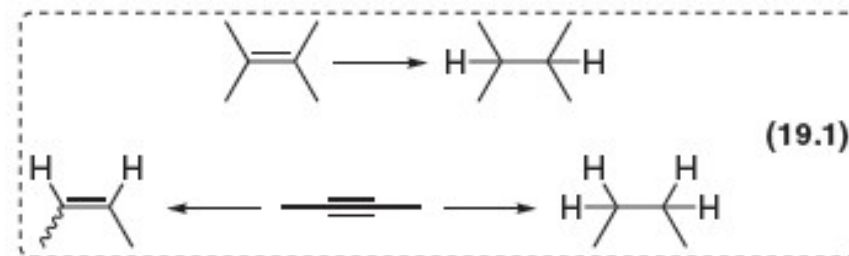
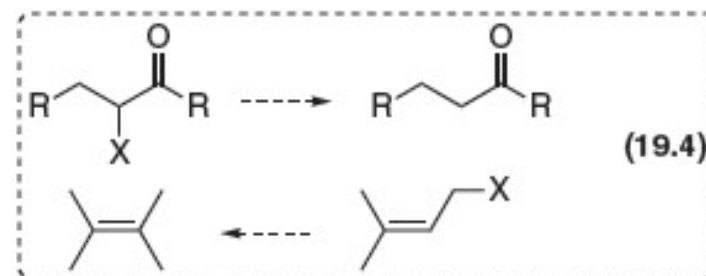
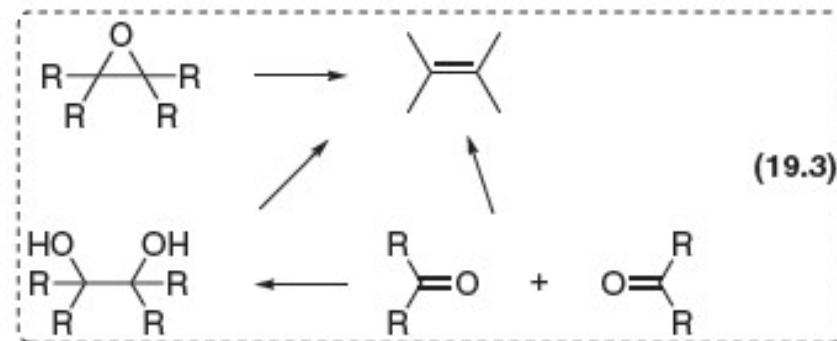
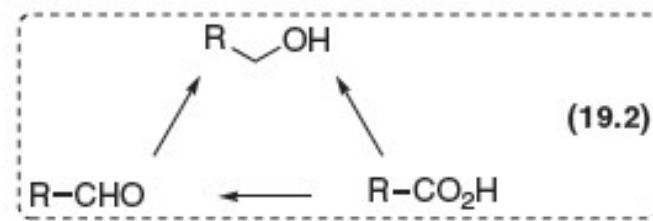


Chapter 19

Figure 19.1

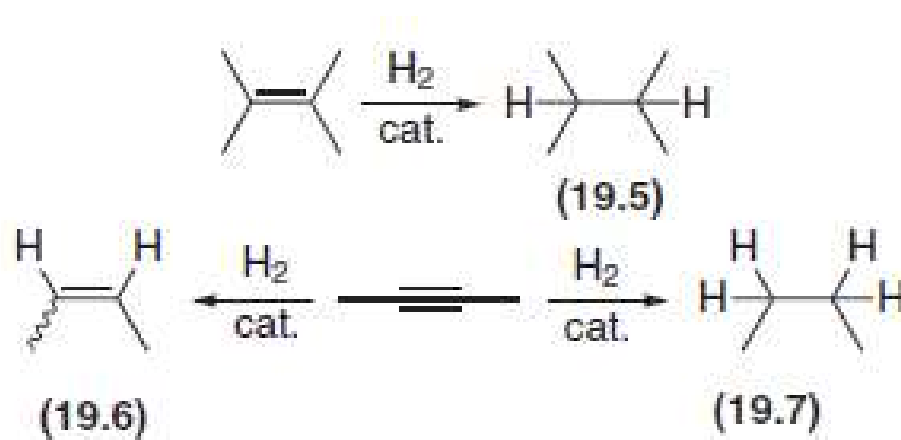


- Major classes of reduction reactions in organic chemistry



Hydrogenation and catalysts

- the most active (and widely used) catalysts are Ni, Pd and Pt, in increasing order of reactivity
- chiral ruthenium and rhodium catalysts are very useful in asymmetric hydrogenations



Fe	Co	Ni
Ru	Rh	Pd
Os	Ir	Pt

↑ catalyst activity

→ catalyst activity

Reactivity of substrates in catalytic hydrogenation

- alkynes are most reactive; carboxylic acids and amides are essentially inert
- catalyst activity can be modulated by appropriate use of catalyst poisons (e.g. diphenyl sulfide)

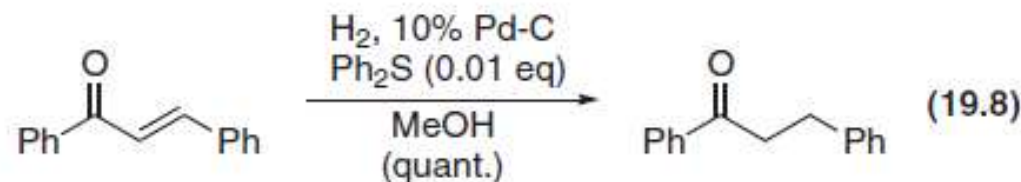
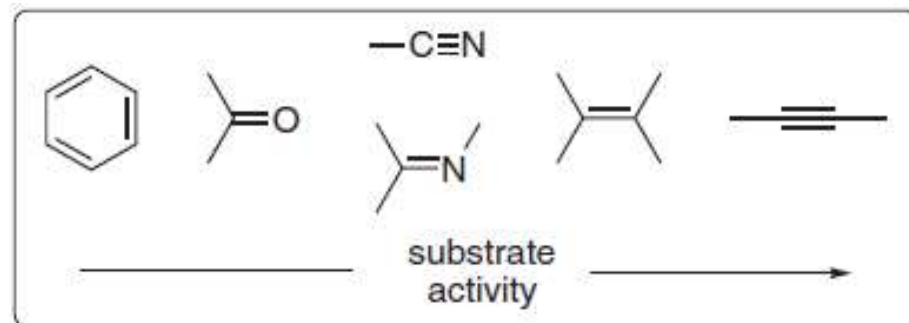
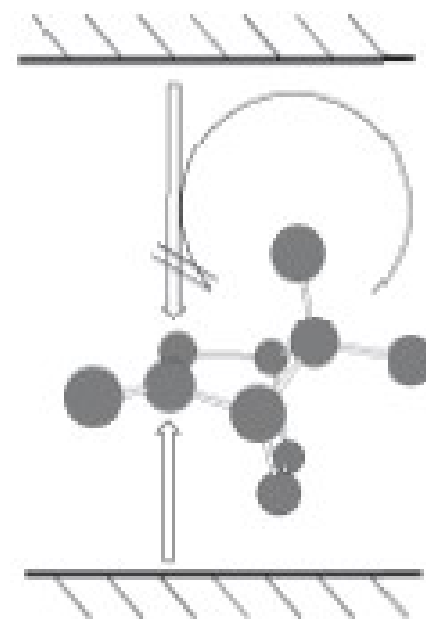
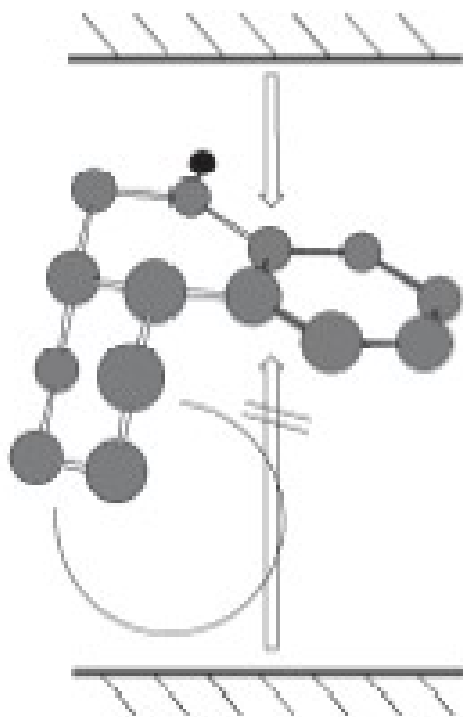


Figure 19.2

The initial step of catalytic hydrogenation is the chemisorption of the alkene on the catalyst surface. If one face of the double bond is blocked from close approach to the metal surface so efficient orbital overlap between the π bond and the metal atoms cannot occur, hydrogenation will occur from the other side.



