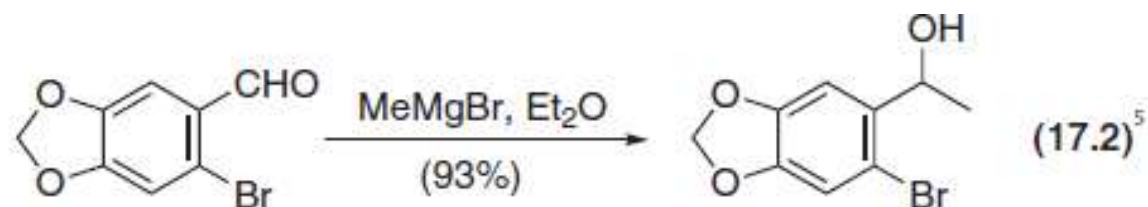


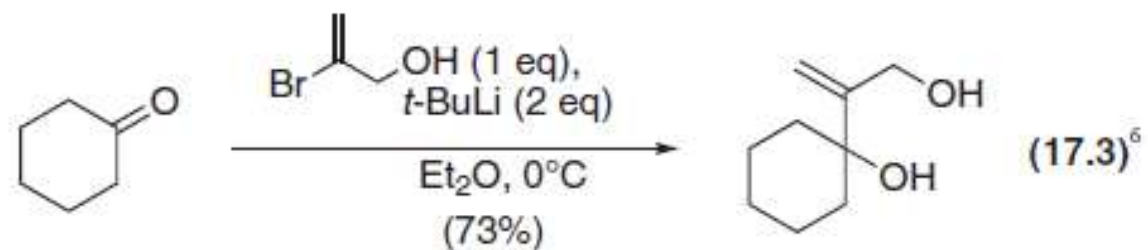
Chapter 17

Organometallic reactions

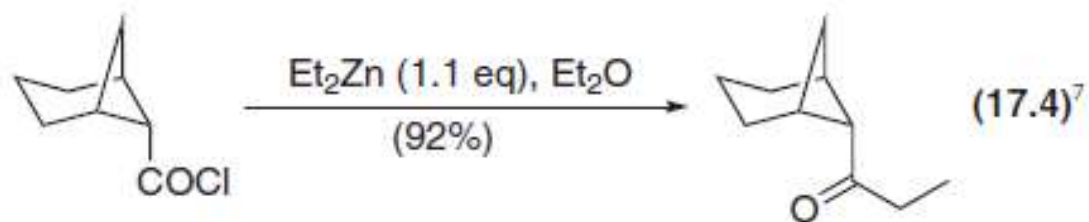
addition of a Grignard reagent to a ketone



addition of an alkyllithium reagent to a ketone



substitution of an acid chloride with a dialkylzinc



substitution of an acid chloride with a lithium dialkylcuprate

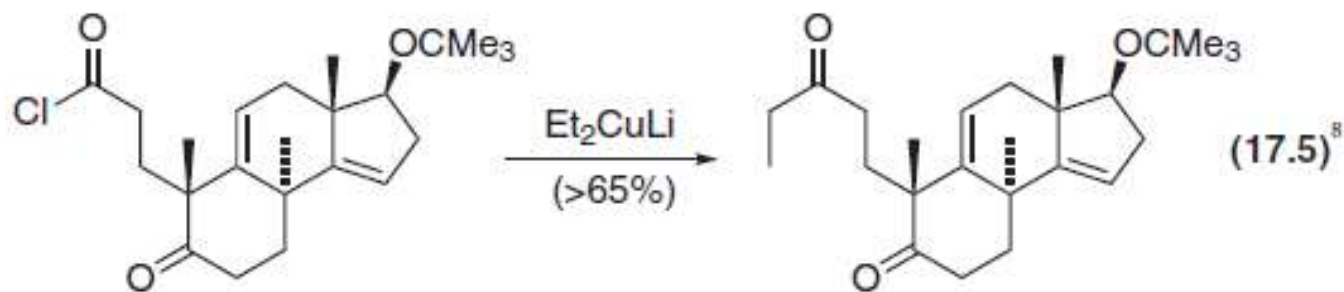
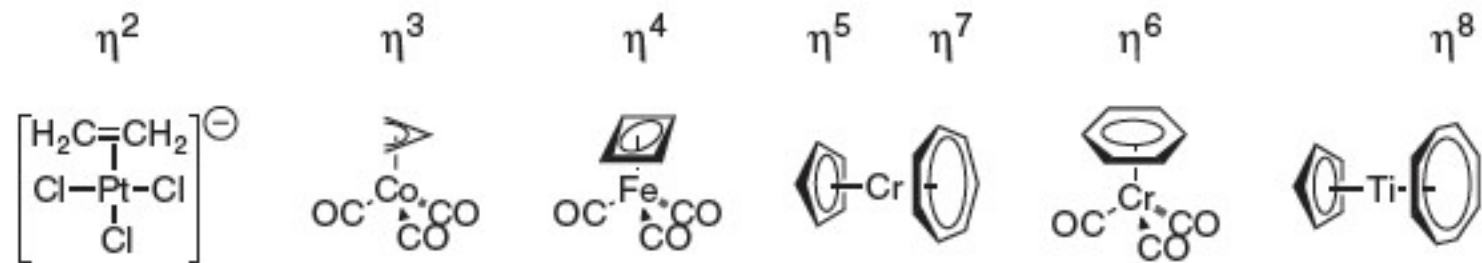


Figure 17.1



Hapto numbers for a series of common ligands

Table 17.1

Electrons donated by neutral ligands for electron accounting by the 18-electron rule

Electrons	Typical Examples of Ligands
1	alkyl, aryl, alkynyl, H, halogen
2	CO, phosphines, η^2 alkene, η^2 alkyne
3	η^3 allyl, NO
4	η^4 diene (e.g. 1,3-butadiene; cyclobutadiene; norbornadiene)
5	η^5 dienyl (e.g. cyclopentadienyl, Cp; cyclohexadienyl)
6	η^6 arene (e.g. benzene; mesitylene)
7	η^7 trienyl (e.g. cycloheptatrienyl)
8	η^8 tetraenyl (e.g. cyclooctatetraenyl)

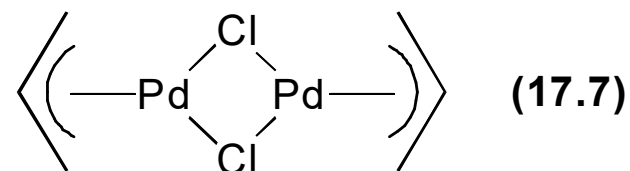
Table 17.2

Electrons donated by ionic ligands for electron accounting by the 18-electron rule

Electrons	Typical Examples of Ligands
2	halide ion, alkoxide ion, carboxylate ion
4	η^3 allyl anion, η^4 diene
6	η^5 dienide anion, η^6 arene, η^7 trienyl cation
8	η^8 tetraenyl (e.g. cyclooctatetraenyl)

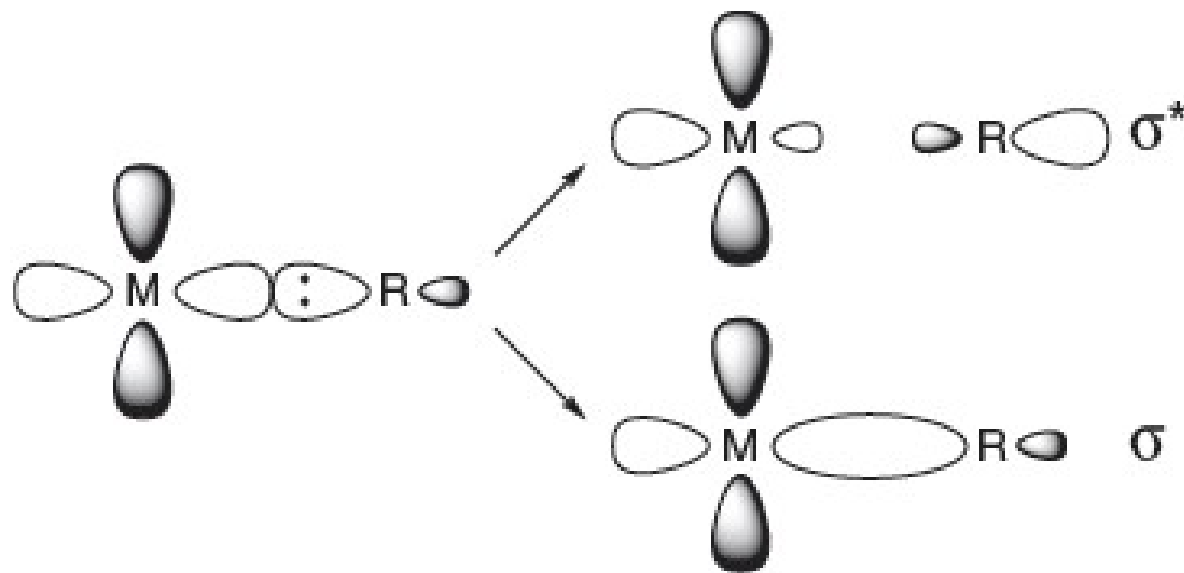
Electron accounting in the π -allylpalladium chloride dimer

the 18-electron rule predicts that the palladium in this complex is in the +2 oxidation state



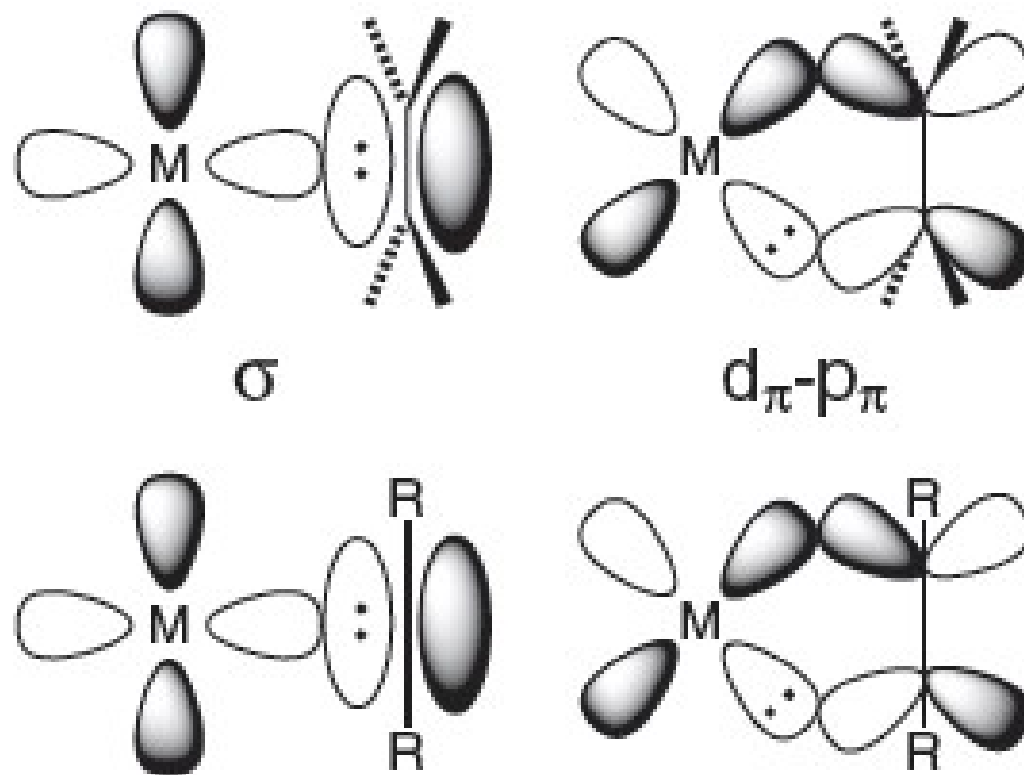
Pd^{2+} ($3d^8$)	8
C_3H_5 (allyl anion $4 e^{\ominus}$)	4
Cl (anion, 2 @ $2e^{\ominus}$)	4
<hr/>	
Total	16
<hr/>	

Figure 17.2



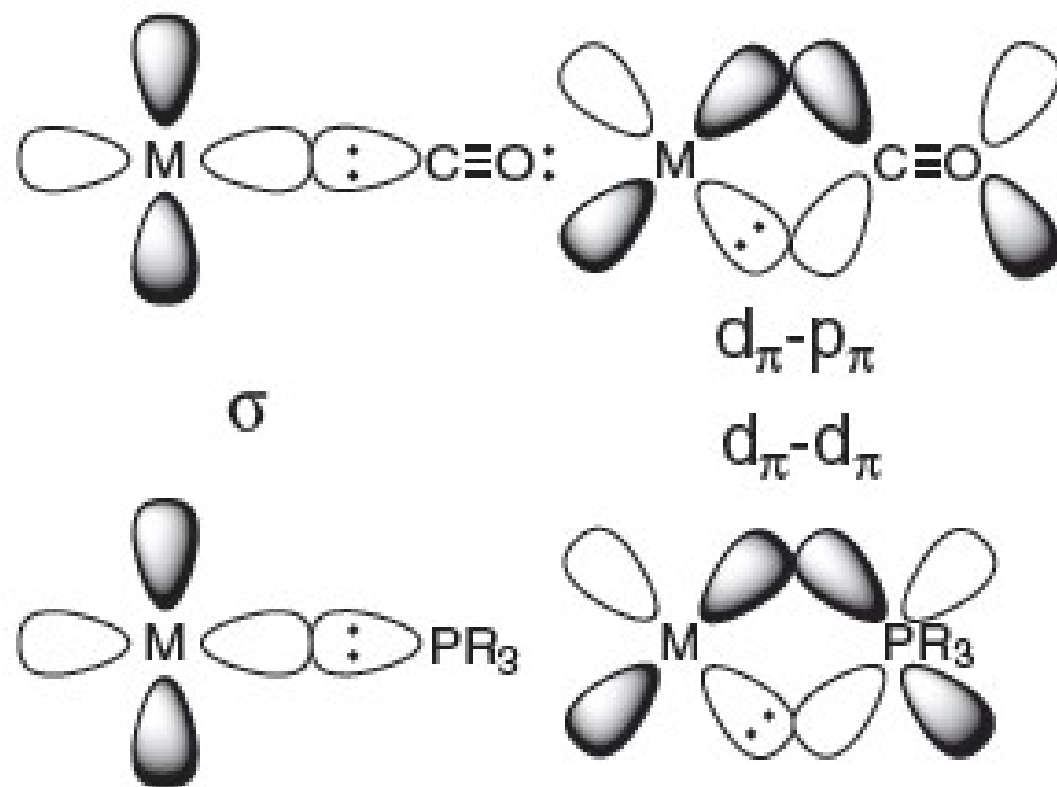
Orbital overlap between a metal atom LUMO and a ligand HOMO to give the σ and σ^* orbitals of a metal-carbon bond.

Figure 17.3



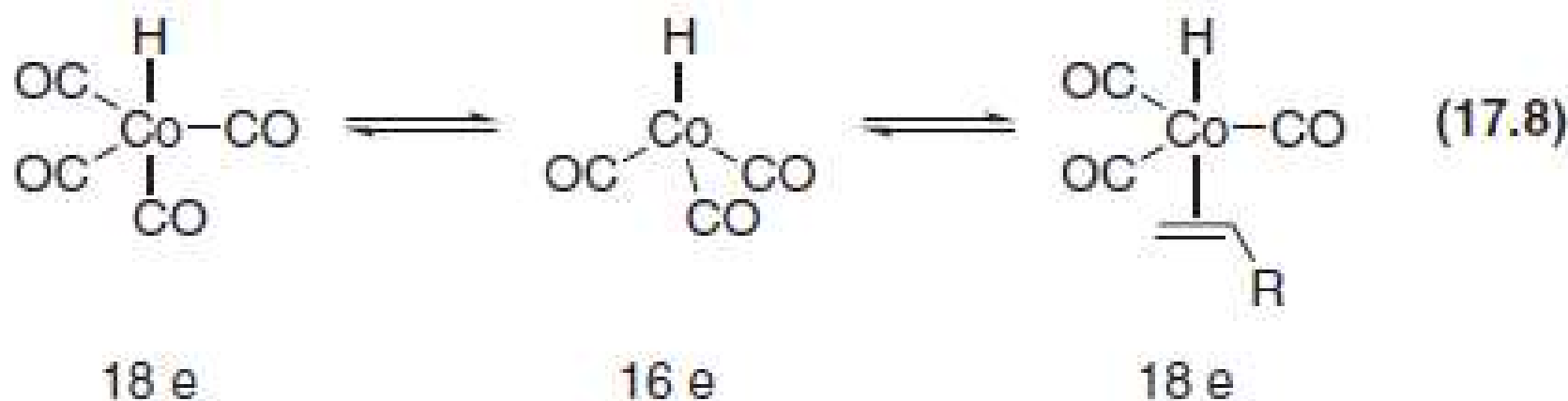
Metal-alkene (top) and metal-alkyne (bottom) σ bonding (left) and $d\pi-p\pi$ backbonding (right).

Figure 17.4



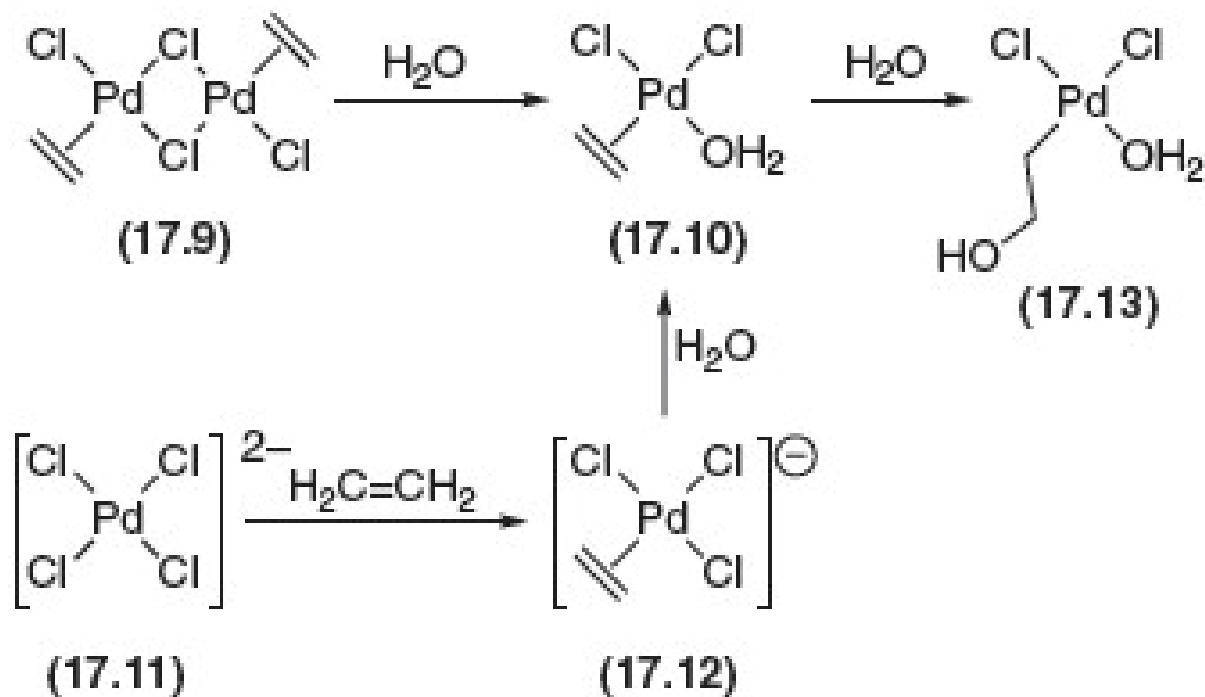
Bonding in carbonyl (top) and phosphine (bottom) complexes

Ligand substitution



Often an important part of metal-catalyzed organic reactions. First steps of oxo process involve ligand substitution by a dissociative mechanism through a coordinatively unsaturated intermediate.

Figure 17.5

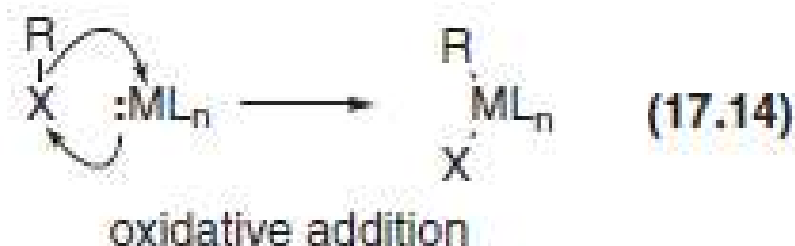


Metal substitution can dramatically affect ligand reactivity

- In the dimeric palladium complex (**17.9**), the alkene ligand is labile towards displacement, but is not reactive towards nucleophilic attack
- In the monomeric complexes (**17.11**, **17.12**), incorporating one water ligand and one alkene ligand gives a complex (**17.10**) where the alkene π bond is quite susceptible to attack by nucleophiles

Oxidative addition and reductive elimination

In oxidative addition, a coordinatively unsaturated complex with a lone pair on the metal reacts with a neutral molecule to give a coordinatively saturated product; the reaction accompanied by an increase in the formal oxidation number of the metal center. The lone pair is essential in this reaction



In reductive elimination, a coordinatively saturated complex eliminates a neutral molecule to give a coordinatively unsaturated product; the reaction accompanied by a decrease in the formal oxidation number of the metal center

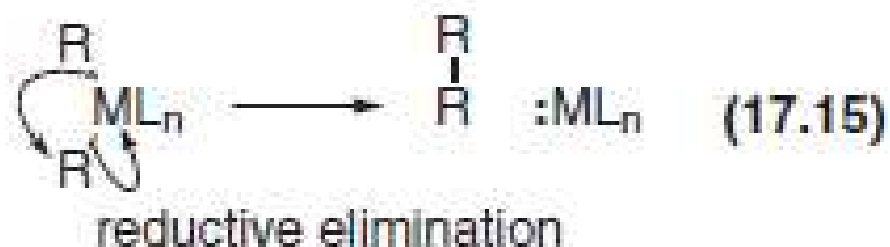
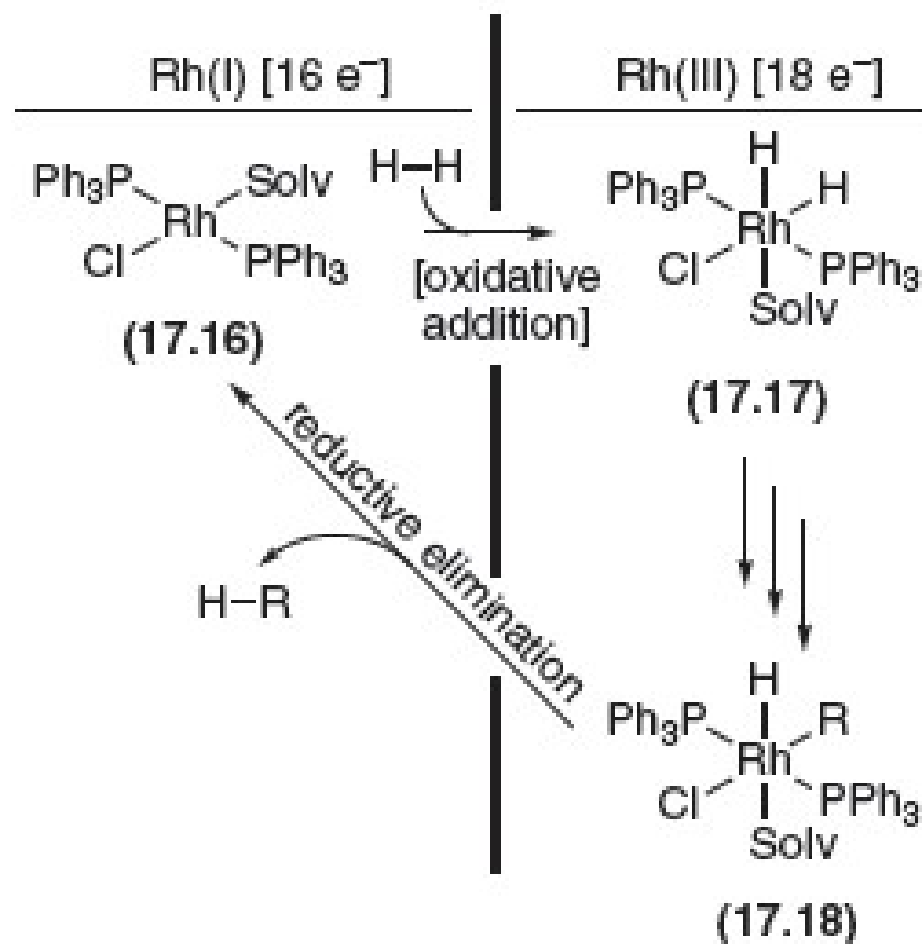


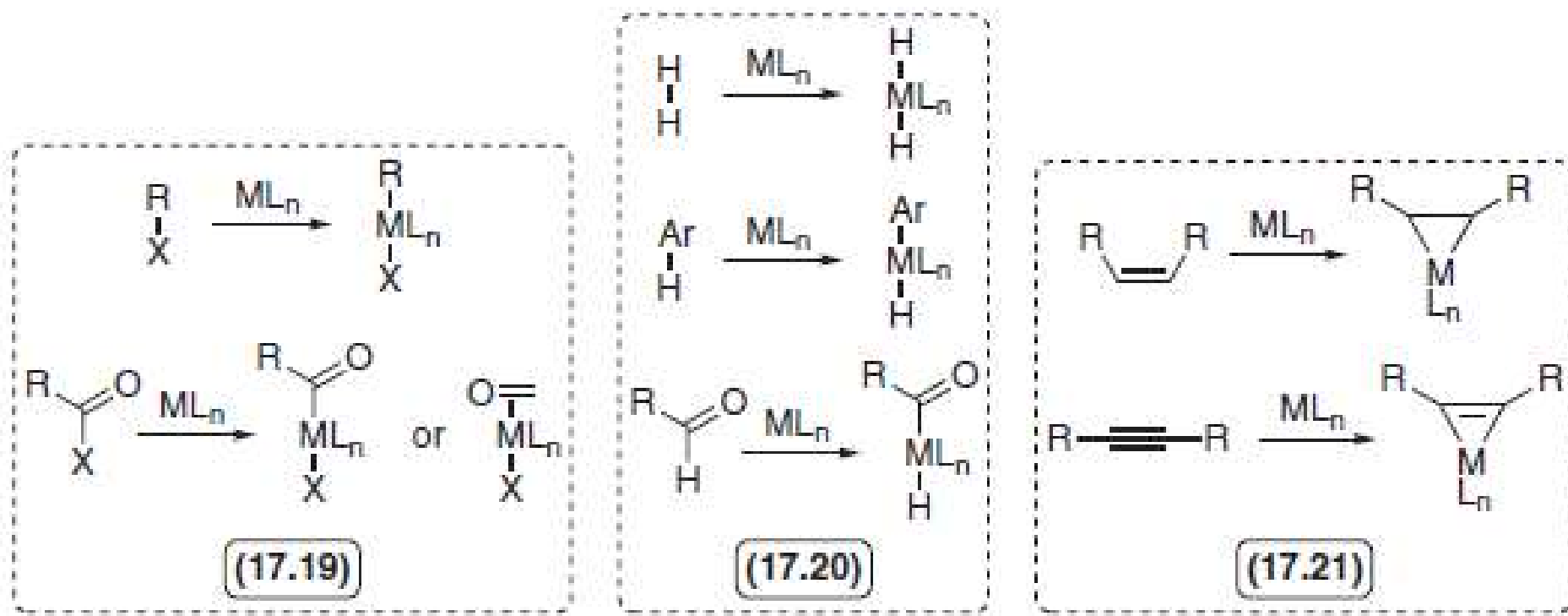
Figure 17.6

Oxidative addition and reductive elimination

- addition of H_2 converts unsaturated Rh (I) complex to saturated Rh (III) complex
- elimination of the alkane converts saturated Rh (III) complex to unsaturated Rh (I) complex



