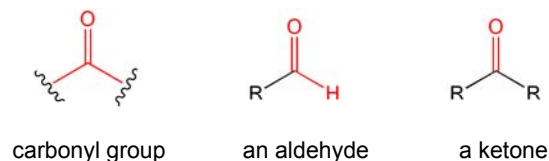
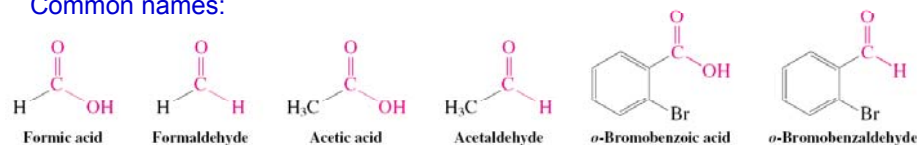


Aldehydes and Ketones

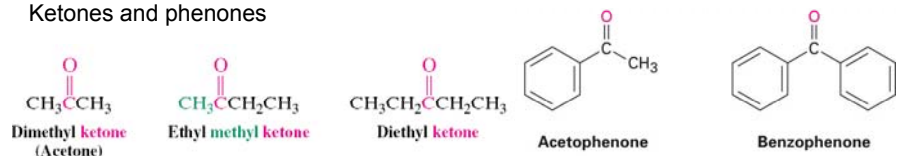


Naming aldehydes and ketones

Common names:



Ketones and phenones

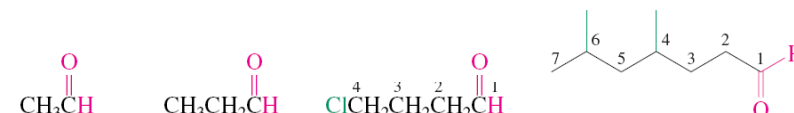


16-1

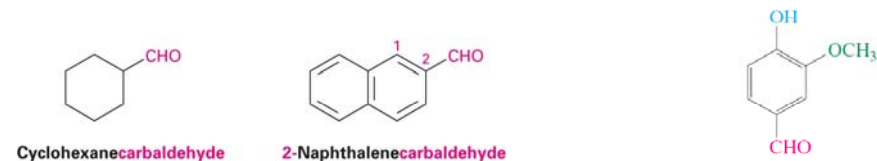
IUPAC Names

Aldehydes:

- IUPAC nomenclature treats aldehydes as derivatives of alkanes. The ending -e is replaced by -al. An alkane becomes an alkanal.
- The aldehyde carbon is numbered C1 and does not have to be specified.



- When -CHO is attached to a ring the compound is called **carbaldehyde**.

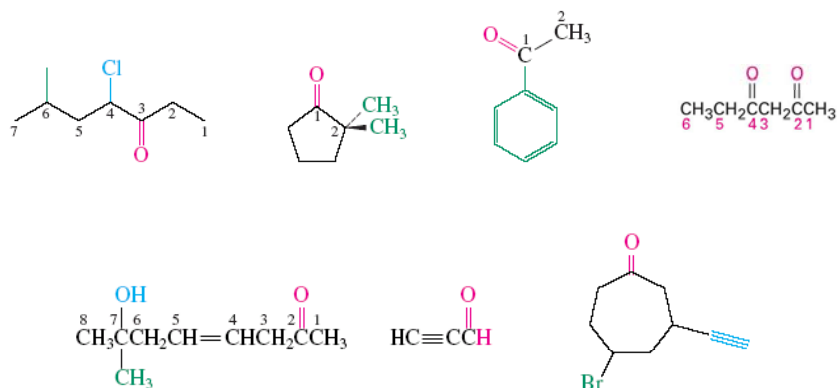


16-2

IUPAC Names

Ketones:

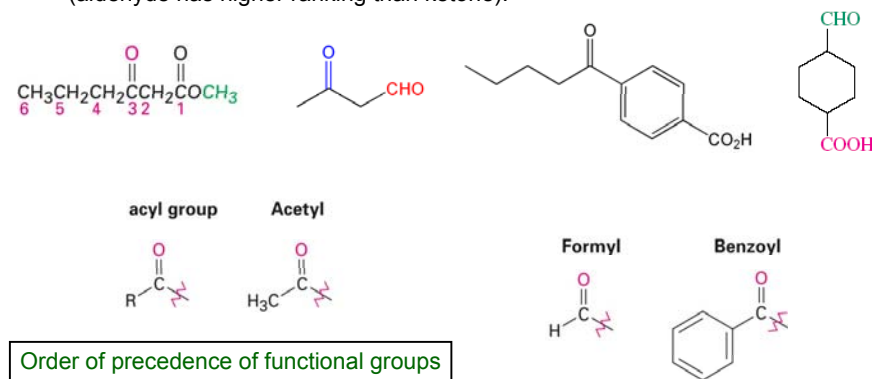
- Ketones are named by replacing the terminal -e of the corresponding alkane name with -one.
- The carbonyl carbon is assigned the lowest possible number.
- carbonyl has higher priority than -OH, C=C, and C≡C.



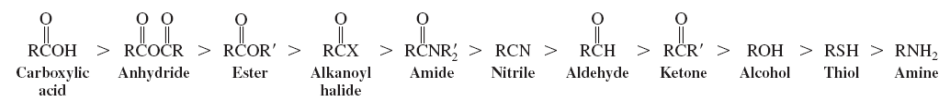
16-3

Naming the Carbonyl Compounds

- When functional group of higher ranking than carbonyl is present, the doubly bonded oxygen is considered a substituent and the prefix oxo- is used (aldehyde has higher ranking than ketone).