Hydrogenation where the two faces of the π bond are not equivalent

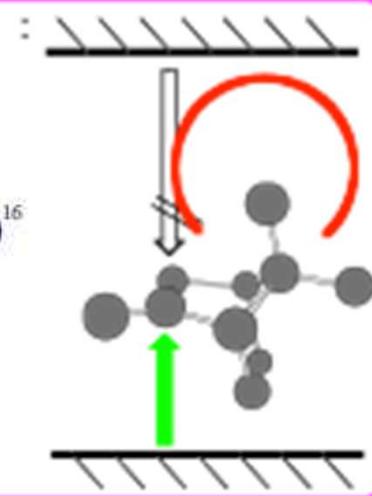
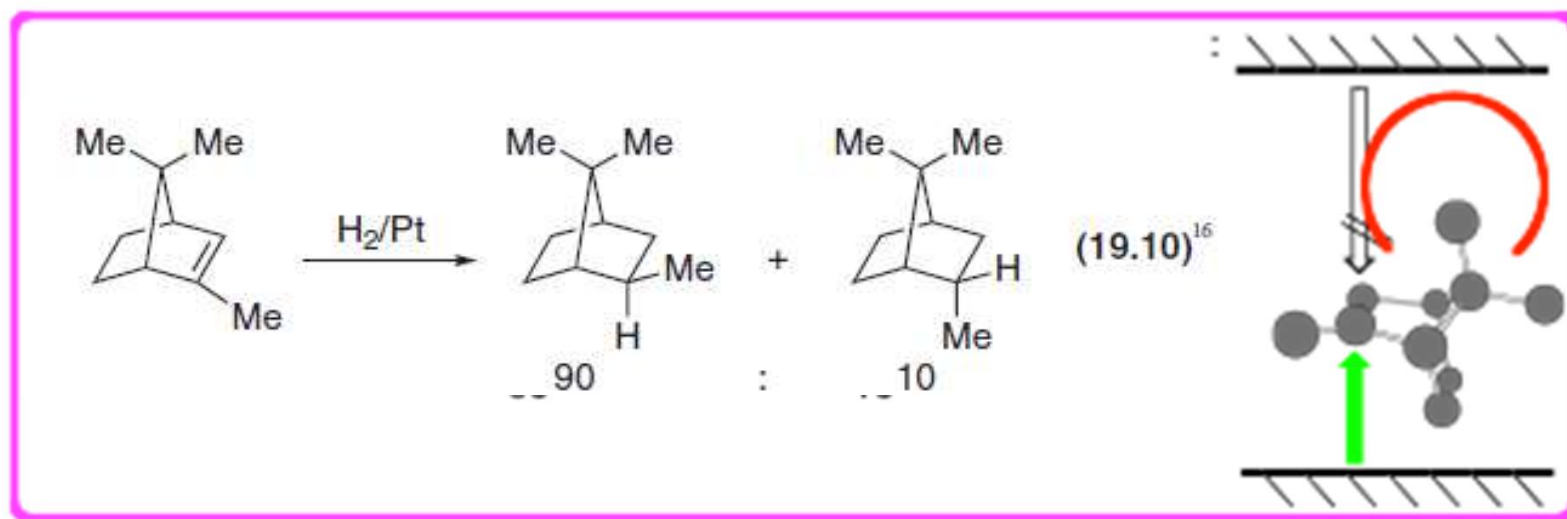
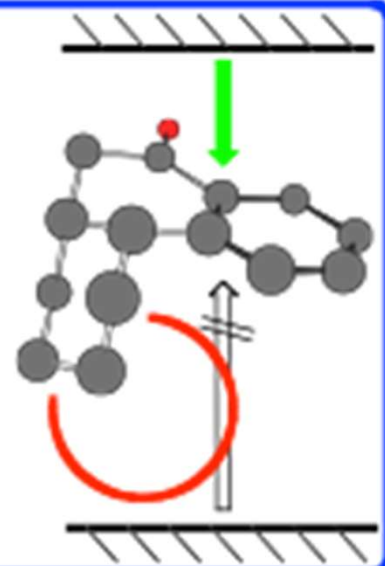
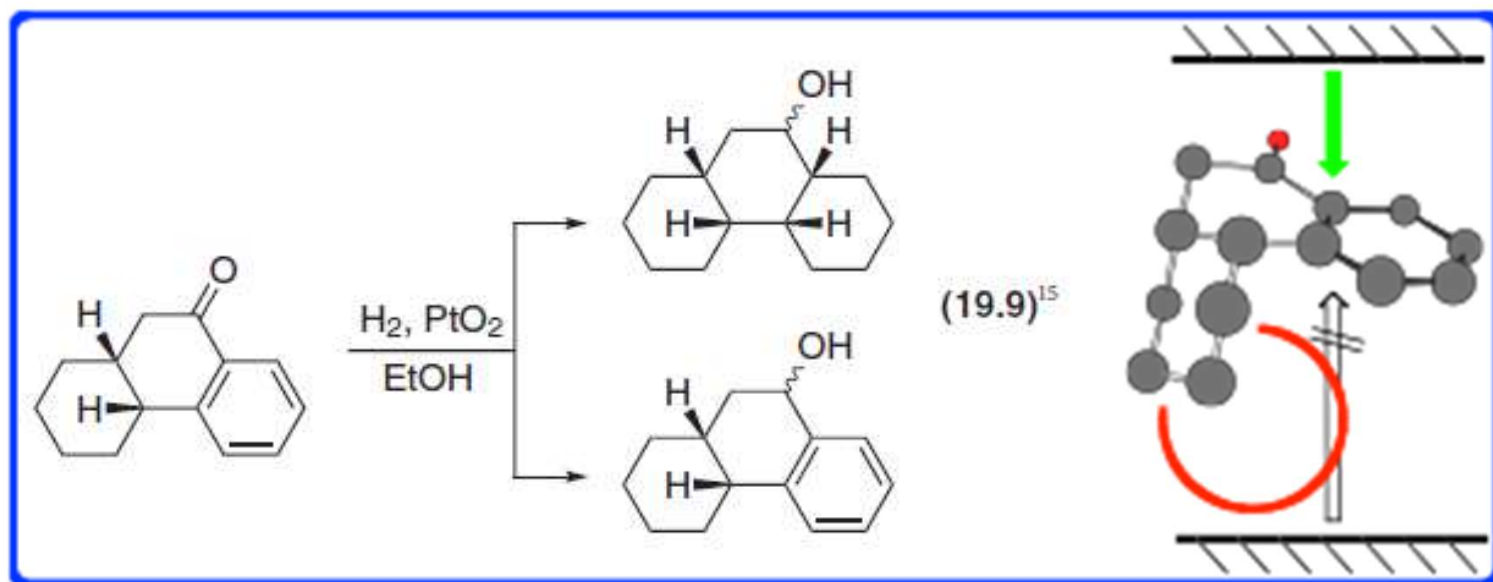


Table 19.1: Hydrogenations over Pd


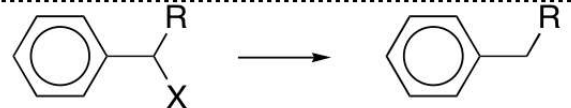
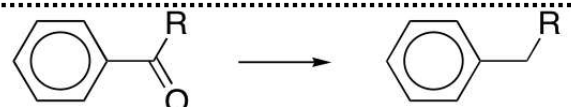
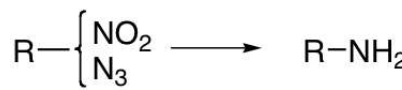

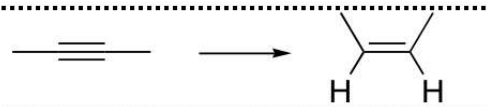
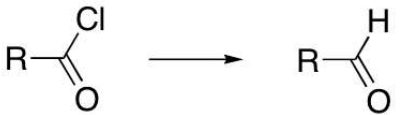
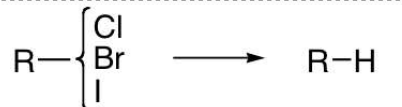

Reaction	Comments
	can cause π bond migration during reaction. To prevent this use Ni or Ru.
	
	To avoid this reaction, Rh catalysts should be used
	
	may be halted at alkene stage by limited catalyst and hydrogen
	Lindlar catalyst, or Pd/PEI
	Pd catalyst poisoned with S and/or quinoline
	
	

Table 19.1: Hydrogenations over Pt


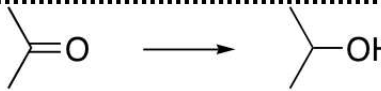


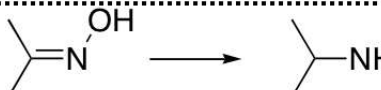
Reaction	Comments
	
	reduction of aldehydes usually requires Fe^{2+} as an accelerator
	
	
	

Table 19.1: Hydrogenations over Ni


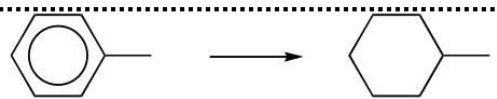
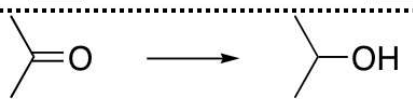


Reaction	Comments
	1 atm.; ambient temp.
	100-200 atm.; 100-200°C
	50-100°C; high pressure
	1-4 atm.; 50-100°C
	50-100°C; high pressure; NH ₃ added to minimize yield of secondary amine

Table 19.1: Hydrogenations over Rh and Ru







Catalyst	Reaction	Comments
Rh		1 atm.; ambient temp.
		5-10 atm.; 50-100°C. Does not usually lead to loss of benzyl substituents
		50-100°C; high pressure; NH ₃ added to minimize yield of secondary amine
Ru		only heterogeneous catalyst for this transformation; 300-600 atm. H ₂ required in H ₂ O
		
		

Figure 19.3: Accepted mechanism for hydrogenation

- 1) chemisorption of hydrogen on the metal surface to give metal-hydrogen bonds (**19.11**).
- 2) chemisorption of the alkene on the surface to give metal-carbon bonds by *syn* addition to the p bond (this also anchors the alkene to the metal so that the two faces of the alkene are differentiated) (**19.12**).
- 3) stereospecific replacement of the metal in one metal-carbon bond by hydrogen to give a carbon-hydrogen bond with retention of configuration at carbon (**19.13**).
- 4) stereospecific replacement of the metal in the other metal-carbon bond by hydrogen with retention of configuration at carbon (**19.14**).

