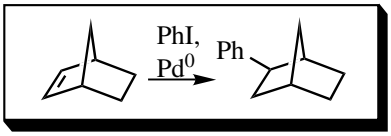

IV.2.4 Carbopalladation of Alkenes not Accompanied by Dehydropalladation

SERGEI I. KOZHUSHKOV and ARMIN DE MEIJERE

A. INTRODUCTION

The metal residue in σ-alkylpalladium(II) complexes of type **2** can be released from the organic fragment not only via β-dehydropalladation (**Scheme 1**, path A), but also via anion capture and/or reductive elimination (path B).

In this latter reaction mode, which is observed much more rarely than β-dehydropalladation, a wide variety of ligands can be coupled to each other with the formation of new C—C, C—H, C—N, C—O, and C—Hal bonds. This section does not cover the numerous cascade couplings in which a number of successive intramolecular additions of **2** onto double bonds is eventually completed by β-dehydropalladation[1],[2] as well as the numerous [2 + 2 + 2] and [4 + 2] cyclotri- and cyclodimerizations of alkynes, enynes, and related compounds.[3]–[7] The Pd(0)-catalyzed Cope rearrangement[8] also will not be considered here, as it proceeds via bis(η^3-allyl)palladium(II) intermediates. The carbopalladation reactions of allenes, which have been reviewed recently,[9] are covered in **Sect. IV.7**. (For new examples see also refs. [10]–[12]). On the other hand, the numerous Pd-catalyzed formal [3 + 2] cycloadditions of trimethylenemethane (TMM) complexes may be classified as carbopalladations of alkenes without subsequent dehydropalladation. As the subject of this section has partially been covered in several newly published reviews,[1],[2] the attention here will be on the most recent and interesting communications.

B. REACTIONS OF STABLE PALLADIUM COMPLEXES

The type of reaction under consideration has been reported for several stable palladium(II) complexes containing Pd—C σ-bonds. Thus, the reaction of the σ,π-complex **5** with halogens in dichloromethane gave mixtures of *exo*,*endo*-2-halo-6-methoxybicyclo[3.3.0]octane **6** and its *endo*,*endo*-diastereomer **7** in quantitative yields (**Scheme 2**).[13] The second step of this transformation can be described as a Pd-mediated carbohalogenation of the double bond in **5**.

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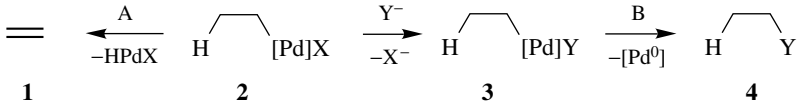
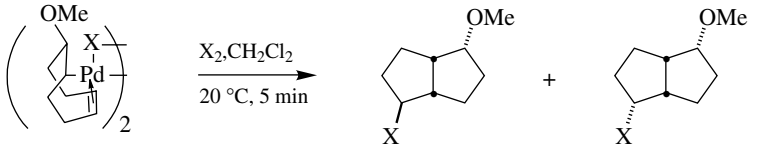
The bis(1-methoxynaphthalene-8-*C*,*O*)palladium(II) **9** reacts stoichiometrically with ethylene, butadiene, and isoprene. Among several other products, the 1,2-bis[1′-(8″-methoxynaphthyl)]ethane **10**, which must have arisen via reductive elimination from an intermediate Ar—CH_2CH_2—Pd—Ar complex, was also isolated, albeit in low yield (10%). The corresponding 1,4-addition of **9** onto butadiene and isoprene gave moderate yields of **8a,b** (**Scheme 3**).[14]

A metal release in the σ,π-complexes **5** and **12** has also been achieved by carbonylation with subsequent anion capture to produce *trans*-2-methoxy-substituted methyl esters **11** and **13** with retention of configuration at the carbon to which the palladium had been σ-bound (**Scheme 4**).[15]



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

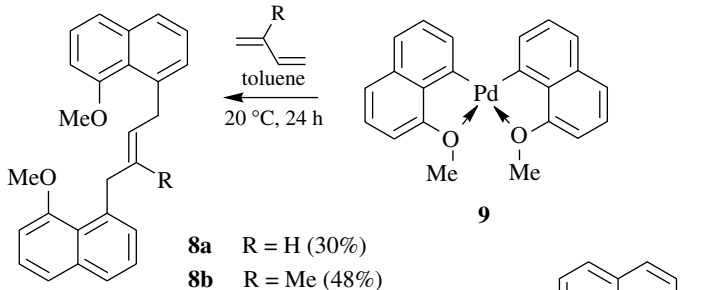
Scheme 1



5a X = Cl
5b X = Br

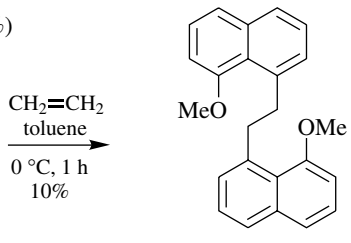
6a X = Cl (72%) **7a** X = Cl (28%)
6b X = Br (95%) **7b** X = Br (5%)

Scheme 2



9

8a R = H (30%)
8b R = Me (48%)



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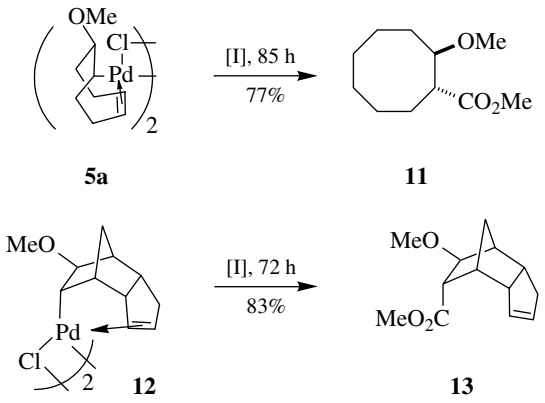
Scheme 3



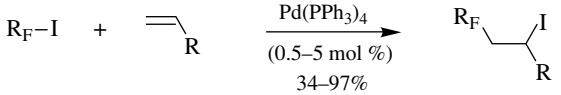
[I] = CO (40–43 atm), AcONa, MeOH, 20 °C.

