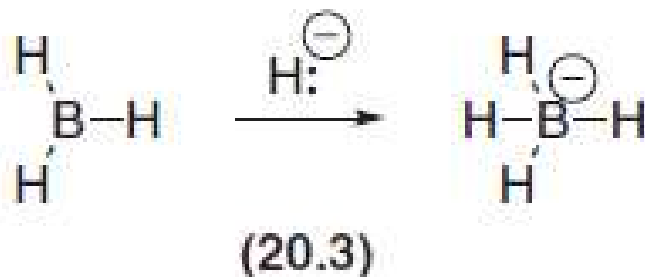
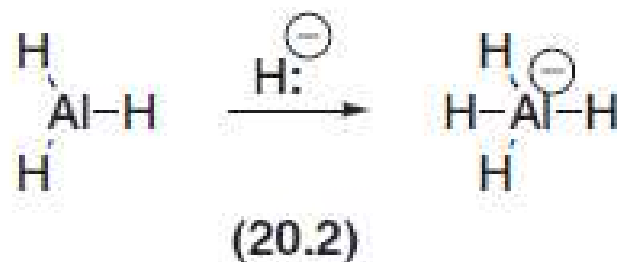
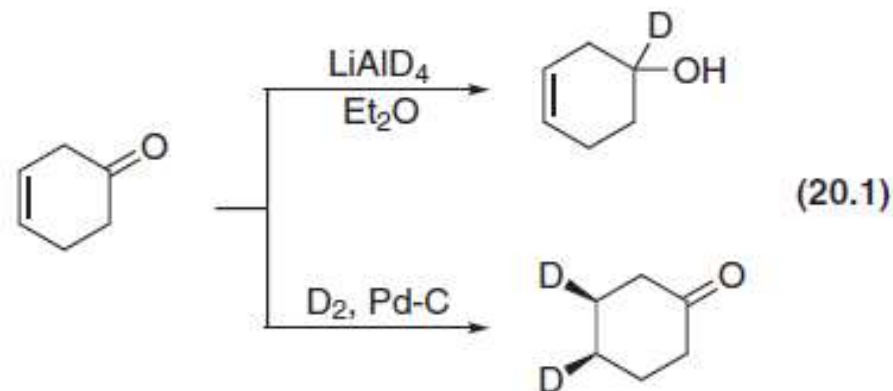

































































# Chapter 20

# Hydride reducing agents

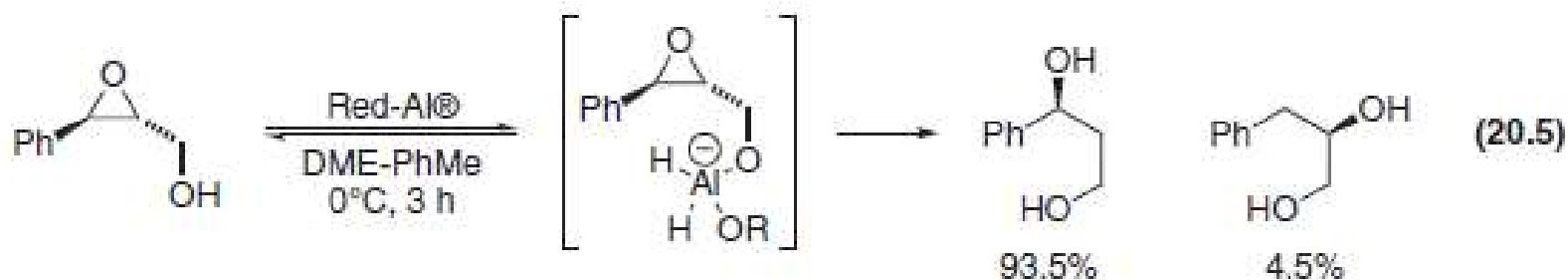
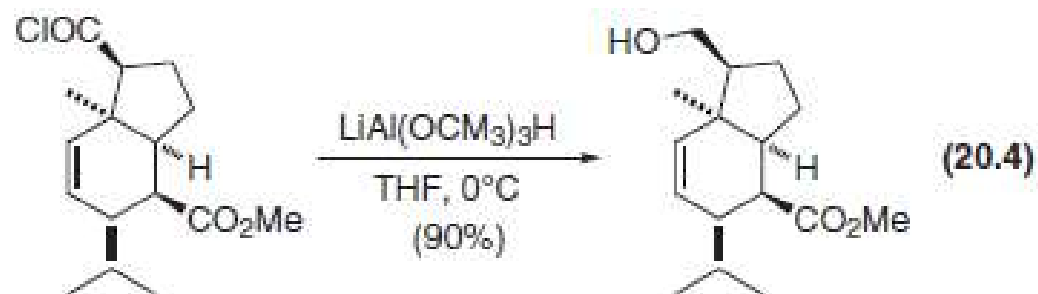
- the reduction of this non-conjugated ketone gives different products depending on the method of reduction used
- the base strength of hydride anion is mitigated by forming a complex with a Lewis acid



# Table 20.1

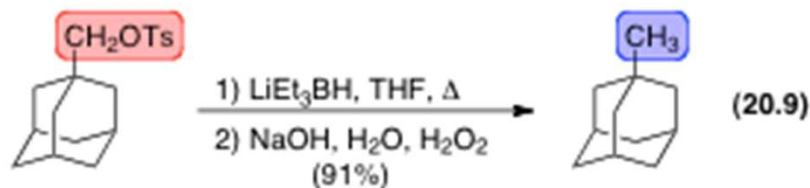
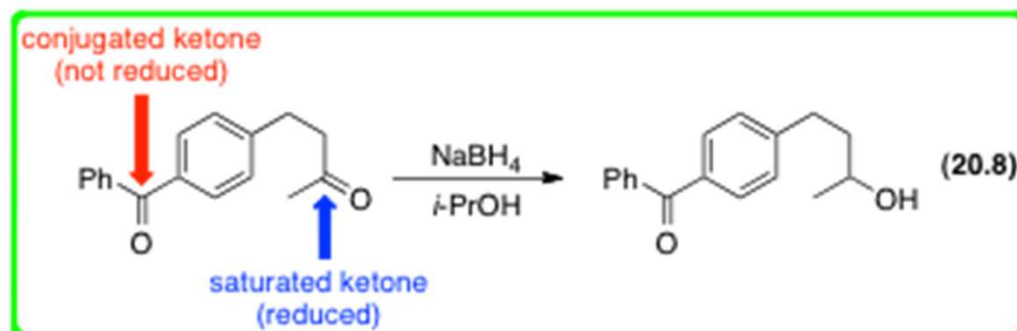
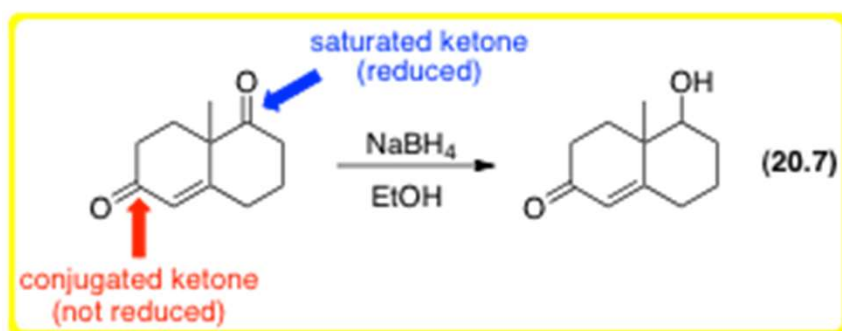
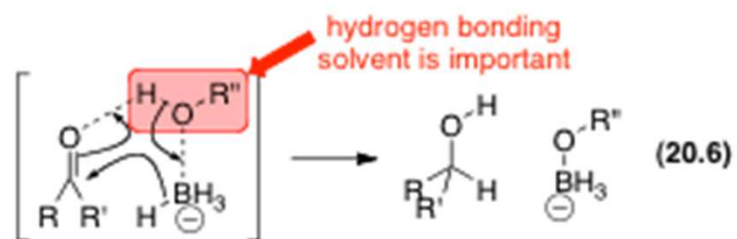
Reducing Agent	Acronym or Trade Name									
LiAlH <sub>4</sub>	LAH									
NaAl(OR) <sub>2</sub> H <sub>2</sub> *	Red-Al® or Vitride™									
LiAl(OBu <sup>t</sup> ) <sub>3</sub> H										
NaBH <sub>4</sub>										
LiBH <sub>4</sub>										
*R=CH <sub>2</sub> CH <sub>2</sub> OMe.										
**Not commercially available.										
***Acidic conditions usually required for reduction.										
LiEt <sub>3</sub> BH	Super Hydride™									
LiBu <sup>s</sup> <sub>3</sub> H	L-Selectride™									

# Representative reductions with aluminum hydride reagents



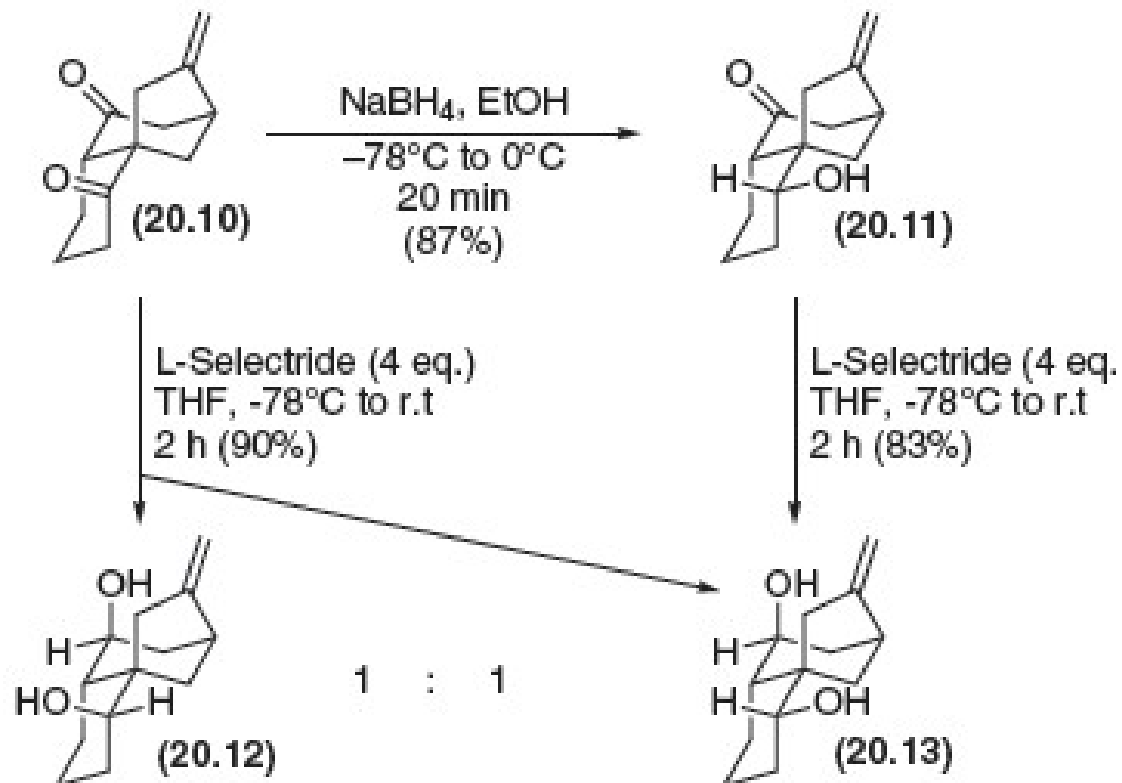
- lithium tri-*tert*-butoxyaluminum hydride reduces acid chlorides and aldehydes, but not esters
- complexation of the aluminum of Red-Al<sup>®</sup> by exchange with the alcohol group in the glycidyl alcohol leads to preferred formation of the 1,3-diol by reduction of the epoxide

# Representative borohydride reductions



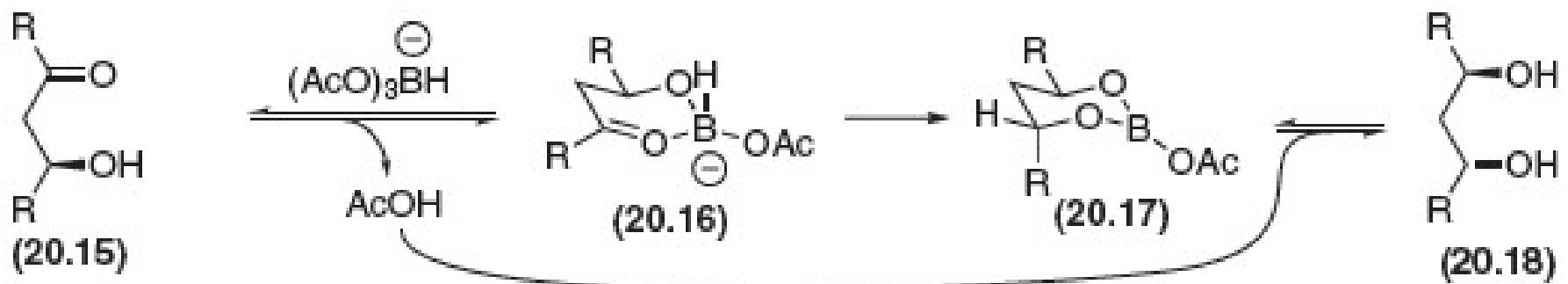
# Figure 20.1

Reduction of an intermediate in the total synthesis of ( $\pm$ )-platensimycin

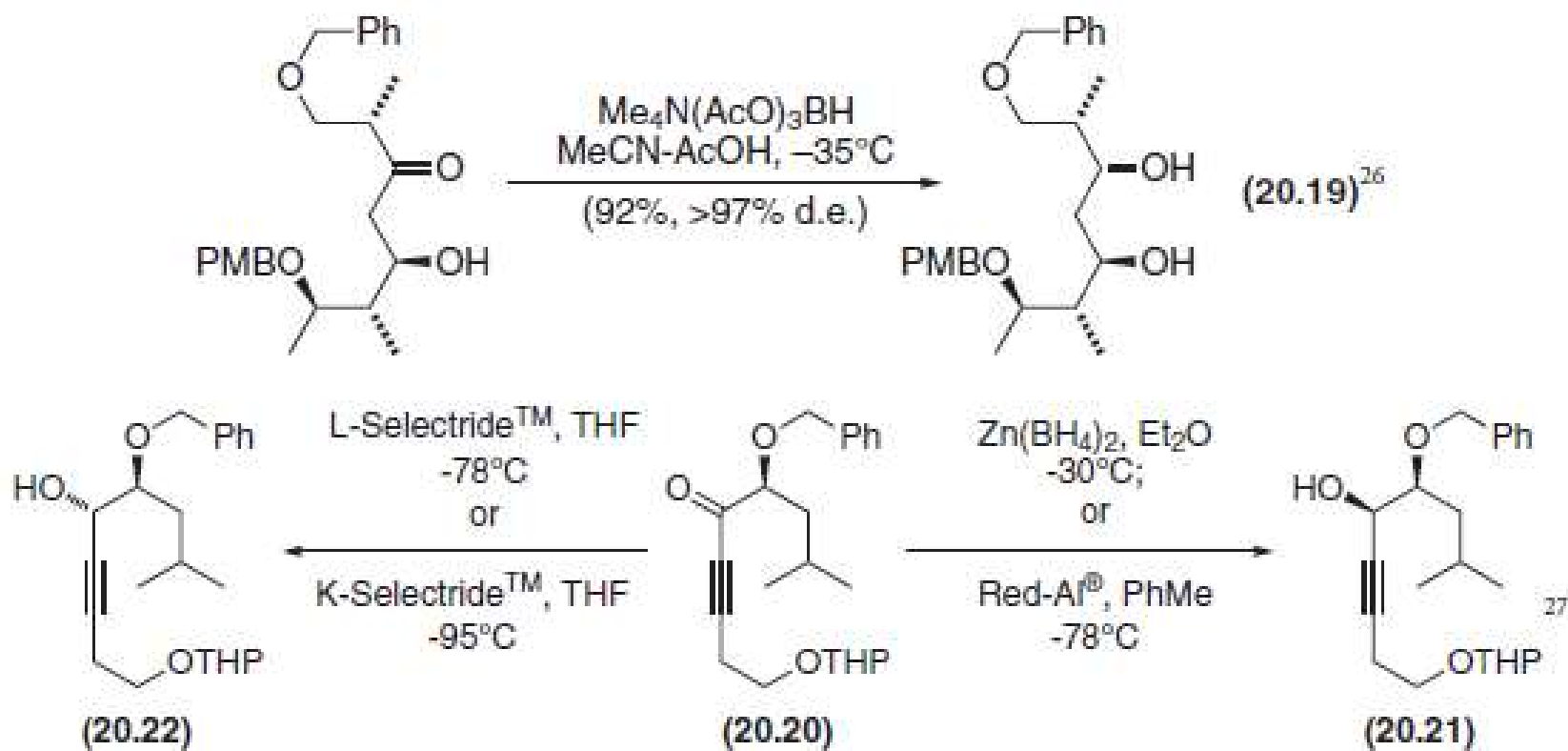


# Figure 20.2

Putative mechanism for the reduction of  $\beta$ -hydroxyketones by triacetoxyborohydrides