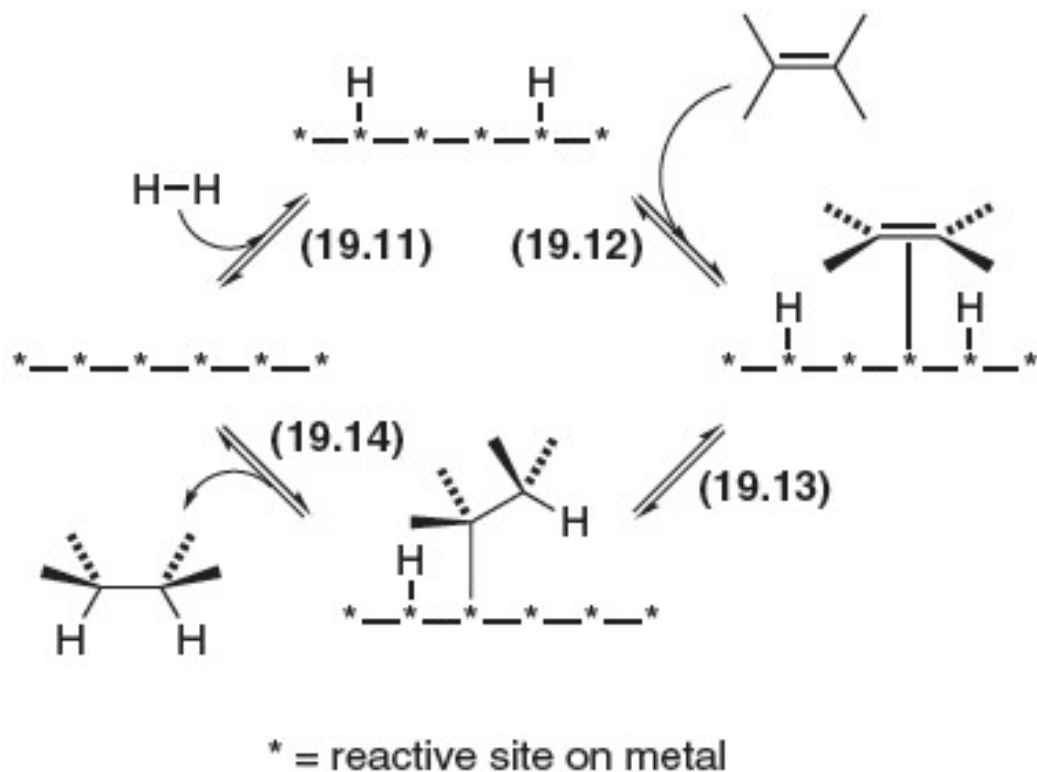
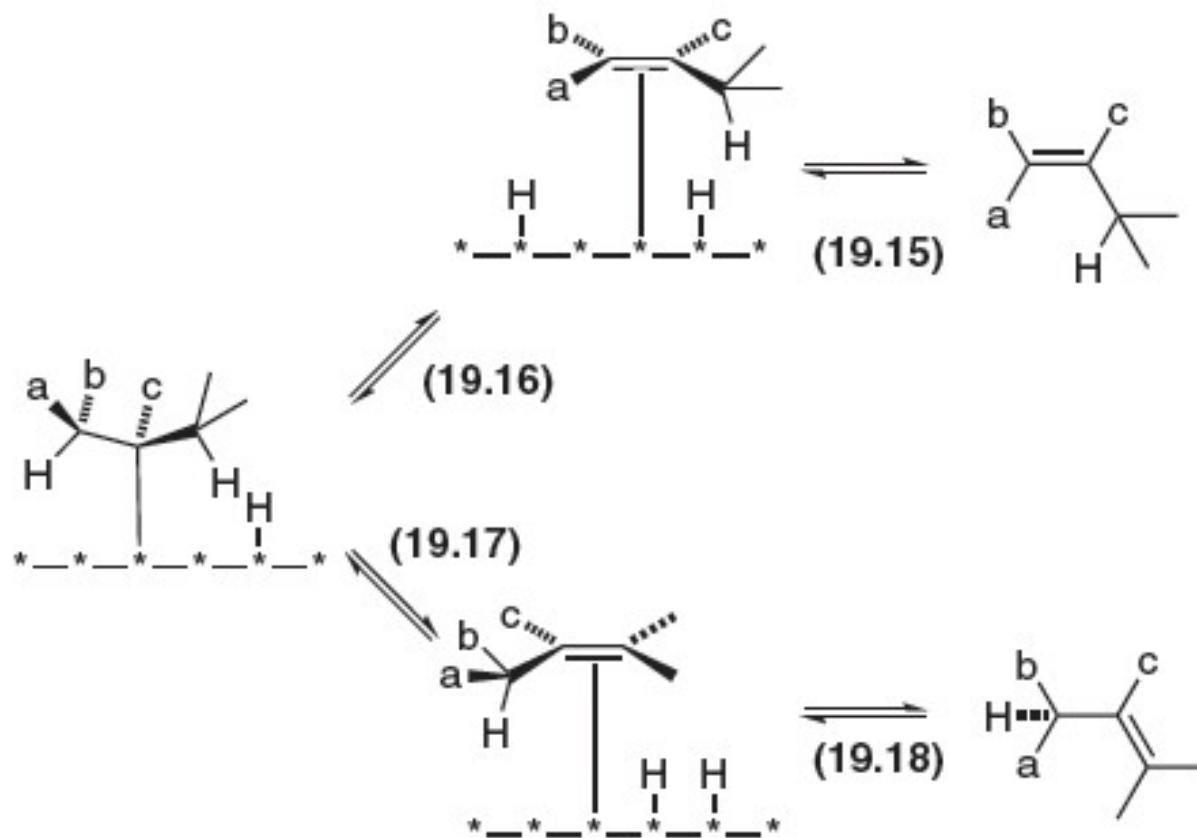
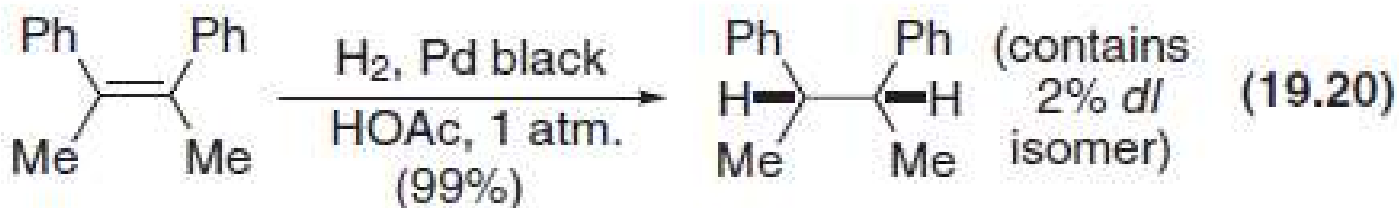
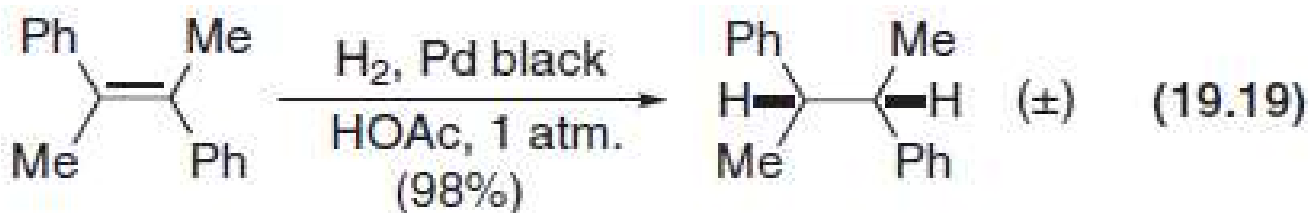


Figure 19.4



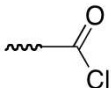
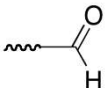
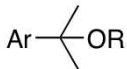
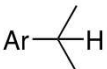
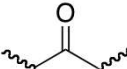
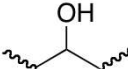

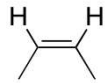
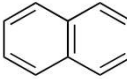
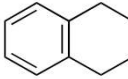
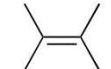

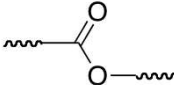
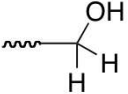
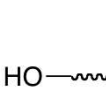
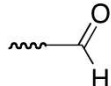
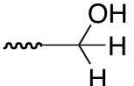
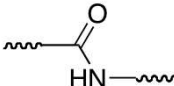
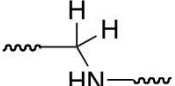
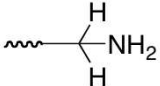


- Mechanism whereby isomerization of the π bond regiochemistry or stereochemistry may occur