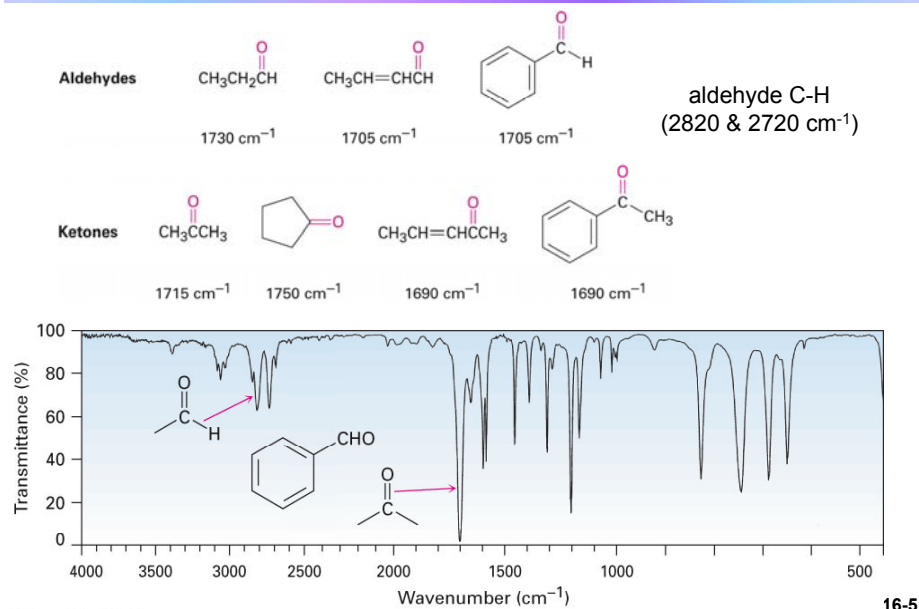


Order of precedence of functional groups



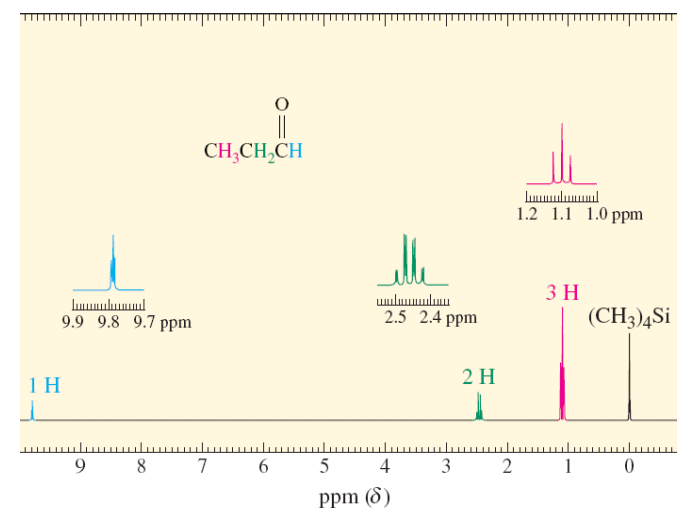
16-4

Reviewing IR Characteristics of Aldehydes & Ketones



16-5

Reviewing NMR Characteristics of Aldehydes & Ketones

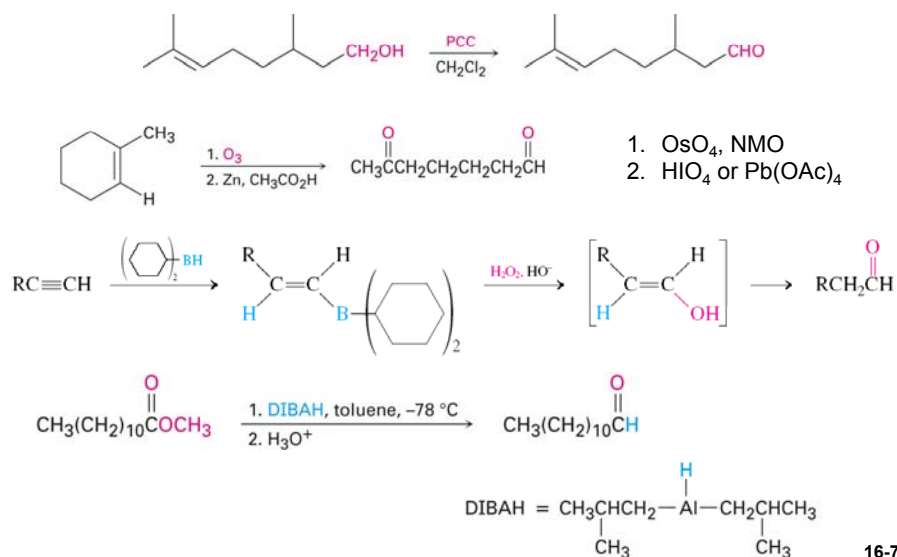


1. Similar to alkenes, the movement of the π electrons in the magnetic field strengthens the external field;
2. The partially positive carbonyl carbon causes additional deshielding.

16-6

Preparation of Aldehydes

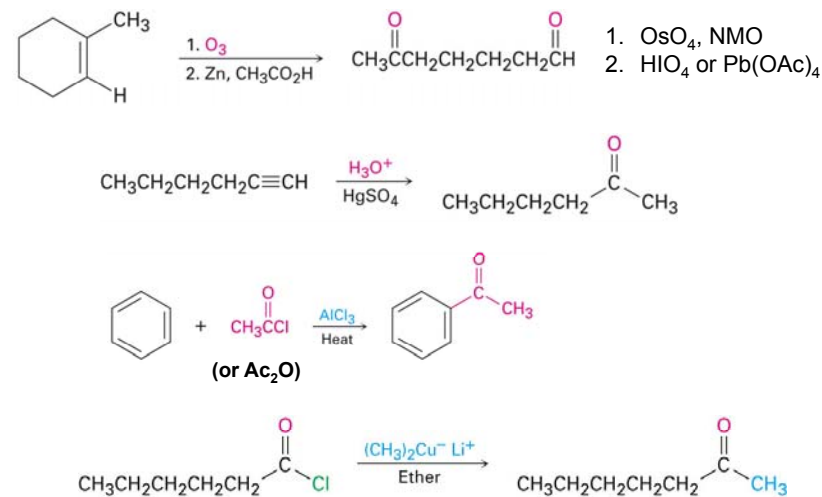
DCC / DMSO, H_3PO_4 (Pfitzner-Moffatt reagent)



16-7

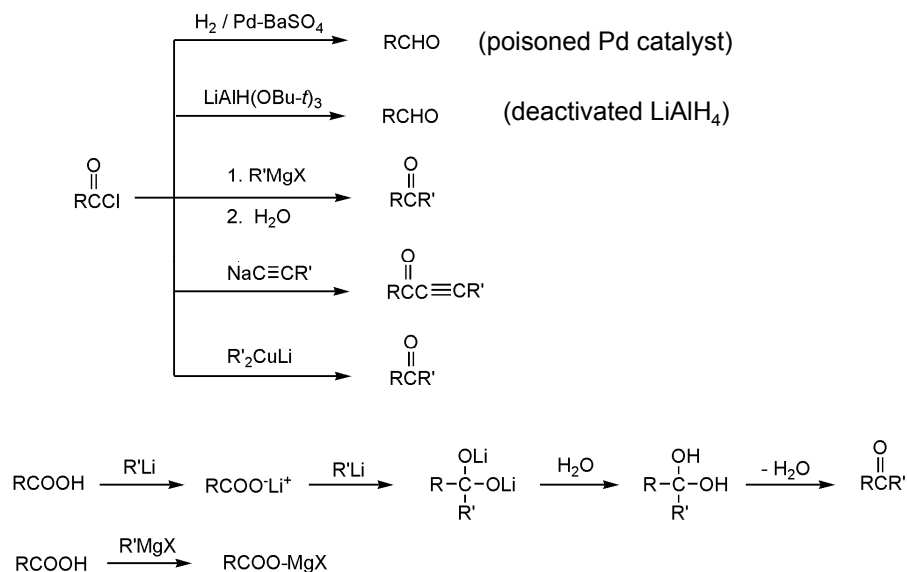
Preparation of Ketones

Oxidation of 2° alcohols: $\text{K}_2\text{Cr}_2\text{O}_7$ or CrO_3 / H_2SO_4 , PCC