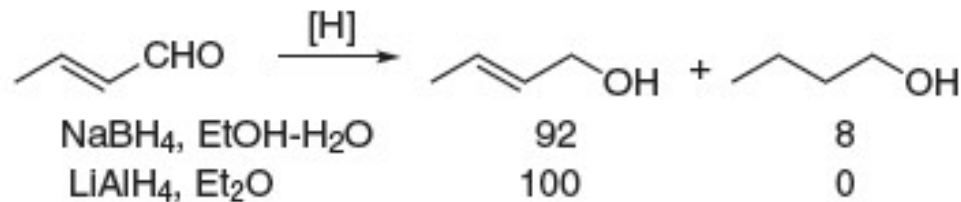
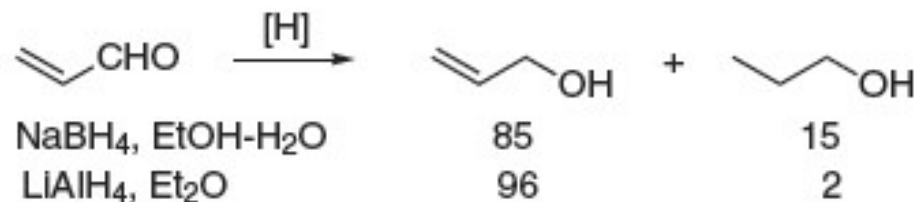
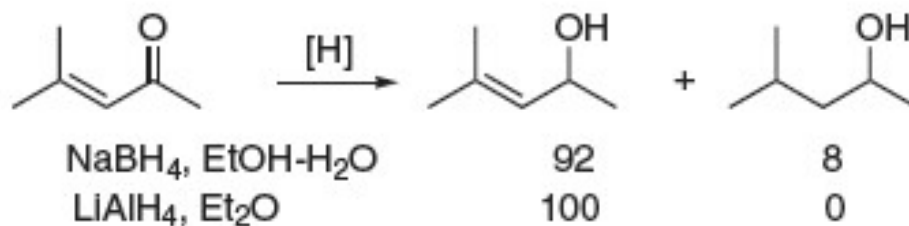
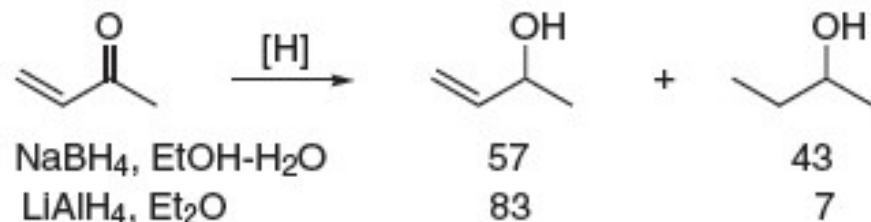


# Representative reductions with modified borohydride reagents



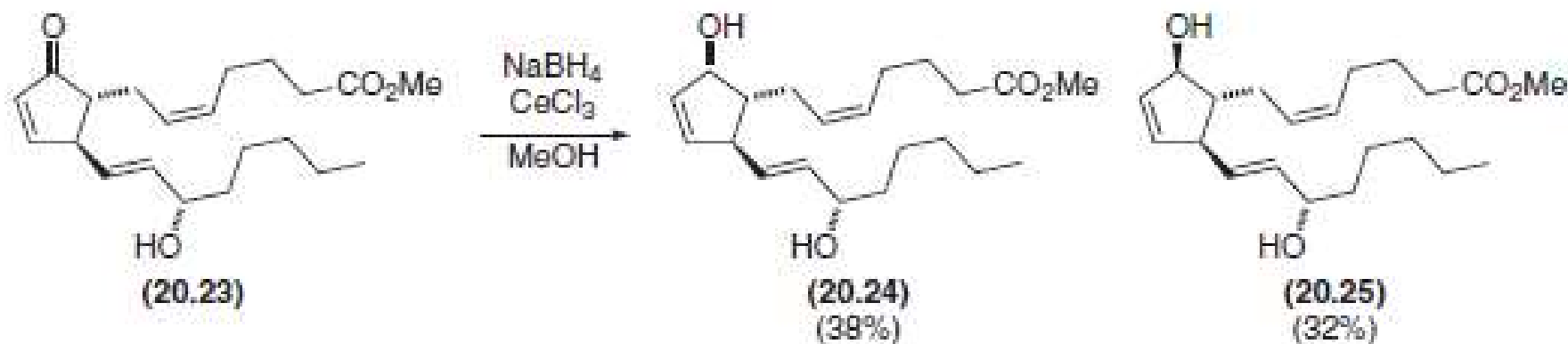


# Figure 20.3



Regiochemistry of reduction of  
representative conjugated  
aldehydes and ketones

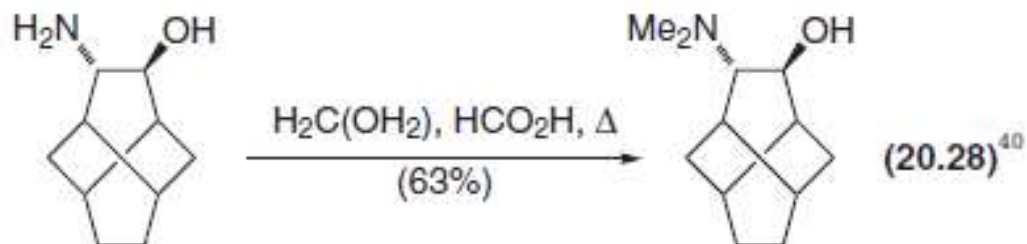
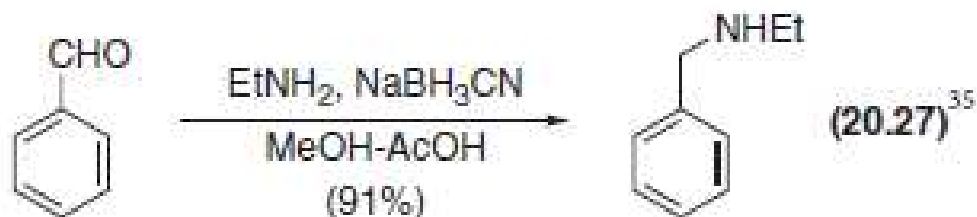
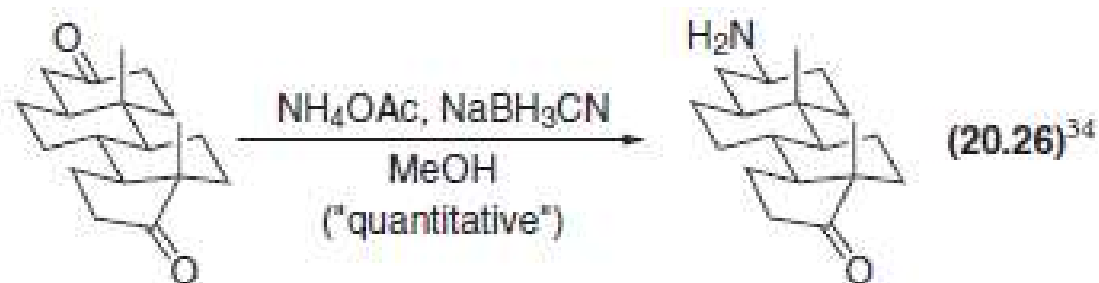
# Representative reductions of enones with Ce (III) modified borohydride



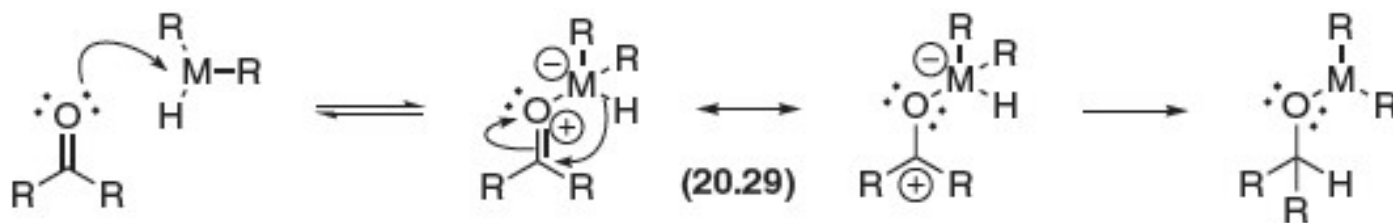
- The reaction in this prostaglandin synthesis shows little diastereoselectivity

# Representative reductive amination reactions

- sodium cyanoborohydride is a reducing agent that is selective for iminium ions, and that can be used at lower pH.
- In Example **20.26**, note that the less hindered carbonyl group reacts more rapidly
- The Eschweiler-Clark reaction gives a tertiary amine product with the nitrogen completely methylated



# Figure 20.4

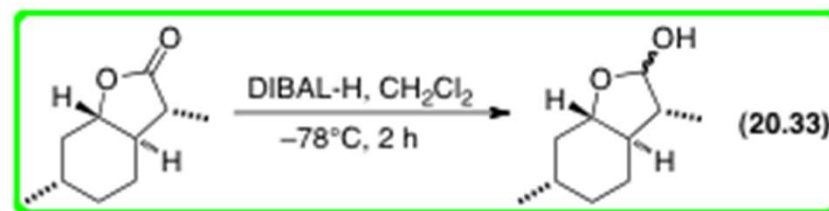
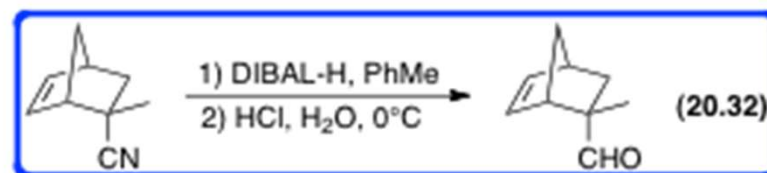
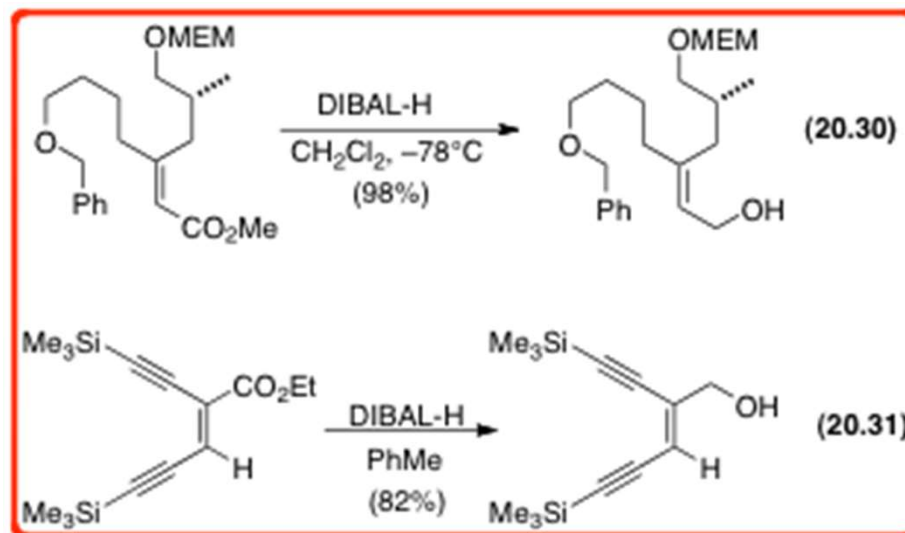


note how the complexation of the carbonyl oxygen with the metal simultaneously renders the carbonyl carbon more electrophilic and the metal hydride more nucleophilic

- Reduction of carbonyl compounds with electrophilic reducing agents

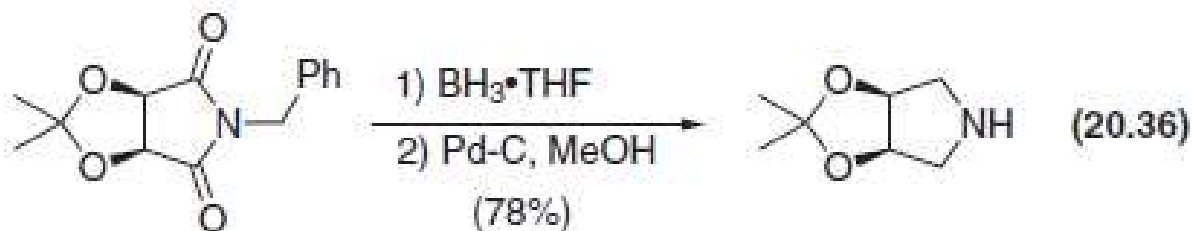
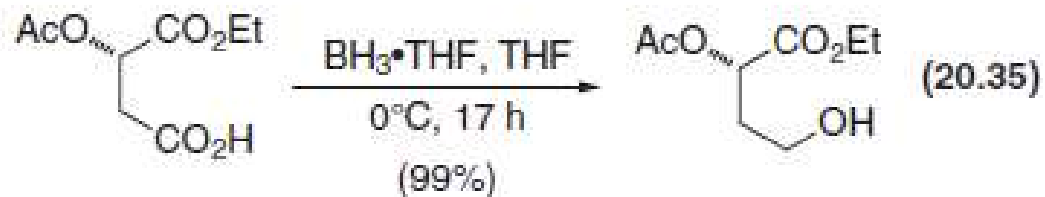
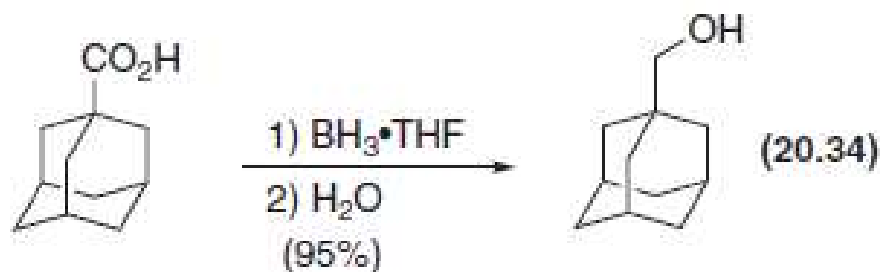
# Representative reductions with DIBAL-H

- reductions of conjugated esters give allylic alcohols
- reductions of nitriles give imines from which aldehydes are liberated by hydrolysis
- reductions of lactones at low temperature give hemiacetals



