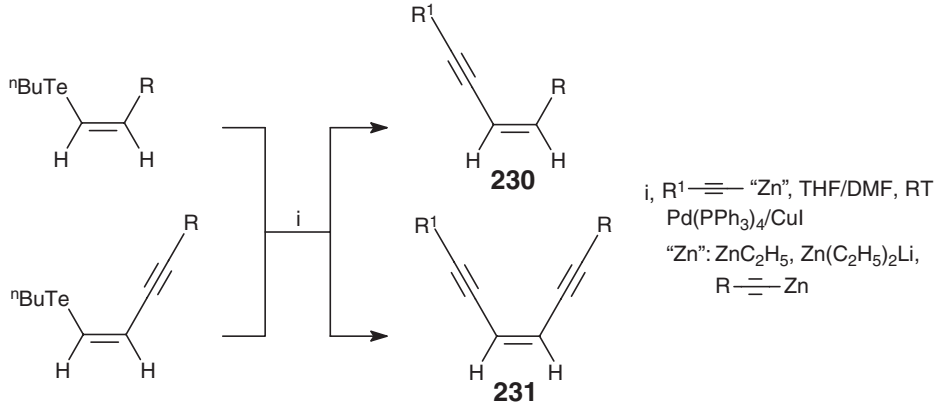
Scheme 124

compounds catalyzed by Pd and Ni were synthetically explored to construct unsaturated systems in a stereoselective way. Free radical processes were developed using organotellurium compounds to promote transformations into organic substrates. The first stereoselective total synthesis of natural products making use of tellurium-based methodologies have been published.

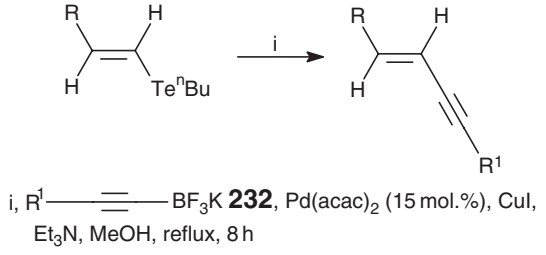
We can conclude that organic chemists dominated the preparative aspects of this branch of organic chemistry and introduced a number of advantageous synthetic methodologies based on tellurium. It is expected that these methods will be used more frequently in the synthesis of complex molecules, since they present some unique features, as it was remarked on in this chapter.



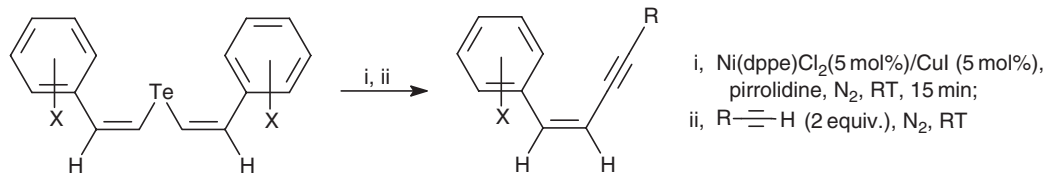
Scheme 125



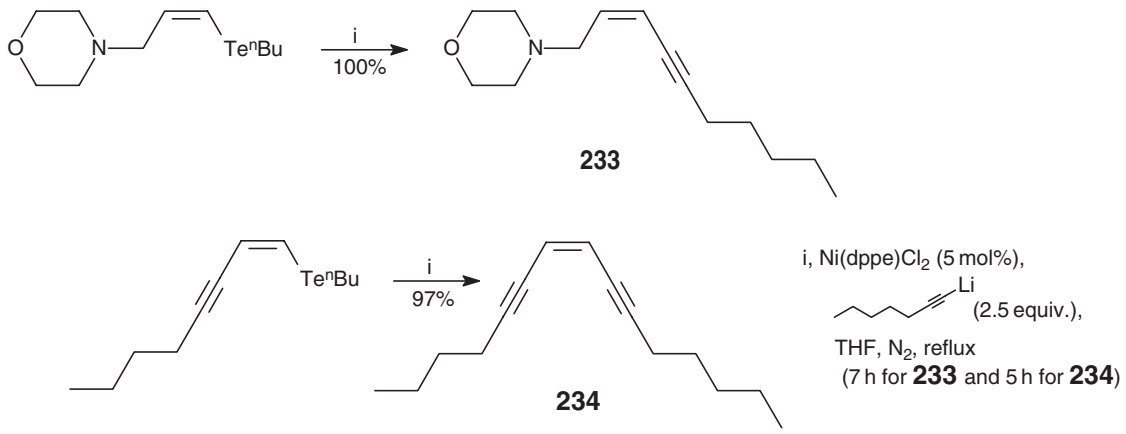
Scheme 126



Scheme 127



Scheme 128



Scheme 129

References

1. Wöhler, F. *Liebigs Ann. Chem.* **1840**, *35*, 111.
2. Wöhler, F. *Liebigs Ann. Chem.* **1852**, *84*, 69.
3. Heeren, M. *Chem. Zentralbl.* **1861**, 916.
4. Rheinboldt, H. In *Schwefel, Selenen und Tellurverbindungen, Methoden der Organischen Chemie* (Houben-Weyl); Müller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1955; Vol. IX.
5. Irgolic, K. C. In *Organotellurium Compounds, Methods of Organic Chemistry* (Houben-Weyl); Klamann, D., Ed., Georg Thieme Verlag: Stuttgart, 1990; Vol. E12b.
6. Petragnani, N.; Comasseto, J. V. *Synthesis* **1991**, 793.
7. Petragnani, N.; Comasseto, J. V. *Synthesis* **1991**, 897.
8. Comasseto, J. V.; Ling, L. W.; Petragnani, N.; Stefani, H. A. *Synthesis* **1997**, 373.
9. Comasseto, J. V.; Barrientos-Astigarraga, R. E. *Aldrichim. Acta* **2000**, *33*, 66.
10. Petragnani, N.; Stefani, H. A. *Tetrahedron* **2005**, *61*, 1613.
11. Petragnani, N. *Tellurium in Organic Synthesis – Best Synthetic Methods*; Academic Press: London, **1994**.
12. Petragnani, N. Tellurium. In In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Elsevier: Oxford, 1995; Vol. 11.
13. Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* **2004**, *104*, 6255.
14. Dabbousi, B. O.; Bonasia, P. J.; Arnold, J. *J. Am. Chem. Soc.* **1991**, *113*, 3186.
15. Liesk, V. J.; Schultz, P.; Klar, G. *Z. Anorg. Allg. Chem.* **1977**, *435*, 98.
16. Piette, J. L.; Renson, M. *Bull. Soc. Chim. Belg.* **1971**, *80*, 669.
17. Lang, E. S.; Fernandes, R. M.; Silveira, J. E. T.; Abram, U.; Vásquez-López, E. M. *Z. Anorg. Allg. Chem.* **1999**, *625*, 1401.
18. Rheinboldt, H. In Schwefel, *Selenen und Tellurverbindungen, Methoden der Organischen Chemie* (Houben-Weyl); Müller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1955; Vol. IX, p. 971.
19. Goodman, M. M.; Knapp, F. F. *Organometallics* **1983**, *2*, 1106.
20. Kirsch, G.; Goodman, M. M.; Knapp, F. F. *Organometallics* **1983**, *2*, 357.
21. Chen, J.; Zhou, X. J. *Synthesis* **1987**, 586.
22. Trofimov, B. A.; Gusarova, N. K.; Tatarinova, A. A.; Potapov, V. A.; Sinegovskaya, L. M.; Amosova, S. V.; Voronkov, M. G. *Tetrahedron* **1988**, *44*, 6739.
23. Lue, P.; Chen, B.; Yu, X.; Zhou, X. Y. *Synth. Commun.* **1986**, *16*, 1849.
24. Ferreira, J. T. B.; de Oliveira, A. R. M.; Comasseto, J. V. *Synth. Commun.* **1989**, *19*, 239.
25. Suzuki, H.; Manabe, H.; Kawaguchi, T.; Inouye, M. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 771.
26. Suzuki, H.; Padmanabhan, S.; Inouye, M.; Ogawa, T. *Synthesis* **1989**, 468.
27. Trofimov, B. A.; Amosova, S. V.; Gusarova, N. K.; Musorin, G. K. *Tetrahedron* **1982**, *38*, 713.
28. Trofimov, B. A.; Amosova, S. V.; Gusarova, N. K.; Potapov, V. A.; Tatarinova, A. A. *Sulfur Lett.* **1983**, *1*, 151.
29. Sandman, D. J.; Stark, J. C.; Acampora, L. A.; Gagne, P. *Organometallics* **1983**, *2*, 549.
30. Huang, Z.; Xie, L.; Huang, X. *Synth. Commun.* **1988**, *18*, 1167.
31. Haller, W. S.; Irgolic, K. J. *J. Organomet. Chem.* **1972**, *38*, 97.
32. Akiba, M.; Lakshmikantham, M. V.; Jen, K.; Cava, M. P. *J. Org. Chem.* **1984**, *49*, 4819.

33. Detty, M. R.; Murray, B. J.; Smith, D. L.; Zumbulyadis, N. *J. Am. Chem. Soc.* **1983**, *105*, 875.
34. Dabdoub, M. J.; Dabdoub, V. B.; Comasseto, J. V.; Petragnani, N. *J. Organomet. Chem.* **1986**, *308*, 211.
35. Dabdoub, M. J.; Comasseto, J. V. *J. Organomet. Chem.* **1988**, *344*, 167.
36. Hope, E. G.; Kemmitt, T.; Levason, W. *Organometallics* **1988**, *7*, 78.
37. Piette, J. L.; Renson, M. *Bull. Soc. Chim. Belg.* **1970**, *79*, 367.
38. Engman, L.; Cava, M. P. *Synth. Commun.* **1982**, *12*, 163.
39. Engman, L.; Cava, M. P. *Organometallics* **1982**, *1*, 470.
40. Engman, L.; Persson, J. *J. Organomet. Chem.* **1990**, *388*, 71.
41. Tucci, F. C.; Chieffi, A.; Comasseto, J. V.; Marino, J. P. *J. Org. Chem.* **1996**, *61*, 4975.
42. Zeni, G.; Formiga, H. B.; Comasseto, J. V. *Tetrahedron Lett.* **2000**, *41*, 1311.
43. Piette, J. L.; Renson, M. *Bull. Soc. Chim. Belg.* **1970**, *79*, 383.
44. Clive, D. L. J.; Chittattu, G. J.; Farina, V.; Kiel, W. A.; Menchen, S. M.; Russel, C. G.; Singh, A.; Wong, C. K.; Curtis, N. J. *J. Am. Chem. Soc.* **1980**, *102*, 4438.
45. Knapp, F. F.; Ambrose, K. R.; Callahan, A. P. *J. Med. Chem.* **1981**, *24*, 794.
46. Uemura, S.; Fukuzawa, S. *J. Am. Chem. Soc.* **1983**, *105*, 2748.
47. Chieffi, A.; Menezes, P. H.; Comasseto, J. V. *Organometallics* **1997**, *16*, 809.
48. Cunha, R. L. O. R.; Omori, A. T.; Castelani, P.; Toledo, F. T.; Comasseto, J. V. *J. Organomet. Chem.* **2004**, *689*, 3631.
49. Suttle, J. F.; Smith, C. R. F. *Inorg. Synth.* **1956**, *III*, 140.
50. Morgan, G. T.; Kellett, R. E. *J. Chem. Soc.* **1926**, 1080.
51. Drew, H. D. K. *J. Chem. Soc.* **1926**, 223.
52. Reichel, L.; Kirschbaum, E. *Liebigs Ann. Chem.* **1936**, *523*, 211.
53. Petragnani, N. *Tetrahedron* **1960**, *11*, 15.
54. Sadekov, I. D.; Sayapina, L. M.; Bushkov, A. Y.; Minkin, V. I. *J. Gen. Chem. USSR* **1971**, *41*, 2747.
55. Bergman, J. *Tetrahedron* **1972**, *28*, 3323.
56. Günther, W. H. H.; Nepywoda, J.; Chu, J. Y. C. *J. Organomet. Chem.* **1974**, *74*, 79.
57. Ahmed, M. A. K.; McWhinnie, W. R.; Hamor, T. A. *J. Organomet. Chem.* **1985**, *281*, 205.
58. Farrar, W. V. *Research* **1951**, *4*, 177.
59. Campbell, I. G. M.; Turner, E. E. *J. Chem. Soc.* **1938**, 37.
60. Clark, A. R.; Nair, R.; Fronczek, F. R.; Junk, T. *Tetrahedron Lett.* **2002**, *43*, 1387.
61. O'Brien, D. H.; Huang, C. K.; Irgolic, K. C. *Heteroat. Chem.* **1990**, *1*, 215.
62. Engman, L. *Organometallics* **1986**, *5*, 427.
63. Backwall, J.; Bergman, J.; Engman, L. *J. Org. Chem.* **1983**, *48*, 3918.
64. Ali, M. E. S.; Malik, M. A.; Smith, B. C. *Inorg. Chim. Acta* **1989**, *162*, 157.
65. Engman, L. *Organometallics* **1989**, *8*, 1997.
66. Campos, M. M.; Petragnani, N. *Chem. Ber.* **1960**, *93*, 317.
67. Bergman, J.; Engman, L. *J. Am. Chem. Soc.* **1981**, *103*, 5196.
68. Cunha, R. L. O.; Zukerman-Schpector, J.; Caracelli, I.; Comasseto, J. V. *J. Organoment. Chem.* **2006**.
69. Zukerman-Schpector, J.; Camillo, R. L.; Comasseto, J. V.; Santos, R. A.; Caracelli, I. *Acta Cryst.* **1999**, *C55*, 1577.
70. Zukerman-Schpector, J.; Camillo, R. L.; Comasseto, J. V.; Cunha, R. L. O. R.; Lemos, F. C. D.; Caracelli, I. *Acta Cryst.* **1999**, *C55*, 1930.
71. Zukerman-Schpector, J.; Haiduc, I.; Camillo, R. L.; Comasseto, J. V.; Cunha, R. L. O. R.; Caracelli, I. *Acta Cryst.* **2001**, *C57*, 749.
72. Zukerman-Schpector, J.; Camillo, R. L.; Comasseto, J. V.; Cunha, R. L. O. R.; Caracelli, I. *Acta Cryst.* **2000**, *C56*, 897.
73. Zukerman-Schpector, J.; Haiduc, I.; Camillo, R. L.; Comasseto, J. V.; Cunha, R. L. O. R.; Jorge, A. *Can. J. Chem.* **2002**, *80*, 1530.
74. Wynne, K. J.; Pearson, P. S. *Inorg. Chem.* **1970**, *9*, 106.
75. Wynne, K. J.; Pearson, P. S. *Inorg. Chem.* **1971**, *10*, 1871.
76. Sadekov, I. D.; Bushkov, A. Y.; Minkin, V. I. *J. Gen. Chem. USSR* **1972**, *42*, 124.
77. Alcock, N. W.; Harrison, W. D. *J. Chem. Soc., Dalton Trans.* **1982**, 251.
78. Vicentini, G.; Giesbrecht, E.; Pitombo, L. R. M. *Chem. Ber.* **1959**, *92*, 40.
79. Engman, L. *J. Org. Chem.* **1989**, *54*, 2964.
80. Petragnani, N.; Torres, L.; Wynne, K. J. *J. Organomet. Chem.* **1975**, *92*, 175.
81. Engman, L.; Pearson, J. *Synth. Commun.* **1993**, *23*, 445.
82. Detty, M. R. *J. Org. Chem.* **1980**, *45*, 274.
83. Ley, S. V.; Meerholz, C. A.; Barton, D. H. R. *Tetrahedron* **1981**, *37(suppl. 9)*, **1981**, 213.
84. Petragnani, N.; Vicentini, G. *Universidade de São Paulo, F. F. C. L. Bol. Quim.* **1959**, *5*, 75.

84a. Petragnani, N.; Vicentini, G. *Chem. Abst.* **1963**, *58*, 11256.

85. Thavomyuticam, P.; Whinnie, W. R. *J. Organomet. Chem.* **1973**, *50*, 135.
86. Barton, D. H. R.; Finet, J. P.; Thomas, M. *Tetrahedron* **1986**, *42*, 2319.
87. Comasseto, J. V.; Ferreira, J. T. B.; Fontanillas, J. A. *J. Organomet. Chem.* **1984**, *277*, 261.
88. Chen, D. W.; Chen, Z. C. *Synth. Commun.* **1995**, *25*, 1605.
89. Kambe, N.; Kondo, K.; Morita, S.; Murai, S.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1009.
90. Akiba, M.; Cava, M. P. *Synth. Commun.* **1984**, *14*, 1119.
91. Suzuki, H.; Nakamura, T. *J. Org. Chem.* **1993**, *58*, 241.
92. Gemal, A. L.; Luche, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
93. Barton, D. H. R.; Fekih, A.; Lusinchi, X. *Tetrahedron Lett.* **1985**, *26*, 3693.
94. Kambe, N.; Inagaki, T.; Miyoshi, N.; Ogawa, A.; Sonoda, N. *Chem. Lett.* **1987**, 1275.
95. Suzuki, H.; Manabe, H.; Inouye, M. *Chem. Lett.* **1985**, 1671.
96. Ozuka, A.; Shimizu, H.; Suzuki, H. *Chem. Lett.* **1983**, 1373.
97. Barton, D. H. R.; Fekih, A.; Lusinchi, X. *Tetrahedron Lett.* **1985**, *26*, 6197.
98. Clive, D. L. J.; Menchen, S. M. *J. Chem. Soc., Chem. Commun.* **1977**, 658.
99. Clive, D. L. J.; Menchen, S. M. *J. Org. Chem.* **1980**, *45*, 2347.
100. Polson, G.; Dittmer, D. C. *Tetrahedron Lett.* **1986**, *27*, 5579.
101. Houveyda, A. H.; Didikuk, M. T. *Curr. Org. Chem.* **1998**, *2*, 489.

102. Discordia, R. P.; Dittmer, D. C. *J. Org. Chem.* **1990**, *55*, 1414.
103. Pepito, A. S.; Dittmer, D. C. *J. Org. Chem.* **1997**, *62*, 7920.
104. Campos, M. M.; Petragnani, N.; Thomé, C. *Tetrahedron Lett.* **1960**, *15*, 5.
105. Butcher, T. S.; Zhou, F.; Detty, M. R. *J. Org. Chem.* **1998**, *63*, 169.
106. Butcher, T. S.; Detty, M. R. *J. Org. Chem.* **1998**, *63*, 177.
107. Clive, D. L. J.; Wickens, P. L.; Sgarbi, P. W. M. *J. Org. Chem.* **1996**, *61*, 7426.
108. Engman, L.; Byström, S. E. *J. Org. Chem.* **1985**, *50*, 3170.
109. Ozuka, A.; Suzuki, H. *Chem. Lett.* **1983**, 119.
110. Clive, D. L. J.; Beaulieu, P. L. *J. Org. Chem.* **1982**, *47*, 1124.
111. Silveira, C. C.; Lenardão, E. J.; Comasseto, J. V. *Synth. Commun.* **1994**, *24*, 575.
112. Suzuki, H.; Takaoka, K.; Ogura, A. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1067.
113. Huang, X.; Pi, J. H. *Synth. Commun.* **1990**, *20*, 2297.
114. Shobana, N.; Shanmugan, P. *Indian J. Chem.* **1986**, *25B*, 658.
115. Suzuki, H.; Padmanabhan, S.; Ogawa, T. *Chem. Lett.* **1989**, 1017.
116. Shobana, N.; Amirthavalli, M.; Deepa, V.; Shanmugan, P. *Indian J. Chem.* **1988**, *27B*, 965.
117. Lakshimikanthan, M. V.; Jackson, Y. A.; Jones, R. J.; O'Malley, C. J.; Ravichandran, K.; Cava, M. P. *Tetrahedron Lett.* **1986**, *27*, 4687.
118. Huang, Y. Z.; Tang, Y.; Zhou, Z.-L. *Tetrahedron* **1998**, *54*, 1667.
119. Li, S. W.; Huang, Y. Z.; Shi, L.-L. *Chem. Ber.* **1990**, *123*, 1441.
120. Matsuki, T.; Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2105.
121. Huang, X.; Xie, L.; Wu, H. *J. Org. Chem.* **1988**, *53*, 4862.
122. Shi, L.-L.; Zhou, Z.-L.; Huang, Y.-Z. *Tetrahedron Lett.* **1990**, *31*, 4173.
123. Tang, Y.; Huang, Y. Z.; Dai, L.-X.; Sun, J.; Xia, W. *J. Org. Chem.* **1997**, *62*, 954.
124. Brandsma, L.; Wijers, H. E. *Recl. Trav. Chim. Pays-Bas* **1963**, *82*, 68.
125. Comasseto, J. V.; Lang, E. S.; Ferreira, J. T. B.; Simonelli, F.; Correia, V. R. *J. Organomet. Chem.* **1987**, *334*, 329.
126. Suzuki, H.; Nakamura, T. *Synthesis* **1992**, 549.
127. Pierini, A. B.; Rossi, R. A. *J. Org. Chem.* **1979**, *44*, 4667.
128. Li, J.; Lue, P.; Zhan, X.-J. *Synthesis* **1992**, 281.
129. Engman, L. *J. Org. Chem.* **1983**, *48*, 2920.
130. Piette, J.-L.; Thibaut, P.; Renson, M. *Tetrahedron* **1978**, *34*, 655.
131. Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, 853.
132. Vieira, M. L.; Zinn, F. K.; Comasseto, J. V. *J. Braz. Chem. Soc.* **2001**, *12*, 586.
133. Barros, S. M.; Dabdoub, M. J.; Dabdoub, V. M.; Comasseto, J. V. *Organometallics* **1989**, *8*, 1661.
134. Luxen, A.; Christiaens, L.; Renson, M. *J. Org. Chem.* **1980**, *45*, 3535.
135. Ohe, K.; Takahashi, H.; Uemura, S.; Sugita, N. *J. Org. Chem.* **1987**, *52*, 4859.
136. Potapov, V. A.; Amosova, S. V. *Phosphorus Sulfur Silicon* **1993**, *79*, 277.
137. Dabdoub, M. J.; Dabdoub, V. B.; Guerrero, P. G.; Silveira, C. C. *Tetrahedron* **1997**, *53*, 4199.
138. Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier B. V.: New York, **1988**.
139. Dabdoub, M. J.; Dabdoub, V. B.; Comasseto, J. V. *Tetrahedron Lett.* **1992**, *33*, 2261.
140. Dabdoub, M. J.; Dabdoub, V. B. *Tetrahedron* **1995**, *51*, 9839.
141. Mo, X. S.; Huang, Y. Z. *Tetrahedron Lett.* **1995**, *36*, 3539.
142. Buzilova, S. R.; Sadekov, I. D.; Lipovich, T. V.; Filippova, T. M.; Vereshchagin, L. I. *J. Gen. Chem. (USSR)* **1977**, *47*, 1828.
143. Uemura, S.; Fukuzawa, S. *Tetrahedron Lett.* **1982**, *23*, 1181.
144. Ohe, K.; Takahashi, H.; Uemura, S.; Sugita, N. *J. Organomet. Chem.* **1987**, *326*, 35.
145. Takahashi, H.; Ohe, K.; Uemura, S. *Nippon Kagaku Kaishi* **1987**, 1508.
146. Detty, M. R.; Murray, B. J. *J. Am. Chem. Soc.* **1983**, *105*, 883.
147. Braga, A. L.; Andrade, L. H.; Silveira, C. C.; Moro, A. V.; Zeni, G. *Tetrahedron Lett.* **2001**, *42*, 8563.
148. Jang, W. B.; Oh, D. Y.; Lee, C.-W. *Tetrahedron Lett.* **2000**, *41*, 5103.
149. Huang, X.; Liang, C. G.; Xu, Q.; He, Q.-W. *J. Org. Chem.* **2001**, *66*, 74.
150. Dabdoub, M. J.; Dabdoub, V. B.; Pereira, M. A. *Tetrahedron Lett.* **2001**, *42*, 1595.
151. Marino, J. P.; Nguyen, H. N. *J. Org. Chem.* **2002**, *67*, 6291.
152. Barrientos-Astigarraga, R. E.; Castelani, P.; Comasseto, J. V.; Formiga, H. B.; Silva, N. C.; Sumida, C. V.; Vieira, M. L. *J. Organomet. Chem.* **2001**, *623*, 43.
153. Raminelli, C.; Silva, N. C.; Dos Santos, A. A.; Porto, A. L. M.; Andrade, L. H.; Comasseto, J. V. *Tetrahedron* **2005**, *61*, 409.
154. Dos Santos, A. A.; Castelani, P.; Bassora, B. K.; Fogo, J. C., Jr.; da Costa, C. E.; Comasseto, J. V. *Tetrahedron* **2005**, *61*, 9173.
155. Sachida, H. *Rev. Heteroatom. Chem.* **2000**, *22*, 59.
156. Sashida, H.; Kurahashi, H.; Tsuchiya, T. *J. Chem. Soc., Chem. Commun.* **1991**, 802.
157. Sashida, H.; Ito, K.; Tsuchiya, T. *J. Chem. Soc., Chem. Commun.* **1993**, 1493.
158. Sashida, H.; Ito, K.; Tsuchiya, T. *Chem. Pharm. Bull.* **1995**, *43*, 19.
159. Sashida, H. *Heterocycles* **2000**, *52*, 49.
160. Sashida, H.; Sadamori, K.; Tsuchiya, T. *Synth. Commun.* **1998**, *28*, 713.
161. Sashida, H.; Yasuike, S. *J. Heterocycl. Chem.* **1998**, *35*, 725.
162. Sashida, H.; Kawamukai, A. *J. Heterocycl. Chem.* **1998**, *35*, 165.
163. Sashida, H. *Synthesis* **1998**, 745.
164. Sashida, H.; Ohyanagi, K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2123.
165. Sashida, H. *Synthesis* **1999**, 1866.
166. Sashida, H. *Heterocycles* **1998**, *48*, 631.
167. Ohe, K.; Takahashi, H.; Uemura, S.; Sugita, N. *Nippon Kagaku Kaishi* **1987**, 1469.
168. Zinn, F. K.; Righi, V. E.; Luque, S. C.; Formiga, H. B.; Comasseto, J. V. *Tetrahedron Lett.* **2002**, *43*, 1625.
169. Minkin, V. J.; Sadekov, I. D.; Rivkin, B. B.; Zakharov, A. V.; Nivorozhkin, V. L.; Kompan, O. E.; Struchkov, Y. T. *J. Organomet. Chem.* **1997**, *536–537*, 233.

170. Barrientos-Astigarraga, R. E.; Castelani, P.; Sumida, C. Y.; Zukerman-Schpector, J.; Comasseto, J. V. *Tetrahedron* **2002**, *58*, 1051.
171. For a discussion of the stereochemical aspects of the nucleophilic vinylic substitution see: Rappoport, Z. *Acc. Chem. Res.* **1992**, *25*, 474.
172. Barrientos-Astigarraga, R. E.; Castelani, P.; Sumida, C. Y.; Comasseto, J. V. *Tetrahedron Lett.* **1999**, *40*, 7717.
173. Dabdoub, M. J.; Comasseto, J. V. *Organometallics* **1988**, *7*, 84.
174. Comasseto, J. V. *Rev. Heteroatom. Chem.* **1993**, *9*, 61.
175. Braga, A. L.; Zeni, G.; Andrade, L. H.; Silveira, C. C. *Synlett* **1997**, 595.
176. Wipf, P.; Kendall, C. *Chem. Eur. J.* **2002**, *8*, 1778.
177. Sung, J. W.; Lee, C. W.; Oh, D. Y. *Tetrahedron Lett.* **1995**, *36*, 1503.
178. Dabdoub, M. J.; Begnini, M. L.; Cassol, T. M.; Guerrero, P. G.; Silveira, C. C. *Tetrahedron Lett.* **1995**, *36*, 7623.
179. Dabdoub, M. J.; Begnini, M. L.; Guerrero, P. G. *Tetrahedron* **1998**, *54*, 2371.
180. Dabdoub, M. J.; Begnini, M. L.; Guerrero, P. G.; Baroni, A. C. M. *J. Org. Chem.* **2000**, *65*, 61.
181. Sung, J. W.; Jang, W. B.; Oh, D. Y. *Tetrahedron Lett.* **1996**, *37*, 7537.
182. Dabdoub, M. J.; Baroni, A. C. M. *J. Org. Chem.* **2000**, *65*, 54.
183. Gerard, J.; Hevesi, L. *Tetrahedron* **2001**, *57*, 9109.
184. Huang, X.; Liang, C. G. *J. Chem. Soc., Perkin Trans. I* **1999**, 2625.
185. Comasseto, J. V.; Stefani, H. A.; Chieffi, A.; Zukerman-Schpector, J. *Organometallics* **1991**, *10*, 845.
186. Zeni, G.; Chieffi, A.; Cunha, R. L. O. R.; Zukerman-Schpector, J.; Stefani, H.; Comasseto, J. V. *Organometallics* **1999**, *18*, 803.
187. Campos, M. M.; Petragnani, N. *Tetrahedron Lett.* **1959**, 11.
188. Comasseto, J. V.; Petragnani, N. *Synth. Commun.* **1983**, *13*, 889.
189. Comasseto, J. V.; Ferraz, H. M. C.; Brandt, C. A.; Gaeta, K. K. *Tetrahedron Lett.* **1989**, *30*, 1209.
190. Comasseto, J. V.; Ferraz, H. M. C.; Petragnani, N.; Brandt, C. A. *Tetrahedron Lett.* **1987**, *28*, 5611.
191. Ferraz, H. M. C.; Comasseto, J. V.; Borba, E. B. *Quim. Nov.* **1992**, *15*, 298.
192. Ferraz, H. M. C.; Sano, M. K.; Scalfo, A. C. *Synlett* **1999**, *5*, 567.
193. Comasseto, J. V.; Grazini, M. V. A. *Synth. Commun.* **1992**, *22*, 949.
194. Moraes, D. N.; Santos, R. A.; Comasseto, J. V. *J. Braz. Chem. Soc.* **1998**, *9*, 397.
195. Petragnani, N.; Stefani, H. A.; Valduga, C. J. *Tetrahedron* **2001**, *57*, 1411.
196. Berry, F. J.; Gupta, A. K.; Khandelwal, B. L.; Raina, K. *J. Organomet. Chem.* **1979**, *172*, 445.
197. Barton, D. H. R.; Ley, S. V.; Merholz, C. A. *J. Chem. Soc., Chem. Commun.* **1979**, 755.
198. Engman, L.; Cava, M. P. *J. Chem. Soc., Chem. Commun.* **1982**, 164.
199. Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *Bull. Chem. Soc. Jpn.* **1983**, *59*, 879.
200. Suzuki, H.; Kawato, S.; Nasu, A. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 626.
201. Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *Tetrahedron Lett.* **1986**, *27*, 6099.
202. Kambe, N.; Fujioka, T.; Ogawa, A.; Miyoshi, N.; Sonoda, N. *Phosphorus Sulfur* **1988**, *38*, 167.
203. Brill, W. F. *J. Org. Chem.* **1986**, *51*, 1149.
204. Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. *J. Org. Chem.* **1989**, *54*, 4398.
205. Kambe, N.; Tsukamoto, T.; Miyoshi, N.; Murai, S.; Sonoda, N. *Chem. Lett.* **1987**, 269.
206. Ogawa, A.; Yokoyama, K.; Yokoyama, H.; Obayashi, R.; Kambe, N.; Sonoda, N. *J. Chem. Soc., Chem. Commun.* **1991**, 1748.
207. Ogawa, A.; Yokoyama, K.; Obayashi, R.; Han, L.-B.; Kambe, N.; Sonoda, N. *Tetrahedron* **1993**, *49*, 1177.
208. Ogawa, A.; Ogawa, I.; Obayashi, R.; Umezu, K.; Doi, M.; Hirao, T. *J. Org. Chem.* **1999**, *64*, 86.
209. Ogawa, A.; Obayashi, R.; Doi, M.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1998**, *63*, 4277.
210. Miyazoe, H.; Yamago, S.; Yoshida, J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3669.
211. Yamago, S.; Miyoshi, M.; Miyazoe, H.; Yoshida, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1407.
212. Yamago, S.; Miyazoe, H.; Iida, K.; Yoshida, J. *Org. Lett.* **2000**, *2*, 3671.
213. Han, L.-B.; Ishihara, K.; Kambe, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 7591.
214. Barton, D. H. R.; Géro, S. D.; Quidclt-Sire, B.; Samadi, M.; Vincent, C. *Tetrahedron* **1991**, *47*, 9383.
215. Barton, D. H. R.; Géro, S. D.; Holliday, P.; Quiclet-Sire, B. *Tetrahedron* **1996**, *52*, 8233.
216. Engman, L.; Gupta, V. *J. Org. Chem.* **1997**, *62*, 157.
217. Berlin, S.; Ericsson, C.; Engman, L. *J. Org. Chem.* **2003**, *68*, 8386.
218. Engman, L.; Laws, M. J.; Malmström, J.; Schiesser, C. H.; Zugaro, L. M. *J. Org. Chem.* **1999**, *64*, 6764.
219. Yamago, S.; Hashidume, M.; Yoshida, J. *Chem. Lett.* **2000**, 1234.
220. Yamago, S.; Hashidume, M.; Yoshida, J. *Tetrahedron* **2002**, *58*, 6805.
221. Ueda, Y.; Watanabe, H.; Uemura, J.; Uneyama, K. *Tetrahedron Lett.* **1993**, *34*, 7933.
222. Yamago, S.; Iida, K.; Yoshida, J. *J. Am. Chem. Soc.* **2002**, *124*, 13666.
223. Yamago, S.; Iida, K.; Yoshida, J. *J. Am. Chem. Soc.* **2002**, *124*, 2874.
224. Yamago, S.; Miyazoe, H.; Yoshida, J. *Tetrahedron Lett.* **1999**, *40*, 2339.
225. Yamago, S.; Miyazoe, H.; Yoshida, J. *Tetrahedron Lett.* **1999**, *40*, 2343.
226. Yamago, S.; Miyazoe, H.; Goto, R.; Yoshida, J. *Tetrahedron Lett.* **1999**, *40*, 2347.
227. Chen, C.; Crich, D. *Tetrahedron Lett.* **1993**, *34*, 1545.
228. Chen, C.; Crich, D.; Papadatos, A. *J. Am. Chem. Soc.* **1992**, *114*, 8313.
229. Crich, D.; Chen, C.; Hwang, J.-T.; Yuan, H.; Papadatos, A.; Walter, R. I. *J. Am. Chem. Soc.* **1994**, *116*, 8937.
230. Lucas, M. A.; Schiesser, C. H. *J. Org. Chem.* **1996**, *61*, 5754.
231. Lucas, M. A.; Schiesser, C. H. *J. Org. Chem.* **1998**, *63*, 3032.
232. Yamago, S.; Miyazoe, H.; Sawazaki, T.; Goto, R.; Yoshida, J. *Tetrahedron Lett.* **2000**, *41*, 7517.
233. Yamago, S. *Synlett* **2004**, 1875.
234. Sharpless, K. B.; Gordon, K. M.; Lauer, R. F.; Patrick, D. W.; Singer, S. P.; Young, H. W. *Chem. Scr.* **1975**, *8A*, 9.
235. Petragnani, N.; Comasseto, J. V. *Synthesis* **1986**, 1.
236. Nishibayashi, Y.; Komatsu, N.; Ohe, K.; Uemura, S. *J. Chem. Soc., Perkin Trans. I* **1993**, 1133.
237. Chiba, T.; Nishibayashi, Y.; Singh, J. D.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **1995**, *36*, 1519.
238. Reich, H. J.; Green, D. P.; Phillips, N. H.; Borst, J. P.; Reich, I. L. *Phosphorus Sulfur Silicon* **1992**, *67*, 83.
239. Reich, H. J.; Bevan, M. J.; Gudmundsson, B. Ö.; Puckett, C. L *Angew. Chem., Int. Ed.* **2002**, *41*, 3436.

240. Nágera, C.; Sansano, J. M.; Yus, M. *Tetrahedron* **2003**, *59*, 9255.
241. Seebach, D.; Beck, A. K. *Chem. Ber.* **1975**, *108*, 314.
242. Brandt, C. A.; Comasseto, J. V.; Nakamura, W.; Petragnani, N. *J. Chem. Res. (S)* **1983**, 156.
243. Hiiro, T.; Kambe, N.; Ogawa, A.; Miyoshi, N.; Murai, S.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1187.
244. Hiiro, T.; Atarashi, Y.; Kambe, N.; Fujiwara, S.; Ogawa, A.; Ryu, I.; Sonoda, N. *Organometallics* **1990**, *9*, 1355.
245. Kanda, T.; Kato, S.; Sugino, T.; Kambe, N.; Sonoda, N. *J. Organomet. Chem.* **1994**, *473*, 71.
246. Sugimoto, O.; Sudo, M.; Tanji, K. *Tetrahedron Lett.* **1999**, *40*, 2139.
247. Sugimoto, O.; Sudo, M.; Tanji, K. *Tetrahedron* **2001**, *57*, 2133.
248. Chieffi, A.; Comasseto, J. V.; Snieckus, V. *Synlett* **2000**, *2*, 269.
249. Hiiro, T.; Morita, Y.; Inoue, T.; Kambe, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *J. Am. Chem. Soc.* **1990**, *112*, 455.
250. Inoue, T.; Atarachi, Y.; Kambe, N.; Ogawa, A.; Sonoda, N. *Synlett* **1995**, 209.
251. Santos, A. A. D.; Comasseto, J. V. *J. Braz. Chem. Soc.* **2005**, *16*, 11.
252. Princival, J. L.; Barros, S. M. G.; Comasseto, J. V.; Santos, A. A. D. *Tetrahedron Lett.* **2005**, *46*, 4423.
253. Cohen, T.; Tong, S. *Tetrahedron* **1997**, *53*, 9487.
254. Luppold, M.; Muller, E.; Winter, W. Z. *Naturforsch.* **1976**, *31b*, 1654.
255. Kauffman, T. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 410.
256. Barros, S. M.; Comasseto, J. V.; Berriel, J. *Tetrahedron Lett.* **1989**, *30*, 7353.
257. Yang, J.; Cohn, S. T.; Romo, D. *Org. Lett.* **2000**, *2*, 763.
258. Kanda, T.; Sugino, T.; Kambe, N.; Sonoda, N. *Phosphorus, Sulfur Silicon* **1992**, *67*, 103.
259. Terao, J.; Kambe, N.; Sonoda, N. *Synlett* **1996**, 779.
260. Knochel, P.; Singer, R. D. *Chem. Rev.* **1993**, *93*, 2117.
261. Studemann, T.; Gupta, V.; Engman, L.; Knochel, P. *Tetrahedron Lett.* **1997**, *38*, 1005.
262. Terao, J.; Kambe, N.; Sonoda, N. *Tetrahedron Lett.* **1996**, *37*, 4741.
263. Huang, W.-H.; Huang, Y.-Z.; Dai, L.-X. *Tetrahedron Lett.* **1998**, *39*, 6953.
264. Uchiyama, M.; Kameda, M.; Mishima, O.; Yokoyama, N.; Koike, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 4934.
265. Comasseto, J. V.; Berriel, J. N. *Synth. Commun.* **1990**, *20*, 1681.
265a. Comasseto, J. V.; Berriel, J. N. *Synth. Commun.* **1992**, *22*, 2431.
266. Tucci, F. C.; Chieffi, A.; Comasseto, J. V. *Tetrahedron Lett.* **1992**, *33*, 5721.
267. Araujo, M. A.; Barrientos-Astigarraga, R. E.; Ellensohn, R. M.; Comasseto, J. V. *Tetrahedron Lett.* **1999**, *40*, 5115.
268. Moraes, D. N.; Barrientos-Astigarraga, R. E.; Castelani, P.; Comasseto, J. V. *Tetrahedron* **2000**, *56*, 3327.
269. Barrientos-Astigarraga, R. E.; Moraes, D. N.; Comasseto, J. V. *Tetrahedron Lett.* **1999**, *40*, 265.
270. Marino, J. P.; Tucci, F. C.; Comasseto, J. V. *Synlett* **1993**, 761.
271. Marino, J. P.; McClure, M. S.; Holub, D. P.; Comasseto, J. V.; Tucci, F. C. *J. Am. Chem. Soc.* **2002**, *124*, 1664.
272. Castelani, P.; Comasseto, J. V. *Organometallics* **2003**, *22*, 2108.
273. Castelani, P.; Luque, S.; Comasseto, J. V. *Tetrahedron Lett.* **2004**, *45*, 4473.
274. Spinet, P.; Echavarren, A. M. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 4704.
275. Sonogashira, K. *J. Organomet. Chem.* **2002**, *653*, 46.
276. Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.
277. Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.
278. Araujo, M. A.; Comasseto, J. V. *Synlett* **1995**, 1145.
279. Araujo, M. A.; Raminelli, C.; Comasseto, J. V. *J. Braz. Chem. Soc.* **2004**, *15*, 358.
280. Smith, A. L.; Nicolaou, K. C. *J. Med. Chem.* **1996**, *39*, 2103.
281. Chieffi, A.; Comasseto, J. V. *Tetrahedron Lett.* **1994**, *35*, 4063.
282. Chieffi, A.; Comasseto, J. V. *Synlett* **1995**, 671.
283. Ogura, A.; Tsuboi, Y.; Obayashi, R.; Yokoyama, K.; Ryu, I.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 1600.
284. Huang, Y.-Z.; Mo, X.-S.; Wang, L. *Tetrahedron Lett.* **1998**, *39*, 419.
285. Castelani, P.; Comasseto, J. V. *J. Braz. Chem. Soc.* **2004**, *15*, 461.
286. Castelani, P.; Comasseto, J. V. *Tetrahedron* **2005**, *61*, 2319.
287. Kawamura, T.; Kikukawa, K.; Takagi, M.; Matsuda, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2021.
288. Uemura, S.; Wakasuki, M.; Okano, M. *J. Organomet. Chem.* **1980**, *194*, 277.
289. Nishibayashi, Y.; Cho, C. S.; Uemura, S. *J. Organomet. Chem.* **1996**, *507*, 197.
290. Kang, S.-K.; Lee, S.-W.; Ryu, H.-C. *Chem. Commun.* **1999**, 2117.
291. Kang, S.-K.; Hong, Y.-T.; Kim, D.-H.; Lee, S.-H. *J. Chem. Res.* **2001**, 283.
292. Kang, S.-K.; Lee, S.-W.; Kim, M.-S.; Kwon, H.-S. *Synth. Commun.* **2001**, *31*, 1721.
293. Zeni, G.; Comasseto, J. V. *Tetrahedron Lett.* **1999**, *40*, 4619.
294. Zeni, G.; Panatieri, R. B.; Lissner, E.; Menezes, P. H.; Braga, A. L.; Stefani, H. A. *Org. Lett.* **2001**, *6*, 819.
295. Zeni, G.; Menezes, P. H.; Moro, A. V.; Braga, A. L.; Silveira, C. C.; Stefani, H. A. *Synlett* **2001**, *9*, 1473.
296. Braga, A. L.; Alves, E. F.; Silveira, C. C.; Andrade, L. H. *Tetrahedron Lett.* **2000**, *41*, 161.
297. Braga, A. L.; Vargas, F.; Zeni, G.; Silveira, C. C.; Andrade, L. H. *Tetrahedron Lett.* **2002**, *43*, 4399.
298. Zeni, G.; Nogueira, C. W.; Panatieri, R. B.; Silva, D. O.; Menezes, P. H.; Braga, A. L.; Silveira, C. C.; Stefani, H. A.; Rocha, J. B. T. *Tetrahedron Lett.* **2001**, *42*, 7921.
299. Zeni, G.; Lüdtke, D. S.; Nogueira, C. W.; Panatieri, R. B.; Braga, A.; Silveira, C. C.; Stefani, H. A.; Rocha, J. B. T. *Tetrahedron Lett.* **2001**, *42*, 8927.
300. Zeni, G.; Perin, G.; Cella, R.; Jacob, R. G.; Braga, A. L.; Silveira, C. C.; Stefani, H. A. *Synlett* **2002**, *6*, 975.
301. Zeni, G.; Nogueira, C. W.; Silva, D. O.; Menezes, P. H.; Braga, A. L.; Stefani, H. A.; Rocha, J. B. T. *Tetrahedron Lett.* **2003**, *44*, 685.
302. Dabdoub, M. J.; Dabdoub, V. B.; Marino, J. P. *Tetrahedron Lett.* **2000**, *41*, 433.
303. Stefani, H. A.; Cella, R.; Dörr, F. A.; Pereira, C. M. P.; Zeni, G.; Gomes, M. *Tetrahedron Lett.* **2005**, *46*, 563.
304. Raminelli, C.; Prechtl, M. H. G.; Santos, L. S.; Eberlin, M. N.; Comasseto, J. V. *Organometallics* **2004**, *23*, 3990.
305. Zeni, G.; Braga, A. L.; Stefani, H. A. *Acc. Chem. Res.* **2003**, *36*, 731.
306. Silveira, C. C.; Braga, A. L.; Vieira, A. S.; Zeni, G. *J. Org. Chem.* **2003**, *68*, 662.
307. Raminelli, C.; Gargalaka, J.; Silveira, C. C.; Comasseto, J. V. *Tetrahedron Lett.* **2004**, *45*, 4927.

9.14
Indium and Gallium

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9.14.1 Introduction

In contrast to boron, aluminum, and thallium, which have widely been used in organic synthesis, the other group 13 elements, indium and gallium, had been less familiar to organic synthetic chemists until the 1980s. In the past two decades, however, organoindium and organogallium compounds have gathered increasing interest in organic synthesis, and now it has been revealed that these compounds have novel and unique properties which are useful for organic transformations.

Organoindium compounds were first prepared in 1928;[1] however, the use of organoindium reagents in organic synthesis was reported only sporadically until the late 1980s.[2,3] In 1988, Araki *et al.* discovered that allylic indium reagents can be readily prepared simply by mixing allylic halides and indium powder in organic solvents, and these compounds have been shown to be useful for allylation of carbonyl compounds.[4] Since then, applications of allylindium reagents and the related organoindium reagents to organic transformations have been studied. In 1991, indium-mediated Barbier-type allylations of carbonyl compounds were achieved in water.[5] After this work, indium-mediated and -catalyzed reactions in aqueous media have been receiving much attention from economical and environmental standpoints.

As the first ionization potential of indium (5.8 eV) is as low as those of Li and Na, indium acts as an effective single-electron-transfer (SET) agent. Organoindium reagents can be prepared by reacting appropriate organic halides with indium metal; *e.g.*, allylindium sesquihalides are obtained in high yields without a formation of Wurtz-coupling by-products. Owing to the less basic and mild nucleophilic nature, organoindium compounds are compatible with several organic functionalities. Organoindium reagents exhibit a strong tendency to coordinate to heteroatoms, in particular to oxygen functionalities such as a hydroxyl or carboxyl group in the substrates. This extraordinally strong oxophilicity sometimes makes the indium-mediated reactions highly regio-, stereo-, and chemoselective. A tolerance toward water characterizes organoindium reagents in organic synthetic tools; their reactions can be performed under aqueous conditions without protection of hydroxyl and other protic groups on reactants, and this property makes the indium reagents unique and important in respect to environmentally benign chemistry. As several reviews on organoindium chemistry in organic synthesis have hitherto been published,[6–24] this chapter concentrates mainly on the recent advances in the indium-mediated organic synthesis. Indium(III) salts, such as indium chloride and indium triflate, have also been used as catalysts in aqueous media as well as in organic solvents. However, these studies are not included in this chapter, because the salts work simply as Lewis acids and no organometallic species having carbon–indium bonds seem to be involved in the reactions.

The systematic studies of organogallium compounds in organic synthesis had to wait further until the 1990s. Recent studies have revealed several novel aspects of organogallium reagents such as clean carbogallation to carbon–carbon triple bonds.[25] Facile electrophilic aromatic substitution and the tendency to undergo radical reactions are additional interesting properties of gallium compounds. These are summarized in Section 9.14.4

9.14.2 Preparation Of Organoindium Compounds

9.14.2.1 Oxidative Addition to Organic Halides

The most widely used preparative method of allylindium(III) or propargylindium(III) compounds is the oxidative addition of metallic indium or indium(I) halides to allylic or propargyl substrates.[4,26,27] Allylic bromides and iodides serve as good allylic sources without any other activation. In the case of allylic chlorides, a proper additive such as lithium iodide is required to promote the oxidative addition. Allylic indium compounds prepared by oxidative addition of metallic indium are considered to exist as the sesquihalide structure ($allyl_3In_2X_3$), which has been

confirmed by ^{1}H NMR spectroscopy.[4] α-Halo carbonyl compounds can be transformed to the corresponding indium enolates by direct insertion of indium metal or indium(I) iodide.[3,27,28]

9.14.2.2 Transmetallation

9.14.2.2.1 Transmetallation with Hg, Li, Mg, or Sn organometallics

Triphenylindium was first prepared from diphenylmercury and metallic indium.[2] Recently, allylindium(I) was prepared via a transmetallation of allylmercury with metallic indium in water and this compound is postulated to be an intermediate in the allylation of carbonyl compounds in aqueous media.[29] Transmetallation of alkyllithium or Grignard reagents with indium trihalides is the most general procedure for preparation of a series of organoindium compounds.[30] Tetraorganoindium ate complexes (indates) can be obtained by an addition of 1 equiv. of alkyllithium or Grignard reagents to organoindium(III) compounds.[31] Transmetallation of allylstannane with indium trichloride also gives allylindium(III).[32–41] Similarly, alkynylstannane is transformed to alkynylindium compounds.[42]

9.14.2.2.2 Redox transmetallation with Pd or Ni compounds

A new preparative method for allylic indium(III) reagents via a reductive transmetallation of π-allylpalladium(II) or π-allylnickel(II) complexes with indium(I) salts is reported. This method enables the use of a wide variety of allylic compounds, such as allylic chlorides, acetates, and even allylic alcohols, in combination with Pd or Ni catalysts.[43–50] π-Allylpalladium(II) resulting from the addition of arylpalladium(II) to allene is also transformed by metallic indium to the corresponding allylindium.[51–54] Similarly, propargylindium(III) can be prepared from the corresponding propargyl alcohol derivatives.[55–58]

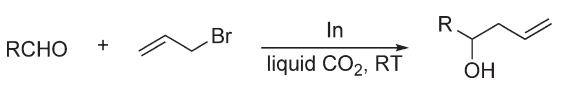
9.14.3 Reaction Of Organoindium Compounds

A large part of organoindium chemistry so far reported deals with reactions of allylic and propargylic indium reagents. These are summarized in Sections 9.14.3.1–9.14.3.9. Reactions of other type of organoindium compounds are overviewed in Sections 9.14.3.10–9.14.3.14.

9.14.3.1 Allylation and Propargylation of Carbonyl Compounds

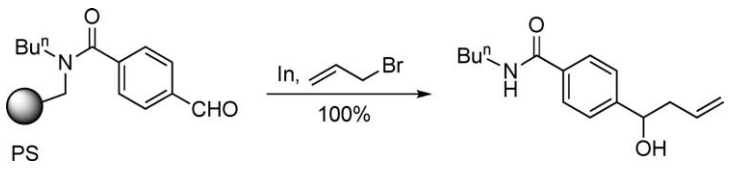
After the first report on the allylation of carbonyl compounds with allylndium reagents in organic solvents,[4] extensive studies on this reaction have been published so far. Earlier allylation and propargylation of carbonyl compounds in organic and aqueous media have been surveyed.[6–17] This part as well as the following sections focus on recent advances of carbonyl allylation/propargylation reactions with emphasis on the regio- and stereochemical aspects.