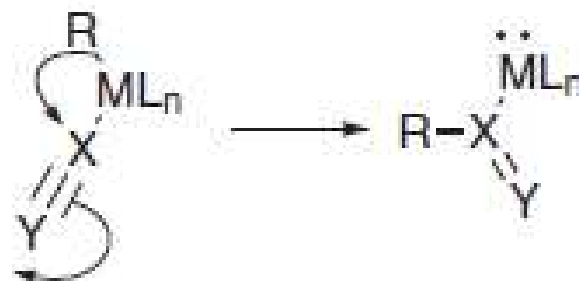
Oxidative additions



- Three types of covalent bonds in neutral molecules add to coordinatively unsaturated complexes
 - polar σ bonds
 - non-polar σ bonds
 - π bonds

Migratory insertion

- Two major types
 - bonding between the non-migrating ligand and the metal remains unaltered
 - metal migrates to the other end of the π bond to give a net addition, and conversion of a π complex to a σ complex

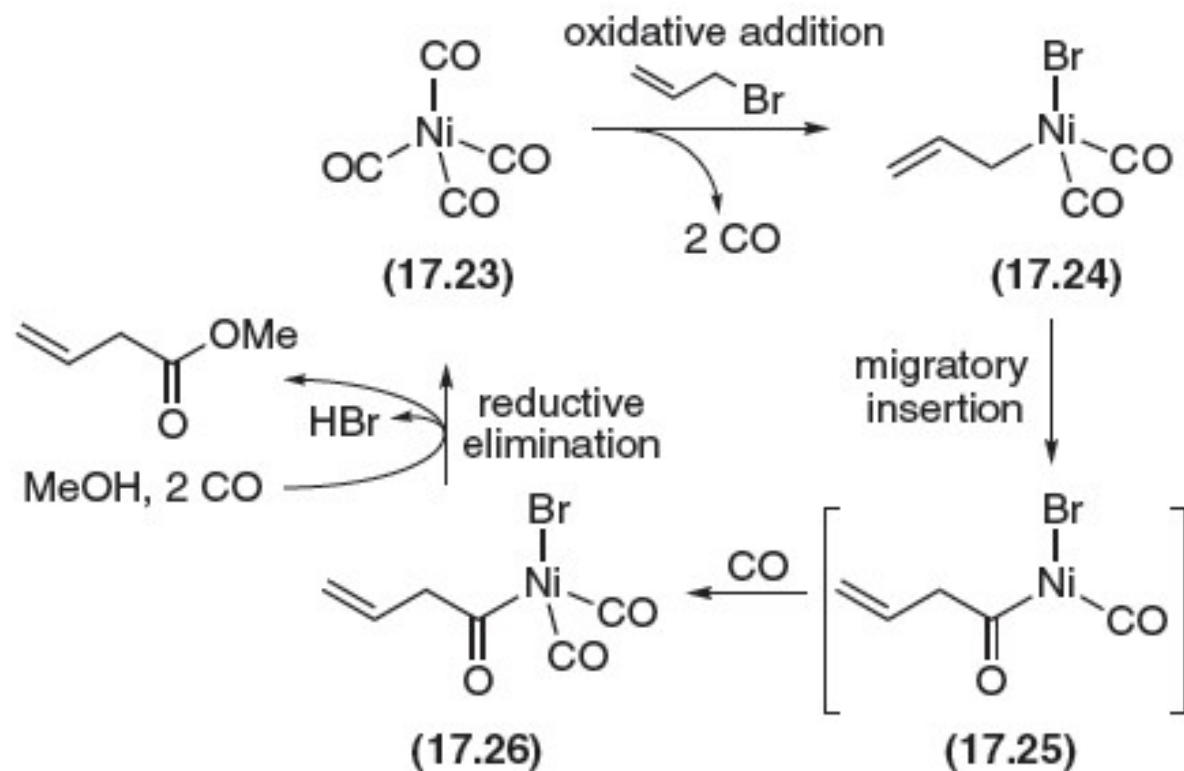


migratory insertion



(17.22)

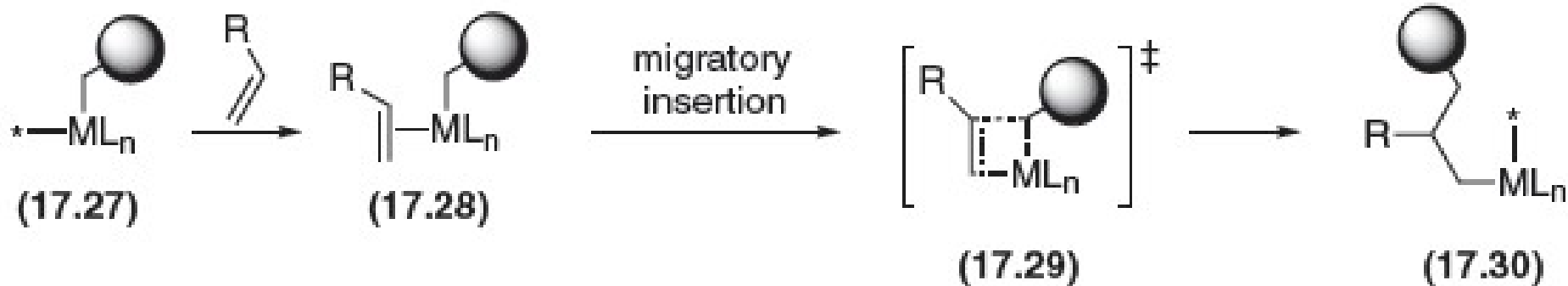
Figure 17.7



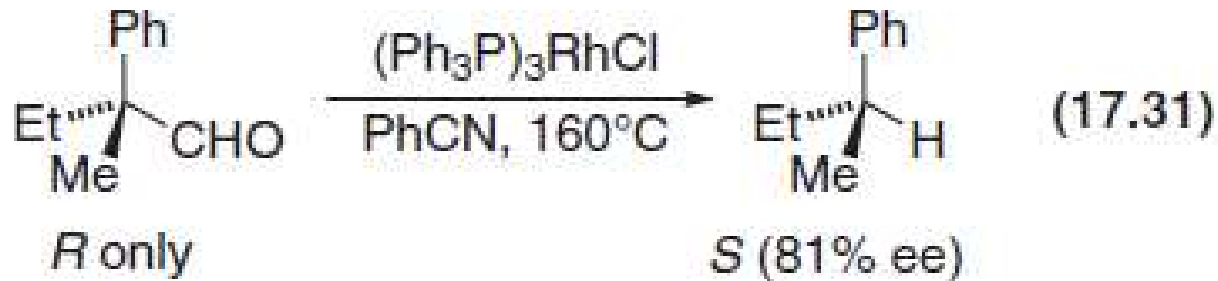
Carbonylation of allyl bromide by carbon monoxide in the presence of nickel tetracarbonyl

Figure 17.8

Migratory insertion in the Ziegler-Natta polymerization. The asterisk denotes a vacant coordination site on the metal atom



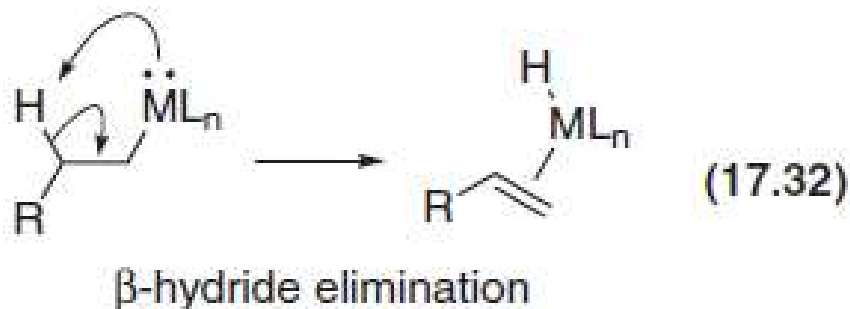
Decarbonylation



- mechanistically, the reverse of migratory insertion
- occurs with retention of configuration
- often a side reaction in hydrogenation of aldehydes with Wilkinson's catalyst

β -Hydride elimination

β -elimination of hydride from transition metal-alkyl σ -bonded complexes gives an η^2 alkene-metal hydride complex.



This step of the Wacker process converts σ complex **17.33** to the acetaldehyde enol η^2 complex of the palladium hydride (**17.34**)

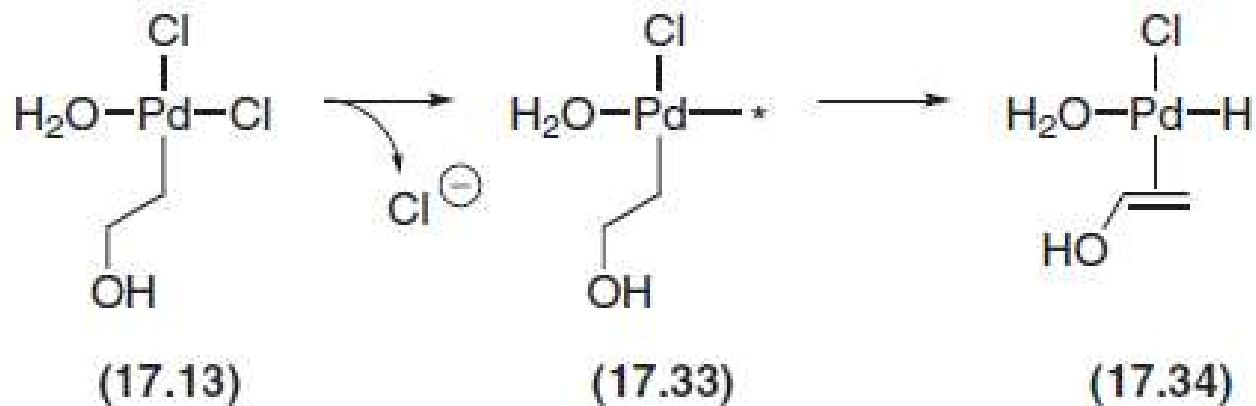
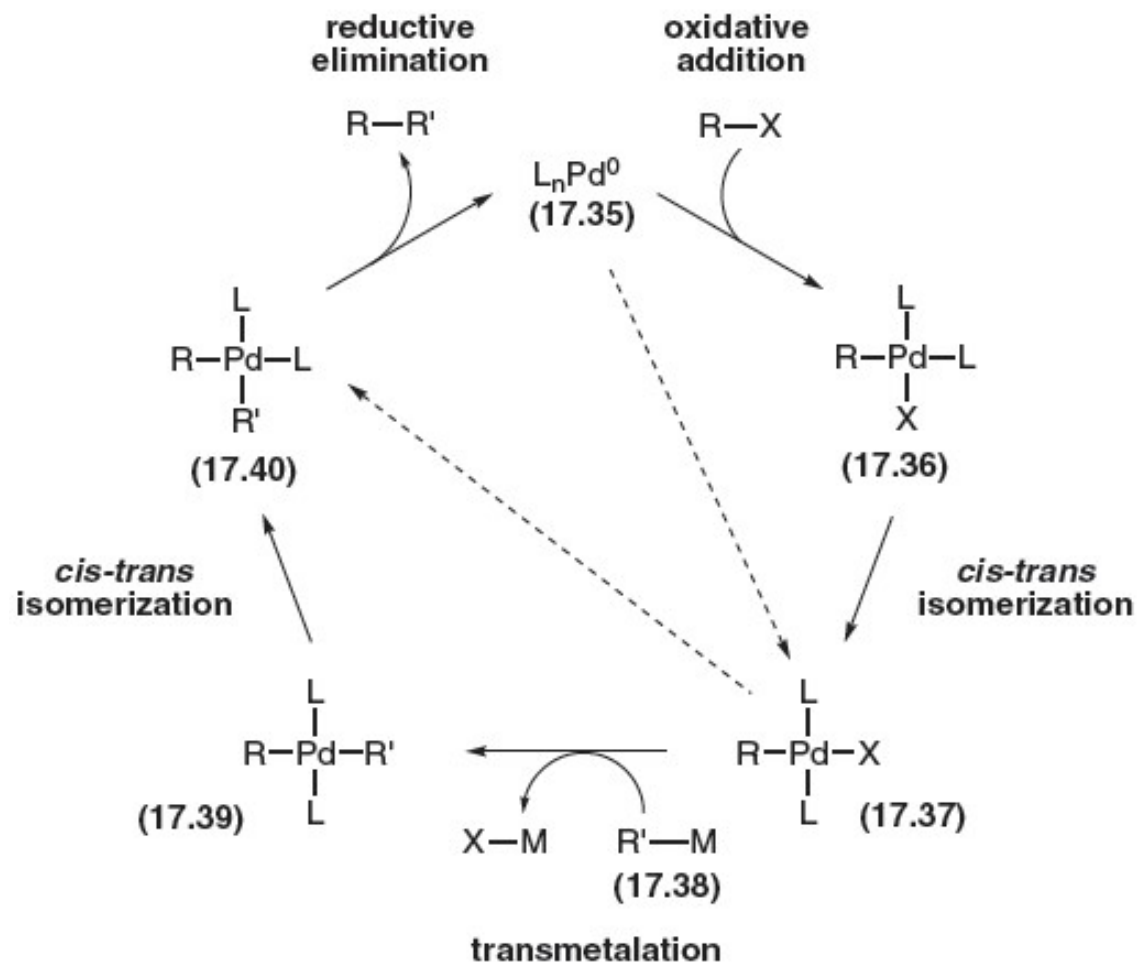
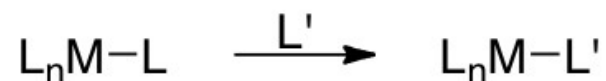


Figure 17.9

The catalytic cycle for metal-catalyzed coupling reactions

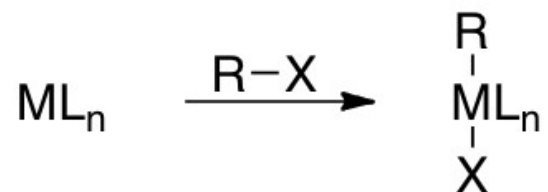


Reaction synopsis: Ligand substitution



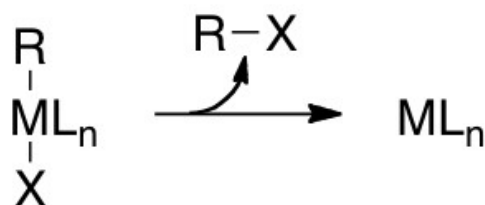
Reaction may proceed by a dissociative or an associative mechanism

Reaction synopsis: Oxidative addition



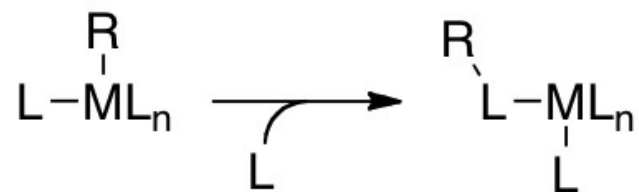
Reaction converts coordinatively unsaturated complex to coordinatively saturated complex by effectively inserting metal into R—X σ bond.

Reaction synopsis: Reductive elimination



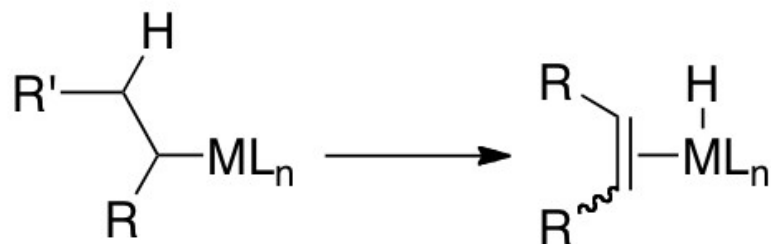
Reaction eliminates σ -bonded product from a coordinatively saturated complex to give a coordinatively unsaturated complex.

Reaction synopsis: Migratory insertion



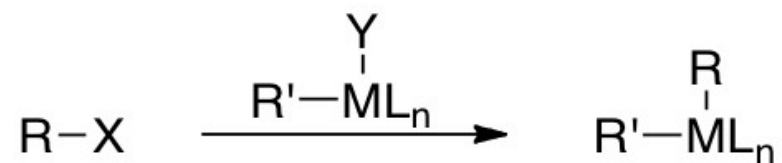
Reaction results in coordinatively unsaturated complex in migration step; reaction is almost always assisted by additional ligand to satisfy need for coordinative saturation. Most common with η^2 alkene or carbonyl ligands. With carbonyl ligands, reaction may be reversible.

Reaction synopsis: β -Hydride elimination



Reaction may lead to direct loss of alkene and formation of hydride complex, or to hydride complex with a bound to η^2 alkene ligand.

Reaction synopsis: Transmetalation



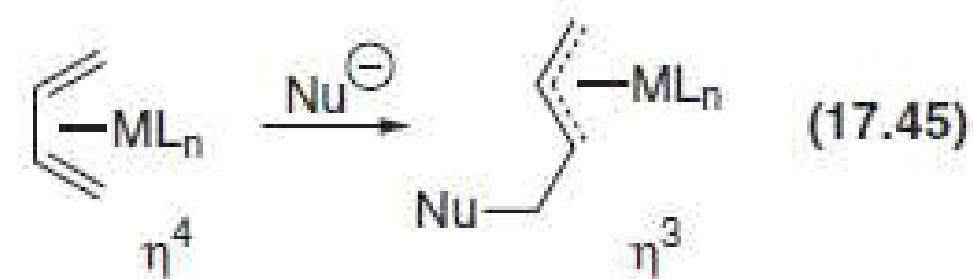
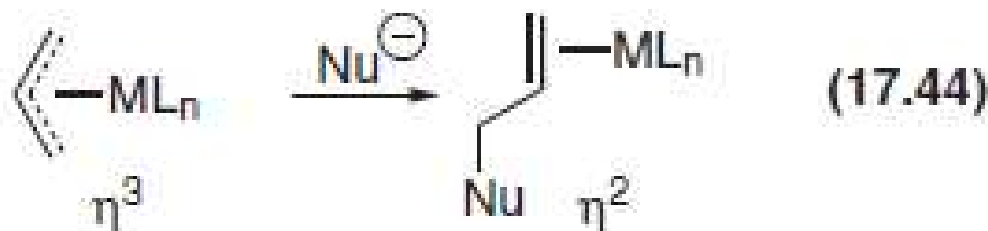
X: MgX, MgR, ZnX, ZnR, HgX, HgR, SnR₃, AlR₂, Cu,
SiR₃, B(OH)₂ etc.

Nucleophilic addition to ligands

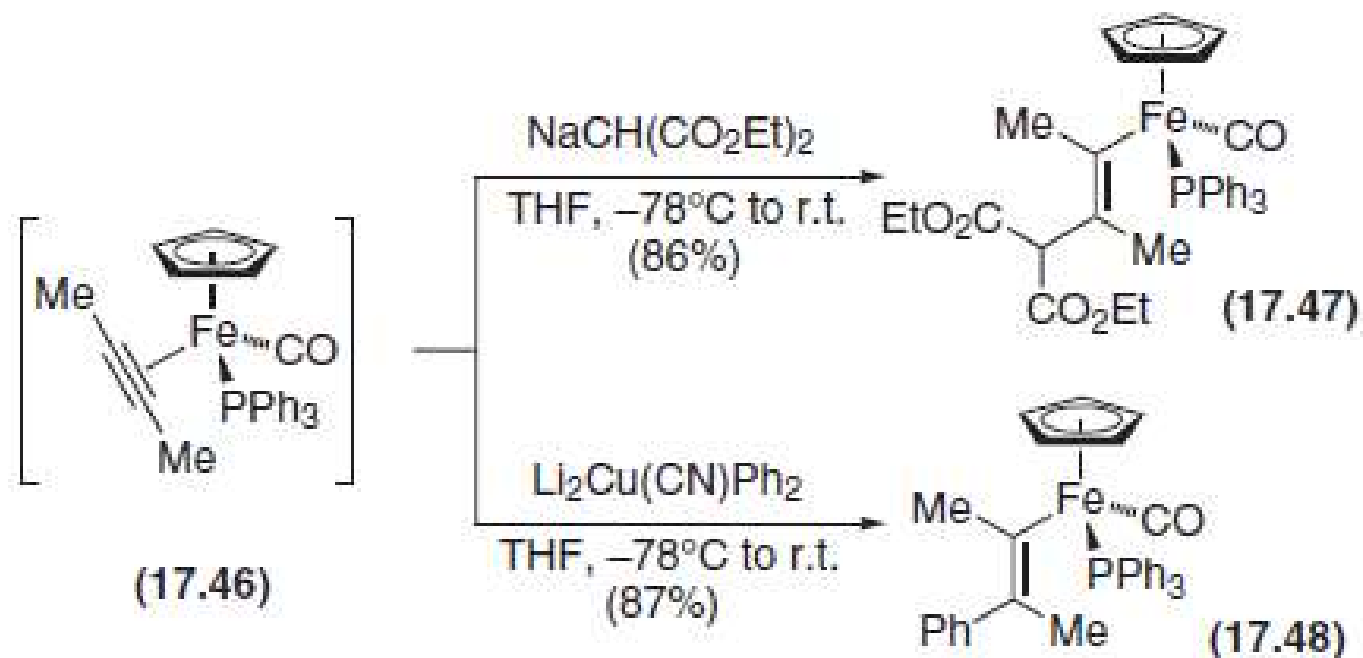
Alkene and alkyne complexes of iron (II), palladium (II) and platinum (II) are especially useful in reactions where a nucleophile attacks the haptic ligand.

In the process, an η^2 ligand is converted to a σ ligand.

The haptic number of higher order haptic ligands is reduced by one.



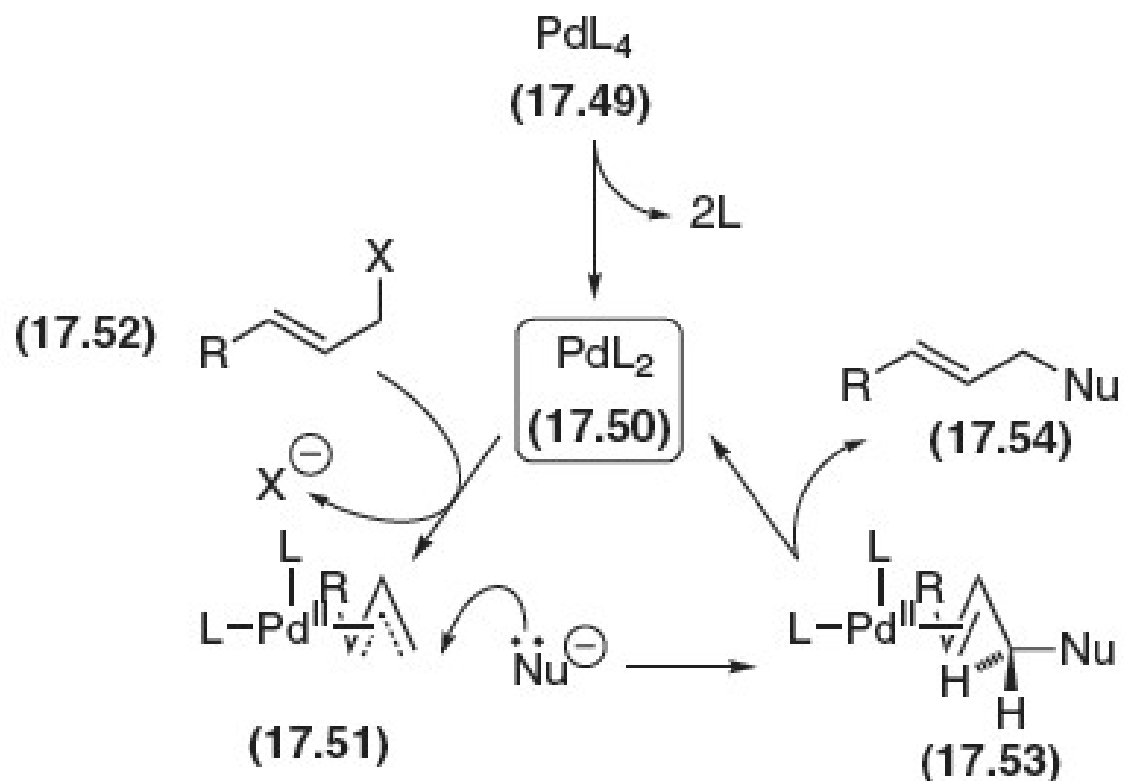
Addition of nucleophiles to a cationic η^2 iron (II) complex



Note how the η^2 iron alkyne complex becomes a vinyliron (II) σ complex

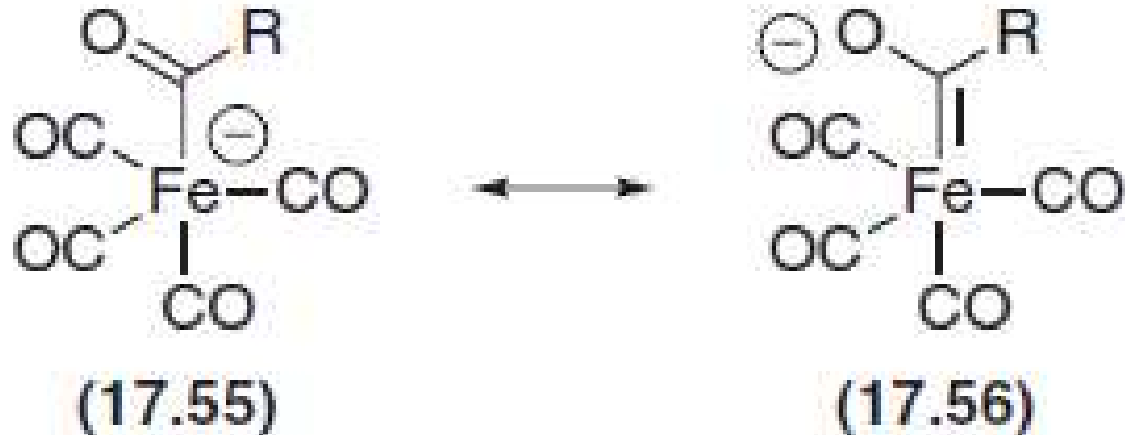
Figure 17.10

The catalytic cycle of the Tsuji-Trost reaction with soft nucleophiles



$\text{L} = \text{PPh}_3$, etc.
 $\text{X} = \text{Cl}, \text{Br}, \text{OAc}, \text{OCOPh}$, etc.