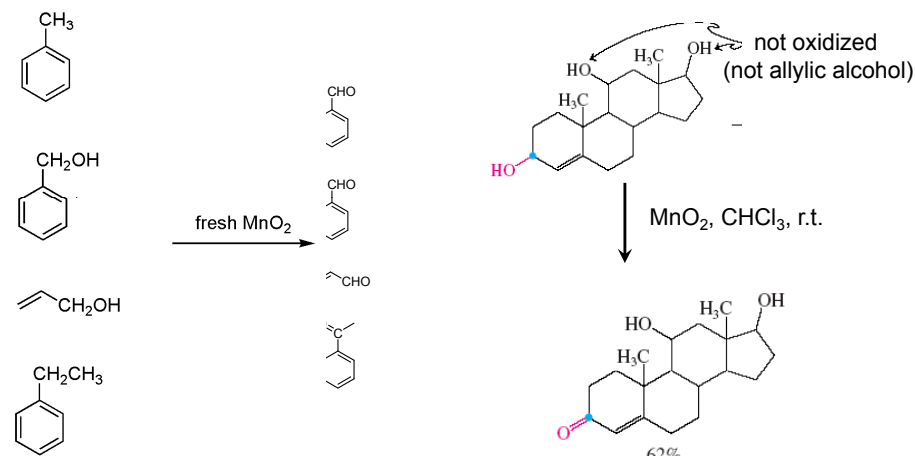
16-8

Preparations of Aldehydes and Ketones



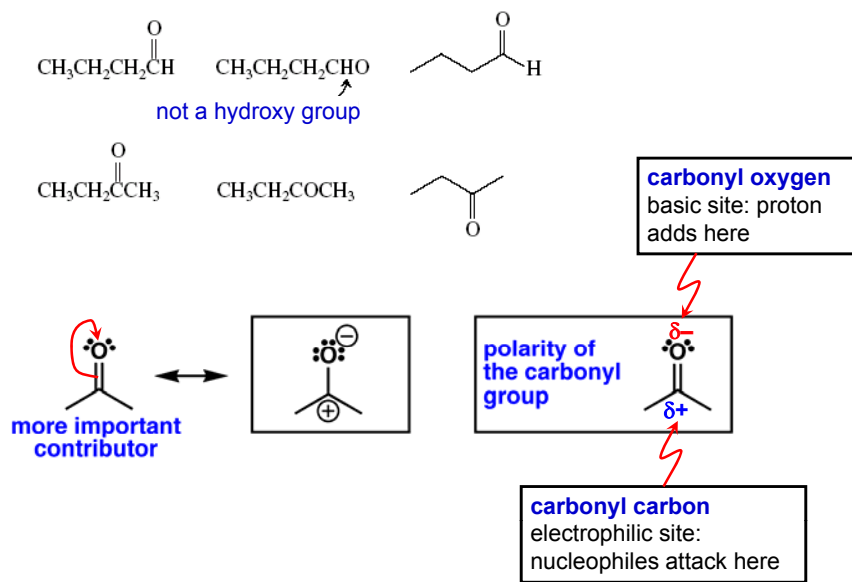
16-9

Selective Oxidation of Allyl and Benzyl C-H Bond with MnO_2



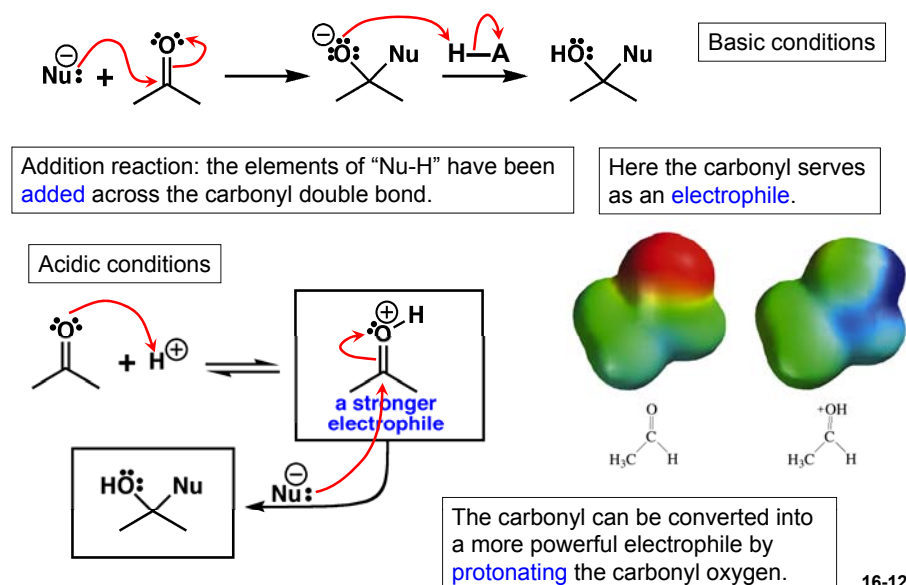
16-10

Description of a Carbonyl Group



16-11

Nucleophilic Addition Reactions



16-12

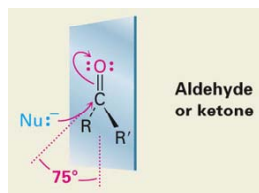
Generalization of Nucleophilic Addition to Aldehydes and Ketones

Some negatively charged nucleophiles

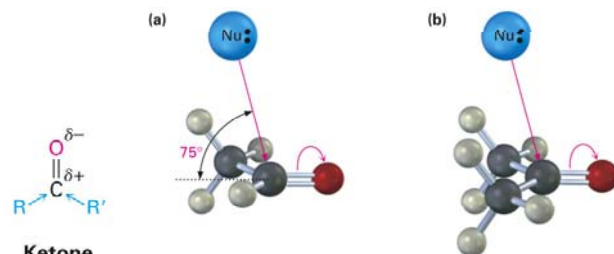
HO^- (hydroxide ion)
 H^- (hydride ion)
 R_3C^- (a carbanion)
 RO^- (an alkoxide ion)
 $\text{N}\equiv\text{C}^-$ (cyanide ion)

Some neutral nucleophiles

HOH (water)
 ROH (an alcohol)
 H_3N (ammonia)
 RNH_2 (an amine)



Aldehyde or ketone

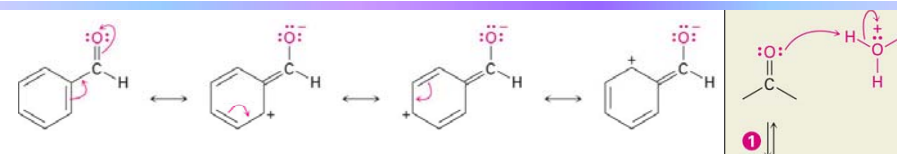


Ketone
 (more stabilization of δ^+ , less reactive)

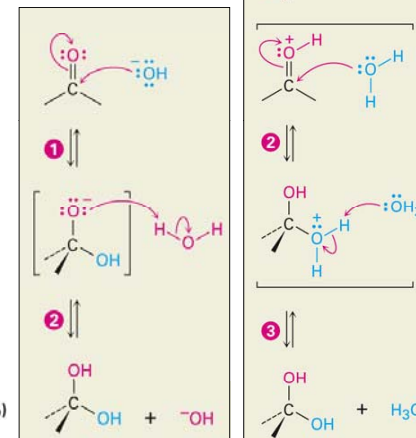
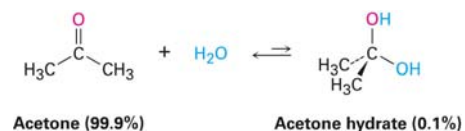
Ketones are less reactive than aldehydes for both steric and electronic reasons.

16-13

Nucleophilic Addition of Water: Hydration

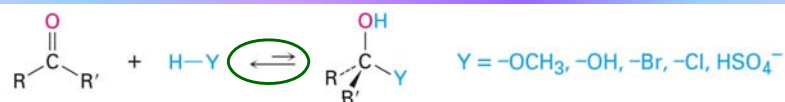


Aromatic aldehydes are less reactive than aliphatic aldehydes due to delocalization of the positive charge.

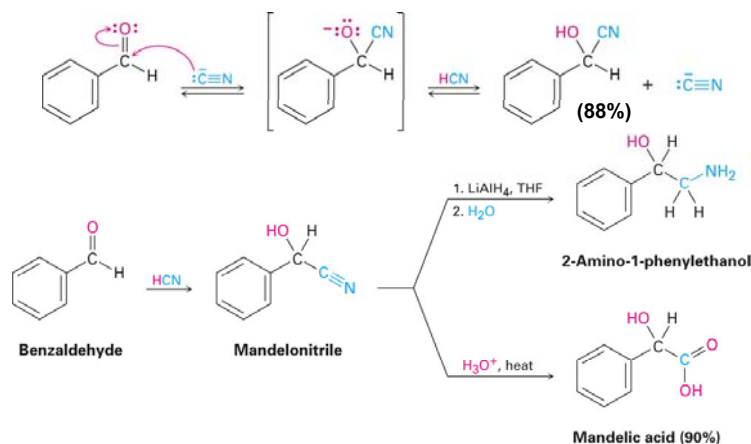


16-14

Nucleophilic Addition of HCN: Cyanohydrin Formation

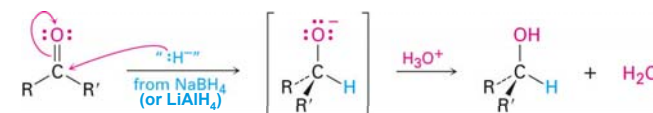
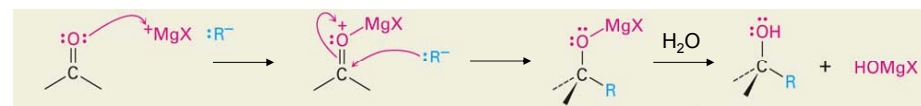


