

IV.4 Allylpalladation and Related Reactions of Alkenes, Alkynes, Dienes, and Other π -Compounds

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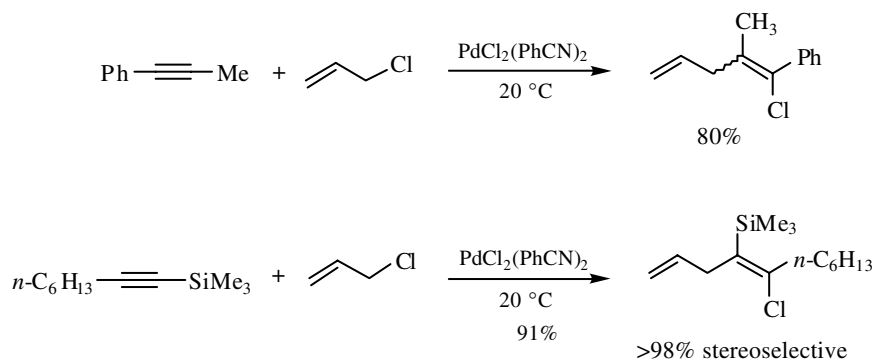
A. INTRODUCTION

Allylic halides react intermolecularly with alkynes in the presence of palladium(II) catalysts (**Scheme 1**).^{[1],[2]} The products are vinylic halides, which have further been elaborated by Ni(CO)₄-mediated carbonylation^[3] and Pd-catalyzed cross-coupling reaction, for example, with organotin compounds (**Scheme 2**).^[4]

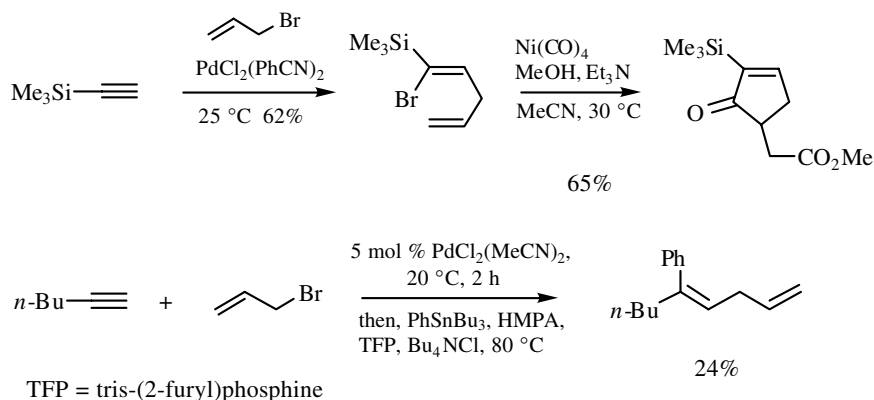
There are only a few cases of an intermolecular reaction of a π -allylpalladium complex with an alkene. The carbopalladation of norbornadiene with a stoichiometric amount of a π -allylpalladium complex to yield an allyl-substituted σ -norbornenylpalladium species has been reported.^[5] In the context of mechanistic studies of Pd-catalyzed alkene dimerization, the insertion of ethylene into a cationic π -allylpalladium complex was also reported as a stoichiometric reaction in 1996 (**Scheme 3**).^[6]

B. INTRAMOLECULAR REACTION OF A π -ALLYLPALLADIUM COMPLEX WITH ALKENES AND DIENES

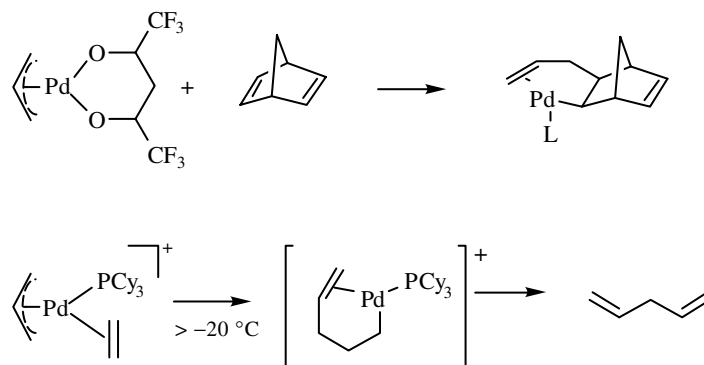
In 1987, Oppolzer and Gaudin reported an intramolecular version of the reaction of a π -allylpalladium complex with an alkene.^[7] The reactions of various 2,6-octadienyl acetate derivatives were achieved in the presence of Pd(dba)₂-PPh₃ at 70–80 °C leading to 2-vinyl-1-alkenylidenecyclopentane derivatives in yields ranging from 20% to 98% (**Schemes 4 and 5**). With one or two methyl groups attached at the alkenyl terminus, the acyclic alkenylallyl acetates under Pd(II) catalysis cyclized to yield 1-alkenyl-2-vinylcyclopentane derivatives (**Scheme 6**).^{[7]–[11]} A π -allylpalladium intermediate generated from an allyl ester can also intramolecularly carbopalladate a terminal diene or allene unit (**Scheme 7**, for the latter see also **Sect. IV.7**).^{[12],[13]} These cyclizations lead to new π -allylpalladium intermediates, which are eventually trapped by acetate to yield allyl acetates.



