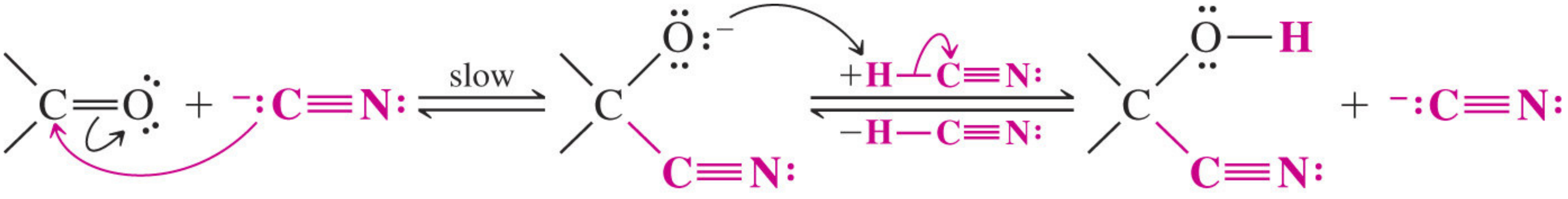
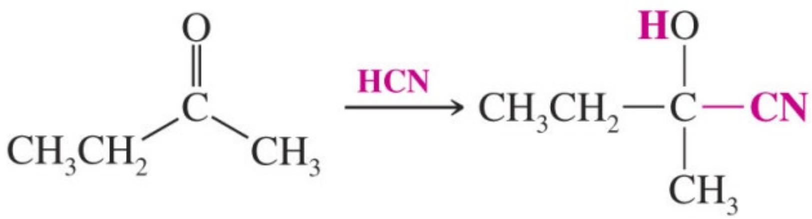
9.10 The Addition of Hydrogen Cyanide

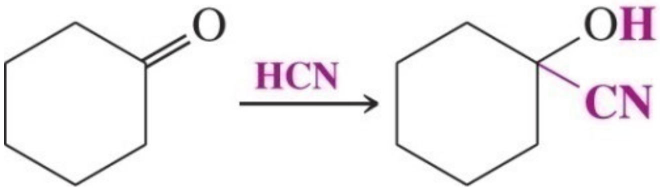
- Aldehydes and ketone react with HCN to form a cyanohydrin
  - A catalytic amount of cyanide helps to speed the reaction



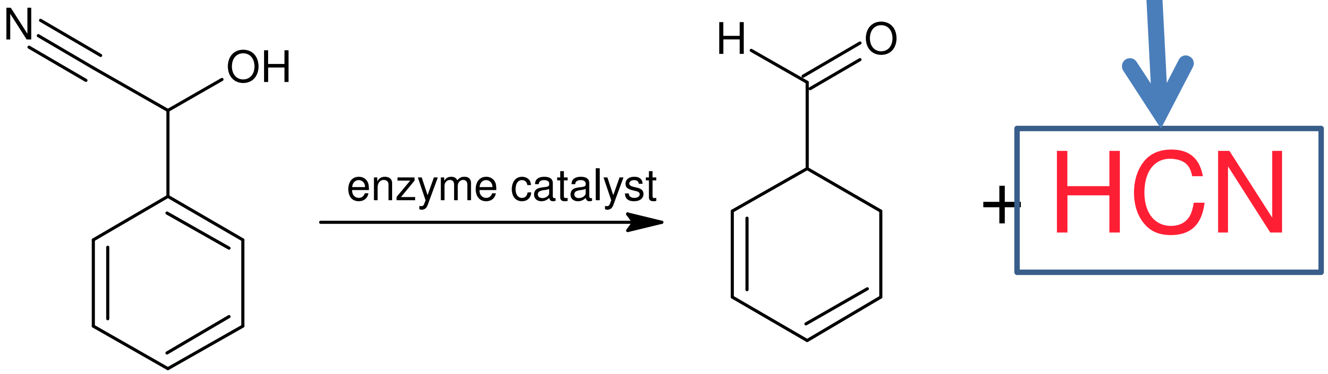
Cyanohydrin



$$CH_3CH_2C(=O)CH_3 \xrightarrow{HCN} CH_3CH_2-\overset{HO}{\underset{CH_3}{C}}-CN$$



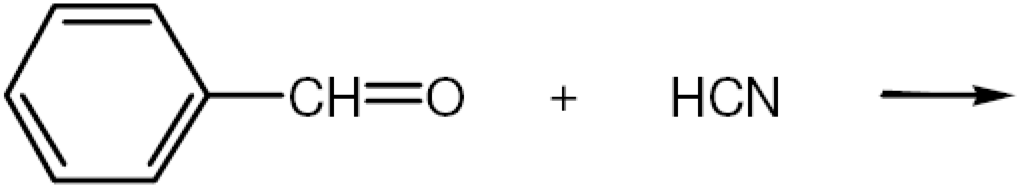
Defense system of millipede & bombardier beetle (*apheloria corrugata*)