HCN is an exception: equilibrium favors cyanohydrin formation



16-15

Nucleophilic Addition of Grignard Reagent and Hydride: Alcohol Formation

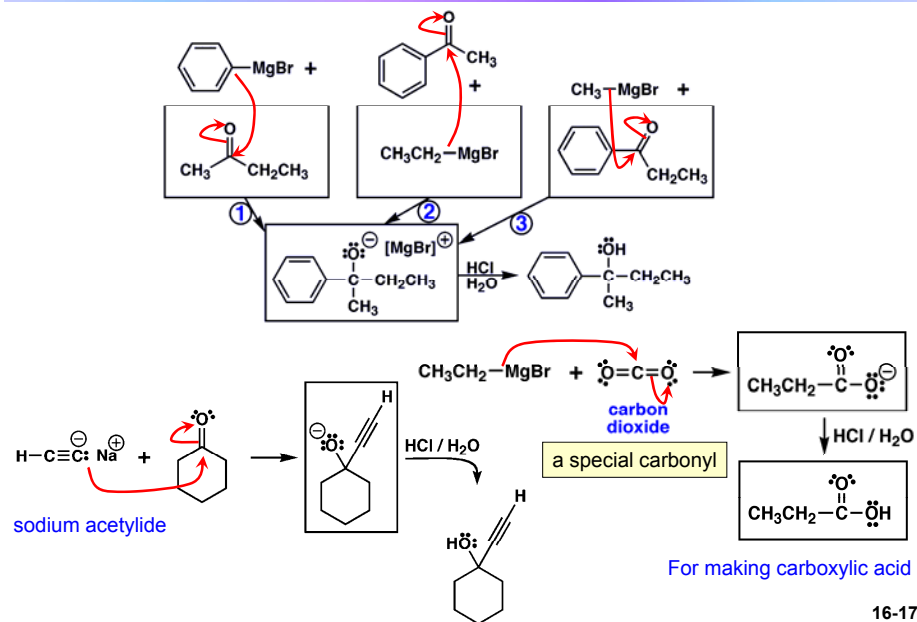


Reaction	Equation	
1. Aldehyde + hydride reagent	$\text{RCHO} \xrightarrow{\text{NaBH}_4, \text{CH}_3\text{CH}_2\text{OH}} \text{RCH}_2\text{OH}$	Primary alcohol
2. Ketone + hydride reagent	$\text{R}_2\text{CO} \xrightarrow{\text{NaBH}_4, \text{CH}_3\text{CH}_2\text{OH}} \text{R}_2\text{CHOH}$	Secondary alcohol
3. Formaldehyde + Grignard reagent	$\text{H}_2\text{CO} \xrightarrow{\text{R}'\text{MgX}, (\text{CH}_3\text{CH}_2)_2\text{O}} \text{R}'\text{CH}_2\text{OH}^a$	Primary alcohol
4. Aldehyde + Grignard reagent	$\text{RCHO} \xrightarrow{\text{R}'\text{MgX}, (\text{CH}_3\text{CH}_2)_2\text{O}} \text{R}'\text{RCHOH}^a$	Secondary alcohol
5. Ketone + Grignard reagent	$\text{R}_2\text{CO} \xrightarrow{\text{R}'\text{MgX}, (\text{CH}_3\text{CH}_2)_2\text{O}} \text{R}'\text{R}_2\text{COH}^a$	Tertiary alcohol

^aAfter aqueous acid work-up.

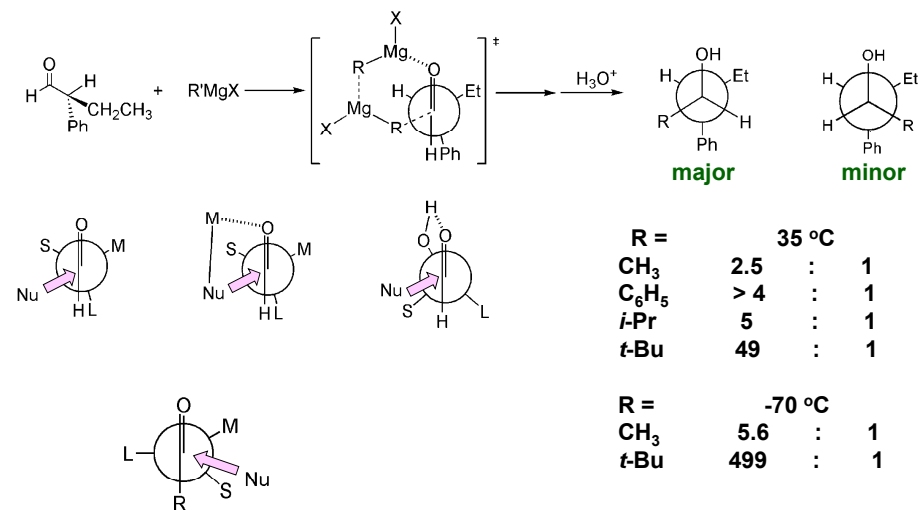
16-16

Nucleophilic Addition of Grignard Reagent



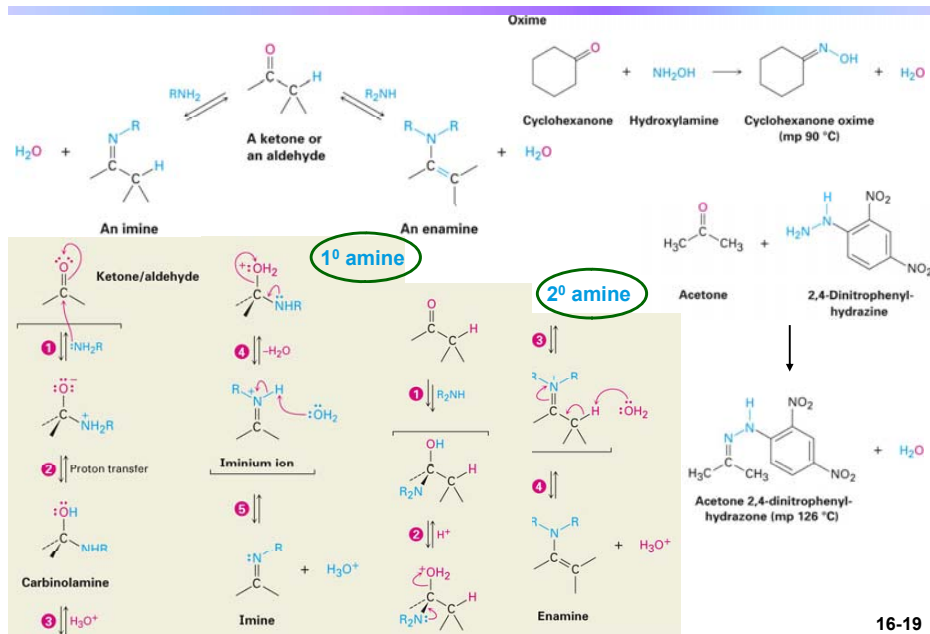
16-17

Stereoselectivity of Nucleophilic Addition to Carbonyl Group: Cram's Rule



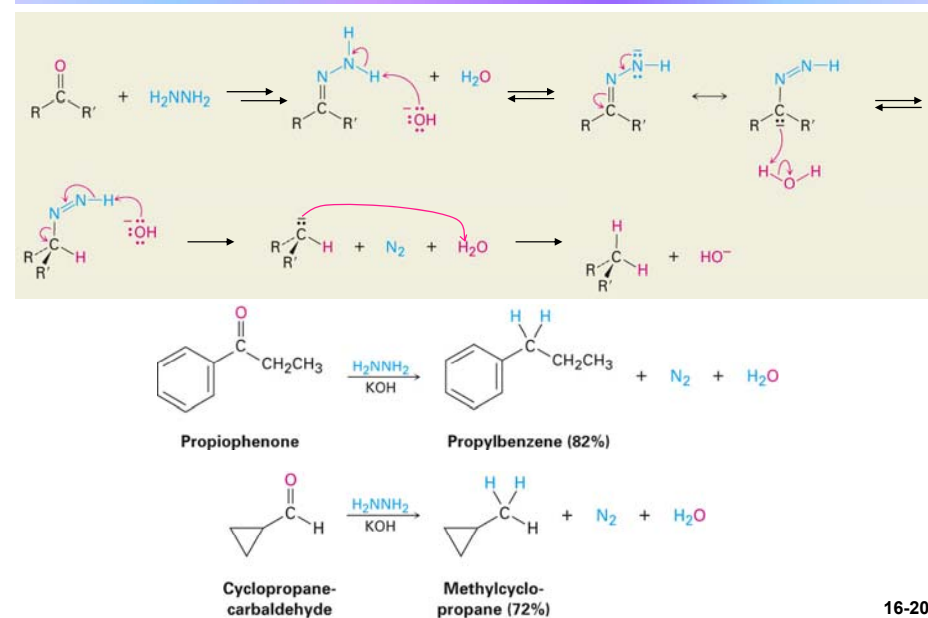
16-18

Imine and Enamine Formation



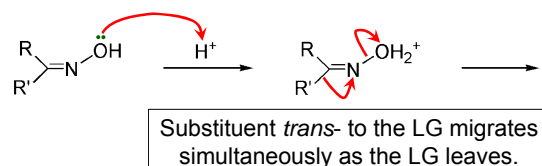
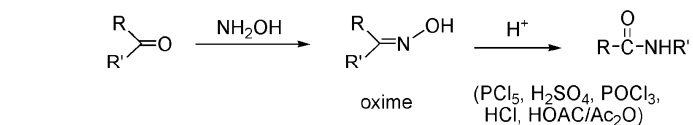
16-19