Scheme 1

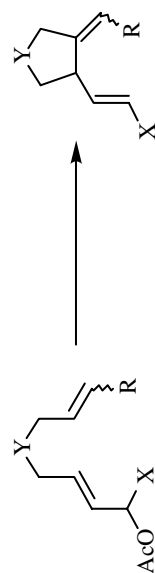


Scheme 2



Scheme 3

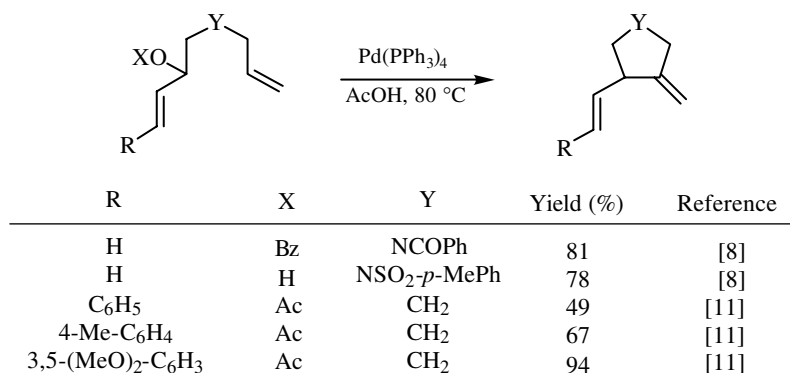
The key reactive intermediate in all these cyclizations is an alkene-coordinated cationic π -allylpalladium complex (**Scheme 8**), the formation of which is probably promoted by protonation of the acetoxy group when allylic acetates are used as starting materials.^{[6],[14]} It is thus understandable why acetic acid is mostly used as a crucial solvent. The σ -alkylpalladium intermediate generated through alkene insertion can undergo



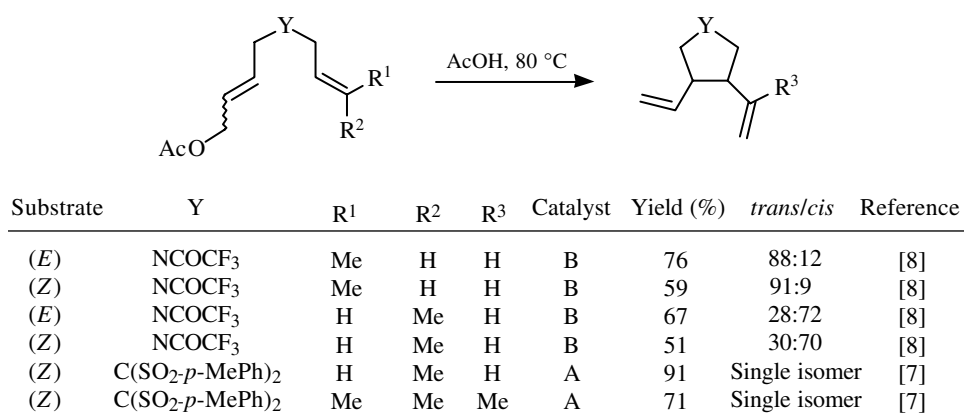
X	Y	R	Catalyst	Solvent	Temperature [°C]	Yield (%)	Ratio	Reference
H	C(SO ₂ - <i>p</i> -MePh) ₂	H	A	THF	70	82		[7]
H	C(CO ₂ Me) ₂	H	A	THF	80	20		[7]
H		H	A	MeOH	80	65		[7]
H		H	A	AcOH	80	77		[7]
H		H	A	AcOH	80	75		[7]
H	C(COO) ₂ CMe ₂	H	A	AcOH	80	72		[8]
H	NCH ₂ Ph	H	B	AcOH	80	69		[8]
H	NCO ₂ CH ₂ Ph	H	B	AcOH	80	72		[8]
H	N-Ts	H	B	AcOH	80	72		[8]
H		(<i>Z</i>)-Ph	A	AcOH	80	Not noted	(<i>Z</i>) only	[9]
H		(<i>E</i>)-Ph	A	AcOH	80	Not noted	96:4 (<i>Z/E</i>)	[9]
H		(<i>E</i>)-SiMe ₃	C	AcOH	80	57	(<i>E</i>) only	[9]
H	N(Ts)-CH ₂	H	B	AcOH	80	77		[8]
OAc	C(CO ₂ Et) ₂	H	B	AcOH	80	80		[10]
OAc		H	C	AcOH	80	98		[10]
OAc	C(SO ₂ Ph) ₂	H	C	AcOH	80	99		[10]

A: Pd(dba)₂, 3 PPh₃; B: Pd(PPh₃)₄; C: Pd(dba)₂, P(*o*-tolyl)₃.