Stereochemistry of hydrogenation



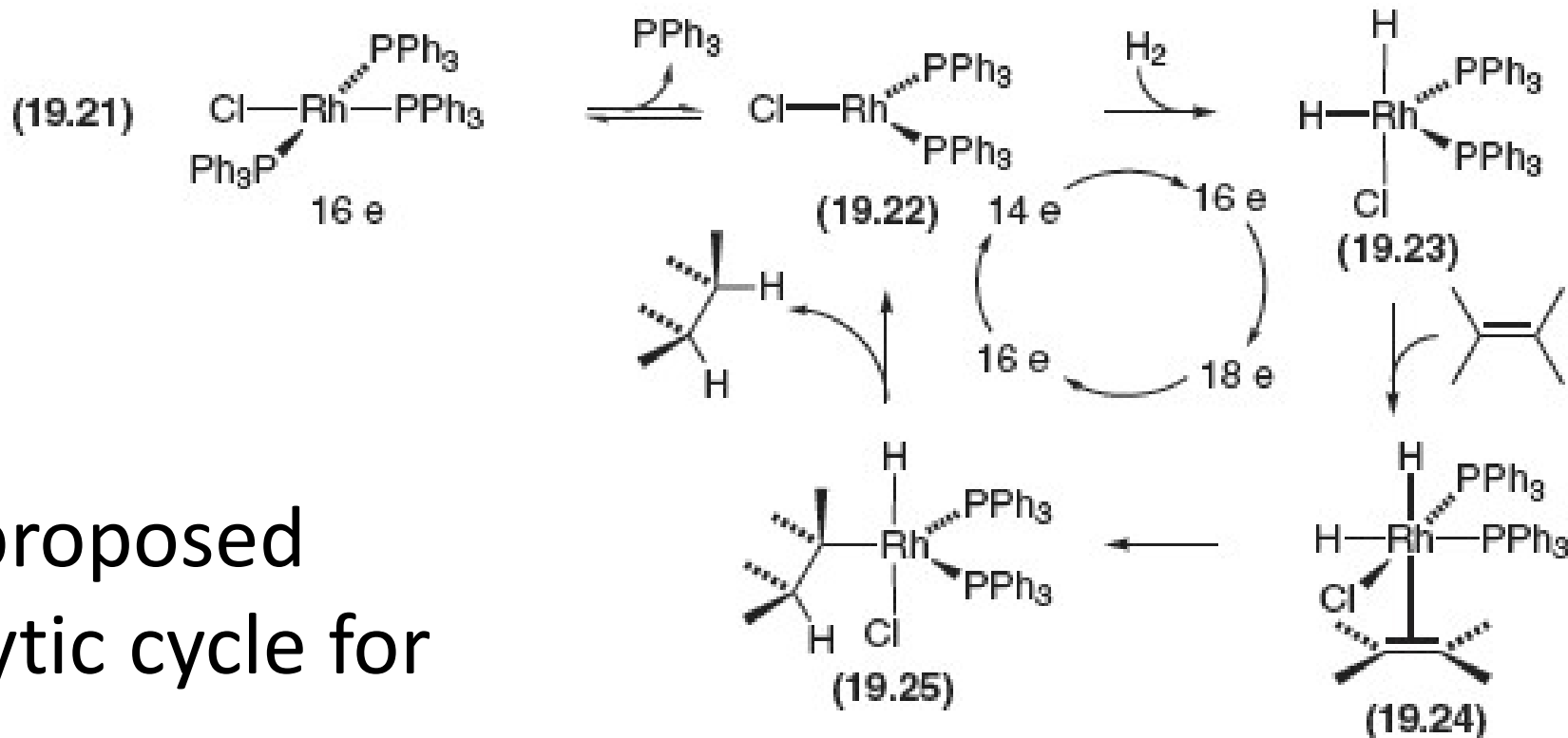
- the addition of hydrogen is either stereospecific, and suprafacial (*syn*), or highly stereoselective in favor of suprafacial addition of H₂.

Table 19.2: Relative ease of hydrogenation of functional groups

Approx. Rank	Functional Group	Reduction Product	Approx. Rank	Functional Group	Reduction Product
1			7		
2	$-\text{NO}_2$	$-\text{NH}_2$	8		
3 ^b			9		
4			10		 
5 ^c			11		
6	$-\text{C}\equiv\text{N}$		12		

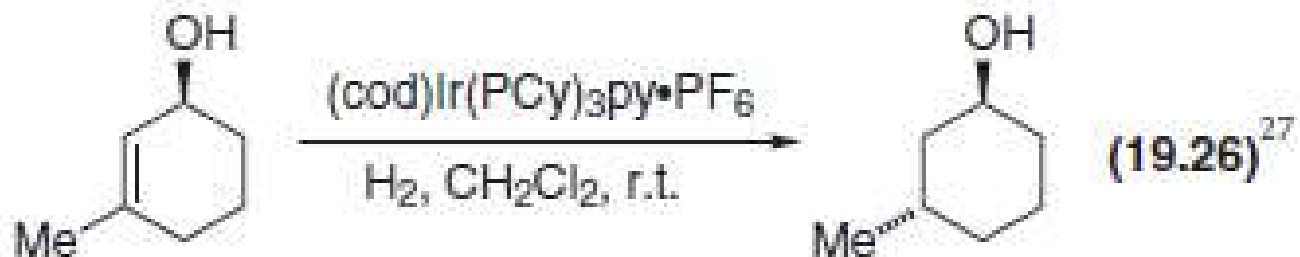
^aThe order is catalyst-dependent. Functional groups not listed (e.g. carboxylate anions) are considered resistant to hydrogenation. ^bThe high level of reactivity of alkynes is due to the much stronger chemisorption of the alkyne on the catalyst surface. ^c Fe^{2+} or Fe^{3+} is required as an accelerator with Pt. Pd often leads to decarbonylation competing with hydrogenation

Figure 19.5

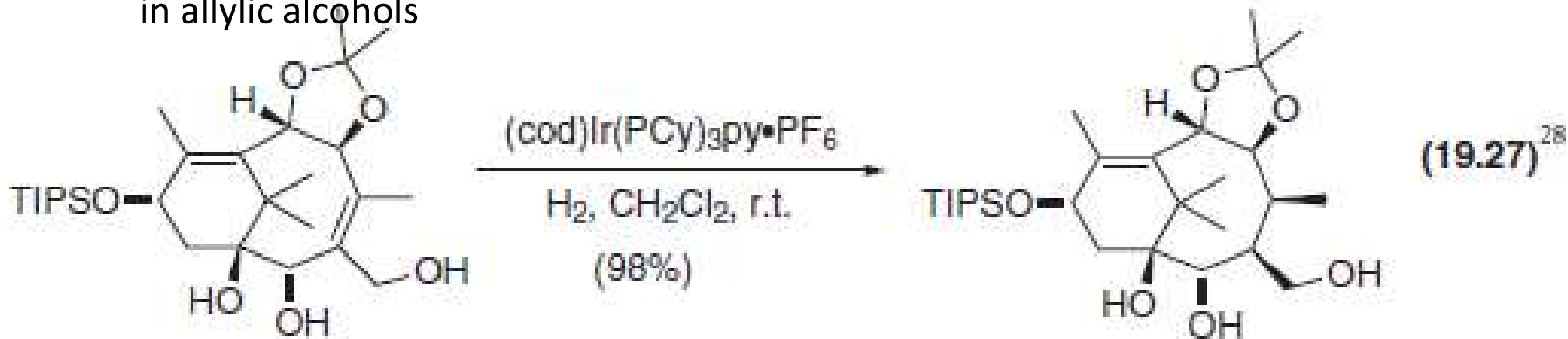


- The proposed catalytic cycle for homogeneous hydrogenation over Wilkinson's catalyst

Hydrogenations using Crabtree's catalyst



- catalyst allows the hydrogenation of double bonds to be directed by an OH group in allylic alcohols



- catalyst is highly efficient at hydrogenating tetrasubstituted double bonds

Reaction Synopses: Catalytic hydrogenation



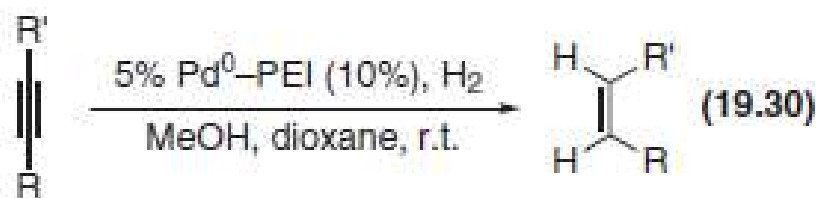
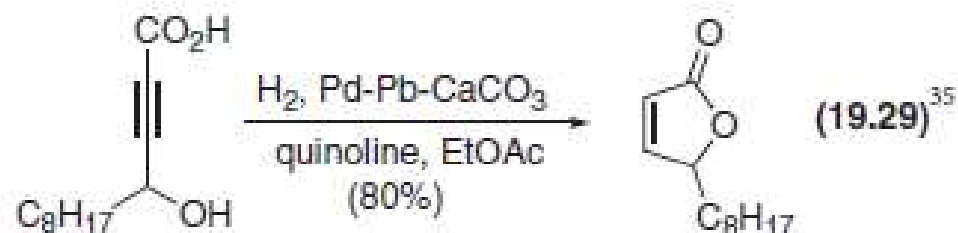
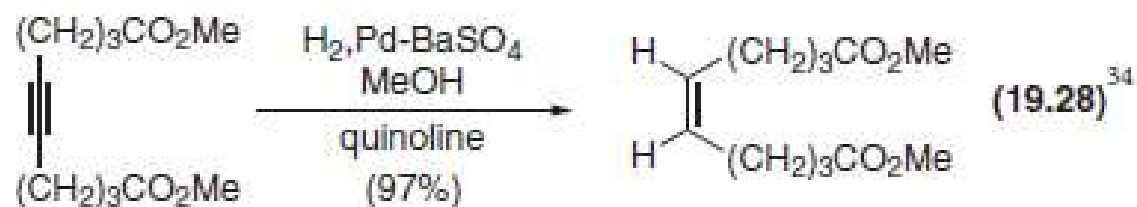
[H]: H_2 ; NH_4OCHO , HCO_2H ; cyclohexene;
 R_2CHOH ; etc.

catalyst: Ni; PtO_2 ; Pd; Os; Ru; etc; heterogeneous
catalysts may be powders or supported metals
(on C, BaSO_4 , CaCO_3 , etc)
 $(\text{Ph}_3\text{P})_3\text{RhCl}$; etc.