Scheme 4

C. ANION CAPTURE AND REDUCTIVE ELIMINATION

The classification of catalytic carbopalladations can be difficult at first glance, since the overall transformation does not necessarily proceed via an alkylpalladium halide intermediate of type **2**. Thus, in the very efficient Pd-catalyzed iodoperfluoroalkylations of alkenes **15** with perfluoroalkyl iodides **14** (**Scheme 5**; only selected examples are listed),[16]–[18] the palladium(0) species participate only to the extent that they mediate the generation of perfluoroalkyl radicals from **14**, which subsequently add onto the double bond in **15**.[16]

Carbopalladations may be succeeded by hydride capture[1]; the reaction of an alkene with an aryl halide under appropriate choice of reaction conditions can thus lead to an

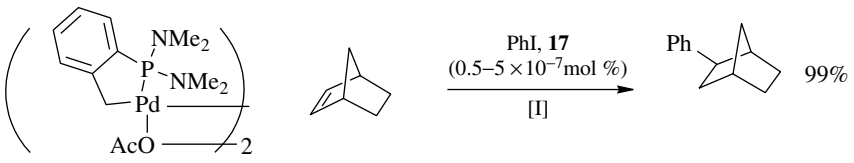


14 **15** **16**

R_F	R	Solvent	T(°C)	t (h)	Yield(%)	Reference
CF_3CF_2	*n*-Bu	Neat	20	0.3	97	[16]
$Cl(CF_2)_4$	*n*-C_5H_{11}	Neat	40	0.5	96	[16]
$CF_3(CF_2)_5$	Me_3Si	Neat	100	8	80	[16]
$CF_3(CF_2)_2$	$(CH_2)_2OH$	Hexane	20	6	65	[17]
$CF_3(CF_2)_3$	*n*-C_6H_{13}	Hexane	20	6	78	[17]
$CF_3(CF_2)_5$	*n*-C_6H_{13}	Hexane	20	6	73	[17]
$CF_3(CF_2)_3$	$(CH_2)_4CH(OH)CH_2OH$	Neat	20	2	76	[18]
$CF_3(CF_2)_3$	$(CH_2)_2CH(OH)CH_2OH$	Neat	20	2	75	[18]
$CF_3(CF_2)_2$	$(CH_2)_4CH(OH)CH_2OH$	Neat	20	2	88	[18]

Scheme 5

overall hydroarylation. The recently prepared new phosphapalladacycle **17** has been found to be particularly efficient for the hydroarylation of norbornene (**Scheme 6**)[19] under reductive conditions (Et_3N/formic acid) as developed by Larock and Johnson.[20] In this reaction *exo*-2-phenylnorbornane **18** was formed in quantitative yield.[19]

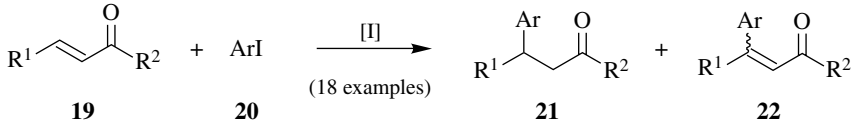


17 **18**

[I] = DMSO, Et_3N, 120 °C, 16 h.

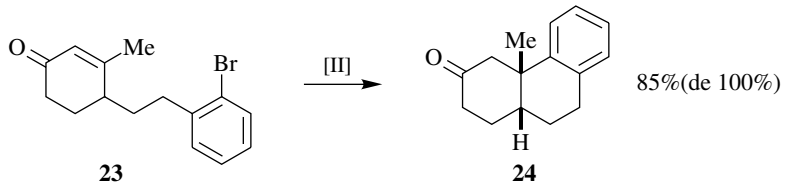
Scheme 6

Under palladium catalysis, α,β-unsaturated ketones can undergo Michael-type Heck hydroarylations.[21],[22] Recently, the intermolecular hydroarylation of **19** has been realized in supercritical carbon dioxide as a solvent to furnish the products **21** (**Scheme 7**).[21] Triethylamine is believed to be the source of hydride in these transformations.[23],[24] With certain combinations of substituents R^1, R^2 on the enone **19** and the aryl iodide, significant fractions of the β-dehydropalladation products **22** were also formed, and the aryl-substituted unsaturated **22** was the sole product when acrylates **19** (R^2 = OEt) were subjected to these conditions. The highly *cis*-diastereoselective hydroarylation of an α,β-unsaturated ketone **23** (**Scheme 7**)[22] has been applied in an intramolecular fashion toward the synthesis of the octahydrophenanthrene derivative **24**, a novel biomarker from Brazilian marine evaporitic Carmopolis oil.



19 **20** **21** **22**

R^1	Ph	Ph	Ph	Ph	*p*-MeO-C_6H_4	Ph
R^2	Me	Me	Me	Me	Me	Ph
Ar	Ph	*p*-MeO-C_6H_4	*m*-MeCO-C_6H_4	*m*-CF_3-C_6H_4	*p*-MeO-C_6H_4	*p*-MeO-C_6H_4
Yield of **21** (%)	88	88	55	74	90	97

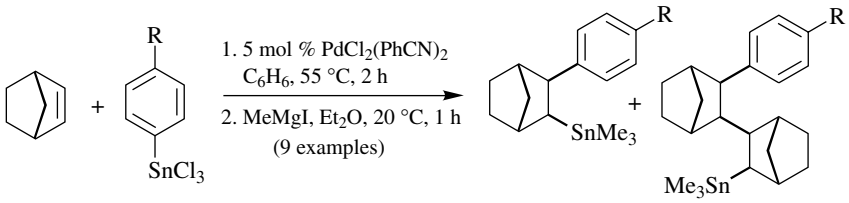


23 **24**

[I] = $Pd(OAc)_2$, Et_3N, $scCO_2$, 80 °C, 100 atm.
[II] = 10 mol % $Pd(OAc)_2$, Et_3N, $Bu_4N^+Br^-$, MeOH, DMF.

Scheme 7

A Pd-catalyzed reaction of aryltin trichlorides **25** with norbornene provided the corresponding arylstannylation products **26** and **27** after treatment of the reaction mixture with methylmagnesium iodide (**Scheme 8**).[25] The more electron-donating the substituent on the aromatic ring is, the more stable and long-lived the intermediate σ-norbornylpalladium complex is, and this leads to an increasing proportion of the product **27**.