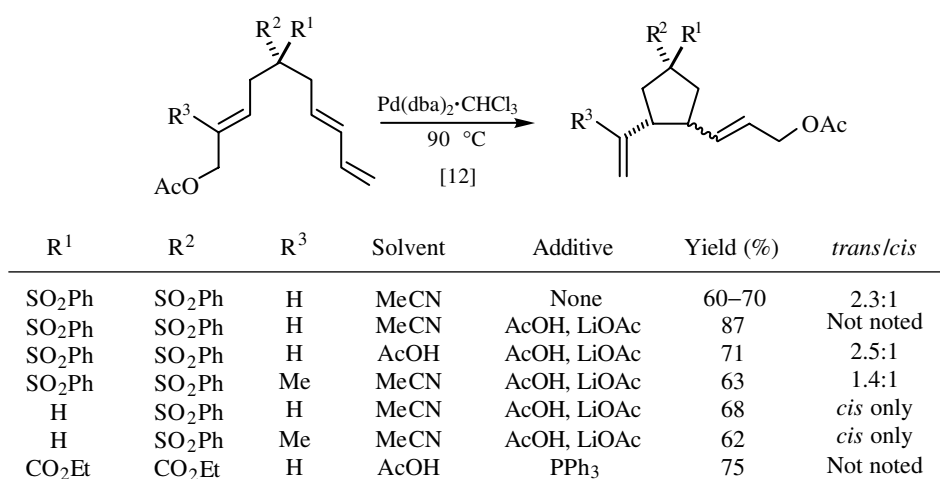
Scheme 4



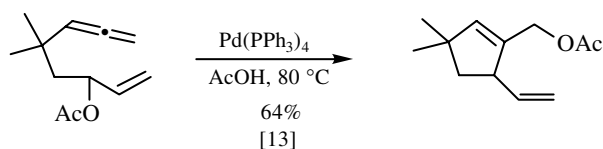
Scheme 5

A: Pd(dba)₂, 3 PPh₃; B: Pd(PPh₃)₄.

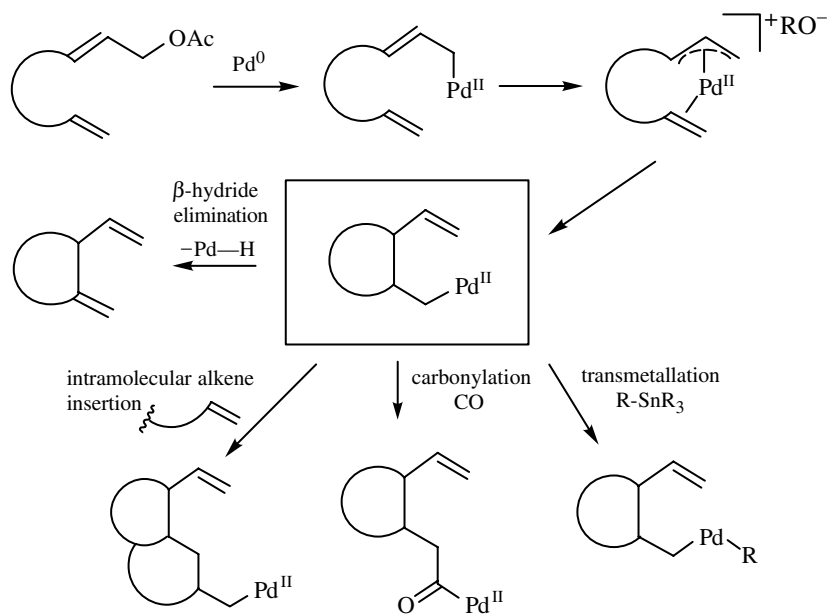
Scheme 6



Scheme 7



Scheme 7 (Continued)



Scheme 8

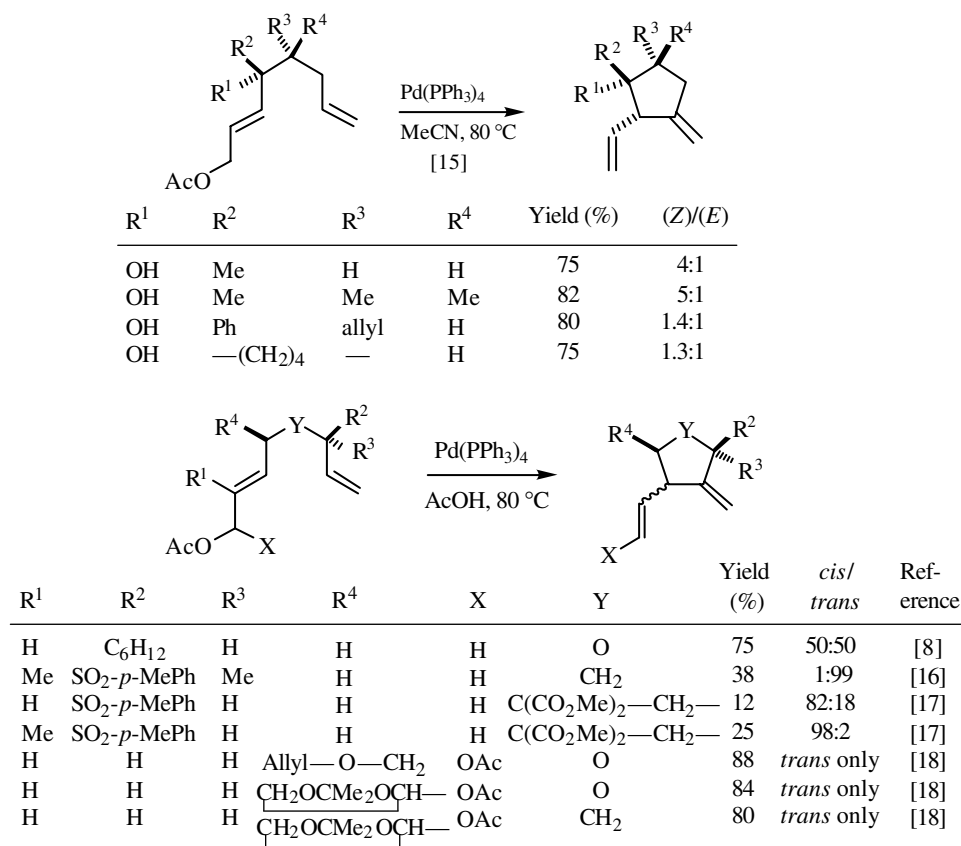
β -hydride elimination to terminate the reaction sequence leading to a diene. Domino-type reaction sequences are possible in that another intramolecular alkene insertion, a carbonylation, or a transmetalation forming a further new carbon-carbon bond can occur. These cases are discussed below.