Indium-mediated Barbier-type coupling between carbonyl compounds and allyl halides has been revealed to proceed effectively in diverse reaction media. Even under solvent-free conditions, allylation works well, although no reaction is observed with benzyl bromide and α-halo carbonyl compounds.[59] Various aldehydes react with allyl bromide mediated by indium in liquid carbon dioxide to give homoallylic alcohols (Scheme 1). In contrast to the corresponding neat allylation, the liquid CO_2-mediated reaction can allylate solid aldehydes successfully.[60] Indium-mediated allylations of carbonyl compounds with allyl bromide proceed in room temperature ionic liquids. In [bmim][BF_4] and [bmim][PF_6] (bmin: 1-butyl-3-methylimidazolium), the desired homoallylic alcohols are formed with good levels of conversion.[61] Homoallyllic alcohols are also prepared by the reaction of resin-bound aldehydes (Equation (1)).[62]



R	*Yield* (%)
Ph	82
p-C_6H_4CN	58
n-C_6H_{13}	59

Scheme 1

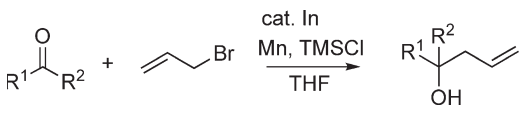


(1)

In indium-mediated reactions, a catalytic use of expensive indium is desirable from an economical standpoint, and it has been achieved in combination with more electron-positive metals. Thus, allylation of aldehydes and ketones, as well as prenylation of 2-chlorobenzoquinone, has been performed by using metallic aluminum or zinc in combination with a catalytic amount of indium(III) chloride.[63] Also, allylation of aldehydes and ketones with allyl bromide is carried out with a catalytic amount of indium powder (from 0.01 to 0.1 equiv.) in THF in the presence of manganese and chlorotrimethylsilane as the reducing and oxophilic agents, respectively (Scheme 2).[64,65]

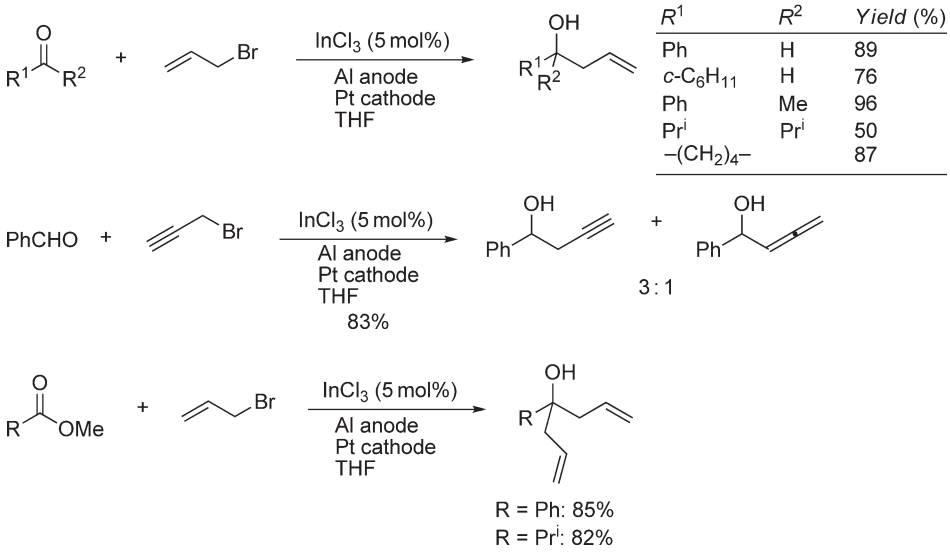
From $InCl_3$, highly reactive low-valent indium(I) species are electrochemically generated and regenerated. These are used for allylation and propargylation of carbonyl compounds (Scheme 3). Of special interest are bisallylations of aromatic and aliphatic esters, since such conversions cannot be achieved by using conventional stoichiometric allylations of esters by means of indium metal or InI.[66]

Allylindium prepared *in situ* from allylmagnesium bromide with indium trichloride reacts with aldehydes in THF–H_2O to afford homoallylic alcohols. The yield is higher when water is present rather than under anhydrous conditions (Equation (2)).[67]



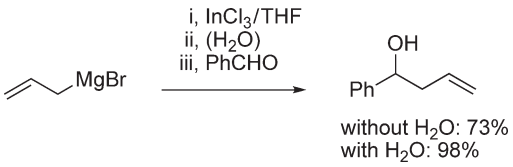
R^1	R^2	*Yield* (%)
Ph	H	86
n-C_7H_{15}	H	77
Bu^t	H	57
PhCH=CH	H	39
–$(CH_2)_5$–		91
Ph	Me	80

Scheme 2



R^1	R^2	*Yield* (%)
Ph	H	89
c-C_6H_{11}	H	76
Ph	Me	96
Pr^i	Pr^i	50
–$(CH_2)_4$–		87

Scheme 3



(2)

Allylindium and propargylindium reagents have successfully been applied to the total syntheses of several natural products.[68–101]

9.14.3.2 Regioselective Carbonyl Allylation

Allylindium reagents bearing substituents at the γ-position react with carbonyl compounds in organic and aqueous media regioselectively at the γ-position, via a six-membered transition state, to afford the corresponding branched homoallylic alcohols, if no sterically bulky carbonyl or allyl substituent is involved.[102] For example, the indium-mediated reaction of aldehydes with 3-bromo-1-cyano-1-propene proceeds readily in water to give α-cyano-β-ethylenic secondary alcohols (Scheme 4).[103]

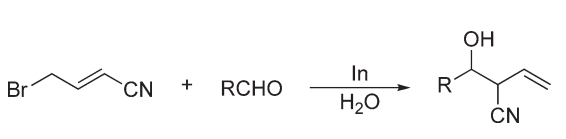
The reaction of benzaldehyde with unsymmetrical allylic bromides in the ionic liquid bmim also proceeds regioselectively to realize a carbon–carbon bond formation at the more substituted allylic carbon (Scheme 5). In the coupling of crotyl bromide with benzaldehyde, the product is a nearly 50 : 50 mixture of *anti*/*syn* diastereomers. Cinnamyl bromide predominantly gives the *anti*-diastereomer. The regio- and diastereoselectivity is similar to that observed for these in aqueous media.[104]

Interestingly, the indium-mediated reactions of crotyl or cinnamyl bromide with aldehydes in the presence of 10 M water exclusively give the α-adducts regardless of the bulkiness of aldehydes (Scheme 6).[105,106] NMR study has proved that the initially formed γ-homoallylic alcohol is converted to the thermodynamic α-homoallylic alcohol.

Pentadienylindium, a vinylog of allylindium, reacts with carbonyl compounds regioselectively at the γ-position to give 1,4-pentadiene derivatives (Scheme 7).[107–109] In the presence of $InCl_3$, pentadienylstannane similarly reacts with α-alkoxyaldehydes to produce the corresponding γ-adducts (Scheme 8).[110]

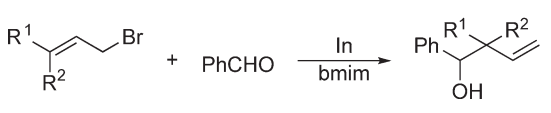
Indium-mediated coupling of propargyl bromides with aldehydes in aqueous media occurs regioselectively to give either homopropargyl alcohols or allenyl alcohols depending on the γ-substitutent of the propargyl bromides.[111,112] For example, the reaction of (trialkylsilyl)propargyl bromide with an aldehyde selectively gives the homopropargylic alcohol **1** or the allenyl alcohol **2** by changing the substituents at the silyl group and reaction conditions (Scheme 9).[113]

Indium-mediated propargylation of 4-oxoazetidine-2-carboxaldehydes gives the homopropargyl alcohol **3** and the allenyl alcohol **4** with moderate selectivities. In the case involving propargyl bromides bearing an aliphatic or aromatic substituent at the terminal position, *anti*-allenyl alcohols **5** are selectively formed over *syn*-alcohols **6** (Scheme 10).[114]



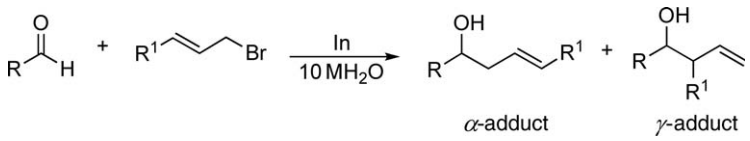
R	*Yield* (%)
Ph	65
Bu^n	64
Pr^i	64
Bu^t	58

Scheme 4



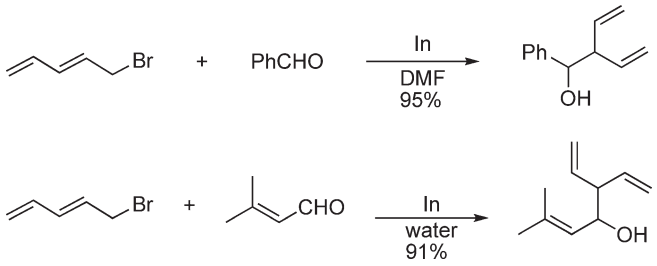
R^1	R^2	*Yield* (%)	*syn* : *anti*
Me	H	87	58 : 42
Ph	H	100	37 : 63
Me	Me	91	

Scheme 5

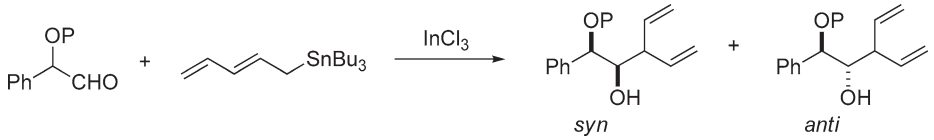


R	R^1	*Yield* (%)	$\alpha:\gamma$	*E*:*Z*
Ph	Me	60	99:1	55:45
c-C_6H_{11}	Me	85	99:1	70:30
n-C_5H_{11}	Me	75	98:2	65:35
$PhCH_2CH_2$	Me	67	97:3	55:45
Ph	Ph	72	98:2	*E*
c-C_6H_{11}	Ph	71	99:1	90:10
$PhCH_2CH_2$	Ph	50	99:1	95:5

Scheme 6

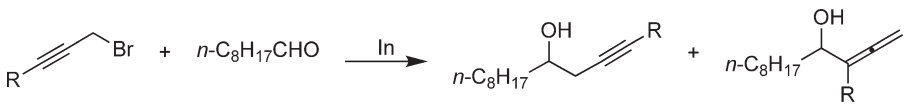


Scheme 7



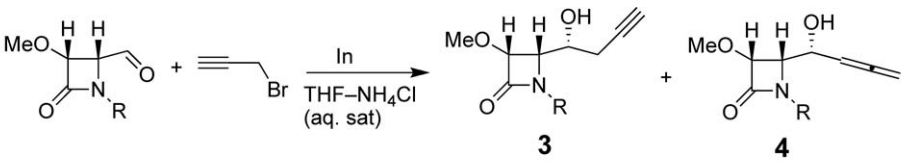
P	*Solvent*	*Yield* (%) (*syn*:*anti*)
Bn	MeCN	76 (>99:1)
TBS	CH_2Cl_2	78 (78:22)
TBS	MeCN	70 (43:57)
TBS	EtOH	70 (25:75)

Scheme 8

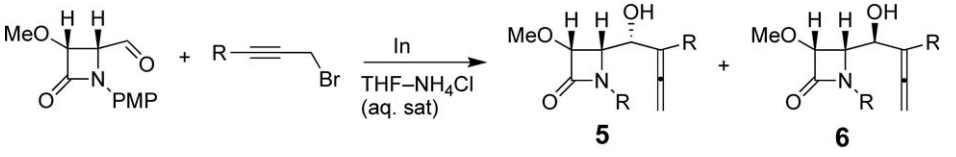


R	*Conditions*	*Yield* (%) **1**:**2**
Me_3Si	THF, InF_3 (10 mol%)	93 (99:1)
Pr^i_3Si	THF–H_2O (1:5)	52 (5:95)

Scheme 9



R	**3** : **4**	*Yield* (%)
2-Propenyl	55 : 45	72
2-Propynyl	57 : 43	65
4-Pentynyl	55 : 45	66



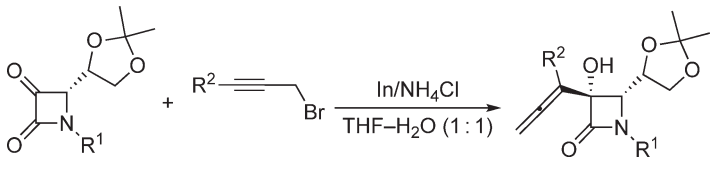
R	**5** : **6**	*Yield* (%)
Me	91 : 9	77
Ph	90 : 10	84

Scheme 10

For azetidine-2,3-diones, α-allenic alcohols are obtained as essentially regio- and diastereoisomerically pure products (Scheme 11).[115]

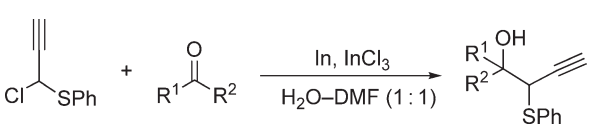
Indium-mediated reaction of α-chloropropargyl phenyl sulfide and aldehydes gives β-hydroxysulfides regio- and stereoselectively in aqueous media (Scheme 12).[116,117]

Fluorinated organoindium reagents show unique regio- and stereoselectivities. The allylindium reagent containing a CF_2 unit reacts with aldehydes at the CF_2 terminus to give the corresponding 1-substituted 2,2-difluoro-3-buten-1-ols (Equation (3)).[118–121] The reaction of 1-substituted 3-bromo-3,3-difluoropropyne with aldehydes in the presence of $InCl_3$ and Sn also proceeds exclusively at the CF_2 terminus to afford the corresponding *gem*-difluorohomopropargyl alcohols (Equation (4)).



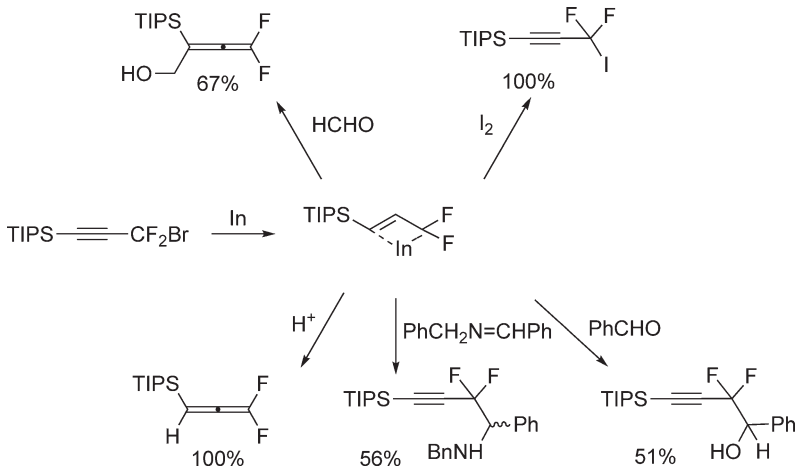
R^1	R^2	*Yield* (%)
4-$MeOC_6H_4$	Me	74
2-Propenyl	Me	63
4-$MeOC_6H_4$	Ph	76
4-$MeOC_6H_4$	Ph	75 (without NH_4Cl)
2-Propenyl	Ph	62
2-Propynyl	Ph	48

Scheme 11

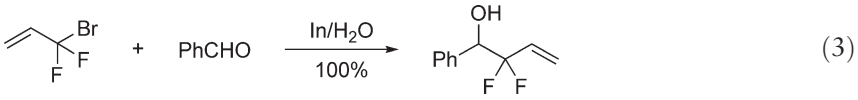


R^1	R^2	*Yield* (%) (*syn* : *anti*)
Ph	H	84 (88 : 12)
n-C_5H_{11}	H	46 (53 : 47)
(*E*)-PhCH=CH	H	75 (90 : 10)
c-C_6H_{11}	H	77 (87 : 13)

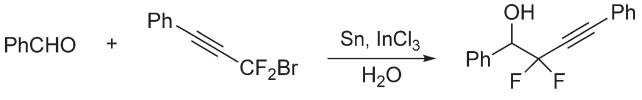
Scheme 12



Scheme 13



(3)



(4)

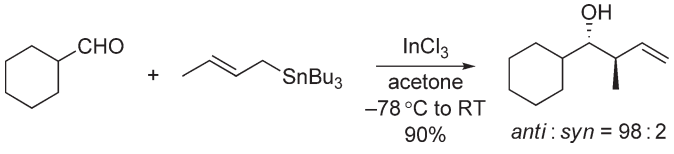
gem-Difluoroallenylindium(I) has been prepared from bromodifluoromethyl silyl acetylene. This compound reacts with various electrophiles (Scheme 13). Aldehydes give homopropargylic *gem*-difluoro alcohols, whereas allenyl alcohols are obtained with aqueous formaldehyde.[122–124]

9.14.3.3 Diastereoselective Carbonyl Allylation

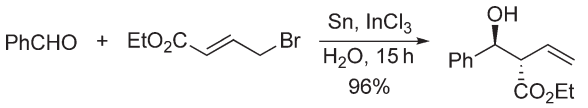
9.14.3.3.1 Introduction

The control of diastereoselectivity in the allylation reaction of carbonyl compounds with allylic indium reagents has been an important issue since the discovery of the indium-mediated carbonyl allylation. As earlier discussions have been summarized in the precedent reviews,[6–24] only relatively recent references are cited below.

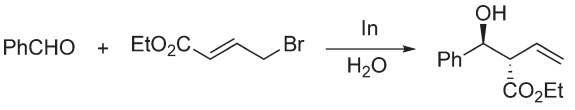
In various donor solvents such as acetone and acetonitrile, $InCl_3$ undergoes transmetallation with crotylstannane, and the resulting allylic indium compound affords *anti*-adducts with aldehydes (Equation (5)).[32] The allylation of aldehydes with allylic bromides in water, in the presence of stoichiometric amounts of $InCl_3$ and Sn, proceeds cleanly to give the corresponding *anti*-γ-adducts predominantly (Equation (6)).[33] The transmetallation from allylic stannane to allyllic indium via an S_E2' process is postulated during the reaction, and the high *anti*-selectivity can be explained by a six-membered ring transition state. Metallic indium also mediates the coupling of ethyl 4-bromocrotonate with carbonyl compounds in water to give the corresponding β-hydroxy-α-vinyl carboxylates with *anti*-selectivity. The use of lanthanide triflate increases the rate and selectivity of the reaction (Equation (7)).[125]



(5)

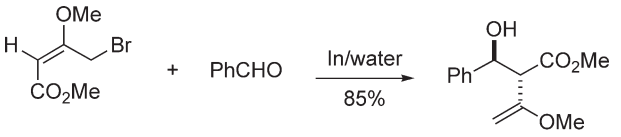


anti : *syn* = 85 : 15 (6)



without $La(OTf)_3$: 59% (*anti* : *syn* = 86 : 14)
with $La(OTf)_3$: 99% (*anti* : *syn* = 90 : 10) (7)

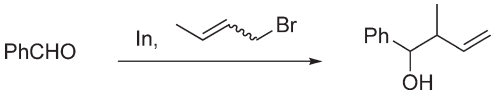
Addition of methyl (*E*)-4-bromo-3-methoxycrotonate to aldehydes in the presence of indium in water provides *β*-hydroxy esters. Their acidic hydrolysis leads to Knoevenagel-like adducts (Equation (8)).[126]



anti : *syn* = 8 : 1 (8)

The indium-mediated aqueous Barbier-type reaction of crotyl bromide with benzaldehyde shows no diastereoselectivity. However, the use of preformed crotylindium sesquibromide in DMF affords *syn*-1-phenyl-2-methyl-3-buten-1-ol (ca. 40% de) after aqueous acidic workup. At 22 °C in DMF prior to workup, a greater relative proportion of *anti*-intermediate is decomposed as compared to its *syn*-diastereomer. The resultant kinetic diastereoselection upgrades the *syn* : *anti* ratio to 99 : 1 with a concomitant drop in overall yield (Scheme 14).[127]

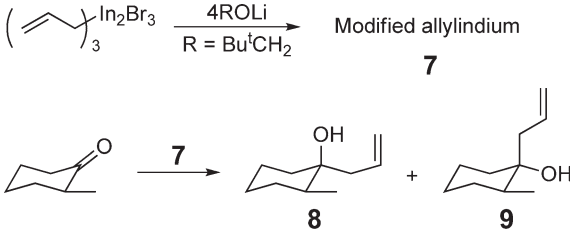
The reaction of allylindium sesquibromide with 4 equiv. of bulky lithium alkoxide results in modified reagents **7**, which show unusual degrees of chemo- and diastereoselectivity in the reactions with carbonyl compounds; for example, allylation of 2-methylcyclohexanone gives a high ratio of axial alcohol **8**/equatorial alcohol **9** (Scheme 15).[128]



Conditions[a]	*syn* : *anti*	*Yield* (%)
A: H_2O, 22 °C, 2 h	50 : 50	78
B: DMF, 22 °C, 20 min	73 : 27	68
B: DMF, 22 °C, 96 h	99 : 1	38

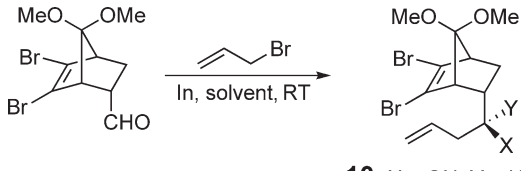
[a]Crotyl bromide ca. 80% *E*, 15% *Z*, 5% 1-methylallyl bromide. **A**: Barbier-type reaction, **B**: Indium was reacted with crotyl bromide in DMF, then benzaldehyde was added.

Scheme 14



without ROLi: 89% (**8** : **9** = 83 : 17)
with ROLi: 95% (**8** : **9** = 93 : 7)

Scheme 15

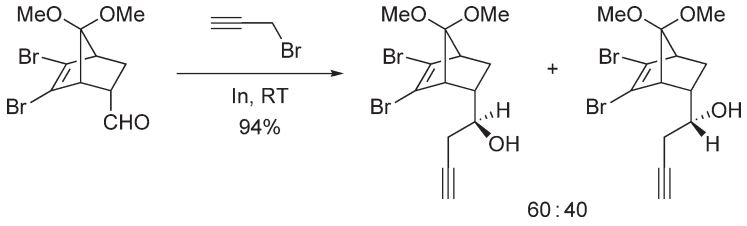


10: X = OH, Y = H
11: X = H, Y = OH

Solvent	*Time*	*Yield* (%)	**10** : **11**
THF–H_2O (1 : 1)	10 h	97	81 : 19
THF–H_2O (1 : 3)	16 h	95	79 : 21
H_2O	12 d	75	81 : 19
THF	6 h	70	77 : 25
DMF	12 h	95	69 : 31
DMSO	12 h	94	86 : 14

Scheme 16

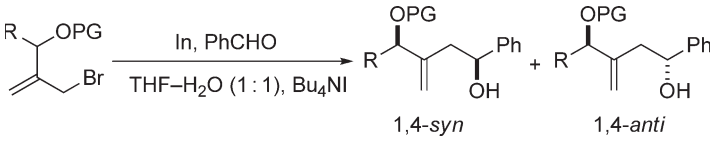
Indium-mediated allylation of *endo*-2-acetoxybicyclo[2.2.1]heptan-7-one shows poor diastereoselectivity.[129] On the contrary, indium-mediated allylation of the bicyclic aldehyde has been performed with different solvent systems, and the homoallylic alcohols **10** and **11** are formed in excellent yields with high diastereoselectivity. The highest diastereoselectivity has been observed in DMSO in 94% yield (Scheme 16).[130] Indium-mediated propargylation of the same aldehyde gives two diastereomers in 94% yield in a ratio of 60 : 40 (Equation (9)).[130]



(9)

9.14.3.3.2 Oxygen-bearing allylindium reagents

Systematic studies have revealed the nature of highly stereoselective 1,4-asymmetric stereoinductions under aqueous conditions by use of oxygen-bearing allylic indium reagents. Thus, the reaction of a series of allyl bromides possessing an ethereal stereogenic substituent at C2 with benzaldehyde gives *syn*-4-alkoxyalkan-1-ols in good yields and diastereoselectivity (Scheme 17).[131] The increase in the bulk of R gives higher diastereoselectivity, whereas altering the nature of the protecting group (PG) shows little difference in stereoselectivity.



1,4-*syn* 1,4-*anti*

R	*PG*	*Yield* (%)	*syn* : *anti*
Me	Bn	72	86 : 14
Ph	Bn	79	88 : 12
Pr^i	Bn	59	96 : 4
Me	TBDMS	67	86 : 14
Ph	TBDMS	75	90 : 10
Pr^i	TBDMS	71	97 : 3
Me	MOM	89	73 : 27
Ph	MOM	83	79 : 21
Pr^i	MOM	85	82 : 18

Scheme 17

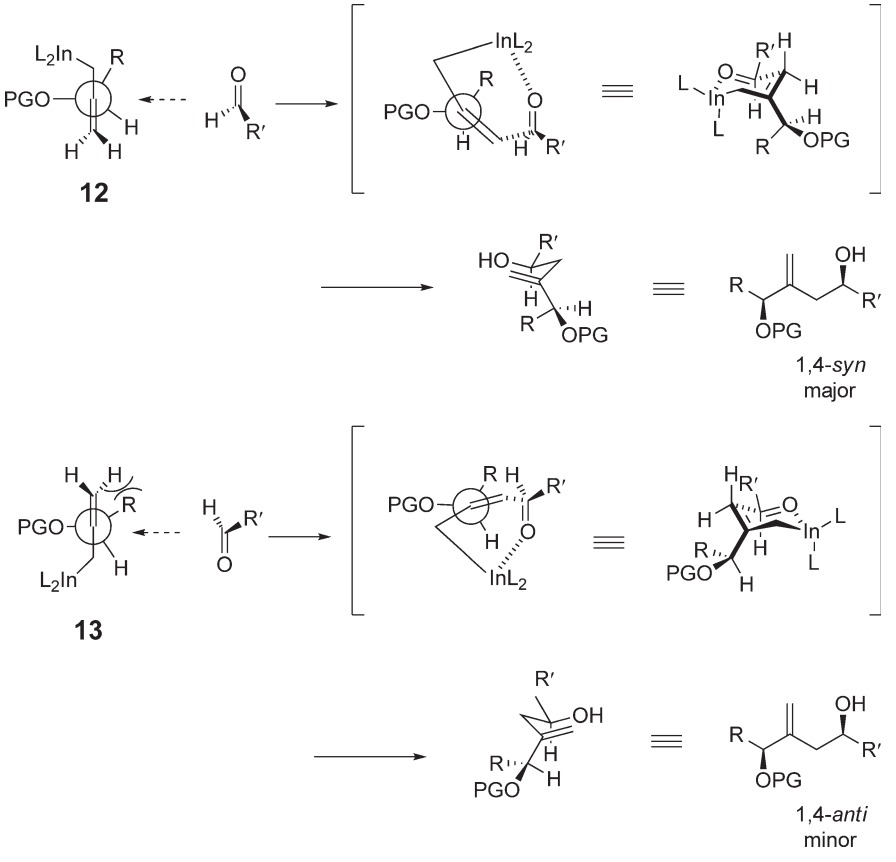
The stereochemical outcome can be rationalized by considering the approach of the aldehyde to the preferred conformation of the allylindium. The approach of the aldehyde is postulated to be in antiperiplanar to the OPG group as for the Felkin–Anh model. The allylindium prefers to adopt the conformation **12** rather than **13**, where the 1,3-allylic strain with R is minimized and the steric interaction with the aldehyde is also reduced (Scheme 18). The facial selection with respect to the aldehyde is determined by the aldehyde residue (R′) to occupy in the least sterically demanding position, away from the substituted allylic carbon. The carbonyl allylation then proceeds via a six-membered chairlike transition state, in which the aldehyde substitutent attains an equatorial position, to afford the 1,4-*syn* product.

The *syn*-stereoselectivity is eroded when the steric bulk of the OPG group is reduced (PG = H, Me) (Scheme 19). It is possible that the decrease of *syn*-selectivity occurs because the *O*-inside conformer **14** is now reasonably populated due to the more closely balanced steric demands of the R and OPG substitutents.[132]

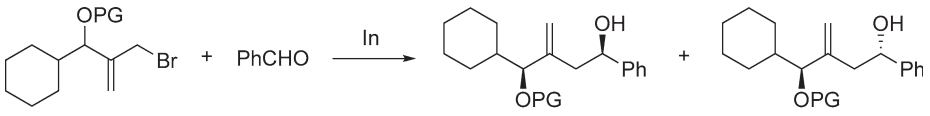
The *O*-silylated allylindium shows moderate *anti*-selectivity, via the Felkin-Anh transition state, while the hydroxy-bearing allylindium exhibits *syn*-selectivity by dual coordination of indium intramolecularly to the hydroxy group and intermolecularly to the aldehyde (Scheme 20).[133] With the CH_2OH now locked below the developing chair, the R substituent could become the key factor. The easy accessibility of the aldehyde in **15** leads to the highly preferred formation of 1,4-*syn* products relative to **16** (Scheme 21).

The chelated transition state **17**, a lower homolog of **15**, is presumably not generated during the reaction of **18** with aldehydes (Scheme 22). The approach of an aldehyde appears to disrupt the coordination between indium and the hydroxyl group as in **19**. In effect, the data suggest that the stereogenic hydroxy-substituted carbon is no longer rigidified in its conformation.

Indium-mediated reaction of 4-bromo-1,1,1-trifluoro-2-butene with aldehydes in water proceeds stereoselectively to afford the *β*-trifluoromethylated homoallylic alcohols. Aldehydes with no chelation ability shows *anti*-selectivity, whereas high *syn*-selectivity has been attained with 2-pyridinecarboxaldehyde and glyoxylic acid (Scheme 23).[134–136]

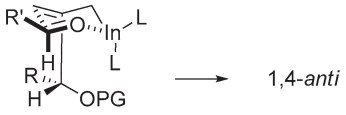


Scheme 18



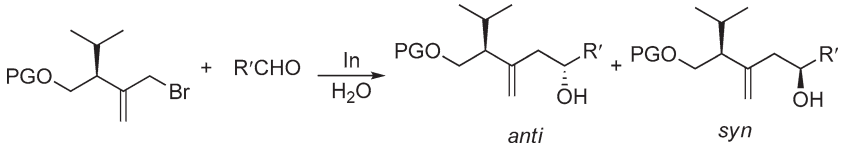
1,4-*syn* 1,4-*anti*

PG	*Solvent*	*Yield* (%)	*syn* : *anti*
TBS	H_2O	90	99 : 1
TBS	H_2O-THF (1 : 1)	81	99 : 1
H	H_2O	87	50 : 50
H	H_2O-THF (1 : 1)	91	47 : 53
Me	H_2O	76	69 : 31
Me	H_2O-THF (1 : 1)	92	83 : 17



14

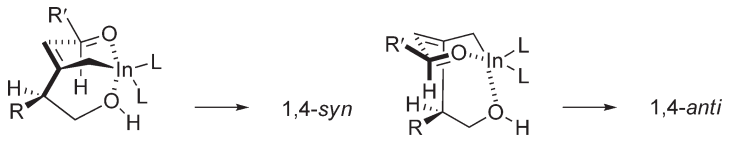
Scheme 19



anti *syn*

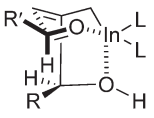
PG	*R′*	*Yield* (%)	*anti* : *syn*
TBS	Pr^i	72	76 : 24
TBS	Ph	83	76 : 24
TBS	*c*-C_6H_{11}	71	75 : 25
H	Pr^i	95	11 : 89
H	Ph	79	13 : 87
H	*c*-C_6H_{11}	91	14 : 86

Scheme 20

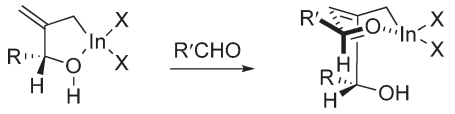


15 **16**

Scheme 21

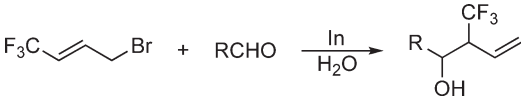


17



18 19

Scheme 22



R	*Yield* (%)(*anti* : *syn*)
Ph	87 (92 : 8)
H	86
c-C_6H_{11}	90 (>99 : <1)
3-Pyridyl	95 (>99 : <1)
2-Pyridyl	88 (<1 : >99)
CO_2H	80 (4 : 96)

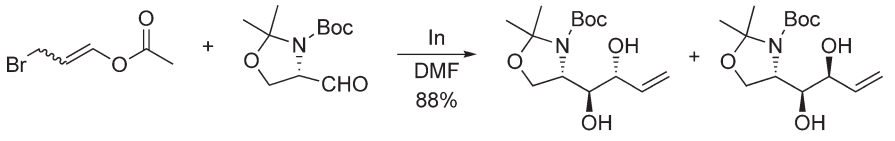
Scheme 23

Paquette *et al*. have investigated the addition of allylindium reagents to 2- and 3-pyridinecarboxaldehyde and to glyoxylic acid in order to assess the level and direction of diastereoselectivity in these coupling reactions. When 2-PyCHO is involved, the results strongly suggest that the ring nitrogen chelates to the indium atom in the aqueous environment (Scheme 24).[137,138]

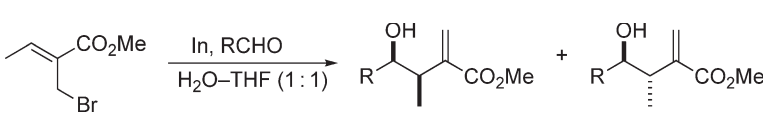
When hydroxy bromide **20** is subjected to the typical coupling conditions, neither 3- nor 2-PyCHO shows high diastereoselectivity (Scheme 25). The low-level stereochemical bias toward 3-PyCHO can be accounted for in terms of the Felkin-Anh transition states **21**. When 2-PyCHO is involved, the intramolecular chelation option **22** is favored over **23**, despite the obvious steric congestion associated with the onset of intermolecular chelation in both transition states.

Where allyl bromide **24** is concerned, 3-PyCHO exhibits higher *syn*-selectivity than the 2-isomer (Scheme 26). The appreciable *syn*-stereoinduction can be explained in terms of models **25** and **26**, where the CH_2OH group is locked below the developing chair because of strong intramolecular chelation. The erosion of *syn*-selectivity evident in the case of 2-PyCHO may originate from a competitive chelation to nitrogen.

γ-Oxygenated allylindium reacts with aldehydes at the oxygenated carbon to give *vic*-diol derivatives, where the *syn*/*anti* selectivity depends on the nature of the aldehydes.[139–143] Whereas conjugated aldehydes preferentially lead to *syn*-adducts, saturated aldehydes favor the formation of *anti*-adducts (Scheme 27). The reaction with the Garner aldehyde in DMF also shows a high-level diastereoselectivity (Equation (10)).

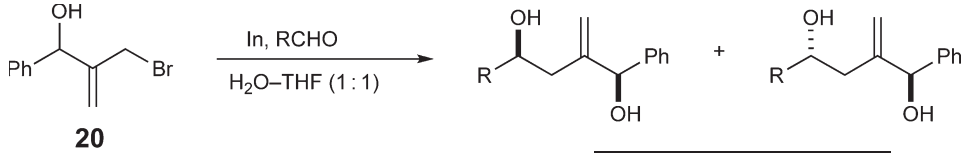


97 : 3 (10)

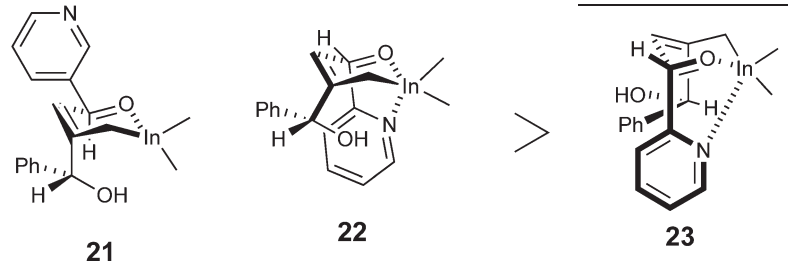


R	*Yield* (%)	*syn* : *anti*
3-Py	82	64 : 36
2-Py	74	6 : 94
CO_2Me	61	81 : 19

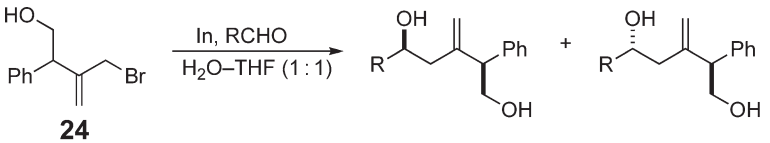
Scheme 24



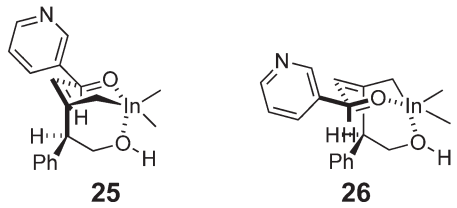
R	*Yield* (%)	*syn* : *anti*
3-Py	65	63 : 36
2-Py	63	40 : 60



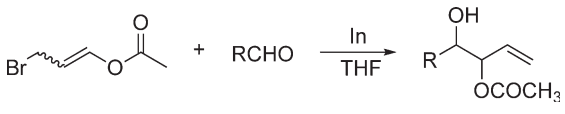
Scheme 25



R	*Yield* (%)	*syn* : *anti*
3-Py	71	80 : 20
2-Py	62	65 : 35



Scheme 26

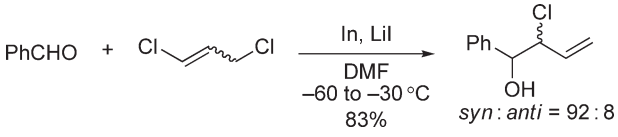


R	*Yield* (%)	*syn* : *anti*
Ph	91	85 : 15
C_6H_{11}	70	10 : 90
$PhCH_2CH_2$	95	30 : 70
Me_2CHCH_2	82	35 : 65
(*E*)-PhCH═CH	79	85 : 15
2-Furyl	72	90 : 10

Scheme 27

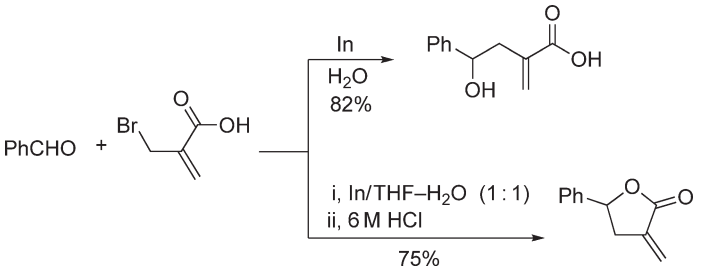
The indium-mediated reaction of 2-(bromomethyl)acrylic acid with carbonyl compounds gives the corresponding γ-hydroxy-α-methylene carboxylic acids, and α-methylene-γ-lactones are obtained after acidic workup (Scheme 28).[80,144–146] The indium-mediated addition of 4-bromocrotonic acid to a variety of aldehydes and ketones proceeds exclusively at the α-carbon of the carboxylic acid. The effect of solvent, including an ionic liquid, is minimal allowing a wide choice of conditions (Scheme 29).[61]

γ-Methoxyallylindium has been prepared by transmetallation of the corresponding γ-methoxyallyllithium with indium trichloride. This allylindium reacts with benzaldehyde to give *vic*-diol monomethyl ether, in high yields with good *syn*-selectivity, via the oxygen-chelated *Z*-configuration (Scheme 30). Similarly, 3,3- or 1,3-dichloropropene reacts with indium in the presence of LiI to generate γ-chloroallylindium, in which indium chelates intramolecularly with the chlorine atom. The reagent reacts with aldehydes to give the corresponding *syn*-chlorohydrins (Equation (11)).[147,148]

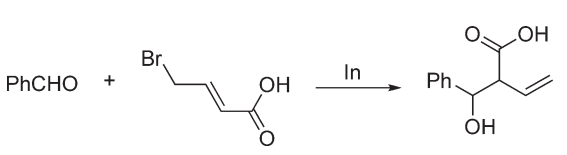


(11)

Indium trichloride-mediated addition of (*R*)-α-(methoxymethoxy)allylic stannane (>95% ee) to cyclohexanecarboxaldehyde affords the *anti*-adduct predominantly (*anti* : *syn* = 98 : 2) and stereoselectively (>95% ee) (Equation (12)). Production of a transient allylic indium reagent is postulated via a stereosepecific *anti*-S_E2' transmetallation. This α-(methoxymethoxy)allylic stannane reacts without allylic inversion, whereas the reaction of crotylstannane in Equation (5) (Section 9.14.3.3.1) proceeds with net allylic inversion. δ-Oxygenated allylic stannane also undergoes transmetallation with $InCl_3$, and *in situ* addition to α-ODPS acetaldehyde leads mainly to the *anti*-adduct, which is a potential precursor to D-(+)-altrose (Scheme 31).[149,150]

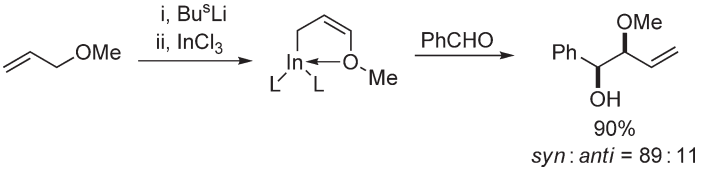


Scheme 28

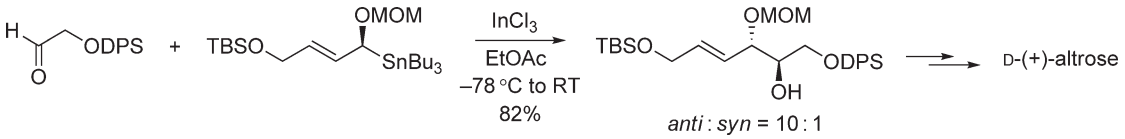


Solvent	*Yield* (%)	*syn* : *anti*
H_2O	84	54 : 46
EtOH–H_2O (20%)	98	52 : 48
[bmim][BF_4]	64	52 : 48

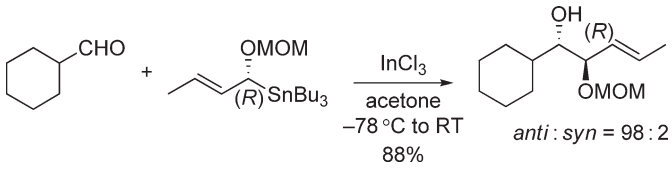
Scheme 29



Scheme 30

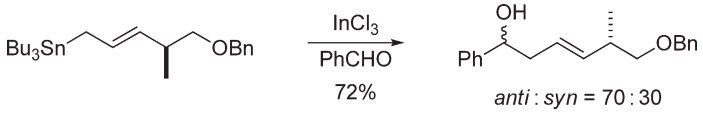


Scheme 31

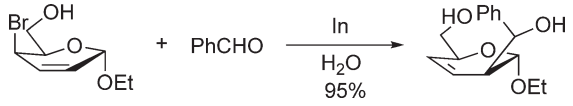


(12)

Allylindium, generated by transmetallation of 5-benzyloxy-4-methyl-2-pentenyl(tributyl)stannane, reacts with benzaldehyde leading to the 1,5-*anti*-(*E*)-stereoisomer with a useful level of 1,5-stereoinduction (Equation (13)).[151] 2-*C*-branched sugars and *C*-disaccharides are prepared diastereoselectively by the indium-mediated reaction of 4-bromo-2-enpyranoside (Equation (14)).[152]



(13)



(14)

9.14.3.3.3 Effect of the substituent adjacent to the carbonyl group

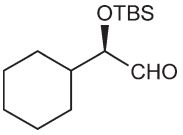
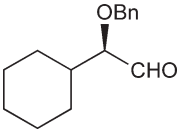
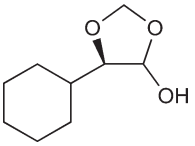
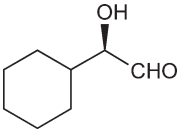
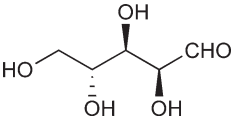
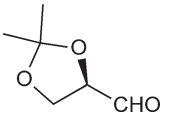
The effect of proximal groups on the diastereoselectivity in the addition of allylindium to a carbonyl group has been extensively surveyed.[153] When α- and β-hydroxy aldehydes are subjected to the allylation, excellent diastereocontrol is realized. *syn*-1,2-Diol and *anti*-1,3-diol products are formed, respectively, at accelerated rates (Tables 1 and 2). Protection of the free hydroxy group results in the alternative formation of 1,2-*anti* products. High stereoselectivities have been observed for indium-promoted allylations of α- and β-hydroxy aldehydes in aqueous media, implying that a chelate control still operates even in water.[72,73,154–158]

The sense of asymmetric induction in the α-oxygenated aldehydes, which shows a strong kinetic preference for the formation of the *syn* diol, is consistent with the classic Cram model as in **27** (Scheme 32). Once the complexation occurs, the allyl group is transferred to the carbonyl carbon from the less hindered π-face opposite to that occupied by the R group. In **28**, the chelation pathway is able to adopt a chair conformation which accommodates the favored formation of the *syn*-diol. For β-chelate reactions, the factors which influence the product formation appear to be the same. When **29** forms, the intramolecular attack occurs *syn* to the hydroxyl group. This reaction trajectory leads preferentially to the *anti*-diol, provided that a chairlike transition states such as **30** is followed.

The coupling addition of crotyl bromide to a triad of conformationally unrestricted α-oxy aldehydes in water, aqueous THF, and anhydrous THF has been examined. The proportion of *syn*-isomers reaches a maximum (*syn* : *anti* = 5.6 : 1) when the neighboring hydroxyl group is unprotected and water is the reaction medium (Scheme 33). Crotyl bromide adds to the hydroxy aldehyde with a preference for the adoption of the cyclic chelated transition states **31** and **32** (Scheme 34).

The reactions involving sulfur derivatives are minimally diastereoselective, indicating that the allylindium reagent is not thiophilic (Table 3).[159] The modest levels of diastereoselectivity observed in all the sulfur examples, which are

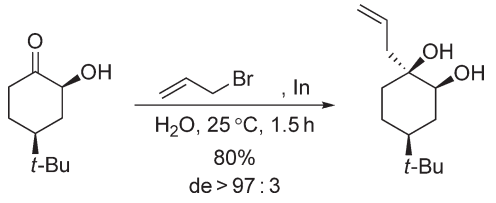
Table 1 Indium-mediated allylation of α-oxygenated aldehydes. Reproduced with permission from ACS Publications

Aldehyde	*Solvent*	*Time* (h)	*syn* : *anti*	*Yield* (%)
	H_2O	3.5	1 : 3.9	90
	H_2O–THF (1 : 1)	2.5	1 : 4.2	87
	THF	36–50	1 : 4.0	92
	H_2O	3	1 : 1.2	92
	H_2O–THF (1 : 1)	2.5	1 : 2.2	93
	THF	40–47	1 : 3.9	87
	H_2O	24–30	2.3 : 1	90–95
	H_2O–THF (1 : 1)	20–26	2.3 : 1	90–93
	THF	No reaction		
	H_2O	5	9.8 : 1	85–90
	H_2O	24–30	10.2 : 1	90
	H_2O–THF (1 : 1)	18–30	8.2 : 1	87
	H_2O–EtOH (1 : 1)	12	9.1 : 1	85
	H_2O	3.5	1 : 3.2	83
	H_2O–THF (1 : 1)	3.5	1 : 3.9	80
	THF	21–25	1 : 5.9	86
	H_2O	2.5–3.5	1 : 2	78
	H_2O–THF (1 : 1)	3.5	1 : 2	82
	THF	20–25	1 : 5.2	89

seen to be relatively insensitive to solvent environment and biased almost universally in the *anti*-direction, necessarily implicate a kinetic preference of a Felkin-Anh transition state trajectory as in **33** (Scheme 35).