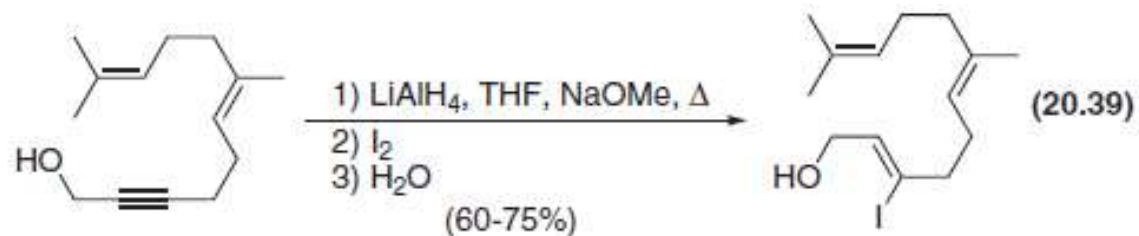
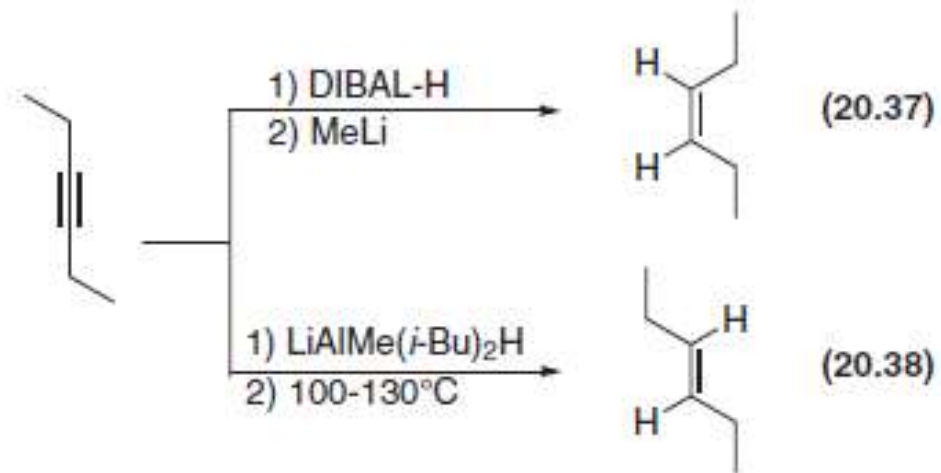
# Representative reductions with borane

- borane is a highly selective reducing agent that reacts rapidly with **carboxylic acids** to give primary alcohols and with **amides or imides** to give amines
- Other carbonyl functionalities are reduced only slowly by borane

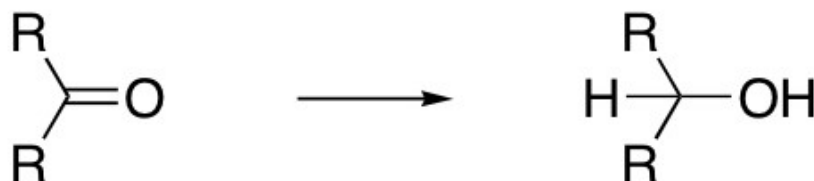


# Representative hydroalumination reactions

- neutral alane reagents give *syn* addition to the triple bond; protonolysis gives the *Z* alkene.
- anionic aluminum hydrides give *anti* addition to the triple bond; protonolysis gives the *E* alkene.
- the vinylalane can be trapped with a suitable electrophilic agent other than protons; the trapping occurs with retention of configuration



# Reaction synopses: Hydride reduction of aldehydes and ketones



Reagents:

or

or

or

THF; etc.

$\text{LiAlH}_4$ ,  $\text{Et}_2\text{O}$  (or THF); Red-Al®; etc.

$\text{NaBH}_4$ ,  $\text{CH}_3\text{OH}$ ;  $\text{LiR}_3\text{BH}$ , THF; etc.

DIBAL-H, hexane

$\text{BH}_3 \bullet \text{THF}$ ;  $\text{BH}_3$ , oxazaborolidine,



# Reaction synopses: Hydride reductions of acyl compounds and nitriles

*To alcohols:*



Reagents:  $\text{LiAlH}_4$ , Red-Al®;  $\text{BH}_3 \cdot \text{THF}$  (X=OH);  
or  
DIBAL-H (X=Cl, OCOR, OR).

*To Amines:*



Reagents:  $\text{LiAlH}_4$ ; Red-Al®; etc.  
or  
 $\text{BH}_3 \cdot \text{THF}$

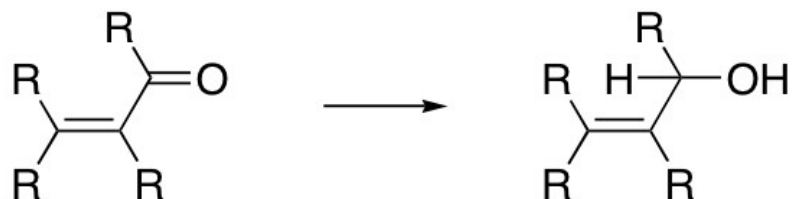
*To Aldehydes:*



Reagents: DIBAL-H, PhMe, 0°C, etc.

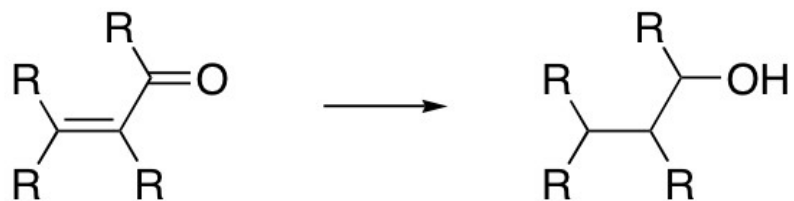
# Reaction synopses: Hydride reduction of conjugated carbonyl compounds

*To Allylic Alcohols:*



Reagents:  $\text{LiAlH}_4 / \text{Et}_2\text{O} / \text{low temp.} / \text{short time};$   
or  $\text{DIBAL-H} / \text{hexane}; \text{etc.}$   
or  $\text{NaBH}_4 / \text{CeCl}_3 / \text{CH}_3\text{OH}; \text{etc.}$

*To Saturated Alcohols:*



Reagents:  $\text{NaBH}_4 / \text{EtOH} / \text{extended time}$

# Reaction synopses: Reductive amination



Reagents:

or

or

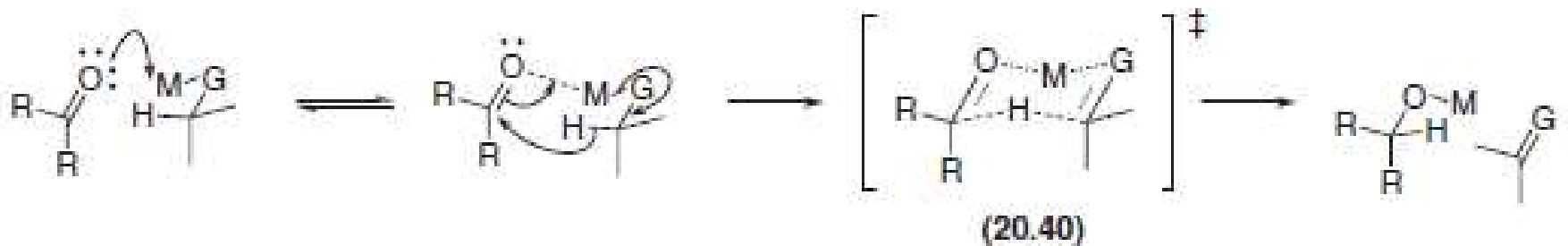
$\text{R}''_2\text{NH}/\text{HOAc}/\text{MeOH}/\text{NaBH}_3\text{CN}$

$\text{NH}_3/\text{HCO}_2\text{H}/\Delta$  (Leuckart)

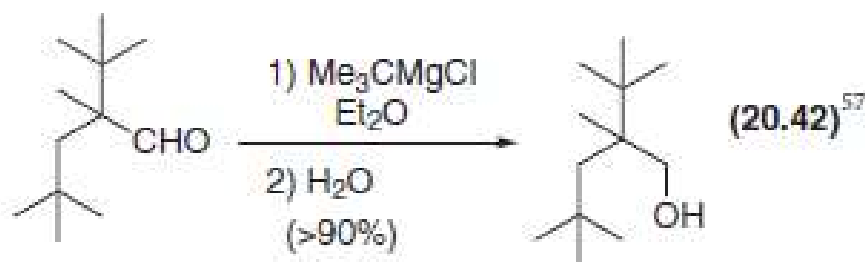
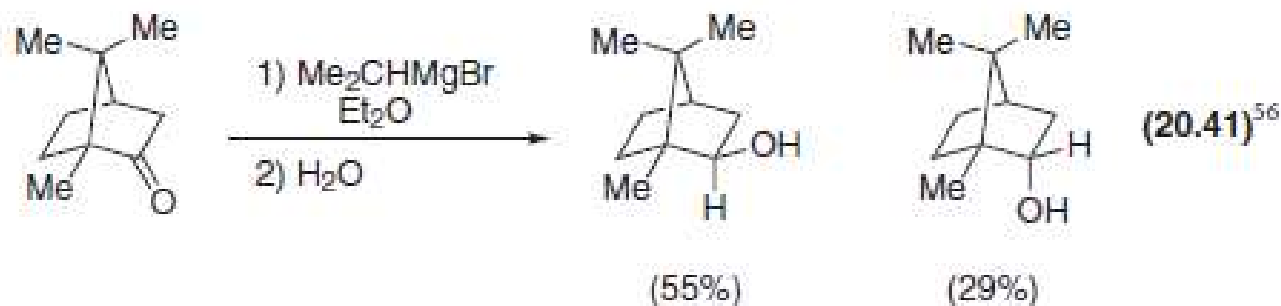
$\text{R}''_2\text{NH}/\text{HCO}_2\text{H}/\Delta$  (Wallach if R, R' = alkyl;  
Eschweiler-Clarke if R, R' = H)

# Reduction by hydrogen transfer from carbon

- hindered organometallic reagents and similar species can transfer hydrogen from one carbon to another, leading to reduction of aldehydes and ketones
- active species include
  - trialkylboranes
  - trialkylalanes
  - hindered Grignard reagents
  - dialkylzinc reagents other than dimethyl and diethylzinc
  - aluminum alkoxides
  - magnesium alkoxides
- hydrogen transfer occurs through a six-membered cyclic transition state



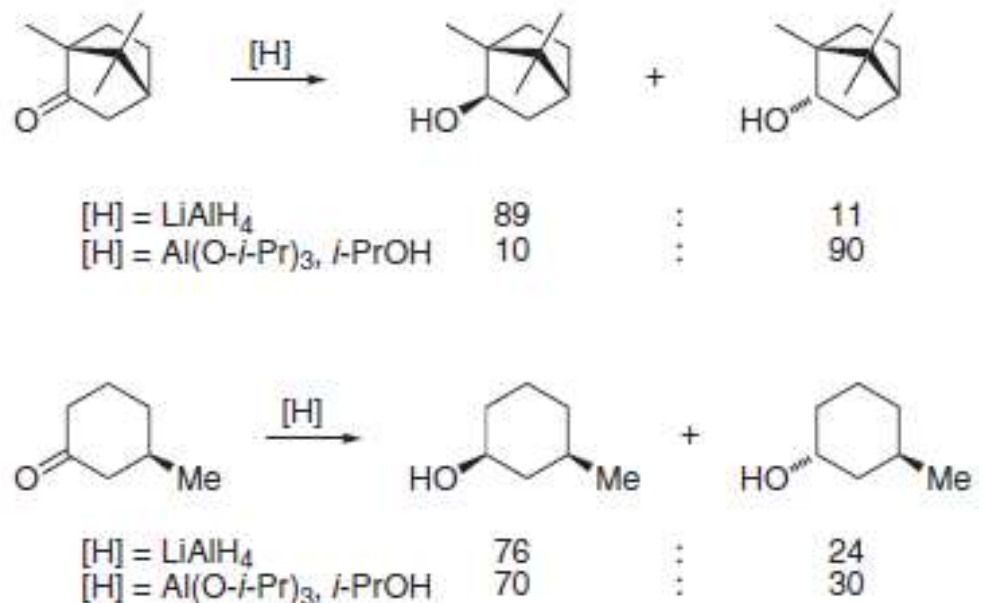
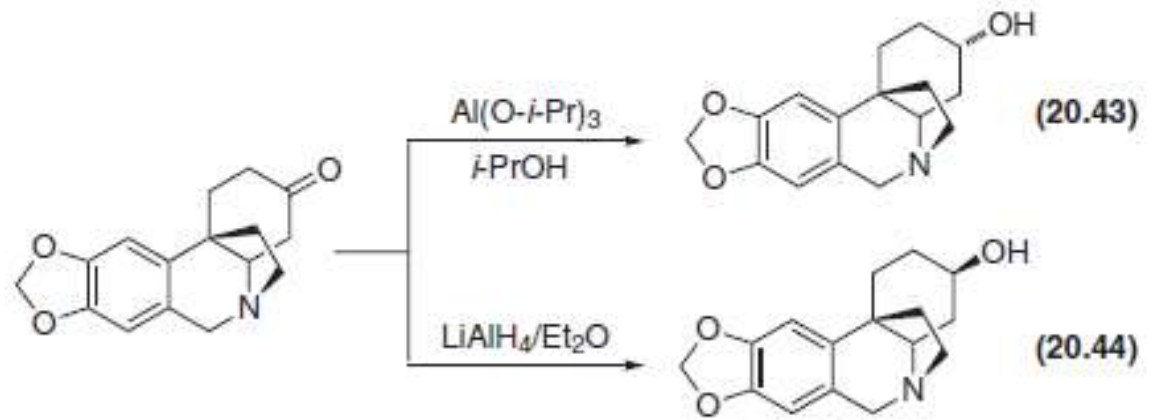
# Reductions with Grignard reagents



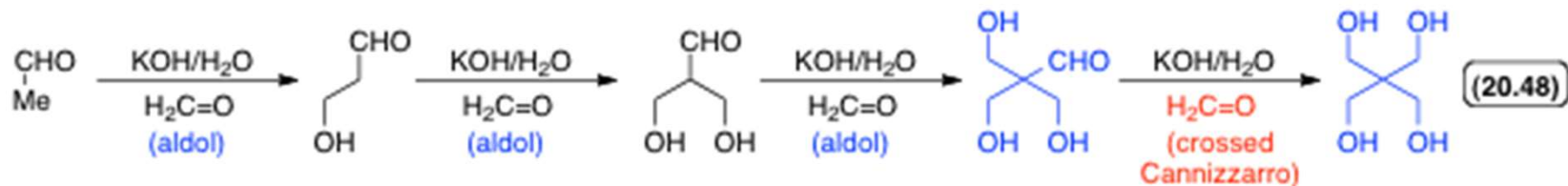
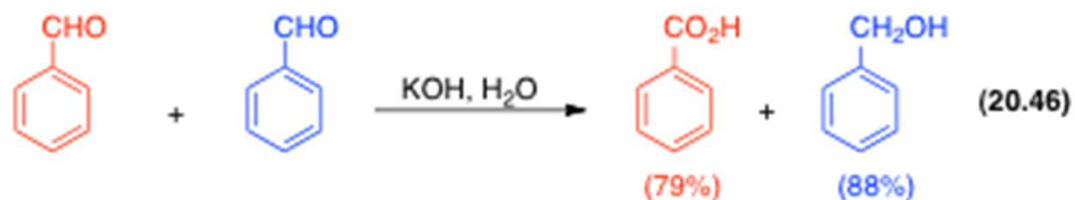
- reduction gives predominantly the product of kinetic control, but selectivity is not high