C. STEREOCHEMICAL ASPECTS

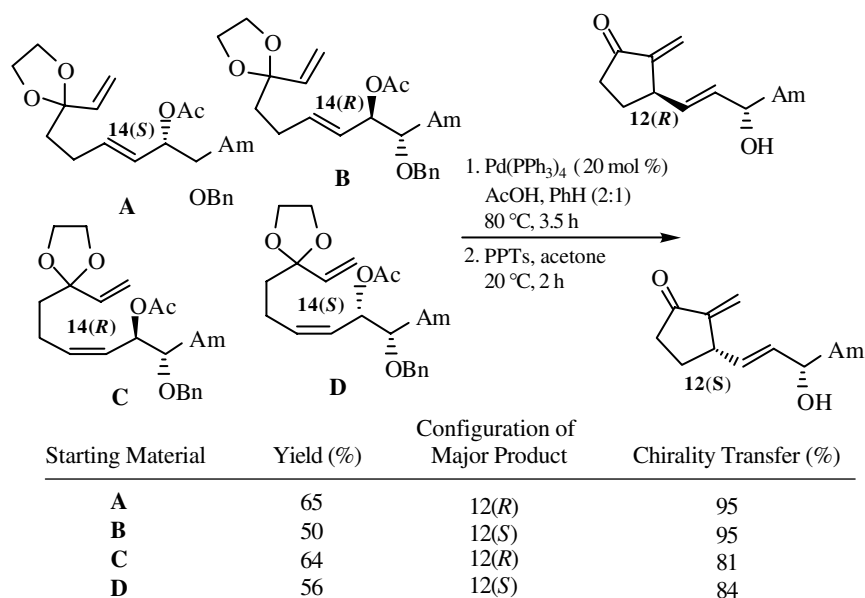
The stereochemical outcome of such intramolecular carbopalladations, which is influenced by the number and nature of the substituents at the various positions of the acyclic system, was examined by several groups (Scheme 9).^{[8],[15]–[18]}

Rather efficient chirality transfer was observed for the alkene insertion into the π -allylpalladium complex prepared from various acyclic allylic acetates in the synthesis of the 11-deoxy analog of Stork's intermediate for the synthesis of prostaglandins (Scheme 10).^[19]

This method was utilized in the preparation of bicyclic compounds consisting of five-, six-, and seven-membered rings. Oxidative addition of allylic acetates to palladium(0) takes place with inversion of configuration and intramolecular alkene insertion into the