25 **26** **27**

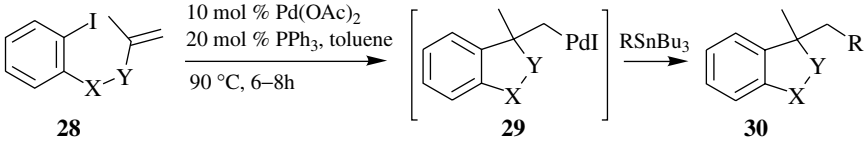
R	*m*-CF_3	*m*-F	H	Me	*p*-MeO
Yield of **26** (%)	69	70	71	60	46
Yield of **27** (%)	8	12	15	24	39

Scheme 8

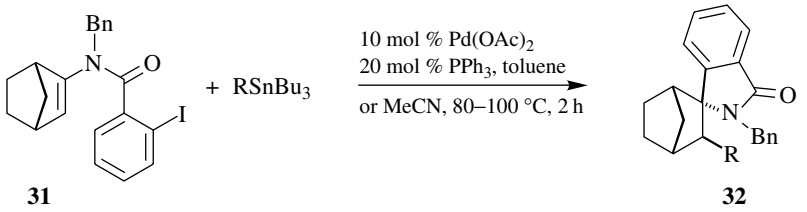
The anion capture by the intermediates of types **2** or **29** can also occur as a nucleophilic substitution on the palladium by an alkenyl or aryl group from an organotin species followed by reductive elimination just as in a Migita–Kosugi–Stille coupling. Pd(0)-catalyzed cascade mono- and biscyclizations with subsequent anion capture starting from a wide variety of all-carbon and heteroatom-containing precursors **28**, **31**, and so on and organotin reagents leading to a range of bridged, fused, and spiro-linked bi- and tricyclic products of types **30**, **32**, and so on have been reported recently (**Scheme 9**, only selected examples from more than 70 are listed).[26]–[28] This type of cascade reaction was developed in its intra–intermolecular as well as intra–intramolecular versions. The latter allowed the preparation of a wide range of bridged and spiro-fused heterobicycles with combinations of 5- and (12–17)-membered rings.[27] A pharmacophore may be attached to the unsaturated moieties, and thus compounds with sugar, nucleoside, purine, benzodiazepinone, and β-lactam moieties were prepared in good yields.[28]

The final step in a reaction sequence after a carbopalladation can also be capture on an acetate anion,[29] or carbon monoxide followed by another nucleophile.[30],[31] The former reaction in an enantioselective version has been used to prepare the key intermediates **34** and **36** en route to the sesquiterpene capnellenol (**Scheme 10**),[29] but with moderate success.

The latter process must play a key role in the recently reported Pd-catalyzed alternative copolymerization of ethene and CO in water.[30] It is also involved as a mechanistic step in a new synthesis of isoindolin-1-ones **40** by Pd-catalyzed intermolecular coupling and heteroannelation between 2-iodobenzoyl chloride (**37**) and imines **38** (**Scheme 11**).[31] In this case, however, a β-hydride elimination in the intermediate **39** would not be possible at all.

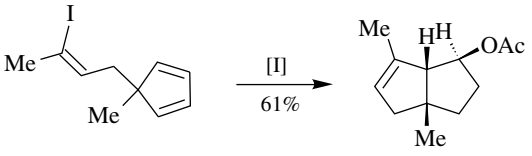


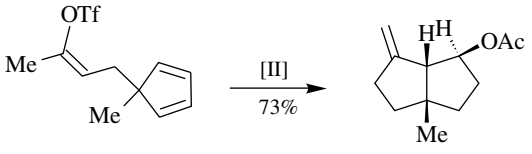
X	NBn	NBn	O	O	O	O
Y	C=O	C=O	CH_2	CH_2	CH_2	CH_2
R	CH=CHPh	2-Furyl	CH=CHPh	2-Furyl	$CH=CH_2$	2-Pyridyl
Yield(%)	89	90	90	95	45	60



R	$CH=CH_2$	Me_3Sn	2-Pyridyl	2-Thiazolyl	2-Furyl
Yield(%)	60	80	40	40	32

Scheme 9

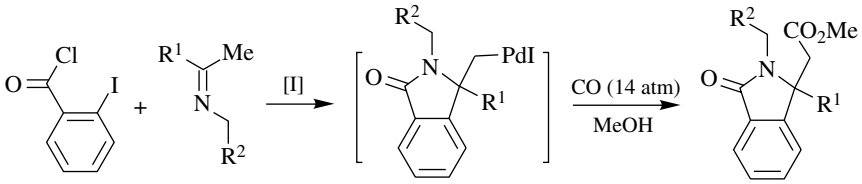




[I] = 10 mol % $[Pd(allyl)Cl]_2$, 10 mol % (*R*,*R*)-CHIRAPHOS, $Bu_4N^+ AcO^-$, toluene, 60 °C, 144 h.

[II] = 5 mol % $Pd(OAc)_2$, 6.4 mol % (*S*)-BINAP, $Bu_4N^+ AcO^-$, DMSO, 50 °C, 0.5 h.

Scheme 10



37 **38** **39** **40**

R^1	Me	Ph	2-Furyl	Me	Me	Me
R^2	*n*-Pr	*n*-Pr	*n*-Pr	Ph	Bn	*n*-Pent
Yield(%)	55	56	42	48	51	51

[I] = 4 mol % $PdCl_2(PPh_3)_2$, 8 mol % PPh_3, Et_3N, MeOH/MeCN, 100 °C, 20 h.

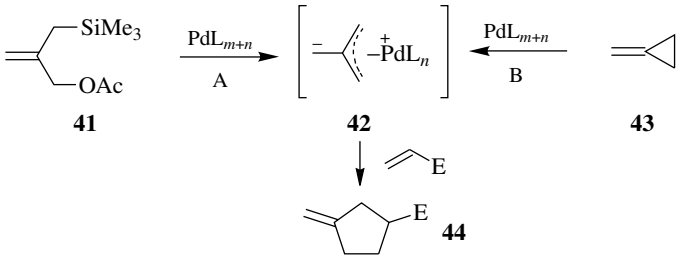
Scheme 11

D. CHEMISTRY OF TRIMETHYLENEMETHANEPALLADIUM (TMM) COMPLEXES AND RELATED INTERMEDIATES

The chemistry of the trimethylenemethanepalladium (TMM) intermediate **42** has been developed as a synthetically useful methodology. Its formal [3 + 2] cycloadditions to electron-deficient and some nonactivated alkenes have been a significant advance in ring construction methodology, as has been demonstrated by facile preparations of cyclopentanes, five-membered heterocycles, and many applications in natural products total synthesis.[32]–[34]

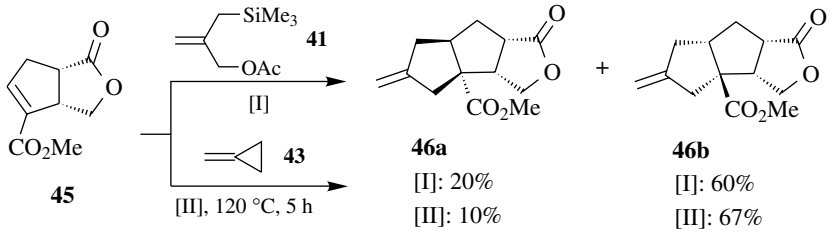
The two known methods to generate **42** (**Scheme 12**), one according to Trost and colleagues from 2-[(trimethylsilyl)methyl]allyl esters of type **41**[32]–[34] and the other according to Binger and co-workers directly from methylenecyclopropane **43** and its derivatives,[35]–[37] lead to intermediates of type **42** that are of slightly different reactivities. The applications of both methods in organic synthesis have been extensively reviewed several times.[32]–[37] In spite of the recently reported evidence for a concerted mode of formation of **44** from **42**,[38] a two-step mechanism for this cocyclization via a zwitterionic intermediate remains to be generally accepted. In a new application of this methodology toward an enantioselective total synthesis of pentalenolactones E and F, the efficiencies of the two methods to generate **42** and its cycloaddition products were compared (**Scheme 13**).[39]