Transition metal acyl complexes



resonance in transition metal acyl complexes

- acylmetal anion and metallocarbene complex structures both contribute to the resonance hybrid

Figure 17.11

Acylmetal complexes react with soft electrophiles to give a metal-acyl product

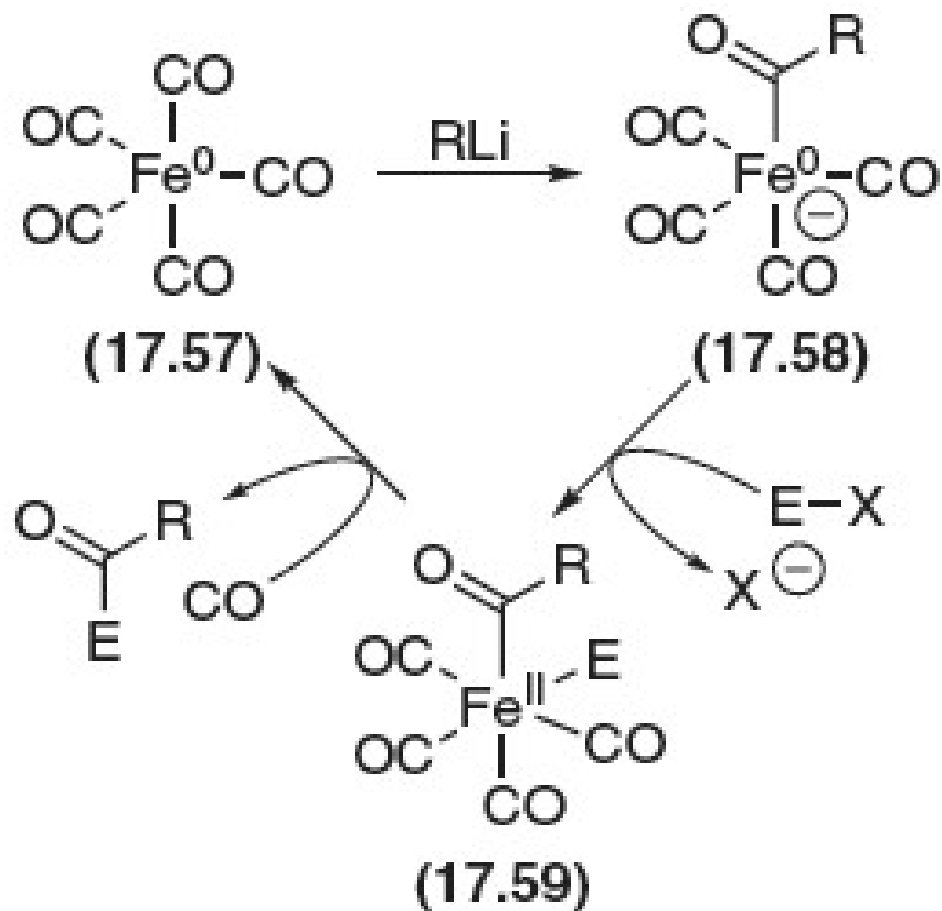
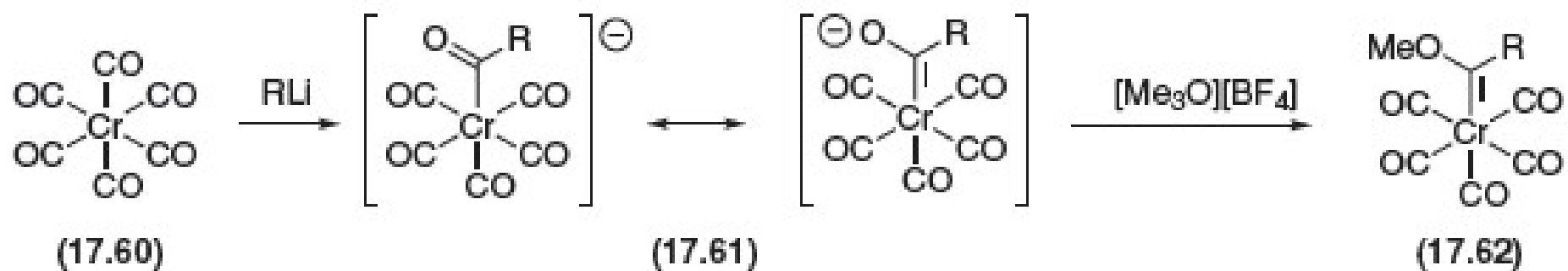
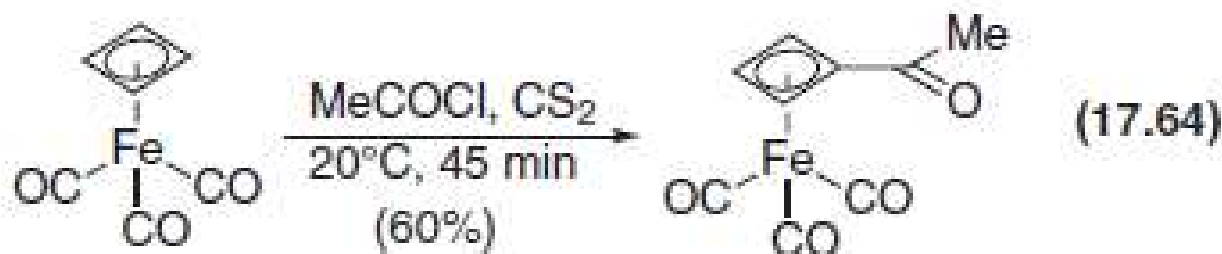
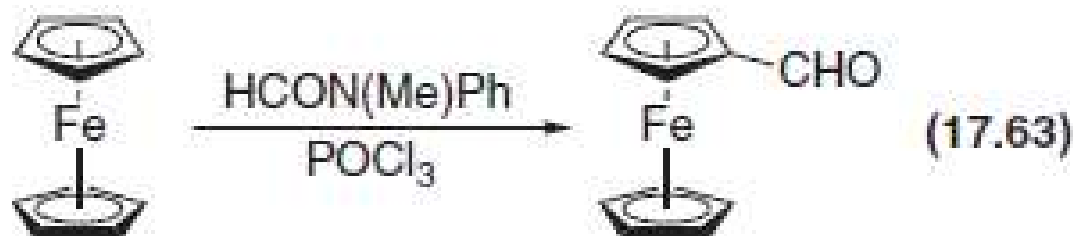


Figure 17.12



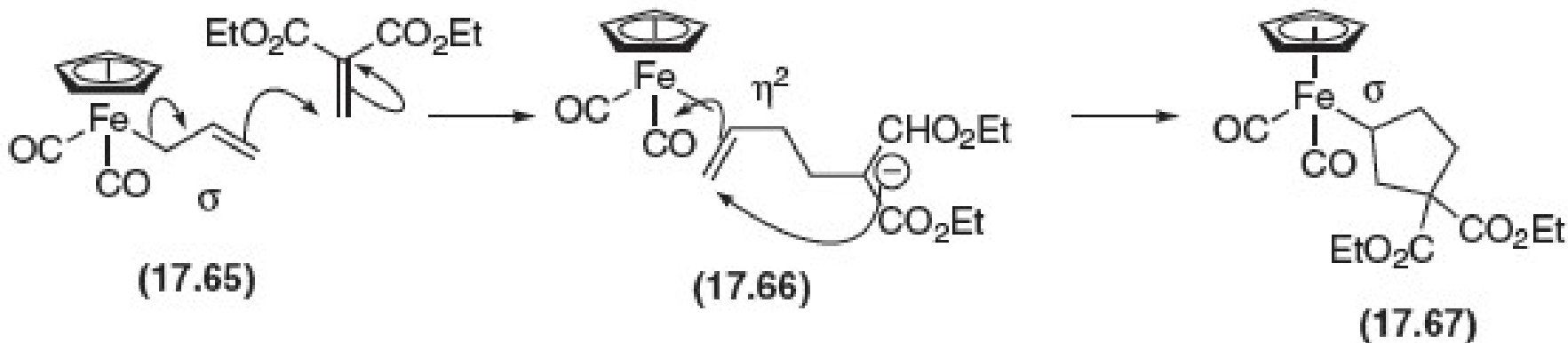
Formation of metal alkylidene complex from an acylmetal anion and a hard electrophile

Electrophilic attack on ligands



- most common form involves electrophilic aromatic substitution.
 - metal complexes with aromatic hydrocarbon ligands react as electron-rich aromatic compounds
 - both alkylation and acylation of the ligand can be accomplished

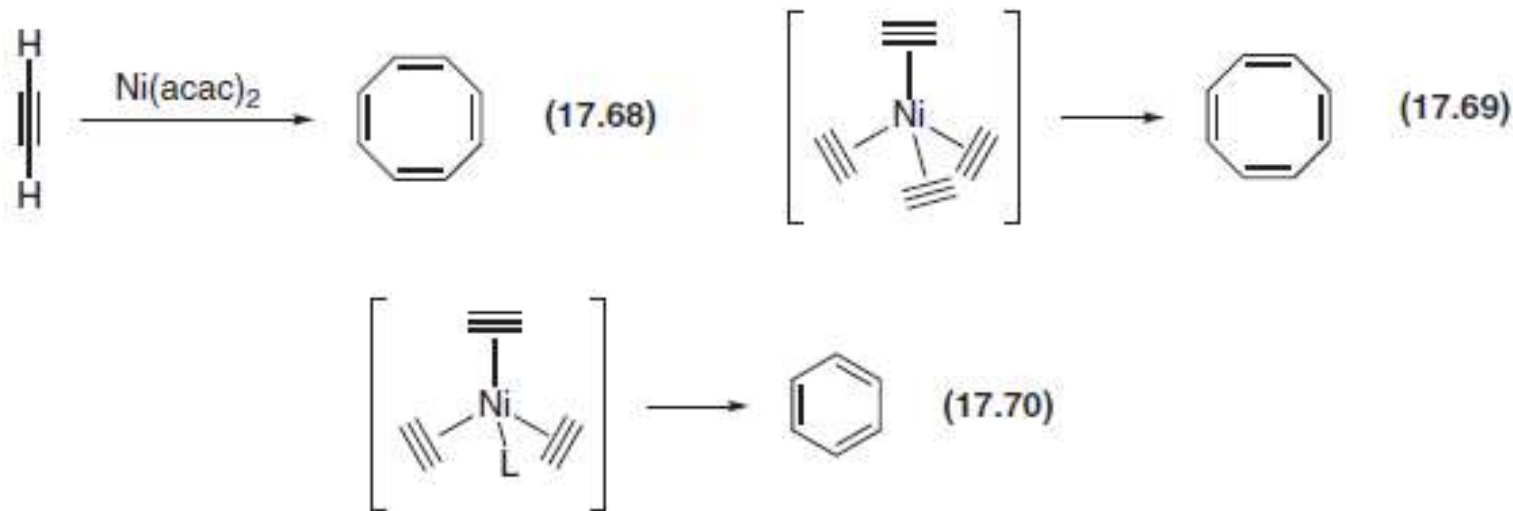
Figure 17.13



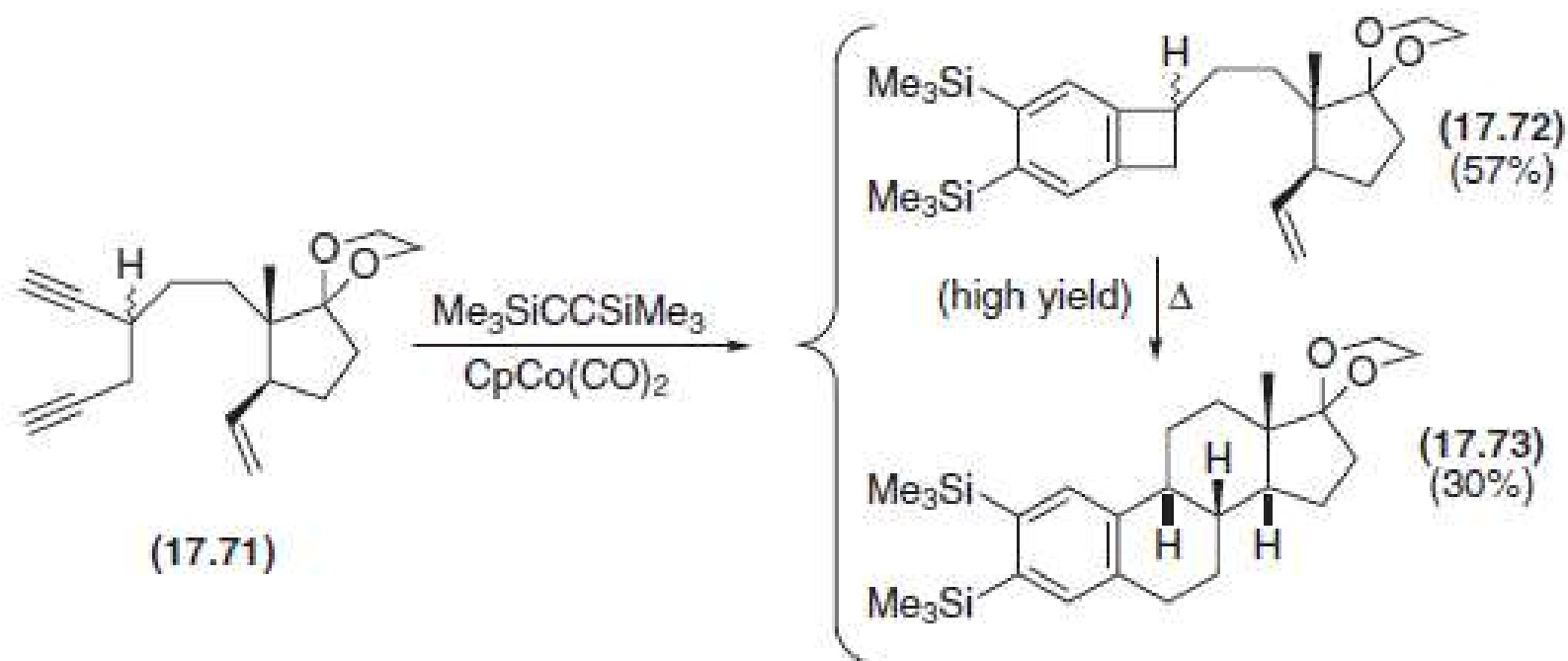
Formation of a cyclopentane by sequential electrophilic addition to a σ -allyl complex and intramolecular nucleophilic addition to an η^2 -alkene complex.

Reppe chemistry

- nickel-catalyzed cyclopolymerization of acetylene to cyclic polyenes, especially cyclooctatetraene (**17.68**)
- reaction is probably a **template reaction**, where all four alkynes are pre-assembled on the metal atom as a template (**17.69**) prior to the oligomerization
- ligands on the nickel that can compete with the acetylene for the metal, make it possible to use the reaction to prepare benzene derivatives



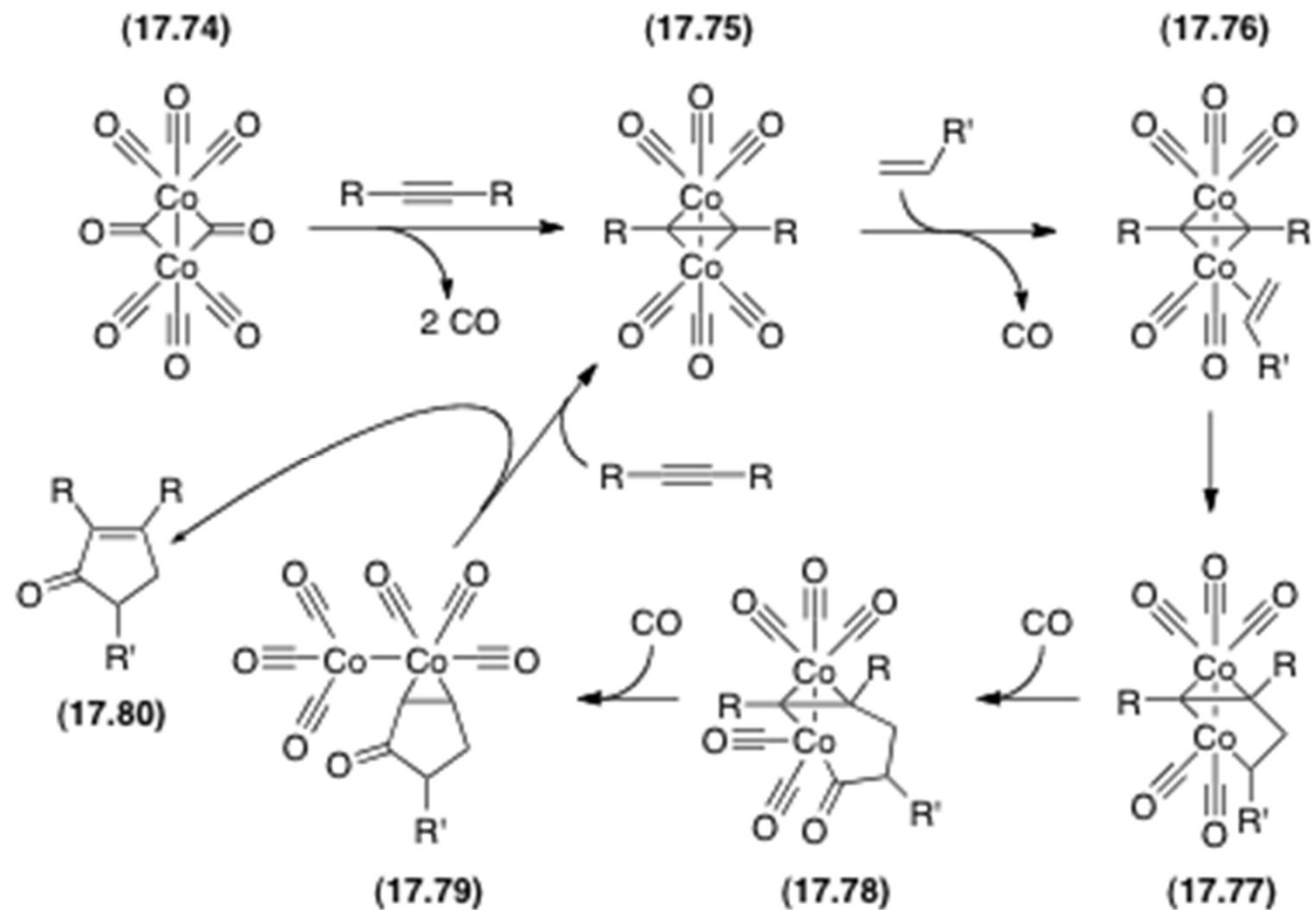
Reppe chemistry in synthesis



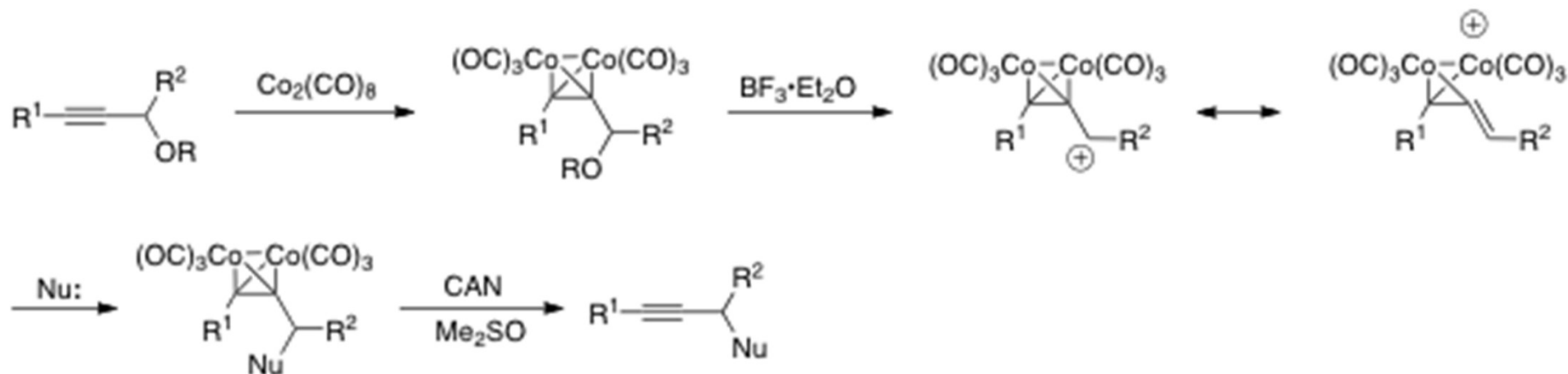
Construction of a steroid nucleus initiated by a cyclooligomerization of a diene with an alkyne catalyzed by cyclopentadienylcobalt (I) dicarbonyl

Figure 17.14

A catalytic cycle for the Pauson-Khand reaction



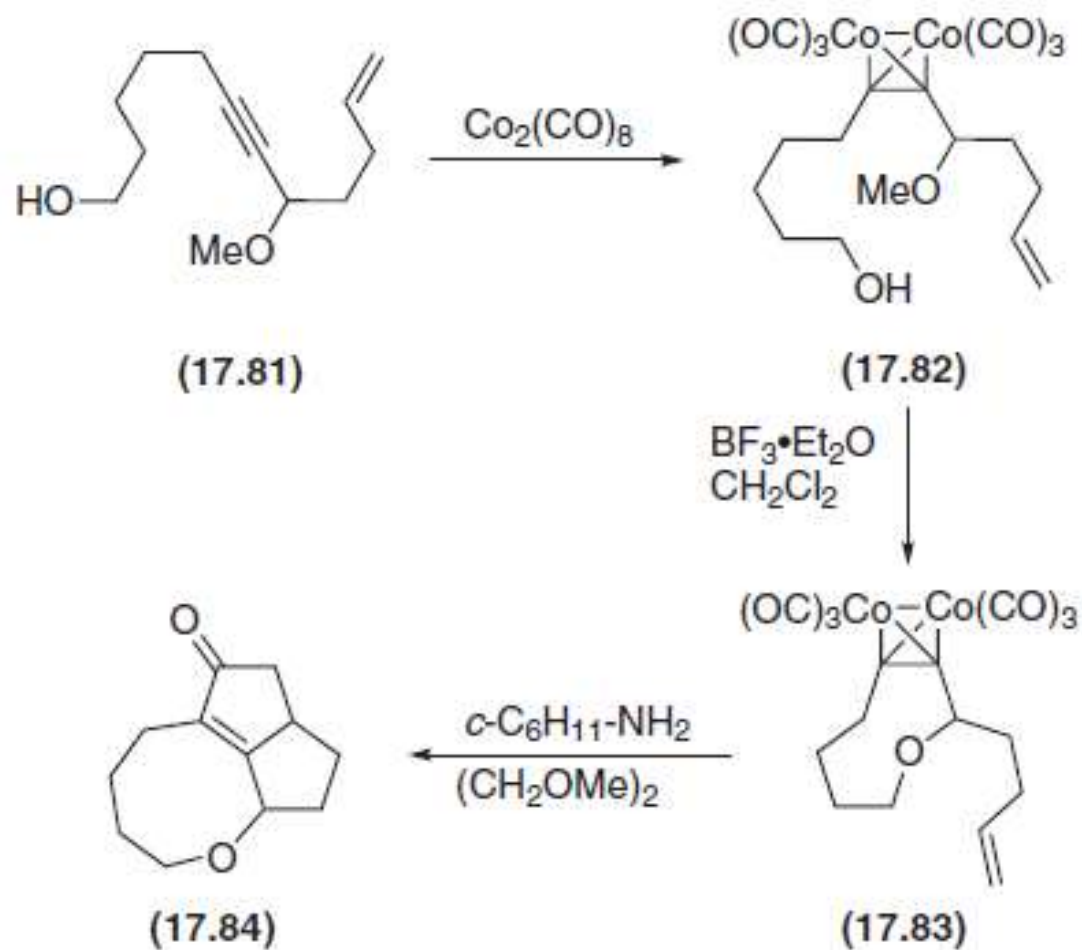
Nicholas reaction



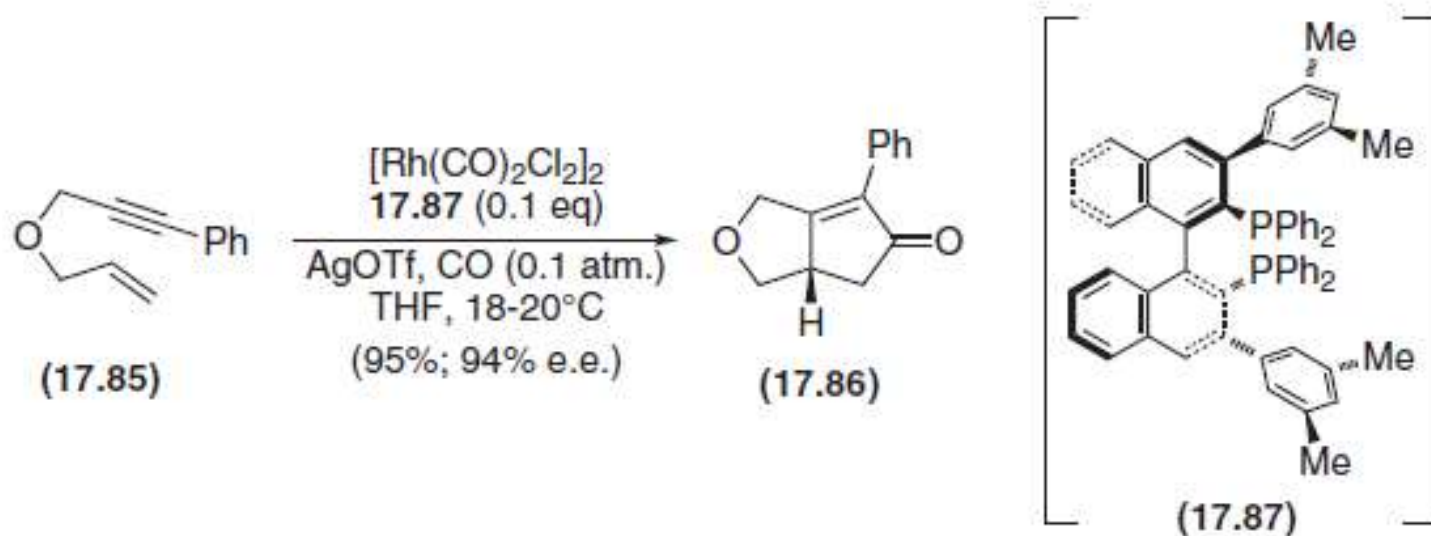
- cobalt complex of an alkyne is electron-rich
- cobalt complex of an alkyne can stabilize an adjacent carbocation (Nicholas cation) by delocalization of cation onto cobalt by resonance
- Nicholas cations react with nucleophiles to give products of nucleophilic substitution by the $\text{S}_{\text{N}}1$ mechanism

Tandem reactions catalyzed by dicobalt octacarbonyl

- The nucleophile in the Nicholas reaction is the intramolecular hydroxyl group.
- Instead of revealing the alkyne by oxidation, the cyclization with the alkene to give the cyclopentenone



Asymmetric Pauson-Khand reaction



- rhodium catalysts with chiral diphosphines can replace the highly toxic dicobalyl octacarbonyl in the Pauson-Khand reaction