Benzaldehyde Cyanohydrin

Problem 9.17

$$CH_3CH{=}O \quad + \quad HCN \quad \longrightarrow$$



Recap

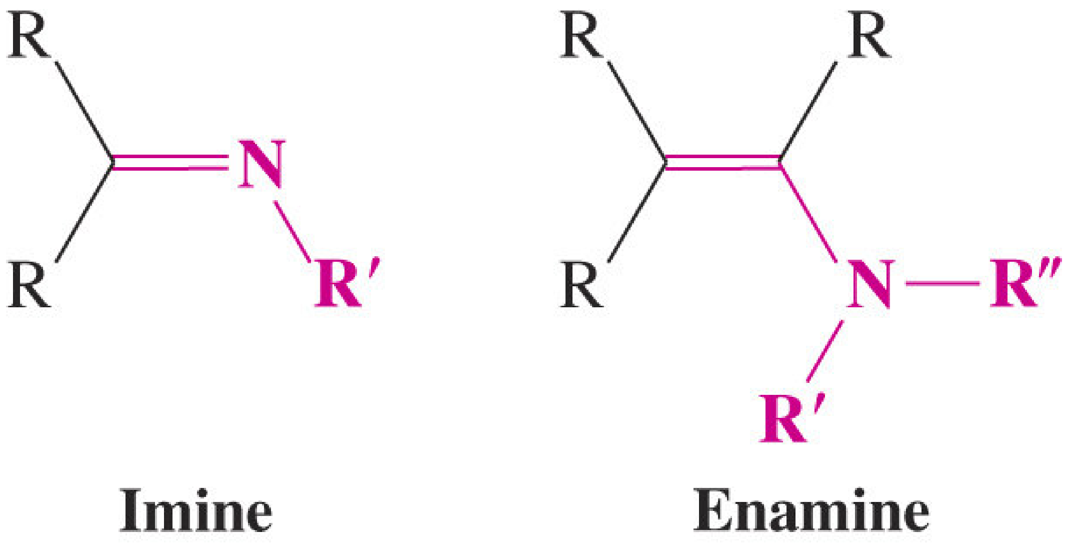
With acid catalysis, alcohols add to the carbonyl group of aldehydes to give **hemiacetals** [RCH(OH)OR']. Further reaction with excess alcohol gives **acetals** [$RCH(OR')_2$]. Ketones react similarly. These reactions are reversible; that is, acetals can be readily hydrolyzed by aqueous acid to their alcohol and carbonyl components. Water adds similarly to the carbonyl group of certain aldehydes (for example, formaldehyde and chloral) to give hydrates. Hydrogen cyanide adds to carbonyl compounds as a carbon nucleophile to give **cyanohydrins** [$R_2C(OH)CN$].

Grignard reagents add to carbonyl compounds. The products, after hydrolysis, are alcohols whose structures depend on that of the starting carbonyl compound. Formaldehyde gives *primary* alcohols, other aldehydes give *secondary* alcohols, and ketones give *tertiary* alcohols.

9.11 Addition of Nitrogen Nucleophiles

Nitrogen nucleophiles add to the carbonyl group. Often, addition is followed by elimination of water to give a product with a $R_2C{=}NR$ group in place of the $R_2C{=}O$ group. For example, primary amines ($R'NH_2$) give **imines** ($R_2C{=}NR'$); **hydroxylamine** (NH_2OH) gives **oximes** ($R_2C{=}NOH$); and **hydrazine** (NH_2NH_2) gives **hydrazones** ($R_2C{=}NNH_2$).

- The Addition of Primary and Secondary Amines
  - Aldehydes and ketones react with primary amines (and ammonia) to yield imines
    - They react with secondary amines to yield enamines