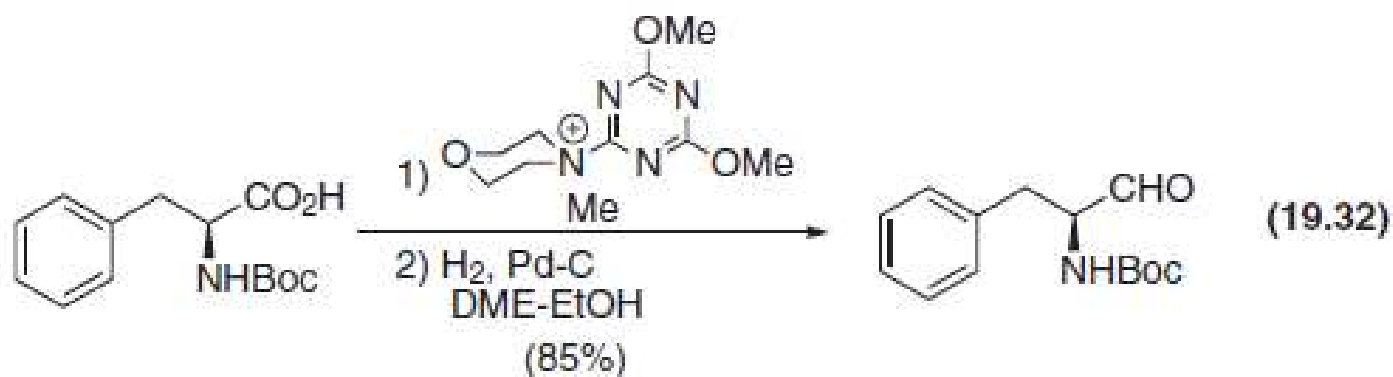
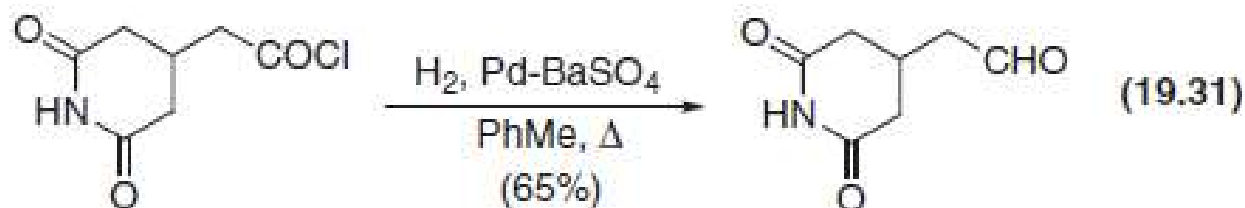
Stereochemistry: *syn* (suprafacial).

Hydrogenation of alkynes to alkenes

- a poisoned palladium catalyst is used
- the most common poisons are lead and the aromatic amine, quinoline
- a modern “green” alternative relies on poly(ethyleneimine), PEI, as the catalyst poison, and does not require lead compounds



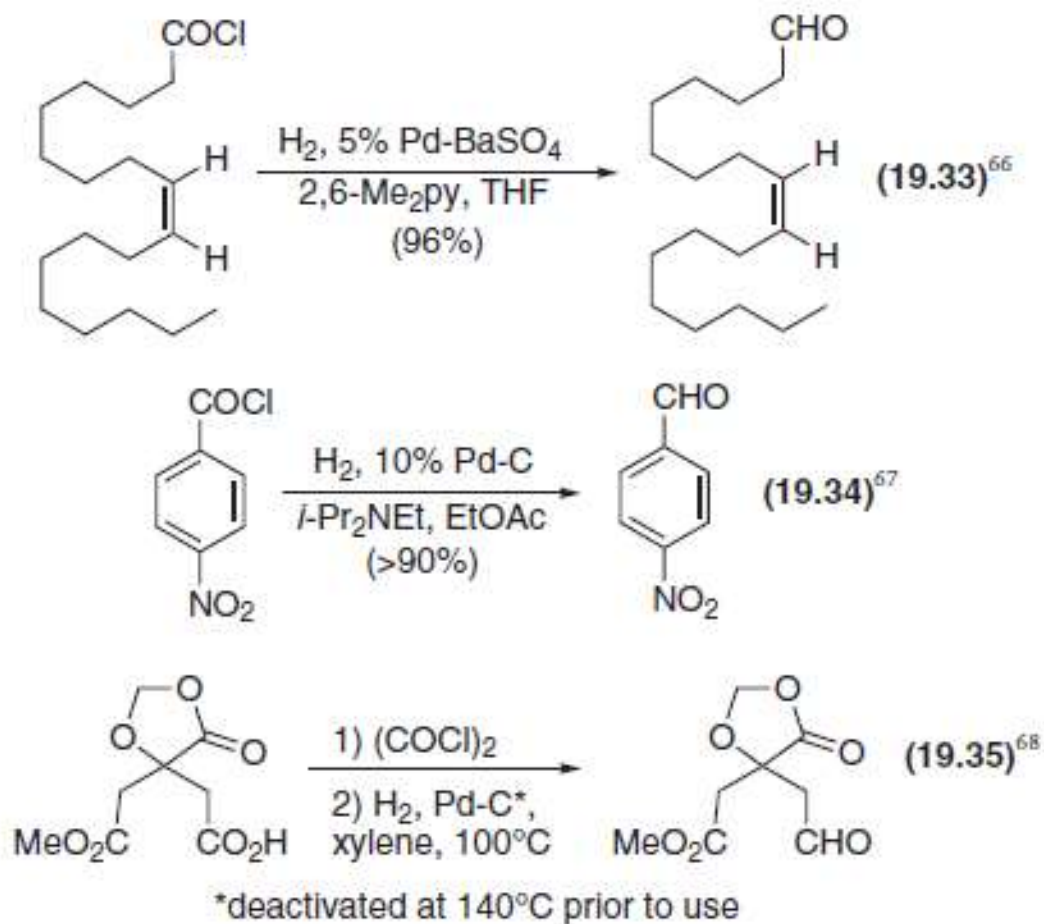
Rosenmund reduction



- the palladium catalyst is frequently modified by a sulfur compound

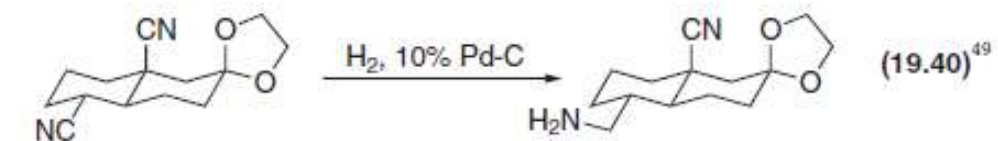
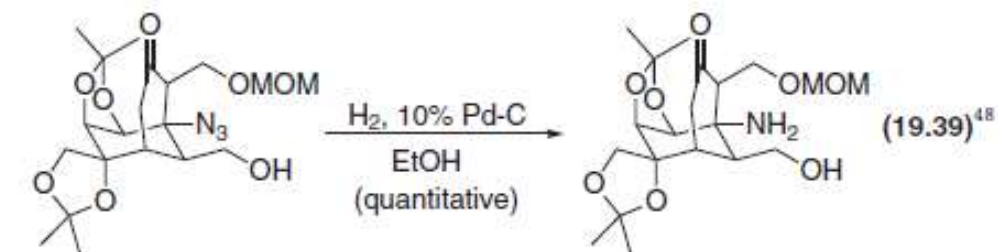
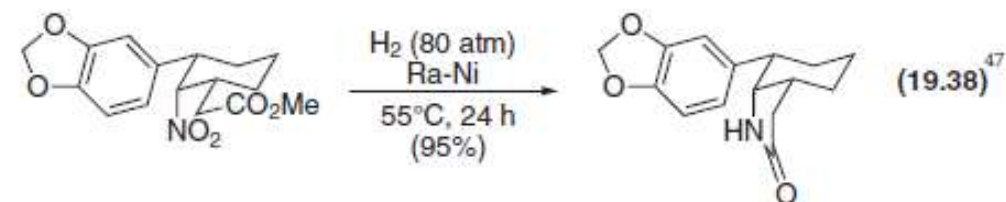
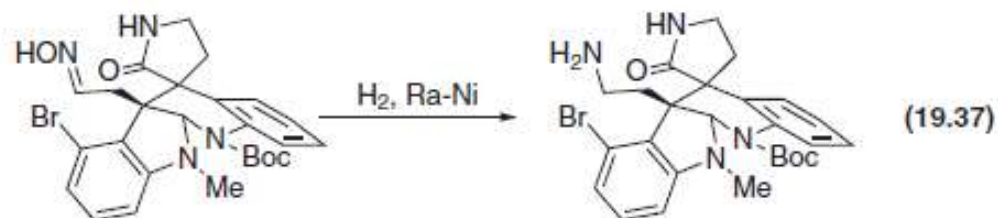
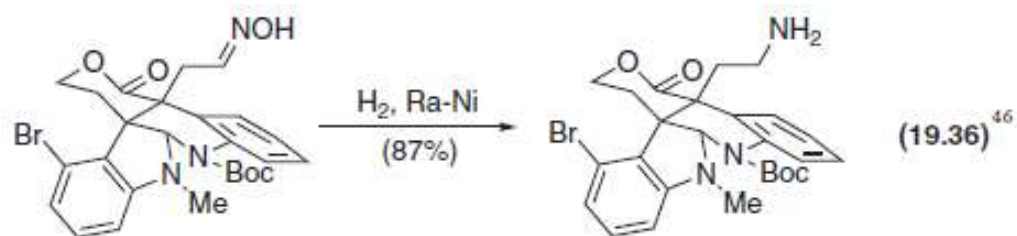
More Rosenmund reductions

- the reduction generates HCl as a by-product
- this leads to variable results
- replacement of the quinoline-sulfur poison by tertiary amines allows the HCl to be intercepted, and also allows the quinoline-sulfur to be replaced: this “greens” the reaction
- the palladium catalyst itself may also be modified by heating at 140°C prior to use



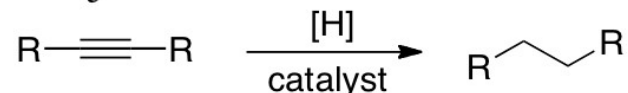
Hydrogenation to amines

- amines can be obtained by hydrogenation of
 - oximes
 - nitro groups
 - azides
 - nitriles
 - imines
- hydrogenation of nitriles is frequently complicated by the formation of primary, secondary, or tertiary amines from the nitrile, depending on the catalyst and exact reaction conditions