# Representative Meerwein-Ponndorf-Verley reductions

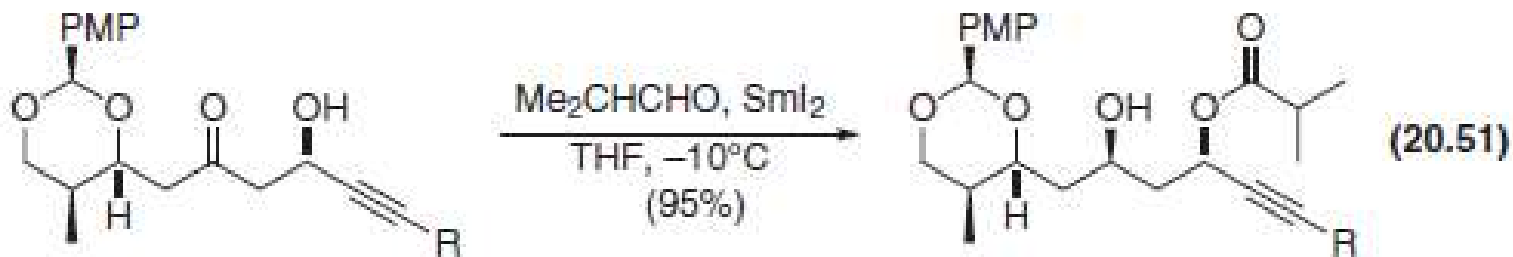
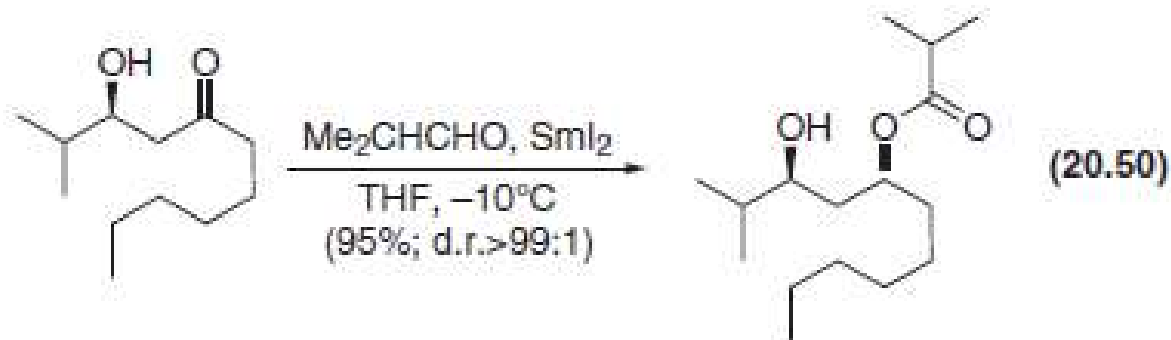
- Unlike the lithium aluminum hydride reduction, this reaction is reversible, which leads to the predominant formation of the more stable alcohol
- when the energy difference between the two alcohol products is small, the ratios of the two isomers produced by the two methods are much more similar



# Representative Cannizzarro and Tishchenko reactions



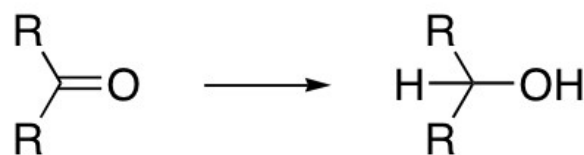
# Representative Evans-Tishchenko reactions



- This reaction results in reduction of the ketone and oxidation of the aldehyde to give the ester of an *anti*-1,3-diol. The more common product has the ester group bonded to the carbonyl oxygen (blue frame above)



# Reaction synopses: Reduction of aldehydes and ketones by hydrogen transfer



Reagents:  $\text{R}_2\text{CH}-\text{CR}_2-\text{MgX}$ ;  $\text{R}_2\text{CH}-\text{CR}_2-\text{ZnX}$ ; etc.

or  $\text{R}_2\text{CH}-\text{CR}_2-\text{BR}_2$ ;

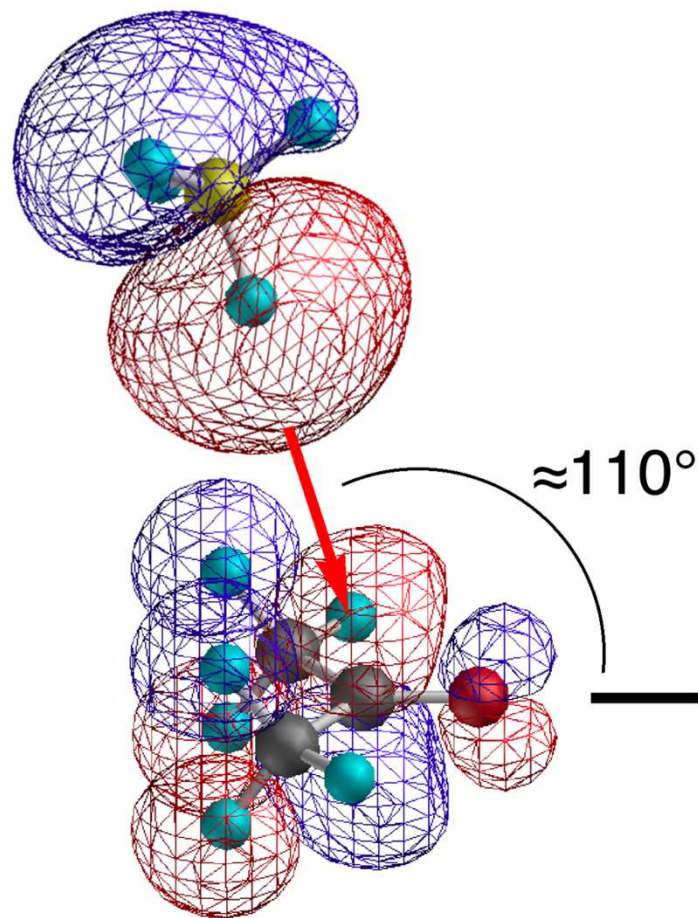
or  $(\text{R}_2\text{CH}-\text{O})_3\text{Al}$ ,  $\text{R}_2\text{CHOH}$ ;  $\text{SmI}_2$ , *i*-PrOH, THF; etc.

or  $\text{H}_2\text{C}=\text{O}$ , KOH (Cannizzarro)

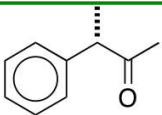
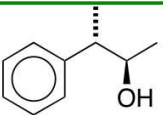
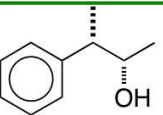
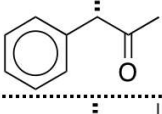
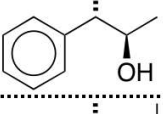
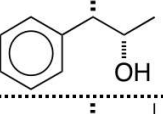
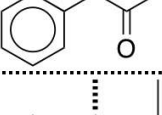
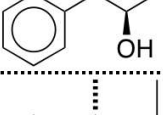
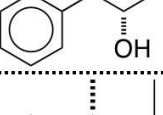
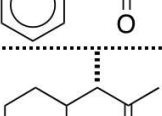
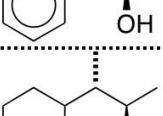
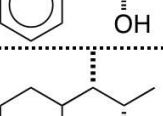
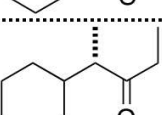
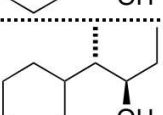
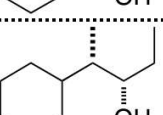
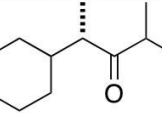
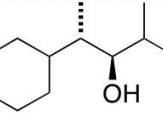
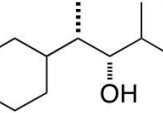



Reduction with organometallic reagents occurs when the systems are hindered.

# Figure 20.5

- Bürgi-Dunitz trajectory for the addition of borohydride anion to acetone

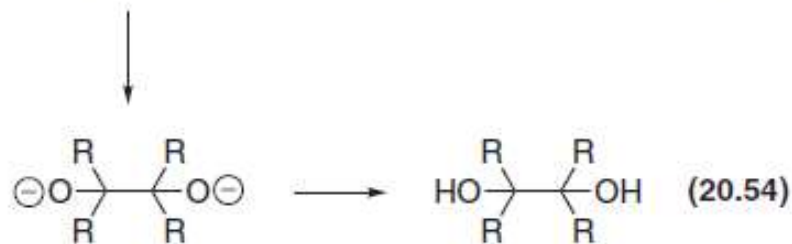
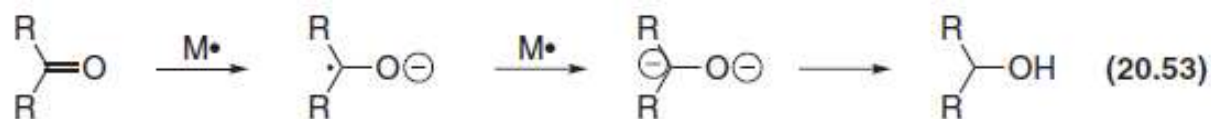
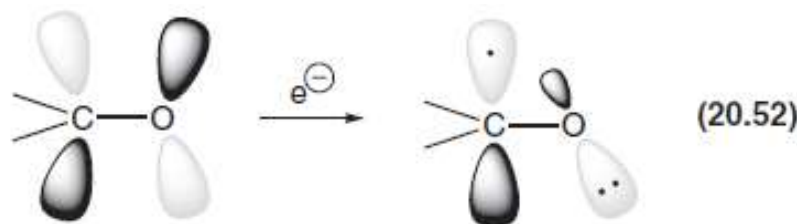


# Table 20.2

Reducing agent	ketone	major (Cram)	minor (anti-Cram)	major: minor	% yield
LiAlH <sub>4</sub> , Et <sub>2</sub> O, 0°C				74:26	97
L-Selectride				>99:1	80
LiAlH <sub>4</sub> , Et <sub>2</sub> O, 0°C				77:23	74
L-Selectride				>99:1	80
LiAlH <sub>4</sub> , Et <sub>2</sub> O, 0°C				58:42	92
LiAlH <sub>4</sub> , Et <sub>2</sub> O, 0°C				68:32	99
LiAlH <sub>4</sub> , Et <sub>2</sub> O, 0°C				81:19	99

- Reduction of  $\alpha$ -substituted ketones with complex hydrides

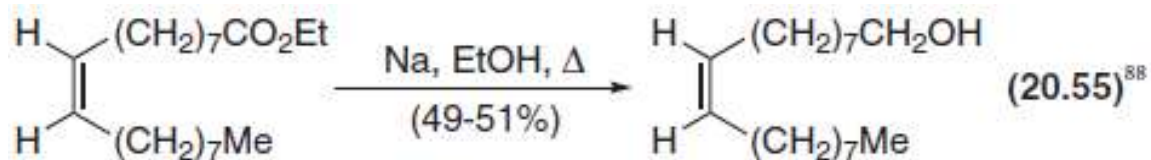
# Dissolving metal reductions: ketyl radical anions



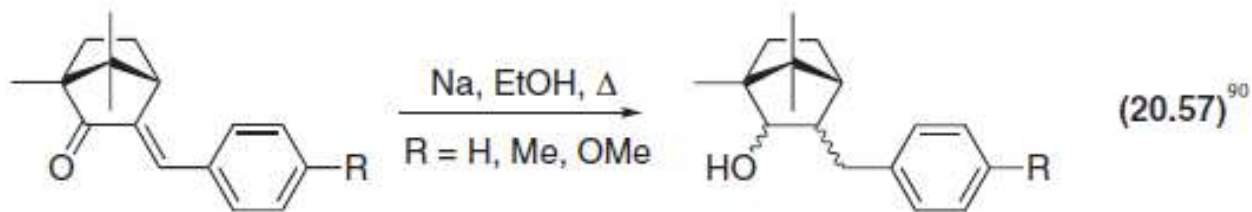
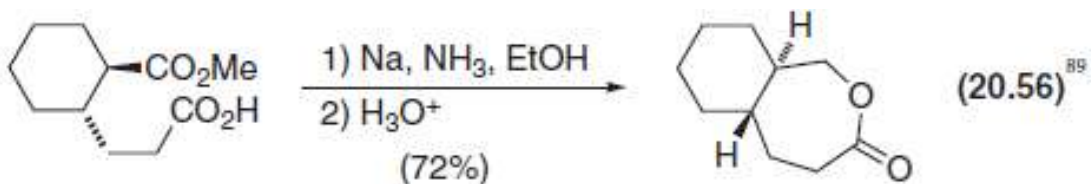
- single electron transfer to the  $\pi^*$  orbital of a carbonyl group gives a strongly stabilized ketyl radical anion
- This radical can react further to give dimeric products, or a strongly basic carbanion that can abstract a proton from the reaction medium

# Representative Bouveault-Blanc reductions

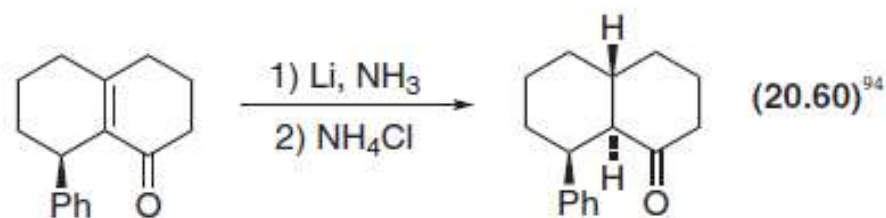
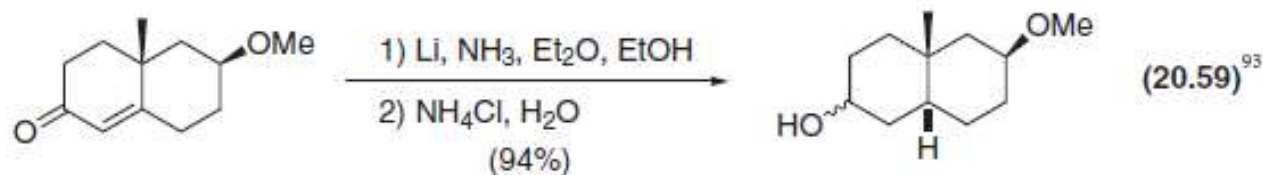
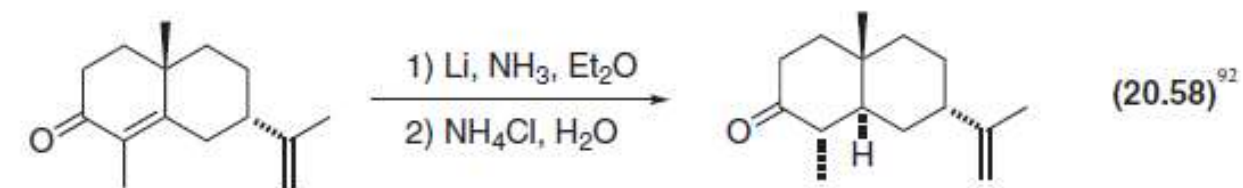
- the reduction with sodium in ethanol allows the selective reduction of esters in the presence of carboxylic acid groups



- the reduction of conjugated enones under Bouveault-Blanc conditions results in the formation of the saturated alcohol



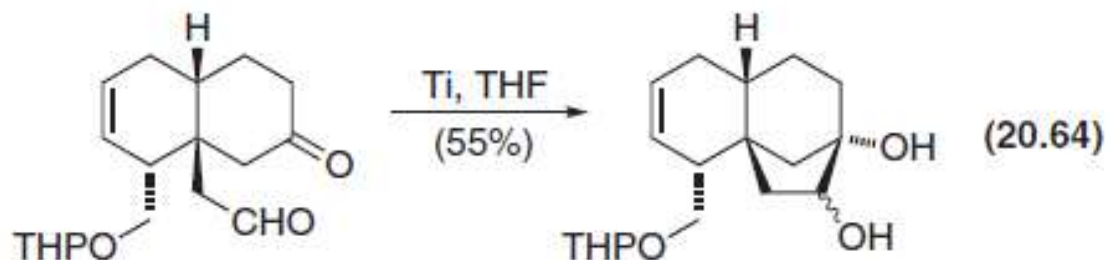
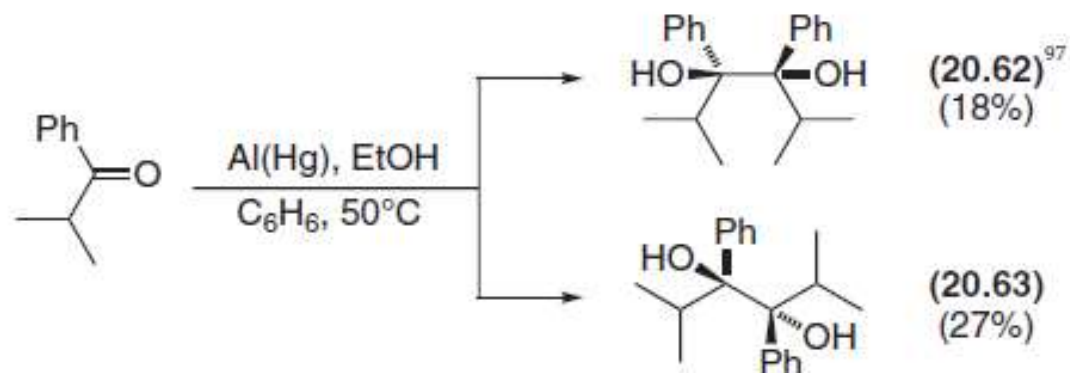
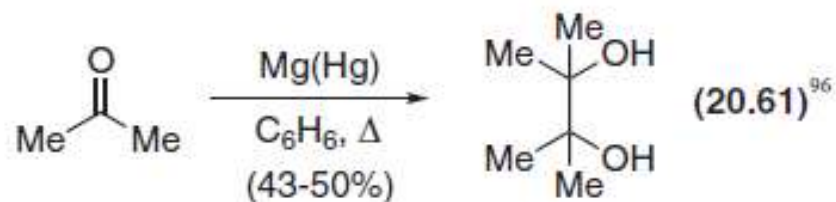
# Stereochemistry of representative Birch reductions of cyclohexenones