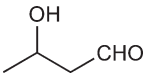
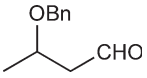
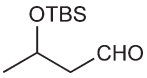
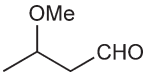
α-Hydroxy ketones and α-keto aldehydes undergo indium-mediated mono- and diallylation reactions to give respectively 1-allyl- and 1,2-diallyl-1,2-diols with high diastereoselectivity (Scheme 36).[160–163]

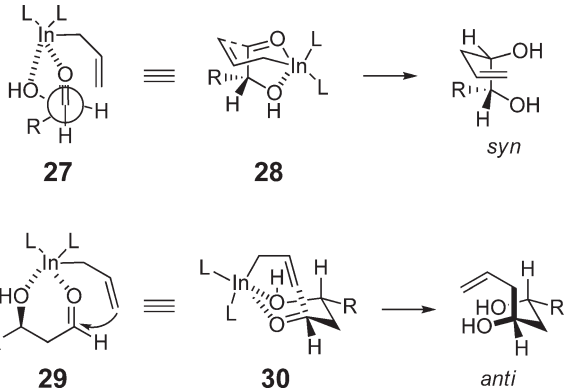
The allylation of 4-*tert*-butyl-2-hydroxycyclohexanone shows a high diastereoselectivity. When the hydroxyl substituent is oriented in the equatorial plane, kinetic acceleration accompanies exclusive entry of the allyl group from the equatorial direction (Equation (15)). The chelation in water has been revealed by competition experiments (Scheme 37).[164,165]



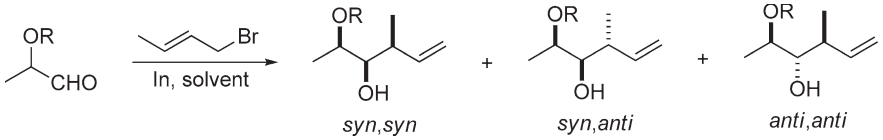
(15)

Table 2 Indium-mediated allylation of β-oxygenated aldehydes. Reproduced with permission from ACS Publications

Aldehyde	*Solvent*	*Time* (h)	*syn* : *anti*	*Yield* (%)
	H_2O	2	1 : 8.5	77
	H_2O–THF (1 : 1)	2	1 : 8.2	74
	THF	No reaction		
	H_2O	2.5	1 : 1	80
	H_2O–THF (1 : 1)	2.7	1 : 1	84
	THF	10	1 : 1	72
	H_2O	3.5	1 : 1	84
	H_2O–THF (1 : 1)	3.5	1.2 : 1	83
	THF	8.5	1.7 : 1	77
	H_2O	2.7	1 : 4	78
	H_2O–THF (1 : 1)	3	1 : 4	78
	THF	8.5	1 : 3.3	69

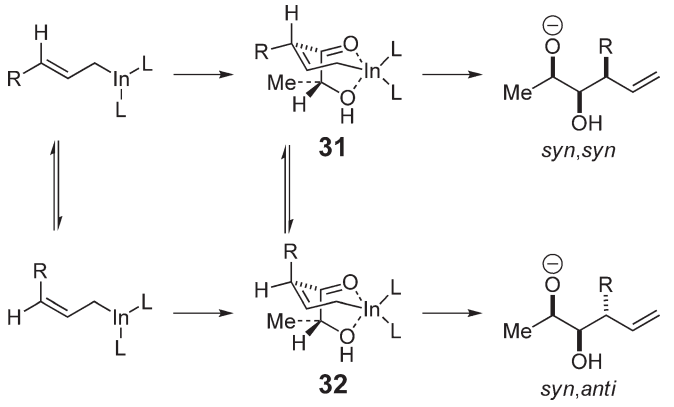


Scheme 32



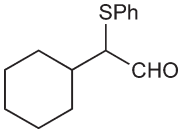
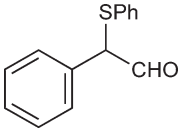
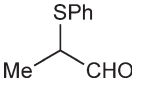
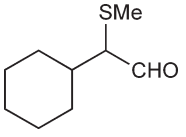
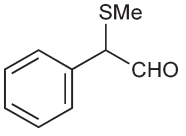
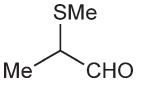
R	*Solvent*	*Yield* (%)	*syn,syn*	*syn,anti*	*anti,syn*
$PhCH_2$	H_2O	89	0.5	0.5	1
$PhCH_2$	H_2O–THF (1 : 1)	87	0.5	0.5	1
$PhCH_2$	THF	74	0.5	0.5	1
H	H_2O	79	2.8	2.8	1
H	H_2O–THF (1 : 1)	78	1.5	1.5	1
H	THF	64	2.3	2.3	1
TBS	H_2O	91	0.5	0.5	3
TBS	H_2O–THF (1 : 1)	88	0.5	0.5	3
TBS	THF	71	0.5	0.5	3

Scheme 33

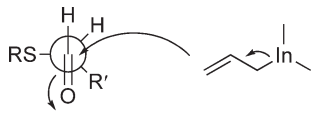


Scheme 34

Table 3 Indium-mediated allylation of α-thioaldehydes. Reproduced with permission from ACS Publications

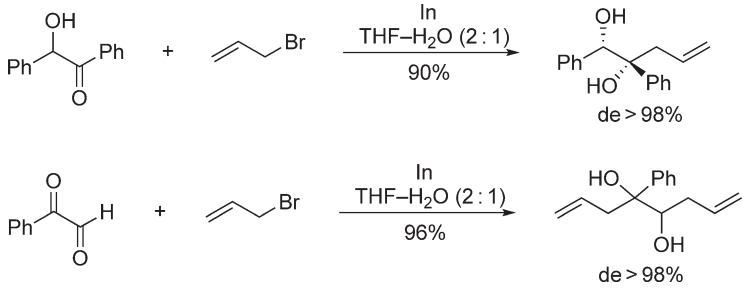
Aldehyde	*Solvent*	*Yield* (%)	*syn* : *anti*
	H_2O	89	1 : 1.4
	H_2O–THF (1 : 1)	91	1 : 1.2
	THF	82	1 : 1.5
	H_2O	89	1.5 : 1
	H_2O–THF (1 : 1)	84	1.5 : 1
	THF	73	1.3 : 1
	H_2O	82	1 : 4
	H_2O–THF (1 : 1)	87	1 : 3
	THF	70	1 : 3
	H_2O	82	1 : 1.5
	H_2O	86	1 : 2.3
	H_2O	58	1 : 1

The intrinsic differences in diastereomer production between indium and other organometallics have been observed in the allylation of α-alkoxy ketone derivatives (Scheme 38). Experiments involving the allylindium reagent as the nucleophile in aqueous solution reveal that the presence of water does not inhibit the operation of chelation control, which often exceeds that attainable with the corresponding magnesium, cerium, and chromium reagents in anhydrous media by significant margins.[166,167]

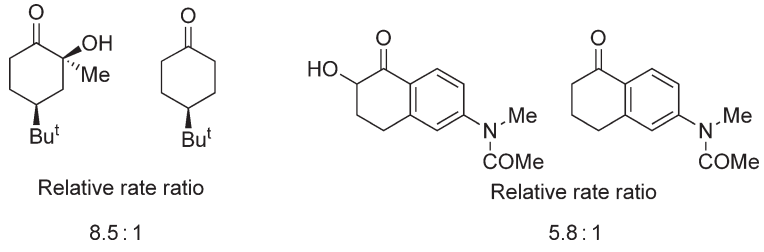


33

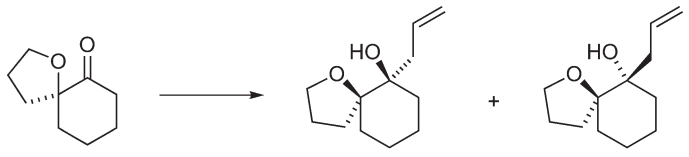
Scheme 35



Scheme 36



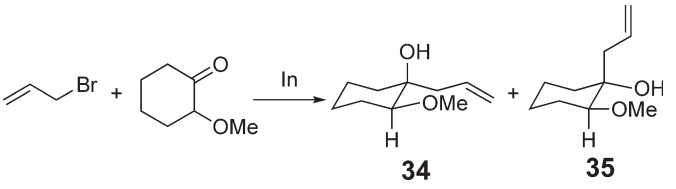
Scheme 37



CH_2=$CHCH_2MgCl$ in THF: 88% (1.2 : 1)
CH_2=$CHCH_2MgCl$, $CeCl_3$ in THF: 96% (1 : 2.4)
CH_2=$CHCH_2Br$, $CrCl_2$ in THF: 90% (1 : 2.6)
CH_2=$CHCH_2Br$, In in THF: 82% (5.6 : 1)
CH_2=$CHCH_2Br$, In in water: 81% (2.7 : 1)

Scheme 38

The effect of ionic liquid solvents on the stereochemical selectivity of allylation of 2-methoxycyclohexanone has been investigated, and found a higher selectivity (axial alcohol **34**/equatorial alcohol **35**) toward the chelation-controlled mechanism in ionic liquid than in conventional solvents such as water and THF. The use of 0.1 equiv. of indium, combined with Mn and TMSCl (2 equiv. of each), results in the isolation of the desired products in good purity, with an overall conversion of 81% (Scheme 39).[168]



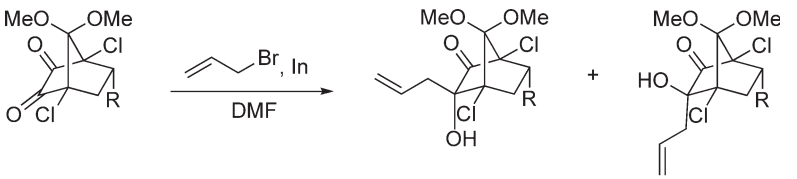
34 **35**

Conditions	*Yield* (%)	**34 : 35**
In, [bmim][BF_4] (30 °C)	83	18.6 : 1
In/Mn/TMSCl, [bmim][BF_4] (30 °C)	37 (81)[a]	6.1 : 1

[a]Conversion in parentheses.

Scheme 39

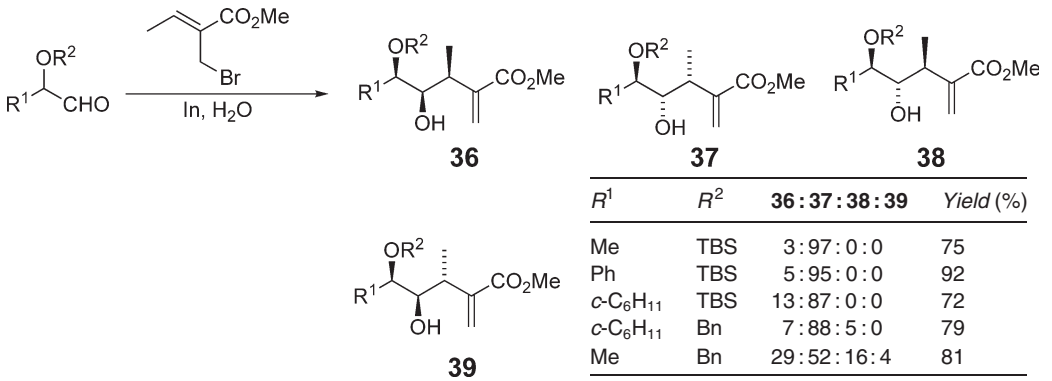
The diastereoselective allylindium addition to norbornyl α-diketones leads to acyloins. The diastereoselection in the case of monoallylation products greatly depends on the nature of 5-*endo* substituents. Non-chelating groups direct the addition from the sterically less congested *exo*-face, diagonal to the substituent, whereas chelating substituents, such as an alkoxy or acetoxy unit, induce a complete reversal in the selectivity (Equation (16)).[169]



(16)

R = OEt: 93% (14 : 86)
R = $SiMe_3$: 91% (91 : 9)

Indium-promoted addition of (*Z*)-2-(bromomethyl)-2-butenoate to α-protected hydroxy aldehydes in water results in the selective formation of diastereomer **37** of the possible four stereoisomers **36–39** via the Felkin-Anh transition state (Scheme 40).[170]

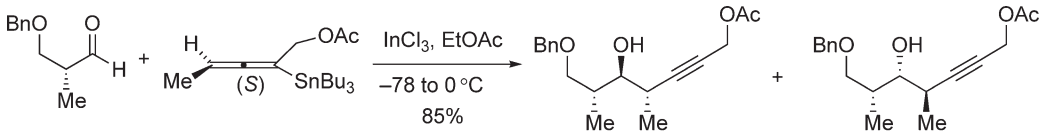


36 **37** **38** **39**

R^1	R^2	**36 : 37 : 38 : 39**	*Yield* (%)
Me	TBS	3 : 97 : 0 : 0	75
Ph	TBS	5 : 95 : 0 : 0	92
c-C_6H_{11}	TBS	13 : 87 : 0 : 0	72
c-C_6H_{11}	Bn	7 : 88 : 5 : 0	79
Me	Bn	29 : 52 : 16 : 4	81

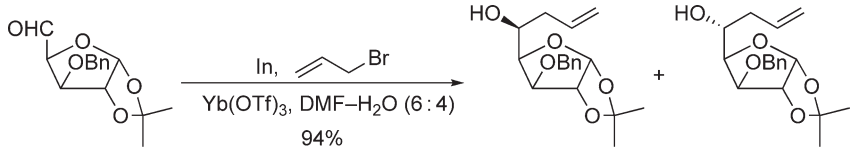
Scheme 40

Transmetallation of allenylstannane with $InCl_3$ and subsequent addition to a chiral aldehyde leads to the *anti,anti* and *anti,syn* adducts (Equation (17)).[171,172]



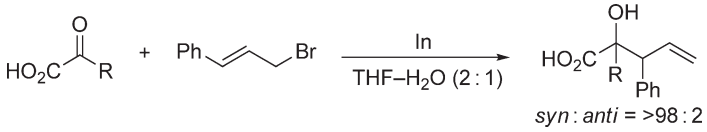
(17)

Indium-mediated allylation of the sugar derivatives in aqueous media proceeds with high *anti* diastereofacial selectivity in the presence of ytterbium triflate as a Lewis acid (Equation (18)).[173]



(18)

A β-carboxyl group on the aldehyde also influences the diastereoselection. The high diastereoselectivity observed with the γ-hydroxy lactone can be rationalized by a chelated transition state with the carboxylic acid group (Scheme 41).[174] 2-Oxocarboxylic acids also undergo diastereoselective allylation with cinnamyl bromide to provide the corresponding α-hydroxy acids as a single diastereomer (Equation (19)).[162]

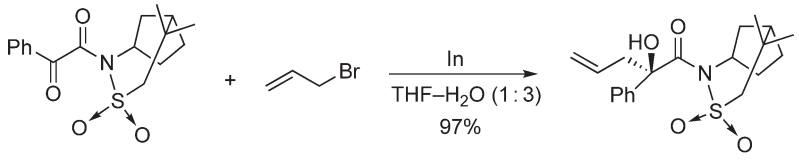


R	*Yield* (%)
H	96
Ph	95

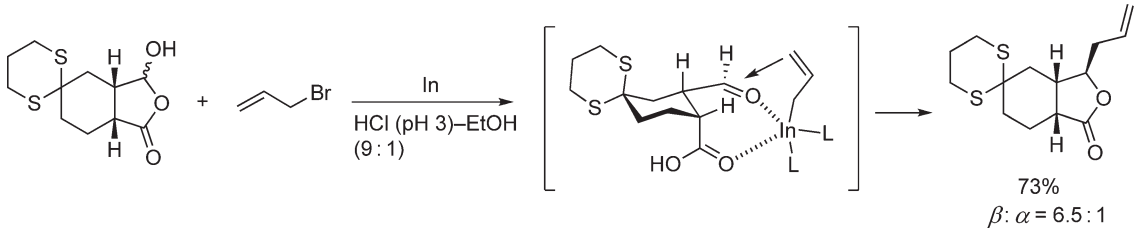
(19)

Indium-mediated allylation of α-keto-β-lactams such as 6-oxopenicillanate and 7-oxocephalospranate proceeds diastereoselectively to afford α-allyl-β-lactams in aqueous media (Scheme 42). In the cinnamylation of the monocyclic compound, the diastereofacial selectivity is directly linked to the (*R*)- or (*S*)-configuration of the exocyclic *N*-substituent (Scheme 43).[175,176–180]

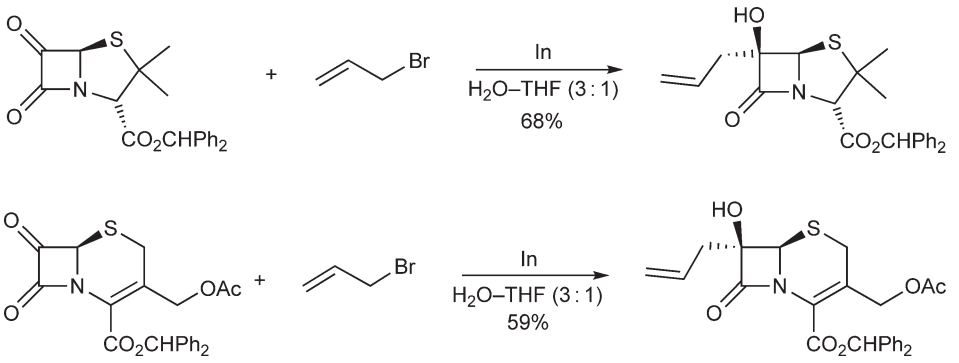
Diastereoselective allylation of α-keto imides derived from Oppolzer's sultam has been realized in aqueous THF (Equation (20)).[181]



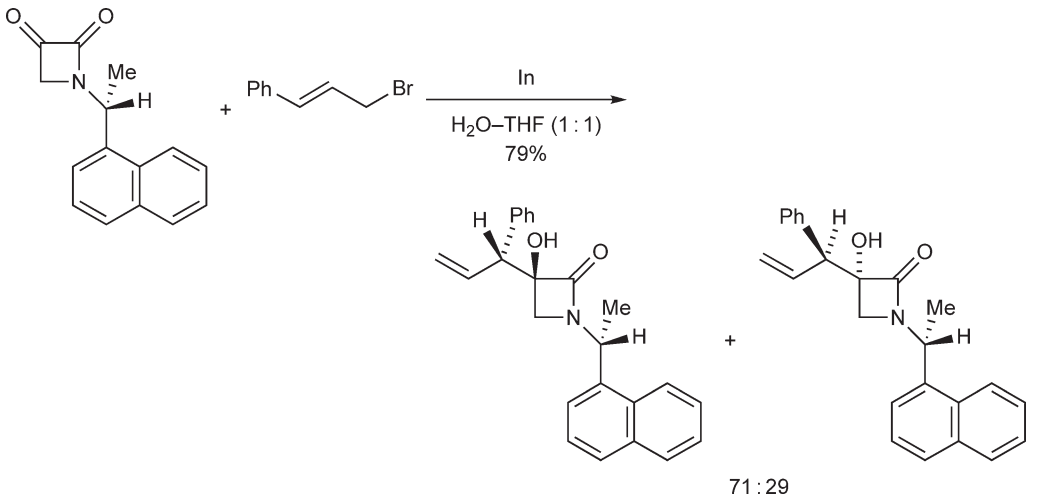
(20)



Scheme 41

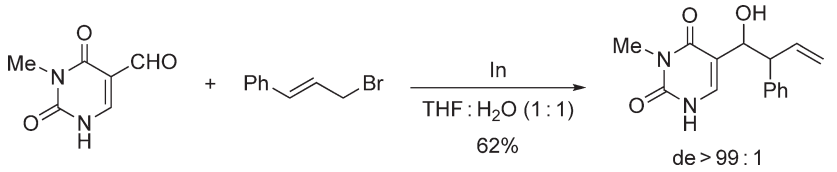


Scheme 42



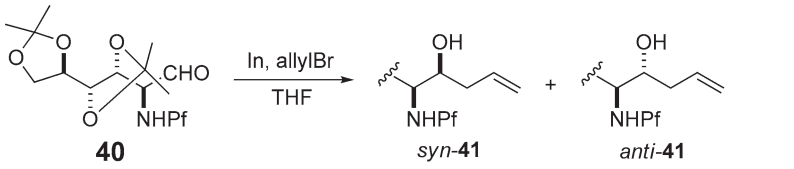
Scheme 43

The indium-mediated reaction of cinnamyl bromide with 5-formyluracil derivatives gives the corresponding homoallylic alcohols (Equation (21)). The presence of C4 carbonyl is essential for high diasteroselection owing to the complexation with indium.[182]



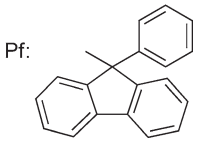
(21)

α-Amino[100,159,183–186] and α-acylamino groups[70,101] on aldehyde also lead to a good diastereoselection. When aminoaldehyde **40** is treated with allyl bromide and indium in the presence of (+)-cinchonine as a chiral promoter, *syn*-aminoalcohol **41** is formed in a 50 : 1 ratio in 87% yield (Scheme 44).[100]



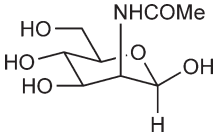
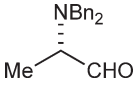
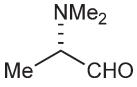
40 *syn*-**41** *anti*-**41**

Promotor	*Ratio (syn : anti)*	*Yield* (%)
(+)-Cinchonine	50 : 1	87
(−)-Cinchonidine	1 : 2	80



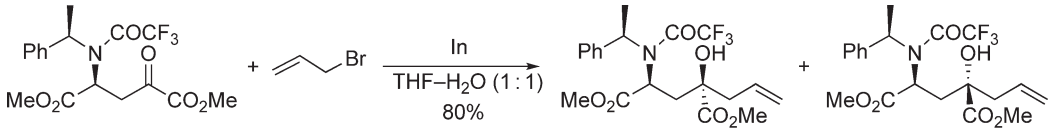
Scheme 44

Table 4 Indium-mediated allylation of α-aminoaldehydes

Substrate	*Conditions*	*Yield* (%)	*syn : anti*
	H_2O	41	3.4 : 1
	0.5 M NH_4Cl	31	8.6 : 1
	H_2O	50	1 : 3.3
	H_2O	50	>99 : 1
	H_2O (pH 7.0)	55	>99 : 1

N-acetylmannosamine undergoes a chelation-controlled reaction and leads to 90% of the *syn*-β-amino alcohol when reacted in a 0.5 M NH_4Cl solution. While a dibenzylamino substitutent of α-aminopropionaldehyde is too bulky to enter complexation, a dimethylamino group is not and leads to high levels (99%) of the *syn*-diastereomer (Table 4).[159]

β-Amino alcohols have been synthesized stereoselectively by the allylation of an α-keto ester possessing an amino substituent at the β-position (Equation (22)).[187]

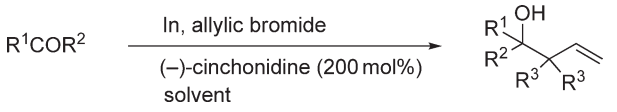


99 : 1 (22)

9.14.3.4 Enantioselective Allylation

An indium-mediated enantioselective allylation of aldehydes has been realized in dichloromethane with (−)-cinchonidine as a chiral promoter (Table 5).[188,189] The isolated yields of the homoallylic alcohol are higher in THF, whereas the enantioselectivity shows an opposite trend. It has been found that the stereoselectivity increases as the reaction temperature is increased from −78 to 25 °C. The allyl tranfer process is accelerated in the presence of an

Table 5 Enantioselective allylation of carbonyl compounds with (−)-cinchonidine as a chiral promoter. Reproduced with permission from Elsevier

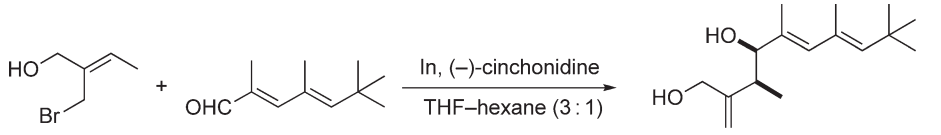


R^1COR^2	*Bromide*	*Solvent*	*Temp.* (°C)	*Additive*	*Yield* (%), *ee* (%)
$PhCOCF_3$	Allyl	THF–hexane (3 : 1)	−78		74, 57
$PhCOCF_3$	Allyl	THF–hexane (3 : 1)	25		100, 62
$PhCOCF_3$	Allyl	CH_2Cl_2–hexane (3 : 1)	−78		63, 64
$PhCOCF_3$	Allyl	CH_2Cl_2–hexane (3 : 1)	25		63, 70
$PhCOCF_3$	Allyl	CH_2Cl_2–hexane (3 : 1)	25	$EtNPr^i_2$ (20 mol%)	83, 72
PhCHO	Allyl	CH_2Cl_2–hexane (3 : 1)	25		55, 75
PhCHO	Prenyl	CH_2Cl_2–hexane (1 : 1)	25		100, 74

amine; however, no dramatic improvement of the stereoselectivity is observed. The highest enantioselectivity has been reached when a mixture of 3 : 1 CH_2Cl_2 and hexane is used. It is noted that in the absence of (−)-cinchonidine, indium does not insert into allylic bromides at room temperature.

Prenyl bromide affords better chemical yields and better enantioselectivities than allyl bromide (Table 6). The best result (99% yield, 90% (*R*) ee) is obtained when benzaldehyde is treated with prenyl bromide in the presence of (−)-cinchonidine. A similar enantioselective propargylation reaction of aldehydes with enantioselectivity up to 85% has been achieved in organic solvents by using stoichiometric amounts of (−)-cinchonidine as the chiral source (Table 7).[190]

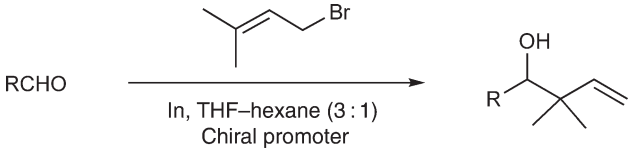
Anomalous *syn*-diastereoselectivity of indium-mediated coupling of aldehydes with bromides (*Z*)- and (*E*)-**42** has been reported (Scheme 45). The reaction affords high *syn*-selectivity (**43**/**44**) regardless of the allylic bromide geometry. Preliminary studies on the enantioselective indium-mediated allylation have been attempted and it has been found that the desired products can be obtained in moderate yield with high *syn*-selectivity and enantioselectivity (Equation (23)).[99]



(23)

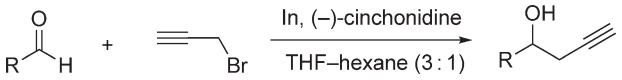
36% (85% ee, *syn* : *anti* = 99 : 1)

Table 6 Enantioselective allylation of aldehydes. Reproduced with permission from ACS Publications

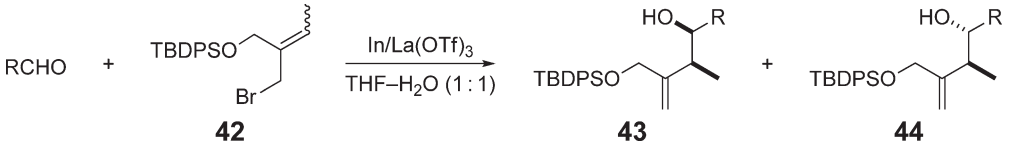


	Chiral promoter	
	(+)-*Cinchonine*	(−)-*Cinchonidine*
R	*Yield* (%), *ee* (%)	*Yield* (%), *ee* (%)
Ph	98, 76 (*S*)	99, 90 (*R*)
3-$MeOC_6H_4$	96, 62 (*S*)	95, 77 (*R*)
4-$MeOC_6H_4$	98, 29 (*S*)	97, 78 (*R*)
1-Naphthyl	91, 41 (*S*)	83, 64 (*R*)
2-Naphthyl	86, 29 (*S*)	95, 81 (*R*)
(*E*)-PhCH═CH	88, 72 (*S*)	98, 56 (*R*)
n-Octyl	87, 27 (*R*)	89, 41 (*S*)

Table 7 Enantioselective propargylation of aldehydes. Reproduced with permission from Elsevier



Aldehyde	*Yield* (%)	*ee* (%)
PhCH═CHCHO	76	36 (*S*)
PhC≡CCHO	74	55
$Ph(CH_2)_2CHO$	63	56
$C_8H_{17}CHO$	70	68
PhC≡CCHO	71	72 (*R*)
c-$C_6H_{11}CHO$	72	76
Cl_3CCHO	49	84
$CF_3C(OH)OEt$	52	85

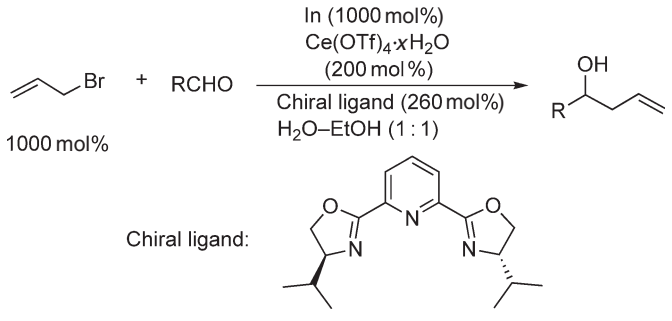


	(*Z*)-**42**		(*E*)-**42**	
R	*Yield* (%)	**43 : 44**	*Yield* (%)	**43 : 44**
Ph	91	>99 : 1	87	91 : 9
(*E*)-PhCH═CH	89	88 : 12	85	83 : 17
c-C_6H_{11}	86	87 : 13	85	87 : 13

Scheme 45

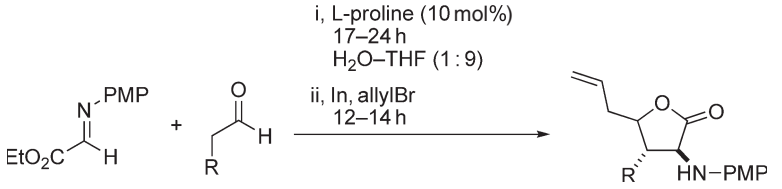
By using (*S*,*S*)-2,6-bis(4-isopropyl-2-oxazolin-2-ly)pyridine as a chiral source, high enantioselectivity (up to 92% ee) has been attained in an aqueous medium H_2O–EtOH (1 : 1) (Scheme 46).[191] Changing to other mixed solvents leads to lower selectivities (72% ee in H_2O–MeCN (1 : 1), 76% ee H_2O–THF (1 : 1), and 66% ee in H_2O–EtOH (1 : 9)). The reaction of allyl iodide in place of allyl bromide decreases the selectivity from 92% to 76% ee.

A one-pot Mannich/indium-promoted allylation sequence affords highly functionalized lactones with 73% and >99% ee as a mixture of two diastereomers. There is no significant asymmetric induction for the allylation step (Equation (24)).[192]



RCHO	*Yield* (%)	*ee* (%)
Benzaldehyde	90	92 (*R*)
3-Methoxy benzaldehyde	83	52 (*R*)
1-Naphthaldehyde	91	56 (*R*)
2-Naphthaldehyde	98	66 (*R*)
(*E*)-cinnamaldehyde	72	51 (*R*)
Hexanal	94	34 (*S*)

Scheme 46



(24)

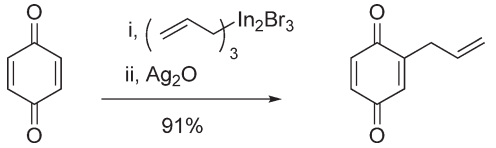
R	*Yield* (%)	*dr*	*ee* (%)[a]
i-Pr	64	2 : 1	73
$Me(CH_2)_4CH{=}CHCH_2$	77	1 : 1	>99

[a]Major isomer.

9.14.3.5 Other Carbonyl Allylation Reactions

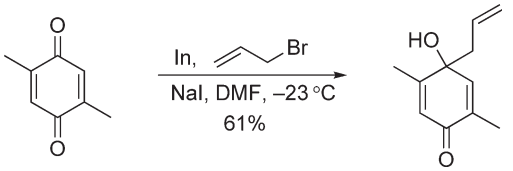
9.14.3.5.1 Allylation of quinones and dicarbonyl compounds

Reactions of unsubstituted *p*-benzoquinone with allylindium, prenylindium, and geranylindium reagents give, after oxidation with silver oxide, the corresponding allylated quinones in good yields (Equation (25)). These reactions are considered to proceed via 1,2-addition of the allylic indium reagents at the γ-carbon followed by [3,3]-sigmatropic rearrangement. Substituted quinones react with allylindium giving excellent yields of allylquinols, whereas with prenylindium and geranylindium, trisubstituted quinones give prenylcyclohexene-1,4-diones in high yields and 2,3-disubstituted quinones give mixtures of prenylhydroquinones and diprenylcyclohexene-1,4-diones (Scheme 47). In the prenylation of haloquinones, l,2-addition, [3,3] sigmatropic rearrangement, and elimination of indium(III) halide occur in sequence yielding prenylquinones. 2-Hydroxy- and 2-methoxy-1,4-naphthoquinones give α-addition products with prenylindium and cinnamylindium reagents.[193]

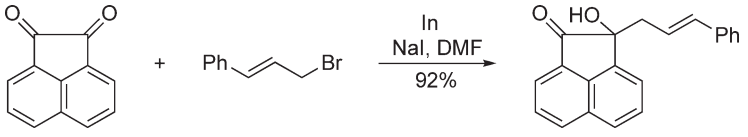


(25)

Pan *et al.* reported similar reactions of *p*-quinones to 4-allyl-4-hydroxycyclohexa-2,5-dienone derivatives (Equation (26)).[194] Unsymmetrical quinones show high selectivity in the addition of allylindium reagents to the carbonyl group. Indium-mediated allylation of 1,2-diones occurs via a γ-coupling fashion to yield α-hydroxy keto compounds. In some cases of cinnamylation, the corresponding α-coupling products are obtained (Equation (27)).[195,196]

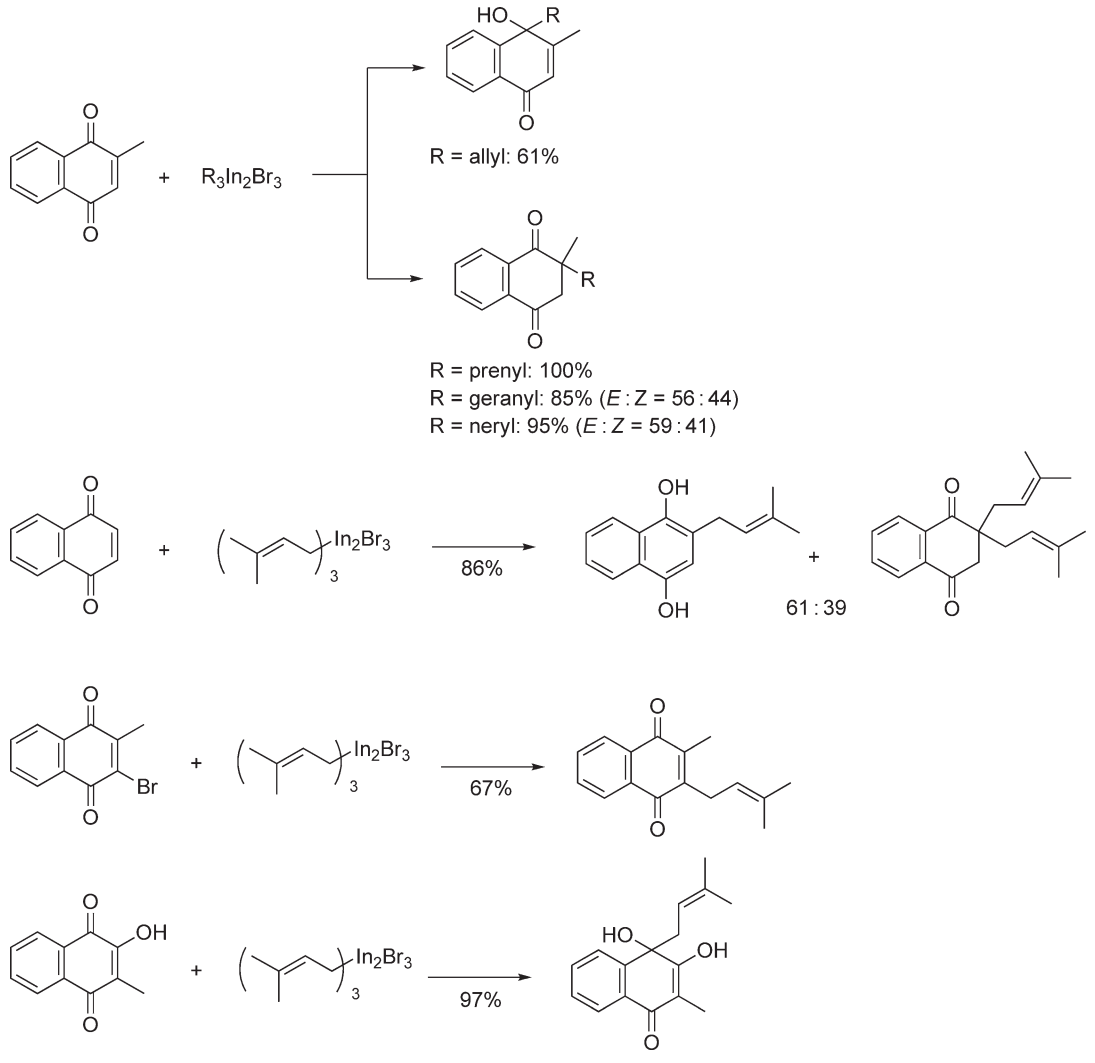


(26)

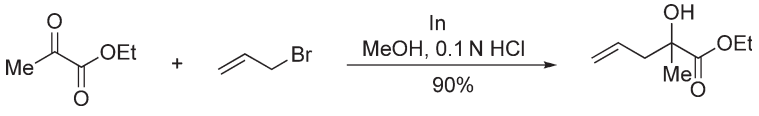


(27)

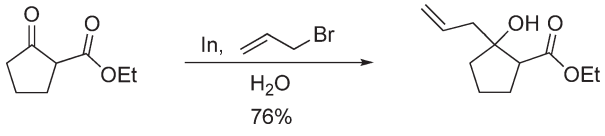
The coupling reaction of α-keto esters with allyl, propargyl, and allenyl halides using indium metal in aqueous solvents affords α-hydroxy-γ,δ-unsaturated esters (Equation (28)).[197,198] 1,3-Dicarbonyl compounds undergo efficient carbonyl allylation reactions in an aqueous medium through a Barbier-type reaction (Equation (29)). The reaction is general and a variety of 1,3-dicarbonyls has been alkylated using allyl bromide or allyl chloride in conjunction with indium.[199]



Scheme 47

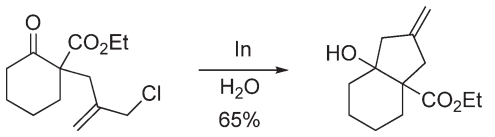


(28)

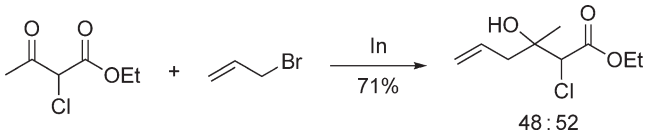


(29)

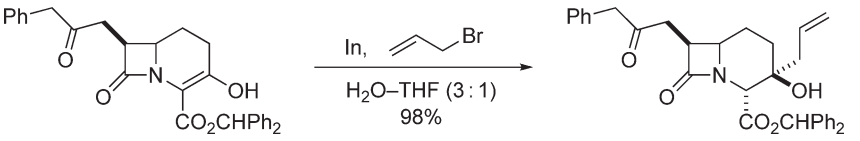
Sequential nucleophilic and electrophilic alkylations of 1,3-dicarbonyl compounds with a trimethylenemethane zwitterion equivalent lead to [3 + 2]-annulation. The nucleophilic carbonyl alkylation step has been carried out via an indium-mediated allylation in water (Equation (30)).[200] Indium-mediated allylation of α-chlorocarbonyl compounds with allyl bromides in aqueous media gives the corresponding homoallylic chlorohydrins, which can be transformed to allyloxiranes (Equation (31)).[201] Allylation of the C3 position of the cephem nucleus has been accomplished by indium-mediated allylation reaction in aqueous media (Equation (32)).[202]



(30)



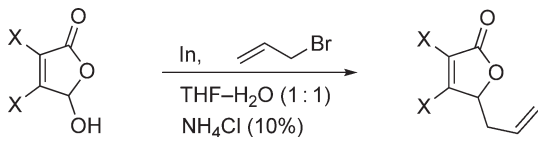
(31)



(32)

Indium-mediated allylation of cyclic and acyclic acid anhydrides gives *gem*-diallyl esters.[203,204] Examples are shown in Scheme 48; the allylation of succinic anhydride or phthalic anhydride with allyl bromide in DMF in the presence of indium metal results in the formation of diallylbutenolides or diallylphthalides. In contrast, monoallylated hydroxy esters are formed exclusively with γ-substituted allylic halides.

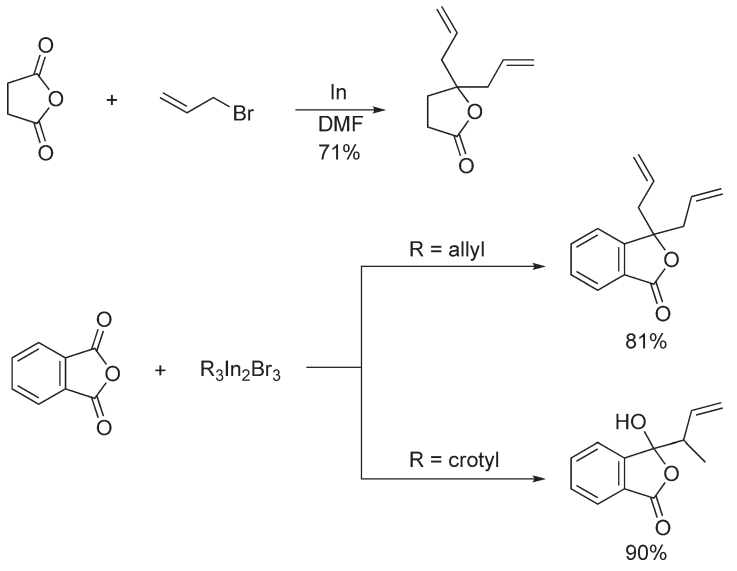
Mucohalic acids (3,4-dichloro- and 3,4-dibromo-5-hydroxy-5*H*-furan-2-one) are used as aldehydes in indium-mediated Barbier-type allylation. γ-Allylic α,β-unsaturated γ-butyrolactones are obtained in good yields (Equation (33)).[205]



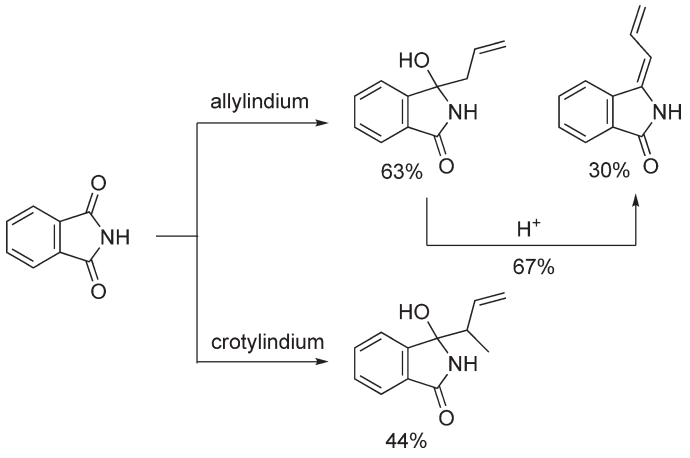
X	*Yield* (%)
Cl	90
Br	70

(33)

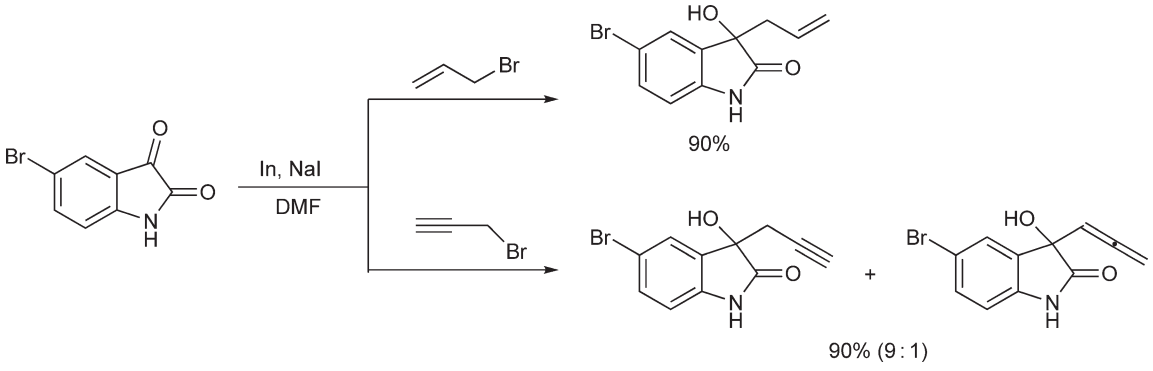
The coupling reaction of allylindium reagents with cyclic imides gives diverse products depending on the structure of both the substrates and the reagents (Scheme 49).[206]



Scheme 48

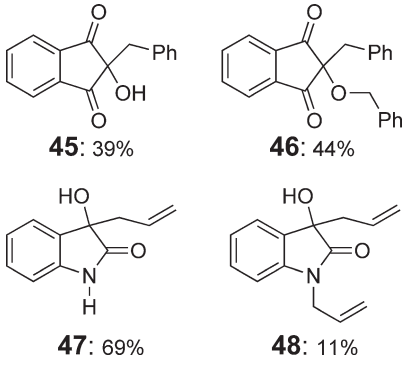


Scheme 49

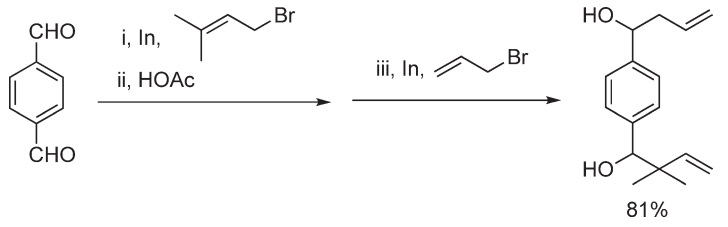


Scheme 50

When reacted with allyl/propargyl bromide in the presence of indium and sodium iodide, isatins undergo efficient allylation/propargylation to afford the corresponding 3-substituted 3-hydroxy-oxindoles (Scheme 50).[206] Indium-mediated Barbier reaction of ninhydrin with benzyl bromide in DMF gives **45** and *O*-benzylated compound **46**. Similarly, the reaction of isatin with allyl bromide affords **47** and **48**.[207]



One-pot sequential double nucleophilic attacks using two different nucleophiles to a molecule having identical functionalities have been established via indium-mediated allylation involving an HOAc quenching after the first allylation (Scheme 51).[208]



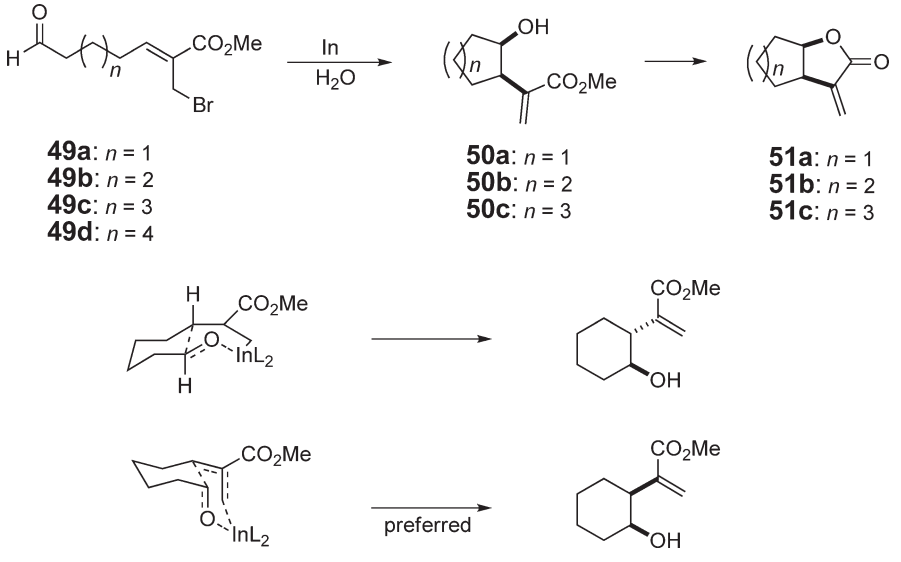
Scheme 51

9.14.3.5.2 Cyclization via intramolecular allylation

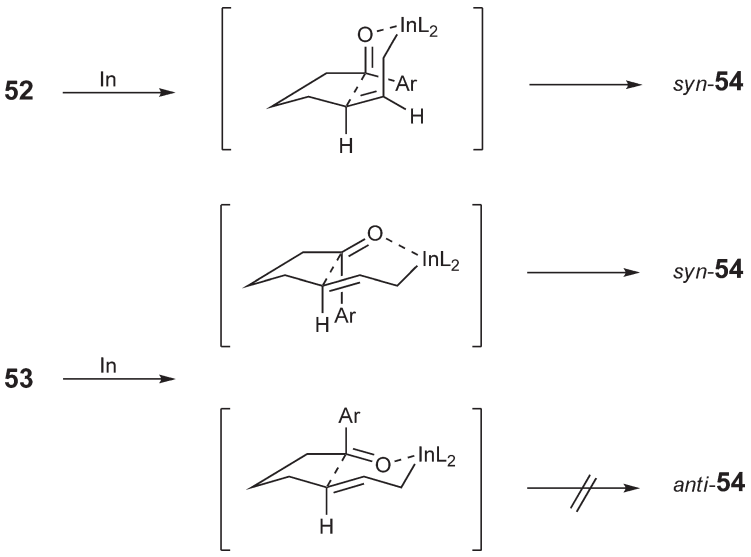
Several indium-mediated intramolecular carbonyl allylation reactions have been investigated, and it has been found that these reactions provide an easy access to a variety of cyclic compounds. The intramolecular cyclization of **49a–c** mediated by indium in aqueous media proceeds smoothly to afford carbocyclic systems containing γ-hydroxy-α-methylene esters **50a–c**, which either spontaneously or readily cyclize to give fused α-methylene-γ-butyrolactones **51a–c** (Scheme 52). The same cyclization of **49d** is too slow to compete with the side-reaction, in which the bromide is substituted by a hydroxy group. The ring junction stereochemistry of fused lactones **51** has been found to be *cis* in all cases. Of the two possible transition states, the one leading to the *cis*-fused compounds is preferred, because the chair–chair conformation is favored over the chair–boat conformation.[209]

The indium-promoted intramolecular cyclization of *p*-substituted (*Z*)- **52** and (*E*)-7-bromo-5-heptenophenones **53** in aqueous THF gives *syn*-2-vinylcyclopentanol **54** irrespective of the double-bond geometry in the starting material. These results suggest that the indium-mediated reactions involve intramolecularly coordinated transition states, where the development of a *cis* 5/6-bicyclic framework is most energetically feasible (Scheme 53).[210]

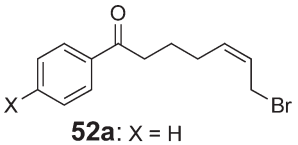
Indium-promoted cyclization of **55** affords 2-vinylcyclohexanol **56** in 32% yield as a single stereoisomer. The configuration has tentatively been assigned as *trans* (Equation (34)).[211] The intramolecular allylation of **57** gives chromane **58** as a mixture of *cis*- and *trans*- isomers (Equation (35)).[212]



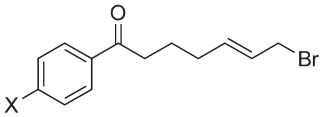
Scheme 52



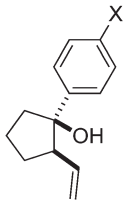
Scheme 53



52a: X = H
52b: X = OMe
52c: X = SMe
52d: X = CF_3
52e: X = F
52f: X = SO_2Me

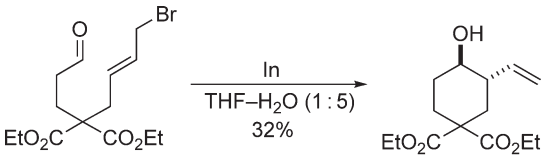


53a: X = H
53b: X = OMe
53c: X = F

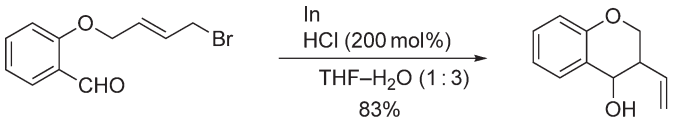


syn : *anti* = >98 : 2

54a: 70% (from **52a**), 82% (from **53a**)
54b: 73% (from **52a**), 70% (from **53a**)
54c: 67%
54d: 79%
54e: 87% (from **52a**), 86% (from **53a**)
54f: 38%



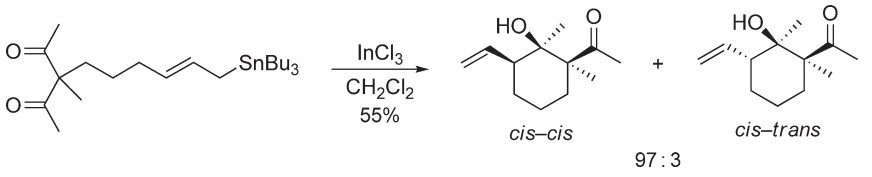
55 **56** (34)



57 **58** (35)

cis : *trans* = 2 : 1

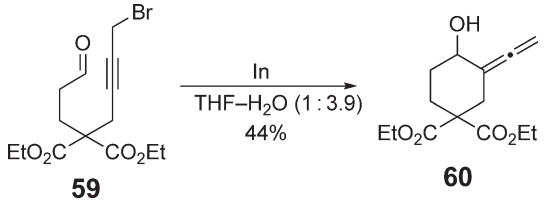
Indium trichloride mediates the intramolecular cyclization of the prochiral allylstannyl diketone to afford the desymmetrized *cis–cis* cyclohexanol predominantly (Equation (36)). The use of $TiCl_4$ in place of $InCl_3$ gives the *cis–trans* diastereomer.[213]



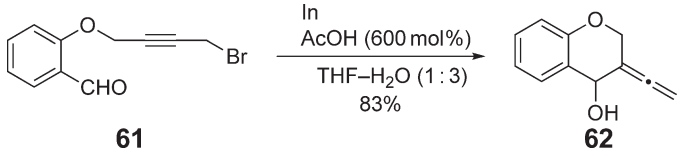
(36)

One- and two-atom carbocycle enlargements have been accomplished via indium-induced Barbier-type reaction in water as shown in Scheme 54.[214–216]

The indium-mediated cyclization of acetylenic aldehyde **59** affords the corresponding ethenylidenecyclohexanol derivative **60** in 44% yield (Equation (37)).[217] A similar intramolecular allenylation of **61** prompted by indium in aqueous THF produces chromane **62** in good yield (Equation (38)).