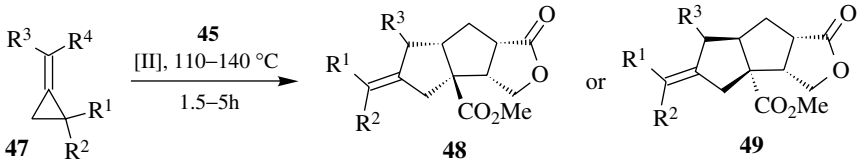
In both cases the addition of **42** onto the butyrolactone-annelated cyclopentenecarboxylate **45** occurred preferentially from the sterically more congested side yielding predominantly the diquinane derivative **46b** with the nonnatural configuration. While in the Trost-type cycloadditions the ratio of **46a**/**46b** varied from 1:1.7 to 1:5.3 depending on the polarity of the solvent, a ratio of 1:6.7 was observed in the Binger-type cocyclization. Analogous results were obtained for the cycloadditions of monosubstituted methylenecyclopropanes **47a,b** onto **45** (**Scheme 13**, only the main product is shown), but the stereochemical outcome of the formal [3 + 2] cycloaddition could be reversed by placing two substituents on the methylenecyclopropane either in the 2,2- or in the 1′,1′-position. For comparison, the product of a Nakamura-type[40]–[42] [3 + 2] cycloaddition of a methylenecyclopropanone acetal onto **45** had the same absolute configuration as **49**.[39]



41 **42** **43** **44**

Scheme 12





Starting Material	R^1	R^2	R^3	R^4	Main Product	R^1	R^2	R^3	Yield (%)
47a	Ph	H	H	H	**48a**	H	H	Ph	70
47b	H	H	H	Ph	**48a**	H	H	Ph	53
47c	Me_3Si	Ph	H	H	**49a**	Me_3Si	Ph	H	45
47d	H	H	Ph	Ph	**49b**	Ph	Ph	H	66

[I] = 15 mol % $Pd(OAc)_2$, 60 mol % Ph_3P, THF, 65 °C, 9 h.
[II] = 3.6 mol % Pd(Cp)(allyl), 3.6 mol % $(i\text{-Pr})_3P$, toluene.

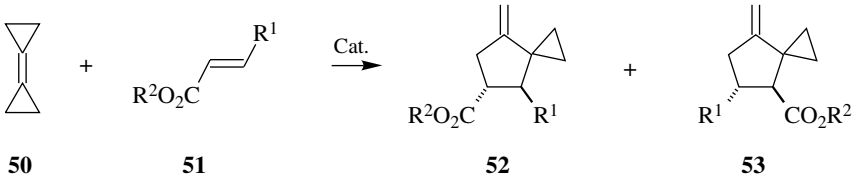
Scheme 13

The highly strained and thus unusually reactive tetrasubstituted alkene bicyclopropylidene (**50**)[43],[44] also turned out to cleanly undergo cocyclizations under palladium catalysis.[45] The TMM species generated from **50** underwent formal [3 + 2] cycloadditions onto electron-deficient (**Scheme 14**) as well as strained alkenes (**Scheme 15**).[45]

With unsymmetrically disubstituted alkenes of type **51**, two regioisomeric products were obtained, but the isomer **53** bearing the alkoxycarbonyl group adjacent to the spiro carbon atom was the minor component in all cases. Norbornadiene and norbornene reacted with **50** by the same mode to give formal [3 + 2] cycloadducts **54** and **55**, **56**, respectively, the latter as a 9:1 mixture of *exo*-**55** and *endo*-isomers **56** (**Scheme 15**). In

the absence of another activated alkene, one molecule of bicyclopropylidene (**50**), after the opening of a distal bond, underwent formal [3 + 2] cycloaddition onto a second molecule of **50** to give 8-cyclopropylidenedispiro[2.0.2.3]nonane (**58**) (**Scheme 15**).[46]

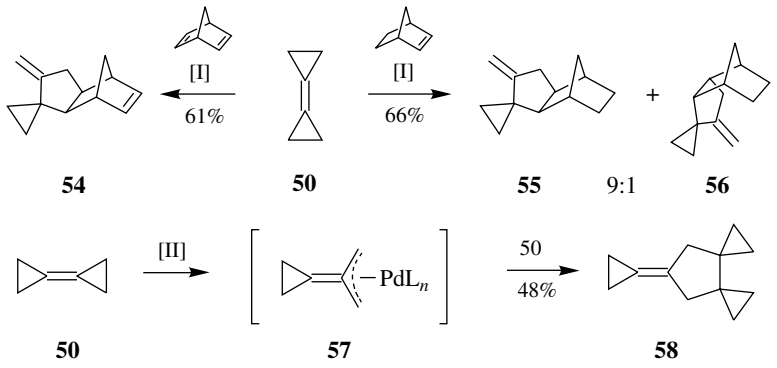
Any hydro- or carbopalladation of the double bond in a methylenecyclopropane moiety proceeds practically irreversibly due to the inherent strain (**Scheme 16**).[44]



50 **51** **52** **53**

R^1	R^2	Catalyst	Conditions	Ratio (**52/53**)	Yield (%)
H	Me	(π-All)PdCp *i*-Pr_3P	130–160 °C 2 h	2.8:1	54
H	Me	$Pd(dba)_2$ *t*-Bu(*i*-Pr)$_2$P	130 °C 2 h	3:1	45
Me	Me	$Pd(dba)_2$ *t*-Bu(*i*-Pr)$_2$P	110 °C 3 h	9:1	60
Ph	Me	$Pd(dba)_2$ *t*-Bu(*i*-Pr)$_2$P	110 °C 3 h	9:1	60
CO_2Et	Et	(π-All)PdCp *i*-Pr_3P	110 °C 3 h	—	77
CO_2Et	Et	$Pd(dba)_2$ *t*-Bu(*i*-Pr)$_2$P	110 °C 3 h	—	83