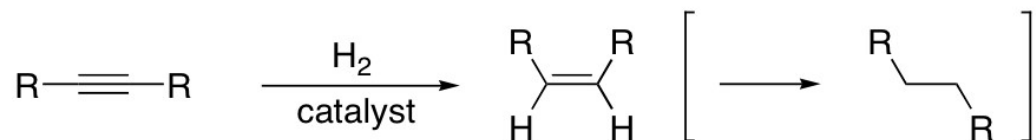
Reaction synopses: Hydrogenation of alkynes

(a) To saturated systems



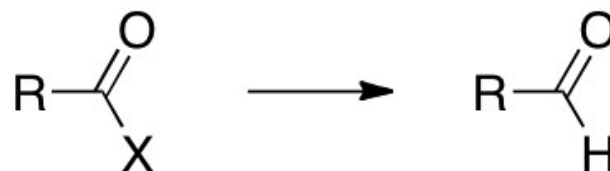
Reagents: see hydrogenation of alkenes

(b) To Z-alkenes



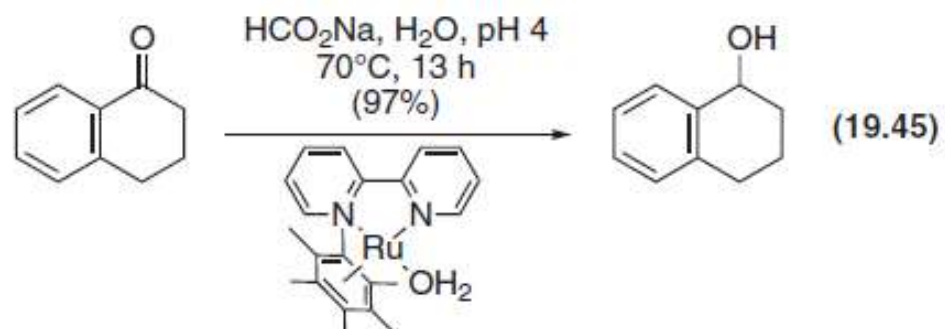
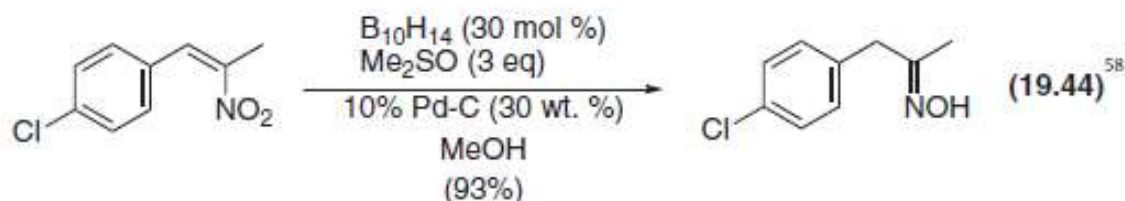
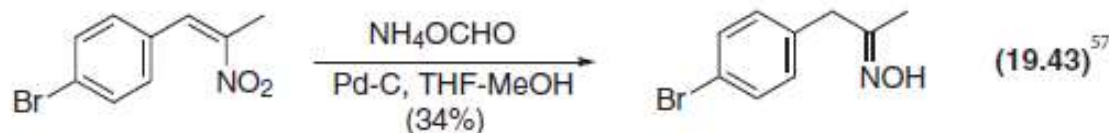
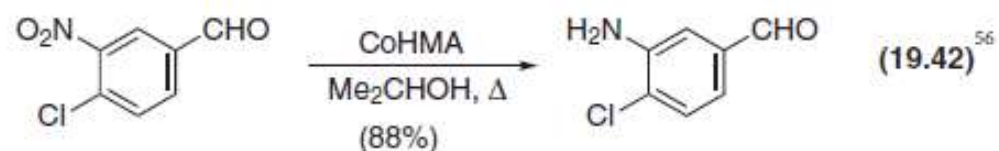
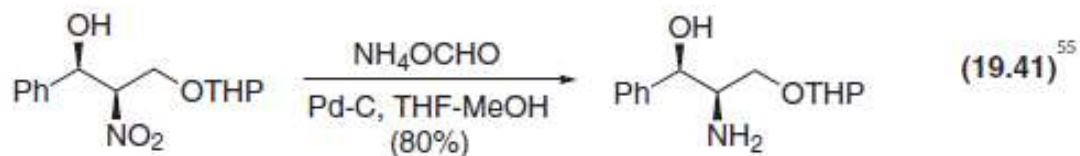
catalyst: Pd-CaCO₃, PbCO₃; Pd-CaCO₃, PbSO₄;
Pd-Al₂O₃, PbSO₄; etc.
H₂, Pd-BaSO₄, PbSO₄, quinoline (Lindlar Pd);
H₂, Pd-CaCO₃, PbSO₄, quinoline (Lindlar Pd);
Pd-PEI, MeOH/dioxane is a green alternative.

Reaction synopses: Rosenmund reduction



Reagent: $\text{X}=\text{Cl}, \text{H}_2, \text{Pd}-\text{BaSO}_4, \text{S}, \text{quinoline};$
 $\text{H}_2, \text{Pd}-\text{C}, \text{R}_3\text{N}; \text{H}_2, \text{Pd}-\text{C}^*; \text{etc.}$
 $\text{X}=\text{triazine ester}, \text{H}_2, \text{Pd}-\text{BaSO}_4; \text{etc.}$

Transfer hydrogenation



- common hydrogen donors: isopropyl alcohol, cyclohexene and cyclohexadiene, ammonium formate, formic acid, boranes
- popular in industry because it does not require gaseous hydrogen, and thus reduces a major hazard for fire or explosion

Reductive amination

an imine or enamine intermediate is involved.

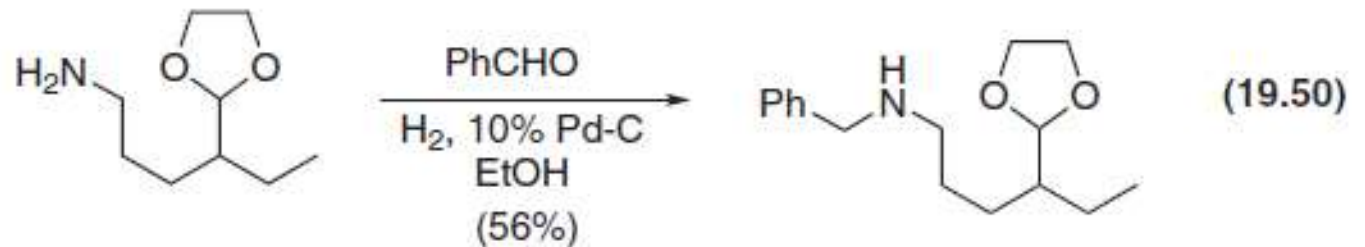
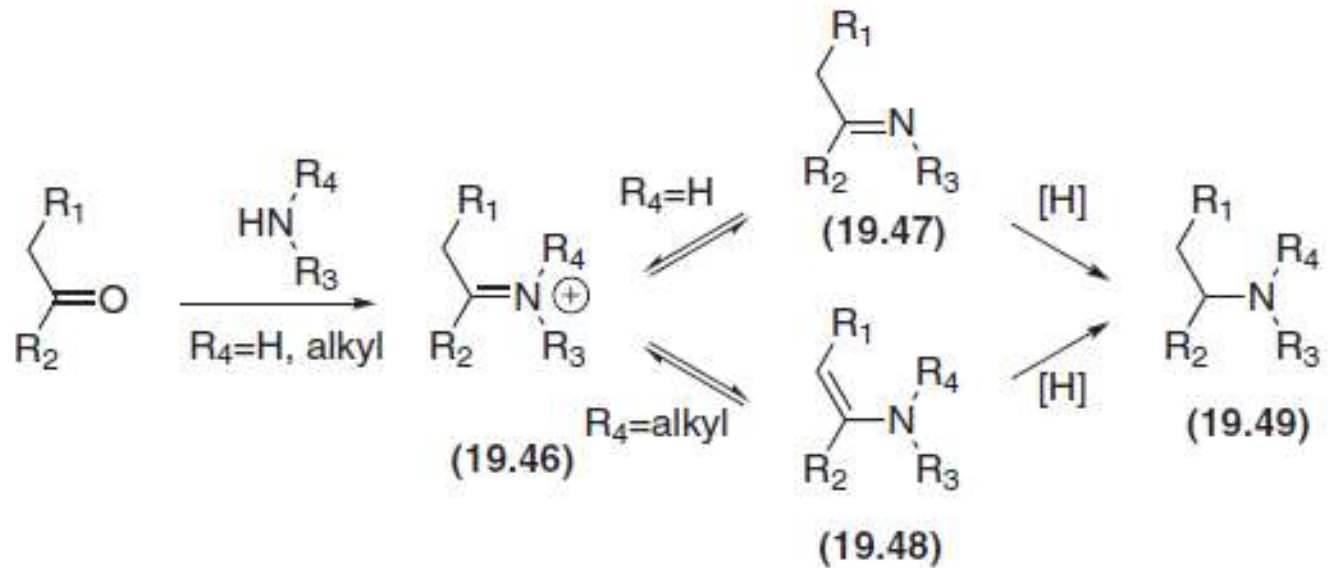
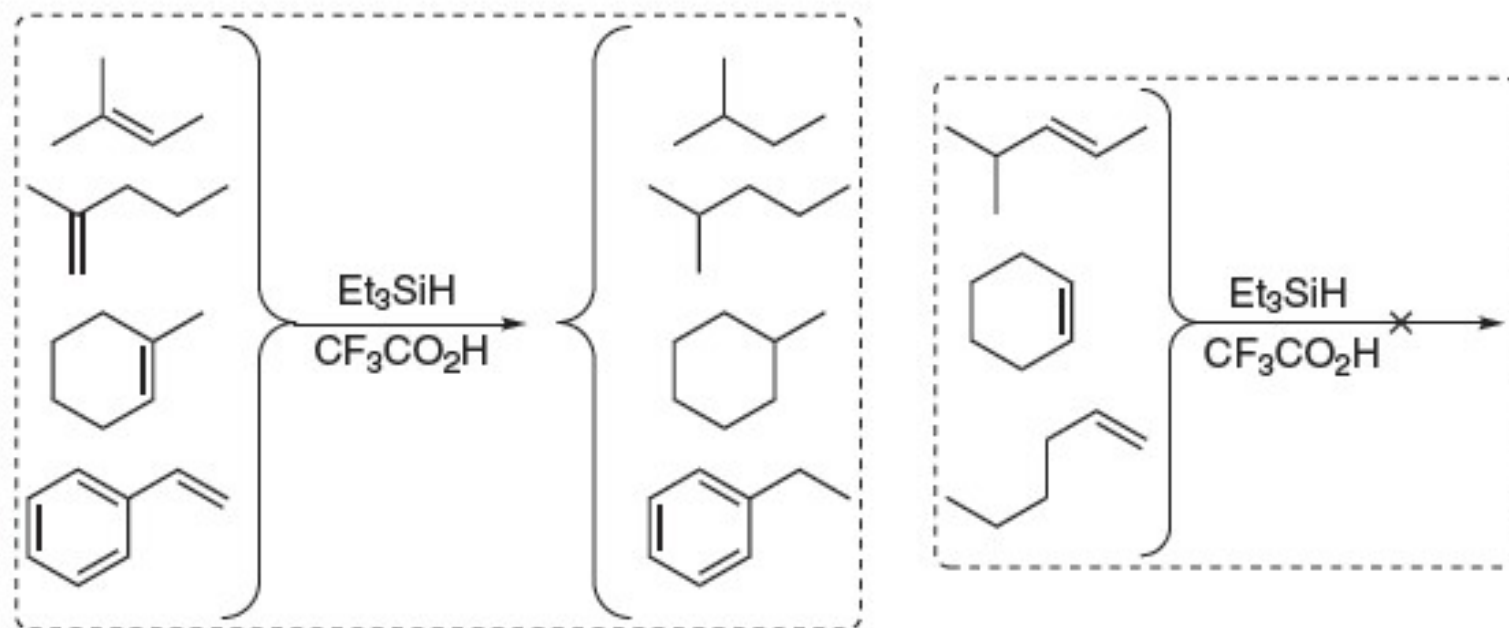