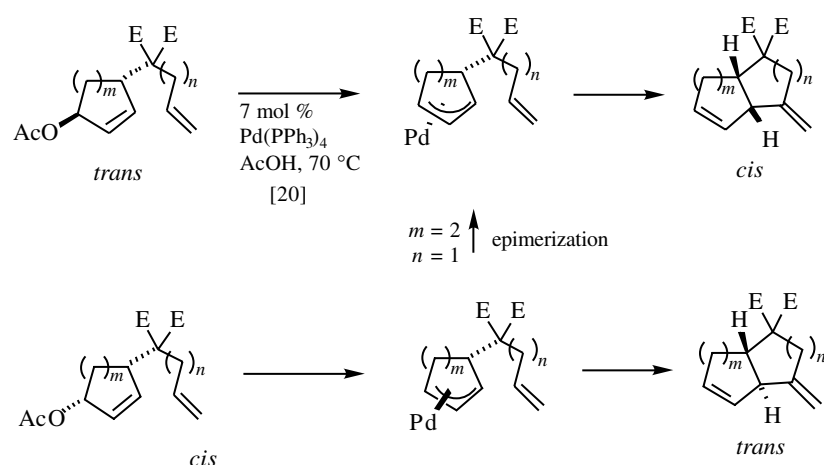


Scheme 9

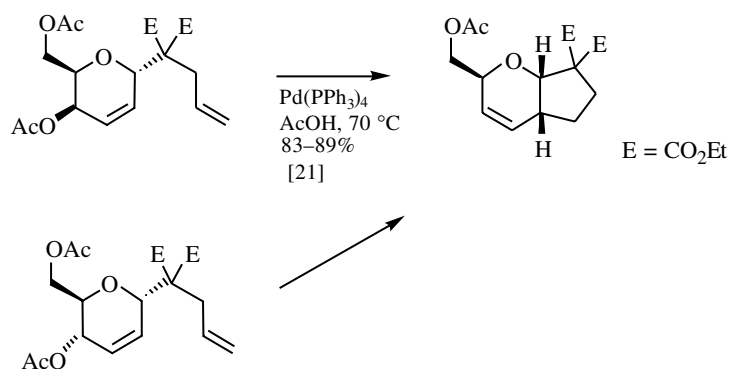


Scheme 10

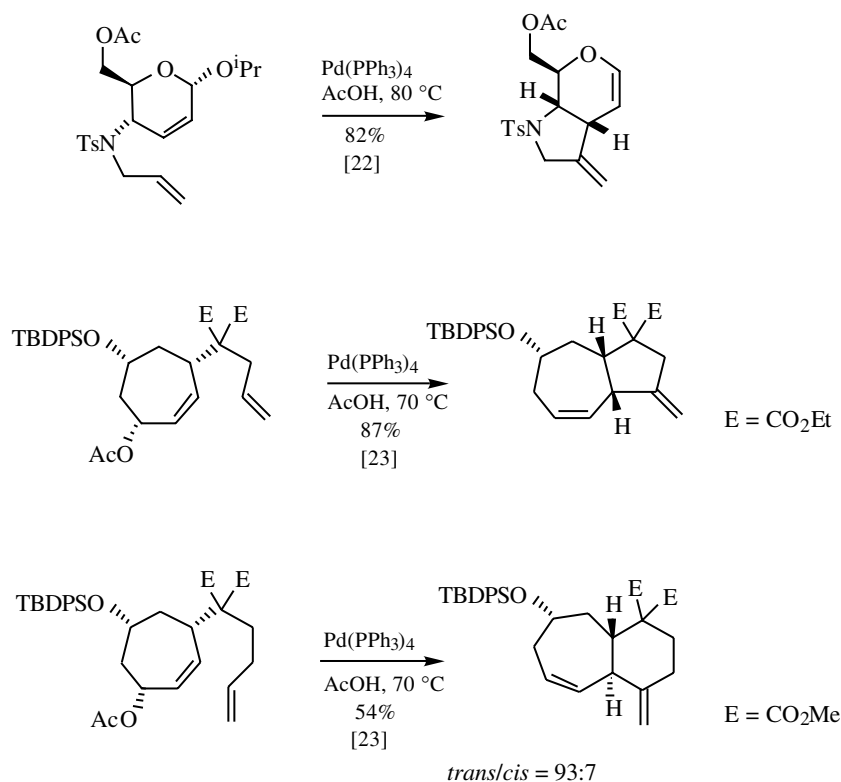
resultant π -allylpalladium complex proceeds with retention of configuration to provide bicyclic products in a stereospecific manner (**Scheme 11**).^{[20]–[23]} However, when the π -allylpalladium moiety produced on a ring is *trans*-positioned with respect to the alkene tether and thus can only insert into the double bond via a highly strained transition structure, epimerization may occur before the bicyclic compound is formed (entry 5 in **Scheme 11**).



Entry	Starting Material	<i>m</i>	<i>n</i>	Yield (%)	Ratio (<i>cis/trans</i>)
1	<i>trans</i>	1	1	67	>99:1
2	<i>trans</i>	2	1	84	>98:2
3	<i>trans</i>	2	2	60	>99:1
4	<i>trans</i>	3	1	73	99:1
5	<i>cis</i>	2	1	55	>98:2
6	<i>cis</i>	2	2	69	5:95
7	<i>cis</i>	3	1	80	2:98



Scheme 11 (Continued)