- The protonation of the anions involved in this reaction (the enolate anion and the radical anions or dianion) occurs preferentially from the axial direction at both the  $\alpha$  and  $\beta$  carbons, leading to the preferential formation of the *trans*-fused cyclohexane

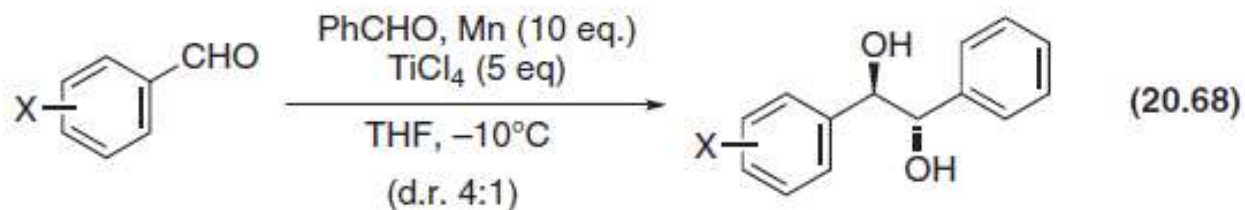
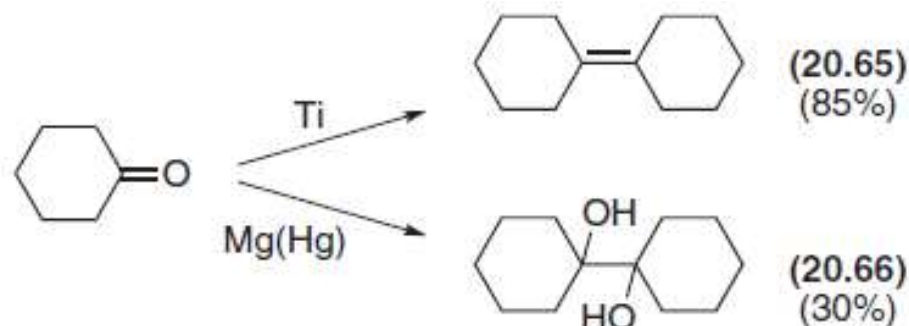
# Representative pinacol coupling reactions

- the diastereoselectivity of the traditional pinacol reaction is not high
- improved yields and stereochemical control are obtained when titanium-based reagents are used.



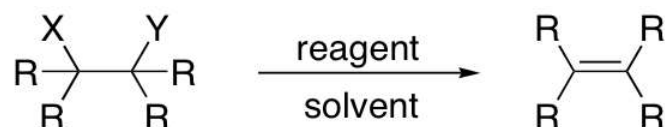
# Representative McMurry and related reactions

- the McMurry reaction, with titanium instead of magnesium, gives the alkene by reductive dimerization of ketones.
- using the reagent from manganese metal and titanium tetrachloride gives mainly the *anti*-1,2-diols from aldehydes





# Table 20.3

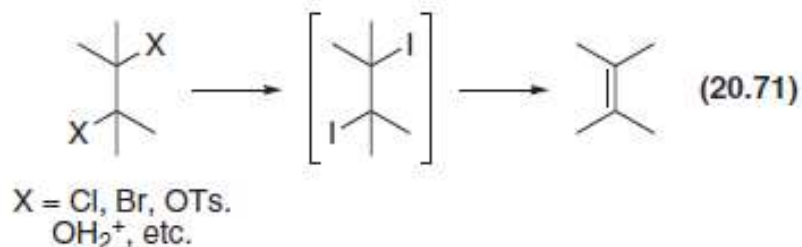
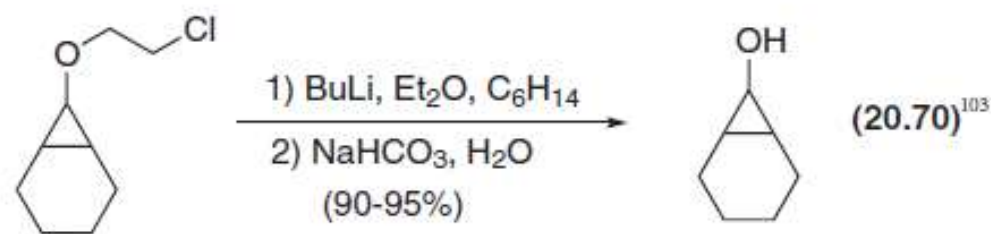
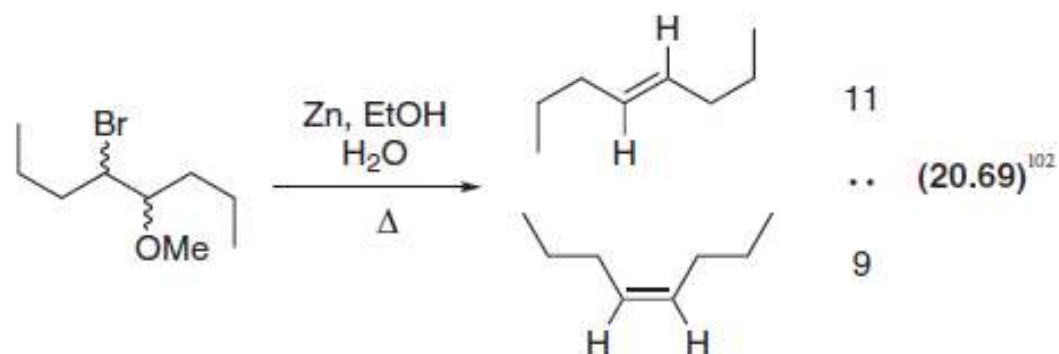


X	Y	Reagent/Solvent
halogen	halogen	Li, NH <sub>3</sub> ; Na, NH <sub>3</sub>
	OR	Na, ROH; Mg, ROH
	OH (acid conditions)	Mg, Et <sub>2</sub> O; Li, Et <sub>2</sub> O
	NHCOR	Zn, CH <sub>3</sub> CO <sub>2</sub> H, Δ; C <sub>4</sub> H <sub>9</sub> Li, THF
OH	OH	1) MeLi; 2) K <sub>2</sub> WCl <sub>6</sub> , THF, Δ
OH	OH	1) Im <sub>2</sub> C=S; 2) P(OR) <sub>3</sub> , Δ
OH	OH	TsOH, NaI
OH	OH	Ti, THF
OTs	OTs	NaI, DMF

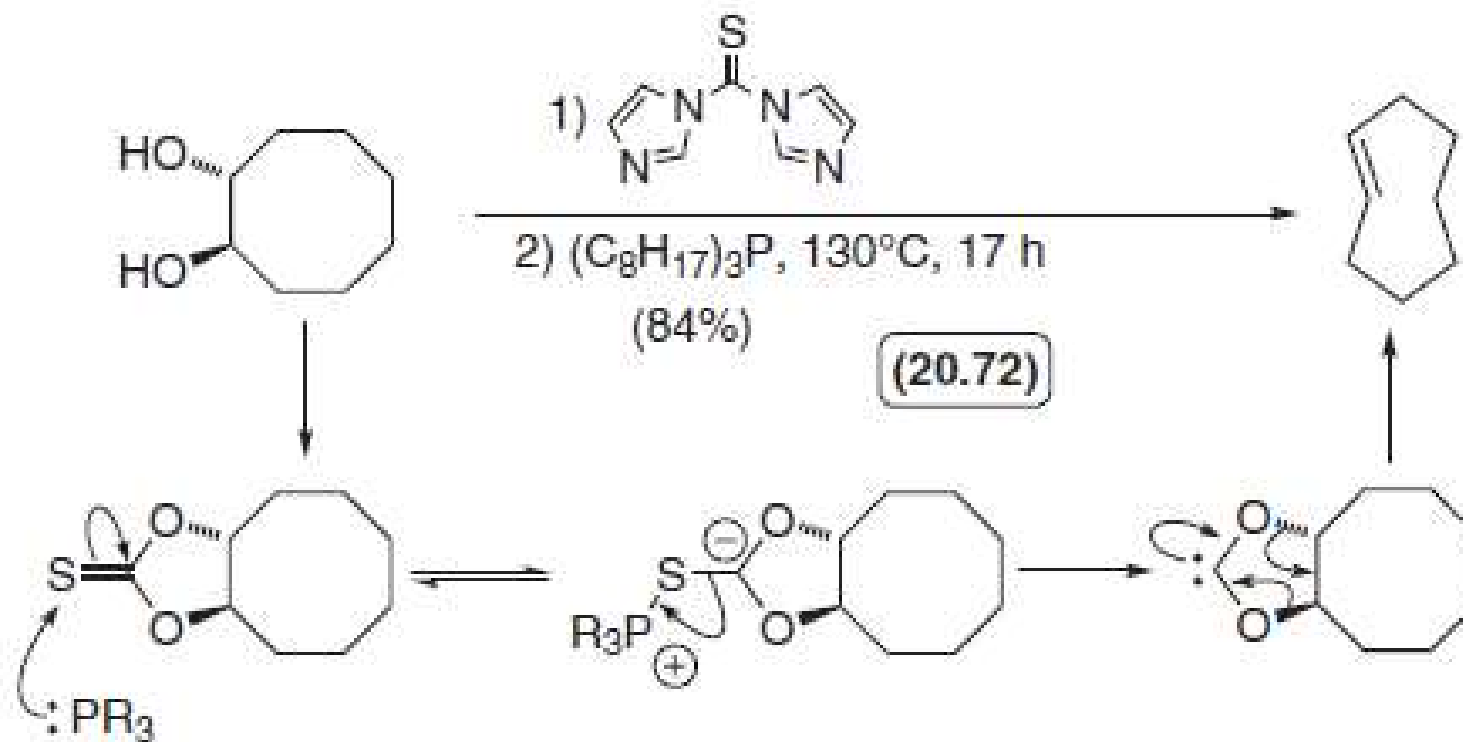
- Reactant and reagent combinations for reductive elimination

# Representative reductive eliminations

- When the leaving group is a halogen, reductive elimination proceeds readily with *anti* stereochemistry by a mechanism that is basically the same as the E2 mechanism.
- As the leaving group becomes more difficult to remove, the reaction mechanism changes to E1cb, with the result that the stereochemistry becomes less rigidly defined.
- the formation of 1,2-diiodoalkanes is always followed by attack of iodide ion to give iodine and the alkene

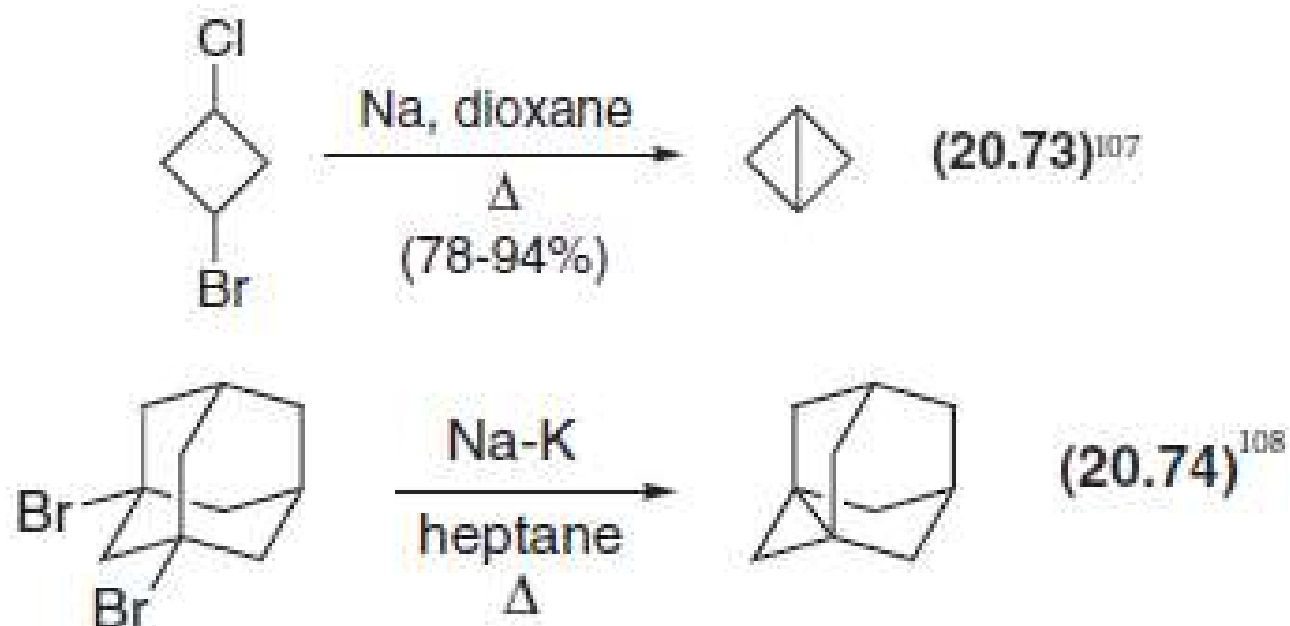


# The Corey-Winter reductive elimination



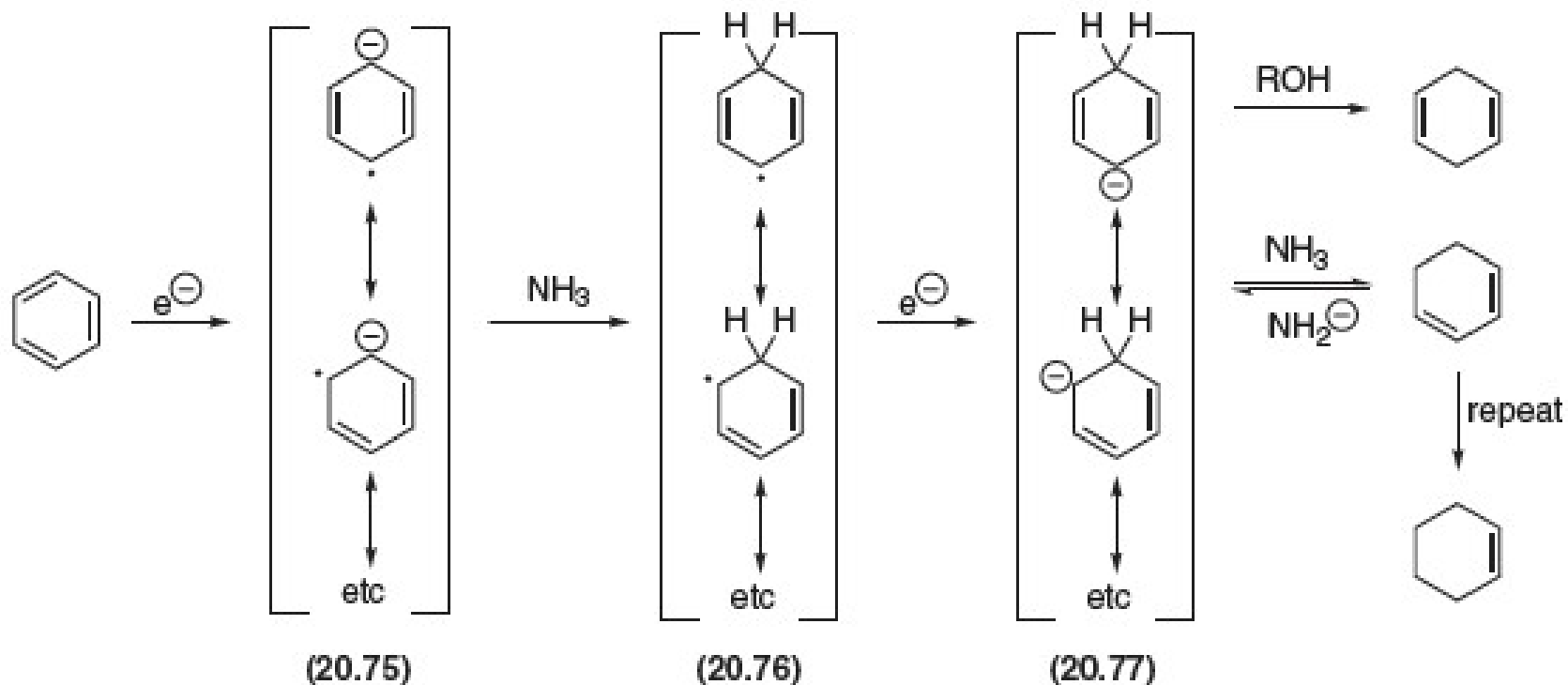
- This *syn* elimination involves a carbene intermediate