Figure 17.15

The catalytic cycle of the Chauvin mechanism for olefin metathesis

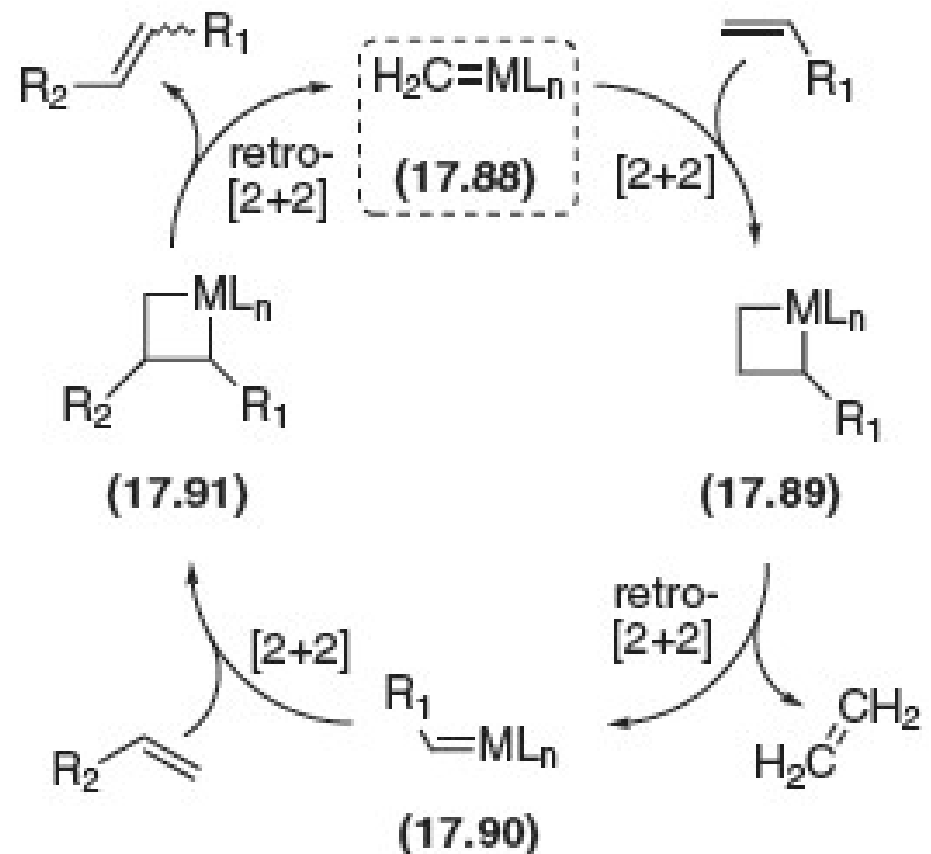
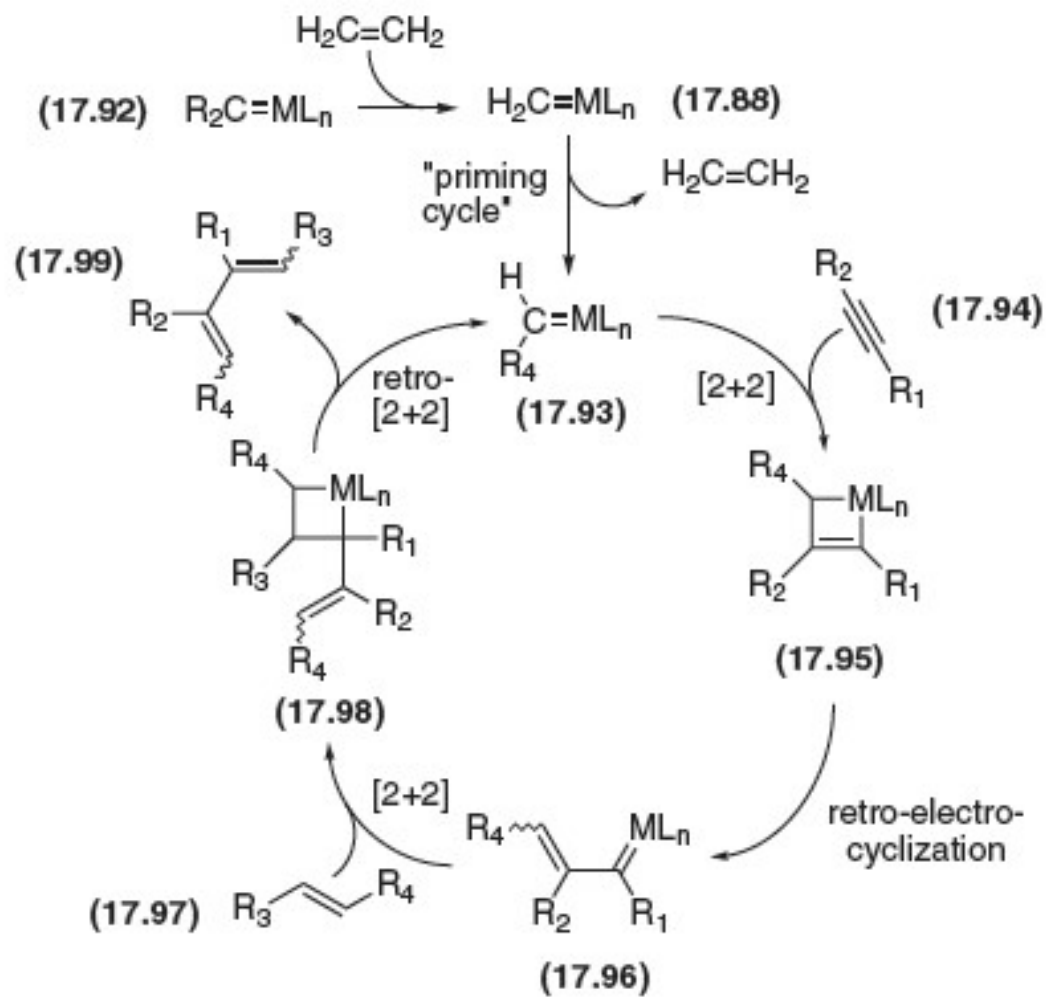


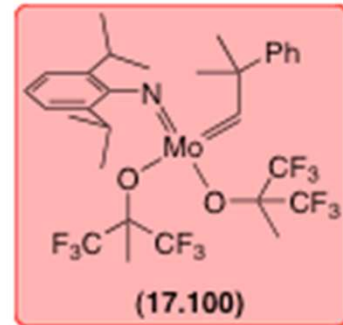
Figure 17.16

The catalytic cycle of the enyne metathesis reaction

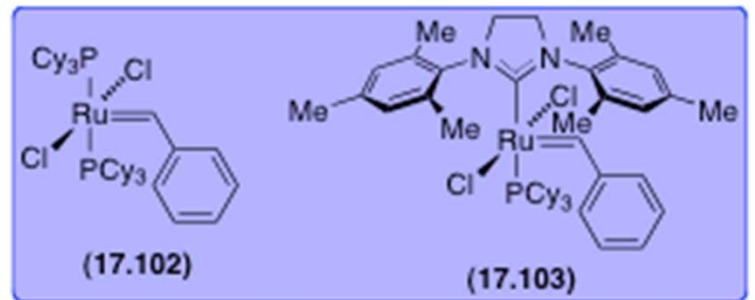


Metathesis catalysts

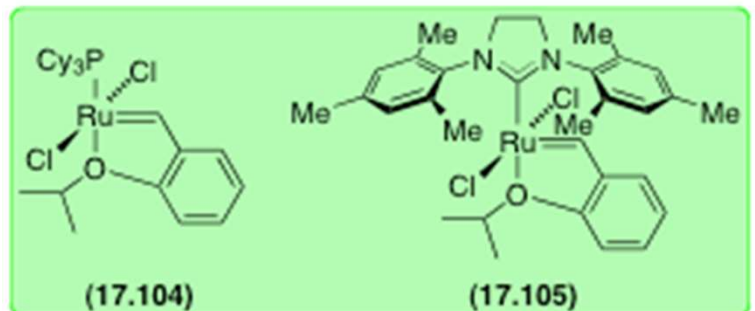
- Schrock catalyst



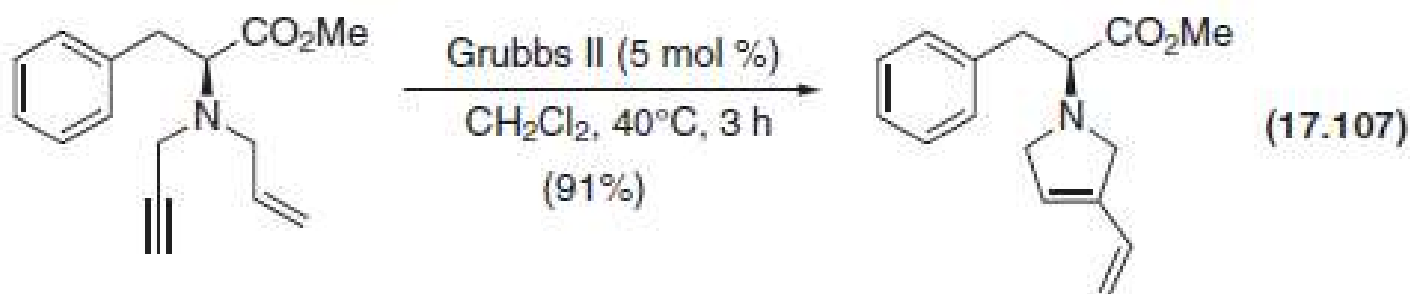
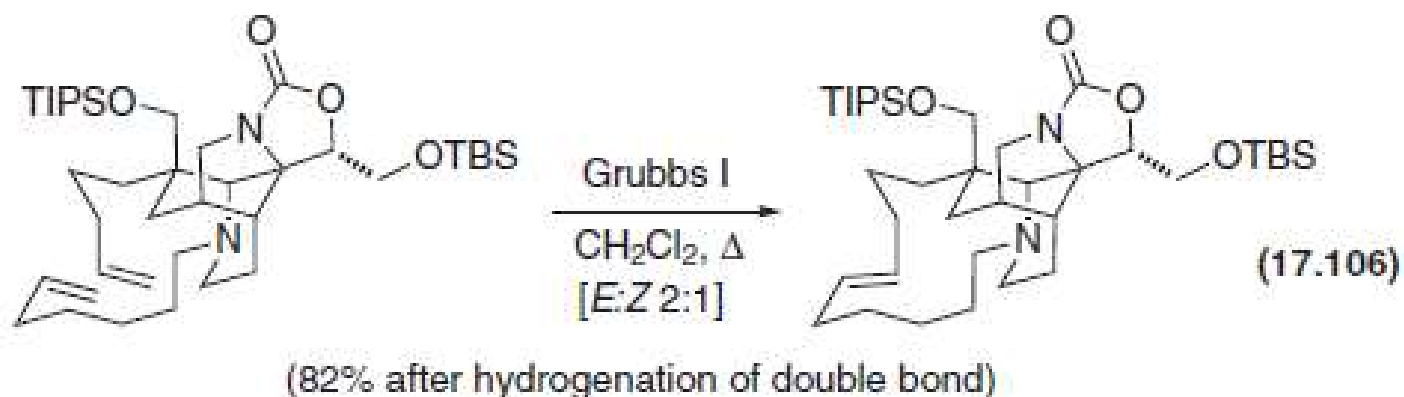
- Grubbs I and Grubbs II catalysts



- Grubbs-Hoveyda I and Grubbs-Hoveyda II catalysts

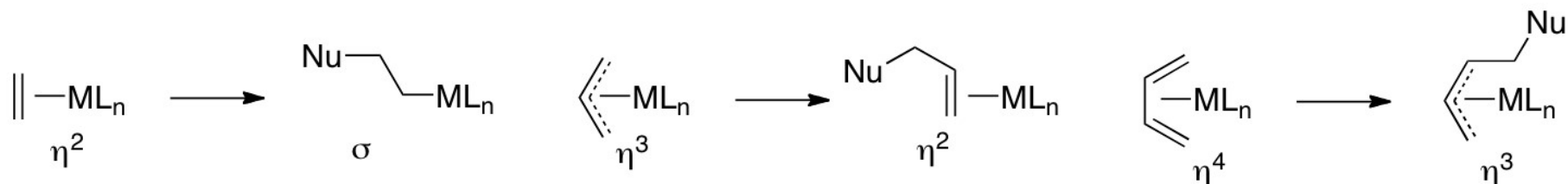


Metathesis in synthesis



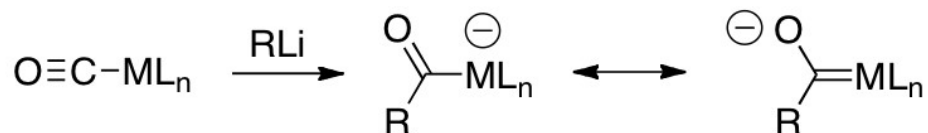
- olefin metathesis is an excellent method for the formation of medium and large rings

Reaction synopsis: Nucleophilic attack on ligands



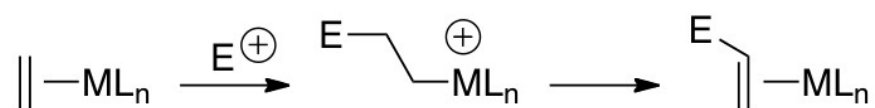
Reagents: RLi, RMgX, R₂Zn, etc.; enolate anions; oxyanions; etc.

Converts an η^n ligand to an η^{n-1} ligand (η^2 to σ), by attack of the nucleophile on the ligand.



Attack on carbonyl ligands gives acylmetal complexes that are resonance-stabilized ambident nucleophiles.

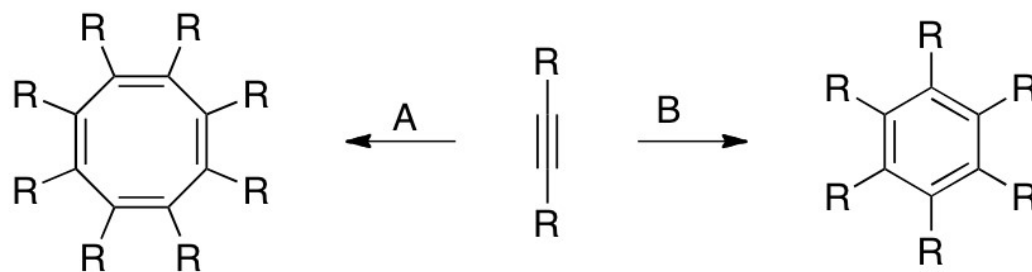
Reaction synopsis: Electrophilic attack on ligands



Reagents: RCOCl , AlCl_3 ; HCONMe_2 , POCl_3 ; etc.

Reaction usually proceeds by conversion of the η^n complex to the cationic η^{n-1} complex, and elimination of the proton to give the new η^n complex with a substituted ligand.

Reaction synopsis: Oligomerization



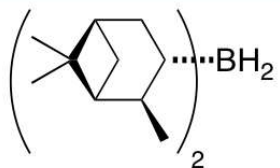

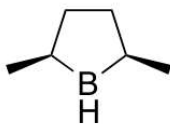
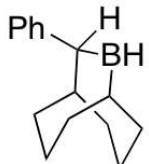
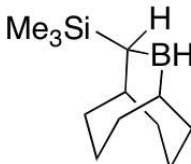
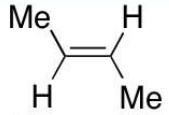
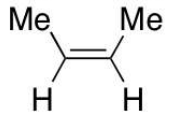
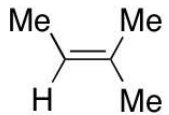
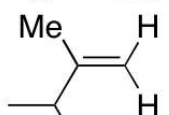
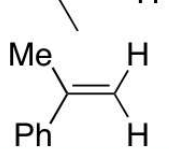
Reagents: A. Ni catalyst, frequently $\text{Ni}(\text{CO})_4$.

B. Ni catalyst with a strongly-binding ligand (e.g. Ph_3P)

Reaction of alkynes with diynes in the presence of $\text{CpCo}(\text{CO})_2$ gives benzenes.

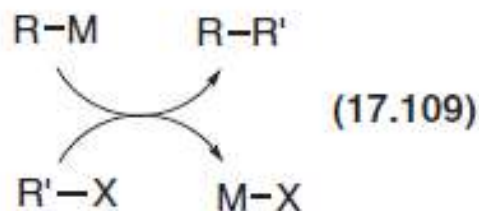
Reaction synopsis: Metathesis and metallocyclobutane formation

Table 17.3 Hydroboration with Chiral Boranes

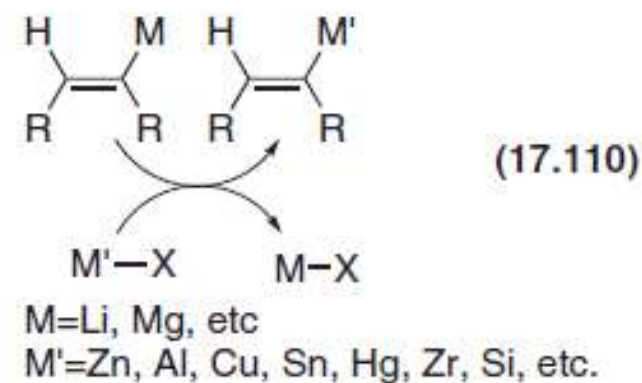
Representative Alkene	 Ipc_2BH	 IpcBH_2	 DMB		
	14	73	99.5	96	95
	99.1	24	97.6	32	84
	15	53	97.6	74	—
	32	—	1.5	38	52
	—	5	—	78	66

Transmetalation

- metal-halogen exchange



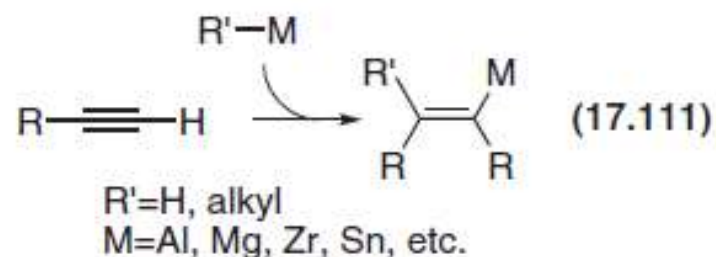
- metal-metal exchange



Carbometallation and hydrometallation

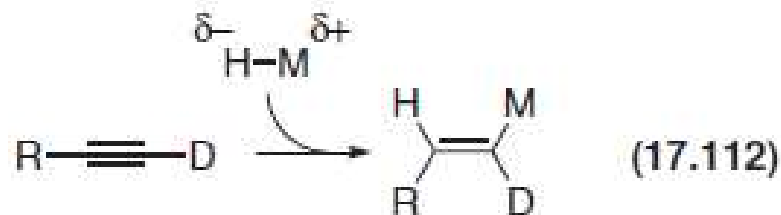
- carbometallation

- addition of metal alkyl across an alkyne occurs with *syn* stereochemistry



- hydrometallation

- addition of metal-hydrogen bond across a π bond occurs with *syn* stereochemistry

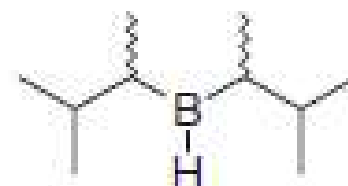


Borane reagents

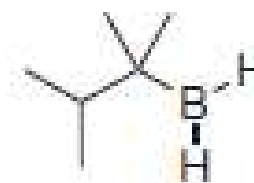
Hindered borane reagents exhibit higher regioselectivity, and regioselectivity increases with the amount of hindrance at boron.

Hindrance increases in the order

disiamylborane <
thexylborane < 9-
borabicyclo[3.3.1]nonane
(9-BBN)



Sia₂BH



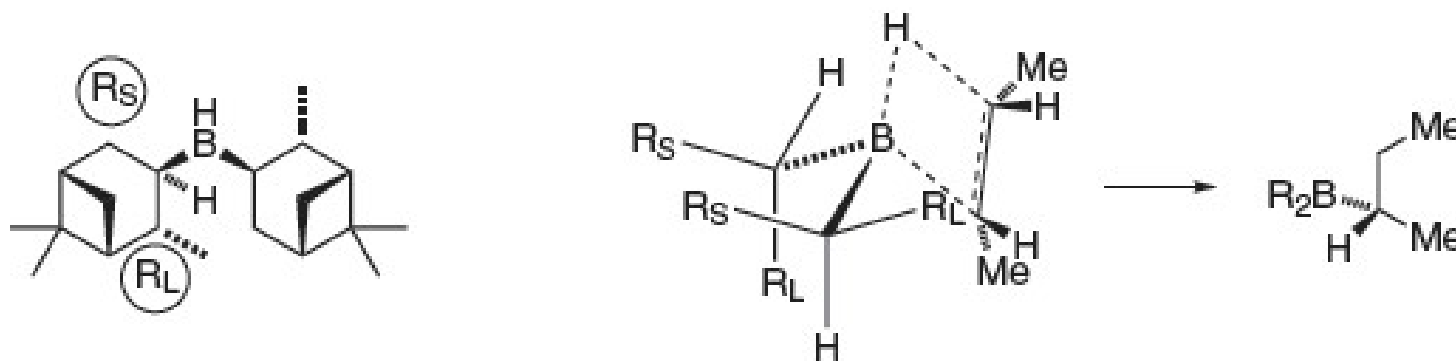
ThBH₂



9-BBN

(17.113)

Figure 17.17



A model for predicting the stereochemistry of addition of diisopinocampheylborane to *cis*-2-butene (a representative *Z* alkene).

Table 17.3

Hydroboration with chiral boranes

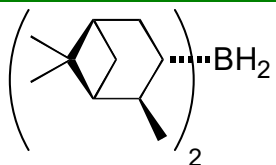
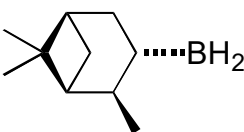
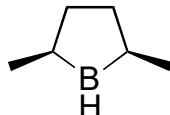
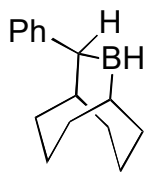
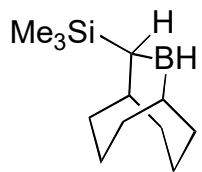
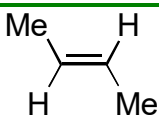
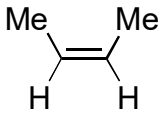
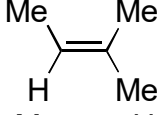
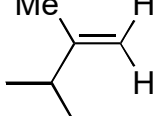
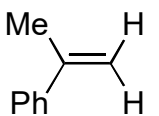
Representative Alkene	 Ipc_2BH	 IpcBH_2	 DMB		
	14	73	99.5	96	95
	99.1	24	97.6	32	84
	15	53	97.6	74	Ĝ
	32	Ĝ	1.5	38	52
	Ĝ	5	Ĝ	78	66

Figure 17.18

The synthesis
of the
Soderquist
boranes

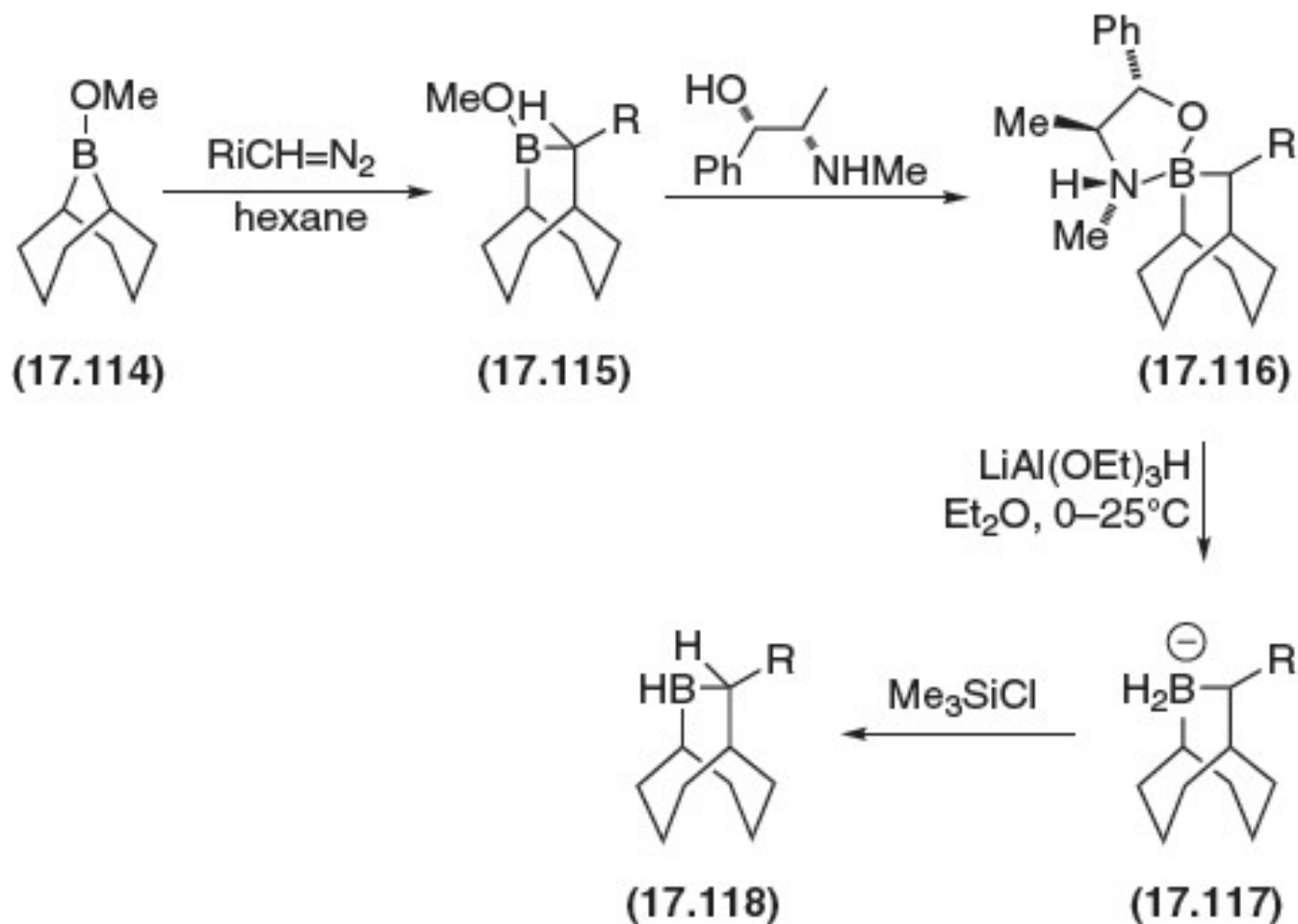
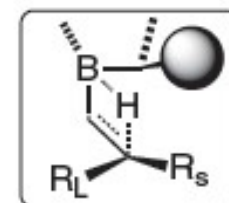
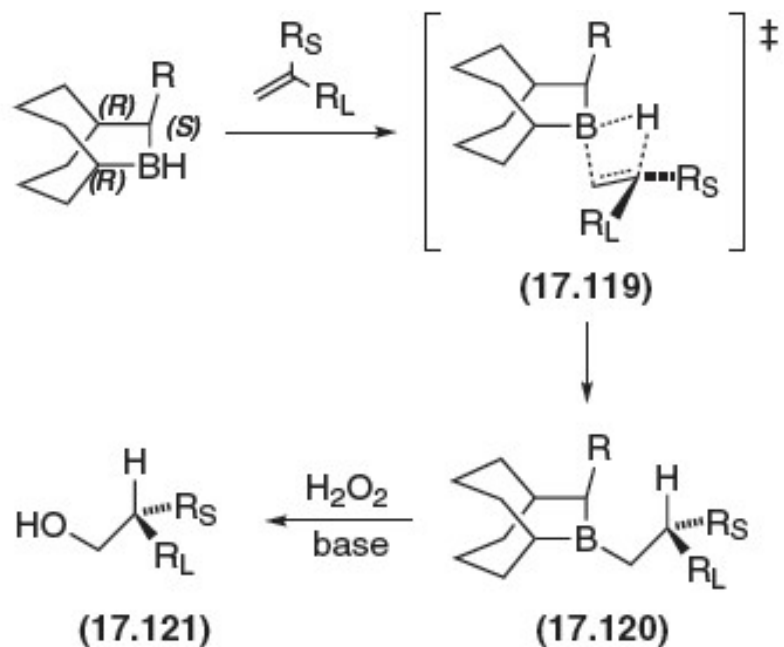


Figure 17.19

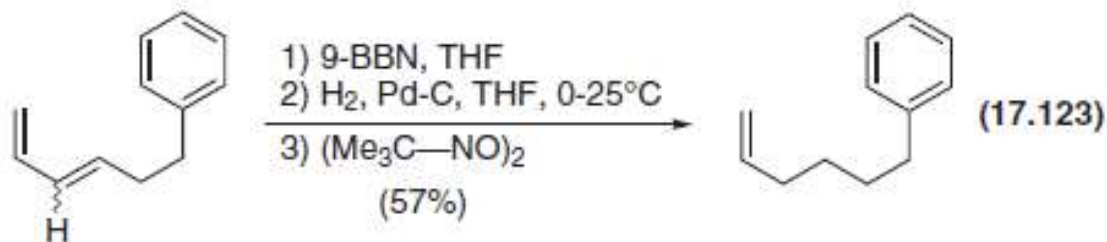
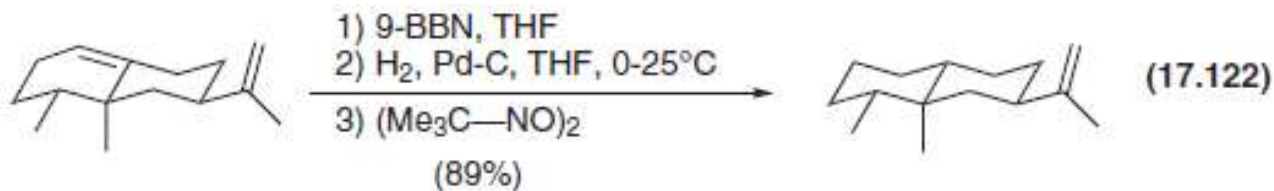


Model for predicting
the stereochemistry of
addition of the
Soderquist borane to a
1,1-disubstituted alkene

Boranes as protecting groups for alkenes

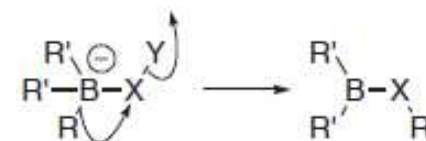
Semi-hydrogenation of dienes

- the less hindered double bond of the diene reacts with one equivalent of a hindered borane such as 9-BBN
- the resultant unsaturated borane is subjected to catalytic hydrogenation.
- the oxidation of the saturated product with a tertiary nitroso compound returns the original alkene.
- the reaction can be applied to either conjugated or



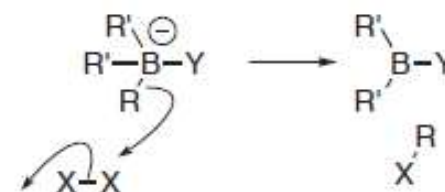
Alkyl transfer in boranes

- intramolecular alkyl migration with displacement of a leaving group occurs with retention of configuration at the migrating center



retention of configuration at R

(17.124)



inversion of configuration at R

(17.125)

- intermolecular alkyl transfer from a borate complex to a halogen or similar electrophile occurs with inversion of configuration at the migrating carbon.