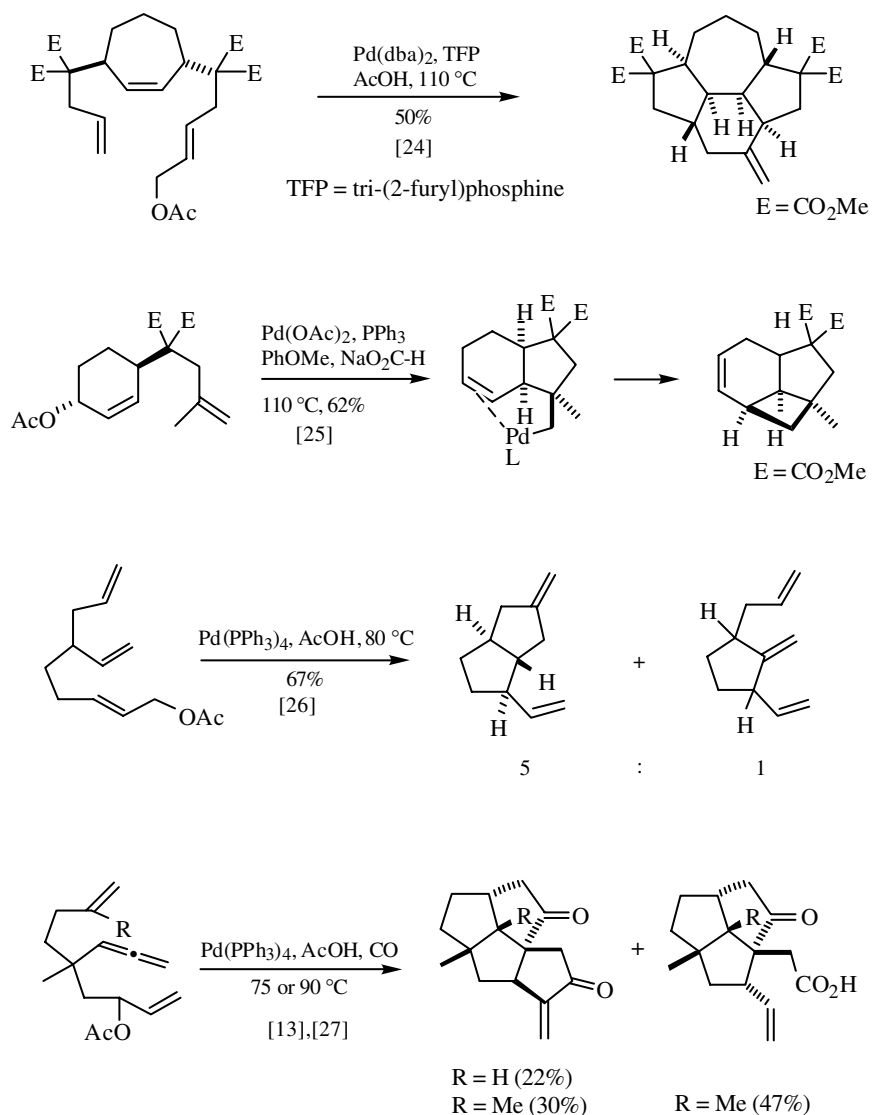
Scheme 11

D. DOMINO AND CASCADE REACTIONS INITIATED BY π -ALLYLPALLADIUM INSERTION INTO ALKENES OR ALKYNES

The Pd-catalyzed cyclization of alkenyl- and alkynyl-tethered allylic acetates gives σ -alkyl- and alkenylpalladium intermediates, respectively, which can undergo further intramolecular alkene insertion, carbonylation, and transmetalation, respectively, to form additional carbon–carbon bonds (**Scheme 8**), as exemplified for such cascade reactions with insertion of a tethered alkene in **Scheme 12**.^{[13],[24]–[27]}

Alkene and alkyne insertions followed by carbonylation are shown in **Schemes 13**,^{[10],[28]–[33]} **14**,^[34] and **15**.^{[21],[35],[36]} Interestingly, alkene insertion occurs faster than CO insertion. In several cases, the carbonylation was succeeded by hydrolysis to provide the corresponding acid or yet another carbon–carbon bond formation in the same operation.

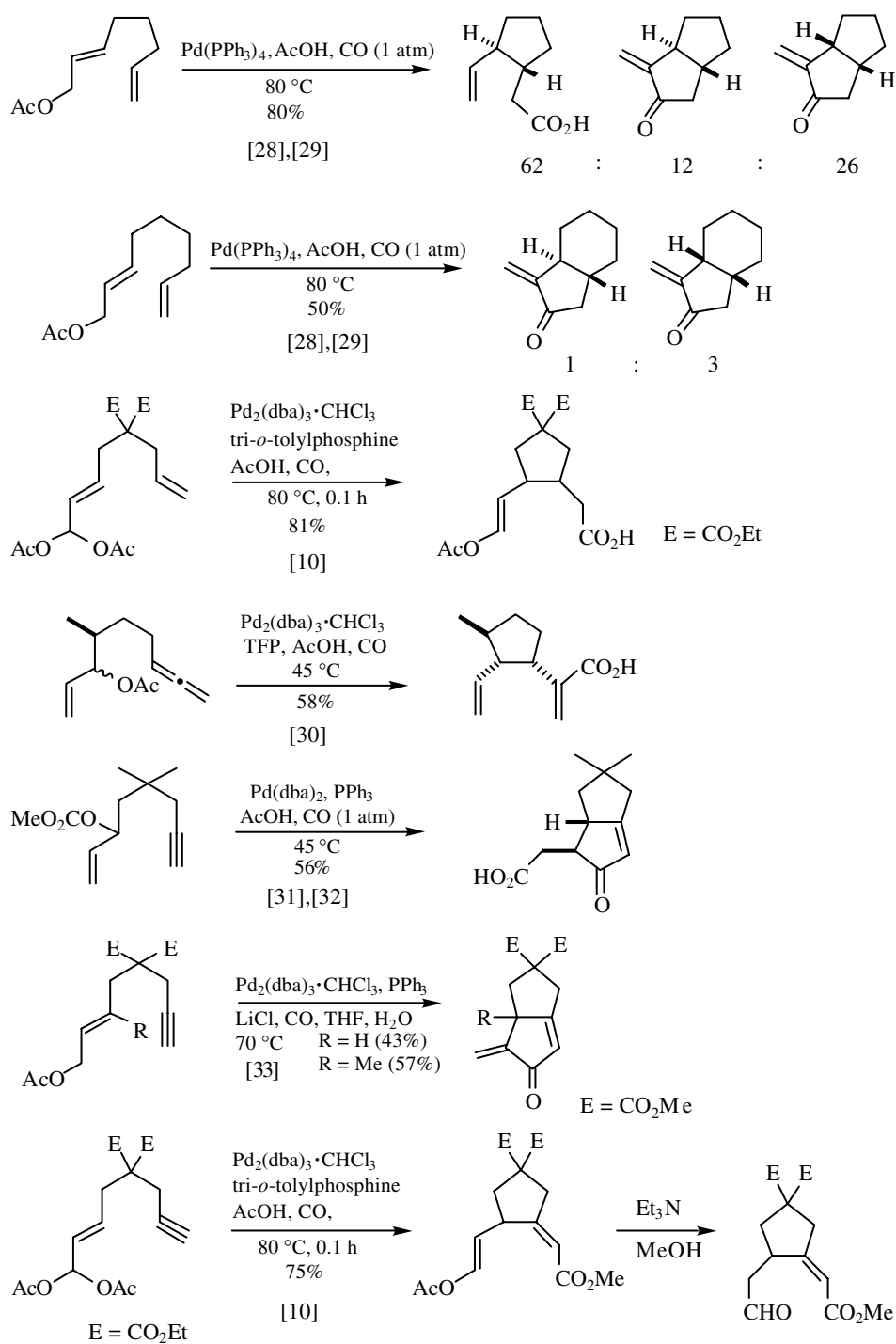
Examples of alkene and alkyne insertions followed by transmetalation with organotin compounds as well as boranates, and eventually reductive elimination are shown in **Scheme 16**.^{[10],[18],[37]–[39]} These reactions do not only require that the transmetalation process as outlined in **Scheme 8** be faster than β -hydride elimination, but also that the alkene insertion prevails over allylic coupling.