# Representative Wurtz couplings



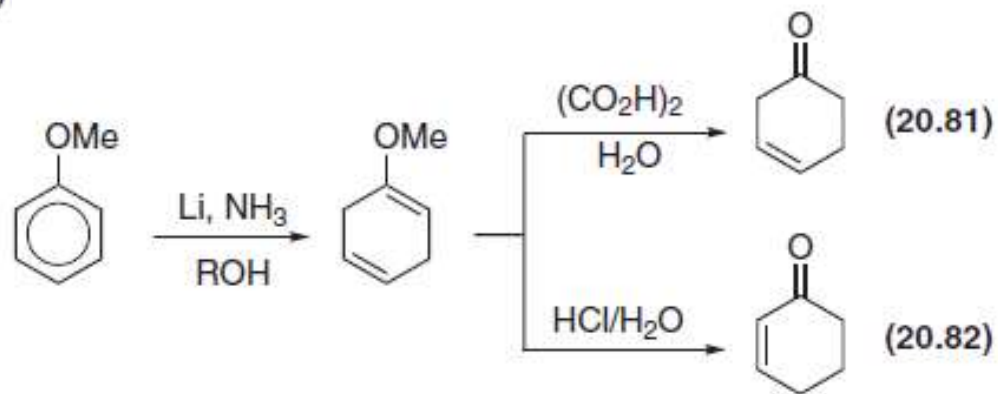
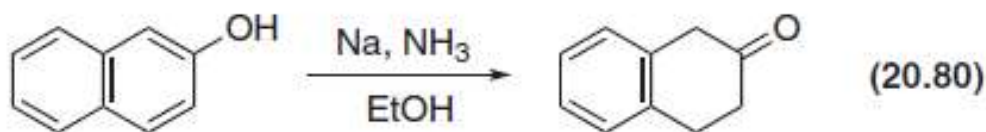
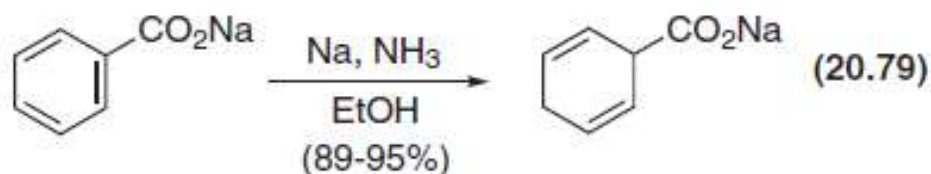
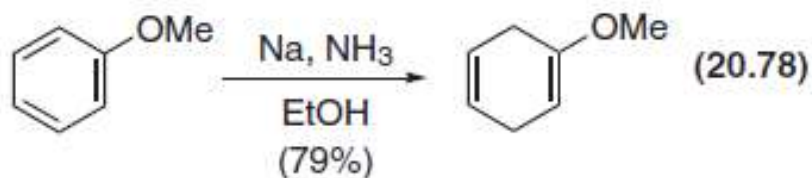
- the intramolecular Wurtz coupling is an excellent method for the non-photochemical formation of highly strained ring systems

# Figure 20.6



- The mechanism of the Birch reduction of aromatic rings in the presence and absence of a proton source.

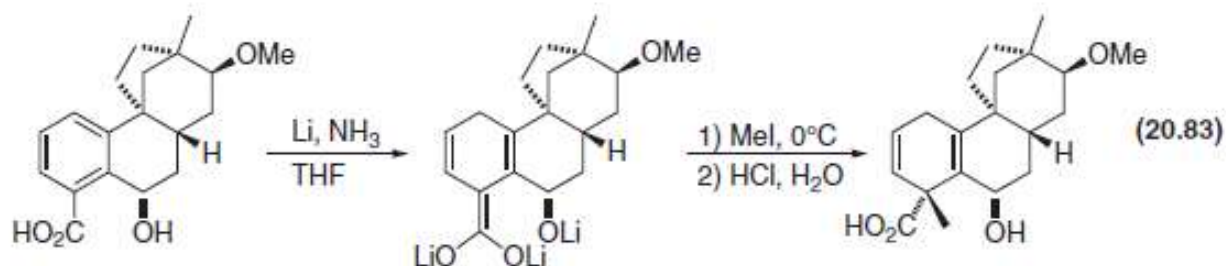
# Representative Birch reductions



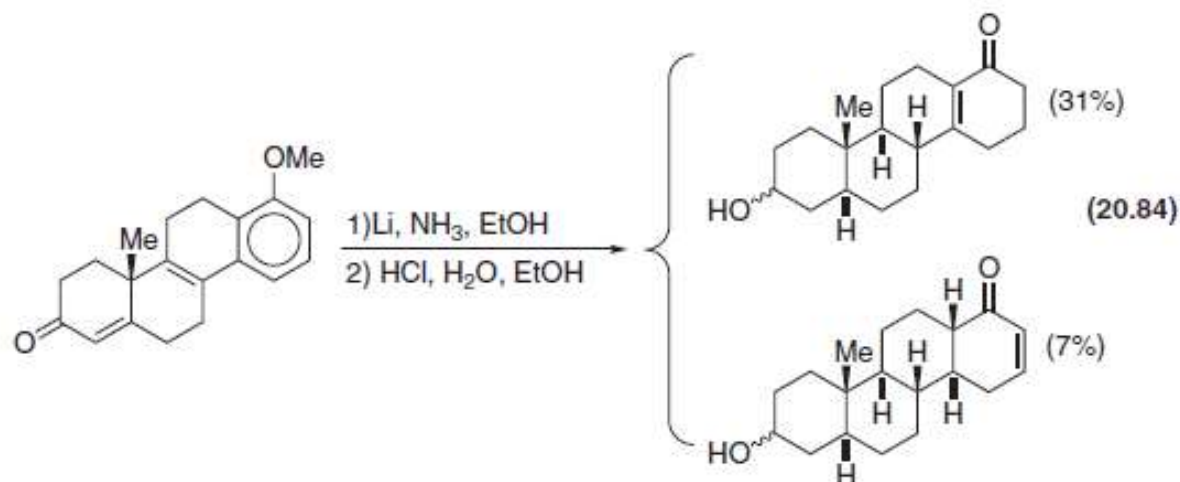
- the regiochemistry of the reduction is determined by the electronic nature of the substituent group

# Birch reduction in synthesis

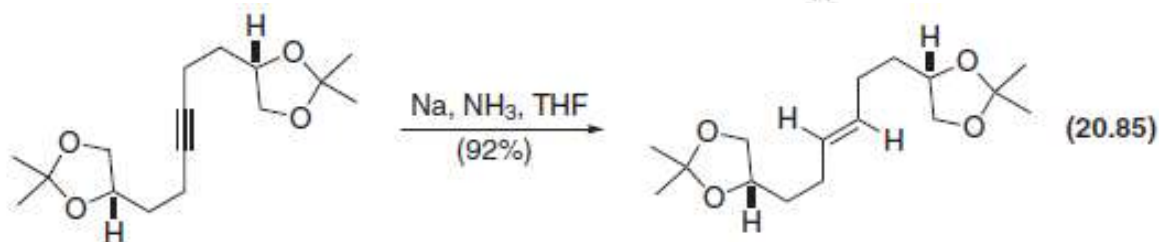
- Birch reduction of carboxylic acids in the absence of a proton source gives carboxylate dianions that can be alkylated *in situ*



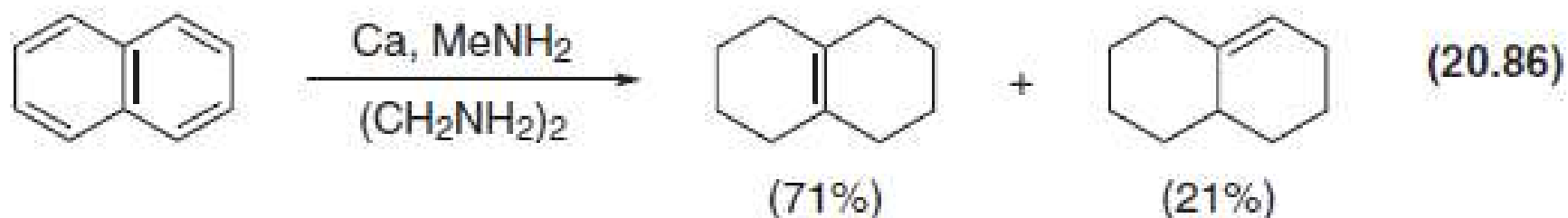
- in this Birch reduction from Johnson's steroid synthesis, spectacular advantage is taken of the reaction's propensity to lead to *trans*-diaxial addition of hydrogen to incorporate up to 5 new chiral centers with the correct relative stereochemistry



- Birch reduction of alkynes gives predominantly *E* alkenes



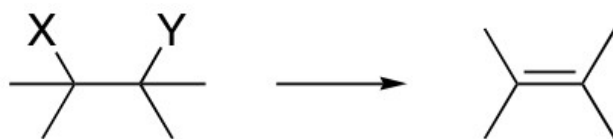
# Benkeser reduction



- this variant of the Birch reduction uses calcium metal in a low-boiling amine solvent
- its better reproducibility has made it popular in large-scale syntheses



# Reaction synopses: Reductive elimination



X, Y: Cl, Br, I, OSO<sub>2</sub>R, NR<sub>3</sub><sup>+</sup>, etc.

Reagents: Li, NH<sub>3</sub>; Mg, Et<sub>2</sub>O; Zn, EtOH, Δ; Zn, CH<sub>3</sub>CO<sub>2</sub>H, Δ;

or BuLi, Et<sub>2</sub>O; etc.

or NaI, DMF, Δ; etc.

Mechanism: E1cb or E2.

Stereochemistry: *anti* (E2); mainly *anti* (E1cb).

# Reaction synopses: Birch and Benkeser reductions

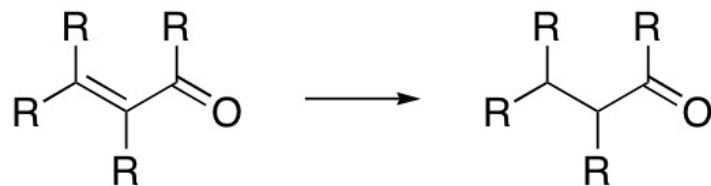


M: Li, Na, K, etc.;      ROH: EtOH, Me<sub>3</sub>COH, etc.

Reagents:      Li, NH<sub>3</sub>, Me<sub>3</sub>COH, THF; etc. (Birch reduction)  
or              Ca, MeNH<sub>2</sub>, (CH<sub>2</sub>NH<sub>2</sub>)<sub>2</sub>; etc. (Benkeser)

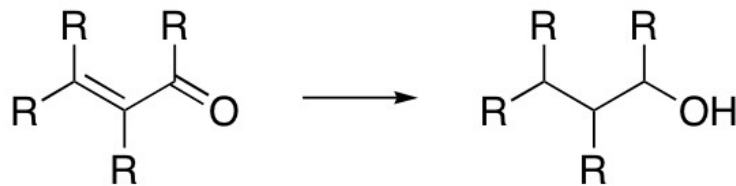
# Reaction synopses: Reduction of conjugated carbonyl compounds

(a) *To Saturated Ketones*



Reagents:  $\text{H}_2$ , Pd-C; etc.  
or Li,  $\text{NH}_3$  (no proton source); etc.

(b) *To Saturated Alcohols*



Reagents: Li,  $\text{NH}_3$ , ROH; etc.  
or  $\text{NaBH}_4$ ,  $\text{CH}_3\text{OH}$ ;  $\text{LiAlH}_4$ ,  $\text{Et}_2\text{O}$ , extended time

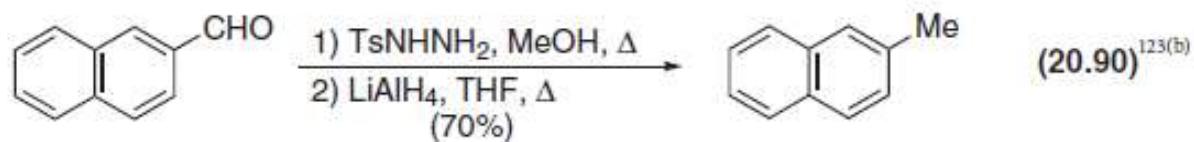
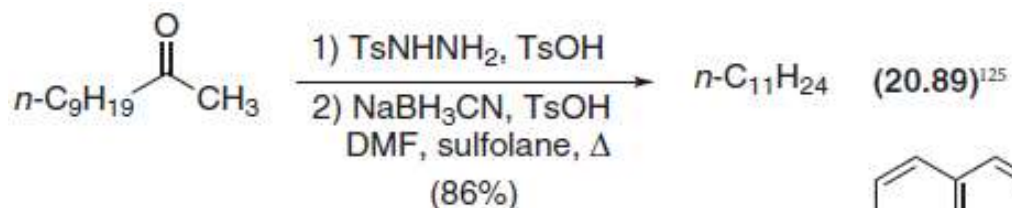
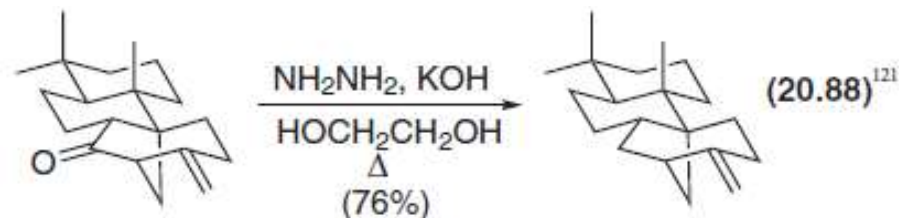
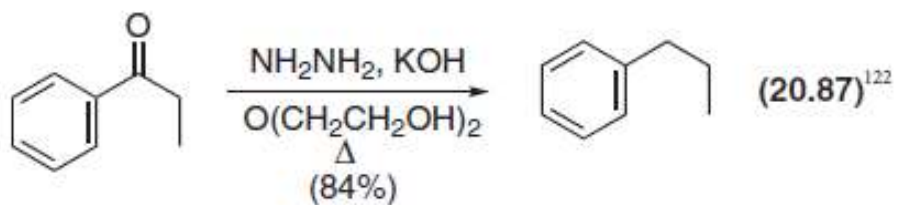
# Reaction synopses: Pinacol and McMurry reactions