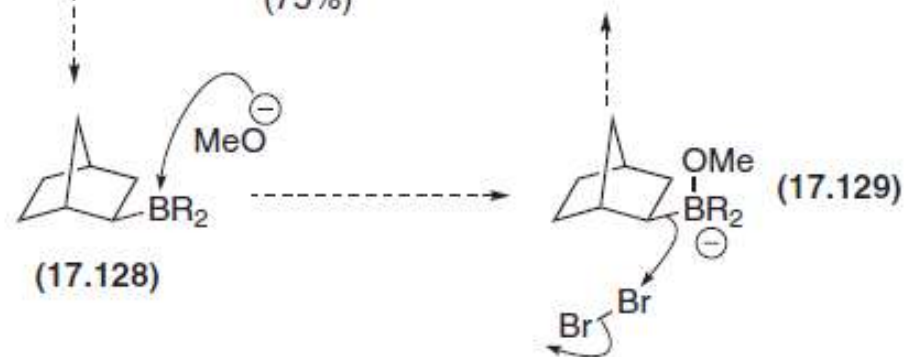
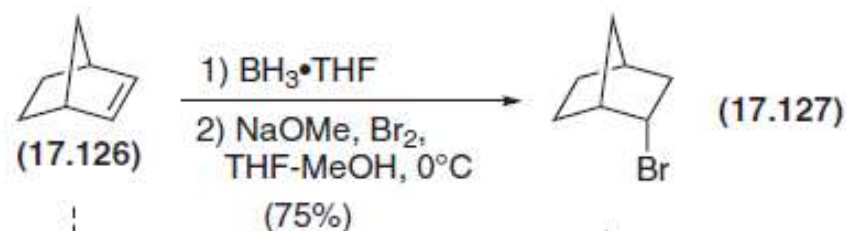
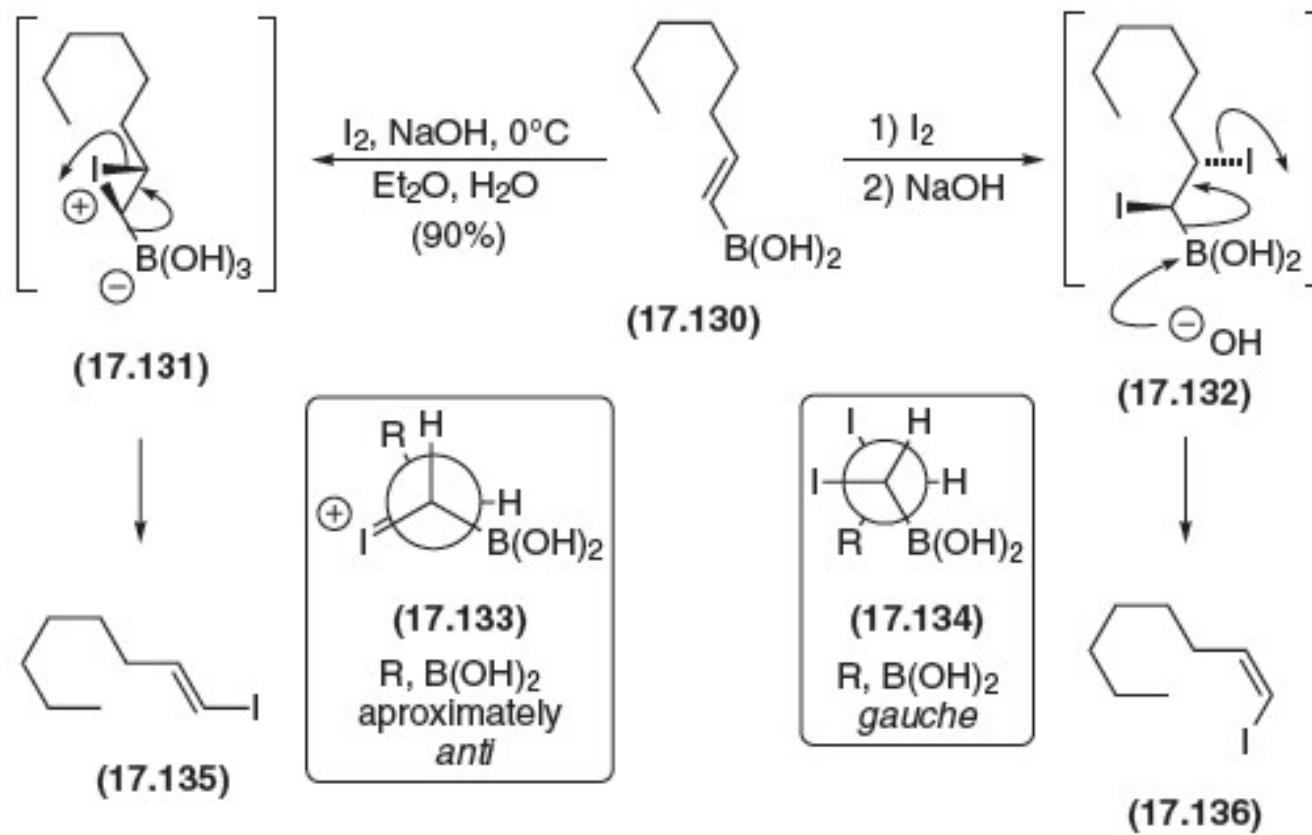


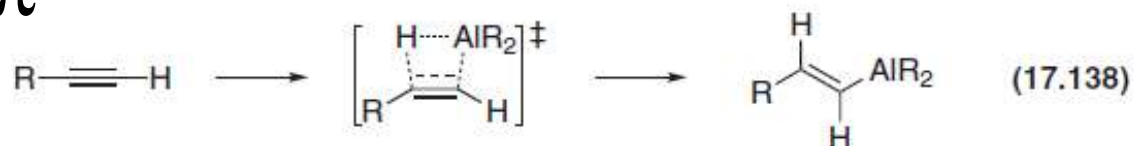
Figure 17.20



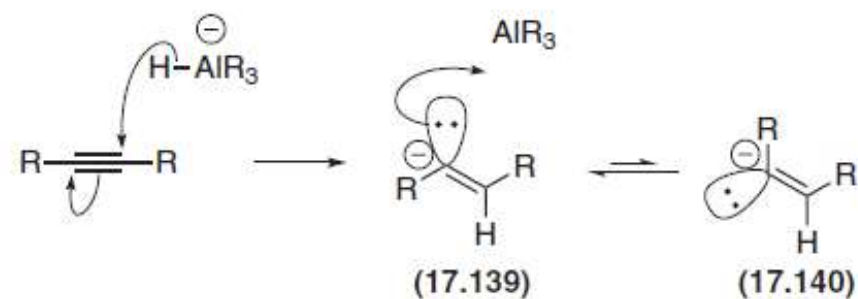
- Variation of stereochemistry in iodination of vinylboronic acids

Hydroalumination of alkynes

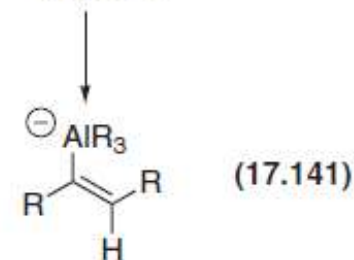
- addition of the Al—H bond across a C—C π bond



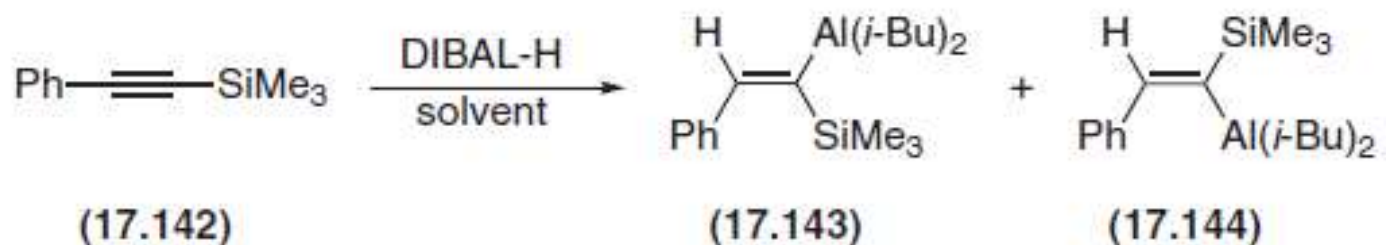
- neutral alanes give products of *syn* addition to alkynes



- anionic aluminates give products of *anti* addition to alkynes



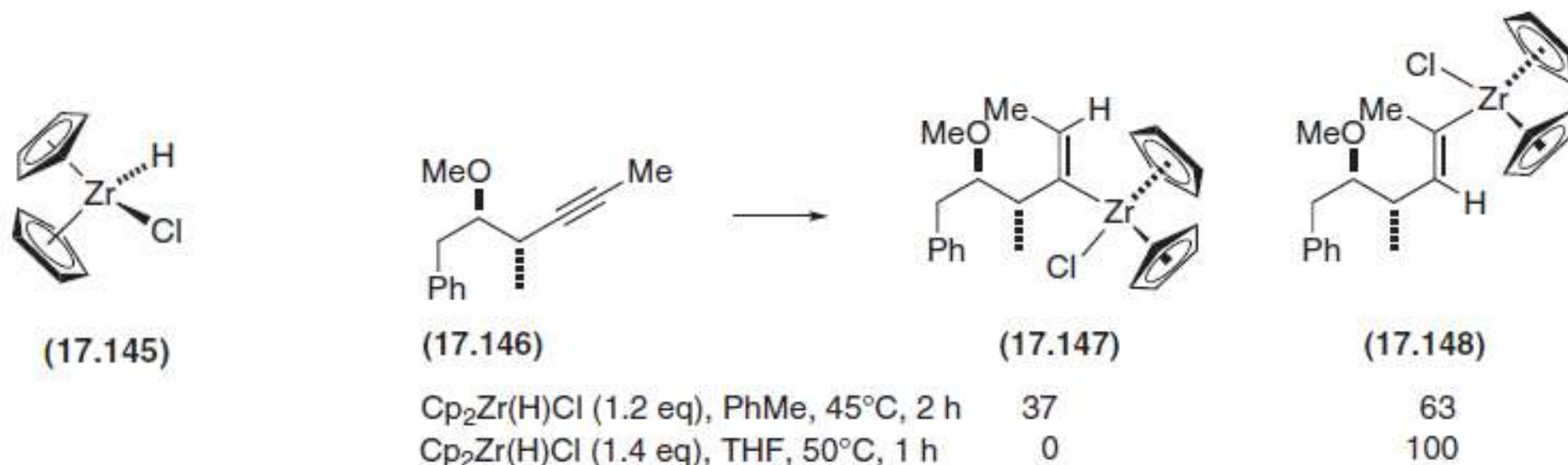
Modulating the stereochemistry of alane addition



solvent = heptane	4	:	96
solvent = heptane, <i>N</i> -Me-pyrrolidine)	96	:	4
solvent = Et ₂ O	65	:	35

- non-coordinating solvents favor *anti* addition of the alane to the alkyne
- strongly coordinating solvents favor *syn* addition of the alane to the alkyne

Zirconium: hydrozirconation



- **Schwartz reagent** adds *syn* to alkenes
- reaction is reversible, which allows the thermodynamic product to be formed in coordinating solvents (e.g. THF) at moderately high temperatures.
- Over longer reaction periods around 50°C, terminal vinylzirconium compounds formed by sequential addition-elimination become the dominant products

Figure 17.21

The Roy and Taylor mechanism for hydrosilylation of alkenes

the coordination number of the metal is denoted by the color of the highlight box

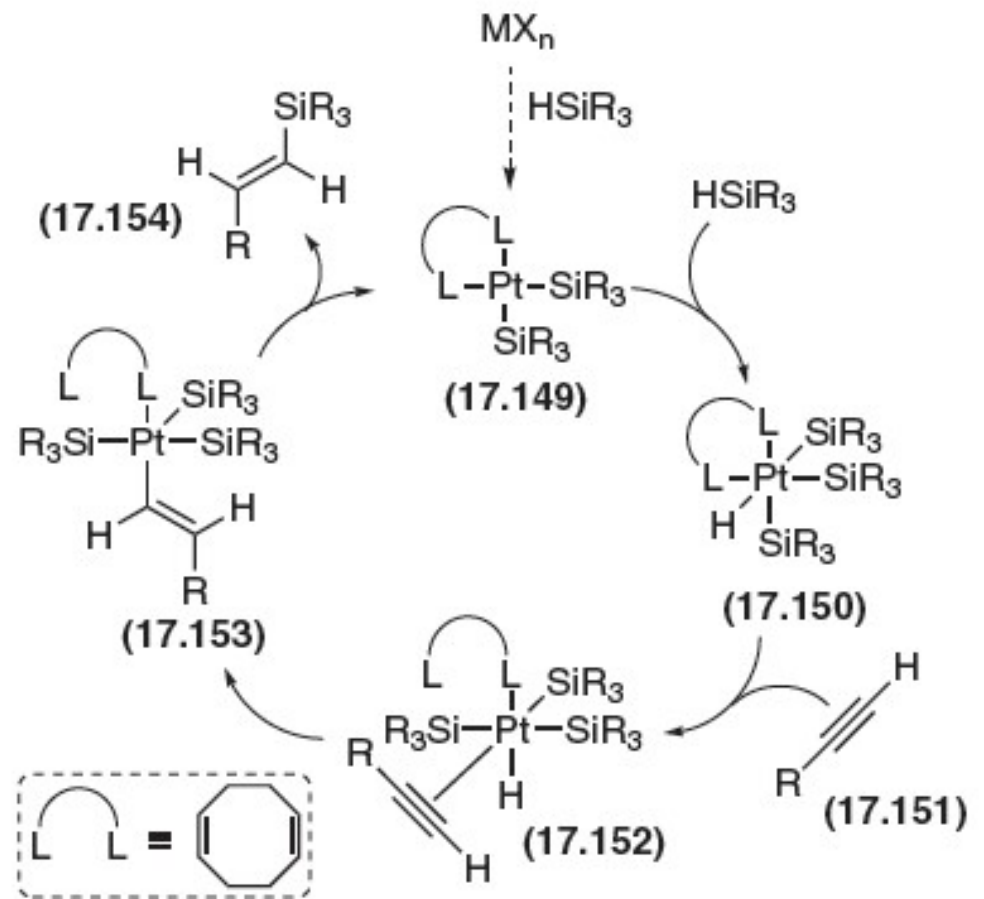
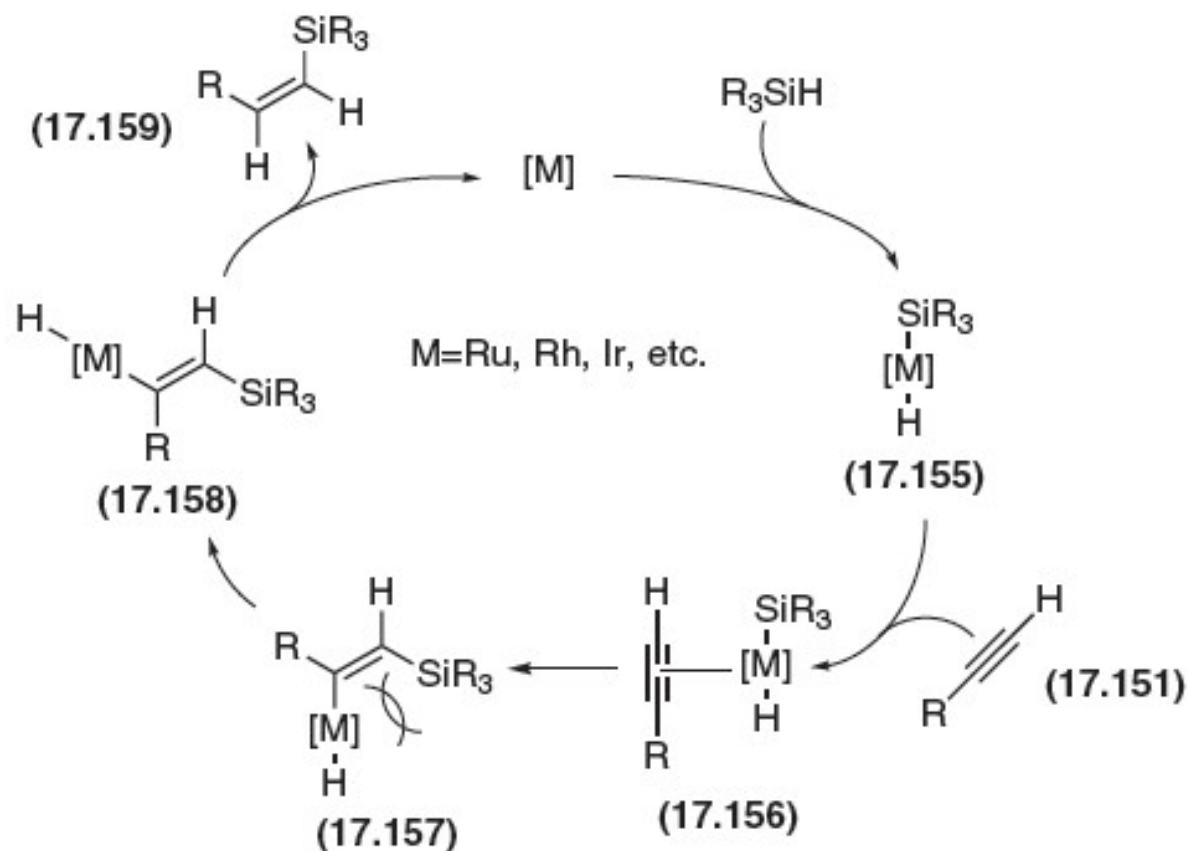


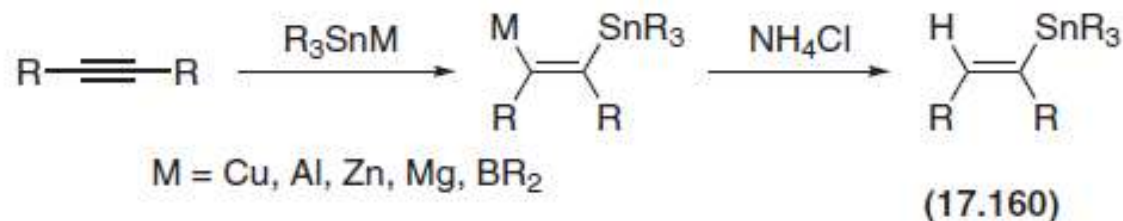
Figure 17.22

A modified Chalk and Harrod mechanism that accounts for the formation of the Z-vinylsilane from an alkyne

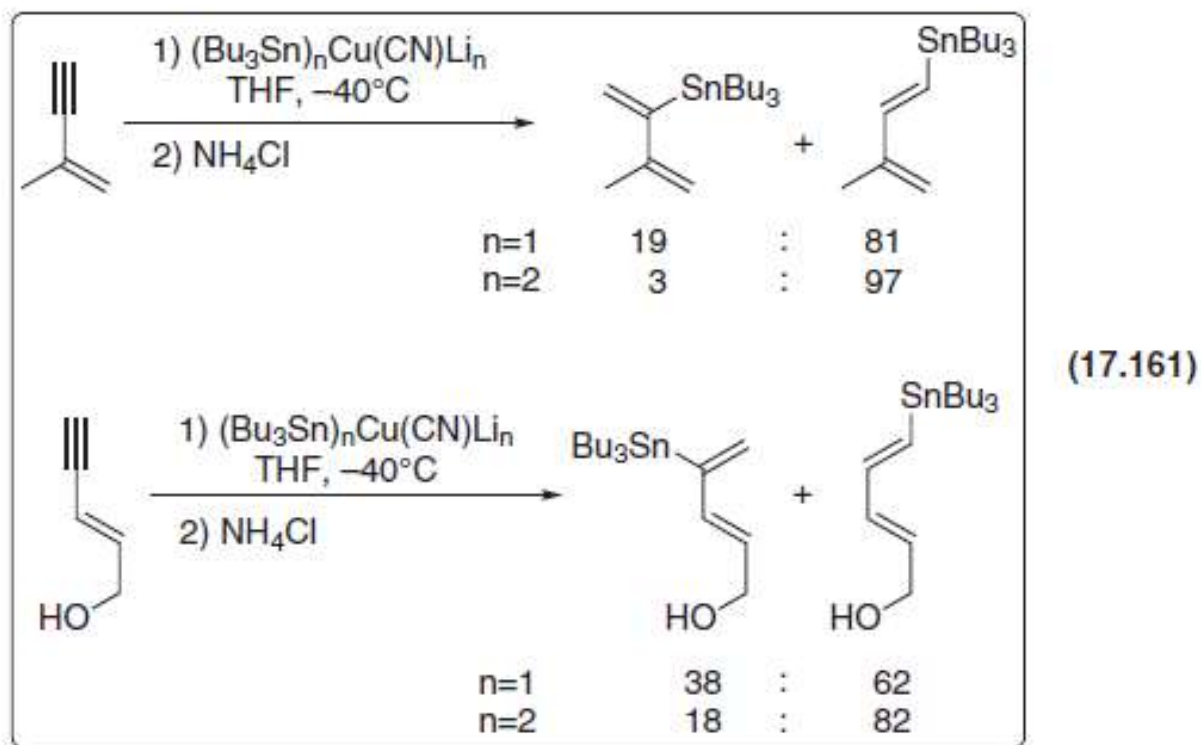
the coordination number of the metal is denoted by the color of the highlight box



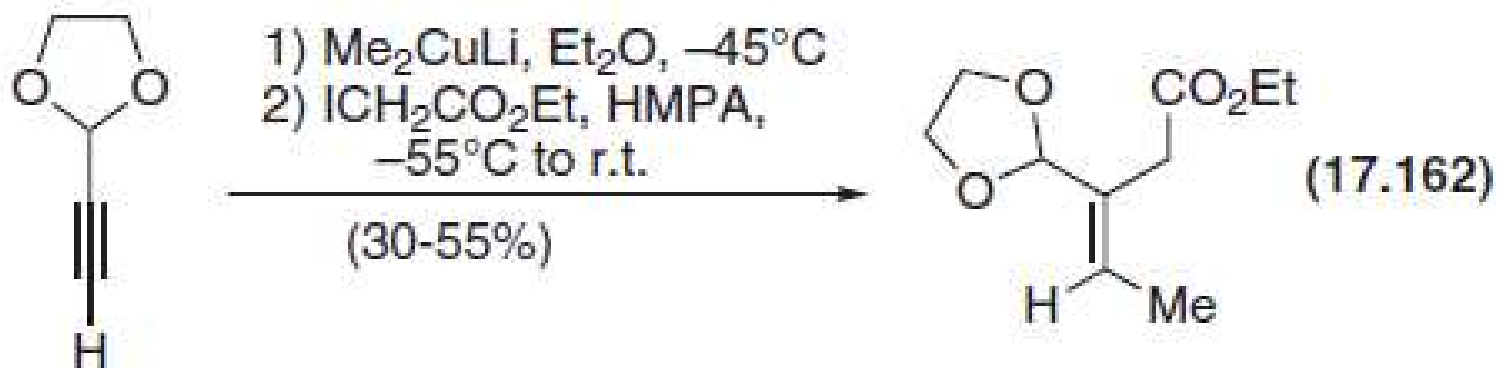
Stannylation-protonolysis of alkynes



- Reaction is most widely used with copper as the second metal
- with lithium stannylcuprates, regioselectivity increases when the Gilman reagent is replaced by the Lipshutz cuprate