R′, R″ = C;
R = C or H

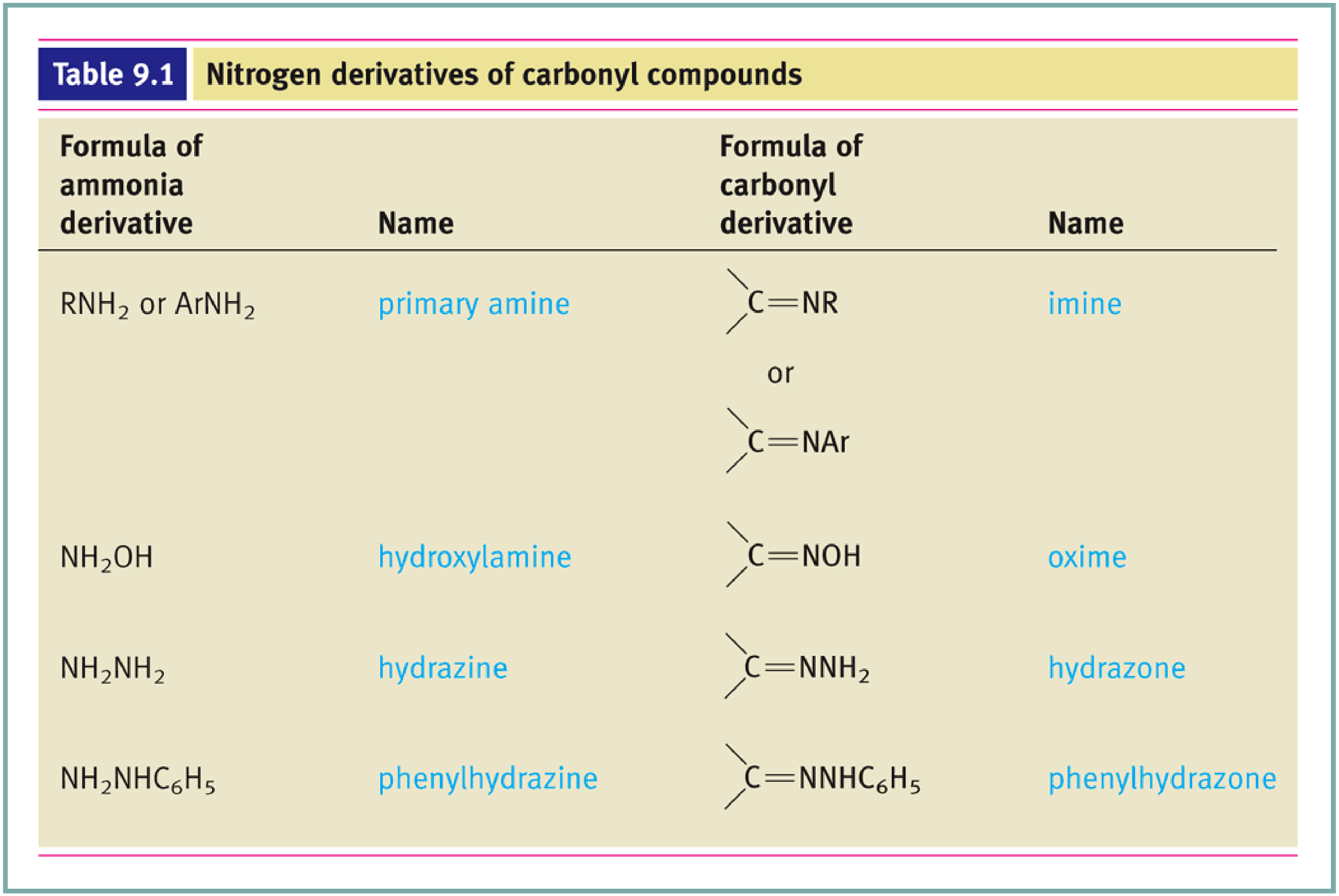
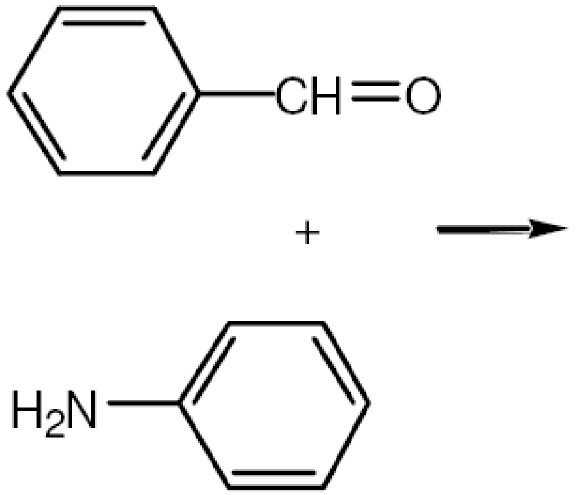


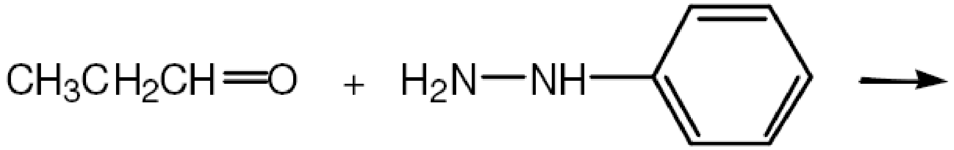
Table 9.1 Nitrogen derivatives of carbonyl compounds

Formula of ammonia derivative	Name	Formula of carbonyl derivative	Name
RNH_2 or $ArNH_2$	primary amine	$>C=NR$ or $>C=NAr$	imine
NH_2OH	hydroxylamine	$>C=NOH$	oxime
NH_2NH_2	hydrazine	$>C=NNH_2$	hydrazone
$NH_2NHC_6H_5$	phenylhydrazine	$>C=NNHC_6H_5$	phenylhydrazone

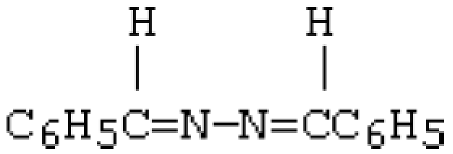
Examples



$$CH_3CH_2CH{=}O \quad + \quad H_2N{-}OH \quad \longrightarrow$$



The compound



$C_6H_5\overset{H}{\overset{|}{C}}=N-N=\overset{H}{\overset{|}{C}}C_6H_5$

is produced by the reaction of an excess of benzaldehyde with which compound?