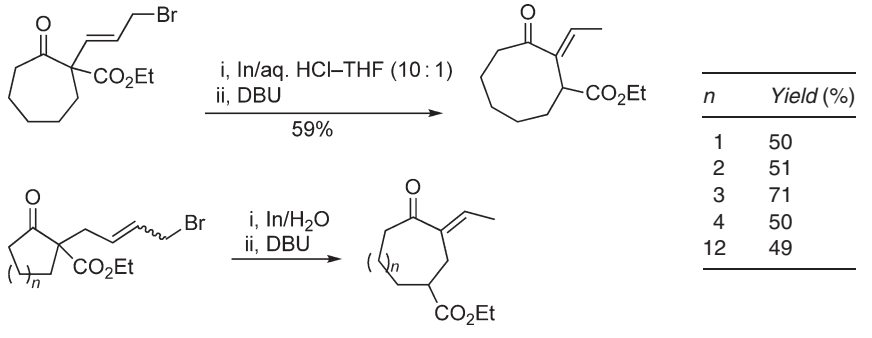
(37)



(38)

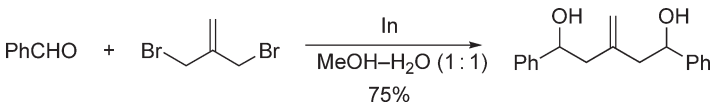
9.14.3.5.3 Reactions of allylindium derived from allylic dihalo compounds

By the action of indium, various allylic or propargylic dihalo compounds can be converted to the respective dianion equivalents. In some cases, the reaction with electrophiles proceeds stepwise, whereas in other cases novel diindium reagents are involved. Via an indium-mediated Barbier-type reaction in an aqueous medium, carbonyl compounds react with a trimethylenemethane dianion equivalent to give the corresponding diols (Equation (39)).[218]



n	*Yield* (%)
1	50
2	51
3	71
4	50
12	49

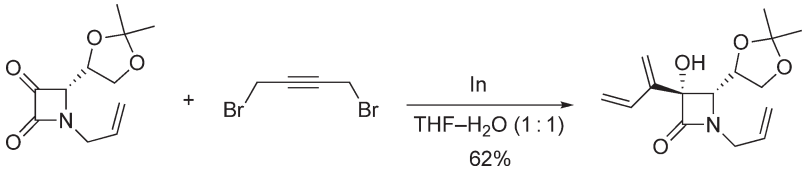
Scheme 54



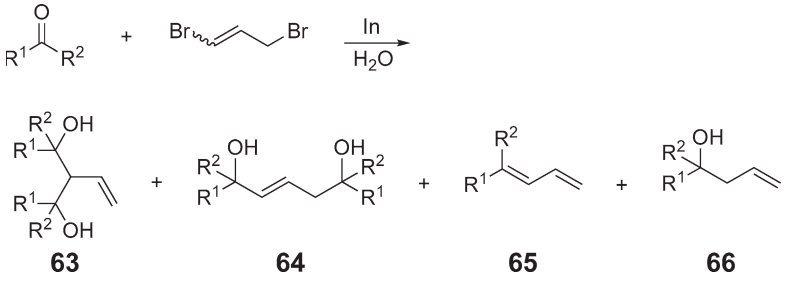
(39)

The reaction of 1,3-dibromopropene with carbonyl compounds mediated by indium in water gives 3,3-disubstituted propene **63** (Scheme 55). In the formation of **63**, 1,3-dibromopropene acts as a *gem*-allyl dianion synthon. Aromatic aldehydes generally have a higher selectivity than aliphatic ones in the product formation. Unsubstituted and electron-withdrawing group-substituted benzaldehydes give mainly 3,3-disubstituted propene **63**. For electron-rich benzaldehydes, the formation of both 3,3- **63** and 1,3-disubstituted propene **64** is dramatically decreased and the selectivity is reversed completely to give diene **65** and homoallylic alcohol **66**.[219]

Indium-promoted reaction of 1,4-dibromo-2-butyne with carbonyl compounds gives 1,3-butadiene derivatives via the allenic indium intermediates (Scheme 56).[220] Similar indium-mediated 1,3-butadien-2-ylation reactions of optically pure azetidine-2,3-diones have been investigated in aqueous media, offering a convenient asymmetric entry to the 3-substituted 3-hydroxy-β-lactam moiety (Equation (40)). The diastereoselectivity of the addition reaction is controlled by the bulky chiral auxiliary at C4.[221,222]

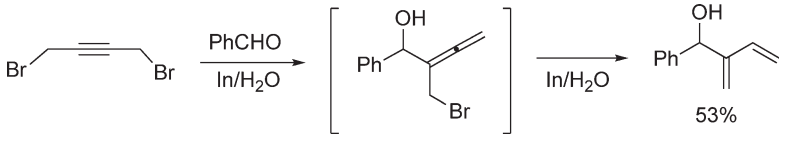


(40)

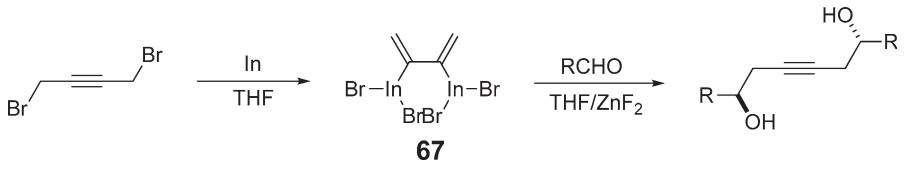


	Product (*isolated yield*, %)			
Substrate	**63**	**64**	**65**	**66**
PhCHO	54	8	7	22
p-$HO_2CC_6H_4CHO$	50	NI	13	17
n-$C_6H_{13}CHO$	31	17	22	21
Me_3CCHO	0	11	NI	10
p-MeC_6H_4CHO	23	2	32	32
p-$HOCH_2C_6H_4CHO$	11	NI	29	51
p-$MeOC_6H_4CHO$	4	0	30	55

Scheme 55



Scheme 56



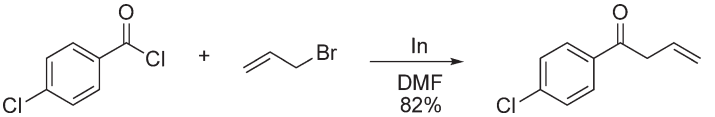
R	*Yield* (%)
n-C_5H_{11}	80
Ph	75
c-C_6H_{11}	73
2-Furyl	89

Scheme 57

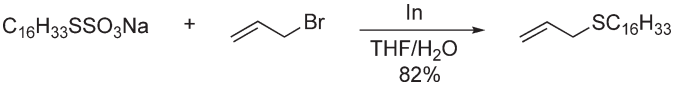
A stable diindium compound, 2,3-butadienyldiindium tetrabromide **67**, is prepared by the reaction of 1,4-dibromo-2-butyne and indium. The reaction between **67** and different carbonyl compounds in the presence of zinc fluoride gives acetyenic diol almost exclusively as a single diastereomer (Scheme 57).[223]

9.14.3.5.4 Reactions with acid halides and related compounds

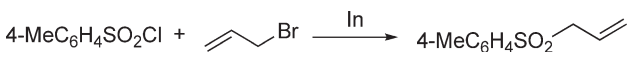
Allyl ketones have been prepared from acid chlorides, allyl bromide, and indium in DMF (Equation (41)).[224] Allylic bromides react with sodium alkyl thiosulfates in the presence of indium in aqueous THF to give allyl sulfides (Equation (42)).[225] Indium-mediated coupling of allyl bromide with aromatic sulfonyl chloride gives the corresponding allylsulfones in aqueous media (Equation (43)).[226] Indium mediates coupling of allylic bromides with acyloyl imidazoles in aqueous media to give the corresponding tertiary alcohols, whereas acyloyl pyrazoles afford allylic ketones selectively (Scheme 58).[227] Indium-mediated allylation of acyl cyanides with allyl halides in aqueous media affords a variety of allylketones (Equation (44)).[228] The reaction of acyl cyanides with propargyl bromides occurs regioselectively under mild conditions to afford either allenic or propargylic ketones depending on the γ-substituent of the propargyl bromides (Equation (45)).[229] Indium is effective in the reaction of 2-pyridyl esters with allyl bromide or iodide in pure water (Equation (46)).[230]



(41)

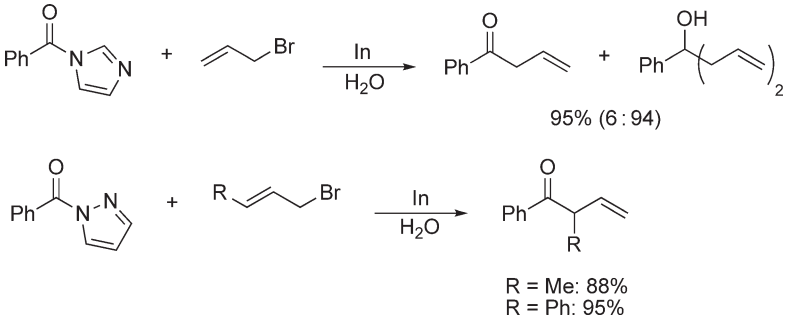


(42)

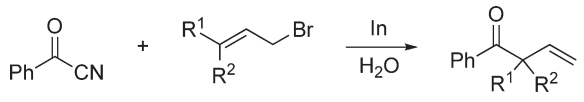


Solvent	*t* (h)	*T* (°C)	*Yield* (%)
H_2O	4	0	67
THF	36	25	45

(43)

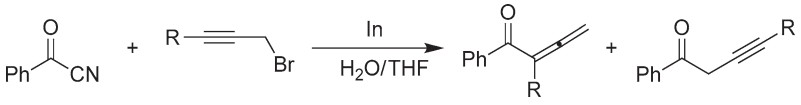


Scheme 58



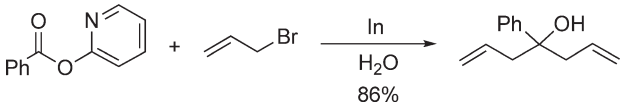
$R^1 = R^2 = H$: 86%
$R^1 = Me$, $R^2 = H$: 75%
$R^1 = R^2 = Me$: 73%

(44)



R	Yield (%)	
H	69	0
Me	0	73
Ph	0	83

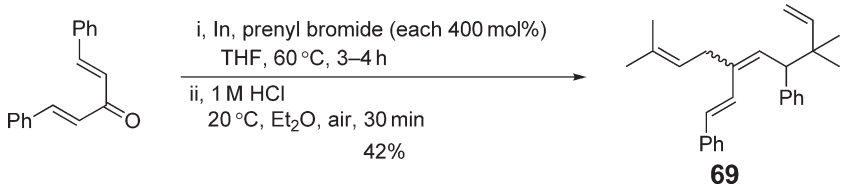
(45)



(46)

9.14.3.5.5 Miscellaneous carbonyl allylation reactions

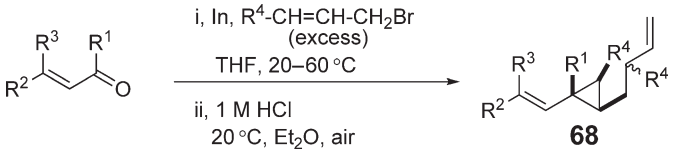
Allylindium reagents, prepared from excess allylic halides (Br or I) with indium metal, react with α,β-unsaturated ketones and aldehydes to give, after an aerobic acidic workup, homoallyl-substituted vinylcyclopropanes (Table 8). In this transformation, the indium-mediated deoxygenation process delivers two allyl units to α,β-unsaturated ketones.[231–234] 1,1-$[D]_2$-allyl bromide reacts with dibenzylidenacetone to give $[D]_4$-**68** in 78% yield as a mixture of four regio-isotopomers in approximately equal ratio. In contrast, the reaction of crotylindium affords essentially a single regioisomer with greater than 95% regioselectivity. When the steric demands of ring formation are increased from crotyl to prenyl, the terpene-like product **69** is obtained as a mixture of *cis*- and *trans*-isomers (1.0 : 1.2) (Equation (47)).



69

(47)

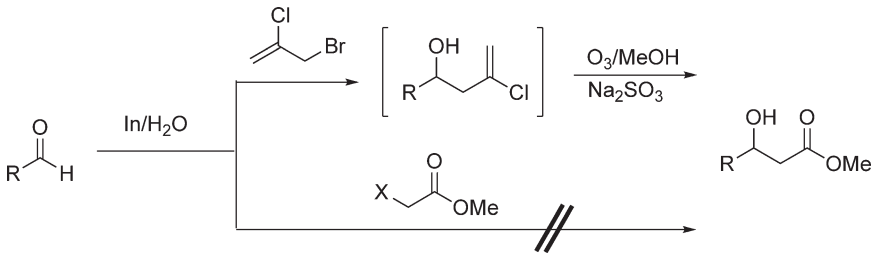
Table 8 Synthesis of vinylcyclopropanes. Reproduced with permission from Wiles



68

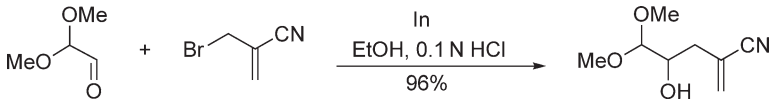
R^1	R^2	R^3	R^4	dr[a]	Yield (%)
(*E*)-stylyl	Ph	H	H		83
(*E*)-*p*-MeO-stylyl	*p*-$MeOC_6H_4$	H	H		60
(*E*)-*p*-Cl-stylyl	*p*-ClC_6H_4	H	H		79
$CH{=}CMe_2$	Me	Me	H		92
Me	Ph	H	H	1 : 1	78
CH_2-R^3	H	–CH_2–	H	4 : 1	49
H	Ph	H	H	2 : 1	52
(*E*)-stylyl	Ph	H	Me	81 : 19[b]	79
$CH{=}CMe_2$	Me	Me	Me	88 : 12[b]	53

[a]For structure of the major diastereomer.
[b]Ratio of the two major *cis*-isomers [at C2-C3] to the two minor *trans*-isomers.



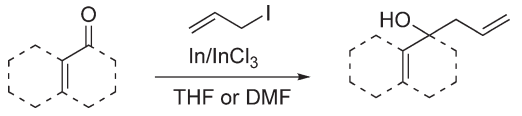
Scheme 59

Indium-mediated Barbier-type reaction of glyoxal monoacetal with bromomethyl acrylonitrile or bromomethyl-acrylate gives a masked α-hydroxy aldehyde (Equation (48)).[91] The reaction of 3-bromo-2-chloro-1-propene, an aldehyde, and indium in water gives the corresponding homoallyl alcohol, which upon ozonolysis in methanol furnishes a β-hydroxy ester. The overall reaction is equivalent to the Reformatsky reaction, which cannot be realized by a direct indium-mediated reaction of an α-halo ester with an aldehyde in water (Scheme 59).[235]

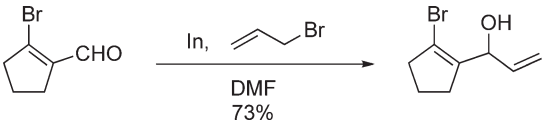


(48)

The 1,2-addition of allyl iodide to cyclic and acyclic α,β-unsaturated carbonyl compounds has been achieved by using indium and indium trichloride. The reactivities of α,β-unsaturated carbonyl compounds depend upon their structure. The reaction of ketones smoothly undergoes in THF or DMF. In the case of cyclic ketones, however, the solvent plays a crucial role, where much improved yields have been obtained in DMF than in THF (Equation (49)).[236] Indium-mediated 1,2-allylation of β-bromoacrolein produces homoallylic alcohol derivatives (Equation (50)), which can be transformed to cyclopentanones by a Pd-catalyzed cyclization.[237,238]

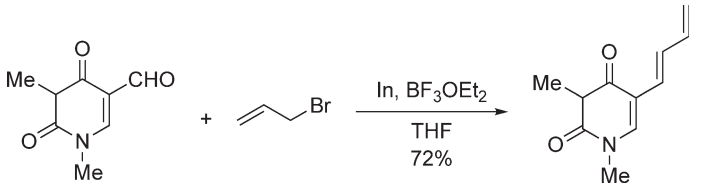


(49)



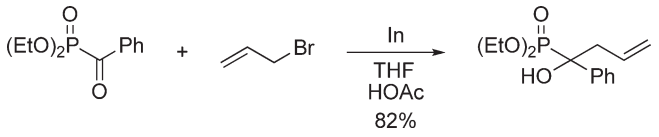
(50)

5-Formyluracils and 4-formylpyrazoles undergo smooth olefinations in THF with indium metal (0.8 equiv.), $BF_3{\cdot}OEt_2$ (1 equiv.), and allyl bromide (1 equiv.) providing the respective diene-substituted heterocycles in a single step (Equation (51)).[239]

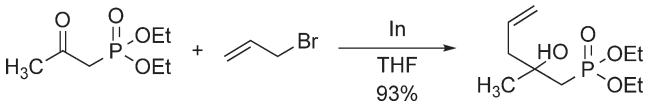


(51)

Treatment of acyl phosphates with allylindium reagents in the presence of acetic acid affords the corresponding α-hydroxy phosphonates in good yields under mild conditions (Equation (52)).[240] β-Keto phosphonates give the corresponding β-hydroxy phosphonates in good yields by indium-mediated allylations (Equation (53)).[241]



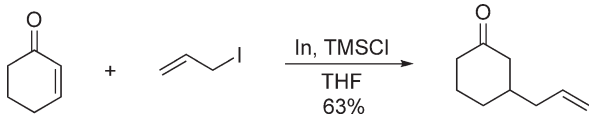
(52)



(53)

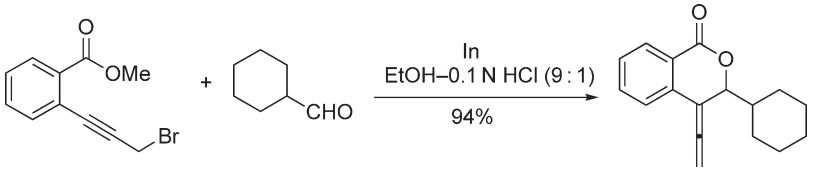
Indium-mediated allylation of trialkyl(difluoroacetyl)silane **70** in aqueous media gives homoallylic alcohol **71** exclusively (Scheme 60). Both water and THF are essential for the allylation reaction. It is worth noting that homoallylic alcohol **71** is formed exclusively under these reaction conditions. On the contrary, enol silyl ether **72** is a major product of the fluorinated acylsilanes reaction with other organometallic compounds than indium via a Brook rearrangement and defluorination.[242,243] Indium-mediated allylsilylation of carbonyl compounds provides a facile route to 2-(hydroxyethyl)allylsilanes. The allene homologs are similarly prepared (Scheme 61).[244,244a]

In the presence of chlorotrimethylsilane, allylindium adds to cyclohexenone to give the Michael adduct in 63% (Equation (54)).[245]



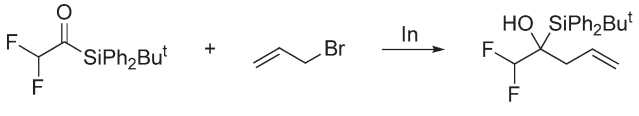
(54)

The allene aryl δ-lactones have conveniently been synthesized via the indium-mediated reaction of aldehydes with (*o*-methoxycarbonylaryl)propargyl bromide in aqueous ethanol (Equation (55)).[246] Indium-mediated ultrasonication reaction between aldehydes and 1-bromo-2-butyne gives 1-substituted (*E*)-2,5-dimethyl-2,5,6-heptatrien-1-ols in moderate to good yields (Scheme 62).[247]



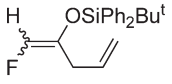
(55)

1-Alkylindole-3-carboxaldehyde **73** and pyrrole-3-carboxaldehyde **74** on stirring with indium (2 equiv.) and allyl bromide (3 equiv.) in THF–H_2O (1 : 1) undergo deoxygenative diallylation at the carbonyl carbon to provide



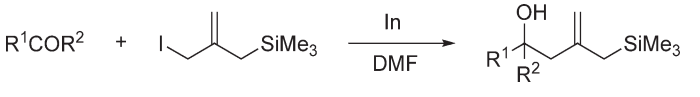
70 **71**

		Ratio	
Solvent	*Time* (h)	**70**	**71**
THF	24	>99	<1
THF–H_2O (9 : 1)	24	0	100
THF–H_2O (1 : 1)	24	0	100
THF–H_2O (1 : 4)	24	9	91
THF–H_2O (1 : 9)	48	31	69
H_2O	48	>99	<1

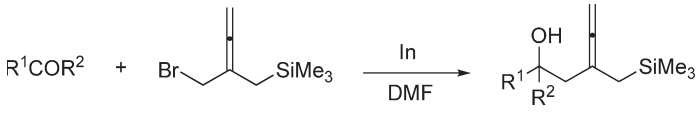


72

Scheme 60

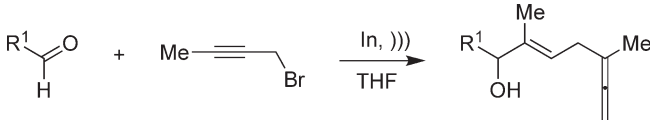


R^1	R^2	*Yield* (%)
Ph	H	90
c-C_6H_{11}	H	60
Ph	Me	71



R^1	R^2	*Yield* (%)
Ph	H	92
c-C_6H_{11}	H	54
Ph	Me	0

Scheme 61



R^1	*Yield* (%)
$PhCH_2CH_2$	53
p-ClC_6H_4	75
p-$MeOC_6H_4$	72
p-MeC_6H_4	66

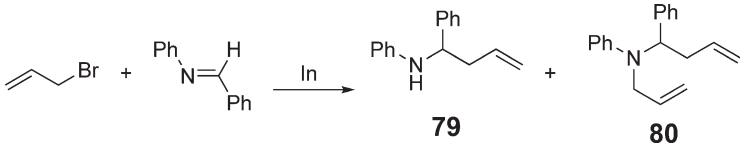
Scheme 62

3-[1,6-heptadien-4-yl]indole **75** and -pyrrole **76**, respectively (Scheme 63). The formation of the usual 1,2-addition product **78** in the case of **77** (R═CO_2Et) points toward the contribution of electronic factors due to the enamine double bond in the deoxygenation process.[248]

3-(*tert*-Butyldimethylsilyloxy)-2-alkenylsulfonium salts, generated *in situ* from the reaction of α,β-enones with dimethyl sulfide in the presence of TBSOTf, undego a nucleophilic substitution with allylindiums to give silyl enol ethers of β-allyl α,β-enones in good yields, which correspond to formal Michael addition products (Table 9). In a similar manner, 1,4-propargylation of propargylindiums onto the sulfonium salts produces the corresponding silyl enol ethers of β-propargyl α,β-enones in good yields. Organoindium reagents derived from γ-substituted propargyl bromide and indium afford the corresponding silyl enol ethers of β-allenyl ketones.[249,250]

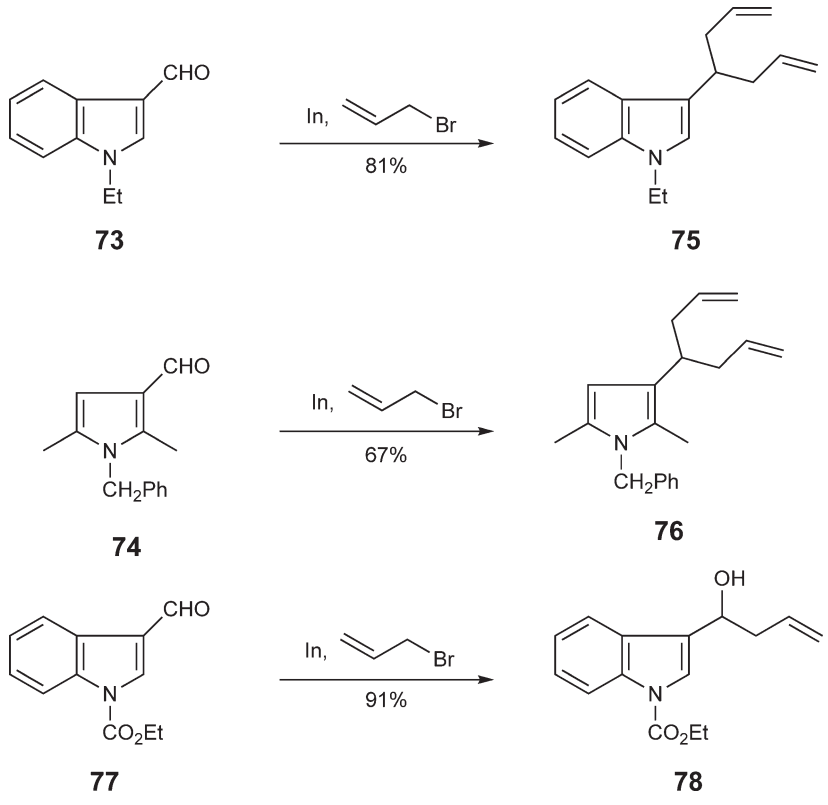
9.14.3.6 Allylation of Imines, Enamines, and Nitriles

The allylation of imines with allylindium reagents in organic solvents gives the corresponding homoallylic amines.[251–253] Under solvent-free conditions, the indium-mediated reaction of *N*-benzylideneaniline furnishes a mixture of mono-allylated **79** and bis-allylated products **80** (Equation (56)). The bis-allylated product **80** presumably arises via a formation of an iminium salt, which is subsequently attacked by the allylindium nucleophiles. Formation of **80** is entirely suppressed by addition of allyl bromide to indium metal prior to any addition of the imine (Grignard-type reaction).[254]



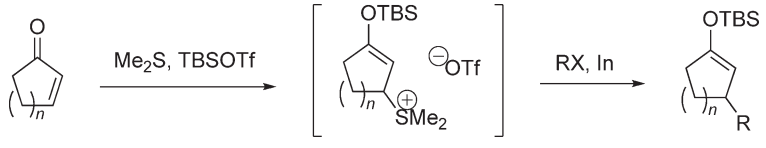
Reactions	*Yield* (%)	
Barbier-type	22	63
Grignard-type	89	0

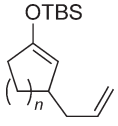
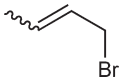
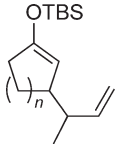
(56)



Scheme 63

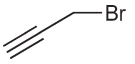
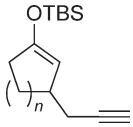
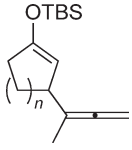
Table 9 Synthesis of silyl enol ethers of 3-substituted enones



RX	*Product*	*Yield (%)*
		$n = 1:62$ $n = 2:65$ $n = 3:65$
 *cis* : *trans* = 1 : 5		$n = 1:64$ (1 : 1)[a] $n = 2:62$ (1 : 1)[a] $n = 3:69$ (1 : 1)[a]

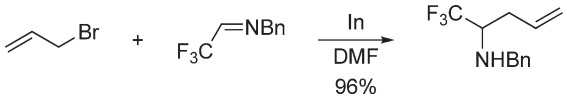
(*Continued*)

Table 9 (Continued)

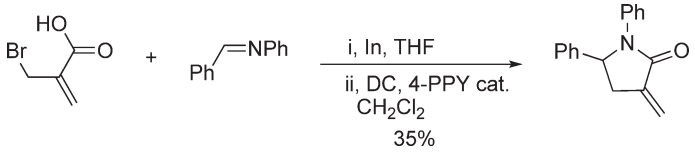
RX	*Product*	*Yield (%)*
		$n = 1:82$ $n = 2:86$
		$n = 1:69$[b] $n = 2:64$[b]

[a]Diastereomeric ratio.
[b]LiI (100 mol.%) was used.

Trifluoromethylaldimine reacts with various allylic bromides, under Barbier conditions in the presence of indium in DMF, to provide the corresponding homoallylamines (Equation (57)).[255] α-Methylene-γ-butyrolactams are prepared by the indium-mediated reaction of 2-(bromomethyl)acrylic acid with aldimines (Equation (58)).[256]

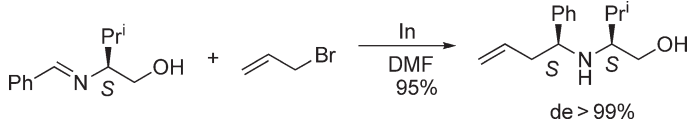


(57)



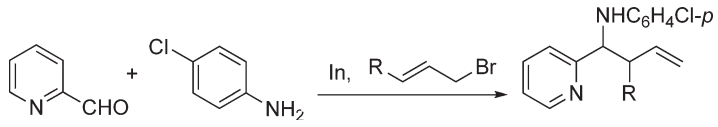
(58)

Diastereoselective Barbier-type allylation of chiral imines bearing a hydroxyl group on the chiral auxiliary has been achieved in DMF (Equation (59)).[257–259] The chelation between the nitrogen and the hydroxyl group of the imine with indium is crucial for the high stereoselectivity. The palladium-catalyzed indium-mediated allylation of imines also proceeds well with InI prepared *in situ* from In and I_2.[259]



(59)

The imines generated *in situ* from 2-pyridinecarboxaldehyde (or 2-quinolinecarboxaldehyde) and arylamines undergo indium-mediated Barbier allylation in aqueous media to provide homoallylic amines. Crotyl and cinnamyl bromides lead to diastereoselective allylation with diastereomeric ratios up to 98:2 (Equation (60)).[260]

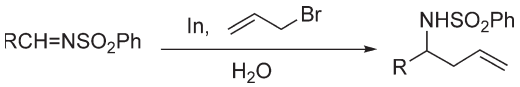


R	*Yield* (%)	(*syn*: *anti*)
Me	63	90 : 10
Ph	22	98 : 2

(60)

The indium-catalyzed coupling of propargyl bromide with a variety of imines and nitrile *N*-oxides affords the corresponding propargylated products in high yields under mild conditions (Scheme 64).[261]

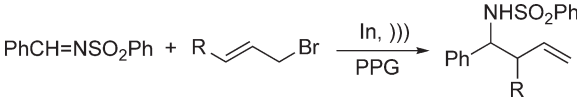
Examples of imine allylation in aqueous media are rather limited compared with the carbonyl version. This is ascribed to the lower electrophilicity of the C═N function of imines and its ease of hydrolysis to carbonyl compounds. In order to overcome the undesired side-reactions, sulfonimines in place of simple imines are successfully used for the allylation under aqueous conditions (Equation (61)).[262,263] Crotylation of α-sulfonimino esters gives the *syn*-adducts as high as 19 : 1 in H_2O/THF (1 : 1) (Table 10).[264]



R	*Yield* (%)
Ph	99
p-ClC_6H_4	50
p-$MeOC_6H_4$	80

(61)

Allylation of aldimines and sulfonimines with indium powder in poly(propylene) glycol (MW ~ 1000), a benign and recyclable reaction medium, results in the formation of the corresponding homoallylic amines and sulfonamides in high yields (Equation (62)).[265]



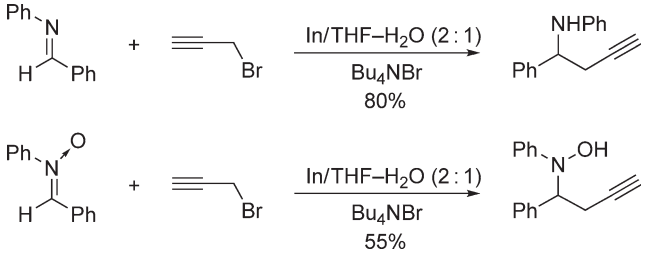
R	*Yield* (%)(*anti*: *syn*)
H	96
Me	93(44 : 56)
Ph	32(1 : 5)

(62)

Binary regiocontrolled pentadienylation of imines with a pentadienyltin reagent has been achieved. While *N*-phenylimines affords ε-adducts (1,3-dienes) exclusively under Lewis-acidic conditions, the combination of *N*-tosylimines and indium chloride or zinc chloride as a Lewis acid gives γ-adducts (1,4-dienes) preferentially (Scheme 65).[266]

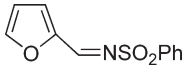
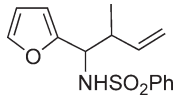
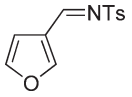
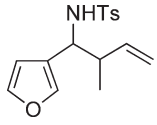
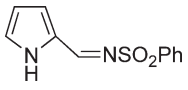
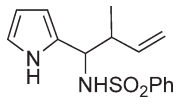
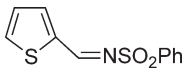
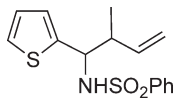
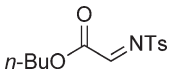
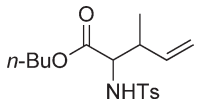
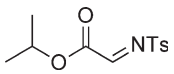
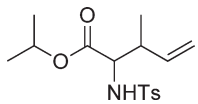
Allylindium reacts with activated *O*-functionalyzed oximes as exemplified by a variety of glyoxylate derivatives (Scheme 66). This method gives the corresponding free (or protected) amines in a one-pot process. The reaction is regiospecific and can be carried out under remarkably mild conditions so that even oxime ethers are subjected to the typical reaction conditions.[267]

Oxime ethers derived from 2-pyridinecarboxaldehyde and glyoxylic acid can be allylated effectively in water with functionalized allylic bromides promoted by indium (Scheme 67). When the metal is positioned in close proximity to flanking heteroatomic centers, chelation by indium is operative and affects both reactivity and stereochemistry (Scheme 68).[268]



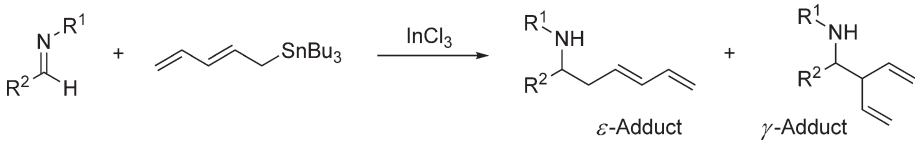
Scheme 64

Table 10 Indium-mediated crotylation of sulfonimines. Reproduced with permission from ACS Publications

Sulfonimine	*Product*	*Solvent* THF : H_2O	*Yield* (%)	*syn* : *anti*
		10 : 1	99	93 : 7
		50 : 50	91	86 : 14
		50 : 50	80	94 : 6
		50 : 50	92	85 : 15
		50 : 50	56	93 : 7
		50 : 50	40	95 : 5

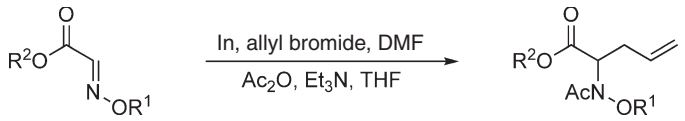
The indium-mediated allylation of the Oppolzer camphorsultam derivatives of glyoxylic oxime ether proceeds with excellent diastereoselectivity in aqueous media, providing a variety of enantiomerically pure α-amino acids.[269]

The indium-mediated allylation of chiral hydrazones has been investigated. Essentially complete diastereoselectivity and quantitative yields have been realized for substrates derived from both aromatic and aliphatic aldehydes (Scheme 69).[270]



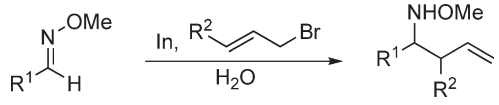
R^1	R^2	ε/γ	*Yield* (%)
Ph	Ph	>99/1	51
Ph	PhCH=CH	>99/1	78
Ph	*n*-C_6H_{13}	>99/1	57
Ts	Ph	<1/99	80
Ts	PhCH=CH	<1/99	77
Ts	*n*-C_6H_{13}	<1/99	89
Ts	*c*-C_6H_{11}	19/81	65

Scheme 65



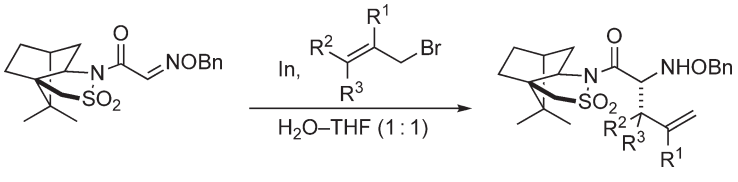
R^1	R^2	*Yield* (%)
Me	Bn	84
Me	Bz	81
Bu^t	Bn	80
Bu^t	Bz	72

Scheme 66



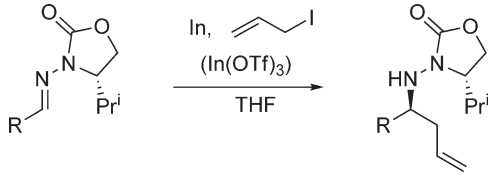
R^1	R^2	*Yield* (%)	*syn*:*anti*
2-Pyridyl	H	70	
2-Pyridyl	Ph	60	>99:1
2-Pyridyl	Me	75	76:24
2-Pyridyl	CO_2Et	96	>99:1
CO_2H	H	65	
CO_2H	Ph	57	>99:1
CO_2H	Me	70	80:20
CO_2H	CO_2Et	70	80:20

Scheme 67



R^1	R^2	R^3	*Yield* (%)	*dr*
H	H	H	98	88
H	Ph	H	91	>98
H	Me	Me	90	>98
Me	H	H	93	63
CO_2Me	H	H	96	58

Scheme 68



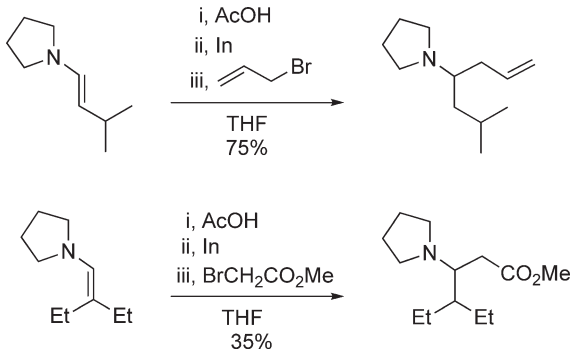
R	*Yield* (%)[a]	*dr*[a]
Ph	99	>99:1
p-$NO_2C_6H_4$	50 (95)	>99:1 (>99:1)
(*E*)-PhCH=CH	99 (90)	55:45 (>99:1)
c-C_6H_{11}	99 (92)	66:33 (>95:5)
Pr^i	99 (90)	66:33 (>95:5)
Et	95 (90)	78:22 (>95:5)

[a]Figures in parentheses refer to the results obtained in the presence of $In(OTf)_3$.

Scheme 69

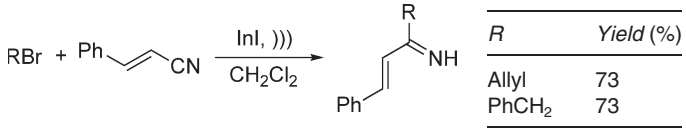
Indium-mediated reaction of enamines with allyl bromides gives homoallylamines. The addition of one equivalent of acetic acid accelerates the reaction. An analogous reaction of methyl bromoacetate in place of allylic bromides is also possible. The iminium salts formed by protonation of the enamines are considered to be the intermediates (Scheme 70).[271,272]

Allyl and benzyl bromides react with α,β-unsaturated nitriles in the presence of indium(I) iodide under sonication to produce the corresponding allylated and benzylated imines, involving exclusive addition of the allyl/benzyl group to the nitrile moiety (Equation (63)).[273] The reaction of allylindium reagents with methyl cyanoacetates affords the corresponding allylation–enamination products (Equation (64)).[274] 1-Acyl-1,2-dihydropyridines are prepared by indium-mediated allylation of 1-acylpyridinium salts (Equation (65)).[275] Quinoline and isoquinoline activated by



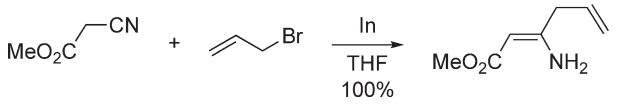
Scheme 70

phenyl chloroformate are allylated using indium and allyl bromides in THF at room temperature to give the corresponding allyldihydroquinoline and allyldihydroisoquinoline in good to high yields (Equation (66)).[276]

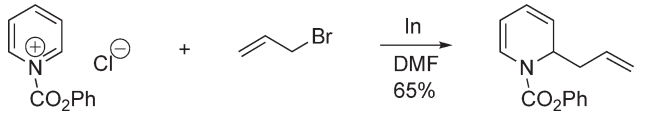


R	*Yield* (%)
Allyl	73
$PhCH_2$	73

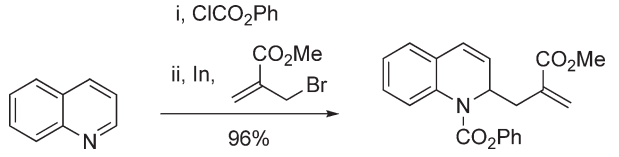
(63)



(64)



(65)



(66)

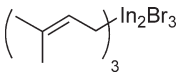
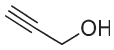
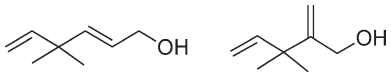
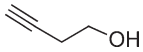
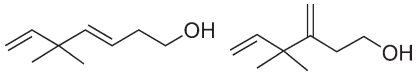
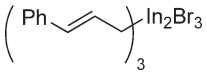
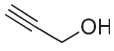
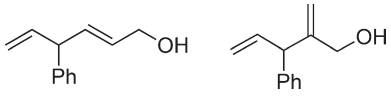
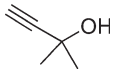
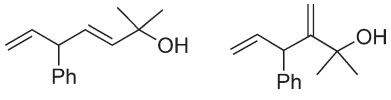
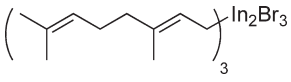
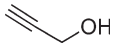
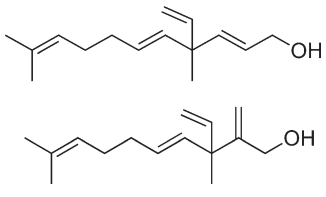
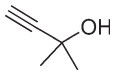
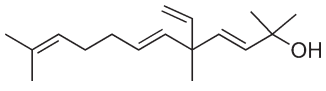
9.14.3.7 Allylindation of Alkenes and Alkynes

Carbometallation of carbon–carbon unsaturated bonds is an important synthetic method for the construction of complex molecules.[277–281] An example of carboindation is described with tri(5-hexenyl)indium, prepared from di(5-hexenyl)mercury and indium metal, which is cyclized to a cyclopentylindium compound.[282]

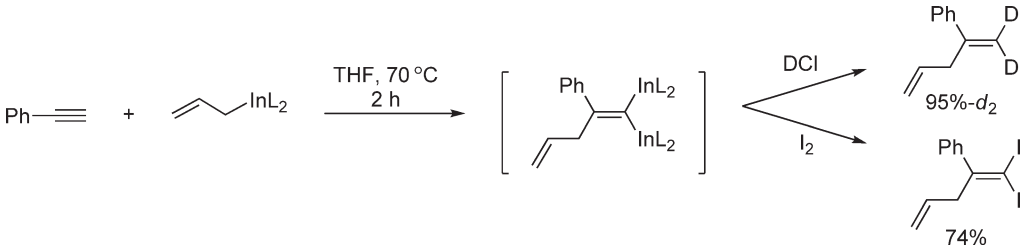
Allylmetallation of alkynes is a useful tool for the synthesis of 1,4-dienes. Various main group allylmetals, as well as allylic transition metals, have been utilized in such transformations. The reaction of allylindium reagents with terminal alkynols was first reported in 1992. The reaction proceeds in DMF giving 1,4-dienes, where the proximal hydroxyl group is essential for the clean allylation (Table 11).[283,284]

By changing the solvent to THF, allylindation of unfunctionalized alkynes also proceeds smoothly.[285–288] When this reaction is quenched with I_2 or D_2O, the diiodinated product or the d_2-containing allylated product is obtained, demonstrating that the allylindation of terminal alkynes in THF proceeds through the double-indation intermediate (Scheme 71). The regioselectivity of the allylindation depends on the presence of an adjacent free hydroxyl group: a predominant formation of linear 1,4-dienes (*anti*-Markovnikov products) is achieved in the case of propargylic alcohols, whereas simple terminal alkynes and alkynes with a protected hydroxyl group give branched 1,4-dienes (Markovnikov products) (Table 12).

Table 11 Allylindation of alkynols. Reproduced with permission from ACS Publications

Allylindium	*Alkynol*	*Products*	*Yield (%)*[a]
			91 (65 : 35)
"			85 (73 : 27)
			56 (14 : 86)
"			68 (90 : 10)
			59 (75 : 25)
"			75

[a]Figures in parentheses refer to the ratio *anti*-Markovnikov : Markovnikov adducts.

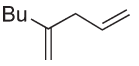
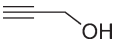
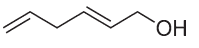
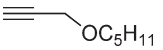
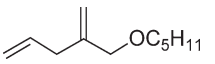
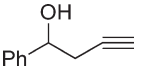
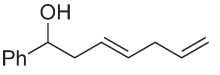
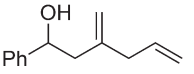
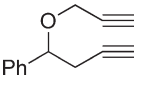
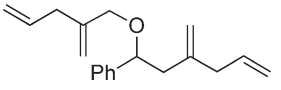


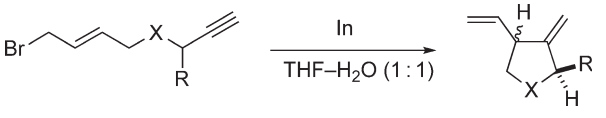
Scheme 71

The intramolecular cyclization of tethered allyl bromides onto terminal alkynes mediated by metallic indium proceeds smoothly and cleanly in a mixture of THF and water to give unsaturated carbocycles and heterocycles in good yields. The reaction does not proceed efficiently under rigorously anhydrous conditions (Scheme 72).[289,290]

Treatment of tethered alkyne-allyl halides with indium metal in halogenated solvents affords carbocyclic vinyl halides via a novel atom-transfer reaction. The reactions are operationally facile and proceed smoothly at room temperature even with sub-stoichiometric quantities of indium. Use of a halogenated solvent containing a different

Table 12 Allylindation of terminal alkynes. Reproduced with permission from the Royal Society of Chemistry

Alkyne	*Product*	*Yield* (%)
		86
		80
		85
	 + 	85 (55 : 45)
		86



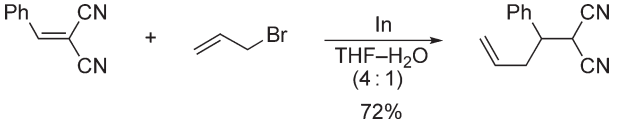
R	*X*	*Yield* (%)	*syn* : *anti*
H	O	62	
Ph	O	50	2 : 1
Pr	O	56	3.5 : 1
C_5H_{11}	O	52	3 : 1
H	NTs	62	

Scheme 72

halide than that contained in the substrate affords a mixture of products **81** and **82** arising from intramolecular halide transfer and abstraction of a halide atom from the solvent (Scheme 73).[291] A total synthesis of proposed amphidinolide A has been achieved via allylindation of terminal alkyne.[94]

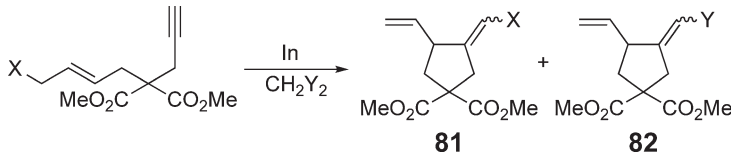
Allylindation of allenols also undergoes regio- and stereoselectively to afford 2,6-heptadien-1-ol derivatives via a hydroxy-chelated bicylic transition state (Scheme 74 and Table 13).[292] The geometry of the carbon–carbon double bond in the products is *E*.

In contrast to the facile allylindation onto alkynes and allenes, allylindation of simple alkenes does not proceed. However, electron-deficient alkenes (Equation (67) and Scheme 75).[293,294] and strained alkenes such as norbornenols[295] undergo smooth allylindation to give allylated products (Scheme 76).



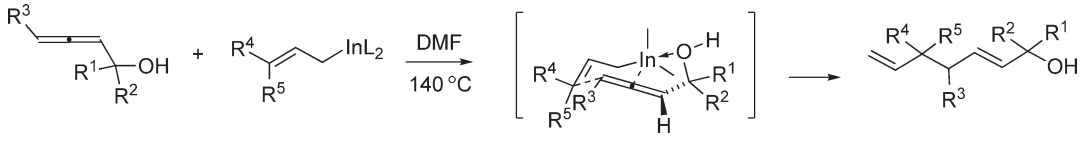
(67)

Cyclopropenes undergo clean allylindation in organic and aqueous media.[296,297] The regio- and stereoselectivity are regulated both by the substituent on the C3 carbon and by the reaction solvents (Scheme 77). In some cases, the regio- and stereoselectivity have been totally reversed between in water and organic solvents (Scheme 78). Stable cyclopropylindium products have been isolated and characterized by X-ray crystallography.



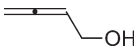
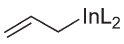
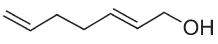
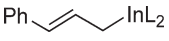
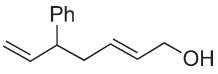
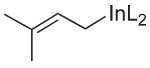
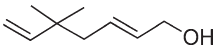
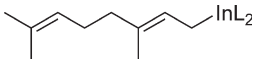
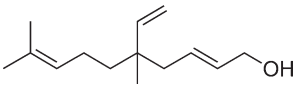
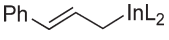
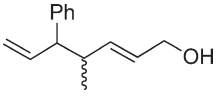
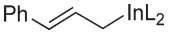
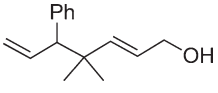
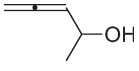
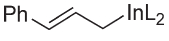
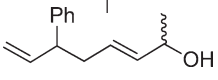
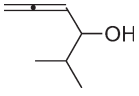
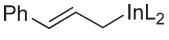
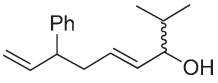
X	*Y*	**81 : 82**	*Yield* (%)
Br	Br		42
Br	Cl	1 : 3.00	76
Br	I	1 : 3.25	43
I	Br	1 : 5.25	75
I	I		46

Scheme 73

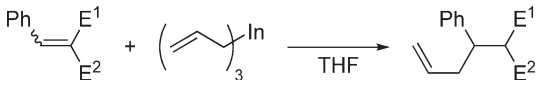


Scheme 74

Table 13 Allylindation of allenols. Reproduced with permission from ACS Publications

Allenol	*Allylindium*	*Product*	*Yield* (%)
			100
			97
			79
			89
			99 (72 : 28)[a]
			54 (61 : 39)[b]
			44 (67 : 33)[a]
			63 (61 : 39)

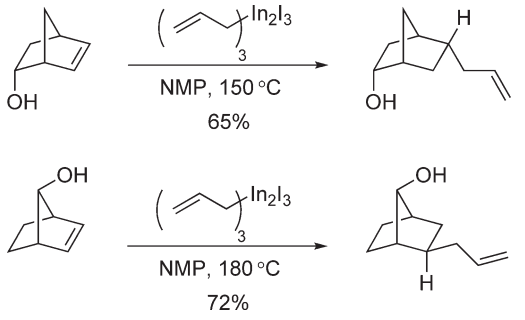
[a]Diastereomeric ratio.
[b]Ratio of products.



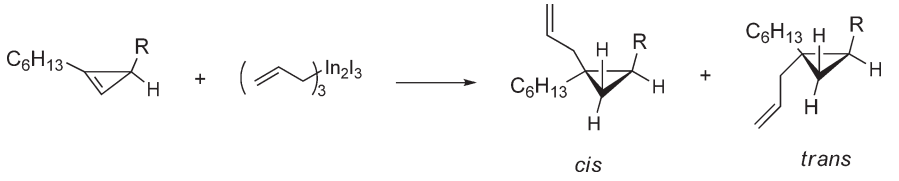
E^1	E^2	*Yield* (%)[a]
CN	CN	88
COMe	COMe	81
CO_2Et	CO_2Et	80
COMe	CO_2Et (*E*:*Z* = 20:80)	84 (61:39)
CN	CO_2Et (*E* only)	85 (53:47)

[a]Figures in parentheses refer to diastereomeric ratio.