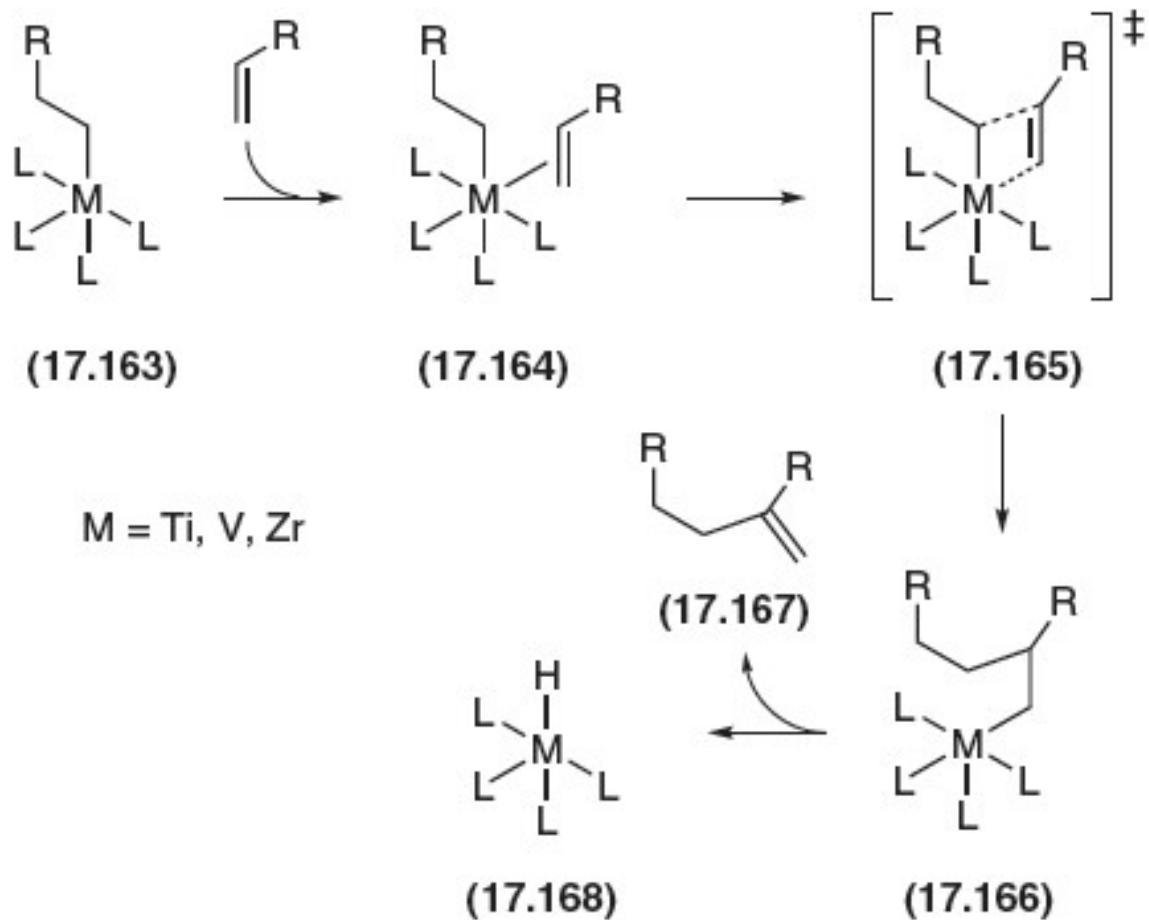
Carbometallation of alkynes



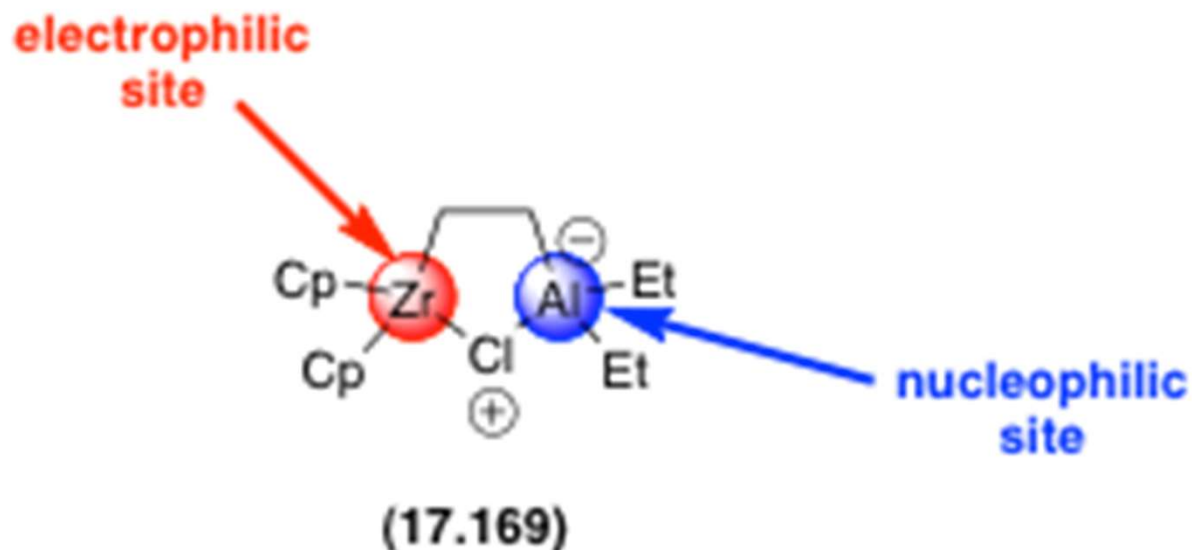
- copper is the most widely used metal, and can be used in stoichiometric or catalytic quantities
- atoms capable of complexing to the copper atom (e.g. the ether oxygens) can exert a major influence over the regiochemistry of the addition
- the addition is *syn*

Figure 17.23

The Cossee
mechanism for the
Ziegler-Natta
polymerization of
an alkene



Carboalumination of Alkynes



- putative bimetallic intermediate in the carboalumination of alkynes catalyzed by zirconium species

Reaction synopsis: Hydroboration

Hydroboration



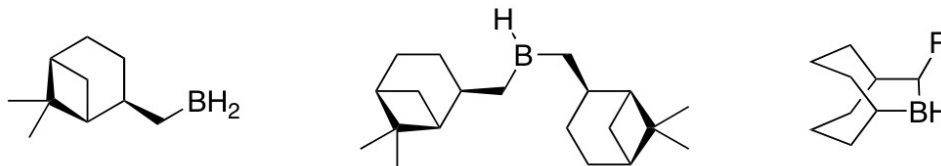
Reagents:

for alkenes: $\text{BH}_3 \cdot \text{THF}$; Sia_2BH , THF; ThBH_2 , THF;
9-BBN, THF;

for alkynes: $[o\text{-C}_6\text{H}_4\text{O}_2]\text{BH}$, THF; $(\text{Me}_2\text{CO})_2\text{BH}$, THF; etc.

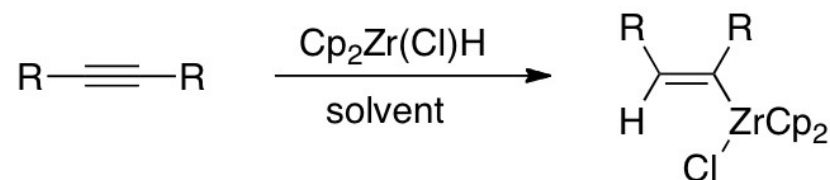
Regiochemistry: Markovnikov; regiochemical control is improved with bulky boranes. Stereochemistry: strictly *syn*

Reaction may be carried out asymmetrically using IpcBH_2 , Ipc_2BH , and Soderquist boranes:



Reaction synopsis: Hydrozirconation

Hydrozirconation

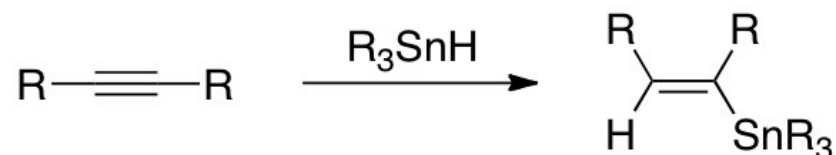


Solvent: PhMe (mixture of regioisomers); THF (Zr bonds to less hindered carbon); etc.

Stereochemistry: *syn*

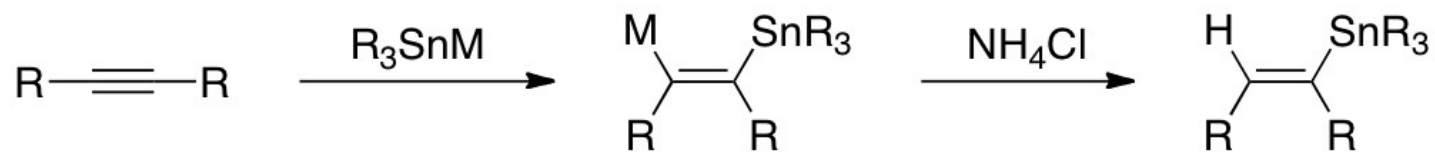
Reaction synopsis: Hydrostannylation

Hydrostannylation



Reagents: R_3SnH , AIBN, $h\nu$; etc. (free radical mechanism);

R_3SnH , Pd (not widely used)

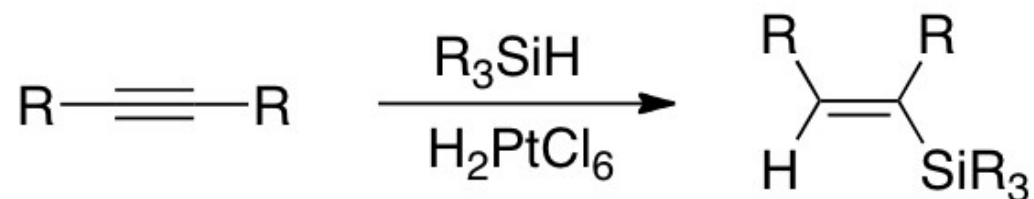


M = Cu, Al, Zn, Mg, BR_2

Copper is most widely used metal.

Reaction synopsis: Hydrosilation

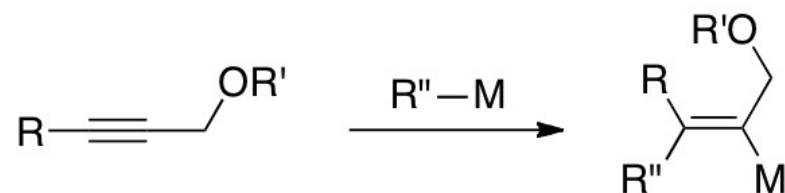
Hydrosilation



Stereochemistry: *syn* when Pt catalysts are used.

Reaction synopsis: Carbometallation

Carbometallation

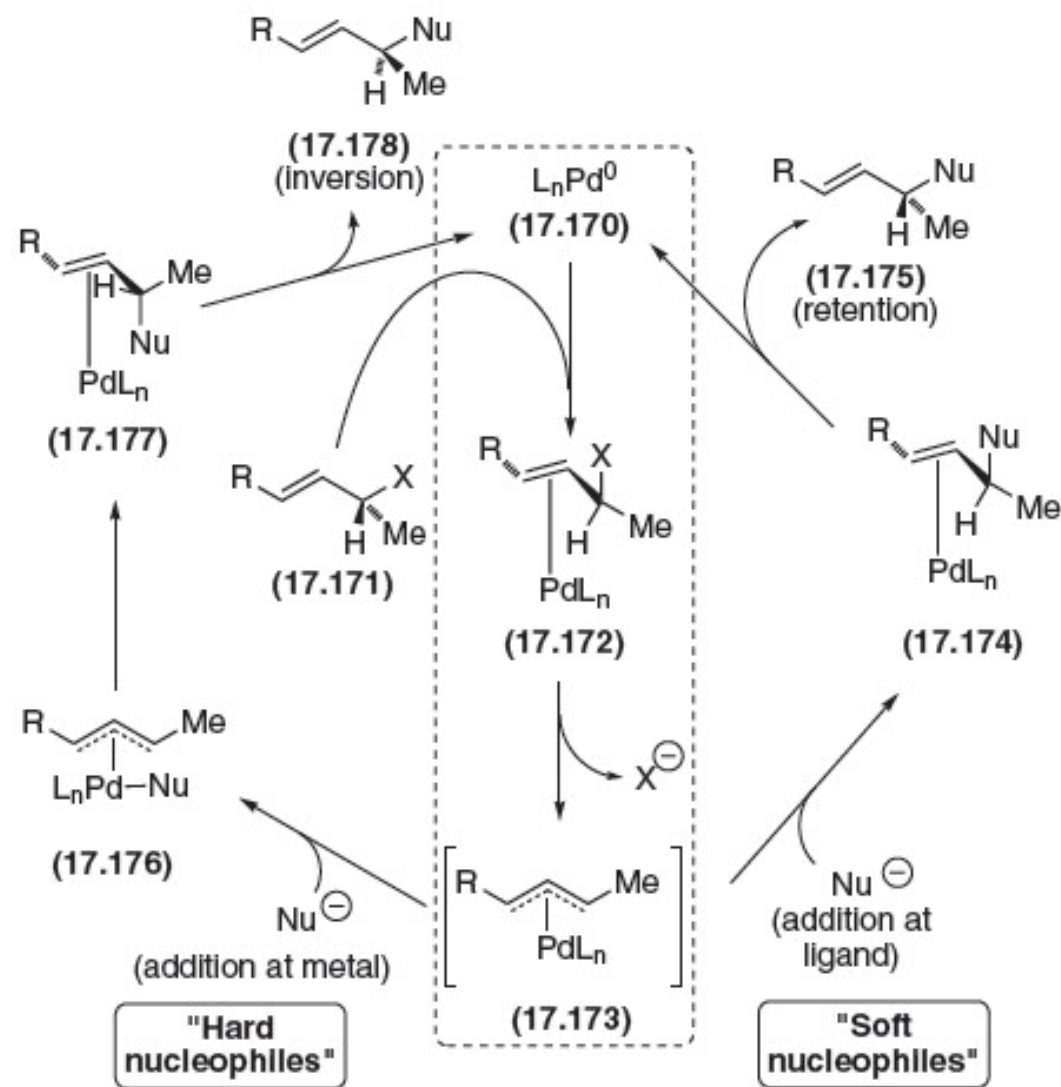


M = Cu, Al, Zr, Ti, etc.

Reagents: $\text{R}''_2\text{CuLi}$, THF; $\text{R}''_2\text{Cu}(\text{CN})\text{Li}_2$, THF (carbocupration);
 $\text{R}''_3\text{Al}$, ZrCl_4 ; R_3Al , $\text{Cp}_2\text{Zr}(\text{Cl})\text{H}$, (carboalumination)

Figure 17.24

Catalytic cycles of the Tsuji-Trost allylation reaction with hard and soft nucleophiles, showing reversal of stereochemistry.



Tsuji-Trost reactions

Tsuji-Trost reactions of allyl esters proceed through an h^3 allyl complex, which reacts with soft carbon nucleophiles to give the net displacement of the ester with retention of configuration

Allylic epoxides can also be used as precursors to the electrophilic palladium complex.

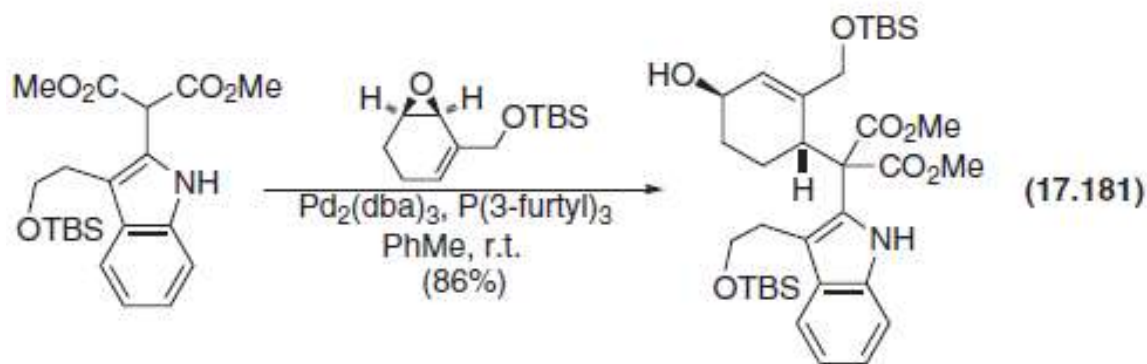
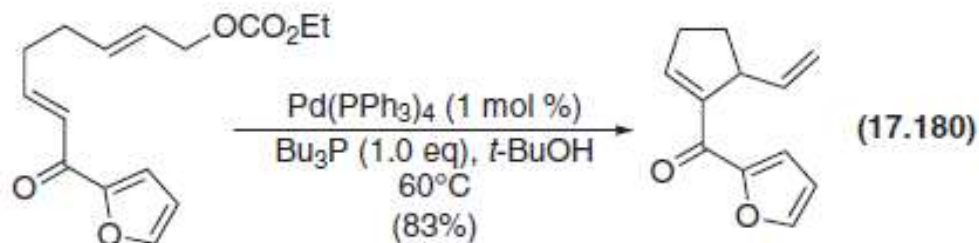
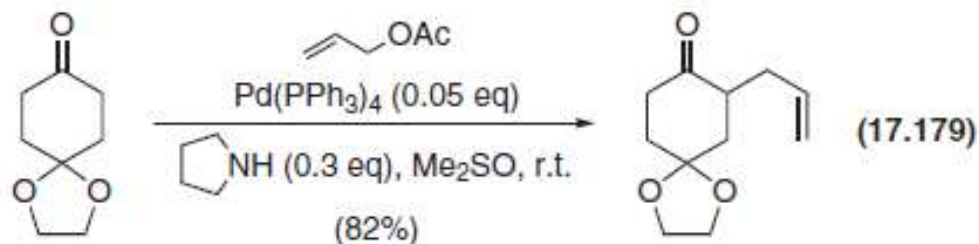


Figure 17.25

The mnemonic for predicting stereochemistry in the asymmetric allylation of *meso* substrates using C_2 -symmetric "Trost" diphosphine ligands

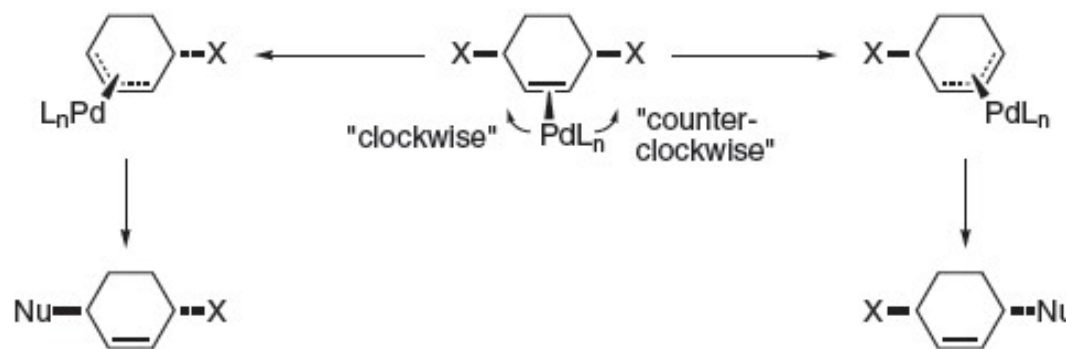
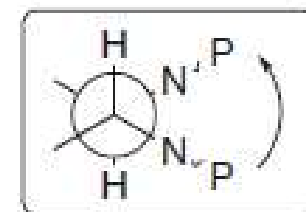
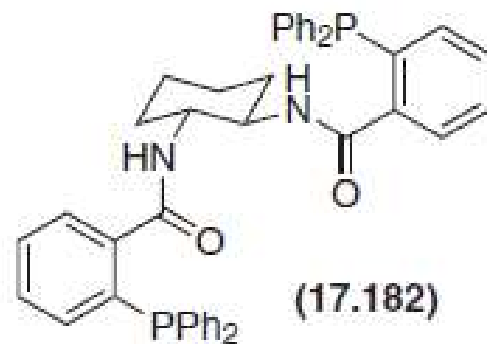
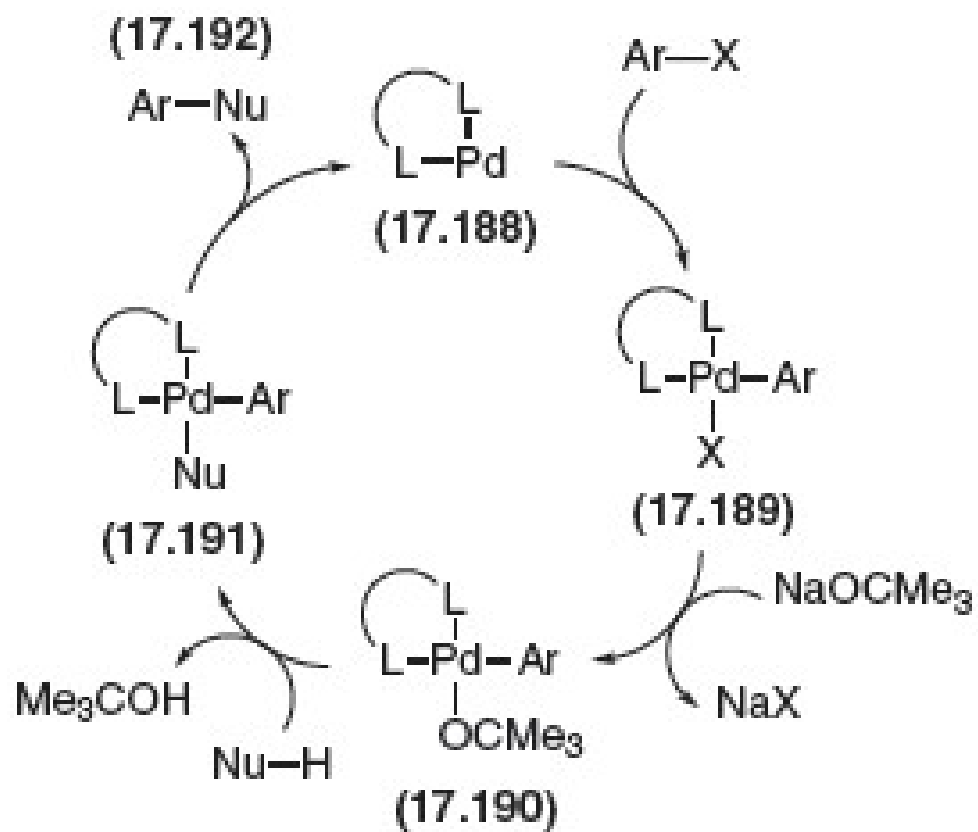
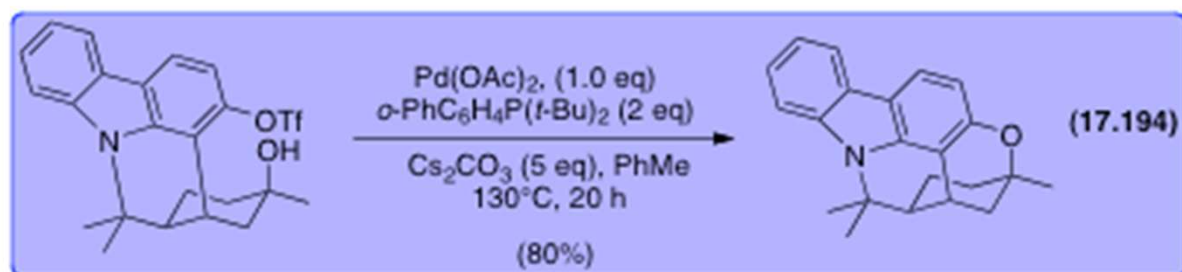
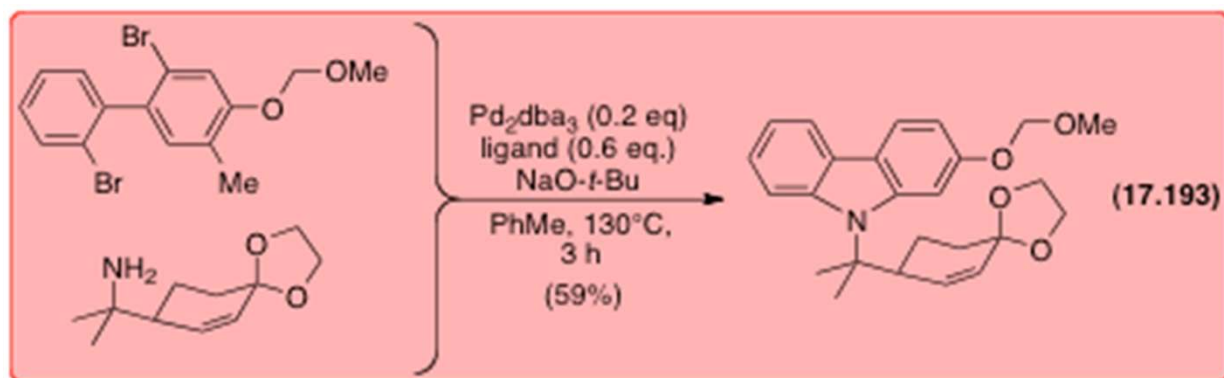


Figure 17.26

The catalytic cycle of the Buchwald-Hartwig coupling reaction

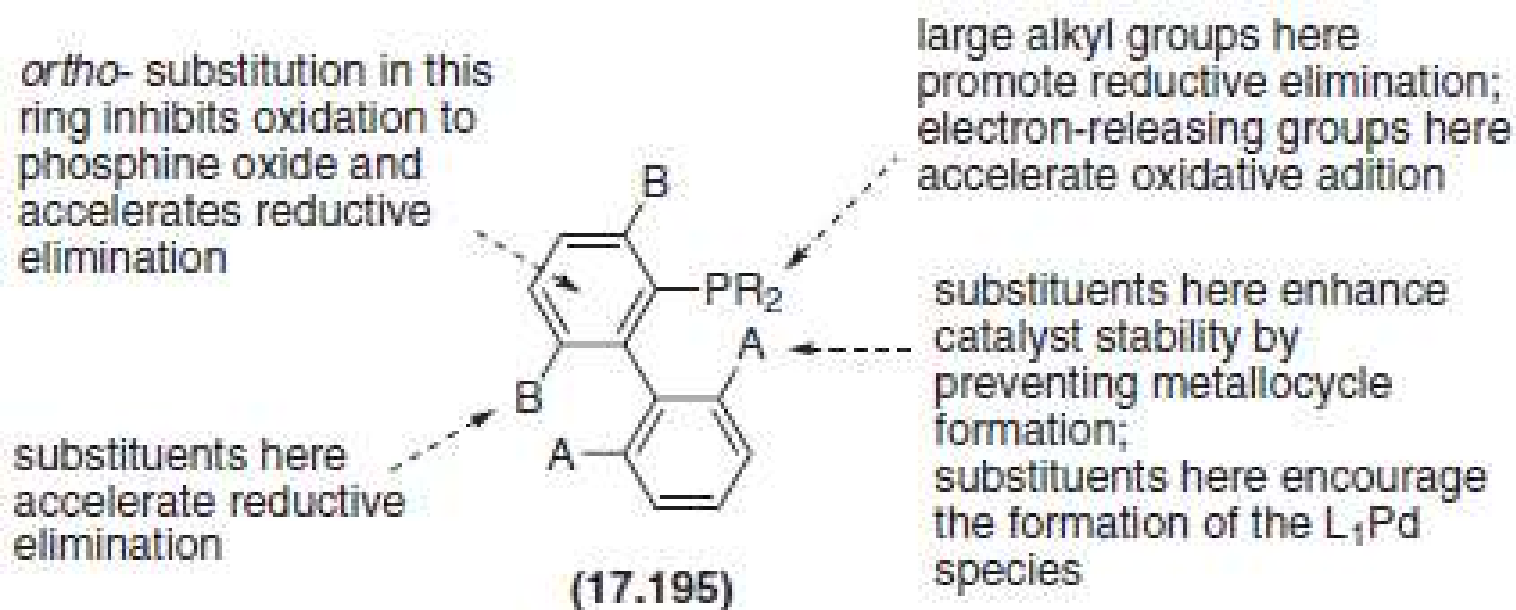


Buchwald-Hartwig reactions



- representative reactions to form aromatic amines and ethers

Ligands for Buchwald-Hartwig aminations



- the effects of each of the structural features of the ligand on its performance in palladium-catalyzed aminations

Reaction synopsis: Tsuji-Trost reaction

Tsuji-Trost Reaction



X: Cl, Br, OAc, OCOPh, OCO₂Et, etc.