A) Ammonia

[✓ B) Hydrazine]

C) Nitrogen

D) Phenylhydrazine

E) Hydroxylamine

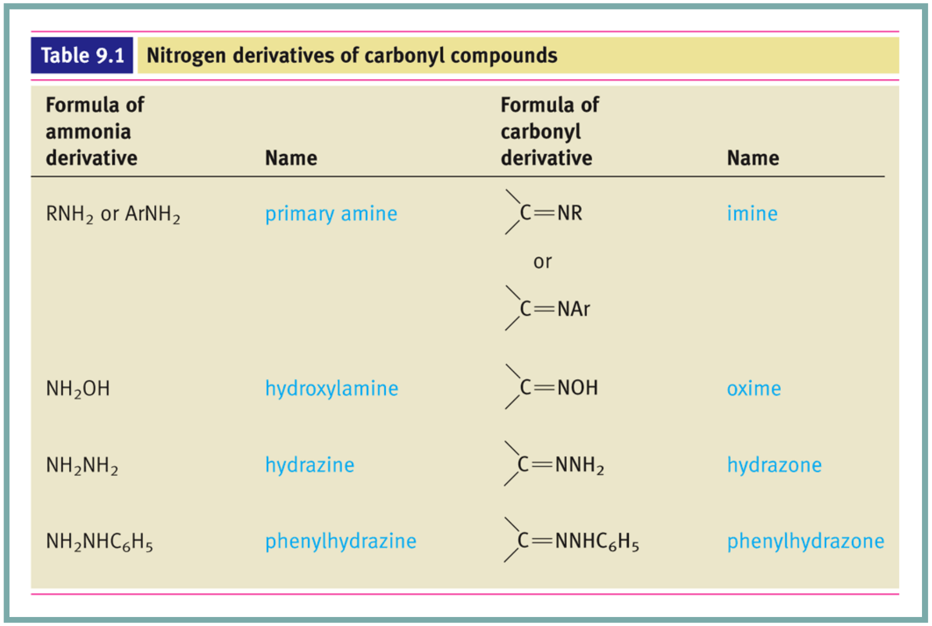
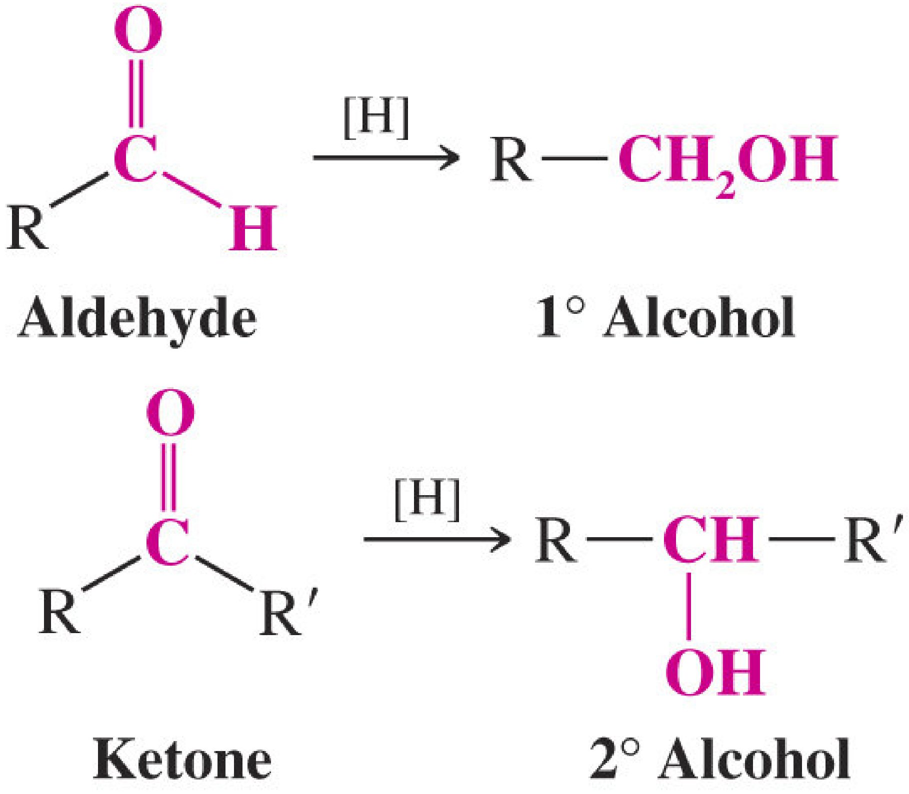