Reagents: Mg(Hg), Et<sub>2</sub>O; Zn(Hg), Et<sub>2</sub>O; Al(Hg), Et<sub>2</sub>O; etc.  
or Ti, THF, TiCl<sub>3</sub>, K, THF; etc. (gives diol if alkene would violate Bredt's rule)  
or Mn, TiCl<sub>4</sub>, THF; etc. (allows the diastereoselective crossed pinacol reaction of aromatic aldehydes)

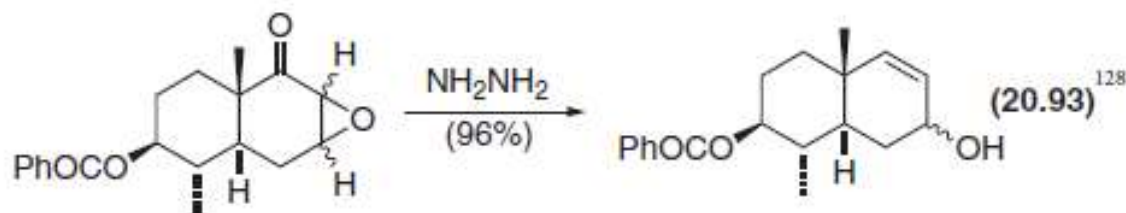
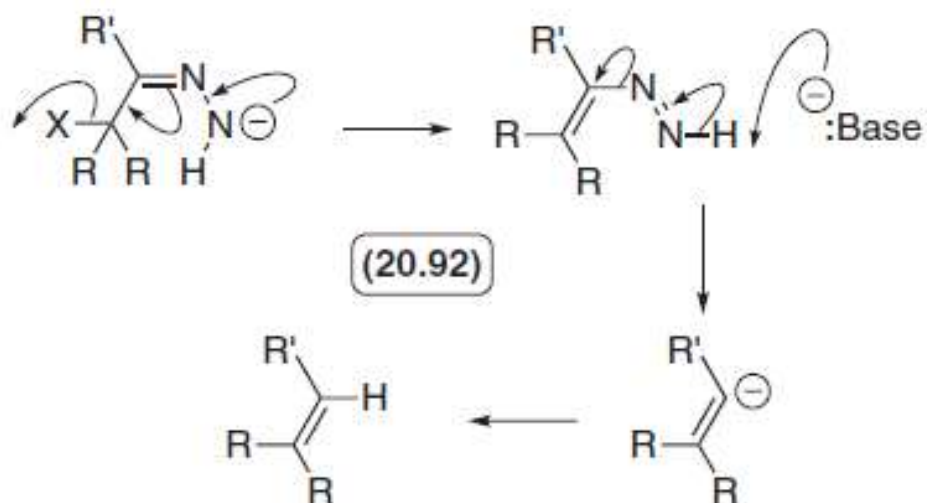


# Representative Wolff-Kishner-type reductions



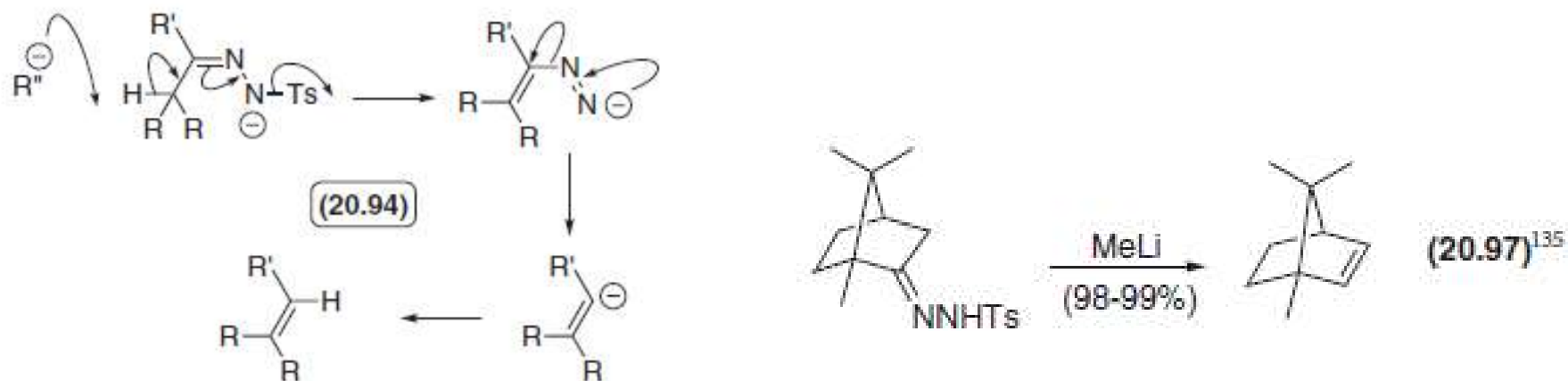
- These reactions are Huang-Minlon modifications of the Wolff-Kishner reduction, which are the most widely used variant of the reaction
- These variants of the reduction use tosylhydrazones instead of the hydrazones; reduction with sodium cyanoborohydride completes the reaction without the need for strong bases

# Wolff-Kishner reduction of $\alpha$ -haloketones and the Wharton reaction



- Wolff-Kishner reduction of  $\alpha$ -haloketones and similar compounds gives alkenes
- the same reaction with an  $\alpha,\beta$ -epoxyketone is known as the Wharton reaction, and gives the allylic alcohol

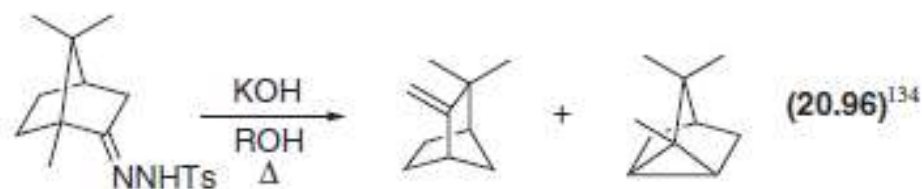
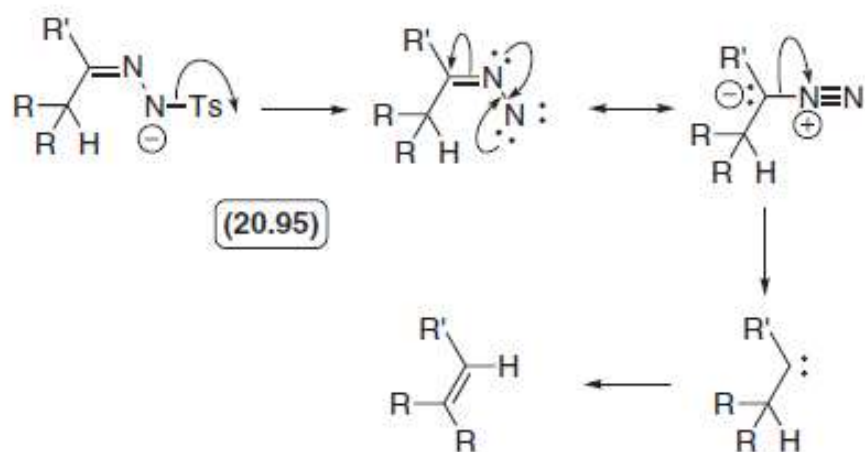
# Fragmentation of tosylhydrazones with methyllithium: the Shapiro reaction



- the treatment of a tosylhydrazone with methyllithium produces a vinyl anion; the reaction is known as the Shapiro reaction

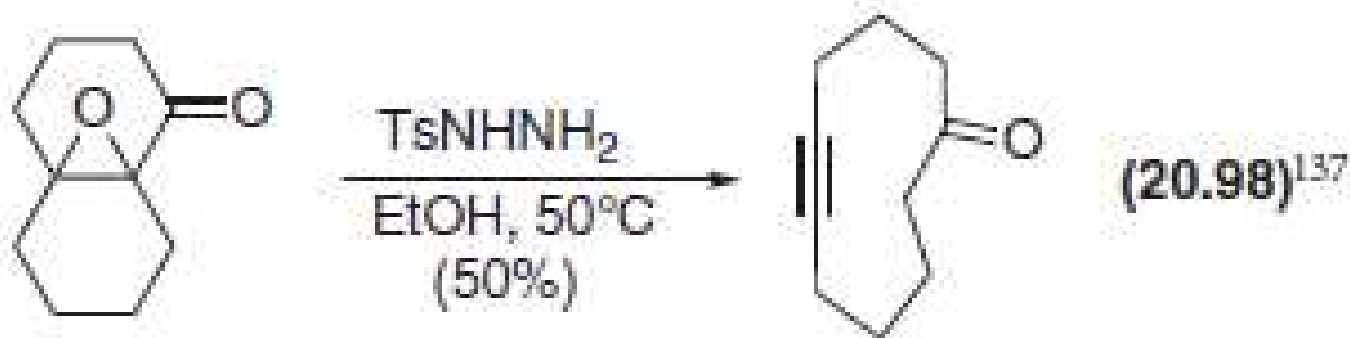


# Fragmentation of tosylhydrazones with oxyanion bases: the Bamford-Stevens reaction



- the treatment of a tosylhydrazone with an oxyanion base produces a carbene; the reaction is known as the Bamford-Stevens reaction

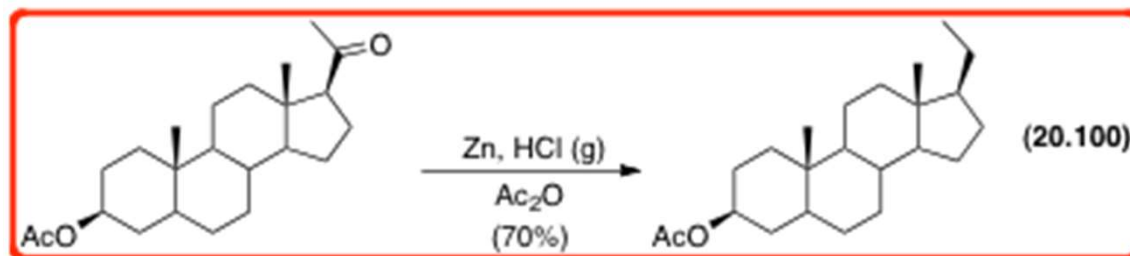
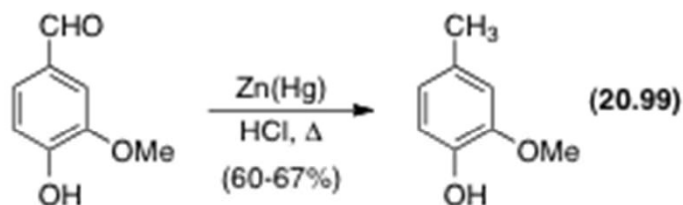
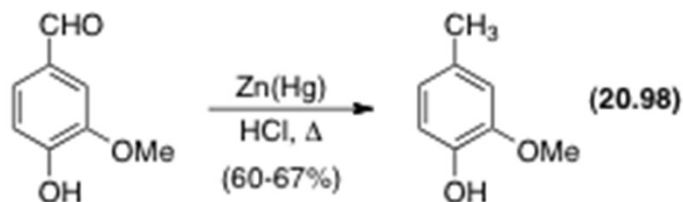
# Eschenmoser-Tanabe fragmentation



- Heating an  $\alpha$ ,  $\beta$ -epoxyketone with tosylhydrazine leads to formation of the tosylhydrazone, followed by fragmentation to give an alkynyl ketone.
- This reaction requires that the  $\beta$  carbon of the epoxyketone not carry a hydrogen atom

# Representative Clemmensen reductions

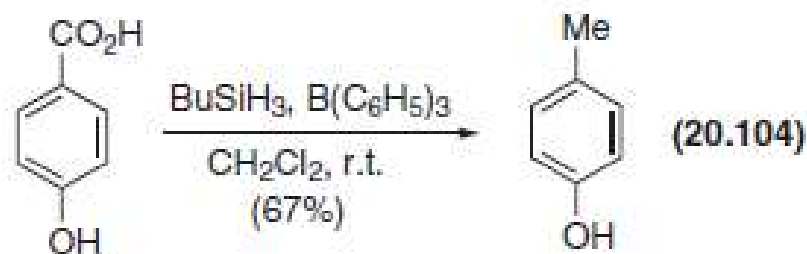
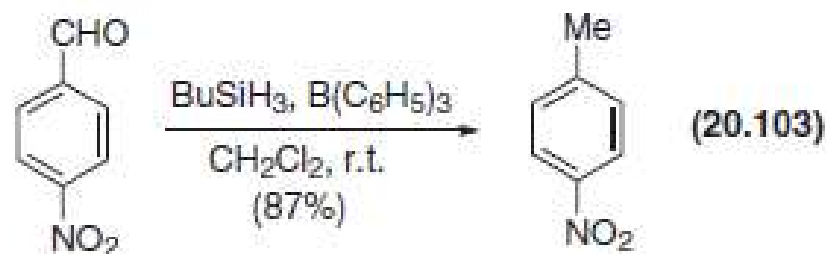
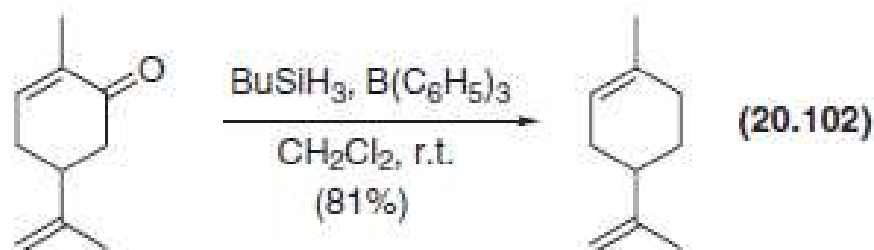
- when an aldehyde or ketone is heated with concentrated hydrochloric acid and zinc amalgam, the carbonyl group is deoxygenated
- rearrangements do occur during some Clemmensen reductions, suggesting that carbocation intermediates may be involved.
- an alternative procedure, using zinc and hydrogen chloride gas, can be used when acid-catalyzed hydrolysis of functional groups is to be avoided



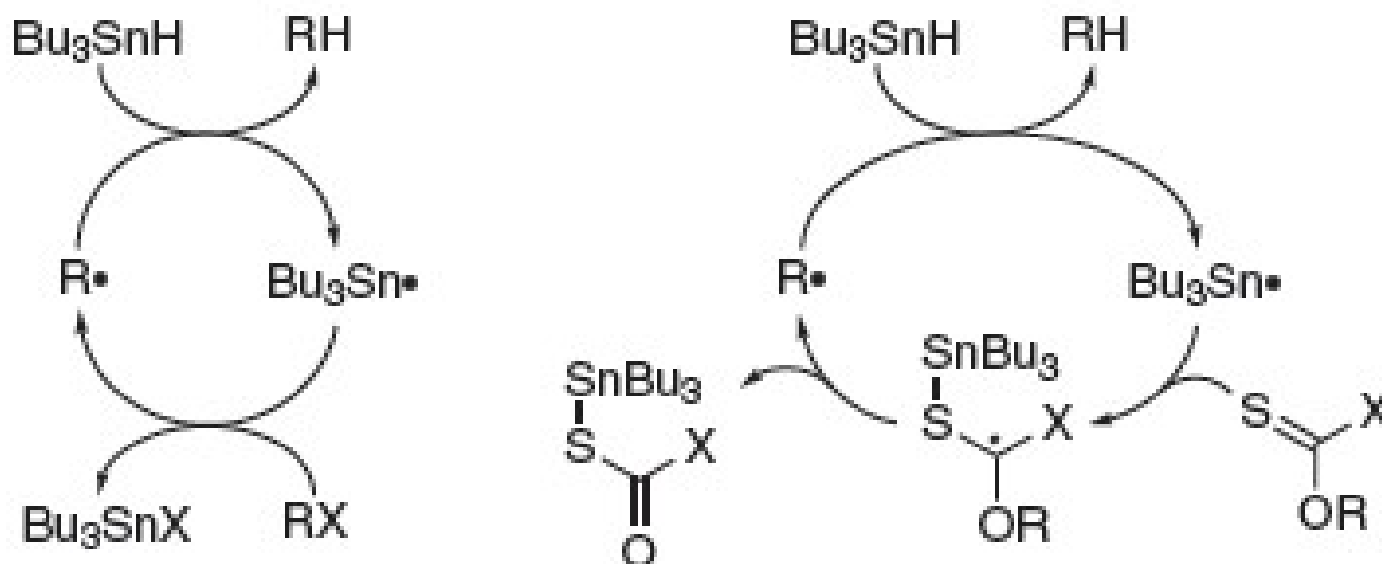


# Deoxygenation with silane reagents

- butylsilane reduces carbonyl groups to the level of the hydrocarbon in the presence of tri(pentafluorophenyl)borane as a Lewis acid activator.
- aldehydes and ketones are reduced to the corresponding alkanes
- unexpectedly, this reagent also reduces carboxyl groups to methyl groups