Pd⁰: Pd(PPh₃)₄, etc.

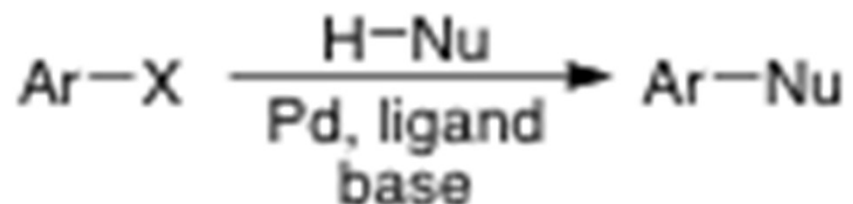
Nu⁻: enolate anions, metal alkyls, etc.

Stereochemistry: net retention of configuration at carbon with soft nucleophiles (e.g. enolates); net inversion with hard nucleophiles (e.g. dialkylzinc reagents).

Chiral ligands allow enantioselective reactions of *meso* diesters to give chiral products.

Reaction synopsis: Buchwald-Hartwig reaction

Buchwald-Hartwig Coupling



X: Br, OTf, I, etc. [Cl and OTs require more active catalysts]

Pd: Pd₂dba₃, Pd(OAc)₂, etc.

ligand: dppf, *o*-ArC₆H₄PR₂, etc.

Nu: Ar'NR, Ar'O, etc. [with stronger bases, enolate anions can be used]

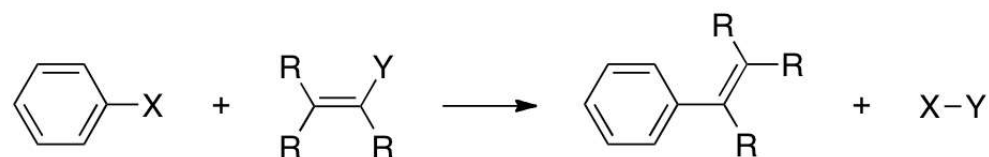
Table 17.4

Number of metal-catalyzed C—C bond-forming reactions cited in 2011

Reaction	Mentions
Suzuki-Miyaura cross-coupling	10,721
Heck cross-coupling	3,157
Sonogashira cross-coupling	2,302
Stille cross-coupling	2,176
Negishi cross-coupling	1,461
Hiyama-Denmark cross-coupling	647
Tsuji-Trost	124
olefin metathesis	7,397

Table 17.5

Transition Metal-Catalyzed Cross-Coupling Reactions



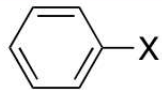
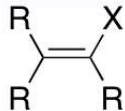
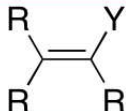
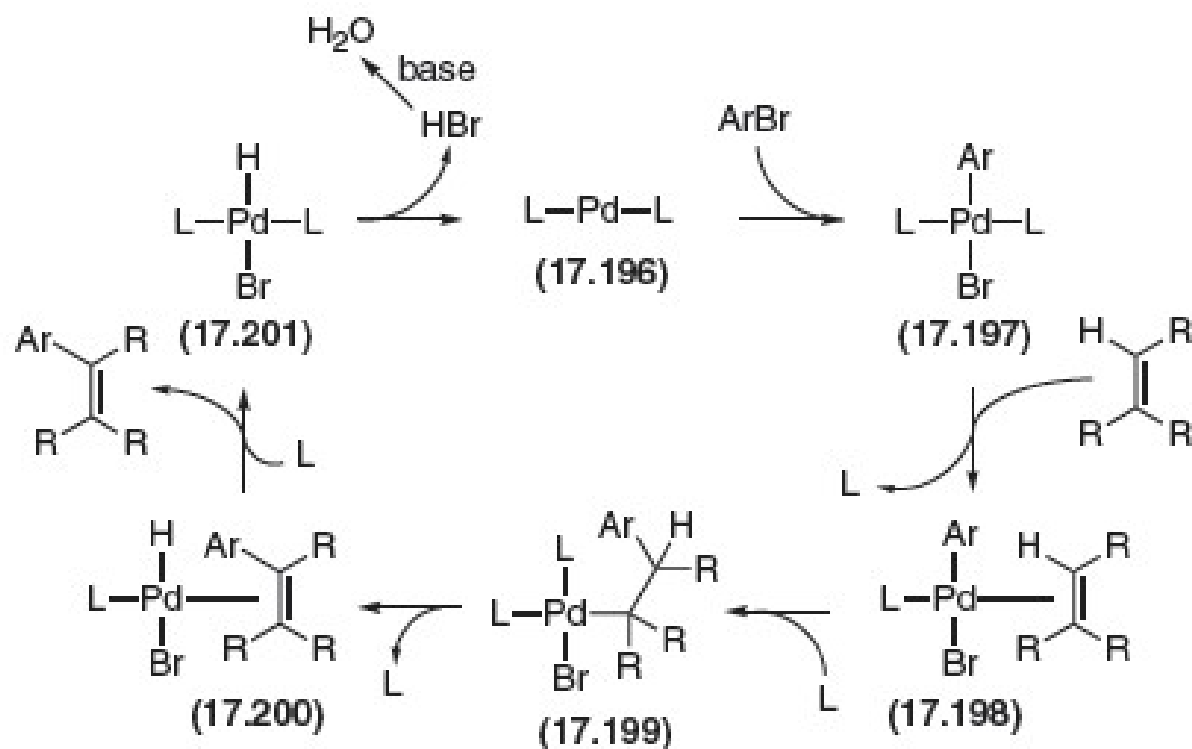
			Catalyst	Reaction Name
X=I, OTf, Br [Cl]		Y=H	Pd	Heck
X=HgX, SnR ₃ , PbR ₃ ,		Y=H	Pd	Heck
X=I, OTf, Br [Cl]		Y=SnR ₃	Pd	Stille
X=I, OTf, Br [Cl]		Y=ZnX, AlX ₂ , ZrL _n	Pd, Ni	Negishi
X=I, OTf, Br [Cl]		Y=SiR ₃ , F ⁻	Pd	Hiyama
X=I, OTf, Br [Cl]		Y=Si(OR) ₃ , RO ⁻	Pd	Hiyama-Denmark
X=I, OTf, Br [Cl]		Y=MgX	Ni, Pd	Corriu-Kumada
X=I, OTf, Br [Cl]		Y=B(OR) ₂	Pd	Suzuki-Miyaura
X=I, OTf, Br [Cl]		RC≡CH	Pd-Cu	Sonagashira

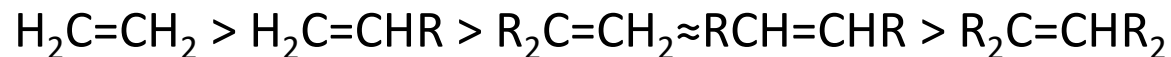
Figure 17.27

The catalytic cycle of the Heck reaction



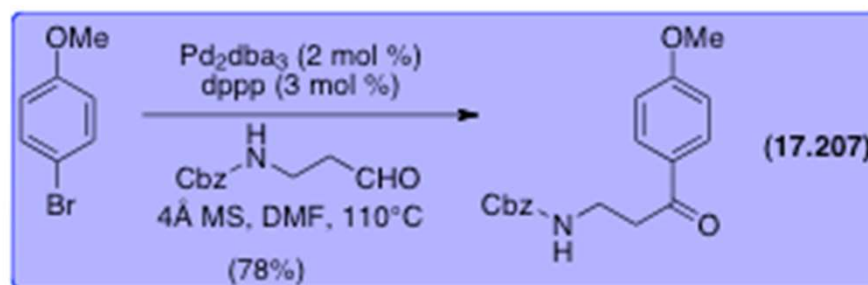
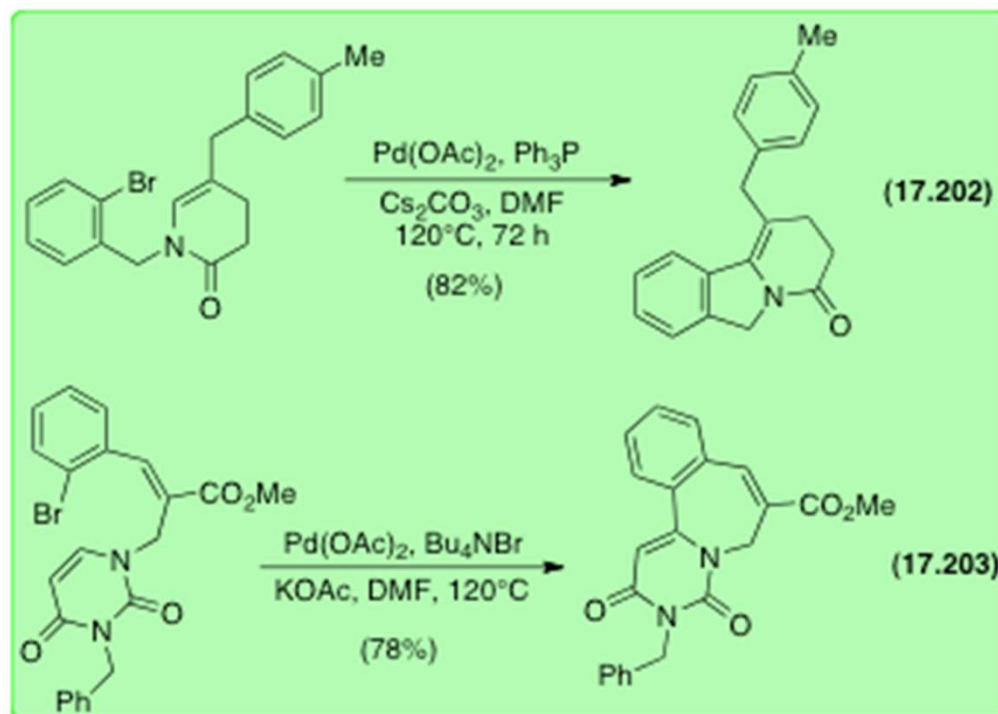
Reactivity of alkene partner

:

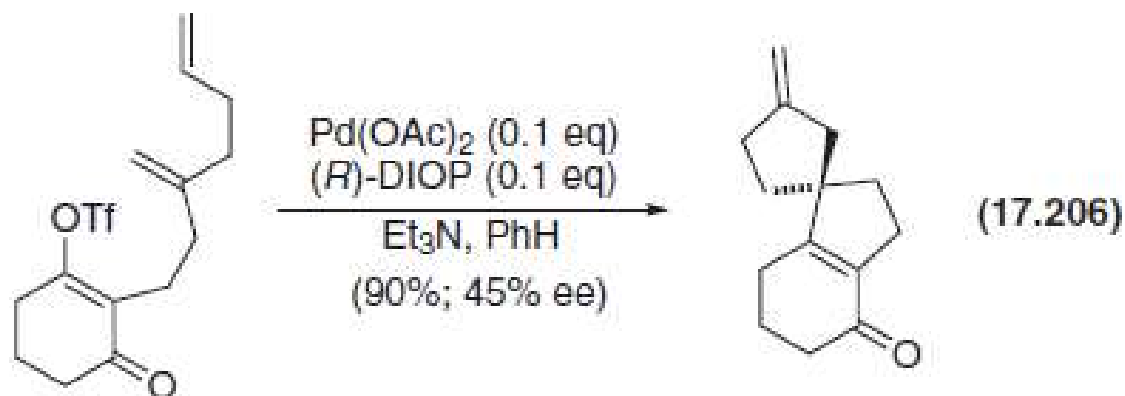
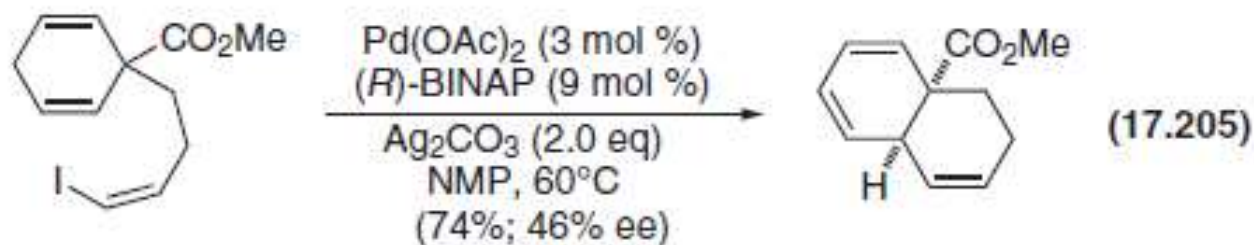


Representative Heck reactions

- Intramolecular Heck reactions are especially useful for ring closures
- The reaction has been extended to allow an aldehyde to be used as the alkene partner



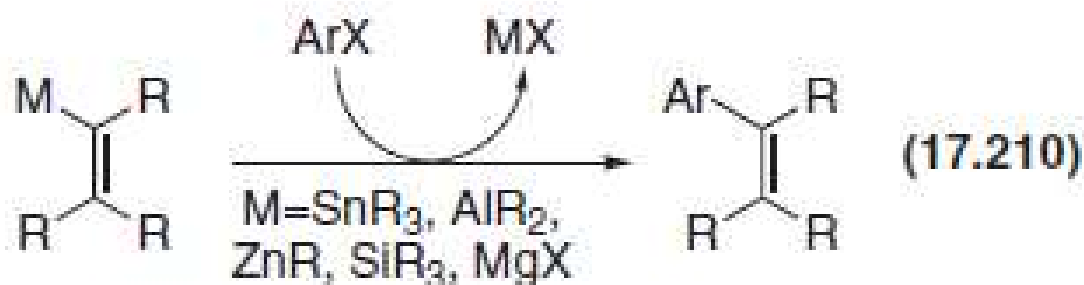
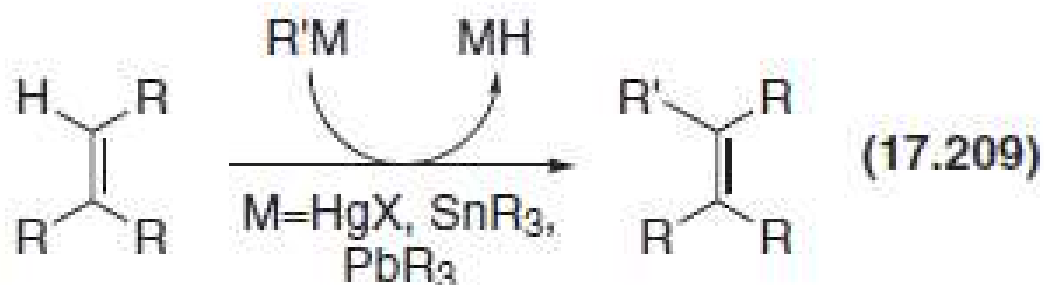
Asymmetric Heck reactions



- Using a chiral diphosphine ligand with the palladium allows reaction to be carried out with a modest level of enantioselectivity

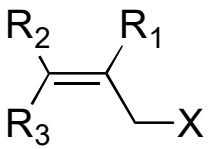
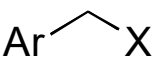
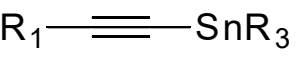
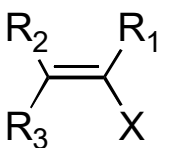
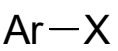
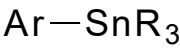
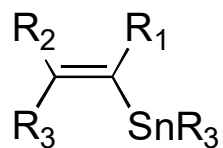
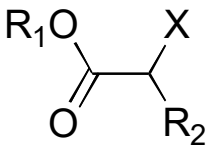
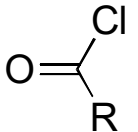
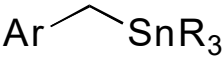
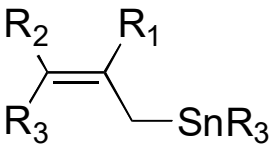
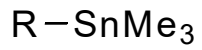
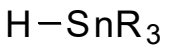
Heck reaction and its successors

- Early Heck reaction used an alkene and an organometallic reagent based on mercury, tin or lead
- Modern successors to the Heck reaction now use alkyl or aryl halides and organometallic reagents based on tin, zinc, aluminum, magnesium or silicon



Stille coupling

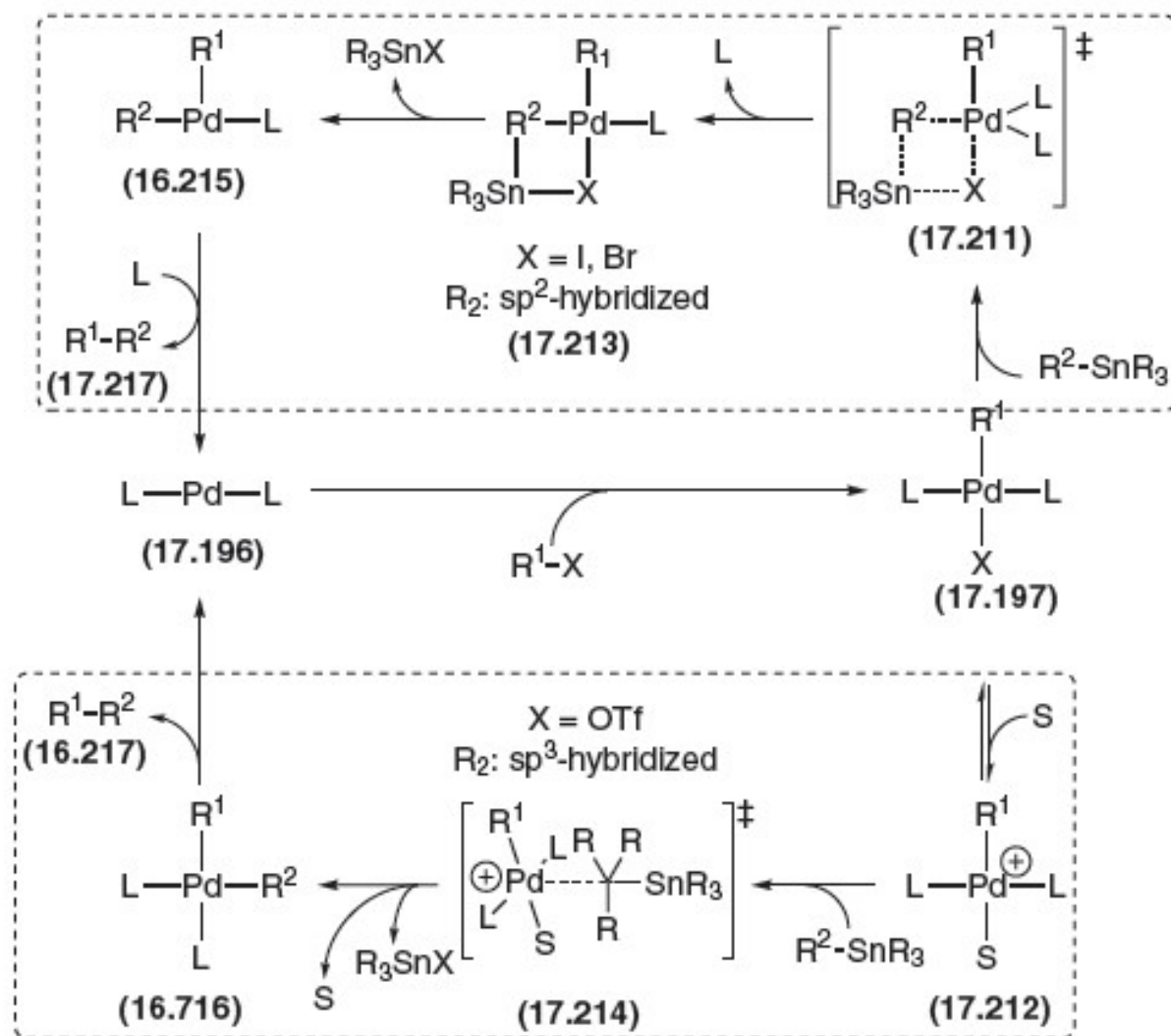
Table 17.6 Substrates for the Stille coupling reaction

Electrophile	Electrophile	Stannane	Stannane
			
			
			
			

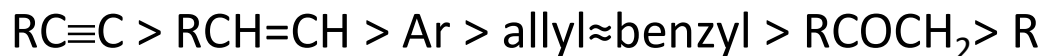
X = Br, I, OTf, Cl; Ar=aromatic residue

Figure 17.28

- The catalytic cycle of the Stille coupling; S represents a molecule of solvent



Relative rates of transmetalation step:



Representative Stille couplings

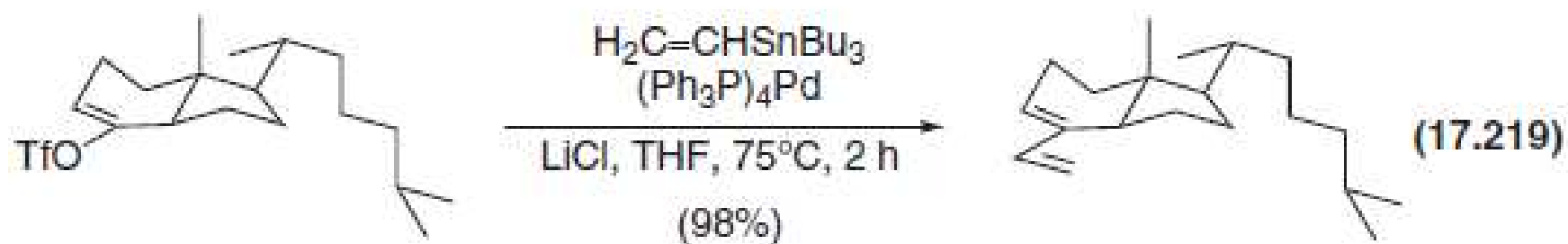
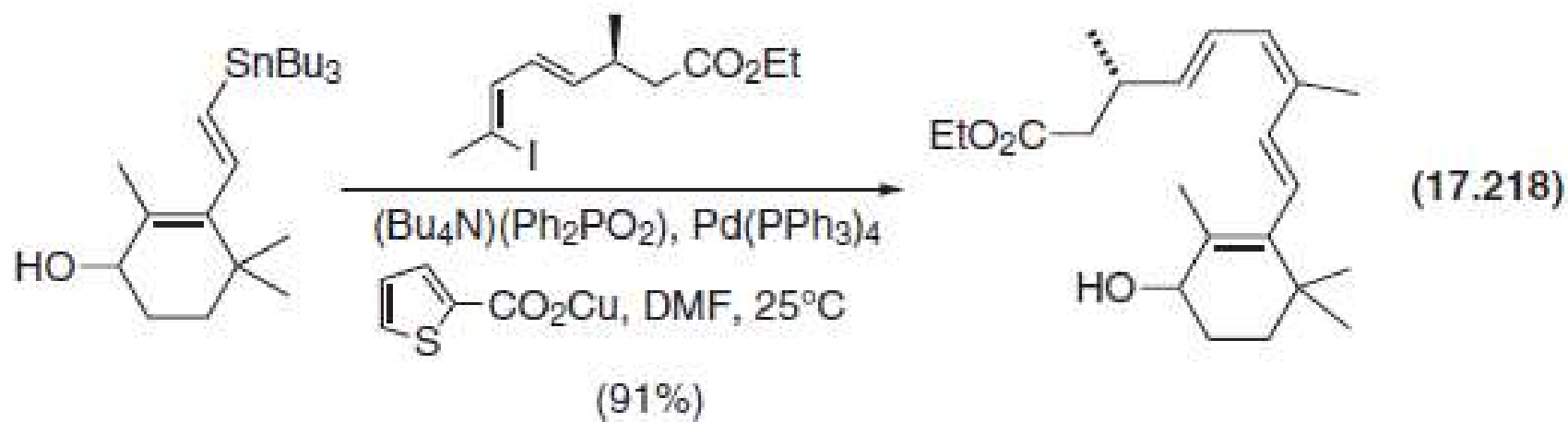
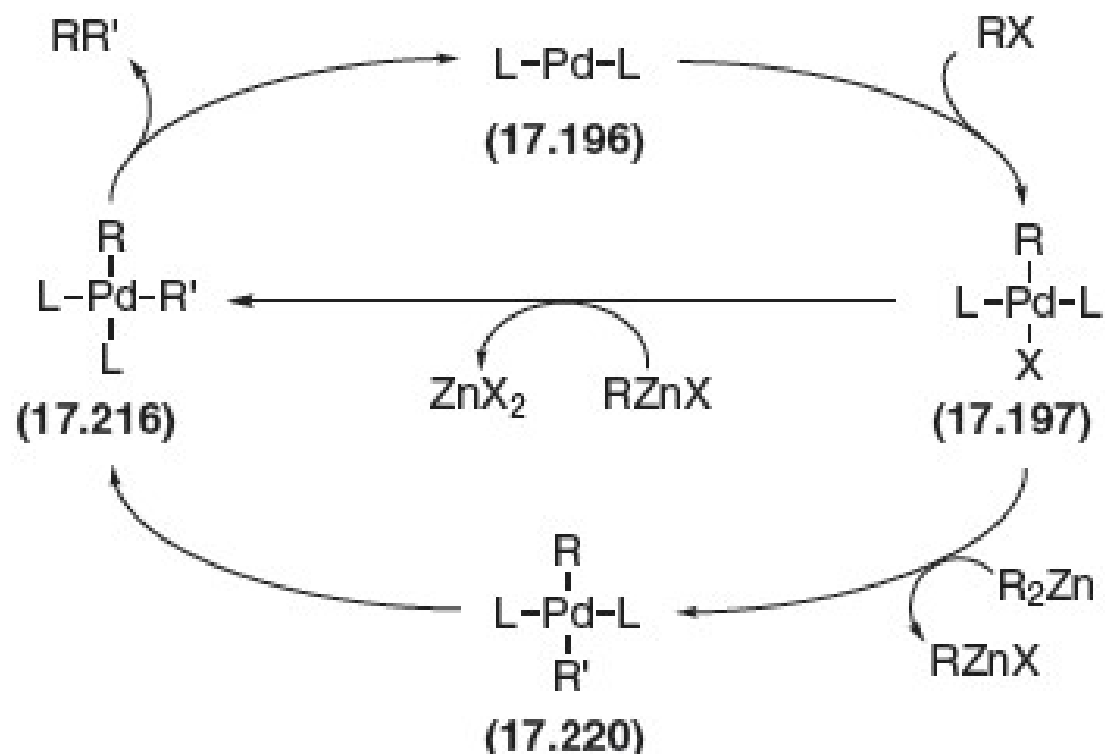
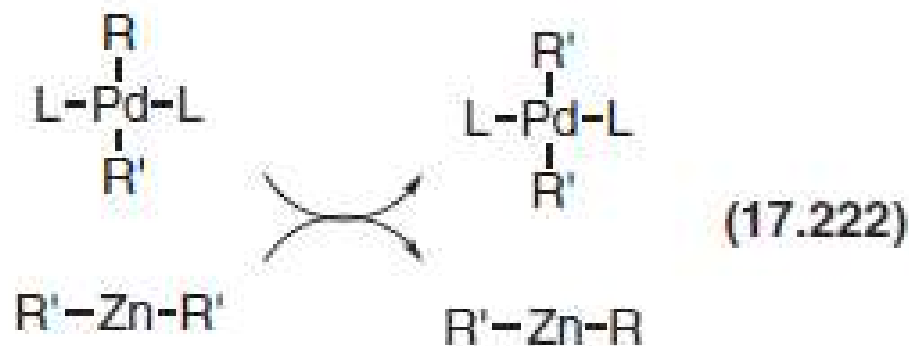