Table 9.1 **Nitrogen derivatives of carbonyl compounds**

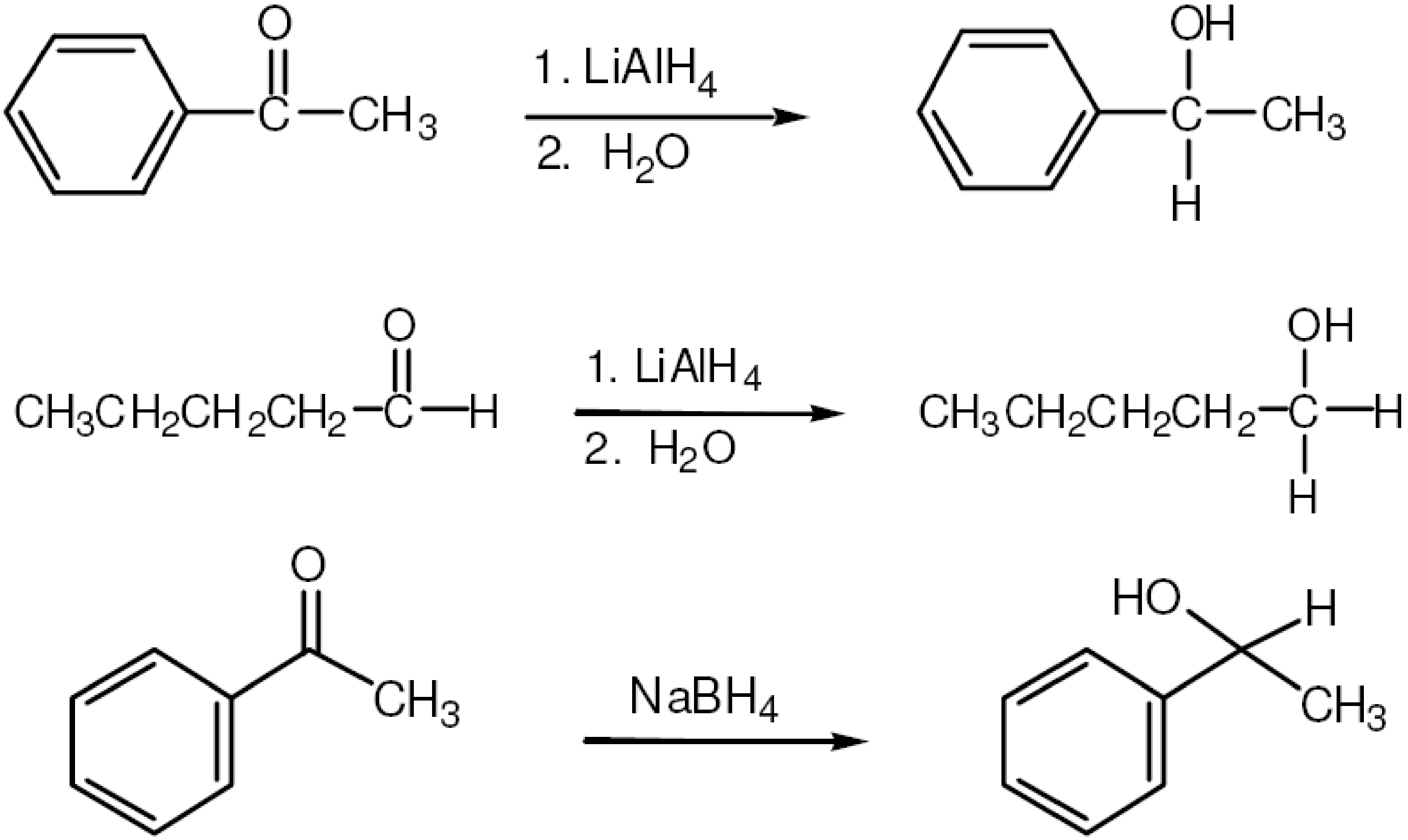
Formula of ammonia derivative	Name	Formula of carbonyl derivative	Name
RNH_2 or $ArNH_2$	primary amine	$>C=NR$ or $>C=NAr$	imine
NH_2OH	hydroxylamine	$>C=NOH$	oxime
NH_2NH_2	hydrazine	$>C=NNH_2$	hydrazone
$NH_2NHC_6H_5$	phenylhydrazine	$>C=NNHC_6H_5$	phenylhydrazone

9.12 Reduction of Carbonyl Compounds

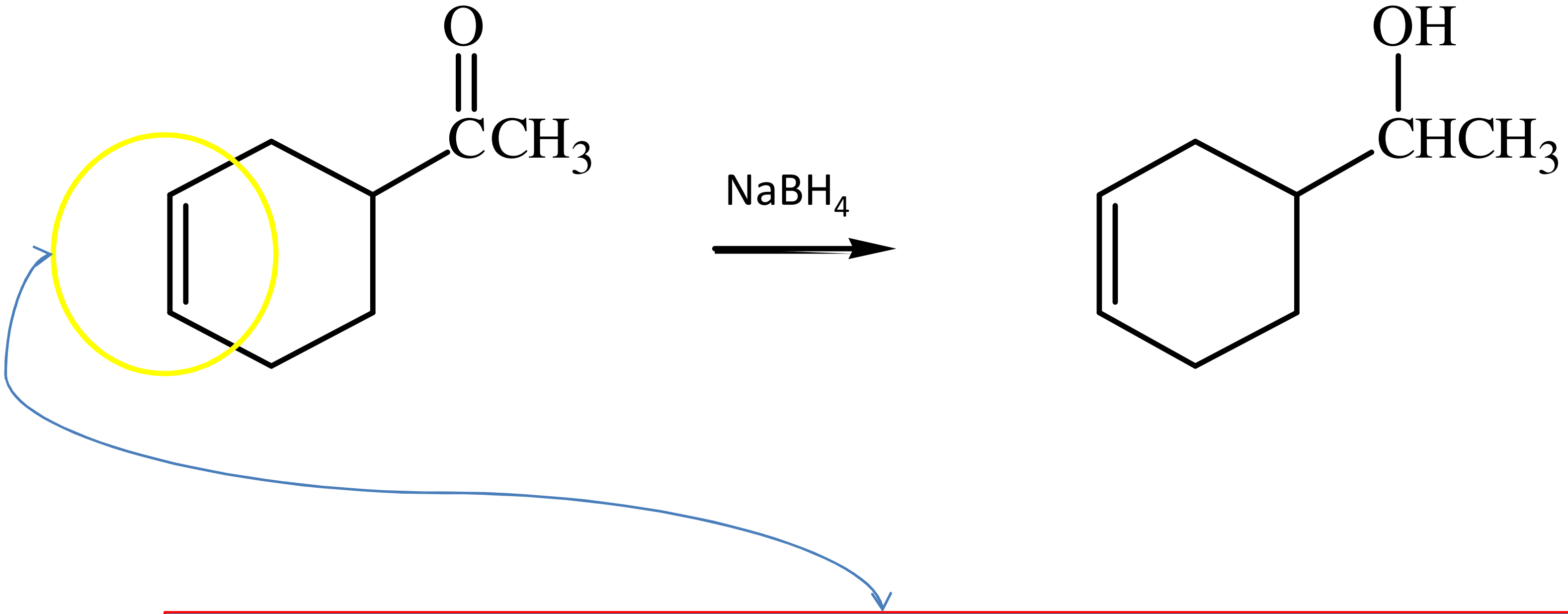
Aldehydes and ketones are easily reduced to primary or secondary alcohols, respectively. Useful reagents for this purpose are various metal hydrides such as **lithium aluminum hydride** ($LiAlH_4$) or **sodium borohydride** ($NaBH_4$).