Wolff-Kishner Reduction: Hydrazine Addition



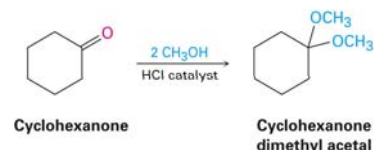
16-20

Beckmann Rearrangement



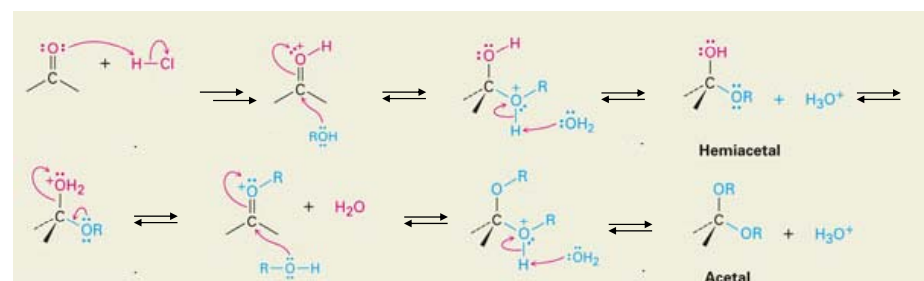
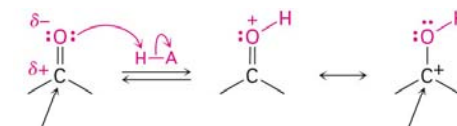
16-21

Nucleophilic Addition of Alcohols: Acetal Formation



Acetals, R₂C(OR')₂, is also called ketals if derived from a ketone.

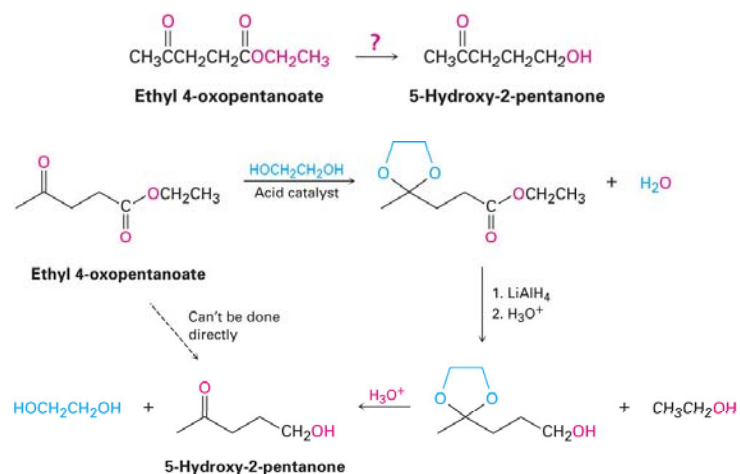
Under acidic conditions, protonated carbonyl becomes a better electrophile.



16-22

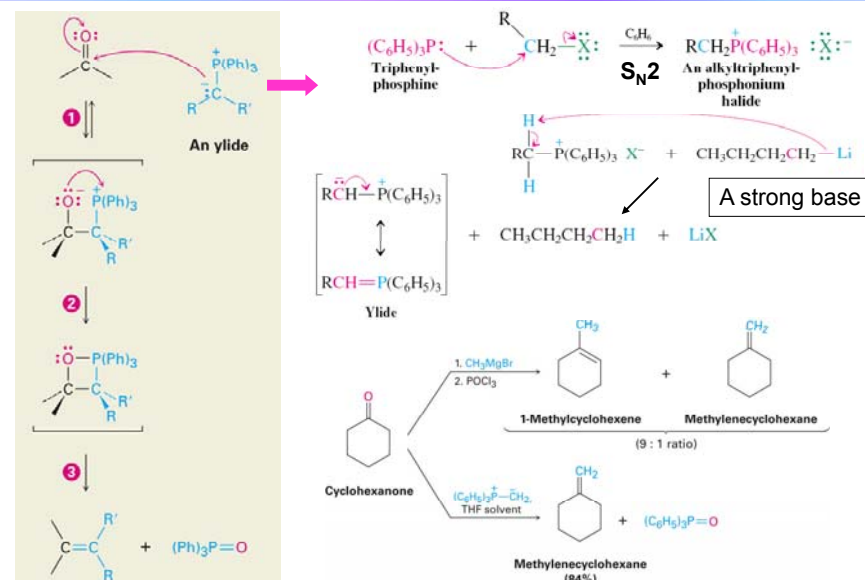
Acetal as Protective Groups for Ketones & Aldehydes

The acetal formation is a reversible equilibrium; in the presence of an acid catalyst it can be shifted in either direction: toward acetal by using excess alcohol or removing water; toward aldehyde or ketone by adding excess water, a process called acetal hydrolysis.



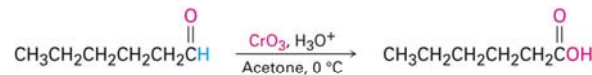
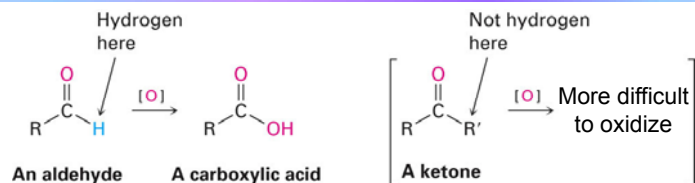
16-23

Nucleophilic Addition of Phosphorus Ylides: the Wittig Reaction

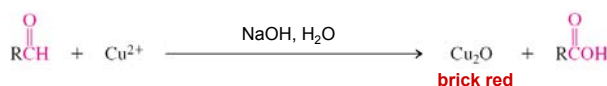
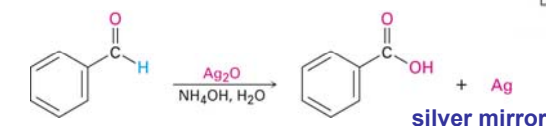
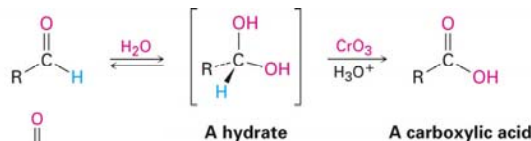


16-24

Oxidation of Aldehydes



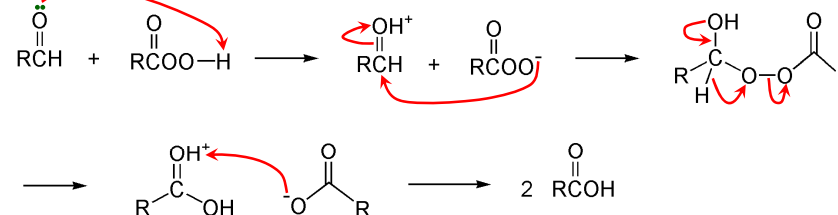
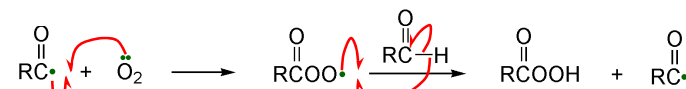
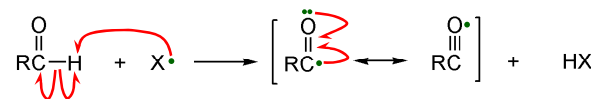
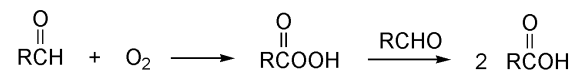
Tollens' test (for both aromatic and aliphatic aldehydes)