Scheme 75

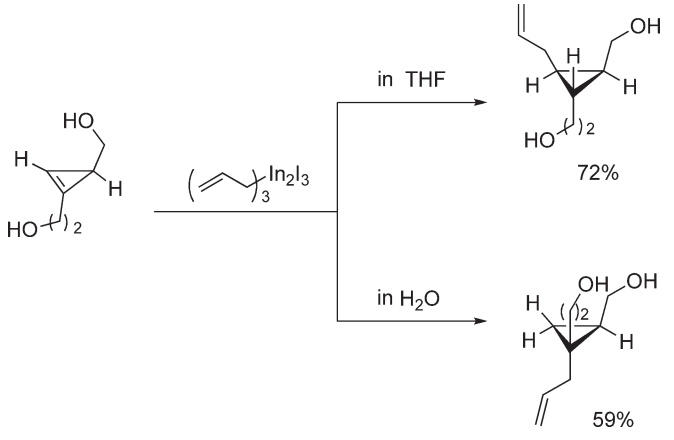


Scheme 76



R	*Conditions*	*Yield* (%)	*cis*:*trans*
CH_2OH	THF, RT	95	95:5
CH_2OH	DMF, RT	74	85:15
CO_2H	THF, rfx	81	100:0
CH_2OAc	THF, RT	66	0:100
CO_2Et	THF, rfx	63	26:74

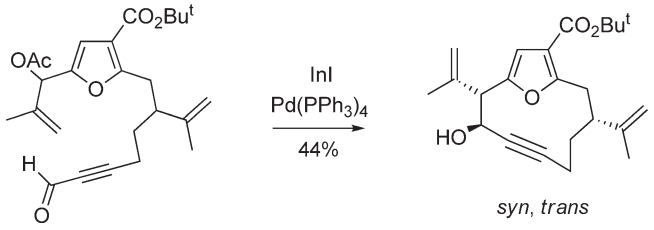
Scheme 77



Scheme 78

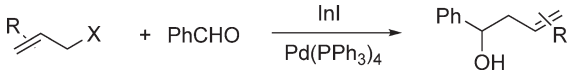
9.14.3.8 Reactions of Allylindium Prepared by Redox Transmetallation with Pd or Ni

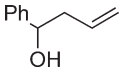
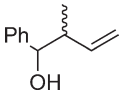
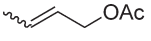
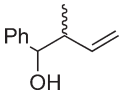
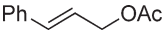
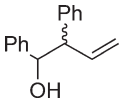
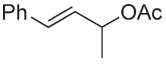
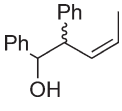
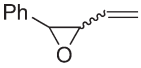
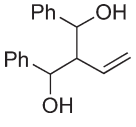
The use of organoindium reagents in combination with transition metal catalysts has recently received much attention, and greatly expands the scope of indium chemistry in organic synthesis. A new preparation of allylic and allenic indium reagents by using Pd catalysts has been disclosed. Allyl acetate and InI react with benzaldehyde in the presence of a catalytic amount of $Pd(PPh_3)_4$ to give the corresponding homoallylic alcohol in high yield (Table 14).[43] The reaction proceeds via a π-allylpalladium(II) complex followed by a reductive transmetallation with InI to give an allylindium compound. The reaction can be carried out in a variety of solvents including THF, 1,3-dimethyl-2-imidazolidinone (DMI), and dichloromethane. Protic solvents such as water, methanol, and ethanol can also be used. Various allylic substrates, such as allyl chloride, vinyloxirane, and acrolein acetal, can be employed. An intramolecular cyclization of the acetate to the macrocyclic alcohol is achieved highly stereoselectively based on the same methodology (Equation (68)).[298]



(68)

Table 14 Indium-mediated palladium-catalyzed allylation. Reproduced with permission from ACS Publications

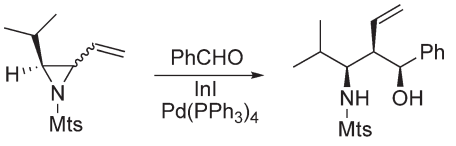


Allylic compound	*Product*	*Yield (%) (syn : anti)*
		91
		92 (58 : 42)
 (*E* : *Z* = 96 : 14)		98 (32 : 68)
		100 (14 : 86)
		79 (11 : 89)
 (*cis* : *trans* = 31 : 69)		80 (85 : 15)[a]

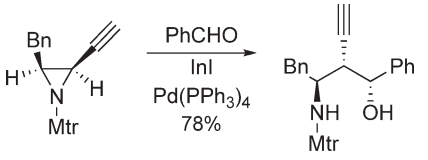
[a]Diastereomeric ratio.

This indium-mediated palladium-catalyzed Barbier-type allylation of aldehydes has been expanded to the cascade reactions with allene, which give the three-component coupling products (Table 15 and Scheme 79).[47,51–53,299–301]

The InI–Pd(0)-promoted allylation of aldehydes (InI, indium(I)iodide) with *N*-activated vinylaziridines proceeds with regio- and stereoselectivity, irrespective of the chirality of the allylic carbon bearing a vinyl group, to provide *syn*,*syn*-2-vinyl-1,3-amino alcohols possessing three contiguous chiral centers (Equation (69)).[45] In a similar manner, 2-ethynyl-1,3-amino alcohols are synthesized from 2-ethnylarizidines (Equation (70)).[302,303]



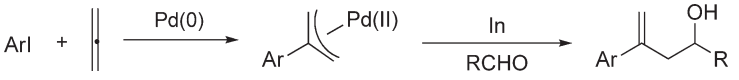
(69)

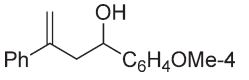
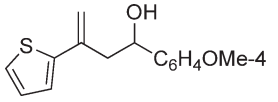
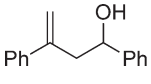


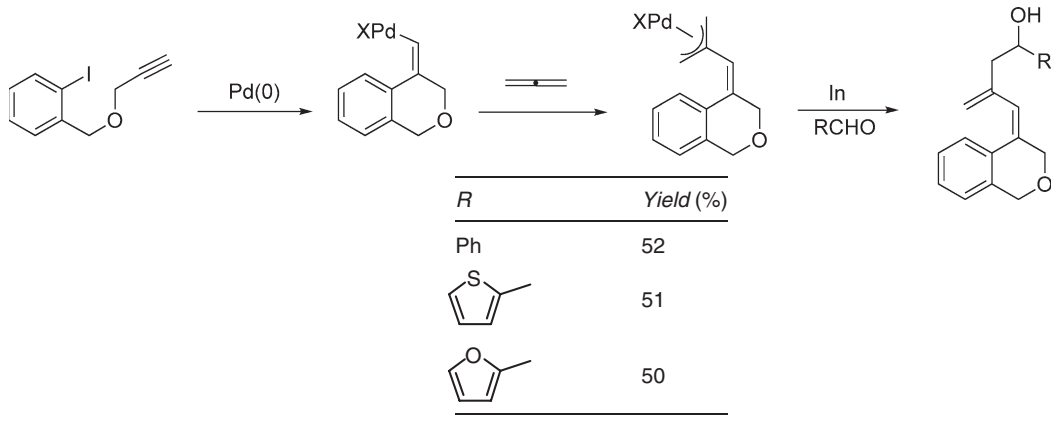
(70)

Allylindium(III) compounds have been generated *in situ* from acylnitroso Diels–Alder cycloadducts or cyclopentenyl acetate with palladium(0) catalysts and indium(I) iodide. The stereo- and regiochemistry of their additions to aldehydes and ketones have been investigated (Scheme 80).[304] The solvent mixture of THF/H_2O with $Pd(OAc)_2{\cdot}PPh_3$ catalysis is optimal. The addition of *N*-acetyl cycloadduct to aliphatic aldehydes affords products in good yields and high regio- and stereoselectivity, with *cis*-1,4-isomers constituting 90–95% of the products. The reaction with *N*-Boc and *N*-methylcarbamate cycloadducts also gives the *cis*-1,4-products predominantly. The same regio- and stereoselectivity have been applied to the reactions of 4-acetoxy-1-(*N*-hydroxyphenylacetamido)cyclopentene. 4-Acetoxy-1-phenylacetamidocyclopentene, however, affords *trans*-1,4-products exclusively.

Table 15 Preparation of homoallyl alcohols via three-component coupling. Reproduced with permission from the Royal Society of Chemistry

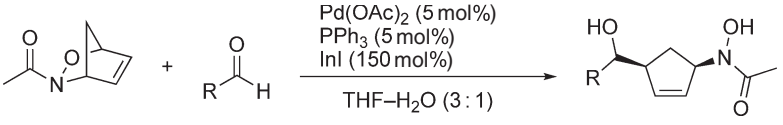


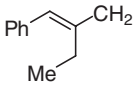
ArI	*RCHO*	*Product and yield* (%)
PhI	4-$MeOC_6H_4CHO$	 64
	4-$MeOC_6H_4CHO$	 66
PhI	PhCHO	 43



R	*Yield* (%)
Ph	52
	51
	50

Scheme 79

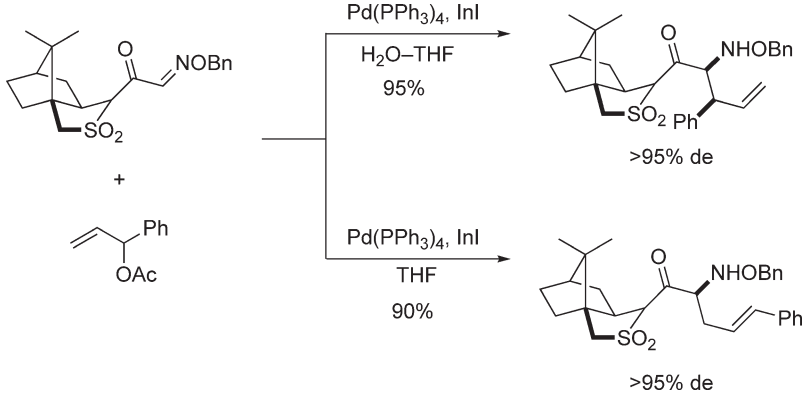


R	*Yield* (%)	*dr*
Pr	59	1.9 : 1
Pr^{i}	56	1.3 : 1
c-C_6H_{11}	57	1.1 : 1
Bu^{t}	64	6 : 1
	59	7 : 1

Scheme 80

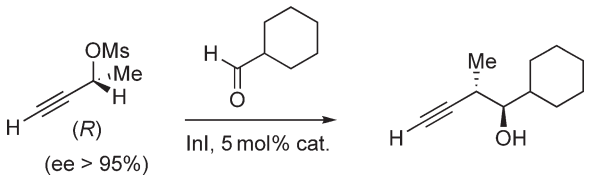
Allylation of electron-deficient imines with allylic acetates and InI proceeds in the presence of a catalytic amount of Pd(0). The reversibility of allylation has been observed in the reaction of glyoxylic oxime ether bearing a camphorsultam moiety (Scheme 81). As an important effect of water on regioselectivity, the branched adducts are kinetically formed from mono-substituted allylic reagents in the presence of water. On the contrary, a selective formation of the thermodynamically stable linear adducts is observed in anhydrous THF.[305,306]

As shown in Table 16, (*R*)-propargyl mesylate (ee > 95%) reacts with cyclohexanecarboxaldehyde in the presence of InI and 5 mol% of a palladium catalyst to give, via an allenylindium intermediate, the adduct with high enantiomeric excess.[55,56] The addition is most efficient in 3 : 1 THF–HMPA and 1 : 1 THF–DMPU solvents. The *Anti* : *syn* ratios are excellent with α-branched aldehydes but only modest with unbranched and conjugated aldehydes.



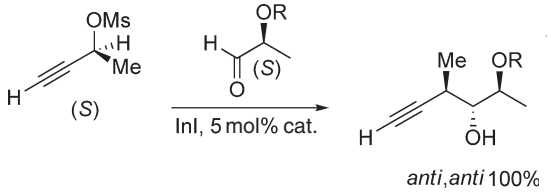
Scheme 81

Table 16 Indium-mediated propargylation of aldehyde with propargyl mesylate. Reproduced with permission from ACS Publications



Catalyst	*Solvent*	*Yield* (%)	*anti* : *syn*	*ee* (%)
None	THF–HMPA (3 : 1)	66	96 : 4	0
$Pd(dppf)Cl_2$	THF–HMPA (3 : 1)	76	95 : 5	95
$Pd(dppf)Cl_2$	THF–DMPU (3 : 1)	63	87 : 13	90
$Pd(dppf)Cl_2$	THF–DMPU (1 : 1)	80	91 : 9	87
$Pd(dppf)Cl_2$	THF–HMPA (20 : 1)	66	93 : 7	91
$Pd(OAc)_2{\cdot}PPh_3$	THF–HMPA (3 : 1)	75	95 : 5	91

The reaction of a matched combination of the mesylate with chiral α-oxgenated aldehydes proceeds with high stereoselectivity giving the *anti*,*anti*-adducts, whereas a mismatched combination affords a mixture of diastereoisomers (Equation (71)).[57] The mesylate of a chiral alcohol undergoes high enantio-, regio-, and diastereoselective additions to various aldehydes, leading to the homopropargylic alcohol adducts (Table 17).[58]

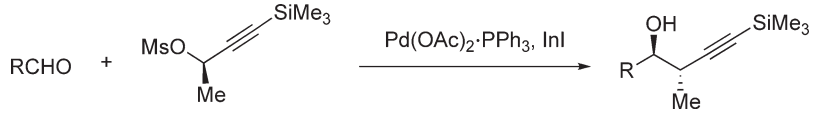


R	*Yield* (%)
Bn	89
TBS	63

(71)

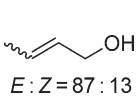
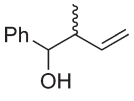
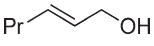
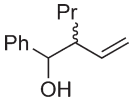
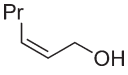
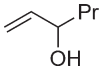
Recently, it has been disclosed that an umpolung of π-allylnickel(II) with InI also provides a new route for allylindium(III) reagents. This process enables a direct use of allylic alcohols as the allylic component. The high availability of a wide range of allylic alcohols greatly enhances the usefulness of this Ni-catalyzed methodology. High *syn*-selectivity is generally observed in the coupling with carbonyl compounds, regardless of the geometry of the starting allylic alcohols (Table 18).[50]

Table 17 Indium-mediated propargylation of various aldehydes. Reproduced with permission from ACS Publications



R	*Yield* (%)	*anti* : *syn*	*er*
c-C_6H_{11}	75	>99 : 1	99 : 1
Pr^i	89	98 : 2	99 : 1
$Ph(CH_2)_2$	69	>99 : 1	>99 : 1
C_6H_{13}	80	98 : 2	99 : 1
(*E*)-BuCH=CH	73	99 : 1	99 : 1

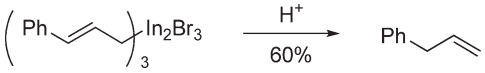
Table 18 Ni(II)-catalyzed allylation of benzaldehyde. Reproduced with permission from ACS Publications

Allylic alcohol	*Product and yield (%)*[a]
 $E:Z = 87:13$	 84 (80 : 20)
	95 (81 : 19)
	 90 (74 : 26)
	88 (82 : 18)
	95 (78 : 22)

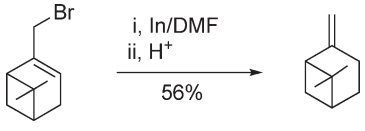
[a]Figures in parentheses show *syn* : *anti* ratios.

9.14.3.9 Other Reactions of Allylindium Reagents

Protonation of allylindium reagents proceeds regiospecifically at the γ-position of the allylic group to give 1-propenes (Equation (72)). A facile transformation of α-pinene to β-pinene has been achieved via protonolysis of a myrtenylindium intermediate (Equation (73)). Oxygenation of allylic indium reagents gives mixtures of allylic alcohol isomers in moderate yields.[26]

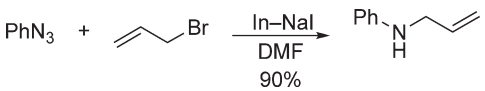


(72)

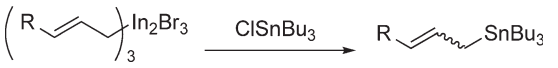


(73)

N-allylic amines are conveniently prepared in high yields by the reaction of azides with allylindium reagents in the presence of sodium iodide at ambient temperature (Equation (74)).[307] Stannylation with tributylchlorostannane occurs exclusively at the α-carbon, yielding allyltributylstannanes; (*E*, *Z*)-isomerization of the allylic double bond depends largely upon the substitution pattern on the allylic moiety (Equation (75)).[26] Allyl and propargyl bromides react with diphenyl diselenides in aqueous media to give allyl and propargyl selenides (Equation (76)).[308,309]



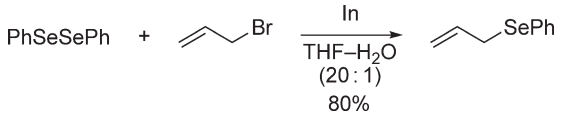
(74)



R	*Yield* (%)	(*E*:*Z*)
Pr^n	83	1:1
Ph	59	9:1[a]

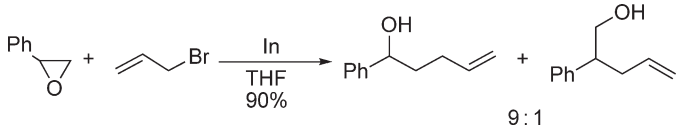
[a]*E* only.

(75)

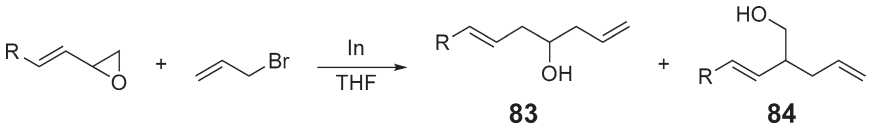


(76)

Allylindium sesquihalides react with terminal epoxides to afford the corresponding bishomoallyl alcohols (Equation (77)).[310] Terminal vinyl epoxides afford various homoallyl alcohols **83** and **84** at room temperature in moderate to high yields via consecutive 1,2-shift and regioselective allylation (Equation (78)).[311] In contrast, allylindium ate complexes give the ring-opening products **85** and **86** without the rearrangement (Scheme 82).[312]



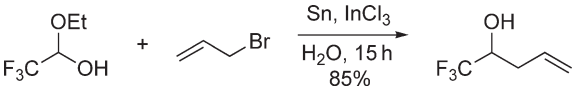
(77)



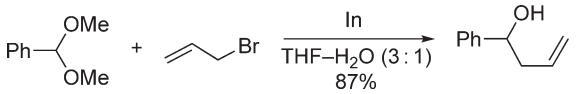
R	*Yield* (%)
H	87% (**83** only)
Ph	70% (**83**:**84** = 8.5:1)

(78)

The reactions of allylindium reagents with trifluoroacetaldehyde hydrate or hemiacetal in water (Equation (79)), or with aldehyde dimethyl acetals in aqueous THF, give the corresponding homoallylic alcohols (Equation (80)).[313–315]

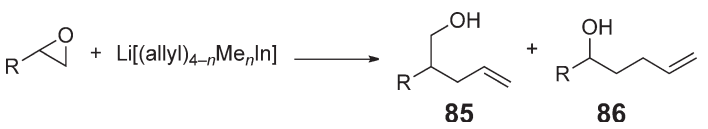


(79)



(80)

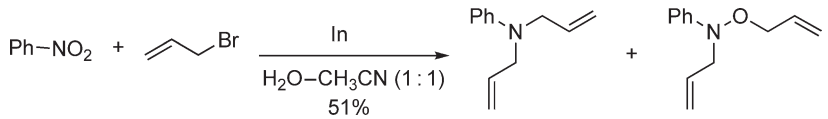
Indium-mediated allylation of a nitro group is achieved in aqueous media to give *N*,*N*-diallylamine and *N*,*O*-diallylhydroxylamine (Equation (81)).[316] *In situ* generated sulfonium salts derived from α,β-enones undergo a nucleophilic substitution with allylindium reagents to give the corresponding Michael addition products (Scheme 83).[317]



R	*Yield* (%) **85**:**86**
Ph	76% (38:62)
(*E*)-PhCH=CH	70% (100:0)[a]
$PhCH_2$	86% (0:100)

[a]The 1,4-adduct was obtained in 2% yield.

Scheme 82

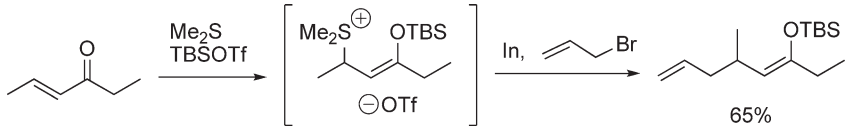


(81)

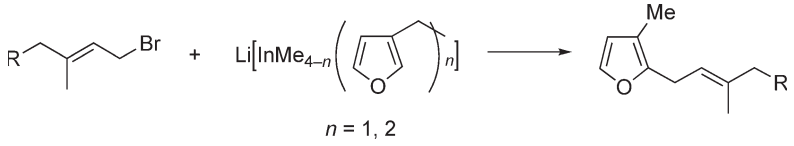
Allylic tetraorganoindium ate complexes, readily prepared by the addition of organolithium reagents to allylic indium sesquihalides, couple with allylic halides regio- and stereo-specifically to give head-to-tail 1,5-dienes in high yields.[31] Tetraalkylindates regioselectively alkylate allylic bromides at the α-carbon. In this way, 1,5-dienes have been regio- and stereoselectively synthesized by the allyl–allyl coupling of allylic bromides and allylic indates. The natural terpenes, rosefuran and sesquirosefuran, have been prepared by this method (Scheme 84).[318]

It has been found that water as a solvent accelerates the indium-mediated Barbier-type allylation and benzylation of β,γ-unsaturated piperidinium cation generated from β,γ-unsaturated α-methoxy-*N*-methoxycarbonylpiperidine, whereas a ring-opened allylated product has been obtained in a case using β,γ-saturated α-methoxy-*N*-methoxycarbonylpiperidine. Other solvents than water result in low yield of the allylated and benzylated products, suggesting that water is essential to generate the piperidinium intermediate from β,γ-unsaturated α-methoxy-*N*-methoxycarbonylpiperidine (Scheme 85).[319]

Indium-mediated allylation of 4-acetoxy-2-azetidinones affords 4-allyl-substituted azetidinones with retention of the stereochemistry (Equation (82)).[320] An aminoalkoxy titanium complex is readily allylated with allylindium reagents to give homoallylic amines (Scheme 86).[321]

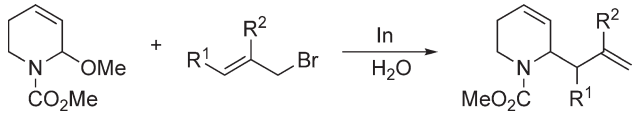


Scheme 83



R	*Yield* (%)
H	88
$CH_2CH{=}CMe_2$	68

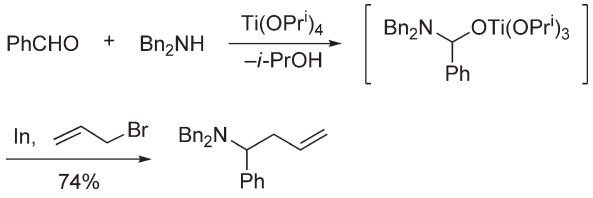
Scheme 84



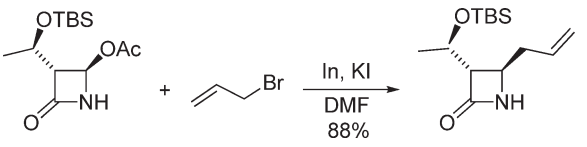
R^1	R^2	*Yield* (%)
H	H	80
Me	H	67 (60 : 40)[a]
Ph	H	67 (51 : 49)[a]
H	CO_2Et	65

[a]Diastereomeric ratio.

Scheme 85



Scheme 86

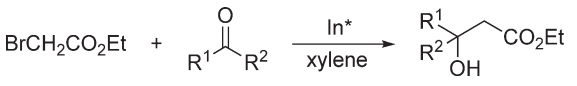


(82)

9.14.3.10 Reformatsky and Related Reactions

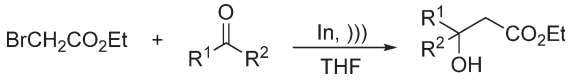
The zinc-mediated Reformatsky reaction is one of the classical methods for carbon–carbon bond formation. To date, various main group metals and transition metals have been used for this reaction. Rieke's activated indium powder mediates readily the coupling of ethyl α-bromoacetate and a variety of carbonyl compounds yielding β-hydroxy esters in good yields (Scheme 87).[3] Later, commercially available indium powder has been found to be equally effective for the indium-based Reformatsky reaction in THF.[28] This indium Reformatsky reaction is accelerated by ultrasound irradiation (Scheme 88).[322,323] Indium(I) iodide also mediates the Reformatsky reaction of aldehydes and ketones to give β-hydroxy esters, presumably via organoindium(III) diiodide (Scheme 89).[27]

The indium-induced Reformatsky reaction with stoichiometric amounts of chiral amino alcohols such as cinnconine and cinchonidine gives optically active β-hydroxy esters with 40%–70% ee (Table 19). In contrast to the smooth reaction with uncomplexed indium-based Reformatsky reagents, ketones do not react with the complexed indium Reformatsky reagents. Other chiral ligands, including (−)-spartein, (−)-norephedrine, (+)-(1-methylpyrrolidin-2-yl)diphenylmethanol, (+)-Dibutyl tartrate and (+)-1,1′-bi-2-naphthol, are not effective for this reaction.[324]



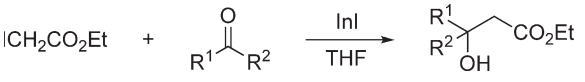
R^1	R^2	*Yield* (%)
$-(CH_2)_4-$		100
$-(CH_2)_5-$		80
Ph	H	83–100
p-MeC_6H_4	Me	59

Scheme 87



R^1	R^2	*Yield* (%)
Ph	H	97
2-(HO)C_6H_4	H	93
$Ph(CH_2)_2$	H	93
(*E*)-PhCH=CH	H	93
Me	Me	73
Ph	Me	90

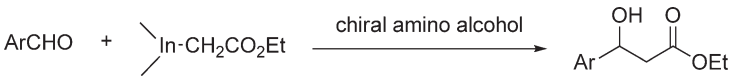
Scheme 88



R^1	R^2	*Yield* (%)
C_7H_{15}	H	69
Ph	H	75
2-(HO)C_6H_4	H	50
(*E*)-PhCH=CH	H	100
$-(CH_2)_5-$		79
$-(CH_2)_4-$		52

Scheme 89

Table 19 Indium-mediated enantioselective Reformatsky reaction. Reproduced with permission from the Royal Society of Chemistry



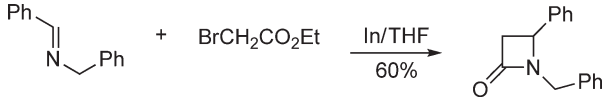
Ar	*Amino alcohol*	*Yield* (%)	*ee* (%)
PhCHO	A	63	71
PhCHO	B	57	64
p-$MeOC_6H_4CHO$	A	58	71
p-$MeOC_6H_4CHO$	B	56	63
2-Naphtaldehyde	A	90	71
2-Naphtaldehyde	B	56	57
2-Naphtaldehyde	C	69	63
2-Naphtaldehyde	D	49	49

A: cinchonine; B: cinchonidine; C: quinidine; D: quinine.

Indium enolates, prepared conveniently via transmetallation of lithium enolates with $InCl_3$, react with aldehydes to give the corresponding β-hydroxy esters (Table 20).[325]

Indium mediates the Reformatsky reaction of *p*-quinones to give good yields of *p*-quinols under mild conditions. Naturally occurring quinol esters such as jacaranone are conveniently prepared in a one-pot synthesis (Scheme 90).[326]

The indium-mediated Reformatsky reaction of phenyl α-bromoalkanoates with ketones or aldehydes gives di-, tri-, and tetrasubstituted β-lactones (Table 21).[327–329] A similar reaction of imines with ethyl bromoacetate gives 3-unsubstituted β-lactams (Equation (83)).[330,331]



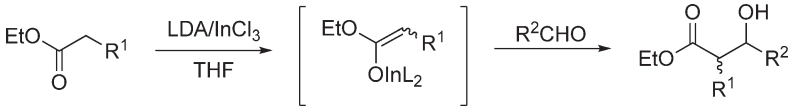
(83)

In the presence of TMSCl, the organoindium reagent derived from indium and dimethyl bromomalonate adds to a wide range of conjugated enones under mild conditions in a 1,4-fashion, to yield oxo-1,3-diesters (Scheme 91).[332]

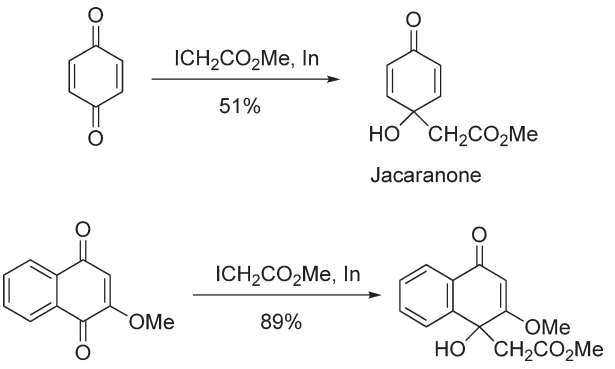
Reaction of phenacyl iodide with indium metal gives 3,4-epoxy-1,3-diphenyl-1-butanone which, on treatment with silica gel, gives 2,4-diphenylfuran and 2,4-diphenyl-4-oxobutanal (Scheme 92). Metallic indium as well as indium(I) iodide mediate the aldol condensation between α-halo ketone and aldehyde.[333]

An indium Reformatsky reagent has been prepared from 2-(chlorodifluoroacetyl)furan, which couples with aldehydes (Equation (84)).[334] A similar Reformatsky-type reaction between some β-aminovinyl chlorodifluoromethyl

Table 20 Reaction of indium enolates with aldehydes. Reproduced with permission from the Royal Society of Chemistry

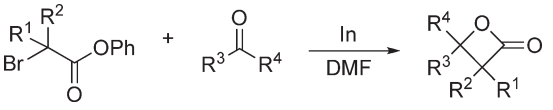


R^1	R^2	*Yield* (%)	*syn* : *anti*
H	Ph	48	
H	2-$(HO)C_6H_4$	57	
Me	Ph	79	66 : 34
Me	$Me(CH_2)_6$	88	60 : 40
Me	(*E*)-PhCH═CH	83	64 : 36
Pr^i	Ph	86	35 : 65
Bu^t	Ph	61	14 : 86

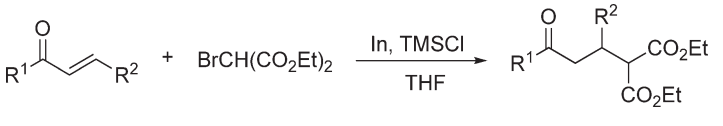


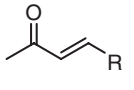
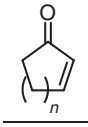
Scheme 90

Table 21 Synthesis of β-lactones. Reproduced with permission from Elsevier

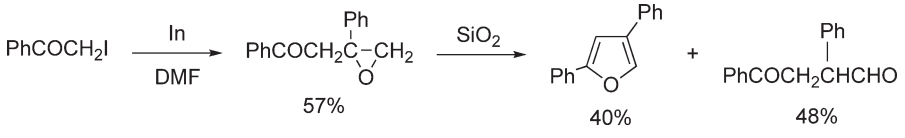


R^1	R^2	R^3	R^4	*Yield* (%)
Me	Me	Me	Me	62
Me	Me	Bu^t	H	59
H	Me	Et	Et	81
H	Me	$-(CH_2)_5-$		77
H	Bu	Et	Et	63
H	Bu	$-(CH_2)_5-$		78
H	Pr^i	Et	Et	11
H	Pr^i	$-(CH_2)_5-$		10



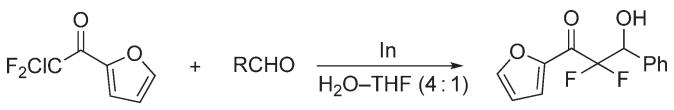
α,β-Enone	*Yield*
	R = H: 80% R = Me: 92% R = Ph: 85%
	*n* = 1: 92% *n* = 2: 92% *n* = 3: 82%

Scheme 91



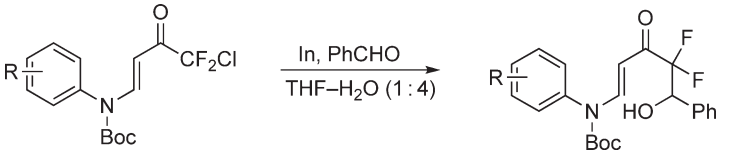
Scheme 92

ketones and aromatic aldehydes is efficiently mediated by indium to afford the corresponding difluoromethylene compounds (Equation (85)).[335]



R	*Yield* (%)
Ph	80
n-C_6H_{13}	60
(*E*)-PhCH=CH	67

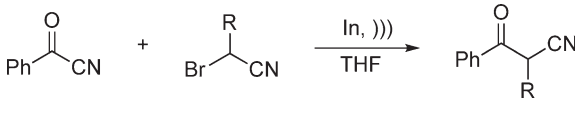
(84)



R	*Yield* (%)
o-CN	82
o-Me	82
p-Me	67

(85)

The organoindium reagent, prepared from indium metal and bromoacetonitrile, reacts with carbonyl compounds in the presence of chlorotrimethylsilane to give β-hydroxy nitriles (Scheme 93).[336,337] Similarly, indium-mediated coupling of bromoacetonitrile or 2-bromopropionitrile with a variety of aromatic acyl cyanides affords the corresponding aromatic α-cyanoketones in moderate to good yields under mild and neutral conditions (Equation (86)).[338] Carbonyl compounds are efficiently transformed into 2,2-dichloro-3-hydroxynitriles by the action of trichloroacetonitrile and indium(I) bromide (Scheme 94).[339] Bromocyanomethylation of carbonyl compounds is also achieved by the reaction of dibromoacetonitrile and indium(I) bromide.[340]



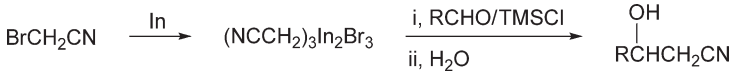
R	*Yield* (%)
R = H	65
R = Me	86

(86)

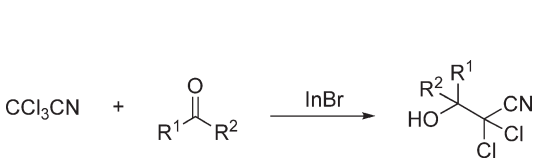
9.14.3.11 Transition Metal-catalyzed Coupling Reactions

Palladium-catalyzed cross-coupling of triorganoindium with vinyl and aryl triflates or iodides proceeds in excellent yields with high chemoselectivity (Scheme 95).[30,341–344] All the three of the organic groups attached to indium are transferred. With acid chlorides, the corresponding ketones are obtained in high yields (Scheme 96). A similar coupling can be performed in aqueous media with diorganoindium compounds under palladium catalysis.[345]

Tetraorganoindate complexes, generated *in situ* from the reaction of 1 equiv. of indium trichloride with 4 equiv. of appropriate organometallics, are efficient nucleophiles in Pd-catalyzed cross-coupling reactions. Tetraorganoindates containing methyl, primary and secondary alkyl, vinyl, alkynyl, and aryl groups transfer the four organic groups to a

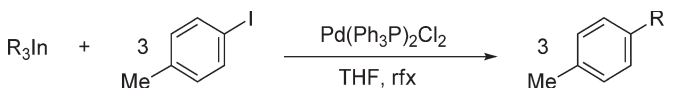


Scheme 93



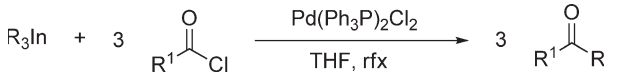
R^1	R^2	*Yield* (%)
Me_2CH	H	70
Bu^t	H	68
Ph_2CH	H	76
(*E*)-PhCH=CH	H	88
$-(CH_2)_5-$		65

Scheme 94



R	*Yield* (%)
Ph	96
CH_2=CH	89
PhC≡C	90
Me_3SiC≡C	93
Bu	82
Me	85
c-C_3H_5	92

Scheme 95

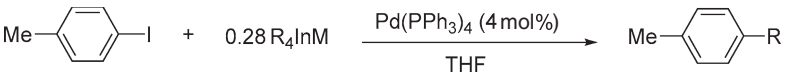


R	R^1	*Yield* (%)
Ph	Ph	89
PhC≡C	Ph	94
Me	Ph	97
Ph	Me_2C=CH	87
PhC≡C	Me_2C=CH	90
Me_3SiC≡C	Me_2C=CH	90

Scheme 96

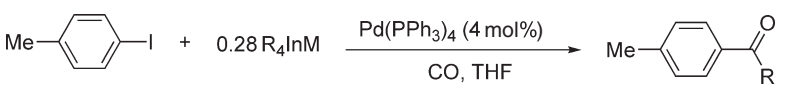
variety of electrophiles (Scheme 97). [346] Tetraorganoindates are also employed as effective nucleophilic cross-coupling partners in Pd-catalyzed carbonylative cross-coupling reactions with a variety of organic electrophiles (Scheme 98).[347]

The alkenylindium compounds, obtained by the addition of benzyl- and allylindium to alkynes, couple with organic halides in the presence of a palladium catalyst to give the three-component coupling products (Scheme 99).[286] 1,3-Dibromopropene or 3-bromo-1-iodopropene reacts with indium to give diindiopropene **87a,b**.[147,148] This dimetallic reagent reacts with two different electrophiles successively; carbonyl compounds and imines are allowed to react with **87** as the first electrophile to give vinylic indium intermediates **88**, which react with



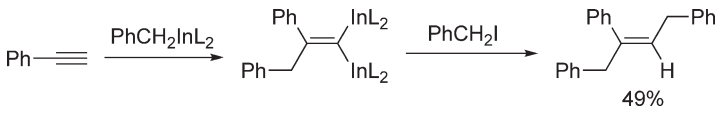
R_4InM	*Yield* (%)
Bu_4InLi	91
$Bu^i{}_4InMgBr$	68
$Bu^s{}_4InMgBr$	47
$Ph_4InMgCl$	79
$(Ph{-}{\equiv}{-})_4InLi$	98

Scheme 97



R_4InM	*Yield* (%)
Me_4InLi	85
$Pr^i{}_4InMgCl$	80
$Bu^i{}_4InMgBr$	70
$Bu^s{}_4InMgCl$	68
$(Ph{-}{\equiv}{-})_4InLi$	38
$Ph_4InMgCl$	72

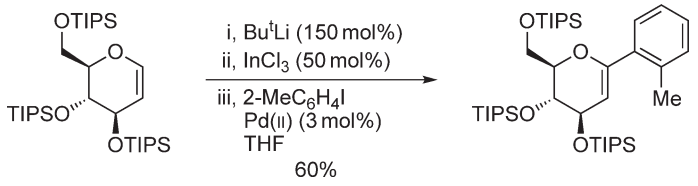
Scheme 98



Scheme 99

aryl, vinyl, or allyl halides as the second electrophile under Pd catalysis to afford a series of linear homoallyl alcohols and homoallyl amines (Scheme 100).[348,349]

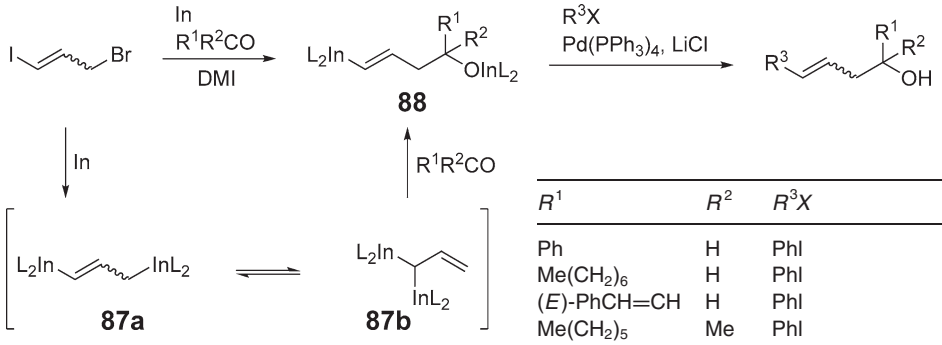
Aryl iodides and electron-deficient aryl bromides couple efficiently with *in situ* generated alkenylindium reagents in the presence of 1–5 mol% $PdCl_2(PPh_3)_2$ to produce substituted dihydropyrans with minimal (<10%) dimer formation (Scheme 101). Organoindium reagents derived from D-glucal also undergo a cross-coupling with aryl iodides to produce *C*-aryl gylcals (Equation (87)).[350]



(87)

The use of a $PdCl_2(PPh_3)_2$–$InBr_3$ reagent system catalyzes cross-coupling reactions of a variety of aryl iodides with several terminal alkynes. The corresponding functionalized alkyne derivatives are produced in good yields (Scheme 102).[351]

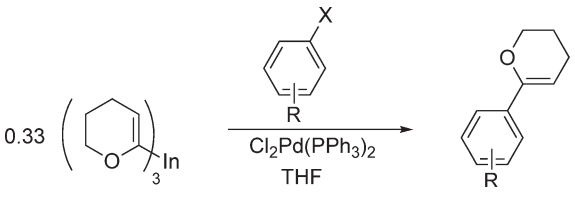
The indium-mediated palladium-catalyzed Ullmann-type coupling of aryl halides proceeds in aqueous media under air (Equation (88)).[352]



R^1	R^2	R^3X	*Yield* (%)	*E*:*Z*
Ph	H	PhI	67	85:15
$Me(CH_2)_6$	H	PhI	43	100:0
(*E*)-PhCH=CH	H	PhI	47	100:0
$Me(CH_2)_5$	Me	PhI	67	70:30
Ph	Me	PhI	81	59:41
Ph	Me	PhCH=CHBr[a]	81	68:32
Ph	Me	AllylCl	49	76:24[b]

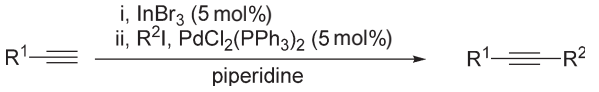
[a] *E*:*Z* = 86:14.
[b] This *E*:*Z* assignment is tentative.

Scheme 100



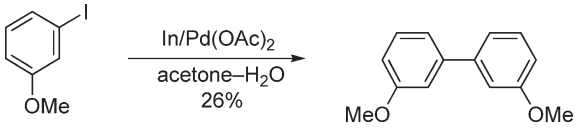
R	*X*	*Yield* (%)
4-COMe	Br	72
4-CO_2Et	Br	87
4-Cl	Br	95
H	I	100

Scheme 101



R^1	R^2	*Yield* (%)
Ph	*p*-MeC_6H_4	95
C_6H_{13}	*p*-MeC_6H_4	93
Me_3Si	*p*-$MeOC_6H_4$	79
Bu^t	*p*-$O_2NC_6H_4$	95

Scheme 102



(88)

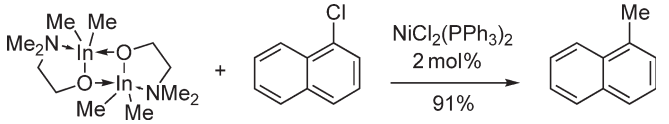
Allylindium reagents can be utilized in the Pd-catalyzed cross-coupling reaction with aryl halides. The Pd-catalyzed allylic substitution of allyl carbonate produces 1,5-dienes (Scheme 103).[353–355]

A similar Pd(0)-catalyzed allylic substitution reaction employing vinyl- and arylindium proceeds with cyclohex-2-enyl esters in the presence of 1–3 mol% $Pd_2(dba)_3$ to produce vinyl- or arylcyclohexenes **89** together with the homocoupling product **90**. The reaction proceeds with inversion of the stereochemical configuration (Scheme 104).[356]

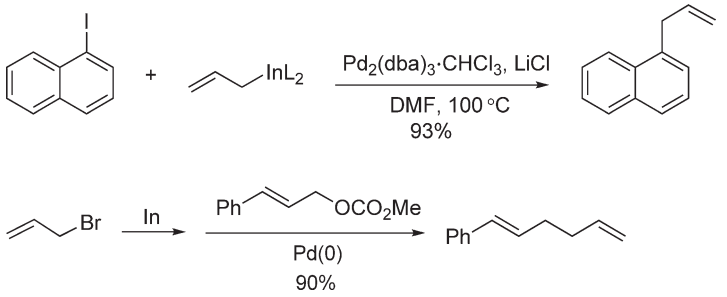
The palladium(0)-catalyzed cross-coupling reaction of allylic halides and acetates with indium organometallics is reported. In this synthetic transformation, triorganoindium compounds and tetraorganoindates (aryl, alkenyl, and methyl) react with cinnamyl and geranyl halides and acetates to afford the S_N2 products regioselectively in good yields. The reaction proceeds with net inversion of the stereochemical configuration (Scheme 105).[357]

Allenylindium reagents, generated *in situ* from the reaction of indium with propargyl bromides, can be employed as effective cross-coupling partners in palladium-catalyzed reactions with a variety of organic electrophiles to produce substituted allenes, polyallenes, unsymmetrical bisallenes in excellent yields (Table 22).[358]

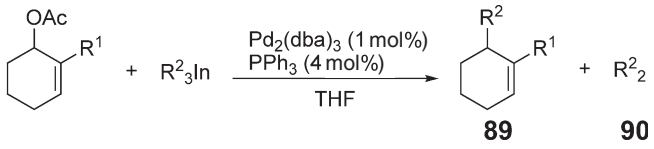
Intramolecularly stabilized alkylindiums react with chloroarenes in the presence of $NiCl_2(PPh_3)_2$ or $PdCl_2(PPh_3)_2$ to give the corresponding alkylated arenes in high yields (Equation (89)).[359–362] The nickel catalyst is equally effective as palladium for a transfer of the three organic groups of trialkylindium in the alkylation of haloarenes.[30,345] A 1,4-conjugate addition of triorganoindium to enones is promoted by a catalytic amount of $Ni(COD)_2$ (Scheme 106).[363]



(89)

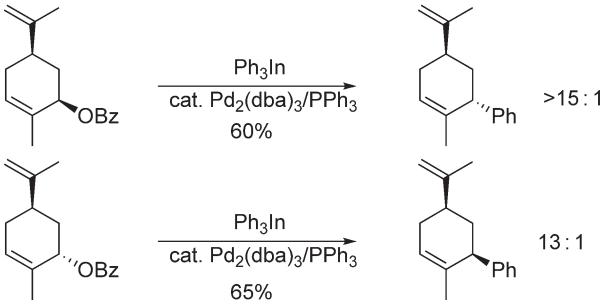


Scheme 103

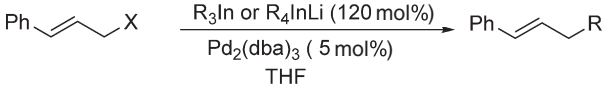


89 **90**

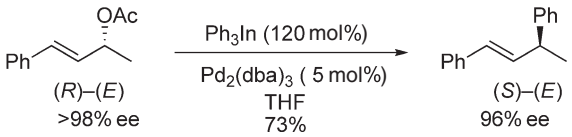
R[1]	*R*[2]	*Yield* (%) **89** : **90**
H		70 (2 : 1)
CN		89 (9 : 1)
Me		60 (>10 : 1)



Scheme 104

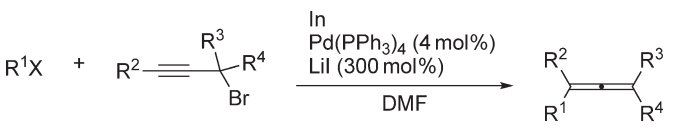


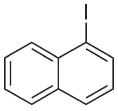
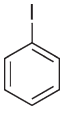
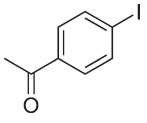
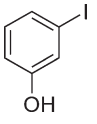
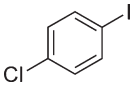
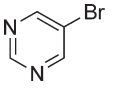
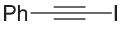
X	*R*$_3$*In or R*$_4$*InLi*	*Yield* (%)
Cl	Ph_3In	85
Cl	$(CH_2{=}CH)_3In$	55
Cl	Me_3In	63
Cl	Ph_4InLi	80
Cl	Me_4InLi	67
Cl	$(CH_2{=}CH)_4InLi$	57
Br	Ph_3In	60
Br	$(CH_2{=}CH)_3In$	62
Br	Me_3In	45
OAc	Ph_3In	70
OAc	$(CH_2{=}CH)_3In$	48
OAc	Me_3In	61



Scheme 105

Table 22 Synthesis of allenes via allenylindium reagents. Reproduced with permission from Wiles



R^1X	R^2	R^3	R^4	*Yield* (%)
	H	H	H	98
	Ph	Me	H	80
	H	H	H	87[a]
	H	H	H	90[a]
	Et	H	H	96
	Me	H	H	92
	Me	H	H	91
	Me	H	H	91

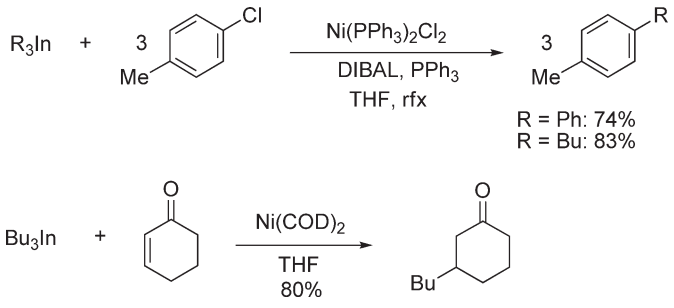
[a]LiCl was used.

9.14.3.12 Reduction

9.14.3.12.1 Reduction of carbonyl compounds

Various indium-based reductions of organic compounds have recently been developed with indium hydride reagents or by the use of the combination of indium salts with hydridosilane, -borane, and -stannane.

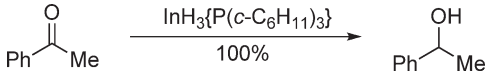
Lithium indium hydride ($LiInH_4$), prepared *in situ* by mixing LiH and $InCl_3$ in ether, readily reduces aldehydes. Reduction of ketones is less effective giving lower yields of alcohols. A carbon–carbon double bond is not reduced.[364] Acid chlorides are converted to esters with this reagent. Esters, in turn, are little affected. The reducing ability of



Scheme 106

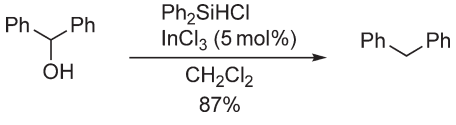
$LiInH_4$ is increased by the introduction of phenyl group(s); $LiPhInH_3$ and $LiPh_2InH_2$ readily reduce aldehydes, ketones, acid chlorides, and even esters to the corresponding alcohols. Hydroxy ketones and diketones are reduced with lithium indium hydride to give *meso*-diols selectively. α-Hydroxy ketones and α-diketones are reduced to *meso*-1,2-diols with high diastereoselectivities, whereas the selectivities of β-hydroxyketones and β-diketones are less satisfactory.[365]

Dichloroindium hydride (Cl_2InH), generated by the reaction of $InCl_3$ with tributyltin hydride, is also successfully used for the reduction of carbonyl compounds and for the debromination of alkyl bromides.[366] This reductant has features such as the chemoselective reduction of functionalized benzaldehydes, chelation-controlled reduction of benzoin methyl ether, and 1,4-reduction of chalcone. The stable carbene and tertiary phosphine adducts of indium trihydride, $InH_3\{CN(Mes)CH{=}CHN(Mes)\}$ and $InH_3\{P(c\text{-}C_6H_{11})_3\}$, reduce ketones to alcohols (Equation (90)).[367]

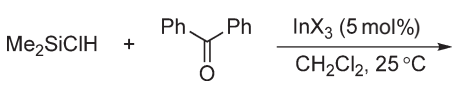


(90)

A combination of chlorodiphenylsilane and a catalytic amount (5 mol%) of $InCl_3$ is used for the reduction of alcohols (Equation (91)).[368] By using chlorodimethylsilane as a hydride source, deoxygenation of aryl ketones and secondary benzylic alcohols to the corresponding hydrocarbons proceeds in the presence of a catalytic amount of $InCl_3$. This system is selective for the reduction of a carbonyl group and the functionalities such as halogen, ester, ether, and nitro groups tolerate the reduction conditions (Equation (92)).[369] The same transformation has been accomplished with $LiAlH_4$–$InBr_3$. It provides a convenient method to complete the transformation from carbonyl compounds to alkenes (Equation (93)).[370]

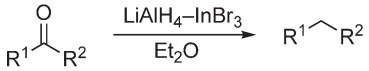


(91)



X	*Yield* (%)
Cl	99
Br	87
I	88

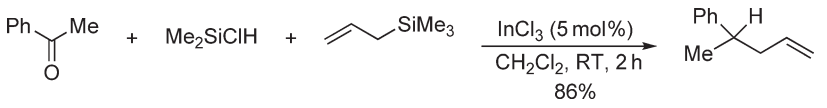
(92)



Substrate	*Yield* (%)
Acetophenone	56
Benzaldehyde	59
Cyclohexanone	82

(93)

A combination of chlorodimethylsilane and allyltrimethylsilane effectively promotes the deoxygenative allylation of aromatic ketones to terminal alkenes in the presence of a catalytic amount of $InCl_3$ (Equation (94)).[371] The choice of solvent is important; the reaction of acetophenone proceeds only in dichloromethane or 1,2-dichloroethane. Aldehydes and aliphatic ketones give complicated mixtures.