Examples


1. $LiAlH_4$
2. H_2O
$CH_3CH_2CH_2CH_2$
1. $LiAlH_4$
2. H_2O
$CH_3CH_2CH_2CH_2$
$NaBH_4$

Reducing C=O without C=C

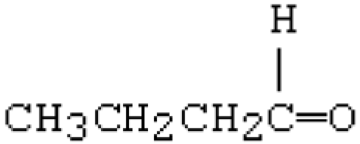


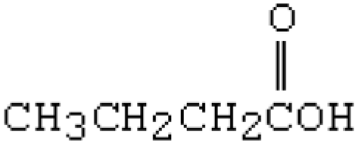
Not readily attacked by nucleophiles, metal hydrides

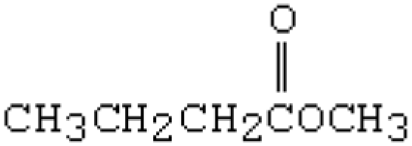
50. In the reaction of carbonyl compounds with $LiAlH_4$, the effective reducing species is:

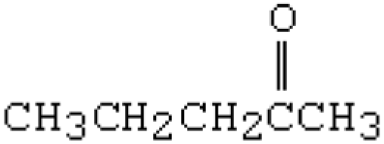
A) Li^+
B) Al^{+3}
C) AlH_4^-
D) AlH_3
[✓ E) H^-]

46. Which of these compounds will <u>not</u> be reduced by $LiAlH_4$?

[✓ A)] $CH_3CH_2CH_2CH{=}CH_2$
B)

$CH_3CH_2CH_2\overset{\overset{H}{|}}{C}{=}O$

C)

$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}OH$

D)

$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}OCH_3$

E)

$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}CH_3$

9.13 Oxidation of Carbonyl Compounds

Aldehydes are more easily oxidized than ketones. The **Tollens' silver mirror test** is positive for aldehydes and negative for ketones.

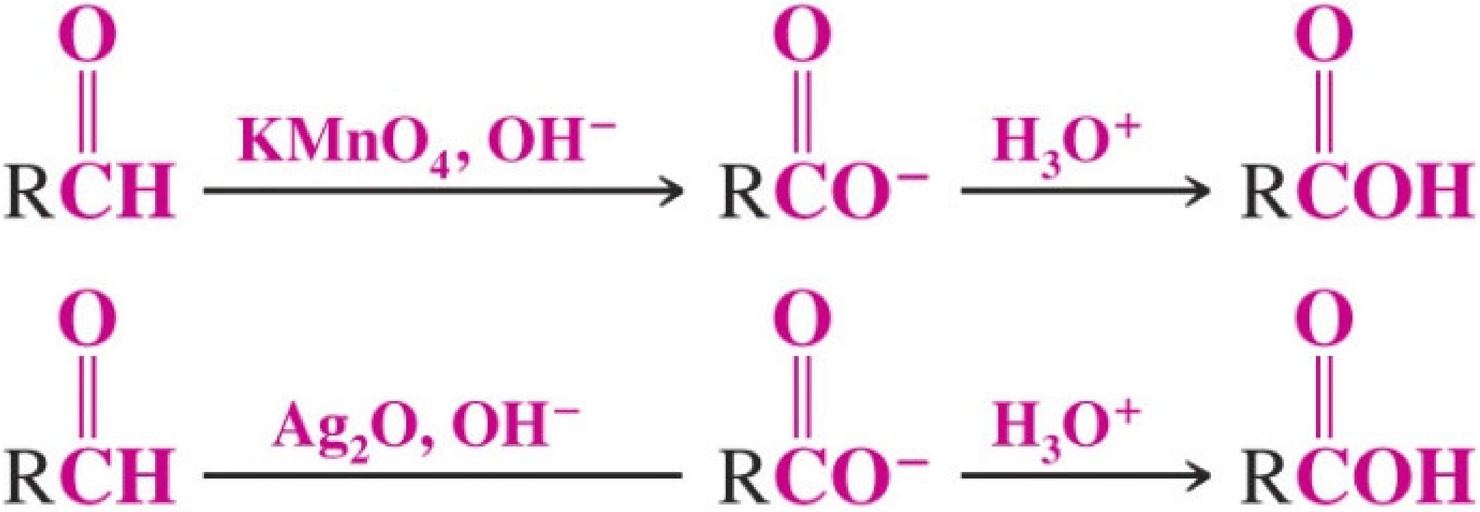
$$\mathrm{RCH{=}O} + 2\ \mathrm{Ag(NH_3)_2^+} + 3\ \mathrm{HO^-} \xrightarrow[\text{test}]{\text{Tollens'}} \mathrm{RCO_2^-} + 2\ \mathrm{Ag^0} + 4\ \mathrm{NH_3} + 2\ \mathrm{H_2O}$$