Fehling's test (only for aliphatic aldehydes)

16-25

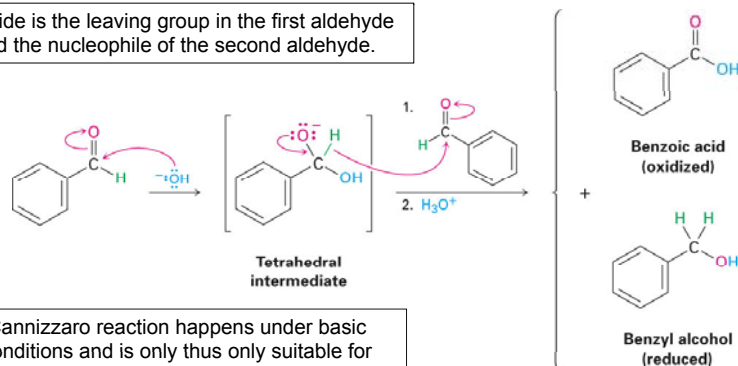
Auto-oxidation of Aldehydes



16-26

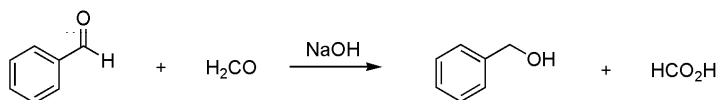
Cannizzaro Disproportionation

Hydride is the leaving group in the first aldehyde and the nucleophile of the second aldehyde.



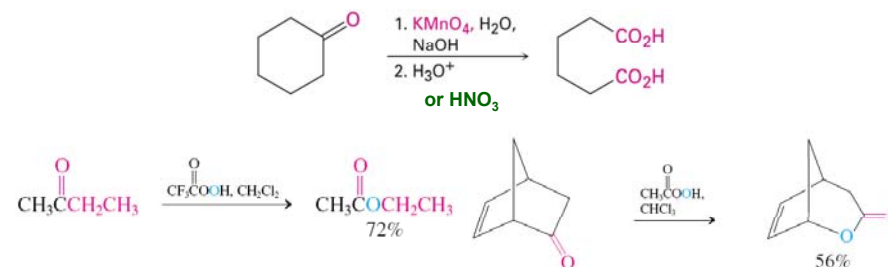
Cannizzaro reaction happens under basic conditions and is only thus only suitable for aldehydes without α -protons (which are acidic).

When two different aldehydes are involved, formaldehyde is usually oxidized (as it's more susceptible to nucleophilic attack).



16-27

Oxidation of Ketones and the Baeyer-Villiger Oxidation



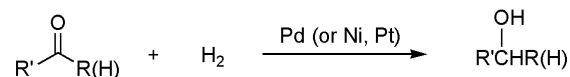
Migratory Aptitudes in the Baeyer-Villiger Reaction

Methyl < primary < phenyl ~ secondary < tertiary

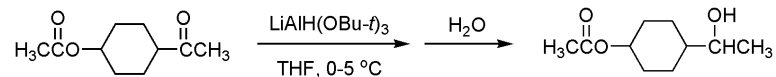
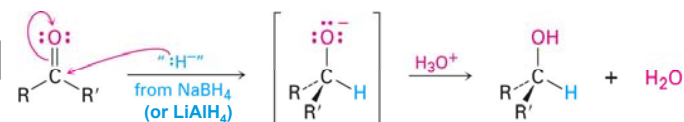
16-28

Reduction of Aldehydes and Ketones into Alcohols

Hydrogenation

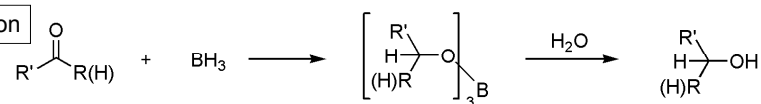


Hydride reduction



Using a deactivated aluminum hydride, ketone is preferably reduced over ester as its carbonyl carbon is more electrophilic; the alkoxy in the ester has an electron-donating resonance effect.

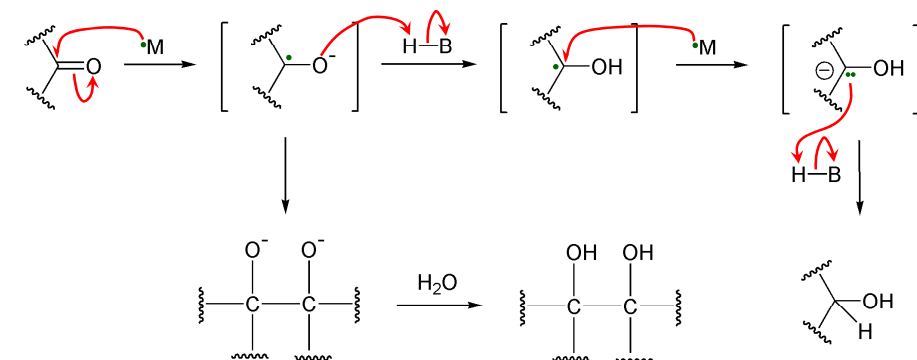
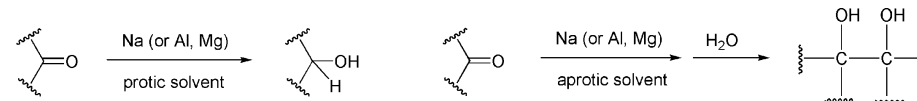
Hydroboration



16-29

Mechanism of Metal Reductions

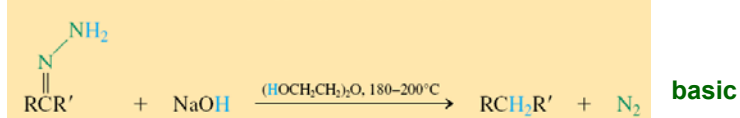
Metal reduction



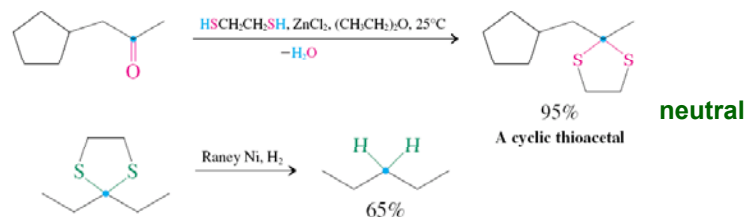
16-30

Deoxygenation of Aldehydes and Ketones

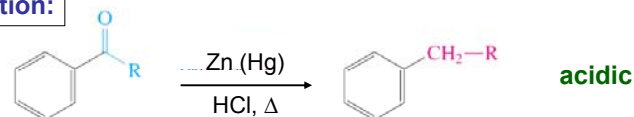
Wolff-Kishner Reduction



Cyclic Thioacetal Formation from a Ketone

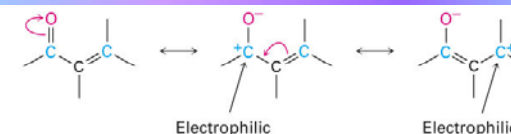


Clemmson reduction:

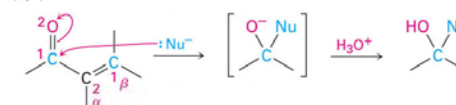


16-31

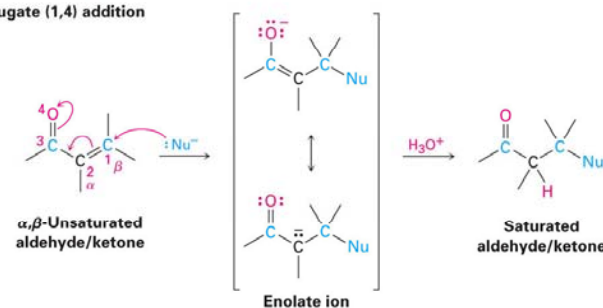
Reactions of α,β -Unsaturated Aldehydes and Ketones



Direct (1,2) addition

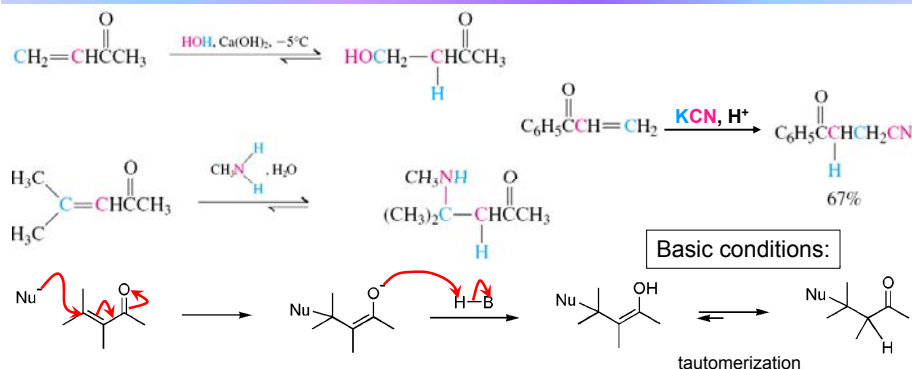


Conjugate (1,4) addition



16-32

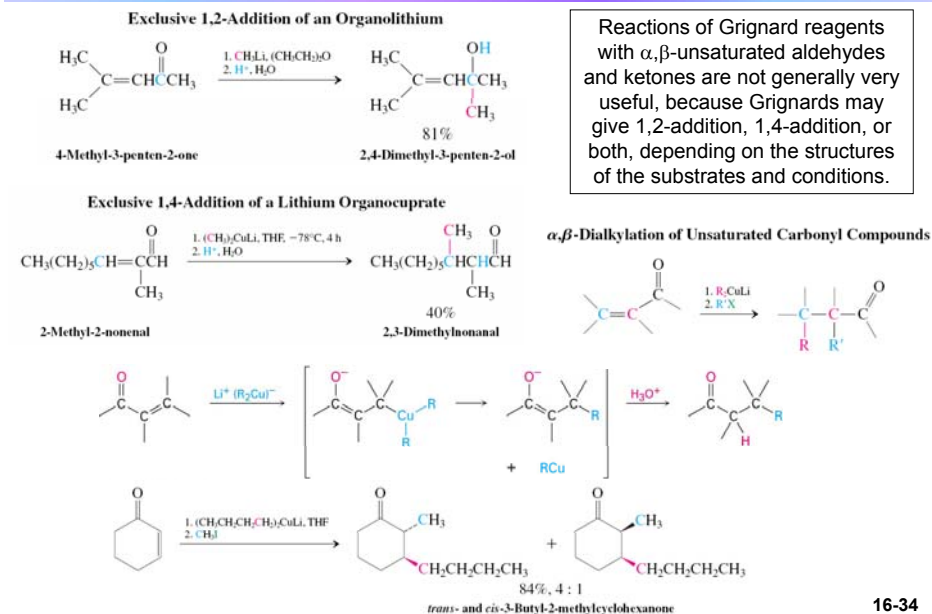
1,4-Conjugate Additions



Acidic conditions:

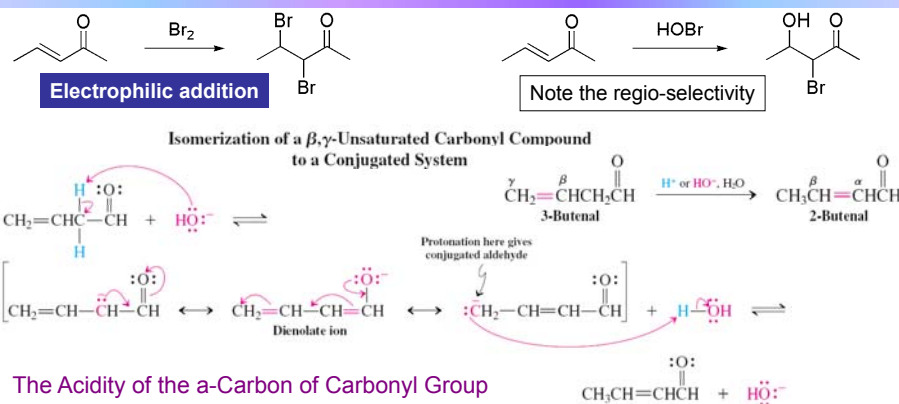
16-33

1,2- and 1,4-Additions of Organometallic Reagents

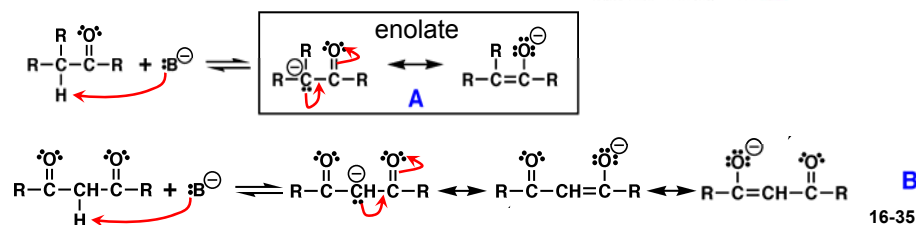


16-34

Other Reactions of α,β -Unsaturated Aldehydes and Ketones

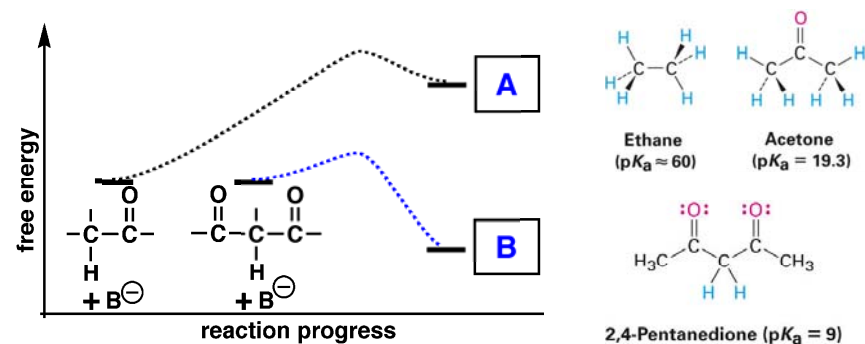


The Acidity of the α -Carbon of Carbonyl Group



16-35

The Acidity of the α -Carbon of Carbonyl Group



Extend this reasoning to explain why the α -hydrogen of esters are less acidic than ketones.



16-36

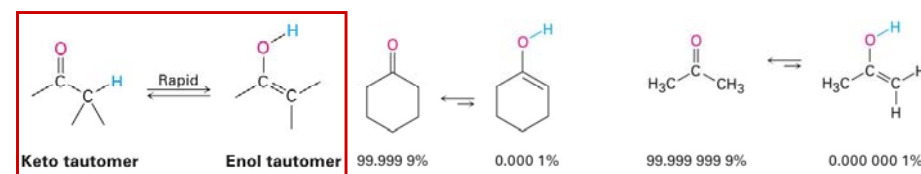
The Acidity of the α -Carbon of Carbonyl Group

TABLE 19.1 The pK_a Values of Some Carbon Acids

	pK_a		pK_a
	30		11.8
	25		10.7
	25		9.4
	20		8.9
	17		5.9
	8.6		3.6

16-37

Keto-Enol Tautomerism

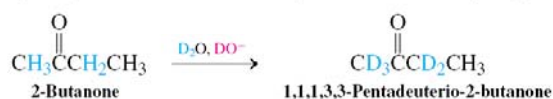


Acid-Catalyzed Enol-Keto Equilibration

16-38

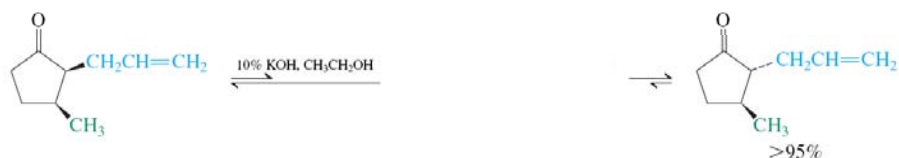
Reactions Facilitated by α -Proton Acidity

Hydrogen-Deuterium Exchange of Enolizable Hydrogens



Would similar processes occur under acidic conditions?