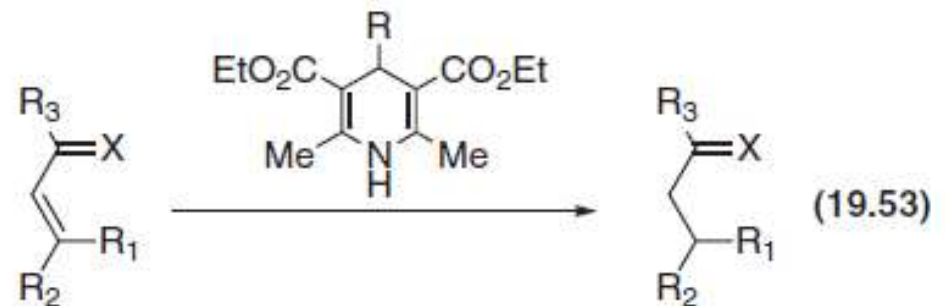
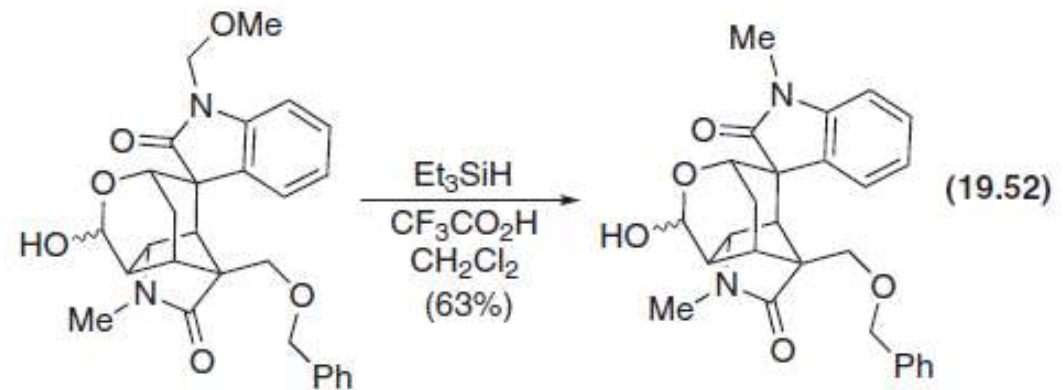
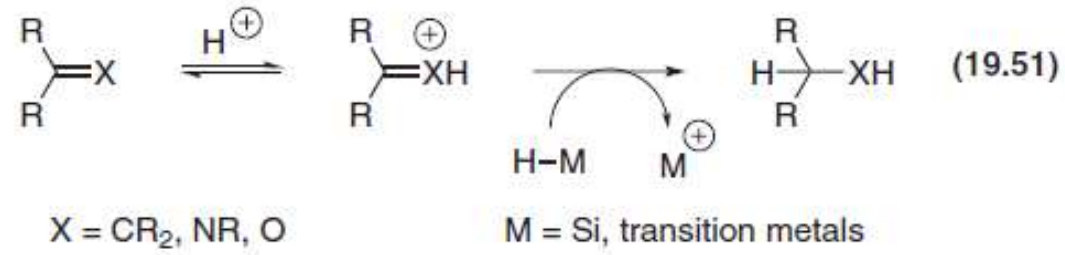
Figure 19.6



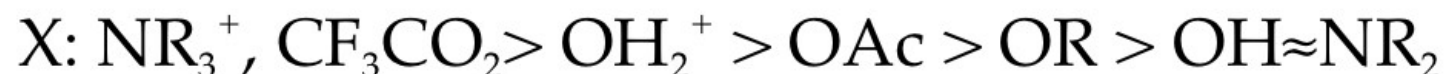
- Ionic hydrogenation of representative alkenes shows that only those alkenes that can give relatively unreactive carbocations on protonation will give hydrogenation products.

Ionic hydrogenation

- reaction requires initial protonation of the π bond, or complexation with a strong Lewis acid catalyst
- hydride donors may be **silanes** or **Hantzsch esters**



Reaction synopses: Ionic hydrogenation



catalyst: Pd preferred; Ni, Pt may be used

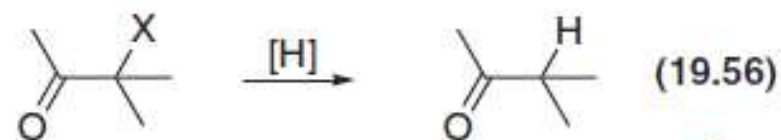
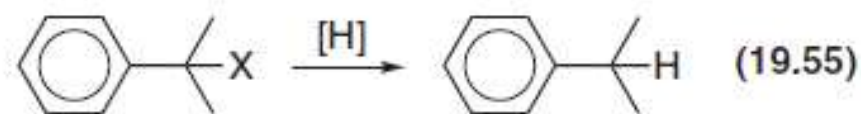
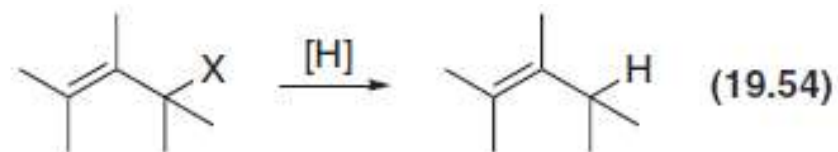
To suppress hydrogenolysis, use Rh, Ru.

regiochemistry of hydrogenolysis of cyclopropane controlled by
substituent groups on ring

stereochemistry: inversion with Pd, retention Ni; Pt variable

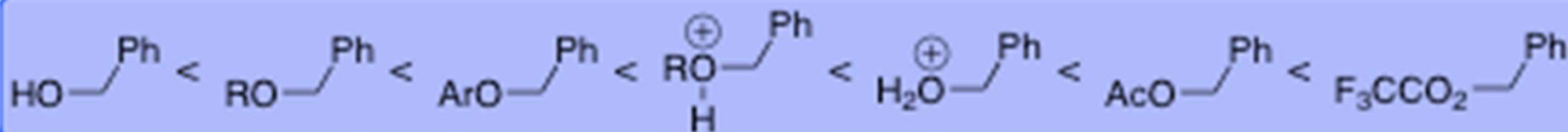
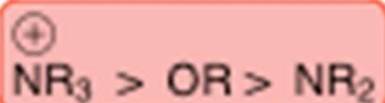
Hydrogenolysis

- allylic, benzylic, and α -substituents of carbonyl compounds are all susceptible to cleavage with hydrogen
- Pd is the preferred catalyst
- activity of leaving groups is as shown below:



X = Cl, Br, I, OH, OR, NR₂, OCOR, NHCOR, OTs, OP(O)(OR)₂, etc.

[H] = H₂, Pd-C; H₂, Ni; etc.