Scheme 14

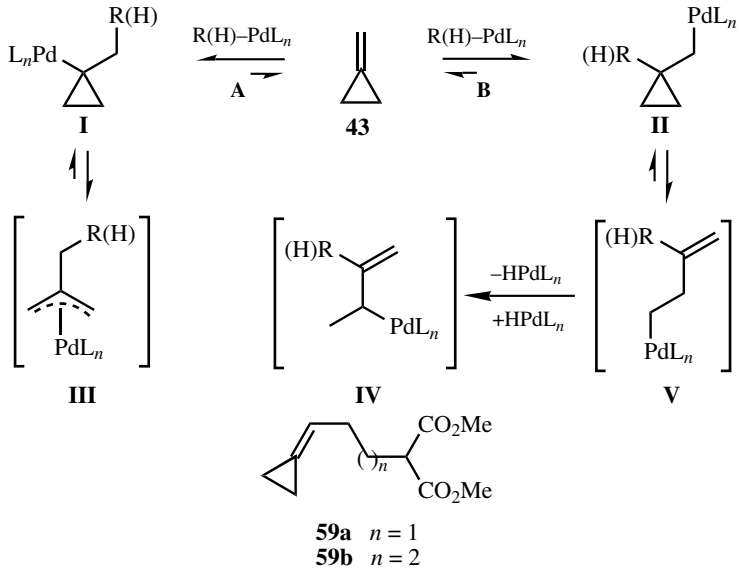


54 **50** **55** **56**

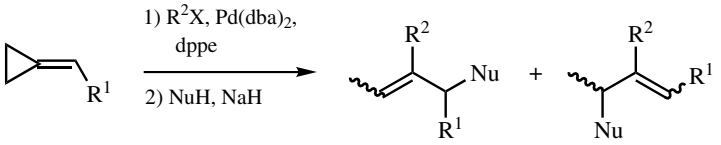
50 **57** **58**

[I] = $Pd(dba)_2$, *t*-Bu(*i*-Pr)$_2$P, 110 °C, 0.5 h.
[II] = $Pd(dba)_2$, (*i*-Pr)$_3$P, 110 °C, 4 h.

Scheme 15



59a $n = 1$
59b $n = 2$



43, **60** **61** **62**

	R^1	R^2X	Conditions	NuH	Products, Yield (%)
43 **60a**	H		THF, 80 °C, 40 h	$H_2C(CO_2Me)_2$	**61aa**, 39 (*E*/*Z* = 7:3) **62aa**, 17
43 **60a**	H		THF, 80 °C, 60 h	$PhSO_2CH_2CO_2Me$	**61ab**, 48 (*E*/*Z* = 8:2) **62ab**, 16
43 **60a**	H	PhI	THF, 80 °C, 40 h	$H_2C(CO_2Me)_2$	**61ac**, 37 (*E*/*Z* = 1:1) **62ac**, 30
60b	*n*-Bu		DMSO, 90 °C, 40 h	$H_2C(CO_2Me)_2$	**61ba**, 38 (*E*/*Z* = 2:8) **62ba**, 7
60b	*n*-Bu	PhI	DMSO, 90 °C, 40 h	$H_2C(CO_2Me)_2$	**61bc**, 58 (*E*/*Z* = 3:7) **62bc**, 6

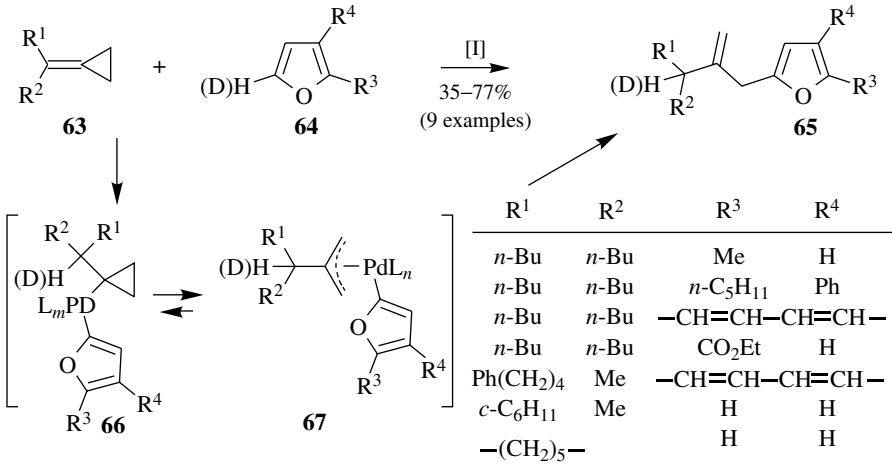
Scheme 16

Both regiochemical modes (**A** and **B**) of insertion of the double bond of **43** into a Pd—C or Pd—H bond leading to the two possible types of intermediates **I** and **II** are accompanied by a significant strain release (~13.5 kcal mol^{-1}), which makes even a hydropalladation practically irreversible. The other conceivable direction of dehydropalladation in one of the two possible intermediates **I** also does not occur as it would lead to a highly strained cyclopropene derivative; therefore, **I** normally undergoes opening of the distal cyclopropyl C—C bond to form an allylpalladium complex **III**. This has its general analogy in the

cyclopropylmetal (or cyclopropyl carbanion) to allylmetal (or allyl anion) ring opening.[47] The other possible intermediate **II** from a methylenecyclopropane usually opens one of the two proximal cyclopropyl bonds, and this corresponds to the well-known (cyclopropylmethyl)metal to homoallylmetal[48],[49] rearrangement, to form the homoallylpalladium intermediate **IV**. The latter can eventually undergo β-dehydropalladation (see **Sects. IV.2.2.1**, **IV.2.1.2**, and **X.3**), yet readdition of $HPdL_n$ can also occur with the reverse regiochemistry to yield a σ-allyl- or π-allylpalladium intermediate **V** (see below).

Both reaction modes **A** and **B** have been observed for carbopalladations of methylenecyclopropane derivatives **59a**,**b** with subsequent intramolecular nucleophilic trapping of the intermediate allylpallatium species **III** or **IV**, respectively, depending on the tether lengths between the methylenecyclopropane and the dimethyl malonate moieties. The same carbopalladations of unsubstituted methylenecyclopropane **43** (≙**60a**) and pentylidene-cyclopropane (**60b**) with subsequent intermolecular trapping by carbon nucleophiles were found to generally proceed by mode **B** via intermediates **II**, **V**, **IV** to yield ring-opening products **61** and **62**, respectively (**Scheme 16**).

Reaction mode **A** (**Scheme 16**) has recently also been realized for the Pd-catalyzed hydrofurylation of alkylidenecyclopropanes **63** in which a hydropalladation is the initial step (**Scheme 17**).[52] Mechanistic investigations of this reaction using a labeled 2-alkyl-5-deuteriofuran demonstrated this transformation to really proceed via intermediates **66** and **67** rather than by a direct insertion of a furylpalladium species into the distal bond of the methylenecyclopropane **63**. The deuterium content at the methyne position of **65** was, however, only 44%.