Base-Catalyzed Isomerism of an α -Substituted Ketone



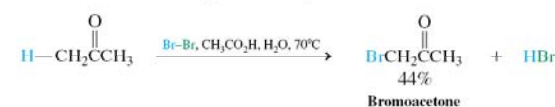
Racemization of Optically Active 3-Phenyl-2-butanone



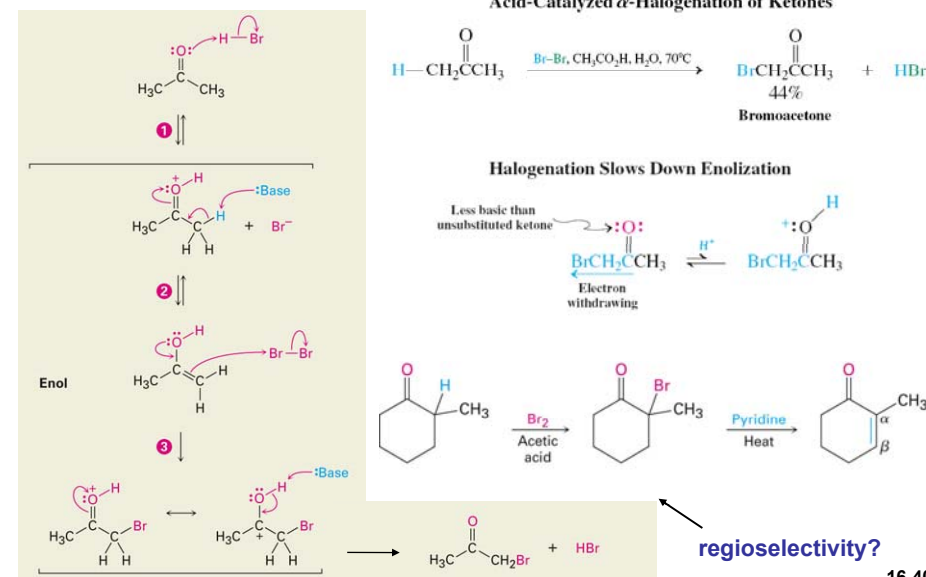
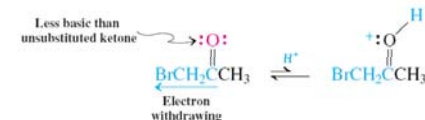
16-39

α -Halogenation of Aldehydes and Ketones

Acid-Catalyzed α -Halogenation of Ketones

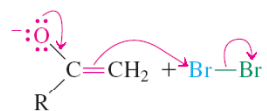


Halogenation Slows Down Enolization

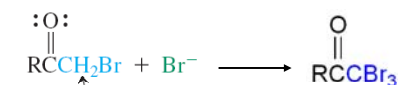


16-40

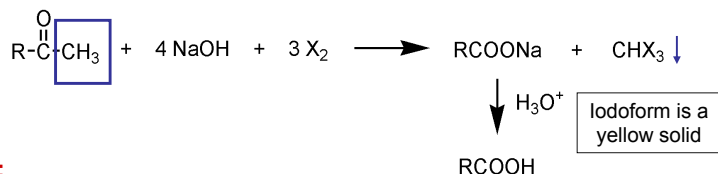
Base-Catalyzed α -Halogenation



The electron-withdrawing power of the halogen substituent makes the remaining α -hydrogens more acidic and complete halogenation of the α -carbon occurs, leaving unreacted starting material (when insufficient halogen is employed).



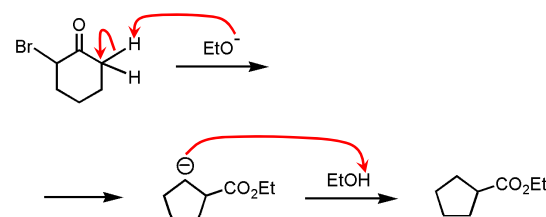
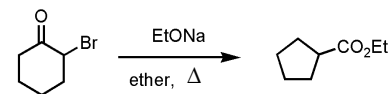
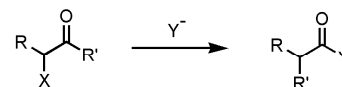
More acidic than unsubstituted ketone



For identifying methyl ketones:

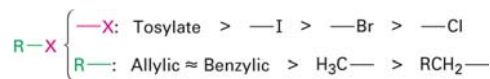
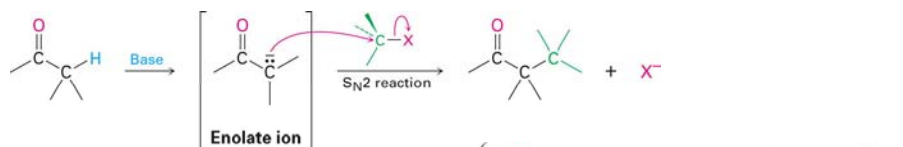
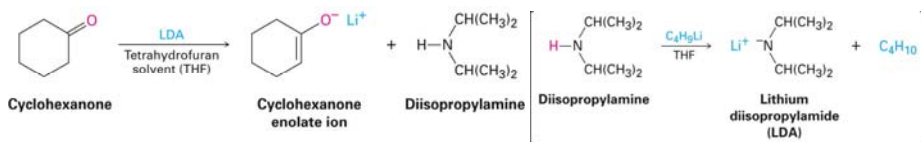
16-41

Favorski Rearrangement



16-42

Alkylation of Enolate Ions

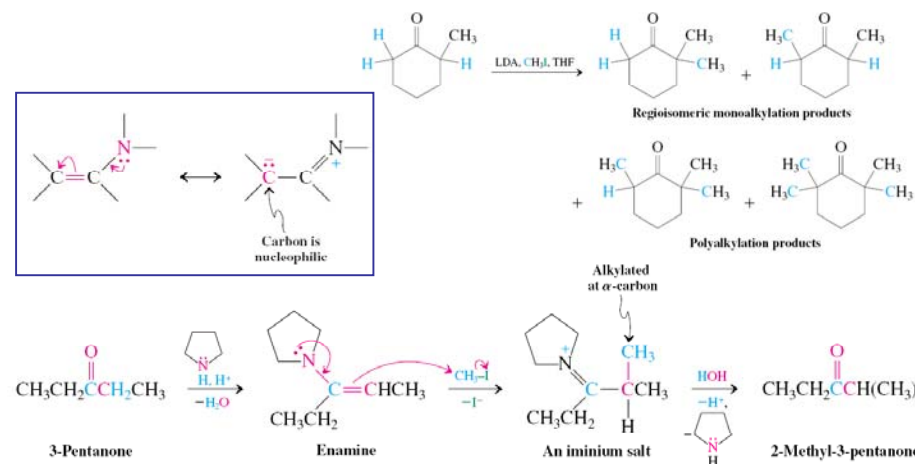


Limitations:

- as enolates are fairly strong bases, only alkylations with halomethane or 1° haloalkanes are feasible, otherwise E2 elimination becomes a significant process;
- Alkylation of aldehydes usually fails due to condensation reactions (to be discussed in a later sections);
- Alkylation of ketones are problematic because polyalkylation occurs.

16-43

Alkylation of Enamines



Alkylation of enamines are far superior to that of enolates, since no strong base is involved, self-condensation can be avoided, and polyalkylation can be minimized because the iminium salt formed after the first alkylation is relatively stable and unable to react with additional alkyl halides.

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