(94)

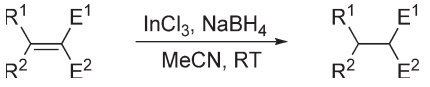
9.14.3.12.2 Hydrogenation of carbon–carbon multiple bonds

The indium hydride compound, generated *in situ* from sodium borohydride and a catalytic amount of indium(III) chloride, selectively reduces carbon–carbon double bonds in conjugated alkenes such as α,α-dicyano olefins, α,β-unsaturated nitriles, cyano esters, cyanophosphonates, diesters, and ketones (Scheme 107).[372] This combined reagent system in acetonitrile reduces exclusively the α,β-carbon–carbon double bond in $\alpha,\beta,\gamma,\delta$-unsaturated diaryl ketones, dicarboxylic esters, cyano esters, and dicyano compounds (Scheme 108).[373]

Highly regioselective radical addition of the indium hydride reagent $HInCl_2$ to alkynes has been achieved. Various functionalities are tolerant under the reaction conditions. The reaction proceeds with complete *trans*-stereoselectivity. Alkenylindium compounds obtained by this hydroindation can be employed for the subsequent cross-coupling reactions with aryl halides in one pot (Scheme 109).[374,375]

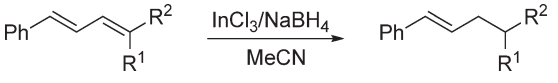
9.14.3.12.3 Dehalogenation and other reactions

Dichloroindium hydride itself is inert to the reduction of acid chlorides. However, by the addition of 20 mol% of triphenylphosphine, high yield reduction to aldehydes has been realized. (Table 23)[376] The over-reduction to alcohols is negligible. This reduction works even with a catalytic amount (10 mol%) of $InCl_3$. Neither electron-withdrawing nor -releasing substituents on aromatic acid chlorides disturb the facile formation of aldehydes. Cyano and nitro substituents tolerate the reduction conditions. Primary aliphatic acid chlorides also give good yields even when terminal olefin or chlorine substituents are present. Bulky aliphatic acid chlorides give low yields accompanied with over-reduction to alcohols. Dichloroindium hydride acts as a radical initiator for the reduction of halides with



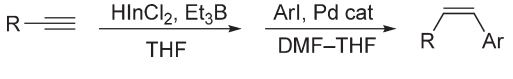
R^1	R^2	E^1	E^2	*Yield* (%)
Ph	H	CN	CN	85
H	CN	H	$PO(OMe)_2$	84
Ph	H	CN	CO_2Et	88
Ph	H	CO_2Et	CO_2Et	87

Scheme 107



R^1	R^2	*Yield* (%)
H	PhCO	91
CO_2Et	CO_2Et	89
CN	CO_2Et	86
CN	CN	97

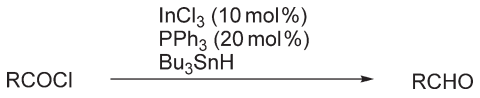
Scheme 108



R	*Ar*	*Yield* (%)	*E*:*Z*
C_6H_{13}	Ph	94	5:95
$EtO_2C(CH_2)_6$	Ph	92	3:97
$TBSO(CH_2)_3$	Ph	70	2:98
$HO(CH_2)_4$	3-$MeOC_6H_4$	99	3:97
$PhCH_2O(CH_2)_3$	3-$MeOC_6H_4$	91	20:80

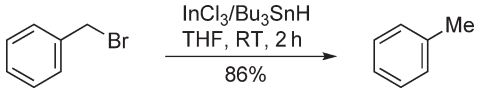
Scheme 109

Table 23 Reduction of acid chlorides to aldehydes. Reproduced with permission from Elsevier

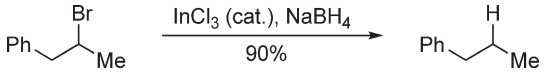


R	*Solvent*	*T* (°C)	*Yield* (%)
Ph	Toluene	−30	97
4-MeC_6H_4	Toluene	−30	93
4-ClC_6H_4	Toluene	−30	80
C_6H_{13}	Toluene	−30	93
$Cl(CH_2)_5$	THF	−30	83
$CH_2{=}CH(CH_2)_8$	THF	−30	92
$C_4H_9(C_2H_5)CH$	THF	RT	42
c-C_6H_{11}	THF	RT	62
Bu^t	THF	RT	39

tributyltin hydride. (Equation (95))[377] The $NaBH_4$–cat.$InCl_3$ system has been found to be a convenient radical reagent and been proposed as an alternative to the tributyltin hydride system. (Equation (96))[378]

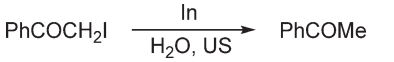


(95)

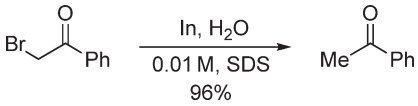


(96)

Indium metal in water reduces α-halocarbonyl compounds and benzyl iodides to the corresponding dehalogenated products in excellent yields under sonication, though simple alkyl and aryl iodides remain inert under these conditions (Equation (97)).[379] Similar dehalogenation in micellar systems in the presence of a catalytic amount of sodium dodecyl sulfate in water affords the corresponding parent carbonyl compounds in excellent yields (Equation (98)).[380] The allylic iodide or acetate is reduced by indium into the corresponding 3-methylcephems and 3-methylenecephams in an aqueous system. The latter are converted into the former quantitatively under basic conditions (Scheme 110).[381]

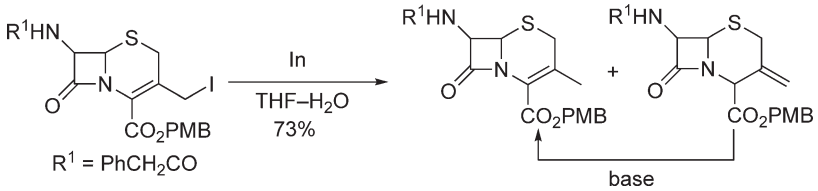


(97)

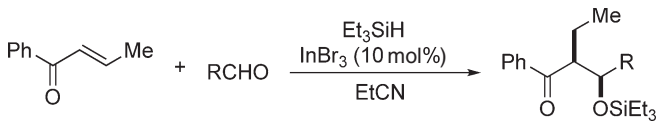


(98)

The Et_3SiH-promoted diastereoselective reductive aldol reaction proceeds by using $InBr_3$ as a catalyst. This three-component reaction affords only silyl aldolates as products without any side-reaction. The *syn*-selectivity obtained here is higher than that of any other reductive aldol reactions (Scheme 111).[382] A catalytic amount of $In(OAc)_3$ also promotes

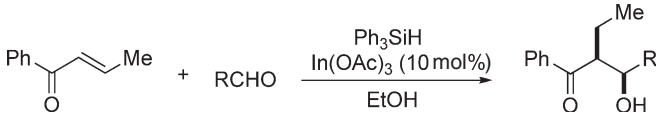


Scheme 110



R	*Yield* (%)	*syn : anti*
4-$MeOC_6H_4$	75	90 : 10
Ph	78	92 : 8
$PhCH_2$	40	>99 : 1
Bu^t	73	>99 : 1

Scheme 111



R	*Yield* (%)	*syn : anti*
1-Naphthyl	83	92 : 8
Ph	84	92 : 8
4-$MeOC_6H_4$	96	96 : 4
4-NCC_6H_4	85	69 : 31
C_7H_{15}	66	77 : 23
c-C_6H_{11}	37	72 : 28

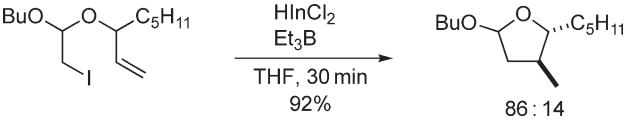
Scheme 112

1,4-reduction of certain α-enones with Ph_3SiH in ethanol at ambient temperature. The intermediary enolates can be used for inter- and intramolecular aldol reactions and intramolecular Michael addition (Scheme 112).[383]

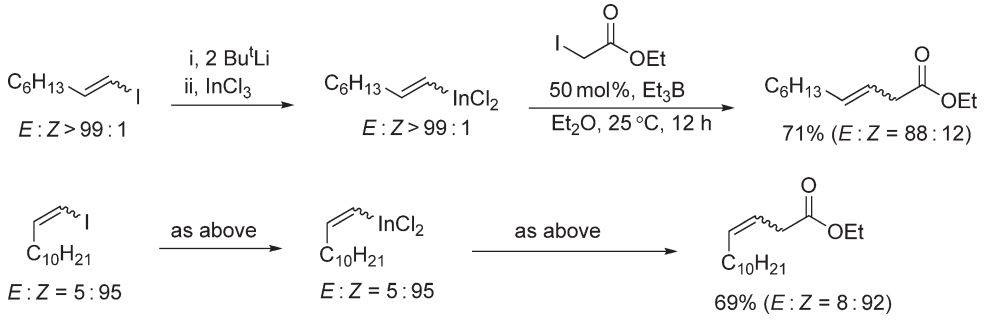
9.14.3.13 Carbon–Carbon Bond Formation via Radical Reactions

The alkenylation reaction of α-halo carbonyl compounds with alkenylindium in the presence of triethylborane proceeds via a radical process. Unactivated alkene moieties as well as a styryl group can be introduced by this method. The geometry of the carbon–carbon double bonds of the alkenylindium is retained. Preparation of alkenylindium via hydroindation of 1-alkyne followed by the radical alkenylation establishes an efficient one-pot strategy (Scheme 113).[384]

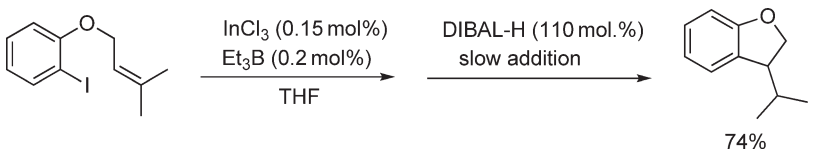
Dichloroindium hydride $HInCl_2$, prepared from indium(III) chloride and DIBAL-H, works as a radical mediator. This compound reduces aryl iodides and bromides in the presence of Et_3B as a radical initiator. Reduction of iodoacetals provides cyclized products in good yields (Equation (99)).[385] Only a catalytic amount of $InCl_3$ is necessary for complete consumption of the starting compound with stoichiometric DIBAL-H as a hydride source (Equation (100)).



(99)



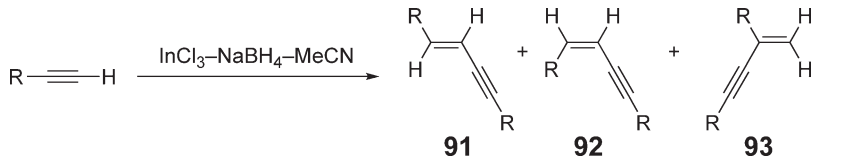
Scheme 113



(100)

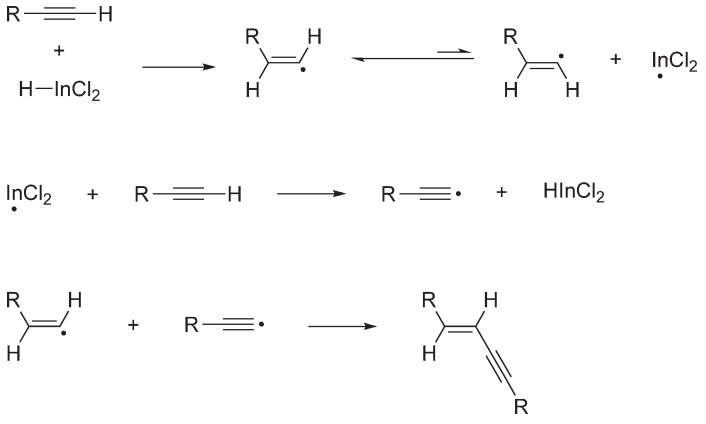
The $InCl_3$–$NaBH_4$–MeCN system shows high regio- and stereoselectivity for the dimerization of terminal alkynes to give enynes **91–93** (Scheme 114). The reaction is considered to proceed via the radical addition and coupling mechanism (Scheme 115).[386]

Indium-mediated radical cyclization reactions of aliphatic iodoalkynes proceeds with a catalytic amount of In and I_2. Iodoalkyne **94** undergoes an atom-transfer 5-exo cyclization to give five-membered iodoalkene. In contrast, the reaction with In (200 mol%) and I_2 (100 mol%) yields the reductive 5-*exo*-cyclization product via the same 5-*exo*-cyclization (Scheme 116).[387–389] The existence of a vinylindium intermediate formed via the radical **95** has been confirmed by a Pd-catalyzed cross-coupling reaction (Scheme 117).[390]

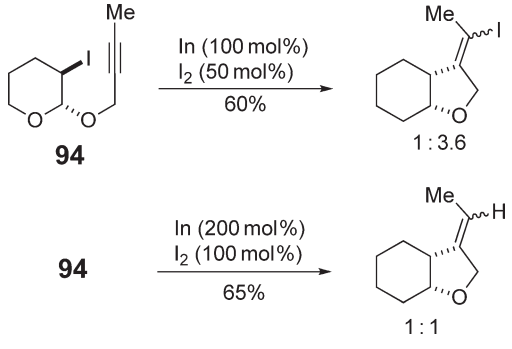


R	*Yield* (%)	**91**:**92**:**93**
Ph	86	92:2:6
Me_2CH	85	91:6:3
Bu^t	78	93:2:5
Bu	81	90:4:6

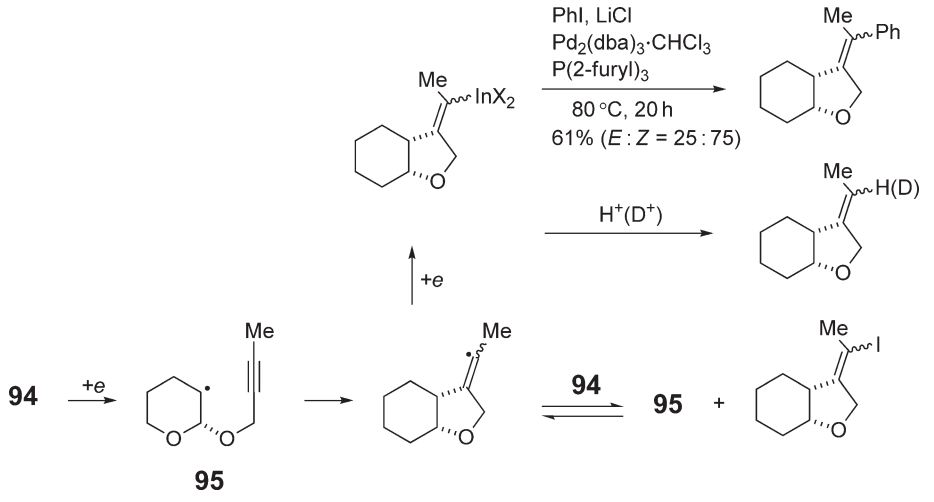
Scheme 114



Scheme 115



Scheme 116



Scheme 117

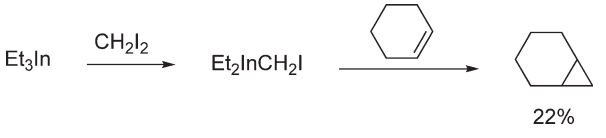
9.14.3.14 Other Reactions

9.14.3.14.1 Cyclopropanation

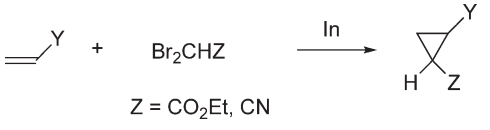
(Iodomethyl)diethylindium undergoes a cyclopropanation reaction with alkenes (Scheme 118).[391] Cyclopropanation of electron-deficient alkenes and the Wideqvist-type transformation of ketones and aldehydes to cyclopropanes are achieved by the action of active methylene compounds with indium.[392] The organoindium reagents derived from ethyl dibromoacetate and dibromoacetonitrile readily reacts with electron-deficient alkenes giving the corresponding cyclopropane. The yields are generally lower than those of the dibromoactive methylene cases (Scheme 119).[147]

9.14.3.14.2 Allylic alkylation

Indium ate complexes (indates) bearing methyl and alkenyl groups have been prepared and both the tendency of emigration and regioselectivity toward cinnamyl bromide have been investigated (Scheme 120). The alkenyl group is

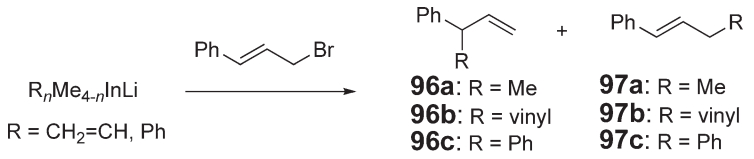


Scheme 118



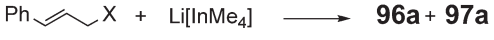
Dibromo compound	*Alkene*	*Yield* (%)	*cis : trans*
Br_2CHCO_2Et	$PhCH{=}C(CN)_2$	69	49 : 51
	$EtCH{=}CH(CN)CO_2Et$	65	57 : 43
Br_2CHCN	$PhCH{=}C(CN)_2$	60	17 : 83
	$EtCH{=}CH(CN)CO_2Et$	42	44 : 56

Scheme 119



Indate	*Solvent*	**96a : 97a : 96b : 97b**	**a : b**	**96 : 97**
$(CH_2{=}CH)_3MeInLi$	THF-Et_2O (1 : 1)	8 : 5 : 21 : 35	19 : 81	42 : 58
	THF-Et_2O-hexane (1 : 5 : 5)	1 : 38 : 1 : 40	49 : 51	2 : 98
$PhMe_3InLi$	THF-*c*-hexane-Et_2O (4 : 7 : 3)	40 : 10 : 9 : 21[a]	62 : 38[b]	61 : 39

[a]**96a : 97a : 96c : 97c**; [b]**a : c**.



X	*Solvent*	*Yield* (%)	**96a : 97a**
Cl	Et_2O	53	<1 : >99
Br	Et_2O	78	0 : 100
I	Et_2O	80	<1 : >99
OC(O)OEt	Et_2O	26	0 : 100
$OP(O)(OEt)_2$	Et_2O	73	0 : 100
OAc	Et_2O	22	<1 : >99
Cl	THFEt_2O (1 : 1)	72	37 : 63
Br	THF–Et_2O (1 : 1)	95	91 : 9
I	THF–Et_2O (1 : 1)	47	74 : 26
$OP(O)(OEt)_2$	THF–Et_2O (1 : 1)	59	61 : 39
OAc	THF–Et_2O (1 : 1)	22	<1 : >99

Scheme 120

more preferably transferred than the Me group, giving a regioisomeric mixture of S_N2'- **96** and S_N2-products **97**. The ratio of S_N2'/S_N2-selectivity can be controlled by solvents; in the presence of polar solvents, such as THF and *N*-butylpyrrolidinone (NBP), the S_N2'-product is mainly obtained, whereas the S_N2-product is selectively produced in less polar solvents. The leaving group also affects the regioselectivity.[393]

2,3-Unsaturated-*C*-aryl glycopyranosides are useful intermediates in the synthesis of medicinally important *C*-aryl glycosides. Treatment of glycal acetates with triarylindium in ether at room temperature gives good yields of *C*-aryl-$\Delta^{2,3}$-glycosides of α-configuration predominantly (Table 24). The mechanism of this reaction very likely involves the formation of an oxocarbenium ion intermediate via indium(III) Lewis acid-assisted ionization of the glycal C3 acetate. Coupling of trivinyl- and trialkynylindium with glycals similarly leads to *C*-vinyl- and *C*-alkynyl-$\Delta^{2,3}$-glycosides in good yields.[394]

9.14.3.14.3 Alkynylation

Indium trichloride promotes catalytically the addition of alkynylstannanes to aldehydes (Table 25).[42] Metallic indium also mediates the same Barbier-type coupling between alkynyl halides and aldehydes or ketones to give secondary or tertiary propargyl alcohols (Table 26). Secondary alcohols can be oxidized *in situ* according an Oppenauer process.[395] Thus, alkynyl ketones have been prepared from aldehydes via an indium-mediated alkynylation reaction followed by an indium-mediated Oppenauer oxidation. They are also obtained via an indium-mediated alkynylation of the relevant acyl chlorides (Table 27).[396]

The use of a novel $InBr_3$–Et_3N reagent system allows addition reactions of 1-alkynes not only to a variety of aromatic or bulky aliphatic aldehydes, but also to *N,O*-acetals. The corresponding propargylic alcohols or amines are formed in good to excellent yields (Table 28).[397]

Table 24 Synthesis of *C*-arylglycosides with triarylindium. Reproduced with permission from Elsevier

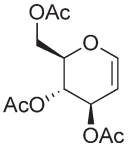
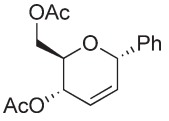
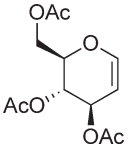
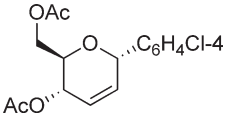
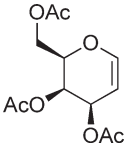
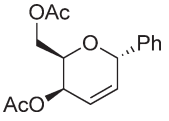
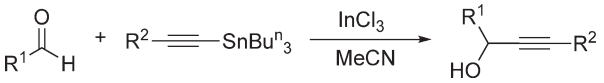
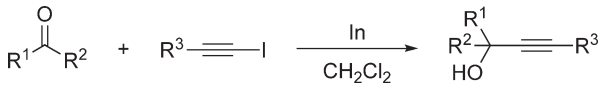
Substrate	*Product*	*Yield* (%) (α : β)
		95 (5 : 1)
		89 (6 : 1)
		50 (10 : 1)

Table 25 Alkynylation of aldehydes with alkynylstannanes. Reproduced with permission from Elsevier



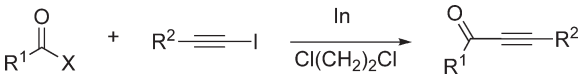
R^1	R^2	*Yield* (%)
Ph	Ph	92
Ph	Pr^n	100
Et	Ph	88
Bu^t	Ph	78
MeCH═CH	Ph	64
MeCH═CH	Pr^n	79

Table 26 Alkynylation of carbonyl compounds with alkynyl iodides. Reproduced with permission from Elsevier



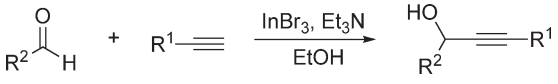
R^1	R^2	R^3	*Yield* (%)
Ph	H	Ph	83
$Me(CH_2)_6$	H	Ph	87
$-(CH_2)_5-$		Ph	94
Et	Et	Ph	89
Ph	H	$Me(CH_2)_3$	83
c-C_6H_{11}	H	$Me(CH_2)_3$	90
$-(CH_2)_5-$		$Me(CH_2)_3$	97

Table 27 Synthesis of alkynylketones. Reproduced with permission from Elsevier



R^1	R^2	X	*Yield* (%)
Ph	Ph	H	86
c-C_6H_{11}	Ph	H	84
Ph	Bu	H	83
C_9H_{19}	Ph	Cl	80
Bu^t	Ph	Cl	82
Ph	Ph	Cl	50
Bu^t	Bu	Cl	55

Table 28 Alkynylation of aldehydes with 1-alkynes. Reproduced with permission from Elsevier

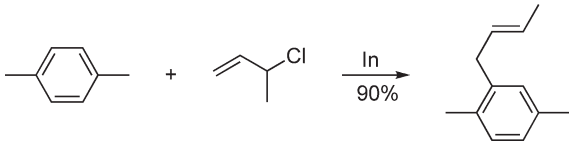


R^1	R^2	*Yield* (%)
C_6H_{13}	*p*-NCC_6H_4	99
Ph	PhCH═CH	46
Ph	3-Pyridyl	99
Ph	2-Thienyl	57
Ph	2-Furyl	93

9.14.3.14.4 Miscellaneous reactions

The reaction of tri-*sec*-butylindium with tetrachloroethylene affords 3-methyl-1,1,2-trichloro-1-pentene and indium trichloride without the use of any catalyst and solvent. Other trialkylindium gives similar results (Table 29). The yield of the product based on the amount of trialkylindium used reaches 287%. This fact shows that all three alkyl groups attached to indium are effectively transferred to the product. Several haloalkenes lead to the selective formation of cross-coupling products under similar conditions. A stereospecific cross-coupling with (*E*)-*β*-bromostyrene gives (*E*)-*β*-*sec*-butylstyrene. In contrast, starting from both (*E*)- and (*Z*)-1,2-dichloroethylene, a mixture of (*E*)- and (*Z*)-l-chloro-3-methyl-1-pentene has been obtained in a ratio of 6 : 4.[398]

The direct allylation of aromatic compounds with allylic chlorides is achieved in the presence of a catalytic amount of indium metal. According to the authors, indium is considered to act as a Lewis acid (Equation (101)).[399] Trialkylindiums react with acid chlorides to give ketones. When trialkylindiums are treated with air prior to the reaction with acid chlorides, esters are formed (Scheme 121).[400] The reaction of cyclopentadienylindium(I) with aldehydes in aqueous media gives mixtures of the isomeric coupling products (Equation (102)).[401]



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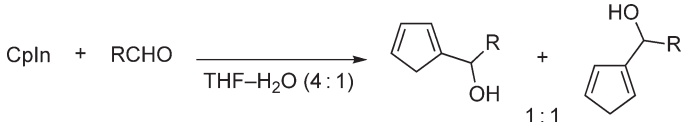
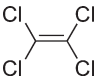
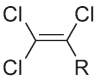
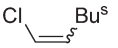
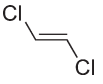
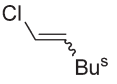
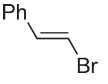
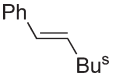
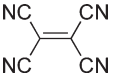
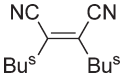
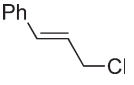
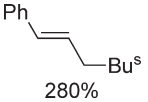
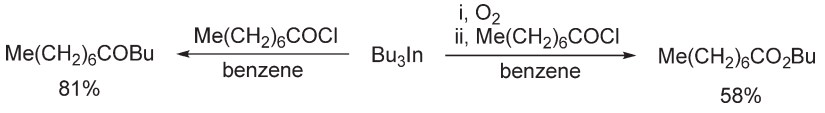


R	*Yield* (%)
C_5H_{11}	51
Ph	60
c-C_6H_{11}	51

(102)

Table 29 Alkylation of haloalkenes. Reproduced with permission from ACS Publications

Starting alkene	*Product and yield (%)*
	 R = Bu^s: 287% R = Bu^n: 252% R = Pr^i: 261%
	 240% (*E* : *Z* = 61 : 39)
	 284% (*E* : *Z* = 67 : 33)
	 206%
	 112%
	 280%



Scheme 121

9.14.4 Preparation and Reactions of Organogallium Compounds

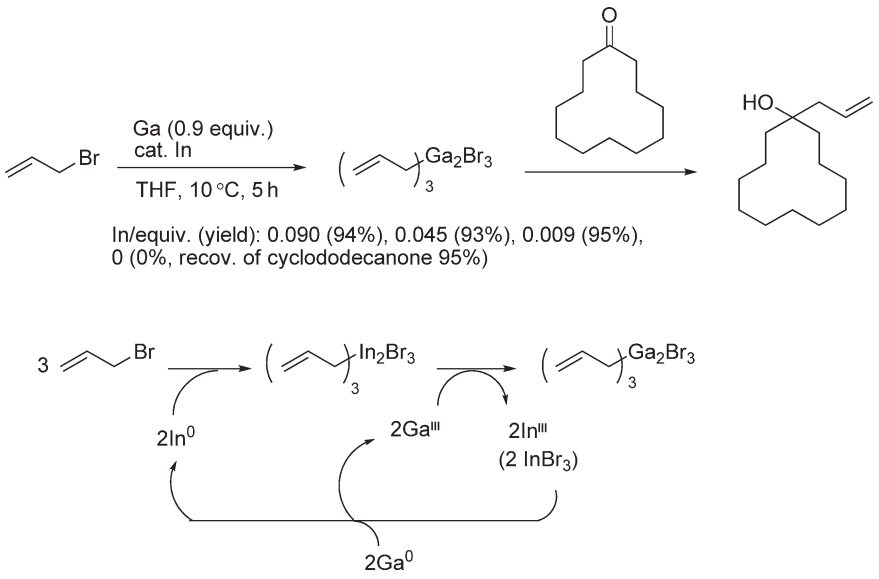
9.14.4.1 Preparation of Organogallium Compounds

9.14.4.1.1 Oxidative addition to organic halides

Allylgallium and propargylgallium compounds can be prepared by the direct reaction of the corresponding bromides or iodides with gallium metal.[402,403] Gallium enolates are also prepared from α-halo carbonyl compounds with gallium.[404]

9.14.4.1.2 Transmetallation

Triphenylgallium is prepared by a transmetallation of diphenylmercury with metallic gallium.[405] Treatment of alkenyl- and allylmagnesium with gallium trichloride gives the corresponding organogallium compounds.[406,407] Various organosilanes are transmetallated to organogallium compounds with gallium trichloride.[408] Tetraorganogallium ate complexes are prepared *in situ* by the addition of an organolithium reagent to triorganogallium compounds.[409]



Scheme 122

Allylgallium sesquibromides can be prepared from allylic bromides and metallic gallium in the presence of a catalytic amount of indium, where the initially formed allylindium is converted to allylgallium. Fast transmetallation of an allyl group from indium to gallium accelerates the formation of allylgallium sesquibromide (Scheme 122).[410,411]

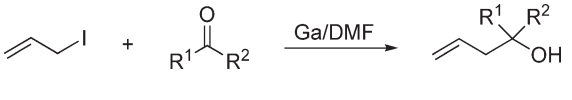
9.14.4.2 Reaction of Organogallium Compounds

9.14.4.2.1 Addition to carbonyl compounds

Organogallium compounds are good nucleophiles for performing addition reactions to carbonyl functionalities. Alkylation, allylation, aldol condensation, and the Reformatsky reaction proceed readily with organogallium reagents.

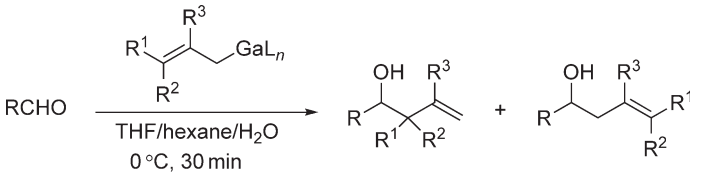
Triphenylgallium, prepared from gallium metal and diphenylmercury, reacts with benzaldehyde at elevated temperature to give benzhydrol in 70% yield. Benzalacetophenone gives β,β-diphenylpropiophenone (85% yield), and benzophenone is formed (79% yield) from benzoyl chloride. All the three phenyl groups of triphenylgallium are available in these reactions.[405] Gallium metal readily promotes the allylation of aldehydes with allyl iodide under Barbier conditions. α,β-Unsaturated carbonyl compounds undergo only 1,2-addition (Scheme 123).[402] Allylic gallium reagents, prepared from gallium trichloride and the corresponding allylic Grignard reagents, allylate carbonyl compounds in good yields in an aqueous medium as well as in organic solvent (Scheme 124).[406]

Gallium-mediated allylation of aldehydes or ketones in water gives the corresponding homoallyl alcohols in high yields without the assistance of either acids or sonication. The diastereoselectivity of the allylation of 2,3-dihydroxypropanal depends on the solvent. When the reaction is carried out in water, the dominant product is the *syn*-isomer. In contrast, the *anti*-isomer is dominant when THF is employed. The *syn*-isomer may be regarded as the chelation-controlled product, due to the hydrogen bond between the two hydroxy groups. The aqueous environment favors



R^1	R^2	*Yield* (%)
C_8H_{17}	H	88
Ph	H	98
PhCH=CH	H	76
C_6H_{13}	Me	75
Ph	Me	57
PhCH=CH	Me	78

Scheme 123

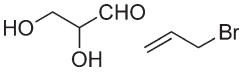
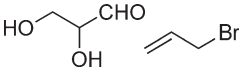
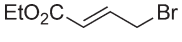


R	R^1	R^2	R^3	*Yield* (%)
Ph	H	H	H	97
Ph	Me (H)	H (Me)	H	90[a]
Ph	Me	Me	H	81[b]
Ph	H	H	Me	97
C_9H_{19}	Me	Me	H	90[c]

[a] *erythro*: *threo*: α = 47 : 42 : 11; [b] γ : α 98 : 2; [c] γ : α = 89 : 11.

Scheme 124

Table 30 Gallium-mediated allylation of aldehydes[a]. Reproduced with permission from Elsevier

Aldehyde	*Halide*	*Solvent*	*Yield* (%)	*syn* : *anti*
		H_2O	86	8.3 : 1
		THF	74	1 : 4.2
PhCHO		H_2O	67	1 : 2.2

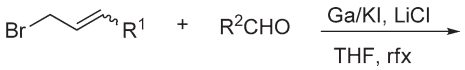
chelation of the α-hydroxyl group. Steric hindrance also governs the diastereoselectivity; benzaldehyde reacts with ethyl 4-bromobutenoate in water to give rise to the *anti*-isomer predominantly (Table 30).[412]

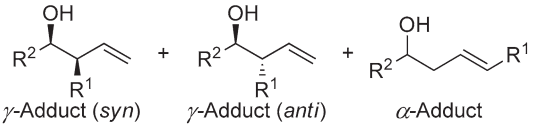
In the presence of potassium iodide and lithium chloride, the reaction of gallium powder, allylic bromides, and aldehydes shows very high selectivity favoring γ-adducts. Under the same conditions, the reaction of propargyl bromide with aldehydes exhibits high acetylenic selectivity (α-adducts), although the regioselectivity drops to almost 1 : 1 with 1-bromo-2-butyne (Scheme 125).[413] On the contrary, γ-(trimethylsilyl)allyl bromide exhibits very high selectivity favoring α-adducts **98** and **99**. The ratios of (*E*)- and (*Z*)-isomers **98**/**99** are generally greater than 90 : 10, irrespective of the isomer proportion of the starting bromide.[403] Trimethylsilylpropargyl bromide shows very high acetylenic selectivity (α-adducts **100**) over allenic γ-adducts **101** (Scheme 126).

The straightforward addition of 1-alkynes to aldehydes mediated by GaI_3 and an amine gives propargylic alcohols in moderate to high yields (Scheme 127).[414]

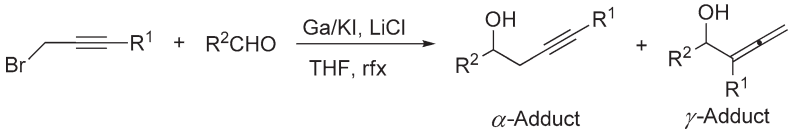
Triorganogallium and -indium reagents react with α,β-unsaturated nitrile, ketone, and ester to give 1,4-addition products regioselectively (Table 31). In contrast, the reaction of allylgallium and allylindium sesquihalides with α,β-unsaturated carbonyl compounds proceed in a 1,2-addition mode, whereas 1,4-addition takes place with α,β-unsaturated nitriles.[294]

Tetraorganogallium ate complexes (gallates), prepared *in situ* by addition of organolithium reagents to triorganogallium, react smoothly with α,β-unsaturated compounds to give Michael addition products in high yields. Alkyl/phenyl mixed gallates display high selectivity in the transfer of the phenyl ligand (Table 32).[415] Tetraorganogallium





R^1	R^2	*Yield* (%)	$\gamma:\alpha$	*syn*:*anti*
Me	Ph	94	>99:1	54:46
Me	*p*-ClC_6H_4	91	>99:1	59:41
Pr	*p*-ClC_6H_4	87	79:21	40:60
Ph	*p*-ClC_6H_4	81	60:40	5:95

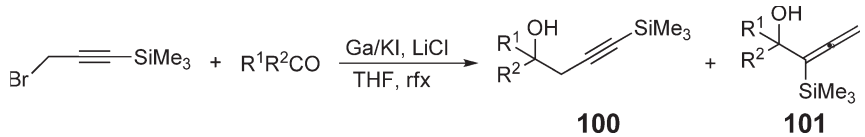


R^1	R^2	*Yield* (%)	$\alpha:\gamma$
H	Ph	90	>99:1
H	*c*-C_6H_{11}	89	>99:1
Me	*c*-C_6H_{11}	96	48:52

Scheme 125

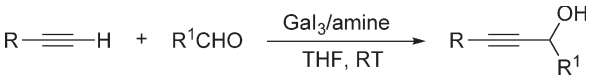
R^1R^2CO	*Time* (h)	*Ratio* **98**:**99**[a]	*Yield* (%)[a]
PhCHO	2	91:9 (91:9)	95 (93)
p-ClC_6H_4CHO	1.5	92:8 (92:8)	96 (97)
$(CH_2)_5CO$	2	85:15 (85:15)	90 (88)

[a]The data in the parentheses show the results with (trimethylsilyl)allyl bromide (*E*:*Z* = 37:63) as the starting material.



R^1R^2CO	*Time* (h)	*Ratio* **100**:**101**	*Yield* (%)
PhCHO	2	>99:1	92
PhCH=CHCHO	3	98:2	78
c-$C_6H_{11}CHO$	3	98:2	89
$C_5H_{11}CHO$	3	97:3	87
$(CH_2)_5CO$	5	>99:1	85
PhCOMe	5	>99:1	87

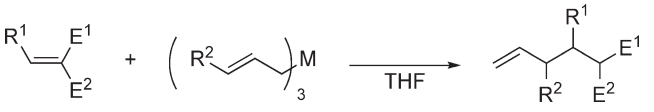
Scheme 126



R	R^1	*Amine*	*Yield* (%)
Ph	Bu^t	DBU	8
Ph	Bu^t	Pyridine	5
Ph	Bu^t	Bu_3N	85
C_5H_{11}	Ph	Bu_3N	64
C_5H_{11}	Bu^t	Bu_3N	74

Scheme 127

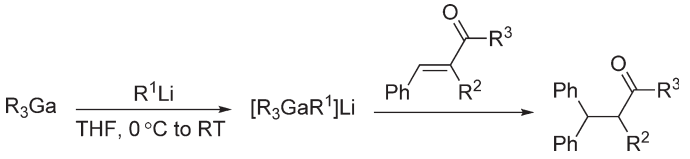
Table 31 Addition of triallylgallium to alkenes. Reproduced with permission from Elsevier



R^1	E^1	E^2	R^2	*Yield* (%)[a]
Et	CN	CN	H	76
Ph	CN	CN	H	78
Ph	CN	CN	Ph	76 (70 : 30)
Ph	COMe	COMe	H	95
Ph	CO_2Et	CO_2Et	H	89
Ph[b]	COMe	CO_2Et	H	95 (61 : 39)

[a]Figures in parentheses refer to diastereomeric ratio.
[b]Alkene ($E:Z = 54:46$) was used.

Table 32 Addition of gallates to α,β-unsaturated carbonyl compounds. Reproduced with permission from Taylor and Francis Group



Substrate	*Gallate*	*Yield* (%)
(*E*)-PhCH═CHCOPh	$[Ph_3GaMe]Li$	85
(*E*)-PhCH═CHCOPh	$[Ph_3GaBu]Li$	85
(*E*)-PhCH═CHCOPh	$[Bu_3GaPh]Li$	79
(*E*)-PhCH═CHCOMe	$[Ph_3GaMe]Li$	67 (8)[a]
(*E*)-PhCH═CHCOMe	$[Ph_3GaBu]Li$	74 (6)[a]
$PhCH═C(CO_2Et)_2$	$[Ph_3GaBu]Li$	95

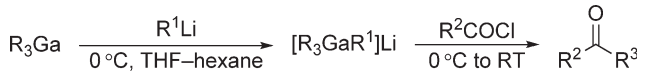
[a]Figures in parentheses refer to the yields of the Ph transfer 1,2-adduct.

ate complexes also react with acyl chlorides to yield ketones in high yields. Again, mixed ate complexes display high selectivity in the transfer of their ligands (Table 33).[409]

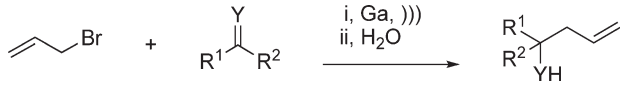
With an application of sonic energy under solvent-free conditions, gallium metal is effective in mediating the allylation of various carbonyl compounds and imines affording the corresponding homoallylic alcohols and amines, respectively. The imines themselves can also be prepared neat in high yields, thereby establishing a two-step solvent-free synthesis of allylated species via an iminium ion intermediate[254] (Scheme 128).

Homoallylic hydroxylamines and homoallylic hydrazines are synthesized in excellent yields from aldonitrones and hydrazones in aqueous media with allylgallium reagent in the presence of 0.1 equiv. of NH_4Cl or Bu_4NBr. The reaction rate can be increased dramatically under microwave activation (Scheme 129).[416]

Table 33 Reaction of gallates with acyl chlorides. Reproduced with permission from Elsevier

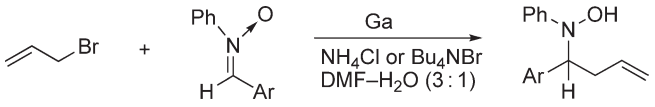


Reagent	R^2	R^3	*Yield* (%)
$[Ph_3GaBu]Li$	Me	Ph	88
$[Ph_3GaMe]Li$	Me	Ph	84
$[Ph_3GaBu]Li$	$PhCH_2$	Ph	82
$[Bu_4Ga]Li$	Ph	Bu	83
$[Ph_3GaBu]Li$	Ph	Ph	90
$[(PhCH_2)_3GaBu]Li$	Ph	$PhCH_2$	58
$[(PhCH_2)_3GaPh]Li$	Ph	$PhCH_2$	69
$[Et_3GaPh]Li$	Ph	Ph	79

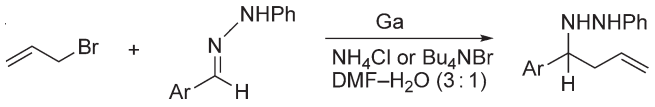


R^1	R^2	*Y*	*Yield* (%)
Ph	H	O	97
PhCH=CH	H	O	74
Ph	Me	O	34
Ph	H	NPh	94
PhCH=CH	H	$N(CH_2)_2Ph$	32

Scheme 128

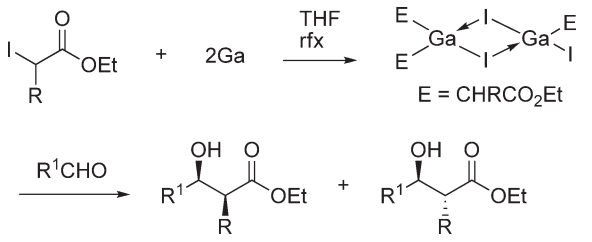


Ar	*Conditions*	*Yield* (%)
Ph	RT, 6 h	65
Ph	Microwave, 4 min	90
$4\text{-}ClC_6H_4$	RT, 7 h	68
$4\text{-}ClC_6H_4$	Microwave, 5 min	92



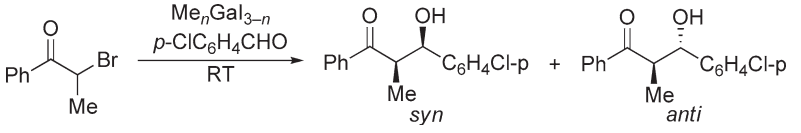
Ar	*Conditions*	*Yield* (%)
Ph	RT, 6 h	62
Ph	Microwave, 5 min	80
$4\text{-}ClC_6H_4$	RT, 7 h	60
$4\text{-}ClC_6H_4$	Microwave, 5 min	92

Scheme 129



R^1	R	Lewis acid	Yield (%)	syn : anti
Ph	H	None	91	–
Ph	Me	None	94	87 : 13
4-ClC_6H_4	Me	None	93	81 : 19
4-ClC_6H_4	Me	LiCl	80	50 : 50
4-ClC_6H_4	Me	$MgBr_2$	78	53 : 47
4-ClC_6H_4	Me	$BF_3{\cdot}OEt_2$	75	66 : 34
Ph	Et	None	92	71 : 29
4-ClC_6H_4	Et	None	82	74 : 26

Scheme 130



Solvent	n	Yield (%)	syn : anti
THF	1	96	25 : 75
DMF	1	95	95 : 5
DME	1	92	46 : 54
Dioxane	1	88	28 : 72
THF	2	98	20 : 80

Scheme 131

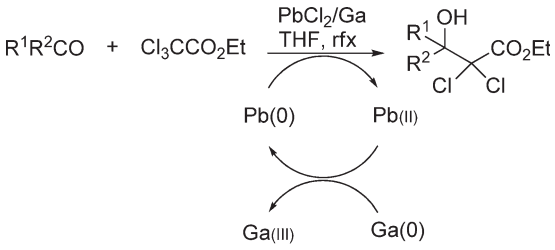
The gallium-mediated Reformatsky reaction gives β-hydroxy esters in excellent yields with *syn*-selectivity. The effect of the molar ratio of gallium : α-iodoacetate : 4-chlorobenzaldehyde shows that the stoichiometric ratio may be 1 : 1.5 : 1 and two-thirds of the CH_2CO_2Et group react with the aldehyde. Some Lewis acids obviously affect the stereochemistry of the reaction (Scheme 130).[404]

Treatment of α-bromo ketone with gallium triiodide or methylgallium iodide provides the corresponding gallium enolate, which reacts with carbonyl compounds and imines to give β-hydroxy ketones and β-amino ketones, respectively, in moderate yields (Scheme 131).[417]

In the presence of a redox system $PbCl_2$/Ga, carbonyl compounds react with trichloroacetate and iodoacetonitrile to afford β-substituted α,α-dichloropropionates and β-hydroxy nitriles, respectively, in moderate to excellent yields (Schemes 132 and 133).[418]

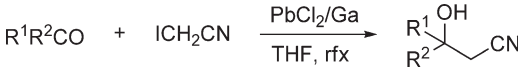
9.14.4.2.2 Carbogallation

Facile carbogallation reactions of organogallium compounds to carbon–carbon triple bonds are one of characteristic features of organogallium reagents. Yamaguchi has found that the treatment of alkynylsilanes with $GaCl_3$ in hydrocarbon solvents furnishes enynes. When the reaction of 1-(trimethylsilyl)-1-heptyne is quenched with D_2O, the corresponding 1,1-dideuterioenyne is formed, confirming that the present dimerization involves transmetallation of



Carbonyl compound	*Time* (h)	*Yield* (%)
4-ClC_6H_4CHO	6	72
4-FC_6H_4CHO	7	60
4-BrC_6H_4CHO	6	80
PhCHO	10	61
4-MeC_6H_4CHO	12	58
(*E*)-PhCH=CHCHO	11	67
Decanal	10	75
Propionaldehyde	12	67
Acetone	10	62

Scheme 132



Carbonyl compound	*Time* (h)	*Yield* (%)
4-ClC_6H_4CHO	5	98
4-FC_6H_4CHO	4	99
4-BrC_6H_4CHO	4	99
PhCHO	6	92
4-MeC_6H_4CHO	8	94
(*E*)-PhCH=CHCHO	7	70
Decanal	5	98
PhCOMe	5	98
4-ClC_6H_4CHO	5	55[a]

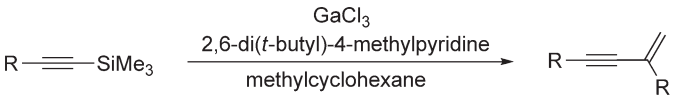
[a]Without $PdCl_2$.