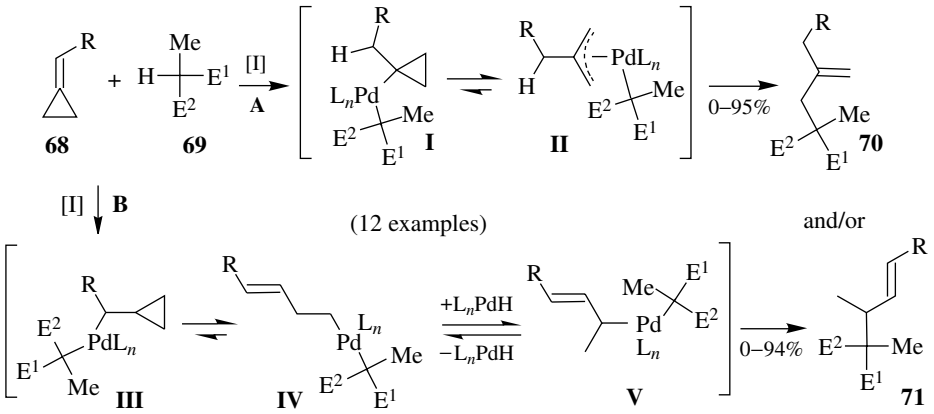
R^1	R^2	R^3	R^4	Yield (%)
n-Bu	*n*-Bu	Me	H	70
n-Bu	*n*-Bu	*n*-C_5H_{11}	Ph	70
n-Bu	*n*-Bu	—CH=CH—CH=CH—		63
n-Bu	*n*-Bu	CO_2Et	H	77
$Ph(CH_2)_4$	Me	—CH=CH—CH=CH—		35
c-C_6H_{11}	Me	H	H	74
—$(CH_2)_5$—		H	H	65

[I]: 5 mol % $Pd(Ph_3P)_4$, 10 mol % $Bu_3P(O)$, neat, 120 °C, 15–39 h.

Scheme 17

In the Pd-catalyzed hydrocarbonation of methylenecyclopropanes **68** with pronucleophiles of type **69** (**Scheme 18**),[53] the direction of the initial hydropalladation depends crucially on the electron density distribution in the double bond of **68**. Thus, a competition of the reactions along both pathways **A** and **B** can be observed. When R = alkyl or substituted alkyl, the reaction proceeds mainly via intermediates **I** and **II** furnishing the hydrocarbonation products **70** in good to very good yields. This type of reaction was performed both as an inter- as well as an intramolecular version. The reaction proceeded

along pathway **B** for methylenecyclopropanes **68** with R = aryl. The opening of a proximal bond in the intermediate **III** corresponds to a cyclopropyl to homoallyl rearrangement. The thus formed intermediate **IV** apparently underwent β-dehydropalladation and readdition of the hydridopalladium species with reverse regioselectivity to yield a σ-allylpalladium intermediate **V**, which is eventually captured by the carbanion from **69** to yield the product of type **71**. This mechanistic rationalization has been checked in experiments with deuterium-labeled protonucleophiles **69**.

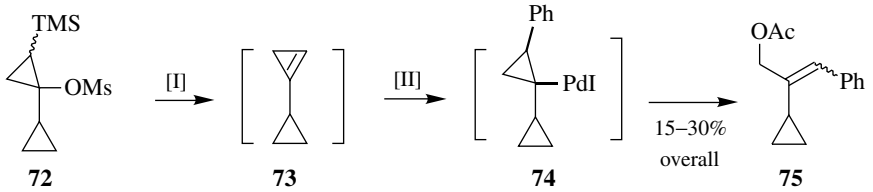


R	$(CH_2)_3Ph$	$(CH_2)_3Ph$	c-C_6H_{11}	Ph	Ph	Ph	p-CF_3-C_6H_4
E^1	CN	CN	CN	CO_2Et	CN	CN	CN
E^2	CN	CO_2Et	CN	CO_2Et	CN	CO_2Et	CN
Yield of **70** (%)	82	95	94	55	0	0	0
Yield of **71** (%)	0	0	0	0	88	83	94

[I]: 10 mol % $Pd(Ph_3P)_4$, THF, 100 °C, 2–3 d.

Scheme 18

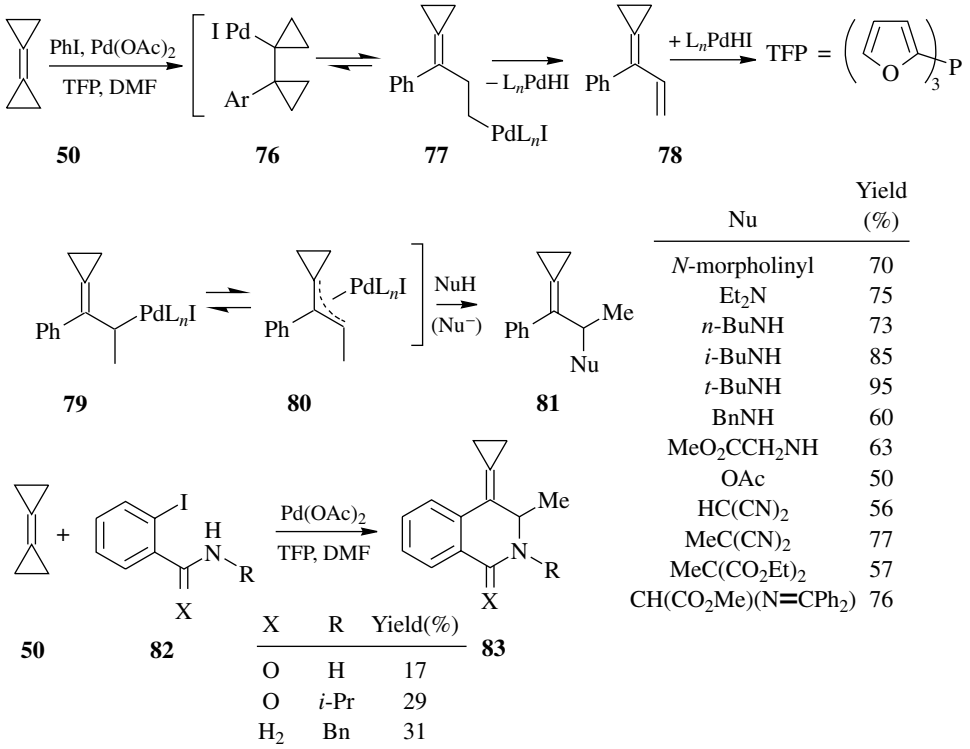
An even more pronounced example of a selectivity in spite of a possible competition between the two reaction modes **A** and **B** was observed in the attempted Heck reaction of phenyl iodide with cyclopropylcyclopropene **73** *in situ* generated from **72** (**Scheme19**).[54] The only isolated product **75** must have been formed by phenylpalladation of the cyclopropene moiety, in such a way as to result in **74**, which at the same time is a cyclopropylpalladium as well as a cyclopropylmethylpalladium species. Apparently, though, the phenyl substituent on the cyclopropane ring favors the cyclopropylpalladium to allylpalladium ring opening, and this is followed by acetate capture to give the allylic acetate **75**.