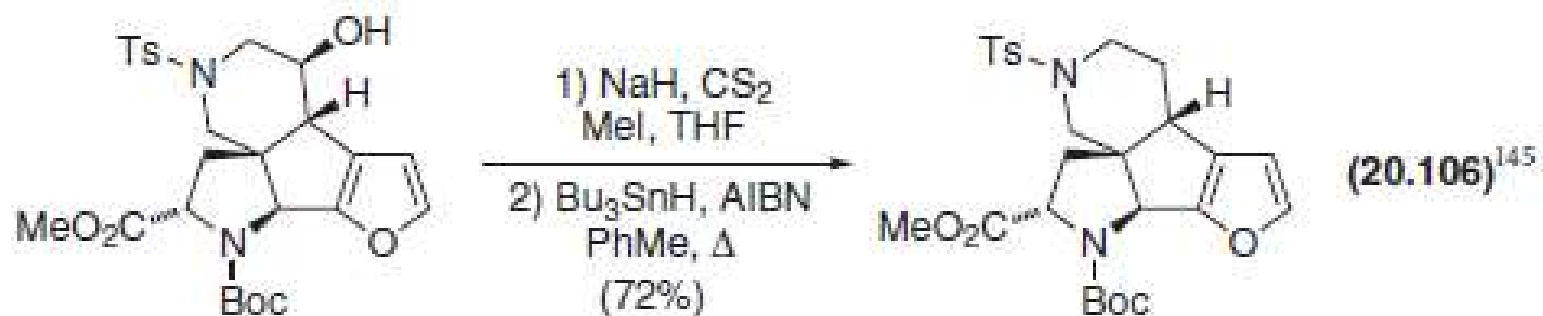
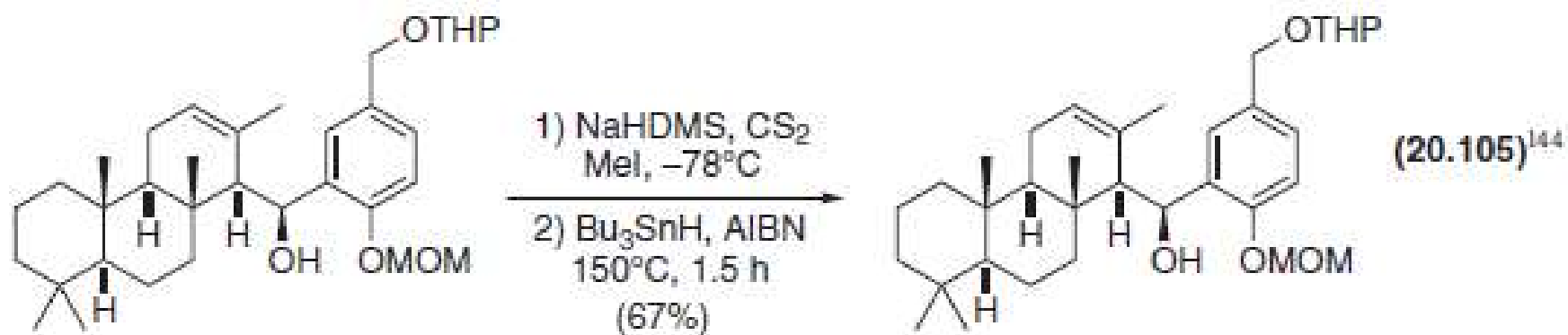


# Figure 20.8

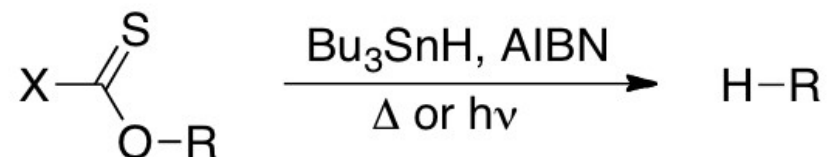


- The free radical chain reaction for reduction of halides (left) or thioesters (right) with tributylstannane.

# Representative Barton-McCombie deoxygenation reactions



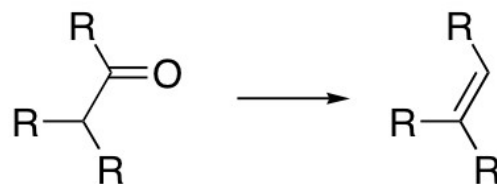
# Reaction synopses: Deoxygenation to alkanes



X: Ar, R, SR, imidazole, ArO, etc.



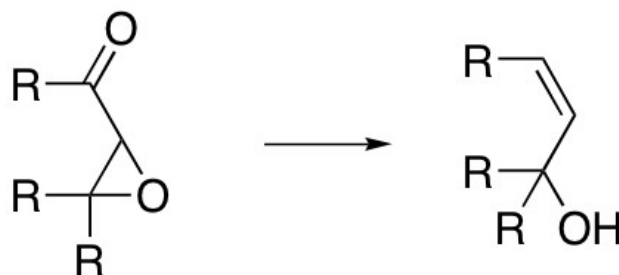
# Reaction synopses: Deoxygenation to alkenes



Reagents: 1) TsNHNH<sub>2</sub>, MeOH, Δ, 2) MeLi, THF (Shapiro)  
or 1) TsNHNH<sub>2</sub>, MeOH, Δ, 2) NaOR, THF (Bamford-Stevens)

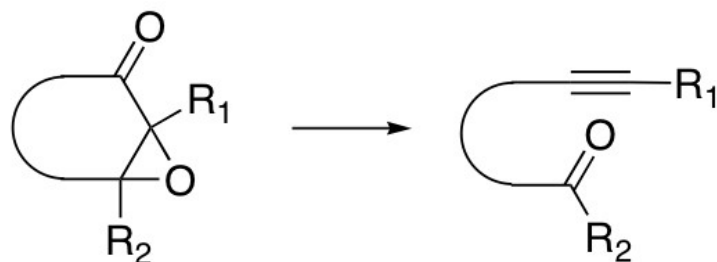
Regiochemistry: Shapiro reaction gives less substituted alkene;  
Bamford-Stevens reaction gives more substituted alkene.

# Reaction synopses: Wharton reaction



Reagents: 1)  $\text{TsNHNH}_2$ ,  $\text{MeOH}$ ,  $\Delta$ , 2) base.

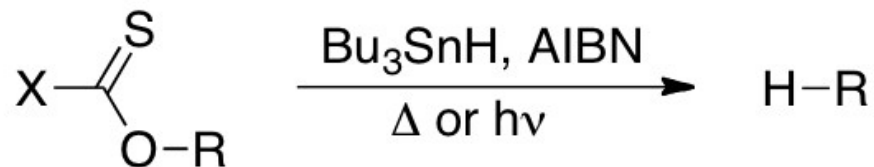
# Reaction synopses: Eschenmoser-Tanabe fragmentation



Reagents: TsNHNH<sub>2</sub>, ROH,  $\Delta$ .





Restrictions: The  $\beta$  position may not carry a hydrogen.

# Reaction synopses: Barton-McCombie deoxygenation

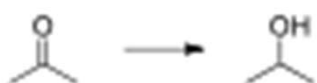


X: Ar, R, SR, imidazole, ArO, etc.


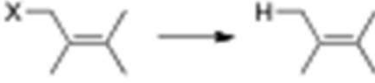

# Catalog of Reduction Reactions-1

Transformation	Reagents	Incompatible Functional Groups; Other Limitations or Features
	$H_2$ , $PtO_2$ ; $H_2$ , Pd-C; $H_2$ , Ra-Ni; $H_2$ , Ru	<i>alkynes, C=N bonds</i> ; addition of H— H is <i>syn</i> . Pt and Pd catalysts can cause $\pi$ bond migration
	$H_2$ , $(Ph_3P)_3RhCl$ , and similar Rh, Ru, Ir compounds	chiral diphosphine ligands on catalyst allow enantioselective reduction
	$R_3SiH$ , $CF_3CO_2H$ ;	alkene must be able to give a stable carbocation ( $3^\circ$ , allyl, benzyl)
	$HCO_2H$ , Pd-C; 1,4- cyclohexadiene, Pd-C; $NH_4OCHO$ , Pd-C; etc.	transfer hydrogenation; tolerates a wide range of functional groups
	$H_2$ , Pd-BaSO <sub>4</sub> , Pb,	gives <i>Z</i> alkene
	Li, $NH_3$ , ROH	gives <i>E</i> alkene
	Hantzsch ester, Brønsted acid	
	Li, $NH_3$ , THF; Na, EtOH; etc.	<i>saturated aldehydes, esters, ketones, nitriles; conjugated dienes; benzyl derivatives</i>
	$H_2$ , catalyst	<i>alkenes, alkynes, benzyl derivatives</i>





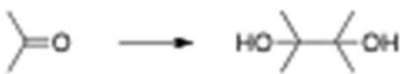




# Catalog of Reduction Reactions-2

Transformation	Reagents	<i>Incompatible Functional Groups; Other Limitations or Features</i>
	LiAlH <sub>4</sub> ; Red-Al®; etc.	reduces esters to primary alcohols
	NaBH <sub>4</sub>	does not reduce esters; reduces conjugated ketones very slowly
	Al(O- <i>i</i> -Pr) <sub>3</sub> , <i>i</i> -PrOH, Δ	reaction is reversible; thermodynamically most stable alcohol predominates
	Na, EtOH; Li, NH <sub>3</sub> , ROH; etc.	<i>conjugated carbonyl compounds</i>
	Et <sub>3</sub> SiH, CF <sub>3</sub> CO <sub>2</sub> H	if conjugated with alkene, alkene π bond reacts first
	HCO <sub>2</sub> Na, Ru-TsDPEN	<i>alkenes in conjugated systems</i> ; allows enantioselective reduction
	DIBAL-H etc.	reduces esters to hemiacetals at low temperature

# Catalog of Reduction Reactions-3

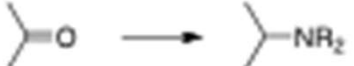


Transformation	Reagents	Incompatible Functional Groups; Other Limitations or Features
	DIBAL-H	<i>other carbonyl compounds, nitriles</i>
	NaBH <sub>4</sub> , CeCl <sub>3</sub>	can also be used to reduce nitriles to primary amines
	H <sub>2</sub> , Pd-C; H <sub>2</sub> , Ni; etc.	stereochemistry depends on metal catalyst
	Li, NH <sub>3</sub> , ROH	<i>carbonyl compounds; conjugated systems</i>
	NH <sub>2</sub> NH <sub>2</sub> , KOH, HOCH <sub>2</sub> CH <sub>2</sub> OH, Δ	<i>groups susceptible to strong bases</i>
		TsNHNH <sub>2</sub> , NaBH <sub>3</sub> CN, HOAc-MeOH
	Zn(Hg), HCl, Δ	<i>groups susceptible to strong acids</i>
	BuSiH <sub>3</sub> , B(C <sub>6</sub> F <sub>5</sub> ) <sub>3</sub>	
	1) HSCH <sub>2</sub> CH <sub>2</sub> SH, BF <sub>3</sub> ; 2) H <sub>2</sub> , Ni or Li, NH <sub>3</sub>	

# Catalog of Reduction Reactions-4

Transformation	Reagents	Incompatible Functional Groups; Other Limitations or Features
	1) TsNHNH <sub>2</sub> , 2) MeLi; or 1) TsNHNH <sub>2</sub> ; 2) KOBu <sup>t</sup>	MeLi gives vinyl anion; carbenes may be involved when KOBu <sup>t</sup> is used as base.
	H <sub>2</sub> , Pd-C	X=halogen
	Bu <sub>3</sub> SnH, AIBN, hv	X=halogen, OC(S)SMe
	L-Selectride®; Hydride <sup>TM</sup> ; etc.	Super-Hydride <sup>TM</sup> ; etc. X=halogen, OSO <sub>2</sub> R; reaction occurs with inversion.
	Ti, THF; TiCl <sub>3</sub> , K, THF; etc.	
	Mg(Hg), Et <sub>2</sub> O; Zn(Hg), Et <sub>2</sub> O; Al(Hg), Et <sub>2</sub> O; etc.	
	Mn, TiCl <sub>3</sub> , THF	
	1) TsNHNH <sub>2</sub> , 2) MeLi; or 1) TsNHNH <sub>2</sub> ; 2) KOBu <sup>t</sup>	MeLi gives vinyl anion; carbenes may be involved when KOBu <sup>t</sup> is used as base.
	Na, THF; Na-K, THF	carbonyl compounds



# Catalog of Reduction Reactions-5

Transformation	Reagents	<i>Incompatible Functional Groups; Other Limitations or Features</i>
	R <sub>2</sub> NH, NaBH <sub>3</sub> CN, HOAc; R <sub>2</sub> NH, Na (OAc) <sub>3</sub> BH <sub>4</sub>	reduction works best under acidic conditions
	1) NH <sub>2</sub> OH; H <sub>2</sub> , Ra-Ni	
	R <sub>2</sub> NH, HCO <sub>2</sub> H, Pd-C; etc.	ammonium formate may also be used
	HCHO, HCO <sub>2</sub> NH <sub>4</sub> , Δ; etc.	gives product where R=Me
	LiAlH <sub>4</sub> , Et <sub>2</sub> O, Δ; etc.	X=CN → G=CH <sub>2</sub> NH <sub>2</sub> ; X=CONR <sub>2</sub> → G=CH <sub>2</sub> NR <sub>2</sub> ;
	H <sub>2</sub> , Pd-C; etc.	X=N <sub>3</sub> → G=NH <sub>2</sub> ; X=NO <sub>2</sub> → G=NH <sub>2</sub> ; etc.
	BH <sub>3</sub> •THF; etc.	X=CN → G=CH <sub>2</sub> NH <sub>2</sub>
	NaBH <sub>4</sub> , CeCl <sub>3</sub>	X=CN → G=CH <sub>2</sub> NH <sub>2</sub>
	H <sub>2</sub> Pd-C; etc.	
	Li, NH <sub>3</sub> , <i>t</i> -BuOH; etc.	<i>carbonyl compounds, conjugated compounds, alkynes</i>

# Catalog of Reduction Reactions-6

Transformation	Reagents	Incompatible Functional Groups; Other Limitations or Features
	1) TsNHNH <sub>2</sub> , 2) base	
	TsNHNH <sub>2</sub> , EtOH, Δ; etc.	β position of epoxyenone must be fully substituted
	Al(OR) <sub>3</sub> ; SmI <sub>2</sub> ; Shvo's Ru catalyst, ROH; etc.	
	NaOH; H <sub>2</sub> CO, NaOH; etc.	
	DIBAL-H, -78°C (ester); DIBAL-H, 0°C (nitrile)	aldehydes, ketones, acid chlorides
	(X=Cl): LiAl(OBu <sup>t</sup> ) <sub>3</sub> ; H <sub>2</sub> , Pd-BaSO <sub>4</sub> , quinoline-S	
	BH <sub>3</sub> •THF	alkenes, amides, nitriles; reaction with carboxylic acids is fastest
	LiAlH <sub>4</sub> , Et <sub>2</sub> O, Δ; etc.	any other carbonyl compound or nitrile