aldehyde

silver mirror

$$2\ \mathrm{RCH{=}O} \xrightarrow{\mathrm{CrO_3,\ H^+}} 2\ \mathrm{RCO_2H}$$

Other Oxidizing Agents

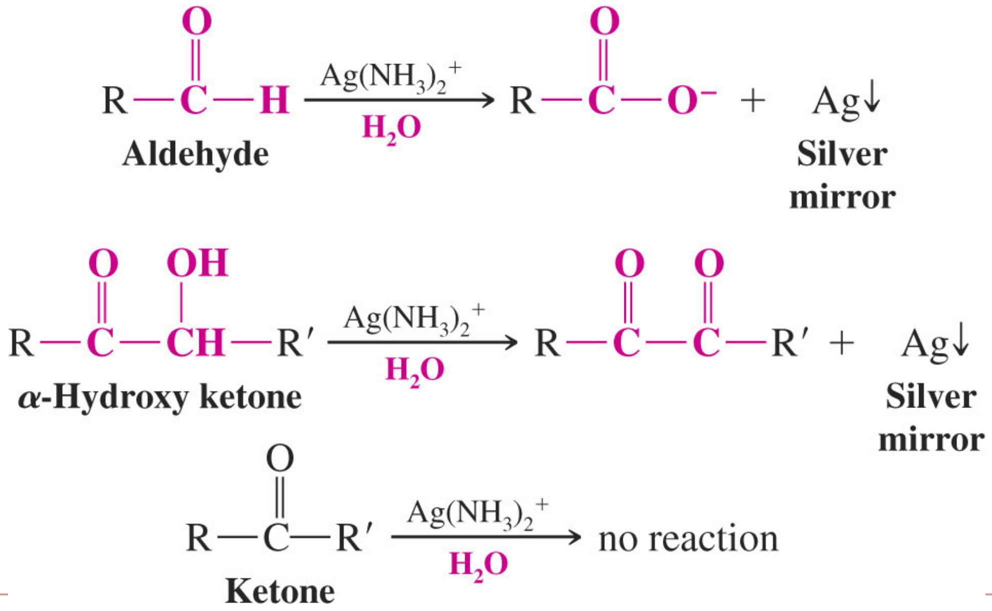


$$\mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{H} \xrightarrow{\mathrm{KMnO_4,\ OH^-}} \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{O^-} \xrightarrow{\mathrm{H_3O^+}} \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$$

$$\mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{H} \xrightarrow{\mathrm{Ag_2O,\ OH^-}} \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{O^-} \xrightarrow{\mathrm{H_3O^+}} \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{OH}$$

Tollens' Test (Silver Mirror Test)

- Aldehydes and ketones can be distinguished from each other on the basis of the Tollens test
  - The presence of an aldehyde results in formation of a silver mirror (by oxidation of the aldehyde and reduction of the silver cation)
  - α-Hydroxyketones also give a positive Tollens' test



$$R-\overset{O}{\overset{\|}{C}}-H \xrightarrow[H_2O]{Ag(NH_3)_2^+} R-\overset{O}{\overset{\|}{C}}-O^- + Ag\downarrow$$

$$R-\overset{O}{\overset{\|}{C}}-\overset{OH}{\overset{|}{CH}}-R' \xrightarrow[H_2O]{Ag(NH_3)_2^+} R-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-R' + Ag\downarrow$$

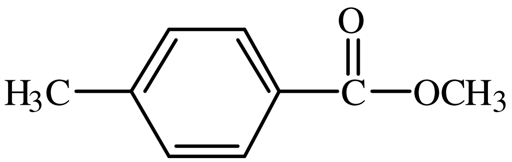
$$R-\overset{O}{\overset{\|}{C}}-R' \xrightarrow[H_2O]{Ag(NH_3)_2^+} \text{no reaction}$$

Examples

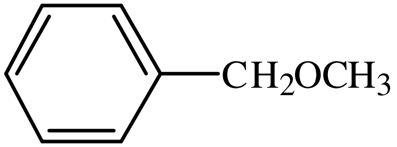
$$H_2C{=}O \;+\; 2\,Ag(NH_3)_2^{+} \;+\; 3\,HO^{-} \longrightarrow HCO_2^{-} \;+\; 2\,Ag\downarrow \;+\; 4\,NH_3\uparrow \;+\; 2\,H_2O$$

Which of the following compounds will give a positive silver mirror test (Tollens' test)?

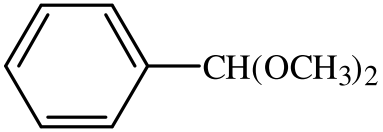
e.



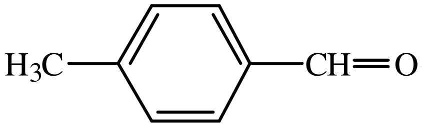
c.