[I]: $Bu_4N^+F^-$, THF.
[II]: 5 mol % $Pd(OAc)_2$, 10 mol % PPh_3, Bu_4N^+ AcO^-.

Scheme 19

In such a situation, but without an additional substituent on the Pd-substituted cyclopropane ring, the reaction mode along pathway **B** normally predominates. This is illustrated by the Heck coupling reaction of bicyclopropylidene (**50**) with iodobenzene, which under normal Heck conditions gave the phenyl-substituted diene **78** in up to 78% isolated yield or, in the presence of a dienophile, the corresponding Diels–Alder product in excellent yield (see **Sects. IV.2.2.1**, **IV.2.1.2**, and **X.3**).[46],[55]–[57] The coupling of **50** with iodobenzene in the presence of palladium acetate and the less basic trisfurylphosphine ligand apparently occurs with a rearrangement of the σ-homoallyl- **77** to a σ-allylpalladium intermediate **80**, most probably via dehydropalladation and subsequent reverse addition of the hydridopalladium species to the newly formed double bond. The σ-allyl- or π-allylpalladium species **80** was then efficiently trapped with various oxygen, nitrogen, and carbon nucleophiles to yield methylenecyclopropane derivatives **81**. An intramolecular version of the latter type of reaction has also been carried out, albeit with lower yields of the products **83** (**Scheme 20**).[57]



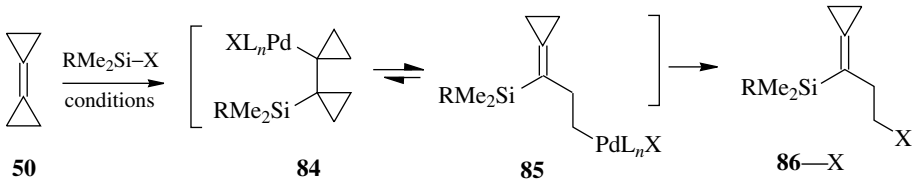
Nu	Yield (%)
N-morpholinyl	70
Et_2N	75
n-BuNH	73
i-BuNH	85
t-BuNH	95
BnNH	60
MeO_2CCH_2NH	63
OAc	50
$HC(CN)_2$	56
$MeC(CN)_2$	77
$MeC(CO_2Et)_2$	57
$CH(CO_2Me)(N{=}CPh_2)$	76

X	R	Yield(%)
O	H	17
O	*i*-Pr	29
H_2	Bn	31

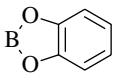
Scheme 20

The formation of homoallylpalladium intermediates of type **77** from the initial carbopalladation products **76** can essentially be described as an intramolecular carbopalladation of one of the proximal cyclopropyl bonds by the adjacent cyclopropylpalladium moiety. Thus, the analogous silyl-substituted homoallylpalladium intermediates **85** also arise via intramolecular carbopalladation, and this is not followed by β-dehydropalladation, but by reductive elimination to give the homoallylsilanes, -boronates, -stannanes, and so on **86**—X (**Scheme 21**).[58] This type of overall transformation of bicyclopropylidene (**50**) is particularly versatile with trimethylsilyl cyanide, as it yields the trimethylsilyl-substituted 4-cyclopropylidenebutyronitrile **86**—CN that can readily be converted to a number

of functionally substituted methylenecyclopropane derivatives with a terminal carboxylic acid, an aldehyde, or an amino substituent. Several of these Pd-catalyzed additions of various silane derivatives to bicyclopropylidene (**50**) open up routes to a variety of building blocks **86**—X containing a methylenecyclopropane end group, which has been found to be beneficial for many intramolecular reactions.



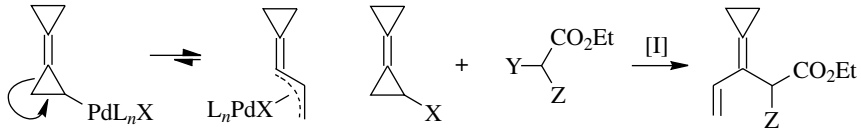
50 **84** **85** **86**—X

R	Conditions	X	Yield(%)
F	$Pd(PPh_3)_2Cl_2$, C_6H_6, 70 °C, 12 h	$SiMe_2F$	75
Ph	$Pd(OAc)_2$,  NC, PhMe, 130 °C, 3 d		71
Ph	$Pd(OAc)_2$,  NC, PhMe, 130 °C, 5 d		56
Me	$Pd(PPh_3)_4$, Et_2O, 50 °C, 3 d	$SnBu_3$	41
Me	$Pd(PPh_3)_4$, Et_2O, 50 °C, 4 d	$SnMe_3$	92
Me	$PdCl_2 \cdot Py_n$, PhMe, 100 °C, 14 d	CN	58

Scheme 21

The palladium hydride elimination from a cyclopropylpalladium derivative **87**, which can be generated by oxidative addition of bromobicyclopropylidene (**89**) onto palladium(0) or metal–palladium exchange on a bicyclopropylidenylmetal derivative such as **90**, would lead to an extremely strained methylenecyclopropene derivative and thus does not occur.[59] In this case, apparently, the ring opening of type **A** leading to the π-cyclopropylideneallylpalladium complex **88** is preferred, and the latter is captured with nucleophiles such as the enolates of ethyl *N*-(diphenylmethylene)glycinate (**91**) and diethyl malonate (**92**). This mode of transformation was observed in the reactions of the chlorozinc derivative **90** with bromomalonate **93** or the acetoxyglycine derivative **94** under $PdCl_2$(dppf) catalysis (**Scheme 22**).[60]

In several cases the nucleophilic attack on a π-allylpalladium complex **97** has been observed to occur on the central carbon atom of the allylic moiety. The resulting palladacyclobutane derivative **98**, instead of β-hydride elimination, underwent reductive elimination furnishing a cyclopropane derivative **99**.[61]–[63] In spite of theoretical predictions which, appear to rule out such reactions,[64] they have been observed experimentally (**Scheme 23**). Thus, in the Pd-catalyzed reactions of cyclopropylideneethyl acetate **100** with ketene alkyl silyl acetals **101**, the spiropentylacetates **103**, albeit in low yield, along with the "normal" products **102** were observed.[61] With η^3-allylpalladium-pyridinylpyrazole complexes **108** as catalysts this reaction mode of allyl acetates **104** with ketene acetals **105** became predominant so that cyclopropylacetates **106** were obtained as the main products (**Scheme 23**).[62] An enantioselective version of this cyclopropane formation has also been reported.[63]