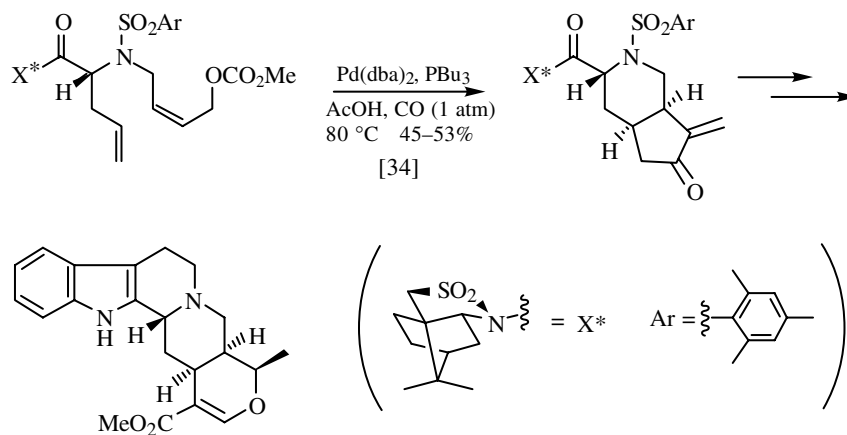
Scheme 12

E. ASYMMETRIC VERSION OF THE ALKENE INSERTION INTO A π -ALLYLPALLADIUM COMPLEX

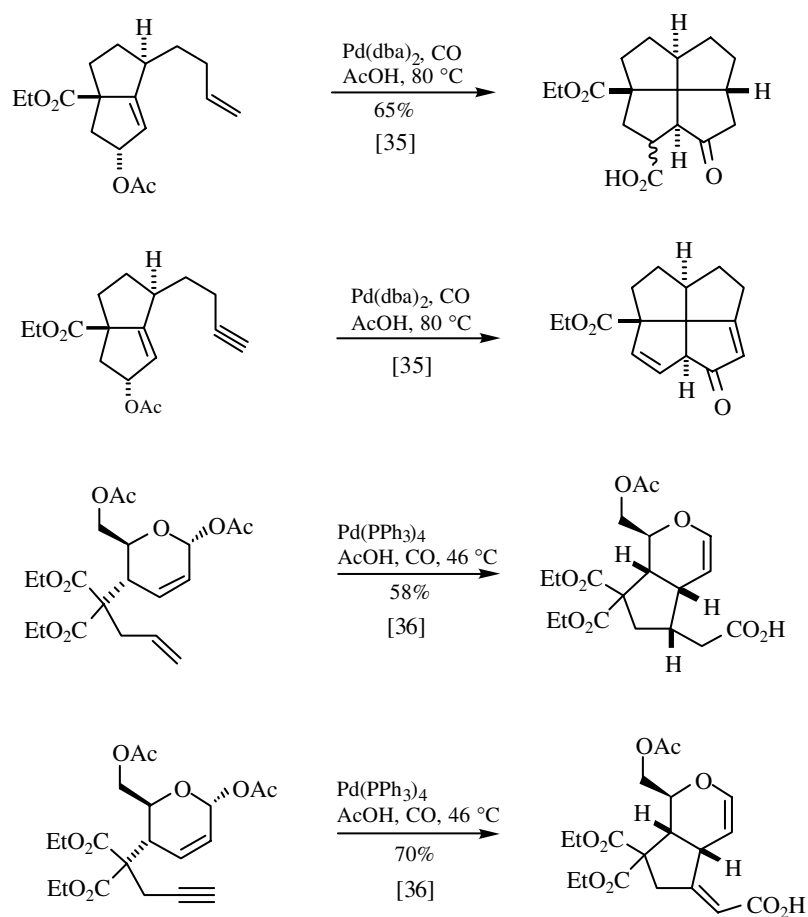
A few examples of asymmetric cyclizations induced by palladium(0) catalysts with various chiral phosphine ligands have been reported, but the achieved enantioselection has been rather low or at best moderate (**Scheme 17**).^[40] Further studies are definitely needed to improve the catalytic asymmetric version of this intramolecular carbopalladation.