Hydrogenolysis: Reactivity and stereochemistry

- Hydrogenolysis of quaternary benzylammonium ion proceeds much more rapidly than hydrogenolysis of the benzyl ether
- hydrogenolysis over nickel occurs with retention of configuration
- hydrogenolysis over palladium results in predominant (but not exclusive) inversion of configuration

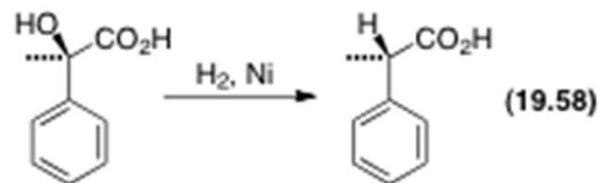
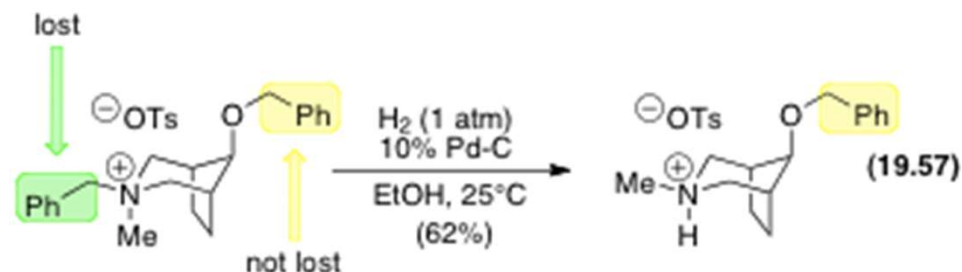


Table 19.3: Stereochemical outcome of hydrogenolysis experiments

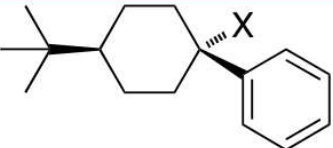
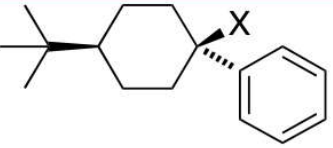
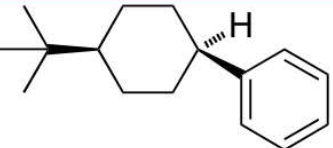
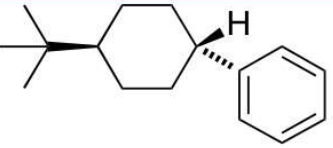
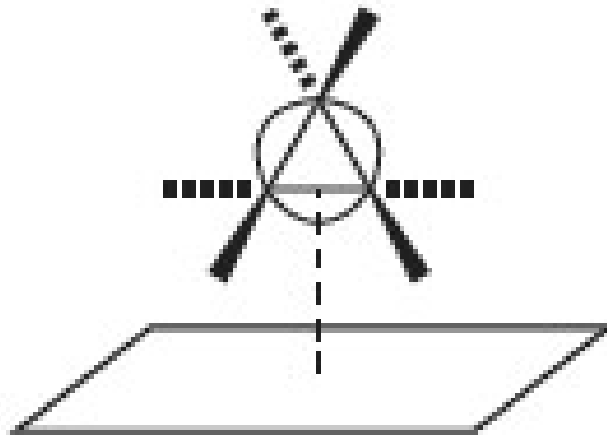
		catalyst		
X=OH		Pt	76	24
	X=OH	Pt	74	26
X=OH		10% Pd-C	80	20
	X=OH	10% Pd-C	90	10
X=OH		Ra-Ni	100	0
	X=OH	Ra-Ni	0	100
X=OAc		Pt	0	100
	X=OAc	Pt	100	0
X=OAc		10% Pd-C	0	100
	X=OAc	10% Pd-C	100	0
X=OAc		Ra-Ni	0	100
	X=OAc	Ra-Ni	100	0
X=OMe		Ra-Ni	100	0
	X=OMe	Ra-Ni	0	100

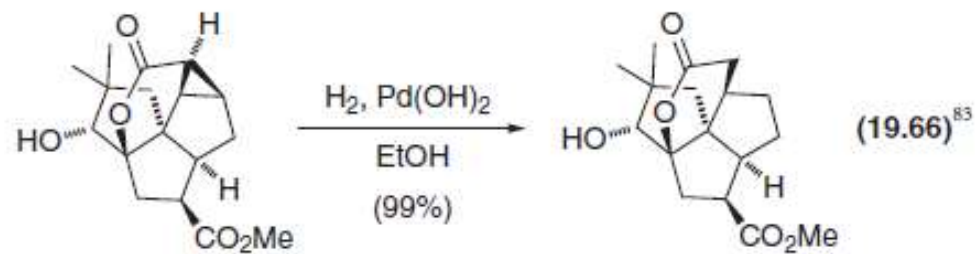
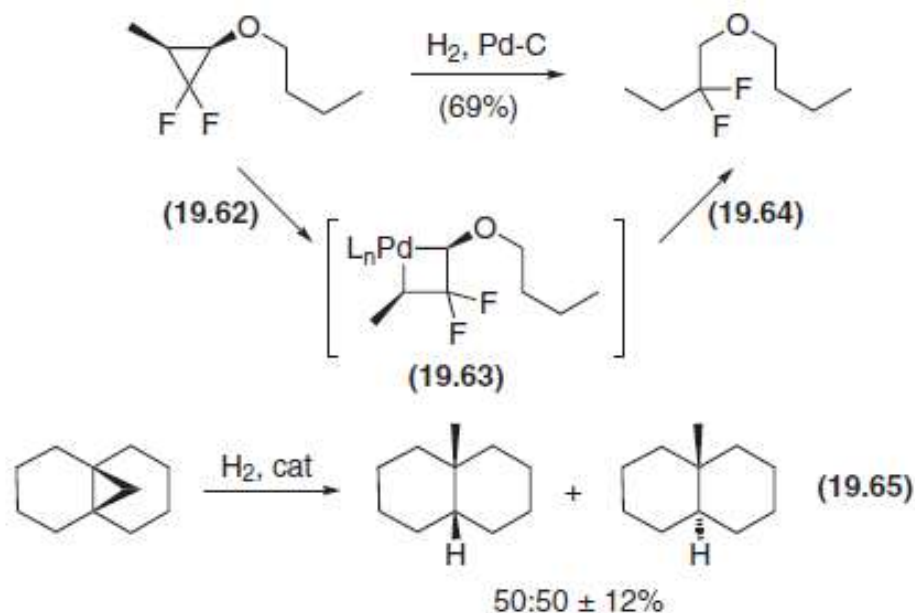
Figure 19.7



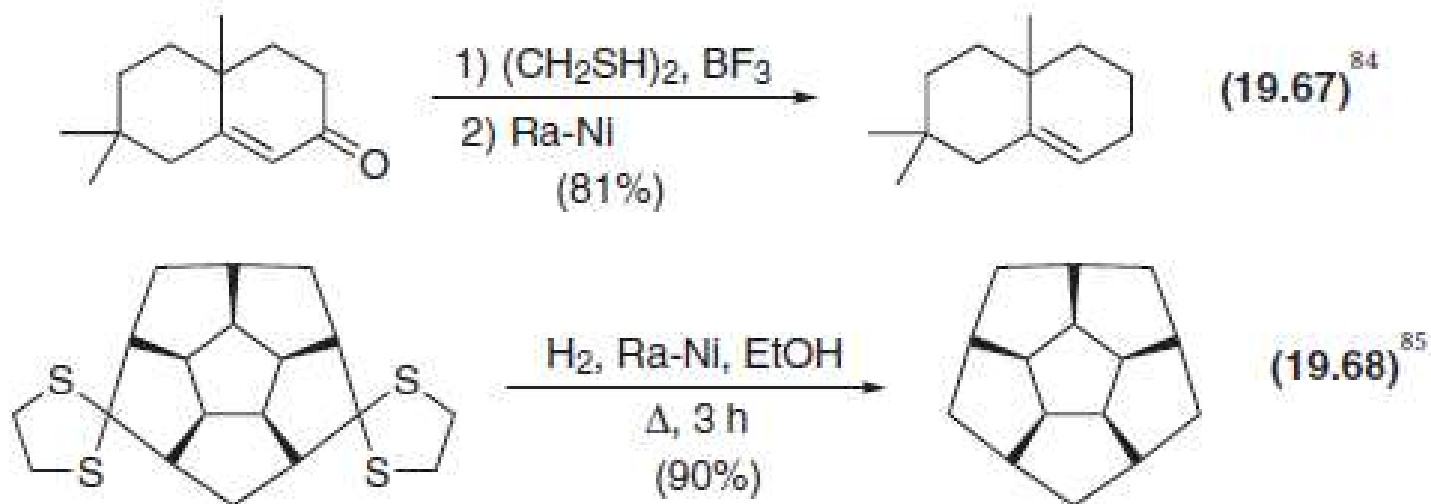
- Chemisorption of a cyclopropane onto a metal surface

Representative hydrogenolysis reactions

- Hydrogenolysis of cyclopropanes most probably occurs through an intermediate metallocyclobutane
- Hydrogenolysis of three-membered rings in propellanes is almost stereorandom
- Hydrogenolysis of the three-membered ring in polycyclic cyclopropyl ketones and acid derivatives leads to cleavage of the axial C—C bond at the α carbon

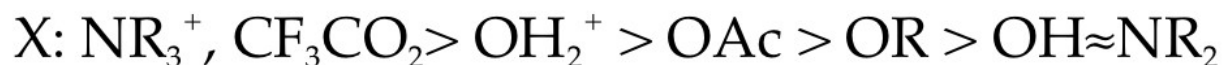


Reductive desulfurization



- W2 Raney nickel is the best reagent for carrying out this reaction
- nickel boride also serves as a suitable catalyst
- this reaction serves as a non-basic alternative to the Wolff-Kishner reduction

Reaction synopses: Hydrogenolysis



catalyst: Pd preferred; Ni, Pt may be used

To suppress hydrogenolysis, use Rh, Ru.

regiochemistry of hydrogenolysis of cyclopropane controlled by
substituent groups on ring

stereochemistry: inversion with Pd, retention Ni; Pt varies