Scheme 133

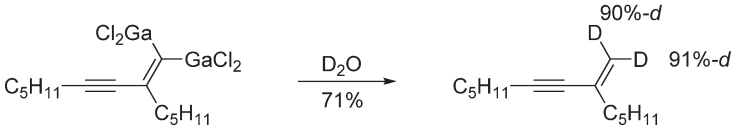
alkynylsilane to alkynylgallium and the carbogallation of the latter yielding 1,1-digallo-1-buten-3-ynes (Scheme 134).[419]

Reaction of alkynes with allyltrimethylsilane mediated by $GaCl_3$ gives 1,4-dienes via allylgallation of allylgallium formed *in situ* (Scheme 135).[408] Allylic gallium sesquibromides, prepared from allylic bromides and gallium metal in the presence of a catalytic amount of indium, similarly add to terminal alkynes with the aid of a tertiary amine to give 1,4-dienes (Scheme 136). The intermediate *gem*-digallium compound has been confirmed by trapping it with iodine to yield 1,1-diiodo-1,4-alkadiene (Scheme 137).[411]

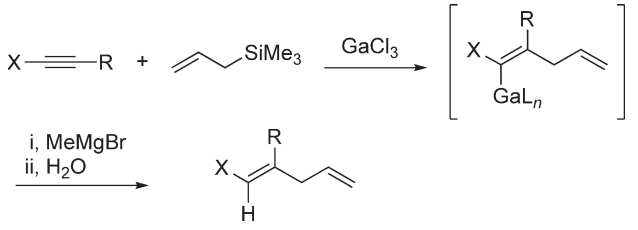
Silyl enol ethers react with silylethyne in the presence of $GaCl_3$ to give α-ethenylated ketones. The process involves the generation of gallium enolates and ethynylgallium via transmetallation; the former undergoes carbogallation to the latter. Various α-ethenylketones are conveniently prepared. Isomerization to conjugated enones is not usually observed (Table 34).[420,421] Similarly, silyl enol ethers derived from either *S*-alkyl or *S*-aryl thioesters give α-ethenyl thioesters by this method (Table 35). Silyl dienolates, derived from α-ethenyl thioesters, also give α,α-diethenyl thioesters.[422] α-Substituted β-keto esters or malonates are ethenylated at the α-carbon atom (Table 36).[423]



R	*Yield* (%)
C_5H_{11}	85
$C_{11}H_{23}$	73
c-C_6H_{11}	81
(*S*)-$Me_2C{=}CH(CH_2)_2CHMeCH_2$	74
$Me(CH_2)_9CHMe$	74
Ph	38

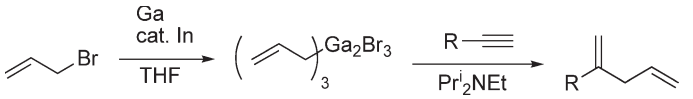


Scheme 134



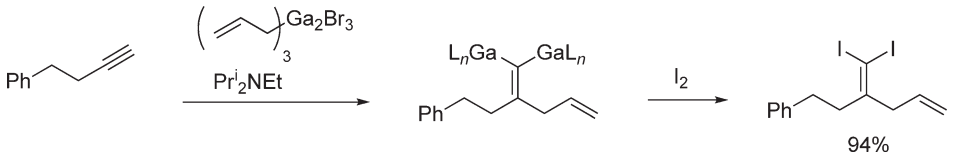
X	*R*	*Yield* (%)
$SiMe_3$	C_5H_{11}	81
$SiMe_3$	*c*-C_6H_{11}	77
$SiMe_3$	Ph	86
$SiEt_3$	H	75
$SiEt_3$	*c*-C_6H_{11}	30
H	C_9H_{19}	74
H	*c*-C_6H_{11}	56
H	Ph	56

Scheme 135



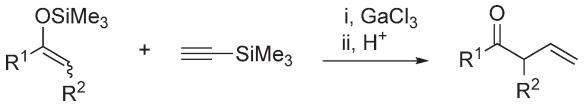
R	*Time* (h)	*Yield* (%)
$C_{10}H_{21}$	4	96
Ph	7	77
$PhCH_2OCH_2$	5	92
$MeO_2C(CH_2)_8$	5	82

Scheme 136



Scheme 137

Table 34 $GaCl_3$-mediated reaction of silyl enol ether with silylethyne. Reproduced with permission from ACS Publications



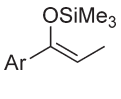
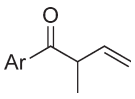
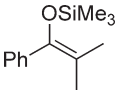
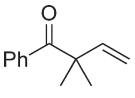
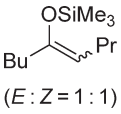
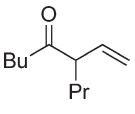
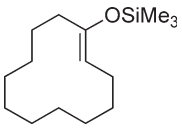
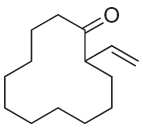
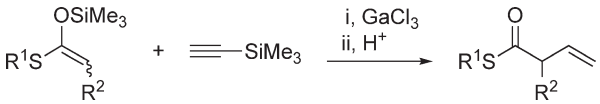
Substrate	*Product*	*Yield*
		Ar = Ph: 75% Ar = *p*-FC_6H_4: 72% Ar = *p*-$MeOC_6H_4$: 70%
		74%
 (*E* : *Z* = 1 : 1)		74%
		68%

Table 35 $GaCl_3$-mediated reaction of silyl enol ether of thioester with silylethyne. Reproduced with permission from CSJ



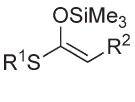
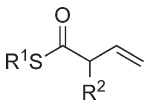
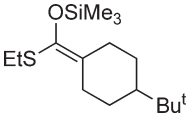
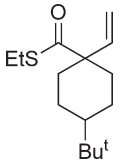
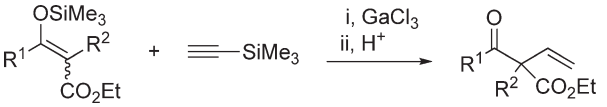
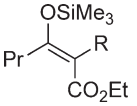
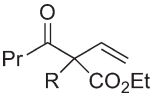
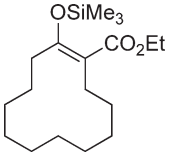
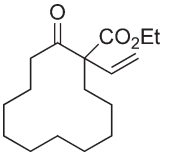
Substrate	*Product*	*Yield* (%)
		
$R^1 = Et$	$R^2 = CH_2Ph$	85
$R^1 = Et$	$R^2 = Bu$	83
$R^1 = Et$	$R^2 = Pr^i$	76
$R^1 = Et$	$R^2 = Bu^t$	72
$R^1 = Ph(CH_2)_2$	$R^2 = Pr^i$	70
$R^1 = c\text{-}C_6H_{11}$	$R^2 = Me$	81
$R^1 = c\text{-}C_6H_{11}$	$R^2 = Pr^i$	92
		78 (dr = 3 : 1)

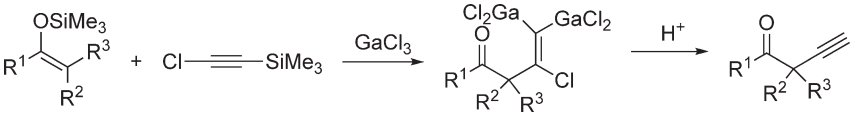
Table 36 $GaCl_3$-mediated reaction of silyl enol ether of β-keto ester with silylethyne



Substrate	*Product*	*Yield (%)*
		
R = Me		74
R = Et		84
R = Pr		85
		88

By using chloro(trimethylsilyl)ethyne in place of silylethyne, silyl enol ethers of aryl ketones are ethynylated at the α-carbon atom, via transmetallation, carbogallation, and β-elimination. This reaction provides α-ethynylated arylketones possessing acidic α-protons without isomerization to conjugated allenyl ketones (Table 37).[424] When only a catalytic amount of $GaCl_3$ is used, the reaction with triethylsilylated chloroethyne proceeds at 130 °C to give α-(silyl)ethynylated ketone (Equation (103)).[425] In the presence of $GaCl_3$, silyl enol ethers are sequentially

Table 37 $GaCl_3$-mediated reaction of silyl enol ether with chlorosilylethyne



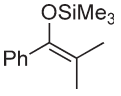
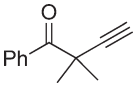
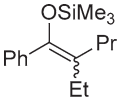
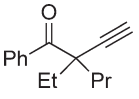
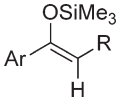
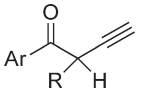
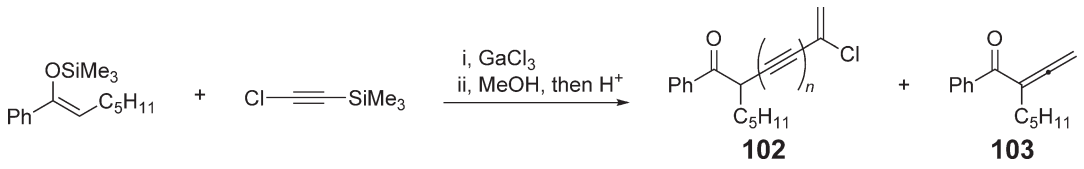
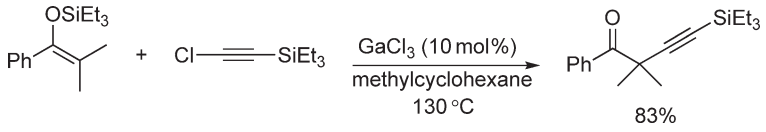
Substrate	*Product*	*Yield (%)*
		73
		69
E : *Z* = 1 : 1		
		
Ar = Ph, R = C_5H_{11}		85
Ar = Ph, R = C_8H_{17}		93
Ar = *p*-MeC_6H_4, R = C_6H_{13}		78

Table 38 $GaCl_3$-mediated sequential ethynylation of silyl enol ether



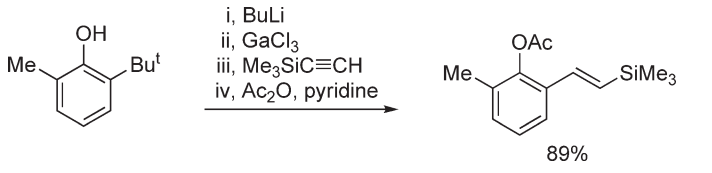
	Yield (%)			
Time (h)	**102** ($n = 1$)	**102** ($n = 2$)	**102** ($n = 3$)	**103**
0.5	55	Trace	ND	30
5	74	ND	ND	4
15	61	10	2	11
30	62	10	1	8

ethynylated at the α-carbon atom with chloro(trimethylsilyl)ethyne giving α-enylated, α-enediynylated, and α-enetriynylated ketones **102** together with allene **103** (Table 38).[426]

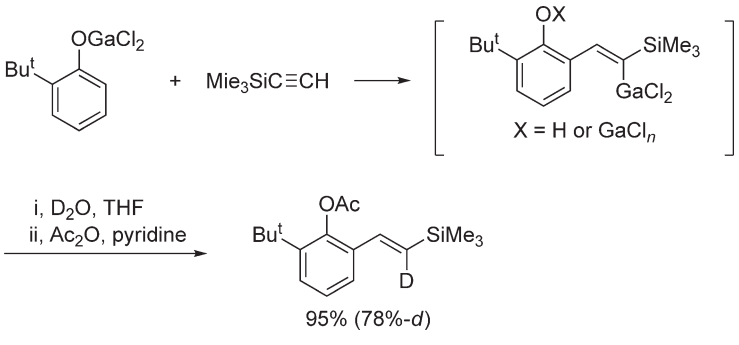


(103)

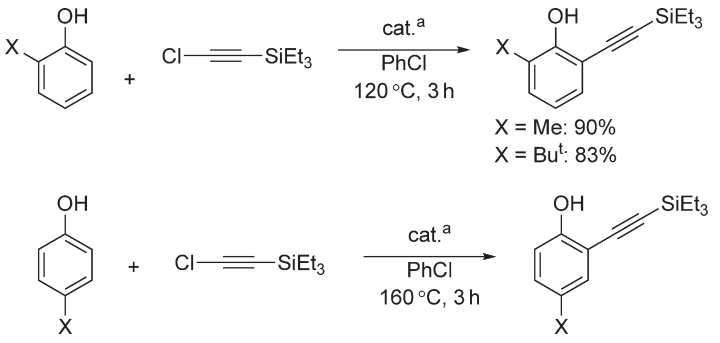
Phenoxygallium also undergoes a smooth carbogallation with silylethyne. Thus, treatment of lithium phenoxide with silylethyne in the presence of $GaCl_3$ gives *o*-(β-silylethenyl)phenol in a high yield (Scheme 138). The reaction of 2,6-disubstituted phenol with one of the substituents being a *t*-butyl group gives the *ipso*-substitution product (Equation (104)).[427] Phenols are ethynylated at the *ortho*-position with chloro(triethylsilyl)ethyne by catalytic amounts of $GaCl_3$, 2,6-di(*t*-butyl)-4-methylpyridine, and butyllithium via carbogallation and β-elimination (Scheme 139).[428]



(104)



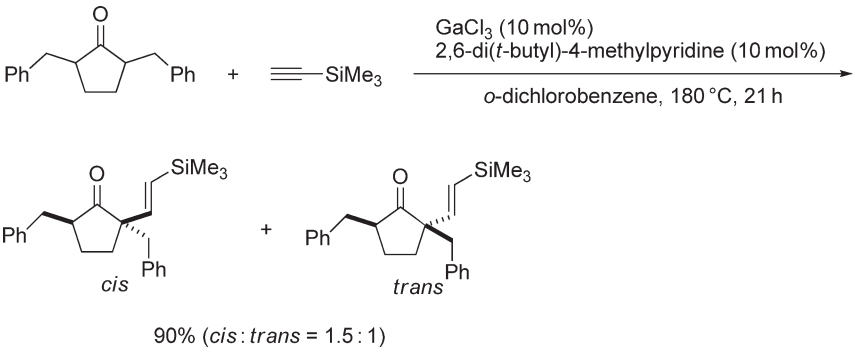
Scheme 138



X	*Yield* (%)
H	80
Bu^t	85
MeO	82 (at 120° C)
Bu^tMe_2SiO	88
Cl	87
Br	81

[a]cat. = $GaCl_3$ (10 mol%), BuLi (30 mol%), and 2,6-di(*t*-butyl)-4-methylpyridine (10 mol%)

Scheme 139



90% (*cis* : *trans* = 1.5 : 1)

Scheme 140

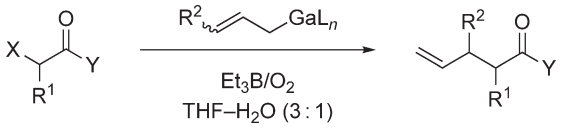
By the catalysis of $GaCl_3$ and 2,6-di(*t*-butyl)-4-methylpyridine, five- or six- membered-ring α,α'-disubstituted ketones are ethenylated at the α-carbon with trimethylsilylethyne at 180 °C. The roles of the base are believed to inhibit decomposition of the products and to promote photodegallation of the organogallium intermediates (Scheme 140).[429]

9.14.4.2.3 Radical reactions

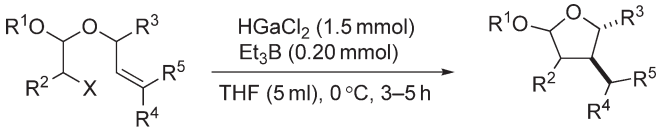
Allylgallium reagents are effective for radical allylation of α-iodo or α-bromo carbonyl compounds. Treatment of benzyl bromoacetate with allylgallium, prepared from allylmagnesium chloride and $GaCl_3$, in the presence of triethylborane in THF provides benzyl 4-pentenoate in good yield via a radical process. α-Halo propionamides also afford good yields of the allylated product. The addition of water as a co-solvent improves the yields of the allylated products. The allylgallium reagents resist immediate decomposition on exposure to water (Table 39).[430,431] Similarly, the reaction of alkynylgallium with α-halo carbonyl compounds gives β,γ-acetylenic carbonyl compounds.[432]

Dichlorogallium hydride $HGaCl_2$, generated form $GaCl_3$ and sodium bis(2-methoxyethoxy)aluminum hydride, acts as a radical mediator like tributyltin hydride. Treatment of alkyl halides with $HGaCl_2$ provides the corresponding dehalogenated products in excellent yields. Radical cyclization of halo acetals **104** is also successful to give **105** with not only the stoichiometric $HGaCl_2$, but also a catalytic amount of gallium trichloride combined with stoichiometric aluminum hydride (Red-Al®) as a hydride source (Scheme 141).[385]

Table 39 Radical allylation of α-halo carbonyl compounds. Reproduced with permission from Elsevier

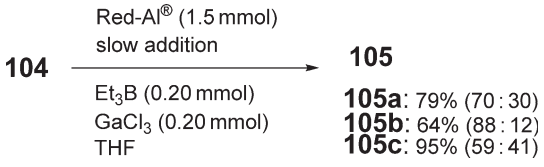


X	*Y*	R^1	R^2	*Time* (h)	*Yield* (%)
Br	OCH_2Ph	H	H	2	78
Br	OCH_2Ph	Me	H	2	63
Br	NMe_2	Me	H	2	64
I	OCH_2Ph	H	H	0.5	89
I	OCH_2Ph	Me	H	0.5	81
I	OCH_2Ph	H	Me	0.5	70
I	NMe_2	Me	Me	7	65 (dr = 2 : 1)



104 **105**

X	R^1	R^2	R^3	R^4	R^5	**105**	*Yield* (%)
I	$(CH_2)_3$		H	Me	Me	**105a**	87 (70 : 30)
Br	$(CH_2)_3$		H	Me	Me	**105a**	82 (71 : 29)
I	$(CH_2)_3$		H	Pr	H	**105b**	85 (84 : 16)
I	$(CH_2)_3$		C_5H_{11}	H	H	**105c**	85 (57 : 43)
I	Bu	H	C_5H_{11}	H	H	**105d**	97 (72 : 28)
Br	Bu	H	C_5H_{11}	H	H	**105d**	79 (72 : 28)



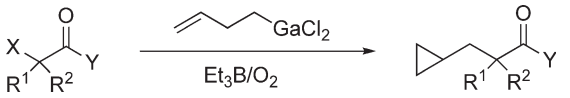
Scheme 141

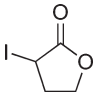
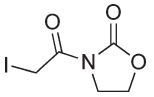
Reaction of α-iodo acetate with 3-butenylgallium dichloride initiated by a catalytic amount of Et_3B provides 3-cyclopropylpropanoate in 79% yield via a radical addition-substitution sequence. Similar reactions are summarized in Table 40.[431]

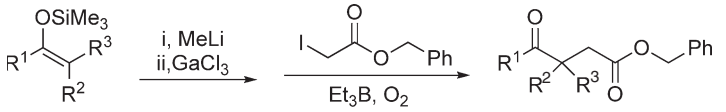
Treatment of silyl enolates with methyllithium followed by an addition of gallium trichloride affords the corresponding gallium enolates. The reaction of the resulting gallium enolates with α-halo carbonyl compounds in the presence of triethylborane provides 1,4-dicarbonyl compounds in good yields (Scheme 142).[433]

Hydrogallation of carbon–carbon multiple bonds with $HGaCl_2$ proceeds in the presence of triethylborane as a radical initiator. Several functionalities do not interfere with this reaction (Scheme 143). Resulting alkenyl- and alkylgallium species can be trapped by several electrophiles.[375] A novel NO_2/alkyl substitution of β-nitrostylene with trialkylgallium has been found, which is considered to proceed via a radical mechanism (Equation (105)).[434]

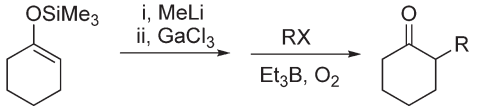
Table 40 Reaction of α-halo acetate with 3-butenylgallium. Reproduced with permission from CSJ

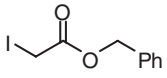
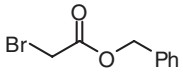
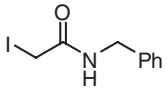
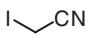


R^1	R^2	X	Y	Et_3Ga (equiv.)	*Time* (h)	*Yield* (%)
H	H	I	OBn	0.2	3	79
Me	H	I	OBn	0.2	5	70
				0.5	12	64
H	H	I	NEt_2	0.5	13	65
				0.5	13	57
H	H	I	Ph	0.2	4	60

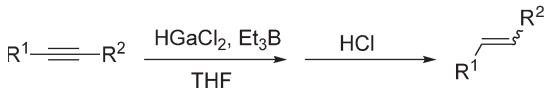


R^1	R^2	R^3	*Time* (h)	*Yield* (%)
C_5H_{11}	H	H	6	76
Bu^t	H	H	2	50
Pr	Et (H)	H (Et)	7	66



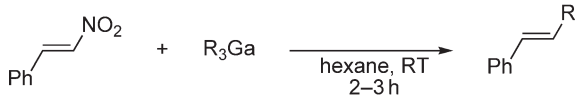
RX	*Yield* (%)
	70
	69
	51
	76

Scheme 142



R^1	R^2	*Yield* (%)	*E*:*Z*
$BnO(CH_2)_4$	H	76	
$EtO_2C(CH_2)_6$	H	74	
$Et_2NCO(CH_2)_8$	H	89	
C_5H_{11}	C_5H_{11}	90	59:41
$MeOCH_2$	C_6H_{13}	75	87:13
$HOCH_2$	C_6H_{13}	69	92:8

Scheme 143



R	*Yield* (%)
Et	68
c-C_5H_9	81
c-C_6H_{11}	54

(105)

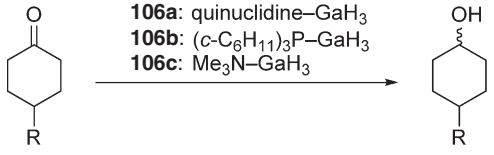
9.14.4.2.4 Reduction

Lithium gallium hydride reduces effectively both primary and secondary alkyl bromides and iodides to the corresponding hydrocarbons (Table 41).[435]

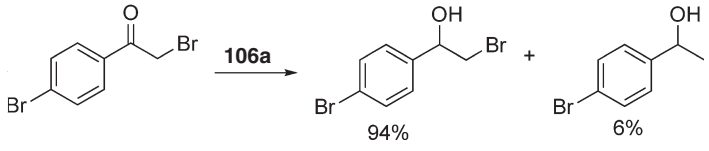
Gallane-tertiary amine or -tertiary phosphine adducts **106**, L-GaH_3 (L = Me_3N, quinuclidine, (*c*-$C_6H_{11})_3P$), reduce a carbonyl group and other unsaturated functional groups. The selectivities are different to those observed for similar alane

Table 41 Reduction of alkyl bromides with lithium gallium hydride. Reproduced with permission from the Korean Chemical Society

		Reduction (%)					
Alkyl halide	*Temp.* (°C)	0.5 h	1 h	3 h	6 h	12 h	24 h
Octyl chloride	65	34	48	80	91	91	92
Benzyl chloride	65	98	98				
Octyl bromide	65	99					
Benzyl bromide	65	99					
Bromobenzene	65	5	18	37	56	71	76
Octyl iodide	65	99					
Iodobenzene	65	62	84	99			



R	**106**	*trans* (%)	*cis* (%)
Bu^t	**106a**	87	13
Bu^t	**106b**	85	15
CO_2Et	**106a**	70	30



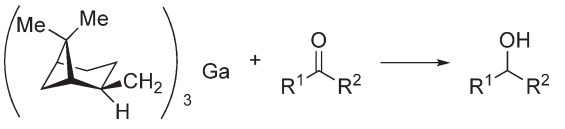
Scheme 144

Table 42 Reduction of esters with sodium gallium hydride. Reproduced with permission from the Korean Chemical Society

Ester	*Time* (h)	*Yield of aldehyde* (%)
Isopropyl acetate	3	78
Phenyl acetate	3	75
Ethyl caproate	3	83
Ethyl benzoate	6	67
Ethyl cinnamate	6	68

adducts (Scheme 144).[436] Sodium gallium hydride reduces aliphatic carboxylic esters to the corresponding aldehydes in good yields. The reduction can be performed at 0 °C and very low temperature is not necessary (Table 42).[437]

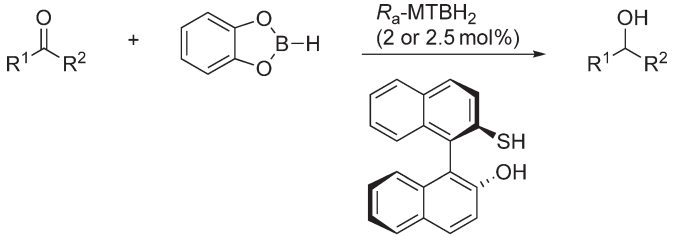
Tris[{(1*S*,2*R*)-6,6-dimethylbicylo[3.1.1]heptan-2-yl}methyl]gallium reacts with ketones above room temperature, and optically active alcohols are obtained as main products (Scheme 145).[438] $LiGaH_4$, in combination with an *S*,*O*-chelate ligand, 2-hydroxy-2′-mercapto-1,1′-binaphthyl ($MTBH_2$), forms an active hydride catalyst for an asymmetric reduction of prochiral ketones with catecholborane. Enantiofacial differentiation is based on the steric requirement of the ketone substituents. Aryl/*n*-alkyl ketones are reduced in 90–93% ee and branched ketones RC(O)Me (e.g., R = Pr^i, *c*-C_6H_{11}, Bu^t) in 60–72% ee (Table 43).[439,440]



Substrate	*Conv.* (%)	*ee* (%)
Ethyl phenyl ketone	77	21 (*R*)
Isopropyl phenyl ketone	58	51 (*R*)
2-Methyl-4-nonyn-3-one	79	75 (*R*)
2,2-Dimethyl-4-nonyn-3-one	89	54 (*R*)

Scheme 145

Table 43 Enantioselective reduction of ketones. Reproduced with permission from Wiles



R_a-$MTBH_2$

R^1	R^2	*Temp.* (°C)	*Time* (h)	*Yield* (%)	*ee* (%)
Ph	Me	−25	18	90	90
2-Furyl	C_6H_{13}	−25	18	76	81
1-Naphthyl	Me	−20	20	82	59
2-Naphthyl	Me	−20	20	83	73
PhCH═CH	Me	−25	18	70	75
Et—≡	Me	−25	18	60	63
Pr^i	Me	−20	18	81	69
Bu^i	Me	−20	18	93	46
c-C_6H_{11}	Me	−25	18	72	72
Bu^t	Me	−20	18	76	79

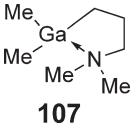
9.14.4.2.5 Coupling reaction

In the presence of a palladium catalyst $PdCl_2(PPh_3)_2$, the intramolecularly stabilized dimethylgallium complexes **107** and **108** methylate bromo- and iodoarenes in a highly selective manner. Substituted bromobenzenes XC_6H_4Br, where X = CHO, COPh, CO_2Et, CN, NO_2, Cl, CH_2Br, or CH═CHCOPh, are methylated by **107** and **108**, usually only at the aromatic ring halogen atom, to give substituted toluenes as single products (Table 44).[441] The methylation rates depend on the nature of the chelating ligands, on the solvent, and on the type of the palladium catalyst employed. With a nickel catalyst $NiCl_2(PPh_3)_2$, **107** reacts with 1-chloronaphthalene to give 1-methylnaphthalene in 43% yield, while **108** hardly reacts with 1-methylnaphthalene at all.[359]

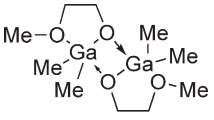
Treatment of aryl iodide **109** with alkenylgallium dichloride, prepared from $GaCl_3$ and alkenylmagnesium bromide, in the presence of a catalytic amount of a palladium catalyst provides high yields of cross-coupling products **110** and **111** (Scheme 146).[407] Gallium metal mediates the reaction of 1-(α-aminoalkyl)benzotriazole with allylic and propargyl bromides to give homoallyl- and homopropargylamines in moderate to good yields (Scheme 147).[442]

Table 44 Palladium-catalyzed methylation of haloarenes. Reproduced with permission from ACS Publications

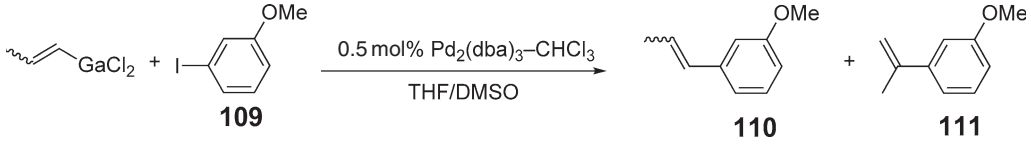
Substrate	*Gallium complex*	*Product and yield* (%)
Bromobenzene	**107**	Toluene (100)
Bromobenzene	**108**	Toluene (90)
4-Bromotoluene	**107**	*p*-Xylene (48)
1-Bromonaphthalene	**107**	1-Methylnaphthalene (99)
1-Bromonaphthalene	**108**	1-Methylnaphthalene (95) Naphthalene (3)
(*Z*)-α-bromostilbene	**107**	(*Z*)-α-Methylstilbene (89) (*E*)-α-Methylstilbene (6)
(*Z*)-α-bromostilbene	**108**	(*Z*)-α-Methylstilbene (100)



107



108

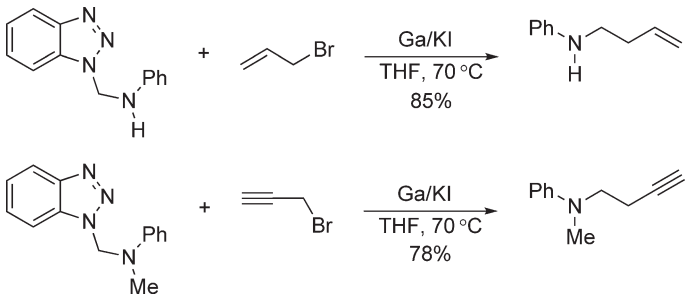


109 **110** **111**

	Yield (%)		
Ligand	**110**	**111**	**109**
None	54		34
Bu_3P	16		71
$(c\text{-}C_6H_{11})_3P$	60	4	24
Ph_3P	54	7	38
$(o\text{-tolyl})_3P$[a]	94	6	

[a] $Pd(dba)_3$-$CHCl_3$ (1.0 mol%) and $(o\text{-tolyl})_3P$ (4 mol%) were used.

Scheme 146

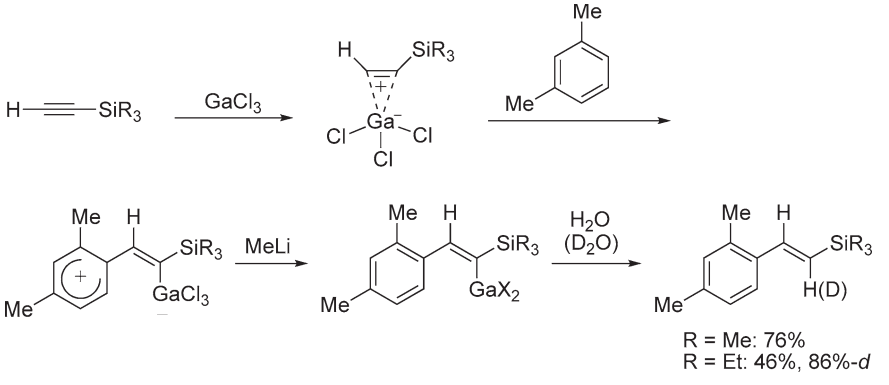


Scheme 147

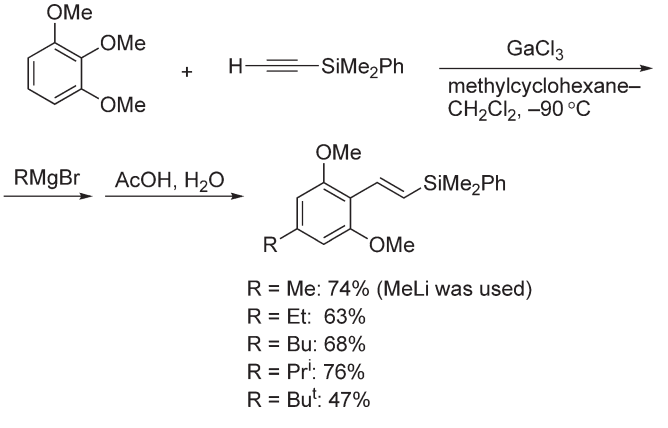
9.14.4.2.6 Use as Lewis acids and bases

Gallium compounds, in particular $GaCl_3$, are known to be useful Lewis acids for several organic transformations. In the presence of $GaCl_3$, silylethyne reacts electrophilically with aromatic hydrocarbons to give β-silylstylenes (Scheme 148). The reaction is believed to proceed via a formation of an electrophilic silylethyne–$GaCl_3$ complex, aromatic substitution, and protonolysis of the resulting vinylgallium compound. Formation of the vinylgallium intermediate before the aqueous workup has been confirmed by deuteration experiments. High reactivity of the gallium complex is demonstrated by the rapid reaction rate at −78 °C using close to the equimolar amount of the substrates. *Ipso*-substitution reaction takes place with 1,2,3-trimethoxybenzene (Scheme 149).[443,444]

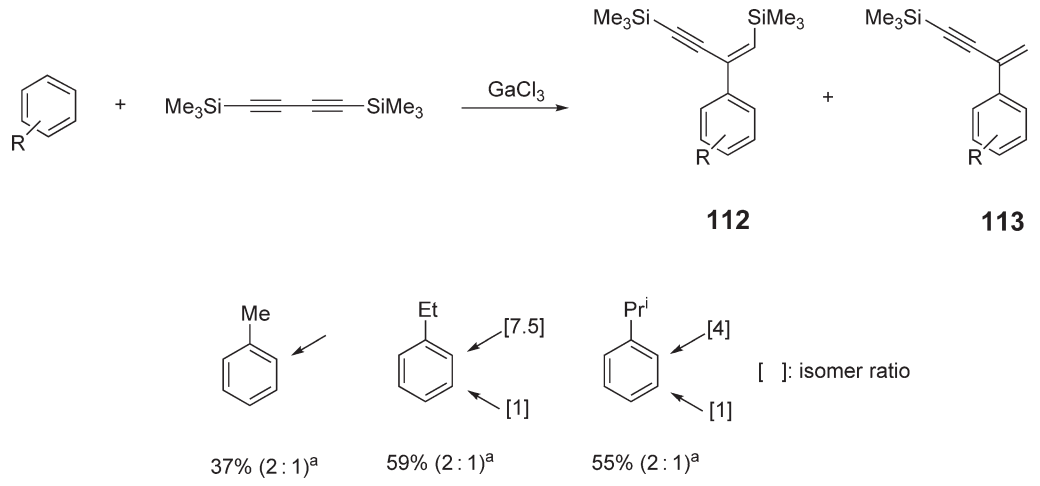
$GaCl_3$ mediates the reaction of 1,4-bis(trimethylsilyl)-1,3-butadiyne with aromatic hydrocarbons at −90 to −100 °C yielding 2-aryl-1-buten-3-ynes **112** and **113**. The reaction exhibits a high tendency to alkenylate the *o*-position of alkyl



Scheme 148



Scheme 149



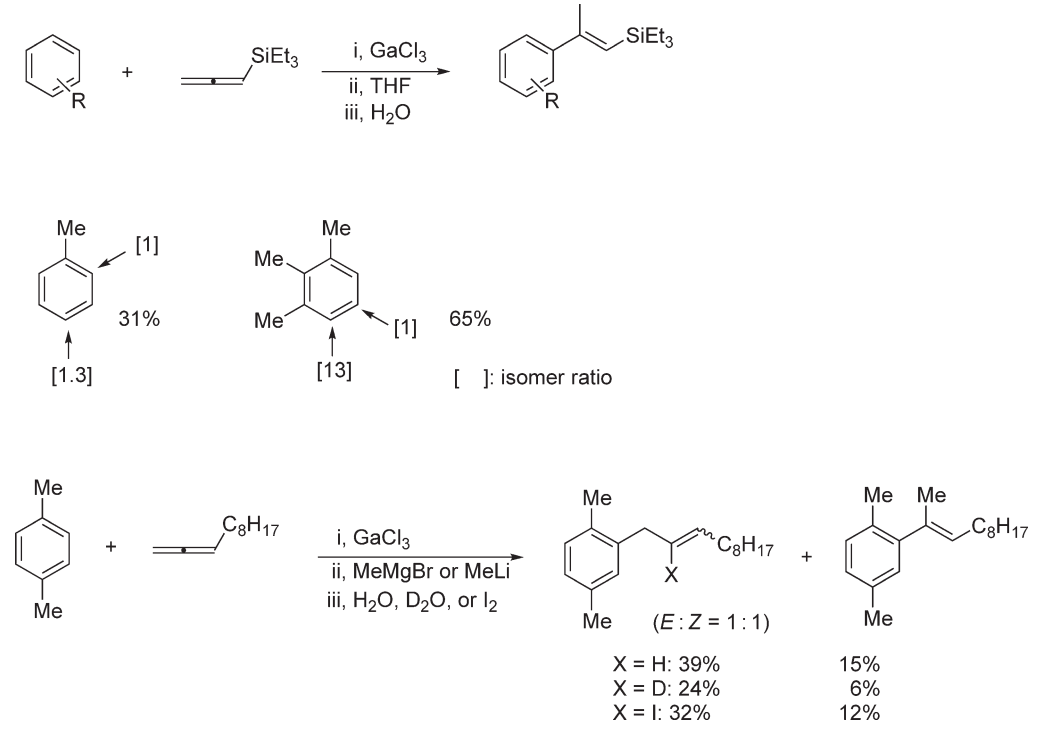
[a]Figures in parentheses indicate the ratio of **112** : **113**.

Scheme 150

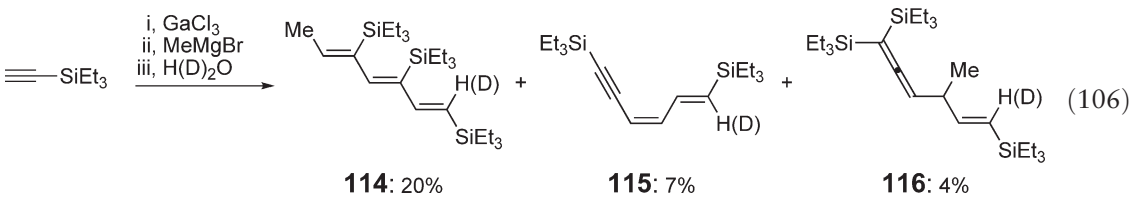
substitutents; toluene, ethylbenzene, and isopropylbenzene react predominantly to exclusively at the *o*-position, whereas *o*-xylene and 1,2,3,4-tetrahydronaphthalene react at the 3- and 5-positions, respectively (Scheme 150).[445]

Aromatic hydrocarbons are alkenylated with allenylsilane in the presence of $GaCl_3$ at −90 °C. A modest level of *ortho*-selectivity is observed. Organogallium electrophiles generated from allenes and $GaCl_3$ are active intermediates in this reaction. While the allenylsilane reacts exclusively at the central carbon, 1,2-alkadiene reacts at the terminal carbon predominantly (Scheme 151).[446]

The reaction of (triethylsilyl)ethyne with $GaCl_3$ in CH_2Cl_2/methylcyclohexane gives heptatriene **114**, hexadienyne **115**, and allene **116** after the treatment of methylmagnesium bromide (Equation (106)).[447]



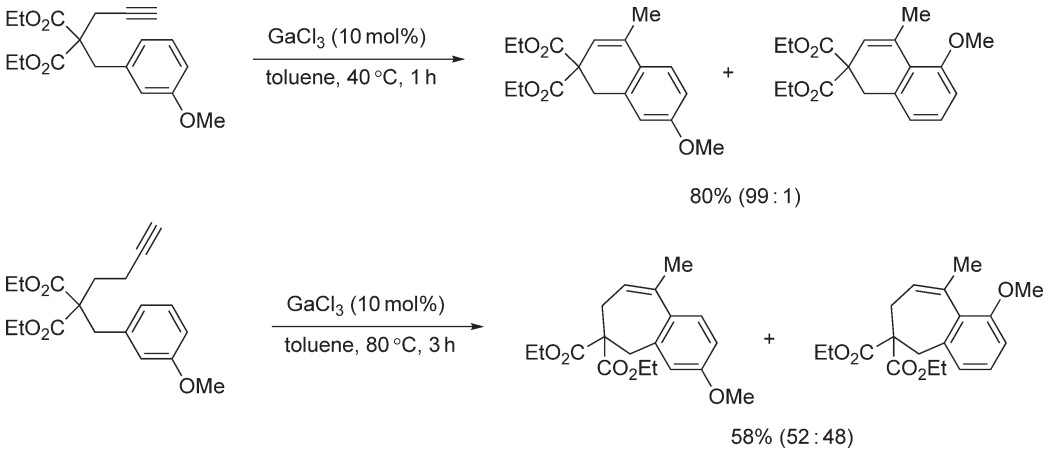
Scheme 151



(106)

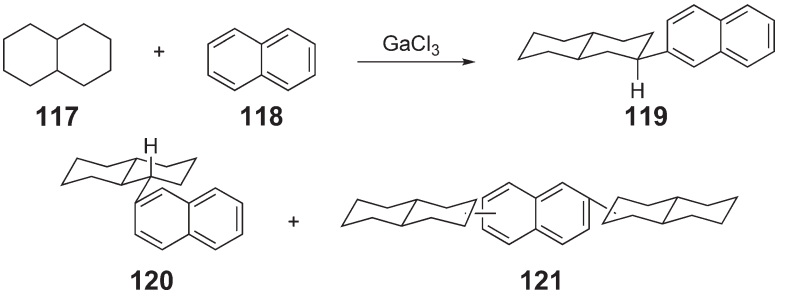
$GaCl_3$-catalyzed cycloisomerization of a variety of ω-aryl-1-alkynes, where $\omega = 5$ or 6, yields dihydronaphthalene or benzocycloheptene derivatives, respectively, in high yields (Scheme 152).[448]

$GaCl_3$ catalyzes the aromatic alkylation of naphthalene **118** or phenanthrene with cycloalkanes such as decalin **117**. The C–C bond formation predominantly takes place at the least hindered positions of the substrates, and equatorial isomers **119** and **120** regarding the cycloalkane moiety are generally obtained together with **121** (Table 45).[449,450]



Scheme 152

Table 45 $GaCl_3$-catalyzed aromatic alkylation

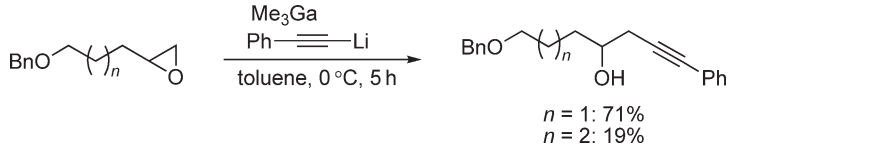


	Yield (%)[a]		
	119 + **120**	**121**	*TON*
cis-**117**; *trans*-**117** (1 : 1)	590 (30) (**119** : **120** = 6 : 1)	237 (12)	10.6[b]
cis-**117**	1188 (30) (**119** : **120** = 4 : 1)	423 (11)	20.3[c]
trans-**117**	11 (0.3) (**119** : **120** = 2 : 1)		0.1[c]

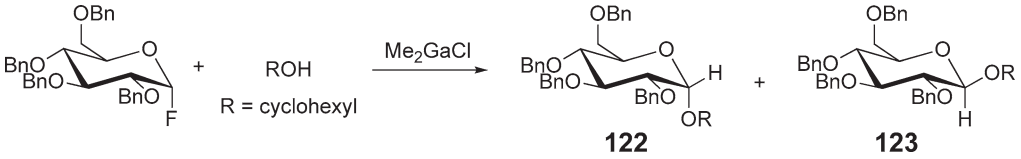
[a]The yield is based on $GaCl_3$. The yield based on **118** is shown in parentheses.
[b]$GaCl_3$ (5 mol%) was used.
[c]$GaCl_3$ (2.5 mol%) was used.

Dimethylgallium chloride and dimethylgallium triflate efficiently promote the glycosidation with several glycopyransyl fluorides to give a mixture of α- **122** and β-products **123**. Examples are shown in Scheme 153.[451] The five-, six-, seven-, and eight-membered lactams **124** are obtained from the corresponding α,ω-amino carboxylic acids in good to high yields by treatment with triethylgallium in toluene or benzene. The dimeric bislactams **125** are the major product for the long-chain α,ω-amino carboxylic acids (Table 46).[452]

Trimethylgallium catalyzes the addition of 1-lithio-1-alkyne to oxiranes, affording 3-alkyn-1-ols in good to excellent yields. A mechanism including activation of the oxiranes by the coordination to trimethylgallium is proposed (Table 47).[453,454] Similarly, regio- and stereoselective ring-opening reaction of hetero-substituted oxiranes with alkynyllithiums is catalyzed by Me_3Ga with remarkable efficiency at 0–20 °C via a pentacoordinated chelate-type complex (Equation (107)).[455]



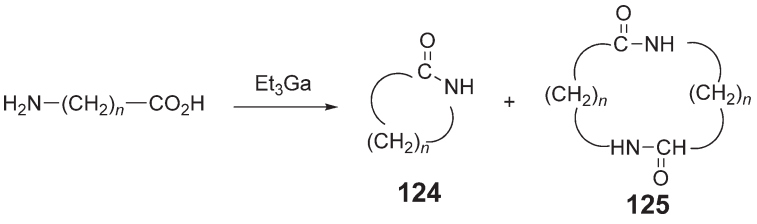
(107)



Solvent	*Time* (h)	*Yield* (%) **122** + **123**	*Ratio* **122** : **123**
Toluene	2	Quant	33 : 67
CH_2Cl_2	1.6	Quant	17 : 83
MeCN	90	Quant	20 : 80
Et_2O		No reaction	

Scheme 153

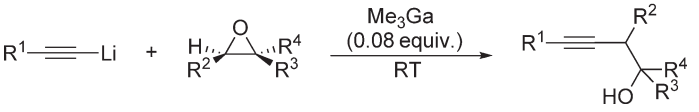
Table 46 Triethylgallium-mediated synthesis of lactams. Reproduced with permission from CSJ



			Product	
n	*Time* (h)	*Conditions*[a]	**124**	**125**
3	5	**A**	88	
4	3	**B**	86	
5	5	**A**	81	
6	5	**A**	18	4
6	5	**C**	43	12
7	5	**A**		6
7	5	**C**	7	8
10	5	**A**		10

[a]**A**: Substrate (1 mmol)/PhMe (10 mL)/reflux. **B**: Substrate (1 mmol)/PhH (10 mL)/reflux. **C**: Substrate (1 mmol)/PhMe (100 mL)/reflux.

Table 47 Trimethylgallium-catalyzed alkynylation of oxiranes. Reproduced with permission from CSJ



R^1	R^2	R^3	R^4	*Time* (h)	*Yield* (%)
C_6H_{13}	H	H	H	1	92 (10)[a]
C_6H_{13}	H	Me	H	1	87 (3)
C_6H_{13}	H	Me	Me	5	70
Ph	H	H	H	2	99 (4)
Ph	H	Me	H	2	88 (3)

[a]Yields in parentheses indicate those obtained by the reaction without Me_3Ga.

References

1. Goddard, A. E.; Goddard, D. A. *Textbook of Inorganic Chemistry*; Griffin: London, 1928.
2. Gilman, H.; Jones, R. G. *J. Am. Chem. Soc.* **1940**, *62*, 2353–2357.
3. Chao, L.-C.; Rieke, R. D. *J. Org. Chem.* **1975**, *40*, 2253–2255.
4. Araki, S.; Ito, H.; Butsugan, Y. *J. Org. Chem.* **1988**, *53*, 1831–1833.
5. Li, C. J.; Chan, T. H. *Tetrahedron Lett.* **1991**, *32*, 7017–7020.
6. Araki, S.; Butsugan, Y. In *Trends in Organometallic Chemistry*; Pandalai, S. C., Ed.; Research Trends: Trivandrum, 1994; pp 1–8.
7. Cintas, P. *Synlett* **1995**, 1087–1096.
8. Li, C.-J. *Tetrahedron* **1996**, *52*, 5643–5668.
9. Marshall, J. A. *Chemtracts: Org. Chem.* **1997**, *10*, 481–496.
10. Coldham, I. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1343–1365.
11. Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149–11176.
12. Chauhan, K. K.; Frost, C. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015–3019.
13. Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347–2356.
14. Babu, G.; Perumal, P. T. *Aldrichim. Acta* **2000**, *33*, 16–22.
15. Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31–47.
16. Marshall, J. A. *Chem. Rev.* **2000**, *100*, 3163–3185.
17. Araki, S.; Hirashita, T. In *Electronic Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: London, 2002.
18. Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Curr. Org. Chem.* **2003**, *7*, 1661–1689.
19. Chan, T. H.; Isaac, M. B. *Pure Appl. Chem.* **1996**, *68*, 919–924.
20. Podlech, J.; Maier, T. C. *Synthesis* **2003**, 633–655.
21. Grasa, G. A.; Singh, R.; Nolan, S. P. *Synthesis* **2004**, 971–985.
22. Nair, V.; Ros, S.; Jayan, C. N.; Pillai, B. S. *Tetrahedron* **2004**, *60*, 1959–1982.
23. Pae, A. N.; Cho, Y. S. *Curr. Org. Chem.* **2002**, *6*, 715–737.
24. Araki, S.; Hirashita, T. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, pp 323–386.
25. Yamaguchi, M. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, pp 307–322.
26. Araki, S.; Shimizu, T.; Johar, P. S.; Jin, S.-J.; Butsugan, Y. *J. Org. Chem.* **1991**, *56*, 2538–2542.
27. Araki, S.; Ito, H.; Katsumura, N.; Butsugan, Y. *J. Organomet. Chem.* **1989**, *369*, 291–296.
28. Araki, S.; Ito, H.; Butsugan, Y. *Synth. Commun.* **1988**, *18*, 453–458.
29. Chan, T.-H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228–3229.
30. Pérez, I.; Sestelo, J. P.; Sarandeses, L. A. *J. Am. Chem. Soc.* **2001**, *123*, 4155–4160.
31. Araki, S.; Shimizu, T.; Jin, S.-J.; Butsugan, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 824–825.
32. Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1995**, *60*, 1920–1921.
33. Li, X.-R.; Loh, T.-P. *Tetrahedron: Asymmetry* **1996**, *7*, 1535–1538.
34. Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1996**, *61*, 105–108.
35. Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1996**, *61*, 4247–4251.
36. Marshall, J. A.; Hinkle, K. W. *J. Org. Chem.* **1997**, *62*, 5989–5995.
37. Marshall, J. A.; Chen, M. *J. Org. Chem.* **1997**, *62*, 5996–6000.
38. Miyai, T.; Inoue, K.; Yasuda, M.; Baba, A. *Synlett* **1997**, 699–700.
39. Muderawan, I. W.; Bott, R. C.; Ypoung, D. J. *Synthesis* **1998**, 1640–1644.
40. Lu, J.; Ji, S.-J.; Qian, R.; Chen, J.-P.; Liu, Y.; Loh, T.-P. *Synlett* **2004**, 534–536.
41. Kobayashi, S.; Aoyama, N.; Manabe, K. *Synlett* **2002**, 483–485.
42. Yasuda, M.; Miyai, T.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1995**, *36*, 9497–9500.
43. Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, *2*, 847–849.
44. Araki, S.; Kameda, K.; Tanaka, J.; Hirashita, T.; Yamamura, H.; Kawai, M. *J. Org. Chem.* **2001**, *66*, 7919–7921.
45. Takemoto, Y.; Anzai, M.; Yanada, R.; Fujii, N.; Ohno, H.; Ibuka, T. *Tetrahedron Lett.* **2001**, *42*, 1725–1728.

46. Anzai, M.; Yanada, R.; Fujii, N.; Ohno, H.; Ibuka, T.; Takemoto, Y. *Tetrahedron* **2002**, *58*, 5231–5239.
47. Kang, S.-K.; Lee, S.-W.; Jung, J.; Lim, Y. *J. Org. Chem.* **2002**, *67*, 4376–4379.
48. Araki, S.; Kambe, S.; Kameda, K.; Hirashita, T. *Synthesis* **2003**, 751–754.
49. Jang, T.-S.; Keum, G.; Kang, S. B.; Chung, B. Y.; Kim, Y. *Synthesis* **2003**, 775–779.
50. Hirashita, T.; Kambe, S.; Tsuji, H.; Omori, H.; Araki, S. *J. Org. Chem.* **2004**, *69*, 5054–5059.
51. Anwar, U.; Grigg, R.; Rasprini, M.; Savic, V.; Sridharan, V. *J. Chem. Soc., Chem. Commun.* **2000**, 645–646.
52. Anwar, U.; Grigg, R.; Sridharan, V. *J. Chem. Soc., Chem. Commun.* **2000**, 933–934.
53. Cooper, I. R.; Grigg, R.; MacLachlan, W. S.; Sridharana, V.; Thornton-Petta, M. *Tetrahedron Lett.* **2003**, *44*, 403–405.
54. Cooper, I. R.; Grigg, R.; Hardie, M. J.; MacLachlan, W. S.; Sridharan, V.; Thomas, W. A. *Tetrahedron Lett.* **2003**, *44*, 2283–2285.
55. Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 696–697.
56. Marshall, J. A.; Grant, C. M. *J. Org. Chem.* **1999**, *64*, 8214–8219.
57. Marshall, J. A.; Chobanian, H. R. *J. Org. Chem.* **2000**, *65*, 8357–8360.
58. Marshall, J. A.; Chobanian, H. R.; Yanik, M. M. *Org. Lett.* **2001**, *3*, 3369–3372.
59. Yi, X.-H.; Haberman, J. X.; Li, C.-J. *Synth. Commun.* **1998**, *28*, 2999–3009.
60. Haberman, J. X.; Irvin, G. C.; John, V. T.; Li, C.-J. *Green Chem.* **1999**, *1*, 265–267.
61. Bowyer, M. C.; Gordon, C. M.; Leitch, S. K.; McCluskey, A.; Ritchie, C. *Aust. J. Chem.* **2004**, *57*, 135–137.
62. Cavallaro, C. L.; Herpin, T.; McGuinness, B. F.; Shimshock, Y. C.; Dolle, R. E. *Tetrahedron Lett.* **1999**, *40*, 2711–2714.
63. Araki, S.; Jin, S.-J.; Idou, Y.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1736–1738.
64. Augé, J.; Lubin-Germain, N.; Thiaw-Woaye, A. *Tetrahedron Lett.* **1999**, *40*, 9245–9247.
65. Augé, J.; Lubin-Germain, N.; Marque, S.; Seghrouchni, L. *J. Organomet. Chem.* **2003**, *679*, 79–83.
66. Hilt, G.; Smolko, K. I. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 3399–3402.
67. Fukuma, T.; Lock, S.; Miyoshi, N.; Wada, M. *Chem. Lett.* **2002**, 376–377.
68. Araki, S.; Butsugan, Y. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2395.
69. Chan, T. H.; Li, C. J. *J. Chem. Soc., Chem. Commun.* **1992**, 747.
70. Gordon, D. M.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 7937–7938.
71. Kim, E.; Gordon, D. M.; Schmid, W.; Whitesides, G. M. *J. Org. Chem.* **1993**, *58*, 5500–5507.
72. Binder, W. H.; Prenner, R. H.; Schmid, W. *Tetrahedron* **1994**, *50*, 749–758.
73. Gao, J.; Härter, R.; Gordon, D. M.; Whitesides, G. M. *J. Org. Chem.* **1994**, *59*, 3714–3715.
74. Prenner, R. H.; Binder, W. H.; Schmid, W. *Liebigs Ann. Chem.* **1994**, 73–78.
75. Choi, S.-K.; Lee, S.; Whitesides, G. M. *J. Org. Chem.* **1996**, *61*, 8739–8745.
76. Loh, T.-P.; Ho, D. S.-C.; Chua, G.-L.; Sim, K.-Y. *Synlett* **1997**, 563–564.
77. Carda, M.; Castillo, E.; Rodríguez, S.; Falomir, E.; Marco, J. A. *Tetrahedron Lett.* **1998**, *39*, 8895–8896.
78. Hua, X.-G.; Mague, J. T.; Li, C.-J. *Tetrahedron Lett.* **1998**, *39*, 6837–6840.
79. Yi, X.-H.; Meng, Y.; Li, C.-J. *J. Chem. Soc., Chem. Commun.* **1998**, 449–450.
80. Chan, T.-H.; Lee, M.-C. *J. Org. Chem.* **1995**, *60*, 4228–4232.
81. Loh, T.-P.; Cao, G.-Q.; Pei, J. *Tetrahedron Lett.* **1998**, *39*, 1453–1456.
82. Loh, T.-P.; Cao, G.-Q.; Pei, J. *Tetrahedron Lett.* **1998**, *39*, 1457–1460.
83. Carda, M.; Casillo, E.; Rodríguez, S.; Murga, J.; Marco, J. A. *Tetrahedron: Asymmetry* **1998**, *9*, 1117–1120.
84. Marshall, J. A.; Hinkle, K. W. *Tetrahedron Lett.* **1998**, *39*, 1303–1306.
85. Marshall, J. A.; Jiang, H. *Tetrahedron Lett.* **1998**, *39*, 1493–1496.
86. Chappell, M. D.; Halcomb, R. L. *Org. Lett.* **2000**, *2*, 2003–2005.
87. Warwel, M.; Fessner, W.-D. *Synlett* **2000**, 865–867.
88. Loh, T.-P.; Lye, P.-L. *Tetrahedron Lett.* **2001**, *42*, 3511–3514.
89. Shieu, J.-C.; Shaw, Y.-J.; Luh, T.-Y. *J. Chin. Chem. Soc. (Taipei)* **2001**, *48*, 1035–1040.
90. Backhaus, D. *Tetrahedron Lett.* **2001**, *41*, 2087–2090.
91. Crestia, D.; Guerard, C.; Veschambre, H.; Hecquet, L.; Demuynck, C.; Bolte, J. *Tetrahedron: Asymmetry* **2001**, *12*, 869–876.
92. Hao, J.; Aiguade, J.; Forsyth, C. J. *Tetrahedron Lett.* **2001**, *42*, 821–824.
93. Vogel, S.; Stembera, K.; Hennig, L.; Findeisen, M.; Giesa, S.; Welzel, P.; Lampilas, M. *Tetrahedron* **2001**, *57*, 4139–4146.
94. Maleczka, R. E., Jr.; Terrell, L. R.; Geng, F.; Ward, J. S., III. *Org. Lett.* **2002**, *4*, 2841–2844.
95. Loh, T.-P.; Song, H.-Y. *Synlett* **2002**, 2119–2121.
96. Carda, M.; Rodríguez, S.; Segovia, B.; Marco, J. A. *J. Org. Chem.* **2002**, *67*, 6560–6563.
97. Sabui, S. K.; Venkateswaran, R. V. *Tetrahedron* **2003**, *59*, 8375–8381.
98. Huang, J.-M.; Xu, K.-C.; Loh, T.-P. *Synthesis* **2003**, 755–764.
99. Loh, T.-P.; Yin, Z.; Song, H.-Y.; Tan, K.-L. *Tetrahedron Lett.* **2003**, *44*, 911–914.
100. Kim, J. H.; Seo, W. D.; Lee, J. H.; Lee, B. W.; Park, K. H. *Synthesis* **2003**, 2473–2478.
101. Chng, S.-S.; Hoang, T.-G.; Lee, W.-W. W.; Tham, M.-P.; Ling, H. Y.; Loh, T.-P. *Tetrahedron Lett.* **2004**, *45*, 9501–9504.
102. Isaac, M. B.; Chan, T.-H. *Tetrahedron Lett.* **1995**, *36*, 8957–8960.
103. Sarrazin, L.; Mauzé, B. *Synth. Commun.* **1996**, *26*, 3179–3191.
104. Law, M. C.; Wong, K.-Y.; Chan, T. H. *Green Chem.* **2002**, *4*, 161–164.
105. Loh, T.-P.; Tan, K.-T.; Yang, J.-Y.; Xiang, C.-L. *Tetrahedron Lett.* **2001**, *42*, 8701–8703.
106. Loh, T.-P.; Tan, K.-T.; Hu, Q.-Y. *Tetrahedron Lett.* **2001**, *42*, 8705–8708.
107. Hirashita, T.; Inoue, S.; Yamamura, H.; Kawai, K.; Araki, S. *J. Organomet. Chem.* **1997**, *549*, 305–309.
108. Melekhov, A.; Fallis, A. G. *Tetrahedron Lett.* **1999**, *40*, 7867–7870.
109. Villalva-Servín, N. P.; Melekov, A.; Fallis, A. G. *Synthesis* **2003**, 790–794.
110. Nishigaichi, Y.; Hanano, Y.; Takuwa, A. *Chem. Lett.* **1998**, 33–34.
111. Issac, M. B.; Chan, T.-H. *J. Chem. Soc., Chem. Commun.* **1995**, 1003.
112. Yi, X.-H.; Meng, Y.; Hua, X.-G.; Li, C.-J. *J. Org. Chem.* **1998**, *63*, 7472–7480.
113. Lin, M.-J.; Loh, T.-P. *J. Am. Chem. Soc.* **2003**, *125*, 13042–13043.
114. Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Eur. J.* **2002**, *8*, 1719–1729.
115. Alcaide, B.; Almendros, P.; Aragoncillo, C.; Rodríguez-Acebes, R. *Synthesis* **2003**, 1163–1170.