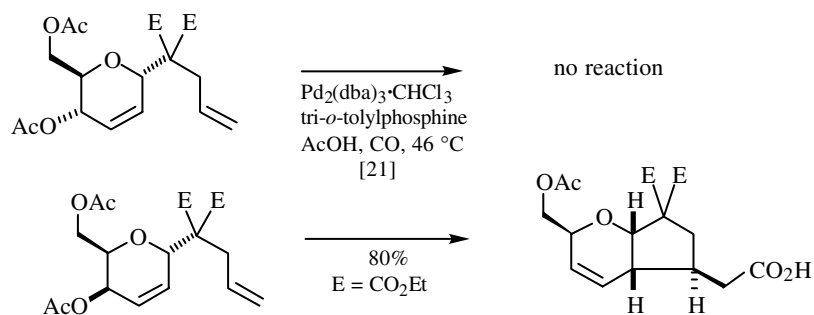
Scheme 13



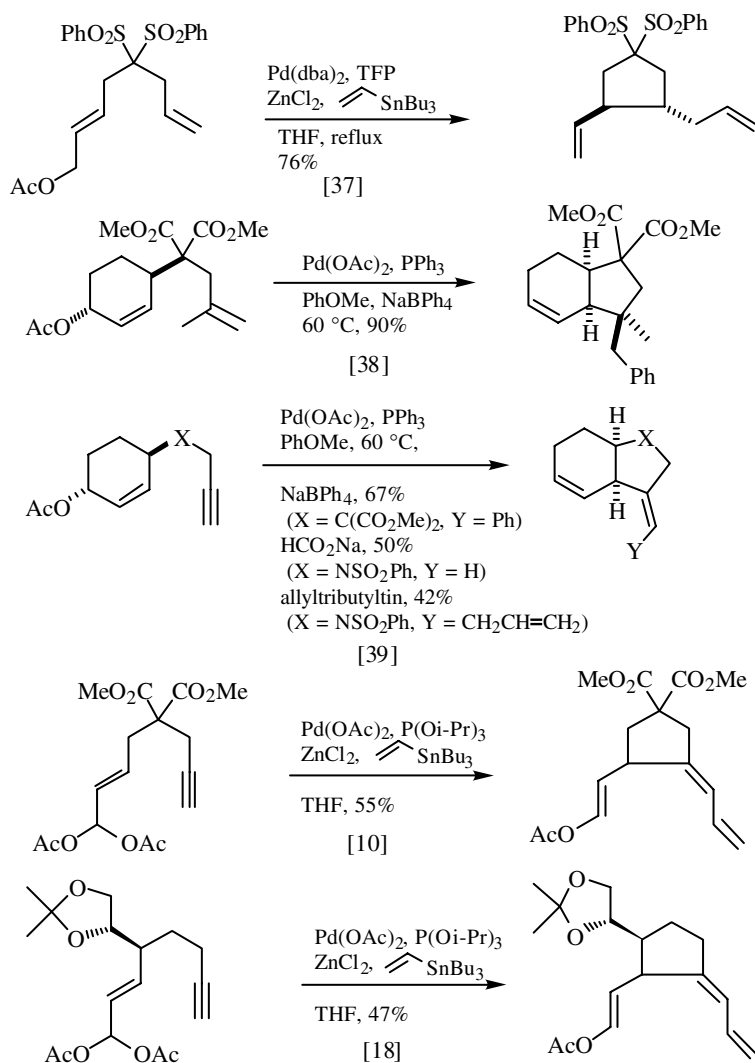
Scheme 14



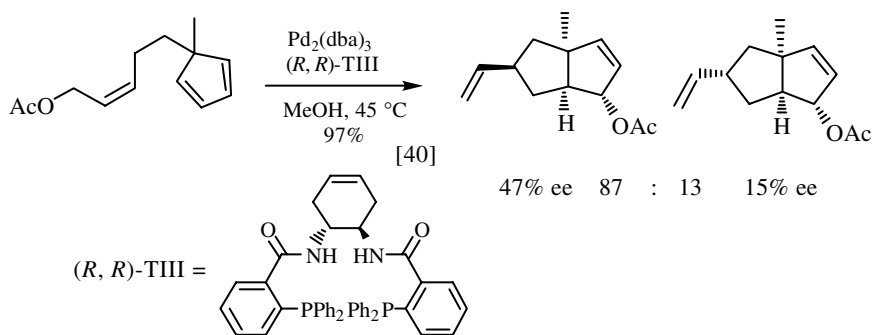
Scheme 15 (Continued)



Scheme 15 (Continued)



Scheme 16



Scheme 17

F. SUMMARY

Allylpalladation of alkenes, alkynes, and dienes is a powerful tool for preparing carbocycles and heterocycles. The combination of allylpalladations with intramolecular alkene insertion, carbonylation, and transmetalation in cascade-type sequences demonstrates the high potential of these Pd-catalyzed cyclization reactions for the synthesis of complex organic molecules.

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