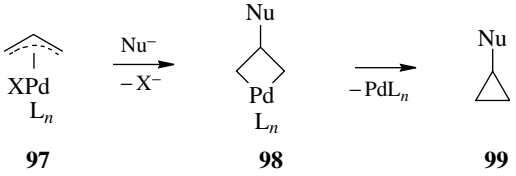


87 **88** **89**, **90** **91–94** **95**, **96**

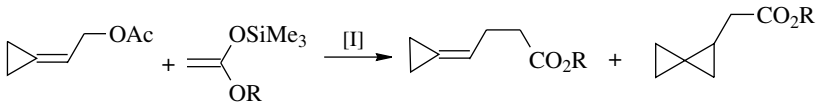
	Starting Materials					
	X		Y	Z	Products	Yield(%)
89	Br	**91**	$ZnCl_2$	N=CPh$_2$	**95**	72
89	Br	**92**	$ZnCl_2$	CO_2Et	**96**	24
90	$ZnCl_2$	**93**	Br	CO_2Et	**96**	27
90	$ZnCl_2$	**94**	OAc	N=CPh$_2$	**95**	29

[I]: $PdCl_2$(dppf), THF, 20 °C, 24 h.

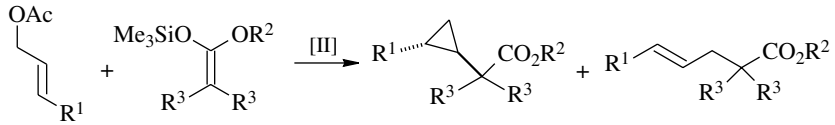
Scheme 22



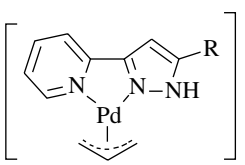
97 **98** **99**



100 **101a** R = Bn **102a** R = Bn (51%) **103a** R = Bn (18%)
101b R = Et **102b** R = Et (44%) **103b** R = Et (19%)



104 **105** **106** **107**



108a R = Me
108b R = *t*-Bu

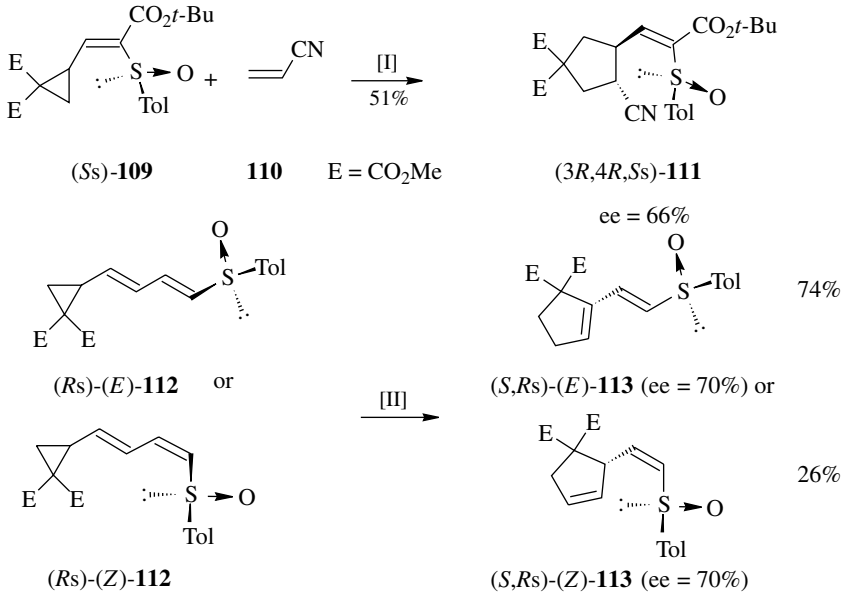
R^1	H	Ph	H
R^2	Et	Et	Me
R^3	Me	Me	$-(CH_2)_5-$
Yield of **102** (%)	68	38	87
Yield of **103** (%)	8	13	7

[I]: 2 mol % Pd(dba)$_2$, 2.5 mol % dppb, THF, 66 °C, 14 h.
[II]: 5 mol % **108a**, 20 mol % NaOAc, DMSO, 20 °C, 0.5 h.

Scheme 23

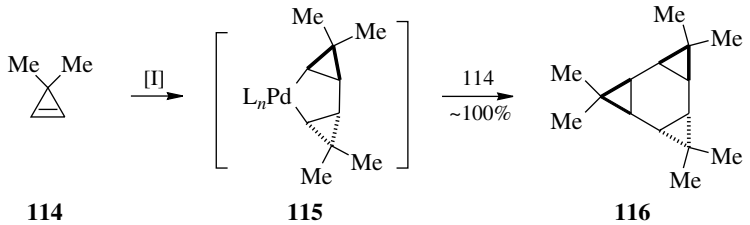
Three more reactions, which presumably proceed via carbopalladation steps without subsequent dehydropalladation, should be mentioned (**Scheme 24**). The first one[63] is the diastereoselective formal [3 + 2] cycloaddition of the chiral nonracemic (β-sulfinyl)vinylcyclopropane derivative **109** onto acrylonitrile (**110**). The second example is the Pd-catalyzed asymmetric vinylcyclopropane to cyclopentene rearrangement of the chiral nonracemic (*E*)- and (*Z*)-arylsulfinyl-1,3-butadienylcyclopropane derivatives **112**.[66] Plausible mechanisms that can rationalize the stereochemical outcome of the reactions were proposed in both publications.[65],[66]

The third reaction is the nearly quantitative Pd(0)-catalyzed cyclotrimerization of 3,3-dimethylcyclopropene (**114**), which resulted in the formation of hexamethyl-*trans*-tris-σ-homobenzene (**116**) (**Scheme 25**).[67],[68] The participation of the intermediate palladabicycloalkane of type **115** has recently been demonstrated by isolation and complete characterization of an analog.[69]



[I]: 10 mol % $Pd(PPh_3)_4$, 20 mol % PPh_3, THF, 65 °C, 3 h.
[II]: 10 mol % $Pd_2(dba)_3 \cdot CHCl_3$, 20 mol % dppe, toluene, 20 °C, 18 h.

Scheme 24



[I]: 0.3 mol % $Pd(PPh_3)_4$, C_6H_6, 40 °C, 4 h.

Scheme 25

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