116. Mitzel, T. M.; Palomo, C.; Jendza, K. *J. Org. Chem.* **2002**, *67*, 136–145.
117. Engstrom, G.; Morelli, M.; Palomo, C.; Mitzel, T. *Tetrahedron Lett.* **1999**, *40*, 5967–5970.
118. Qing, F.-L.; Wan, D.-P. *Tetrahedron* **1998**, *54*, 14189–14200.
119. Kirihara, M.; Takuwa, T.; Takizawa, S.; Momose, T. *Tetrahedron Lett.* **1997**, *38*, 2853–2854.
120. Kirihara, M.; Takuwa, T.; Takizawa, S.; Momose, T.; Nemoto, H. *Tetrahedron* **2000**, *56*, 8275–8280.
121. Audouard, C.; Fawcett, J.; Griffiths, G. A.; Percy, J. M.; Pintat, S.; Smith, C. A. *Org. Biomol. Chem* **2004**, *2*, 528–541.
122. Wang, Z.; Hammond, G. B. *J. Org. Chem.* **2000**, *65*, 6547–6552.
123. Shen, Q.; Hammond, G. B. *Org. Lett.* **2001**, *3*, 2213–2215.
124. Arimitsu, S.; Xu, B.; Kishbaugh, T. L. S.; Griffin, L.; Hammond, G. B. *J. Fluorine Chem.* **2004**, *125*, 641–645.
125. Diana, S.-C. H.; Sim, K.-Y.; Loh, T.-P. *Synlett* **1996**, 263–264.
126. Paquette, L. A.; Kern, B. E.; Méndez-Andino, J. *Tetrahedron Lett.* **1999**, *40*, 4129–4132.
127. Lloyd-Jones, G. C.; Russell, T. *Synlett* **1998**, 903–905.
128. Reetz, M. T.; Haning, H. *J. Organomet. Chem.* **1997**, *541*, 117–120.
129. Mehta, G.; Kumaran, R. S. *J. Chem. Soc., Chem. Commun.* **2002**, 1456–1457.
130. Khan, F. A.; Satapathy, R.; Dash, J.; Savitha, G. *J. Org. Chem.* **2004**, *69*, 5295–5301.
131. Maguire, R. J.; Mulzer, J.; Bats, J. W. *J. Org. Chem.* **1996**, *61*, 6936–6940.
132. Paquette, L. A.; Bennett, G. D.; Chhatriwalla, A.; Isaac, M. B. *J. Org. Chem.* **1997**, *62*, 3370–3374.
133. Paquette, L. A.; Bennet, G. D.; Issac, M. B.; Chhatriwalla, A. *J. Org. Chem.* **1998**, *63*, 1836–1845.
134. Loh, T.-P.; Li, X.-R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 980–982.
135. Loh, T.-P.; Li, X.-R. *Eur. J. Org. Chem.* **1999**, 1893–1899.
136. Loh, T.-P.; Li, X.-R. *Tetrahedron Lett.* **1997**, *38*, 869–872.
137. Paquette, L. A.; Rothhaar, R. R. *J. Org. Chem.* **1999**, *64*, 217–224.
138. Paquette, L. A.; Méndez-Andino, J. *Tetrahedron Lett.* **1999**, *40*, 4301–4304.
139. Hirashita, T.; Kamei, T.; Horie, T.; Yamamura, H.; Kawai, M.; Araki, S. *J. Org. Chem.* **1999**, *64*, 172–177.
140. Lombardo, M.; Girotti, R.; Morganti, S.; Trombini, C. *Org. Lett.* **2001**, *3*, 2981–2983.
141. Lombardo, M.; Licciulli, S.; Trombini, C. *Tetrahedron Lett.* **2003**, *44*, 9147–9149.
142. Lombardo, M.; Gianotti, K.; Licciulli, S.; Trombini, C. *Tetrahedron* **2004**, *60*, 11725–11732.
143. Lombardo, M.; Licciulli, S.; Trombini, C. *Pure Appl. Chem.* **2004**, *76*, 657–669.
144. Choudhury, P. K.; Foubelo, F.; Yus, M. *Tetrahedron Lett.* **1998**, *39*, 3581–3584.
145. Choudhury, P. K.; Foubelo, F.; Yus, M. *Tetrahedron* **1999**, *55*, 10779–10788.
146. Kang, H.-Y.; Ji, Y.; Yu, Y.-K.; Yu, J.-Y.; Lee, Y.; Lee, S.-J. *Bull. Korean Chem. Soc.* **2003**, *24*, 1819–1826.
147. Araki, S.; Hirashita, T.; Shimizu, K.; Ikeda, T.; Butsugan, Y. *Tetrahedron* **1996**, *52*, 2803–2816.
148. Araki, S.; Hirashita, T.; Shimizu, H.; Yamamura, H.; Kawai, M.; Butsugan, Y. *Tetrahedron Lett.* **1996**, *37*, 8417–8420.
149. Marshall, J. A.; Garofalo, A. W. *J. Org. Chem.* **1996**, *61*, 8732–8738.
150. Behnke, D.; Hamm, S.; Hennig, L.; Walzel, P. *Tetrahedron Lett.* **1997**, *38*, 7059–7062.
151. Donnelly, S.; Thomas, E. J.; Arnott, E. A. *J. Chem. Soc., Chem. Commun.* **2003**, 1460–1461.
152. Canac, Y.; Levoirier, E.; Lubineau, A. *J. Org. Chem.* **2001**, *66*, 3206–3210.
153. Paquette, L. A. *Synthesis* **2003**, 765–774.
154. Paquette, L. A.; Mitzel, T. M. *Tetrahedron Lett.* **1995**, *36*, 6863–6866.
155. Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931–1937.
156. Paquette, L. A.; Mitzel, T. M. *J. Org. Chem.* **1996**, *61*, 8799–8804.
157. Warwel, M.; Fessner, W.-D. *Synlett* **2002**, 2104–2106.
158. Skaanderup, P. R.; Madsen, R. *J. Org. Chem.* **2003**, *68*, 2115–2122.
159. Paquette, L. A.; Mitzel, T. M.; Isaac, M. B.; Crasto, C. F.; Schomer, W. W. *J. Org. Chem.* **1997**, *62*, 4293–4301.
160. Méndez-Andino, J.; Paquette, L. A. *Org. Lett.* **2000**, *2*, 1263–1265.
161. Kumar, S.; Kaur, P.; Chimni, S. S.; Singh, P. *Synlett* **2001**, 1431–1433.
162. Kumar, S.; Kaur, P.; Chimni, S. S. *Synlett* **2002**, 573–574.
163. Kang, S.-K.; Baik, T.-G.; Jiao, X.-H. *Synth. Commun.* **2002**, *32*, 75–78.
164. Paquette, L. A.; Lobben, P. C. *J. Org. Chem.* **1998**, *63*, 5604–5616.
165. Lobben, P. C.; Paquette, L. A. *J. Org. Chem.* **1998**, *63*, 6990–6998.
166. Paquette, L. A.; Stepanian, M.; Mallavadhani, U. V.; Cutarelli, T. D.; Lowinger, T. B.; Klemeyer, H. J. *J. Org. Chem.* **1996**, *61*, 7492–7507.
167. Paquette, L. A.; Lobben, P. C. *J. Am. Chem. Soc.* **1996**, *118*, 1917–1930.
168. Gordon, C. M.; Ritchie, C. *Green Chem.* **2002**, *4*, 124–128.
169. Khan, F. A.; Dash, J. *Eur. J. Org. Chem.* **2004**, 2692–2700.
170. Issac, M. B.; Paquette, L. A. *J. Org. Chem.* **1997**, *62*, 5333–5338.
171. Marshall, J. A.; Palovich, M. R. *J. Org. Chem.* **1997**, *62*, 6001–6005.
172. Cossy, J.; Defosseux, M.; Meyer, C. *Synlett* **2001**, 815–817.
173. Wang, R.; Lim, C.-M.; Tan, C.-H.; Lim, B.-K.; Sim, K.-Y.; Loh, T.-P. *Tetrahedron: Asymmetry* **1995**, 1825–1828.
174. Bernardelli, P.; Paquette, L. A. *J. Org. Chem.* **1997**, *62*, 8284–8285.
175. Jayaraman, M.; Manhas, M. S.; Bose, A. K. *Tetrahedron Lett.* **1997**, *38*, 709–712.
176. Paquette, L. A.; Rothhaar, R. R.; Isaac, M.; Rogers, L. M.; Rogers, R. D. *J. Org. Chem.* **1998**, *63*, 5463–5472.
177. Paquette, L. A.; Isaac, M. B. *Heterocycles* **1998**, *47*, 107–110.
178. Cho, Y. S.; Jie, E. L.; Pae, A. N.; Choi, K. I.; Koh, H. Y. *Tetrahedron Lett.* **1999**, *40*, 1725–1728.
179. Alcaide, B.; Almendros, P.; Salgado, N. R. *J. Org. Chem.* **2000**, *65*, 3310–3321.
180. Alcaide, B.; Almendros, P.; Aragoncillo, C.; Rodríguez-Acebes, R. *J. Org. Chem.* **2001**, *66*, 5208–5216.
181. Shin, J. A.; Cha, J. H.; Pae, A. N.; Choi, K. I.; Koh, H. Y.; Kang, H.-Y.; Cho, Y. S. *Tetrahedron Lett.* **2001**, *42*, 5489–5492.
182. Kumar, S.; Kumar, V.; Singh, S.; Chimni, S. S. *Tetrahedron Lett.* **2001**, *42*, 5073–5075.
183. Loh, T.-P.; Wang, R.-B.; Tan, K.-L.; Sim, K.-Y. *Main Group Met. Chem.* **1997**, *20*, 237–240.
184. Steurer, S.; Podlech, J. *Adv. Synth. Catal.* **2001**, *343*, 251–254.
185. Steurer, S.; Podlech, J. *Eur. J. Org. Chem.* **1999**, 1551–1560.

186. Steurer, S.; Podlech, J. *Synthesis* **2002**, 945–950.
187. Loh, T.-P.; Huang, J.-M.; Xu, K.-C.; Goh, S.-H.; Vittal, J. J. *Tetrahedron Lett.* **2000**, *41*, 6511–6515.
188. Loh, T.-P.; Zhou, J.-R.; Yin, Z. *Org. Lett.* **1999**, *1*, 1855–1857.
189. Loh, T.-P.; Zhou, J.-R.; Li, X.-R. *Tetrahedron Lett.* **1999**, *40*, 9333–9336.
190. Loh, T.-P.; Lin, M.-J.; Tan, K.-L. *Tetrahedron Lett.* **2003**, *44*, 507–509.
191. Loh, T.-P.; Zhou, J.-R. *Tetrahedron Lett.* **1999**, *40*, 9115–9118.
192. Cordova, A.; Barbas, C. F. *Tetrahedron Lett.* **2003**, *44*, 1923–1926.
193. Araki, S.; Katsumura, N.; Butsugan, Y. *J. Organomet. Chem.* **1991**, *415*, 7–24.
194. Pan, D.; Mal, S. K.; Kar, G. K.; Ray, J. K. *Tetrahedron* **2002**, *58*, 2847–2852.
195. Nair, V.; Jayan, C. N. *Tetrahedron Lett.* **2000**, *41*, 1091–1094.
196. Nair, V.; Jayan, C. N.; Ros, S. *Tetrahedron* **2001**, *57*, 9453–9459.
197. Lee, P. H.; Lee, K.; Chang, S. *Synth. Commun.* **2001**, *31*, 3189–3196.
198. Lee, P. H.; Seomoon, D.; Lee, K. *Bull. Korean Chem. Soc.* **2001**, *22*, 1380–1384.
199. Li, C.-J.; Lu, Y.-Q. *Tetrahedron Lett.* **1995**, *36*, 2721–2724.
200. Lu, Y.-Q.; Li, C.-J. *Tetrahedron Lett.* **1996**, *37*, 471–474.
201. Shin, J. A.; Choi, K. I.; Pae, A. N.; Koh, H. Y.; Kang, H.-Y.; Cho, Y. S. *J. Chem. Soc., Perkin Trans. 1* **2001**, 946–948.
202. Lee, J. E.; Cha, H.; Pae, A. N.; Choi, K. I.; Koh, H. Y.; Km, Y.; Cho, Y. S. *Synth. Commun.* **2000**, *30*, 4299–4308.
203. Araki, S.; Katsumura, N.; Ito, H.; Butsugan, Y. *Tetrahedron Lett.* **1989**, *30*, 1581–1582.
204. Sabitha, G.; Reddy, C. S.; Babu, R. S.; Yadav, J. S. *Synlett* **2001**, 1787–1789.
205. Zhang, J.; Blazecka, P. G.; Berven, H.; Belmont, D. *Tetrahedron Lett.* **2003**, *44*, 5579–5582.
206. Nair, V.; Ros, S.; Jayan, C. N.; Viji, S. *Synthesis* **2003**, 2542–2546.
207. Gong, J. H.; Lee, K. Y.; Son, J. S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2003**, *24*, 507–510.
208. Babu, S. A.; Yasuda, M.; Shibata, I.; Baba, A. *Synlett* **2004**, 1223–1226.
209. Bryan, V. J.; Chan, T.-H. *Tetrahedron Lett.* **1996**, *37*, 5341–5342.
210. Paquette, L. A.; Mendez-Andio, J. L. *J. Org. Chem.* **1998**, *63*, 9061–9068.
211. Ivkovic, A.; Matovic, R.; Saicic, R. N. *J. Serb. Chem. Soc.* **2002**, *67*, 141–148.
212. Cha, J. H.; Cho, Y. S.; Koh, H. Y.; Lee, E.; Kim, Y.-T.; Yang, H.-H.; Kang, H.-Y. *Bull. Korean Chem. Soc.* **2004**, *25*, 1123–1124.
213. Shimada, T.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 471–474.
214. Li, C.-J.; Chen, D.-L.; Lu, Y.-Q.; Haberman, J. X.; Mague, J. T. *J. Am. Chem. Soc.* **1996**, *118*, 4216–4217.
215. Haberman, J. X.; Li, C.-J. *Tetrahedron Lett.* **1997**, *38*, 4735–4736.
216. Li, C.-J.; Chen, D.-L.; Lu, Y.-Q.; Haberman, J. X.; Mague, J. T. *Tetrahedron* **1998**, *54*, 2347–2364.
217. Kang, H.-Y.; Kim, Y.-T.; Yu, Y.-K.; Cha, J. H.; Cho, Y. S.; Koh, H. Y. *Synthesis* **2004**, 45–48.
218. Li, C.-J. *Tetrahedron Lett.* **1995**, *36*, 517–518.
219. Chen, D.-L.; Li, C.-J. *Tetrahedron Lett.* **1996**, *37*, 295–298.
220. Lu, W.; Ma, J.; Yang, Y.; Chan, T. H. *Org. Lett.* **2000**, *2*, 3469–3471.
221. Alcaide, B.; Almendros, P.; Rodríguez-Acebes, R. *J. Org. Chem.* **2002**, *67*, 1925–1928.
222. Alcaide, B.; Almendros, P.; Campo, T. M.-D.; Rodríguez-Acebes, R. *Tetrahedron Lett.* **2004**, *45*, 6429–6431.
223. Miao, W.; Lu, W.; Chan, T. H. *J. Am. Chem. Soc.* **2003**, *125*, 2412–2413.
224. Yadav, J. S.; Srinivas, D.; Reddy, G. S.; Bindu, K. H. *Tetrahedron Lett.* **1997**, *38*, 8745–8748.
225. Zhan, Z.; Zhang, Y. *Synth. Commun.* **1998**, *28*, 493–497.
226. Wang, L.; Zhaung, Y. *J. Chem. Res. (S)* **1998**, 588–589.
227. Bryan, V. J.; Chan, T.-H. *Tetrahedron Lett.* **1997**, *38*, 6493–6496.
228. Yoo, B. W.; Cho, K. H.; Lee, S. J.; Nam, G. S.; Chang, K. Y.; Kim, S. H.; Kim, J. H. *Synth. Commun.* **2002**, *32*, 839–846.
229. Yoo, B.-W.; Lee, S.-J.; Choi, K.-H.; Keum, S.-R.; Ko, J.-J.; Choi, K.-I.; Kim, J.-H. *Tetrahedron Lett.* **2001**, *42*, 7287–7289.
230. Yoo, J.; Oh, K. E.; Keum, G.; Kang, S. B.; Kim, Y. *Polyhedron* **2000**, *19*, 549–551.
231. Höppe, H. A.; Lloyed-Jones, G. C.; Murray, M.; Peakman, T. M.; Walsh, K. E. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1545–1547.
232. Capps, S. M.; Lloyd-Jones, G. C.; Murray, M.; Peakman, T. M.; Walsh, K. E. *Tetrahedron Lett.* **1998**, *39*, 2853–2856.
233. Capps, S. M.; Clarke, T. P.; Charmant, J. P.; Höppe, H. A.; Lloyd-Jones, G. C.; Murray, M.; Peakman, T. M.; Stentiford, R. A.; Walsh, K. E.; Wothington, P. A. *Eur. J. Org. Chem.* **2000**, 963–974.
234. Lloyd-Jones, G. C.; Murray, M.; Peakman, T. M.; Stentiford, R. A.; Wothington, P. A. *Eur. J. Org. Chem.* **2000**, 975–985.
235. Yi, X.-H.; Meng, Y.; Li, C.-J. *Tetrahedron Lett.* **1997**, *38*, 4731–4734.
236. Kim, H. Y.; Choi, K. I.; Pae, A. N.; Koh, H. Y.; Choi, J. H.; Cho, Y. S. *Synth. Commun.* **2003**, *33*, 1899–1904.
237. Pan, D.; Kar, G. K.; Ray, J. K. *Synth. Commun.* **2003**, *33*, 1–9.
238. Mal, S. K.; Ray, D.; Ra, J. K. *Tetrahedron Lett.* **2004**, *45*, 277–279.
239. Kuma, V.; Chimni, S. S.; Kumar, S. *Tetrahedron Lett.* **2004**, *45*, 3409–3412.
240. Kim, D. Y.; Wiemer, D. F. *Tetrahedron Lett.* **2003**, *44*, 2803–2805.
241. Ranu, B. C.; Samanta, S.; Hajra, A. *J. Org. Chem.* **2001**, *66*, 7519–7521.
242. Chung, W. J.; Higashiya, S.; Welch, J. T. *Tetrahedron Lett.* **2002**, *43*, 5801–5803.
243. Chung, W. J.; Higashiya, S.; Oba, Y.; Welch, J. T. *Tetrahedron* **2003**, *59*, 10031–10036.
244. Bardot, V.; Remuson, R.; Gelas-Mialhe, Y.; Gramain, J.-C. *Synlett* **1996**, 37–38.
244a. Lee, P. H.; Bang, K.; Ahn, H.; Lee, K. *Bull. Korean Chem. Soc.* **2001**, *22*, 1385–1389.
245. Lee, P. H.; Ahn, H.; Lee, K.; Sung, S.-Y.; Kim, S. *Tetrahedron Lett.* **2001**, *42*, 37–39.
246. Hua, X.-G.; Li, C.-J. *Main Group Metal Chem.* **1999**, 533–537.
247. Miao, W.; Chan, T. H. *Synthesis* **2003**, 785–789.
248. Kumar, S.; Kumar, V.; Chimni, S. S. *Tetrahedron Lett.* **2002**, *43*, 8029–8031.
249. Iwasawa, N.; Miura, T.; Kiyota, K.; Kusama, H.; Lee, K.; Lee, P. H. *Org. Lett.* **2002**, *4*, 4463–4466.
250. Lee, K.; Kim, H.; Miura, T.; Kiyota, K.; Kusama, H.; Kim, S.; Iwasawa, N.; Lee, P. H. *J. Am. Chem. Soc.* **2003**, *125*, 9682–9688.
251. Beuchet, P.; Marrec, N. L.; Mosset, P. *Tetrahedron Lett.* **1992**, *33*, 5959–5960.
252. Jin, S.-J.; Araki, S.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1528–1532.
253. Vilaivan, T.; Winotapan, C.; Shinada, T.; Ohfune, Y. *Tetrahedron Lett.* **2001**, *42*, 9073–9076.

254. Andrews, P. C.; Peatt, A. C.; Raston, C. L. *Tetrahedron Lett.* **2004**, *45*, 243–248.
255. Legros, J.; Meyer, F.; Coliboeuf, M.; Crousse, B.; Bonnet-Delpon, D.; Begue, J.-P. *J. Org. Chem.* **2003**, *68*, 6444–6446.
256. Choudhury, P. K.; Foubelo, F.; Yus, M. *J. Org. Chem.* **1999**, *64*, 3376–3378.
257. Loh, T.-P.; Ho, D. S.-C.; Xu, K.-C.; Sim, K.-Y. *Tetrahedron Lett.* **1997**, *38*, 865–868.
258. Basile, T.; Bocoum, A.; Savoia, D.; Umani-Ronchi, A. *J. Org. Chem.* **1994**, *59*, 7766–7773.
259. Yanada, R.; Kaieda, A.; Takemoto, Y. *J. Org. Chem.* **2001**, 7516–7518.
260. Kumar, S.; Kaur, P. *Tetrahedron Lett.* **2004**, *45*, 3413–3416.
261. Prajapati, D.; Laskar, D. D.; Gogoi, B. J.; Devi, G. *Tetrahedron Lett.* **2003**, *44*, 6755–6757.
262. Chan, T. H.; Lu, W. *Tetrahedron Lett.* **1998**, *39*, 8605–8608.
263. Lu, W.; Chan, T. H. *J. Org. Chem.* **2000**, *65*, 8589–8594.
264. Lu, W.; Chan, T. H. *J. Org. Chem.* **2001**, *66*, 3467–3473.
265. Andrews, P. C.; Peatt, A. C.; Raston, C. L. *Green Chem.* **2004**, *4*, 119–122.
266. Nishigaichi, Y.; Ishihara, M.; Fushitani, S.; Uenaga, K.; Takuwa, A. *Chem. Lett.* **2004**, 108–109.
267. Ritson, D. J.; Cox, R. J.; Berge, J. *Org. Biomol. Chem.* **2004**, *2*, 1921–1933.
268. Bernardi, L.; Femoni, V. C.; Pollicino, S.; Ricc, A. *J. Org. Chem.* **2003**, *68*, 3348–3351.
269. Miyabe, H.; Nishimura, A.; Ueda, M.; Naito, T. *Chem. Commun.* **2002**, 1454–1455.
270. Cook, G. R.; Maity, B. C.; Kargbo, R. *Org. Lett.* **2004**, *6*, 1741–1743.
271. Bossard, F.; Dambrin, V.; Lintanf, V.; Beuchet, P.; Mosset, P. *Tetrahedron Lett.* **1995**, *36*, 6055–6058.
272. Tussa, L.; Lebeton, C.; Mosset, P. *Chem. Eur. J.* **1997**, *3*, 1064–1070.
273. Ranu, B. C.; Das, A. *Tetrahedron Lett.* **2004**, *45*, 6875–6877.
274. Fujiwara, N.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 4729–4732.
275. Loh, T.-P.; Lye, P.-L.; Wang, R.-B.; Sim, K.-Y. *Tetrahedron Lett.* **2000**, *41*, 7779–7783.
276. Lee, S. H.; Park, Y. S.; Nam, M. H.; Yoon, C. M. *Org. Biomol. Chem.* **2004**, *2*, 2170–2172.
277. Negishi, E.-i. *Pure Appl. Chem.* **1981**, *53*, 2333–2356.
278. Norman, J. F.; Alexakis, A. *Synthesis* **1981**, 841–870.
279. Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 38–52.
280. Knochel, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; Vol. 4, pp 865–911.
281. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
282. Dolzine, T. W.; Oliver, J. P. *J. Organomet. Chem.* **1974**, *78*, 165–176.
283. Araki, S.; Imai, A.; Shimizu, K.; Butsugan, Y. *Tetrahedron Lett.* **1992**, *33*, 2581–2582.
284. Araki, S.; Imai, A.; Shimizu, K.; Yamada, M.; Mori, A.; Butsugan, Y. *J. Org. Chem.* **1995**, *60*, 1841–1847.
285. Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2318–2319.
286. Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1999**, *64*, 4095–4101.
287. Ranu, B. C.; Majee, A. *J. Chem. Soc., Chem. Commun.* **1997**, 1225–1226.
288. Klaps, E.; Schmid, W. *J. Org. Chem.* **1999**, *64*, 7537–7546.
289. Salter, M. M.; Sardo-Inffiri, S. *Synlett* **2002**, 2068–2070.
290. Lee, P. H.; Kim, S.; Lee, K.; Seomoon, D.; Kim, H.; Lee, S.; Kim, M.; Han, M.; Noh, K.; Livinghouse, T. *Org. Lett.* **2004**, *6*, 4825–4828.
291. Bhatti, N. H.; Salter, M. M. *Tetrahedron Lett.* **2004**, *45*, 8379–8382.
292. Araki, S.; Usui, H.; Kato, M.; Butsugan, Y. *J. Am. Chem. Soc.* **1996**, *118*, 4699–4700.
293. Wang, L.; Sun, X.; Zhang, Y. *Synth. Commun.* **1998**, *28*, 3263–3267.
294. Araki, S.; Horie, T.; Kato, M.; Hirashita, T.; Yamamura, H.; Kawai, M. *Tetrahedron Lett.* **1999**, *40*, 2331–2334.
295. Araki, S.; Kamei, T.; Igarashi, Y.; Hirashita, T.; Yamamura, H.; Kawai, M. *Tetrahedron Lett.* **1999**, *40*, 7999–8002.
296. Araki, S.; Nakano, H.; Subburaj, K.; Hirashita, T.; Shibutani, K.; Yamamura, H.; Kawai, M.; Butsugan, Y. *Tetrahedron Lett.* **1998**, *39*, 6327–6330.
297. Araki, S.; Shiraki, F.; Tanaka, T.; Nakano, H.; Subburaj, K.; Hirashita, T.; Yamamura, H.; Kawai, M. *Chem. Eur. J.* **2001**, 7, 2784–2790.
298. Marshall, J. A.; McNulty, L. M.; Zou, D. *J. Org. Chem.* **1999**, *64*, 5193–5200.
299. Cooper, I. R.; Grigg, R.; MacLachlan, W. S.; Thornton-Petta, M.; Sridharan, V. *J. Chem. Soc., Chem. Commun.* **2002**, 1372–1373.
300. Cleghorn, L. A. T.; Cooper, I. R.; Grigg, R.; MacLachlan, W. S.; Sridharan, V. *Tetrahedron Lett.* **2003**, *44*, 7969–7973.
301. Cleghorn, L. A. T.; Cooper, I. R.; Fishwick, C. W. G.; Grigg, R.; MacLachlan, W. S.; Rasparini, M.; Sridharan, V. *J. Organomet. Chem.* **2003**, *687*, 483–493.
302. Ohno, H.; Hamaguchi, H.; Tanaka, T. *Org. Lett.* **2000**, *2*, 2161–2163.
303. Ohno, H.; Hamaguchi, H.; Tanaka, T. *J. Org. Chem.* **2001**, *66*, 1867–1875.
304. Lee, W.; Kim, K.-H.; Surman, M. D.; Miller, M. J. *J. Org. Chem.* **2003**, *68*, 139–149.
305. Miyabe, H.; Yamaoka, Y.; Naito, T.; Takemoto, Y. *J. Org. Chem.* **2003**, *68*, 6745–6751.
306. Miyabe, H.; Yamaoka, Y.; Naito, T.; Takemoto, Y. *J. Org. Chem.* **2004**, *69*, 1415–1418.
307. Yadav, J. S.; Madhuri, C.; Reddy, B. V. S.; Reddy, G. S. K.; Sabitha, G. *Synth. Commun.* **2002**, *32*, 2771–2777.
308. Bao, W.; Zheng, Y.; Zhang, Y.; Zhou, J. *Tetrahedron Lett.* **1996**, *37*, 9333–9334.
309. Bao, W.; Zhang, Y. *Synlett* **1996**, 1187–1188.
310. Yadav, J. S.; Anjaneyulu, S.; Ahmed, M. M.; Reddy, B. V. S. *Tetrahedron Lett.* **2001**, *42*, 2557–2559.
311. Oh, B. K.; Cha, J. H.; Cho, Y. S.; Choi, K. I.; Koh, H. Y.; Chang, M. H.; Pae, A. N. *Tetrahedron Lett.* **2003**, *44*, 2911–2913.
312. Hirashita, T.; Mitsui, K.; Hayashi, Y.; Araki, S. *Tetrahedron Lett.* **2004**, *45*, 9189–9191.
313. Loh, T.-P.; Li, X.-R. *J. Chem. Soc., Chem. Commun.* **1996**, 1929–1930.
314. Loh, T.-P.; Li, X.-R. *Tetrahedron* **1999**, *55*, 5611–5622.
315. Kwon, J. S.; Pae, A. N.; Choi, K. I.; Koh, H. Y.; Kim, Y.; Cho, Y. S. *Tetrahedron Lett.* **2001**, *42*, 1957–1959.
316. Kang, K. H.; Choi, K. I.; Koh, H. Y.; Kim, Y.; Chung, B. Y.; Cho, Y. S. *Synth. Commun.* **2001**, *31*, 2277–2286.
317. Lee, P. H.; Lee, K.; Kim, S. *Org. Lett.* **2001**, *3*, 3205–3207.
318. Araki, S.; Jin, S.-J.; Butsugan, Y. *J. Chem. Soc., Perkin Trans. 1* **1995**, 549–552.
319. Matsumura, Y.; Onomura, O.; Suzuki, H.; Furukubo, S.; Maki, T.; Li, A. C.-J. *Tetrahedron Lett.* **2003**, *44*, 5519–5522.
320. Kang, S.-K.; Baik, T.-G.; Jiao, X.-H.; Lee, K.-J.; Lee, C. H. *Synlett* **1999**, 447–449.
321. Choucair, B.; Léon, H.; Miré, M.-A.; Lebreton, C.; Mosset, P. *Org. Lett.* **2000**, *2*, 1851–1853.

322. Lee, P. H.; Bang, K.; Lee, K.; Sung, S.-Y.; Chang, S. *Synth. Commun.* **2001**, 3781–3789.
323. Bang, K.; Lee, K.; Park, Y. K.; Lee, P. H. *Bull. Korean Chem. Soc.* **2002**, *23*, 1272–1276.
324. Johar, P. S.; Araki, S.; Butsugan, Y. *J. Chem. Soc., Perkin Trans. 1* **1992**, 711–713.
325. Hirashita, T.; Kinoshita, K.; Yamamura, H.; Kawai, M.; Araki, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 825–828.
326. Araki, S.; Katsumura, N.; Kawasaki, K.-i.; Butsugan, Y. *J. Chem. Soc., Perkin Trans. 1* **1991**, 499.
327. Schich, H.; Ludwig, R.; Schwarz, K.-H.; Kleiner, K.; Kunath, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1191–1193.
328. Schick, H.; Lundwig, R.; Schwarz, K.-H.; Kleiner, K.; Kunath, A. *J. Org. Chem.* **1994**, *59*, 3161–3164.
329. Schick, H.; Lundwig, R.; Schwarz, K.-H.; Kleine, K.; Kunath, A. *Tetrahedron* **1995**, *51*, 2939–2946.
330. Banik, B. K.; Ghatak, A.; Becker, F. F. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2179–2181.
331. Ghatak, A.; Becker, F. F.; Banik, B. K. *Heterocycles* **2000**, *53*, 2769–2773.
332. Lee, P. H.; Seomoon, D.; Lee, K.; Heo, Y. *J. Org. Chem.* **2003**, *68*, 2510–2513.
333. Araki, S.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 727–729.
334. Chung, W. J.; Higashiya, S.; Welch, J. T. *J. Fluorine Chem.* **2001**, *112*, 343–347.
335. Médebille, M.; Onomura, O.; Keiouz, R.; Okada, E.; Yano, H.; Teraichi, T. *Synthesis* **2002**, 2601–2608.
336. Araki, S.; Yamada, M.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1126.
337. Izquierdo, I.; Plaza, M. T.; Tamayo, J. A.; Mota, A. J. *Synthesis* **2004**, 1083–1087.
338. Yoo, B. W.; Hwang, S. K.; Kim, D. Y.; Choi, J. W.; Ko, J. J.; Choib, K. I.; Kim, J. H. *Tetrahedron Lett.* **2002**, *43*, 4813–4815.
339. Nóbrega, J. A.; Goncalves, S. M. C.; Peppe, C. *Tetrahedron Lett.* **2001**, *42*, 4745–4746.
340. Nóbrega, J. A.; Gonçalves, S. M. C.; Peppe, C. *Tetrahedron Lett.* **2000**, *41*, 5779–5782.
341. Pérez, I.; Sestelo, J. P.; Sarandeses, L. A. *Org. Lett.* **1999**, *1*, 1267–1269.
342. Legros, J.-Y.; Primault, G.; Fiaud, J.-C. *Tetrahedron* **2001**, *57*, 2507–2514.
343. Pena, M. A.; Pérez, I.; Sestelo, J. P.; Sarandeses, L. A. *J. Chem. Soc., Chem. Commun.* **2002**, 2246–2247.
344. Pena, M. A.; Sestelo, J. P.; Sarandeses, L. A. *Synthesis* **2003**, 780–784.
345. Takami, K.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Org. Lett.* **2001**, *3*, 1997–1999.
346. Lee, P. H.; Lee, S. W.; Seomoon, D. *Org. Lett.* **2003**, *5*, 4963–4966.
347. Lee, S. W.; Lee, K.; Seomoon, D.; Kim, S.; Kim, H.; Kim, H.; Shim, E.; Lee, M.; Lee, S.; Kim, M., *et al. J. Org. Chem.* **2004**, *69*, 4852–4855.
348. Hirashita, T.; Yamamura, H.; Kawai, M.; Araki, S. *J. Chem. Soc., Chem. Commun.* **2001**, 387–388.
349. Hirashita, T.; Hayashi, Y.; Mitsui, K.; Araki, S. *J. Org. Chem.* **2003**, *64*, 1309–1313.
350. Lehmann, U.; Awasthi, S.; Minehan, T. *Org. Lett.* **2003**, *5*, 2405–2408.
351. Sakai, N.; Annaka, K.; Konakahara, T. *Org. Lett.* **2004**, *6*, 1527–1530.
352. Venkatraman, S.; Li, C.-J. *Org. Lett.* **1999**, *1*, 1133–1135.
353. Lee, P. H.; Sung, S.-y.; Lee, K. *Org. Lett.* **2001**, *3*, 3201–3204.
354. Lee, P. H.; Sung, S.-y.; Lee, K.; Chang, S. *Synlett* **2001**, 146–148.
355. Lee, K.; Lee, J.; Lee, P. H. *J. Org. Chem.* **2002**, *67*, 8265–8268.
356. Baker, L.; Minehan, T. *J. Org. Chem.* **2004**, *69*, 3957–3960.
357. Rodríguez, D.; Sestelo, J. P.; Sarandeses, L. A. *J. Org. Chem.* **2004**, *69*, 8136–8139.
358. Lee, K.; Seomoon, D.; Lee, P. H. *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 3901–3903.
359. Gelman, D.; Schumann, H.; Blum, J. *Tetrahedron Lett.* **2000**, *41*, 7555–7558.
360. Blum, J.; Katza, J. A.; Jabera, N.; Michman, M.; Schumann, H.; Schutte, S.; Kaufmann, J.; Wassermann, B. C. *J. Mol. Catal.* **2001**, *165*, 97–102.
361. Jaber, N.; Gelman, D.; Schumann, H.; Dechert, S.; Blum, J. *Eur. J. Org. Chem.* **2002**, 1628–1632.
362. Shenglof, M.; Gelman, D.; Heymer, B.; Schumann, H. *Synthesis* **2003**, 302–306.
363. Pérez, I.; Sestelo, J. P.; Maestro, M. A.; Mouriño, A.; Sarandeses, L. A. *J. Org. Chem.* **1998**, *63*, 10074–10076.
364. Yamada, M.; Tanaka, K.; Araki, S.; Butsugan, Y. *Tetrahedron Lett.* **1995**, *36*, 3169–3172.
365. Yamada, M.; Horie, T.; Kawai, M.; Yamamura, H.; Araki, S. *Tetrahedron* **1997**, *53*, 15685–15690.
366. Miyai, T.; Inoue, K.; Yasuda, M.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1998**, *39*, 1929–1932.
367. Abernethy, C. D.; Cole, M. L.; Davies, A. J.; Jones, C. *Tetrahedron Lett.* **2000**, *41*, 7567–7570.
368. Yasuda, M.; Onishi, Y.; Ueba, M.; Miyai, T.; Baba, A. *J. Org. Chem.* **2001**, *66*, 7741–7744.
369. Miyai, T.; Ueba, M.; Baba, A. *Synlett* **1999**, 182–184.
370. Fu, N. Y.; Zhao, X. M.; Yuan, Y. F.; Wang, J. T. *Chin. Chem. Lett.* **2003**, *14*, 1018–1020.
371. Yasuda, M.; Onishi, Y.; Ito, T.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 2425–2428.
372. Ranu, B. C.; Samanta, S. *Tetrahedron Lett.* **2002**, *43*, 7405–7407.
373. Ranu, B. C.; Samanta, S. *J. Org. Chem.* **2003**, *68*, 7130–7132.
374. Takami, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2002**, *4*, 2993–2995.
375. Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *J. Org. Chem.* **2003**, *68*, 6627–6631.
376. Inoue, K.; Yasuda, M.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 113–116.
377. Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2001**, *42*, 4661–4663.
378. Inoue, K.; Sawada, A.; Shibata, I.; Baba, A. *J. Am. Chem. Soc.* **2002**, *124*, 906–907.
379. Ranu, B. C.; Dutta, P.; Sarkar, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1139–1140.
380. Park, L.; Keum, G.; Kang, S. B.; Kim, K. S.; Kim, Y. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4462–4463.
381. Chae, H.; Cho, S.; Keum, G.; Kang, S. B.; Pae, A. N.; Kim, Y. *Tetrahedron Lett.* **2000**, *41*, 3899–3901.
382. Shibata, I.; Kato, H.; Ishida, T.; Yasuda, M.; Baba, A. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 711–714.
383. Miura, K.; Yamada, Y.; Tomita, M.; Hosomi, A. *Synlett* **2004**, 1985–1989.
384. Takami, K.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2004**, *6*, 4555–4558.
385. Takami, K.; Mikami, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2003**, *59*, 6627–6635.
386. Wang, C.-Y.; Su, H.; Yang, D.-Y. *Synlett* **2004**, 561–563.
387. Yanada, R.; Nishimori, N.; Matsumura, A.; Fujii, N.; Takemoto, Y. *Tetrahedron Lett.* **2002**, *43*, 4585–4588.
388. Yanada, R.; Obika, S.; Nishimori, N.; Yamauchi, M.; Takemoto, Y. *Tetrahedron Lett.* **2004**, *45*, 2331–2334.
389. Yanada, R.; Obika, S.; Oyama, M.; Takemoto, Y. *Org. Lett.* **2004**, *6*, 2825–2828.
390. Yanada, R.; Koh, Y.; Nishimori, N.; Matsumura, A.; Obika, S.; Mitsuya, H.; Fujii, N.; Takemoto, Y. *J. Org. Chem.* **2004**, *69*, 2417–2422.

391. Maeda, T.; Tada, H.; Yasuda, K.; Okawara, R. *J. Organomet. Chem.* **1971**, *27*, 13–18.
392. Araki, S.; Butsugan, Y. *J. Chem. Soc., Chem. Commun.* **1989**, 1286–1287.
393. Hirashita, T.; Hayashi, Y.; Mitsui, K.; Araki, S. *Tetrahedron Lett.* **2004**, *45*, 3225–3228.
394. Price, S.; Edwards, S.; Wu, T.; Minehan, T. *Tetrahedron Lett.* **2004**, *45*, 5197–5201.
395. Augé, J.; Lubin-Germain, N.; Seghrouchni, L. *Tetrahedron Lett.* **2002**, *43*, 5255–5256.
396. Augé, J.; Lubin-Germain, N.; Seghrouchni, L. *Tetrahedron Lett.* **2003**, *44*, 819–821.
397. Sakai, N.; Hirasawa, M.; Konakahara, T. *Tetrahedron Lett.* **2003**, *44*, 4171–4174.
398. Nomura, R.; Miyazaki, S.-I.; Matsuda, H. *J. Am. Chem. Soc.* **1992**, *114*, 2738–2740.
399. Lim, H. J.; Keum, G.; Kang, S. B.; Kim, Y.; Chung, B. Y. *Tetrahedron Lett.* **1999**, *40*, 1547–1550.
400. Araki, S.; Shimizu, T.; Butsugan, Y. *Chem. Express* **1991**, *6*, 583–586.
401. Yang, Y.; Chan, T. H. *J. Am. Chem. Soc.* **2000**, *122*, 402–403.
402. Araki, S.; Ito, H.; Butsugan, Y. *Appl. Organomet. Chem.* **1988**, *2*, 475–478.
403. Han, Y.; Huang, Y.-Z. *Tetrahedron Lett.* **1994**, *35*, 9433–9434.
404. Han, Y.; Chi, Z.-F.; Huang, Y. Z. *Chin. Chem. Lett.* **1996**, *7*, 713–716.
405. Gilman, H.; Jopnes, R. G. *J. Am. Chem. Soc.* **1940**, *62*, 980–982.
406. Tsuji, T.; Usugi, S.-i.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Chem. Lett.* **2002**, 2–3.
407. Mikami, S.; Yorimitsu, H.; Oshima, K. *Synlett* **2002**, 1137–1139.
408. Yamaguchi, M.; Sotokawa, T.; Hirama, M. *J. Chem. Soc., Chem. Commun.* **1997**, 743–744.
409. Han, Y.; Fang, L.; Tao, W.-T.; Huang, Y.-Z. *Tetrahedron Lett.* **1995**, *36*, 1287–1290.
410. Takai, K.; Ikawa, Y. *Org. Lett.* **2002**, *4*, 1727–1729.
411. Takai, K.; Ikawa, Y.; Ishii, K.; Kumanda, M. *Chem. Lett.* **2002**, 172–173.
412. Wang, Z.; Yuan, S.; Li, C.-J. *Tetrahedron Lett.* **2002**, *43*, 5097–5099.
413. Han, Y.; Chi, Z.; Huang, Y.-Z. *Synth. Commun.* **1999**, *29*, 1287–1296.
414. Han, Y.; Huang, Y.-Z. *Tetrahedron Lett.* **1995**, *36*, 7277–7280.
415. Han, Y.; Huang, Y.-Z.; Fang, L.; Tao, W.-T. *Synth. Commun.* **1999**, *29*, 867–876.
416. Laskar, D. D.; Gohain, M.; Prajapati, D.; Sandhu, J. S. *New J. Chem.* **2002**, *26*, 193–195.
417. Han, Y.; Huang, Y.-Z. *Tetrahedron Lett.* **1998**, *39*, 7751–7754.
418. Zhang, X.-L.; Han, Y.; Tao, W.-T.; Huang, Y.-Z. *J. Chem. Soc., Perkin Trans. 1* **1995**, 189–192.
419. Yamaguchi, M.; Hayashi, A.; Hirama, M. *Chem. Lett.* **1995**, 1093–1094.
420. Yamaguchi, M.; Tsukagoshi, T.; Arisawa, M. *J. Am. Chem. Soc.* **1999**, *121*, 4074–4075.
421. Arisawa, M.; Miyagawa, C.; Yamaguchi, M. *Synthesis* **2002**, 138–145.
422. Arisawa, M.; Miyagawa, C.; Yoshimura, S.; Kido, Y.; Yamaguchi, M. *Chem. Lett.* **2001**, 1080–1081.
423. Arisawa, M.; Akamatsu, K.; Yamaguchi, M. *Org. Lett.* **2001**, *3*, 789–790.
424. Arisawa, M.; Amemiya, R.; Yamaguchi, M. *Org. Lett.* **2002**, *4*, 2209–2211.
425. Amemiya, R.; Fujii, A.; Arisawa, M.; Yamaguchi, M. *J. Organomet. Chem.* **2003**, *686*, 94–100.
426. Amemiya, R.; Fujii, A.; Arisawa, M.; Yamaguchi, M. *Chem. Lett.* **2003**, 298–299.
427. Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *Inorg. Chim. Acta* **1999**, *296*, 67–71.
428. Kobayashi, K.; Arisawa, M.; Yamaguchi, M. *J. Am. Chem. Soc.* **2002**, *124*, 8528–8529.
429. Amemiya, R.; Nishimura, Y.; Yamaguchi, M. *Synthesis* **2004**, 1307–1314.
430. Usugi, S.-I.; Yorimitsu, H.; Oshima, K. *Tetrahedron Lett.* **2001**, *42*, 4535–4538.
431. Usugi, S.; Tsuritani, T.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 841–845.
432. Usugi, S.-I.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 2687–2690.
433. Usugi, S.; Yorimitsu, H.; Shinokubo, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 2049–2052.
434. Han, Y.; Huang, Y.-Z.; Zhou, C.-M. *Tetrahedron Lett.* **1996**, *37*, 3347–3350.
435. Choi, J. H. Y.; Jong Hun; Hwang, B. K.; Baek, D. J. *Bull. Korean Chem. Soc.* **1997**, *18*, 541–542.
436. Raston, C. L.; Siu, A. F. H.; Tranter, C. J.; Young, D. J. *Tetrahedron Lett.* **1994**, *35*, 5915–5918.
437. Choi, J. H.; Oh, Y. J. *Bull. Korean Chem. Soc.* **1995**, *16*, 474–475.
438. Falorni, M.; Lardicci, L.; Giacomelli, G. *Tetrahedron Lett.* **1985**, *26*, 4949–4950.
439. Ford, A.; Woodward, S. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 335–336.
440. Blake, A. J.; Cunningham, A.; Ford, A.; Teat, S. J.; Woodward, S. *Chem. Eur. J.* **2000**, *6*, 3586–3594.
441. Blum, J.; Gelman, D.; Baidossi, W.; Shakh, E.; Rosenfeld, A.; Aizenshtat, Z.; Wassermann, B. C.; Frick, M.; Heymer, B.; Schutte, S., *et al. J. Org. Chem.* **1997**, *62*, 8681–8686.
442. Bao, W.; Zhang, Y. *Synth. Commun.* **1997**, *27*, 615–620.
443. Yamaguchi, M.; Kido, Y.; Hayashi, A.; Hirama, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1313.
444. Kido, Y.; Yoshimura, S.; Yamaguchi, M.; Uchimaru, T. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1445–1458.
445. Yonehara, F.; Kido, Y.; Yamaguchi, M. *J. Chem. Soc., Chem. Commun.* **2000**, 1189–1190.
446. Kido, Y.; Yonehara, F.; Yamaguchi, M. *Tetrahedron* **2001**, *57*, 827–833.
447. Kido, Y.; Yamaguchi, M. *J. Org. Chem.* **1998**, *63*, 8086–8087.
448. Inoue, H.; Chatani, A.; Murai, S. *J. Org. Chem.* **2002**, *67*, 1414–1417.
449. Yonehara, F.; Kido, O.; Morita, S.; Yamaguchi, M. *J. Am. Chem. Soc.* **2001**, *123*, 11310–11311.
450. Yonehara, F.; Kido, O.; Sugimoto, H.; Morita, S.; Yamaguchi, M. *J. Org. Chem.* **2003**, *68*, 6752–6759.
451. Kobayashi, S.; Koide, K.; Ohno, M. *Tetrahedron Lett.* **1990**, *31*, 2435–2438.
452. Yamamoto, Y.; Furuta, T. *Chem. Lett.* **1989**, 797–800.
453. Utimoto, K.; Lambert, C.; Fukuda, Y.; Shiragami, H.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 5423–5426.
454. Fukuda, Y.; Matsubara, S.; Lambert, C.; Shiragami, H.; Nanko, T.; Uchimura, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1810–1813.
455. Ooi, T.; Morikawa, J.; Ichikawa, H.; Maruoka, K. *Tetrahedron Lett.* **1999**, *40*, 5881–5884.