Figure 17.29

- The catalytic cycle of the Negishi cross-coupling

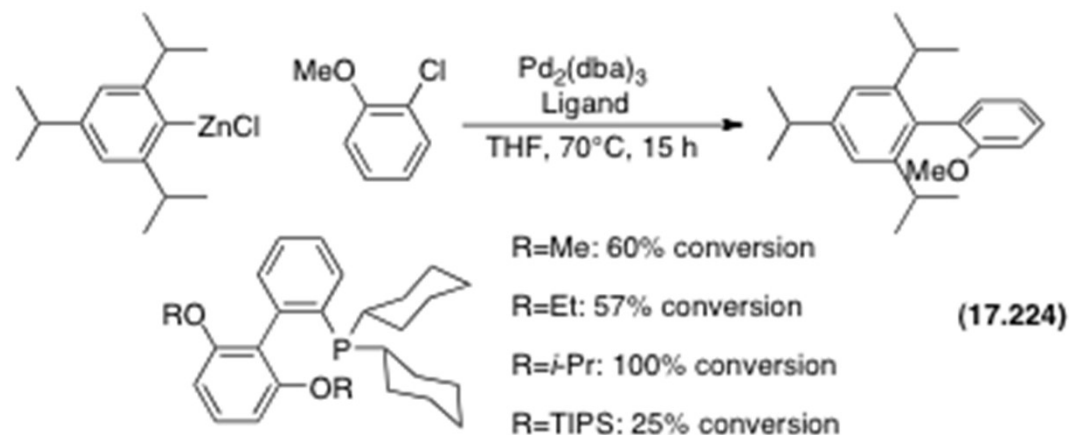


Homocoupling in the Negishi reaction



- If the reductive elimination step is slow, the first transmetallation is followed by a second, so the product of the reductive elimination is the homocoupled dimer

Figure 17.30



- Effects of group size in the catalyst on the two key stages of the Negishi coupling in reaction **17.224**

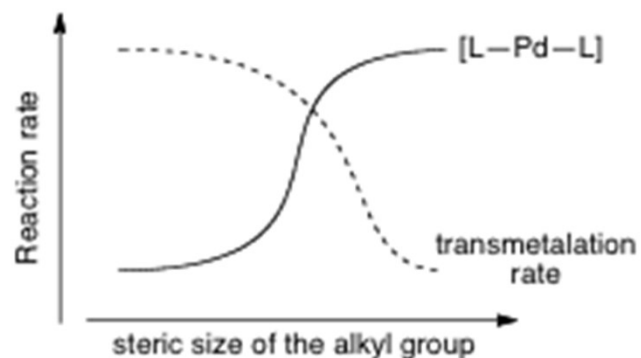
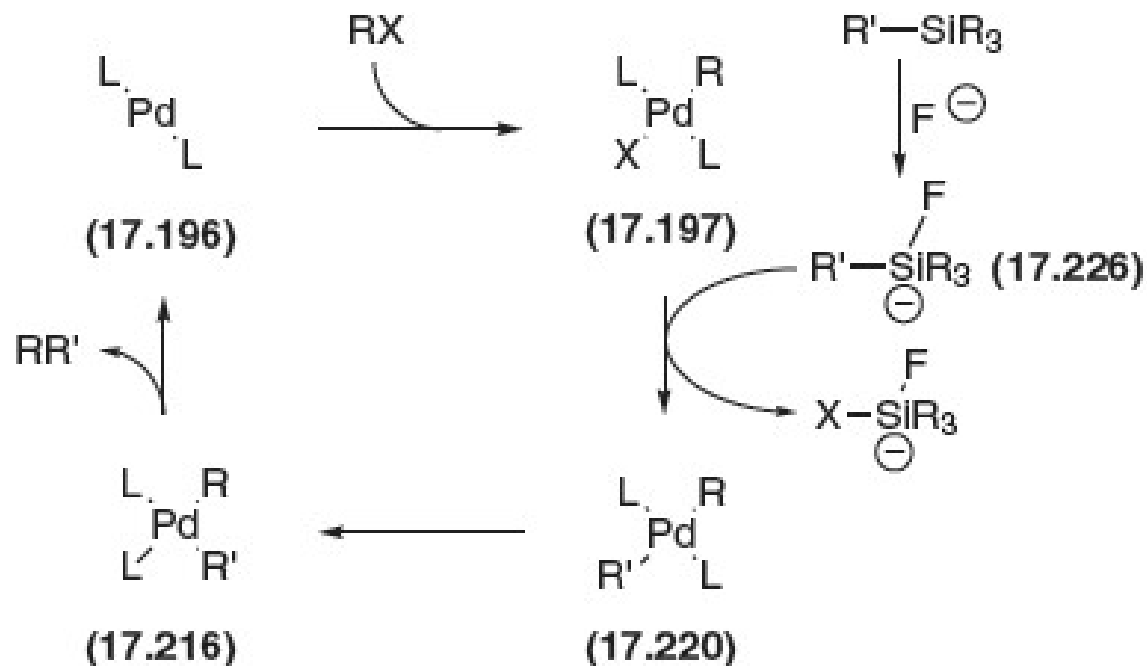
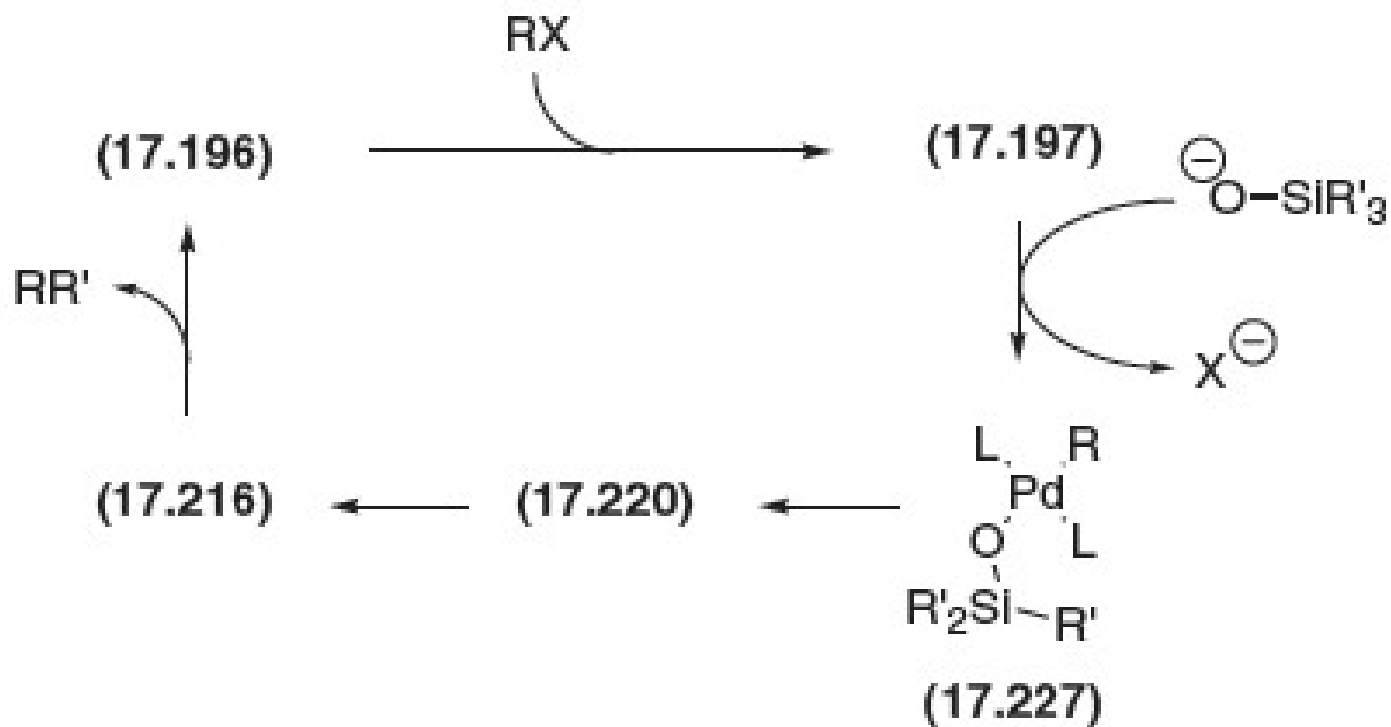


Figure 17.31



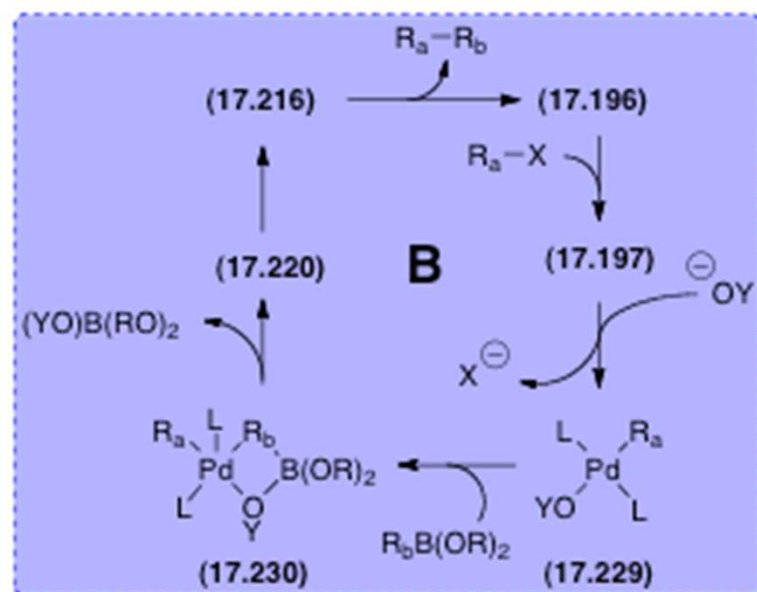
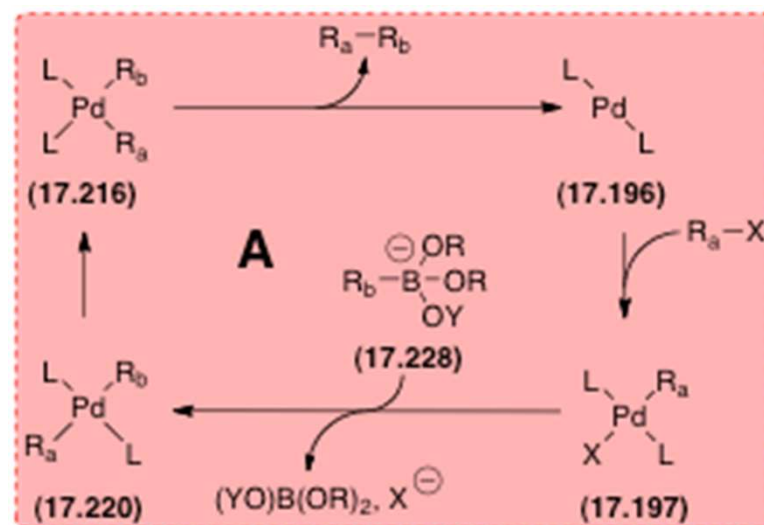
The catalytic cycle of the Hiyama cross-coupling



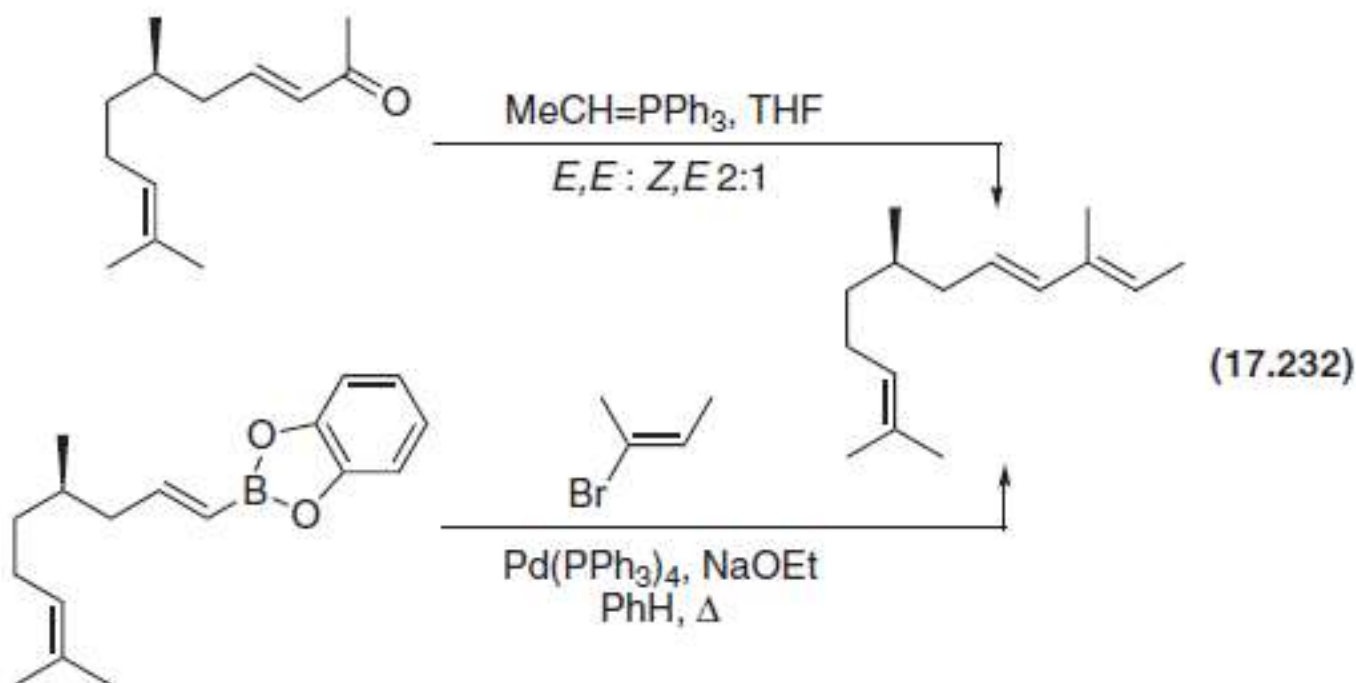
The catalytic cycle of the Hiyama-Denmark reaction

Figure 17.33

- The catalytic cycles for the Suzuki-Miyaura coupling. OY is an oxyanion base.
- The oxyanion attacks boron, to generate the borate complex **17.228** (cycle **A**)
- The oxyanion attacks the metal, to generate the complex **17.229** (cycle **B**)
- Reactivity of halides, etc.: $RI > ROTf > RBr \gg RCl$

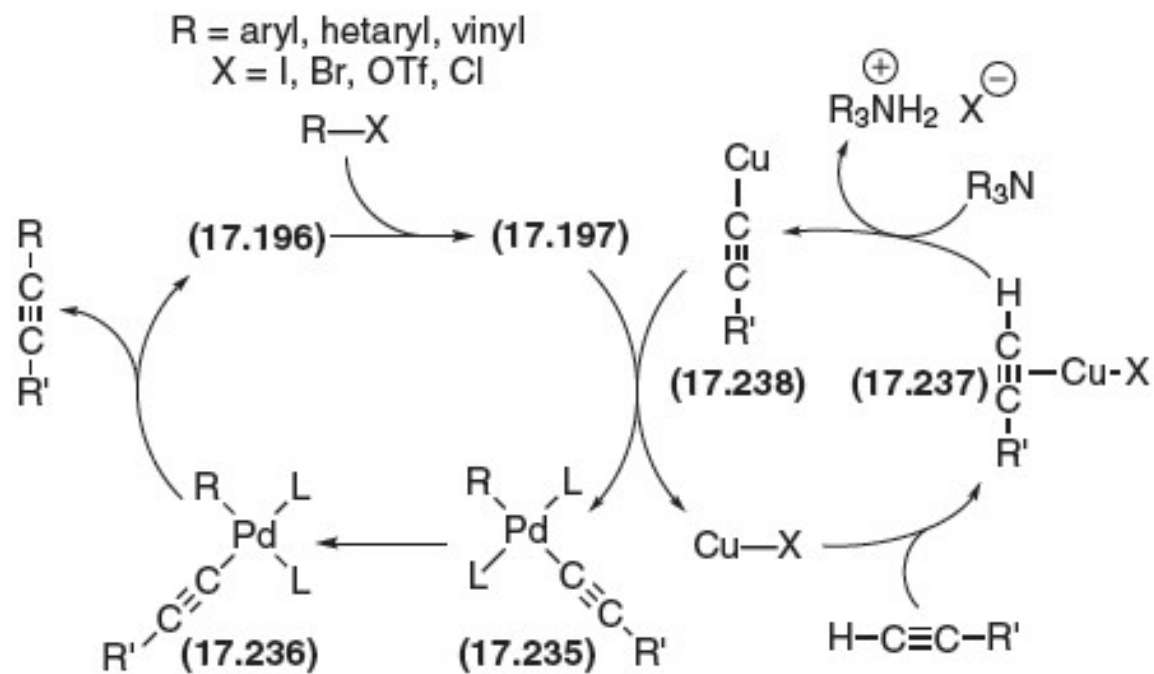


Comparing the Suzuki and Wittig reactions



- The Wittig reaction gives a mixture of geometric isomers of the alkene product
- The Suzuki cross-coupling reaction preserves the stereochemistry at both sp^2 carbon atoms of the diene product

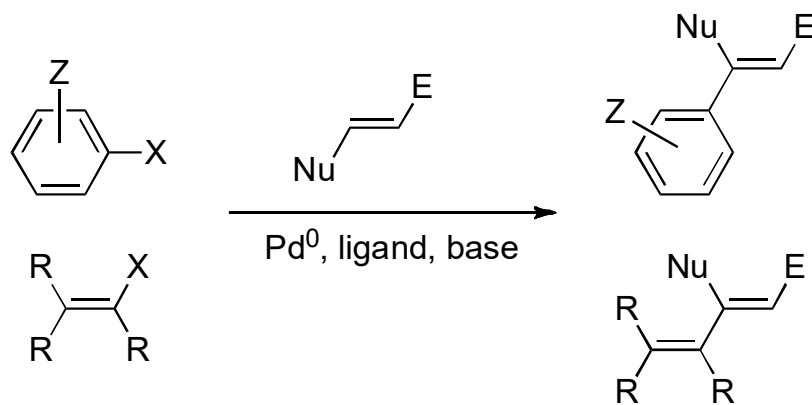
Figure 17.34



- The catalytic cycle of the Sonogashira cross-coupling reaction
 - the reaction involves two linked cycles
 - one based on palladium
 - one based on copper

Reaction synopsis: Heck reaction

Heck reaction



E = COR, CO₂R, SOR, SO₂R, CN, Ar, etc.

Nu = OR, OCOR, NR₂, N(R)COR, etc.

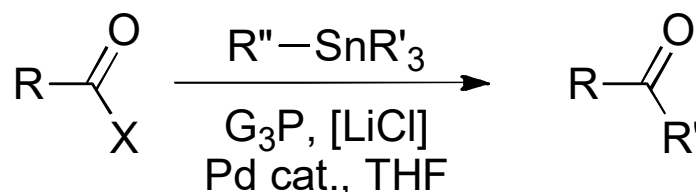
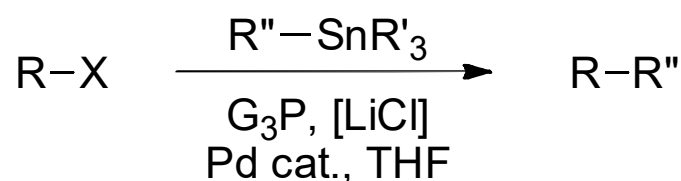
Reagents: Pd(PPh₃)₄, Cs₂CO₃, DMF, 100 °C;
Pd(OAc)₂, dppp, NEt₃, Me₂SO, 115 °C; etc.

Regiochemistry: reaction occurs β to electron-withdrawing substituents, and α to electron-releasing substituents; reaction is much more favorable with electron-deficient alkenes.

Stereochemistry: reaction exhibits strong preference for *trans* product.

Reaction synopsis: Stille reaction

Stille reaction



G = aromatic or hindered alkyl

R = aryl, vinyl, alkyl, acyl

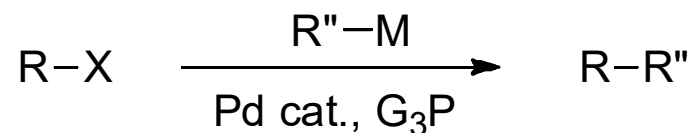
R'' = vinyl, aryl, alkyl, alkynyl

Reagents: PdCl₂, (*t*-Bu)₃P, CuI, CsF, DMF, Δ;
Pd(OAc)₂, DABCO, KF or Bu₄NF, dioxane, Δ; etc.

Migratory preference in stannane: vinyl, aryl > alkyl; this permits the use of reagents such as ArSnBu₃, RCH=CHSnBu₃.

Reaction synopsis: Negishi coupling

Negishi coupling



R: usually aryl

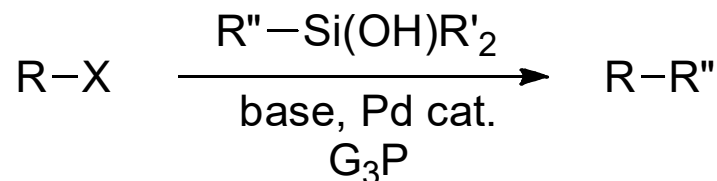
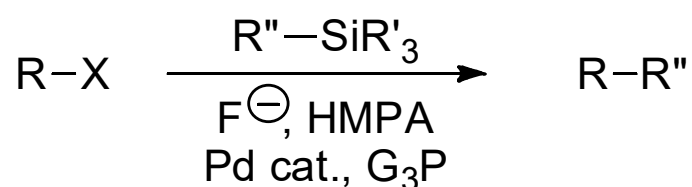
R''-M: R''₂Zn, R''ZnX, R''₃Al, R''ZrCp₂L, etc; organozinc reagents are the most widely used.

G₃P: Ph₃P, 1,1'-(diphenylphosphino)ferrocene [dppf], etc.

Reagents: RZnBr, (*t*-Bu₃P)₂Pd, dioxane;
R₂Zn, Pd₂dba₃, dioxane;
R₂Zn, (dppf)PdCl₂, THF; etc.

Reaction synopses: Hiyama and Hiyama-Denmark couplings

Hiyama and Hiyama-Denmark couplings



R'₃Si: SiMe₃, Si(OR')₃, Me_{3-n}SiF_n, etc.

Pd cat.: PdCl₂, Pd(OAc)₂, Pd₂dba₃, [C₃H₅PdCl]₂, etc.

Reagents: Hiyama coupling

R''Si(OMe)₃, PdBr₂, (*t*-Bu)₂PMe, Bu₄N⁺ F[⊖] (TBAF), THF;

R''Si(OMe)₃, Pd(OAc)₂, DABCO, TBAF, dioxane, Δ.; etc.

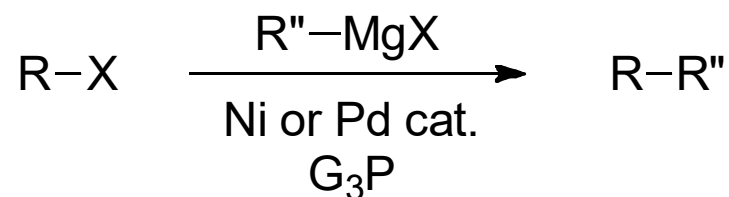
Reagents: Hiyama-Denmark coupling

R''Si(OK)Me₂, [(*t*-Bu)₃P]₂Pd, PhMe, Δ

R''Si(OG)Me₂, Me₃SiOK, Pd₂dba₃, dioxane; etc.

Reaction synopsis: Kumada coupling

Kumada coupling



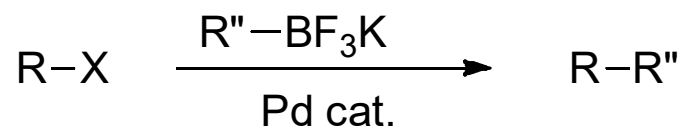
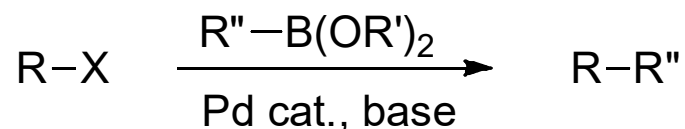
Ni cat: (dppb)NiCl₂; etc.

Pd cat.: (Ph₃P)₄Pd; etc.

Reagents: R''MgBr, Ni(acac)₂, *o*-[MeCH(OH)]C₆H₄PPh₂; etc.

Reaction synopsis: Suzuki-Miyaura coupling

Suzuki-Miyaura coupling



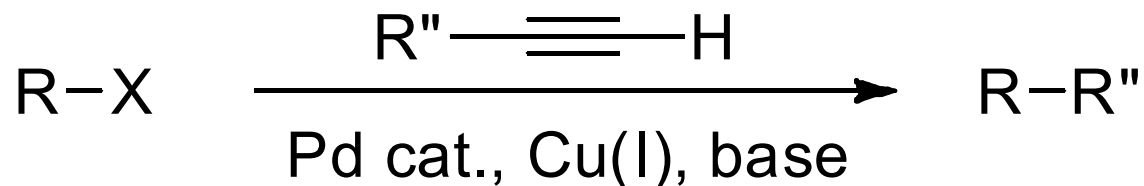
Molander modification

X: Br, I, OTf, etc.; R':H, alkyl; R'': alkyl, aryl

Reagents: $(\text{Ph}_3\text{P})_4\text{Pd}$, Na_2CO_3 , $\text{RN} \tilde{\text{N}} \text{B(OCMe}_2)_2$, $\text{C}_6\text{H}_6\text{-EtOH}$, Δ ;
 Pd(OAc)_2 , $o\text{-(2,6-MeO)}_2\text{C}_6\text{H}_3\tilde{\text{N}} \text{C}_6\text{H}_4\text{PCy}_2$, K_3PO_4 , THF;
etc.

Reaction synopsis: Sonogashira coupling

Sonogashira coupling



X: Cl, Br, I, OTf.

Reagents: $(\text{Ph}_3\text{P})_4\text{Pd}$, CuI , $n\text{-PrNH}_2$, PhH ;
 $(\text{Ph}_3\text{P})_2\text{PdCl}_2$, CuI , Et_3N (solvent); etc.