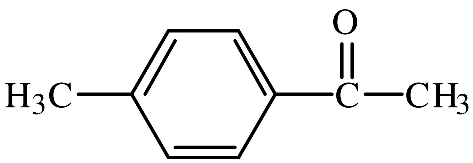
a.



d.



b.

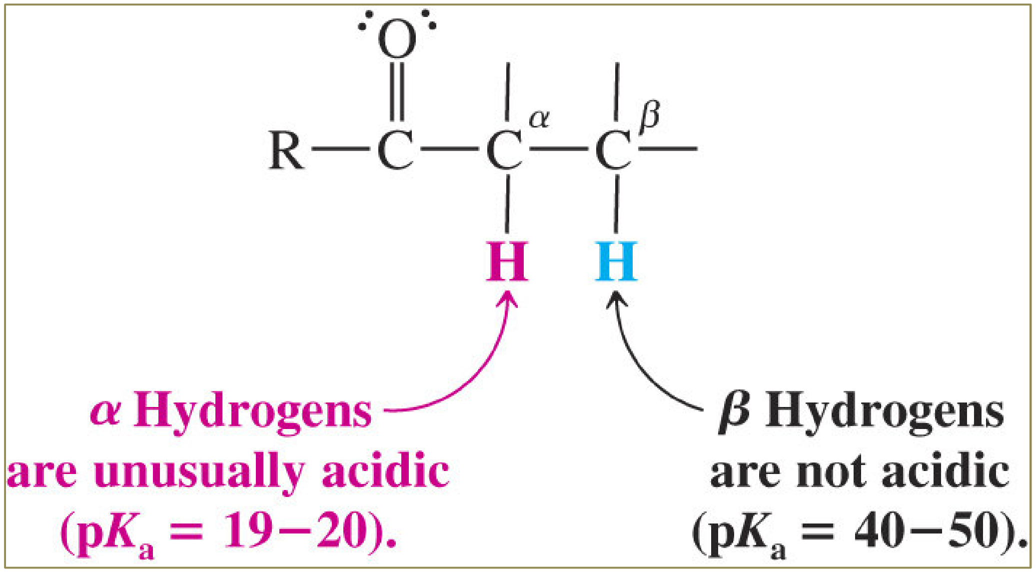


9.14 Keto-Enol Tautomerism

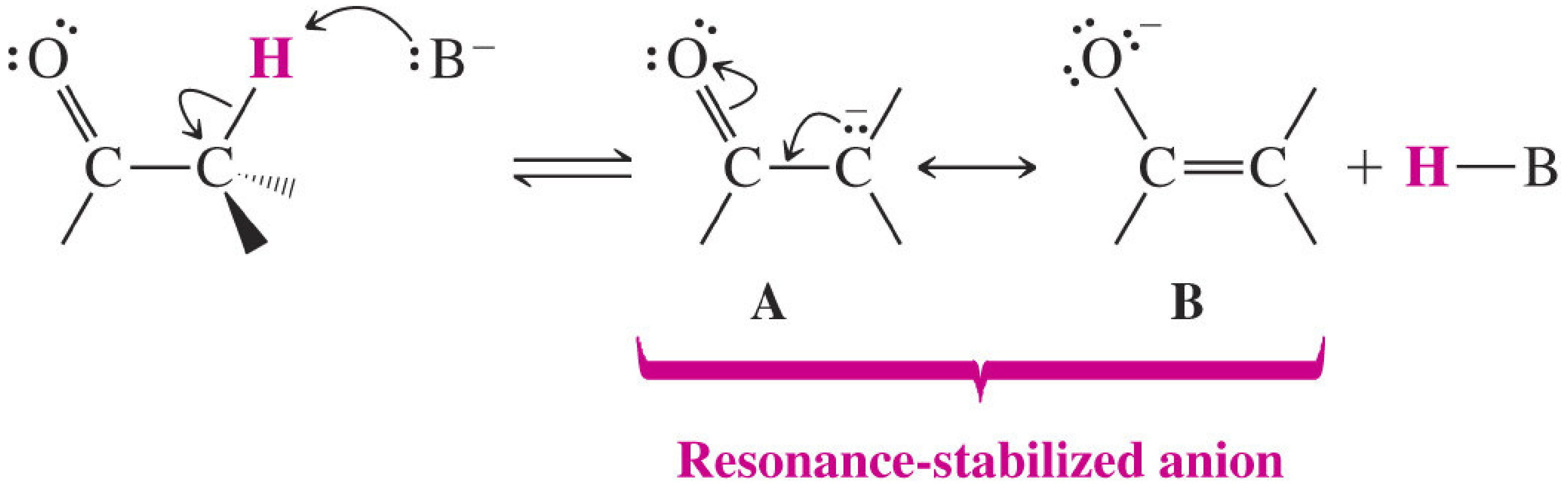
Aldehydes or ketones with an α-hydrogen exist as an equilibrium mixture of **keto** (H–C_α–C=O) and **enol** (C_α=C–OH) **tautomers**. The keto form usually predominates. An α-hydrogen is weakly acidic and can be removed by a base to produce a resonance-stabilized **enolate anion**.

Hydrogens on carbons α to carbonyls are unusually acidic

The resulting anion is stabilized by resonance to the carbonyl



9.15 Acidity of α-Hydrogens; the Enolate Anion



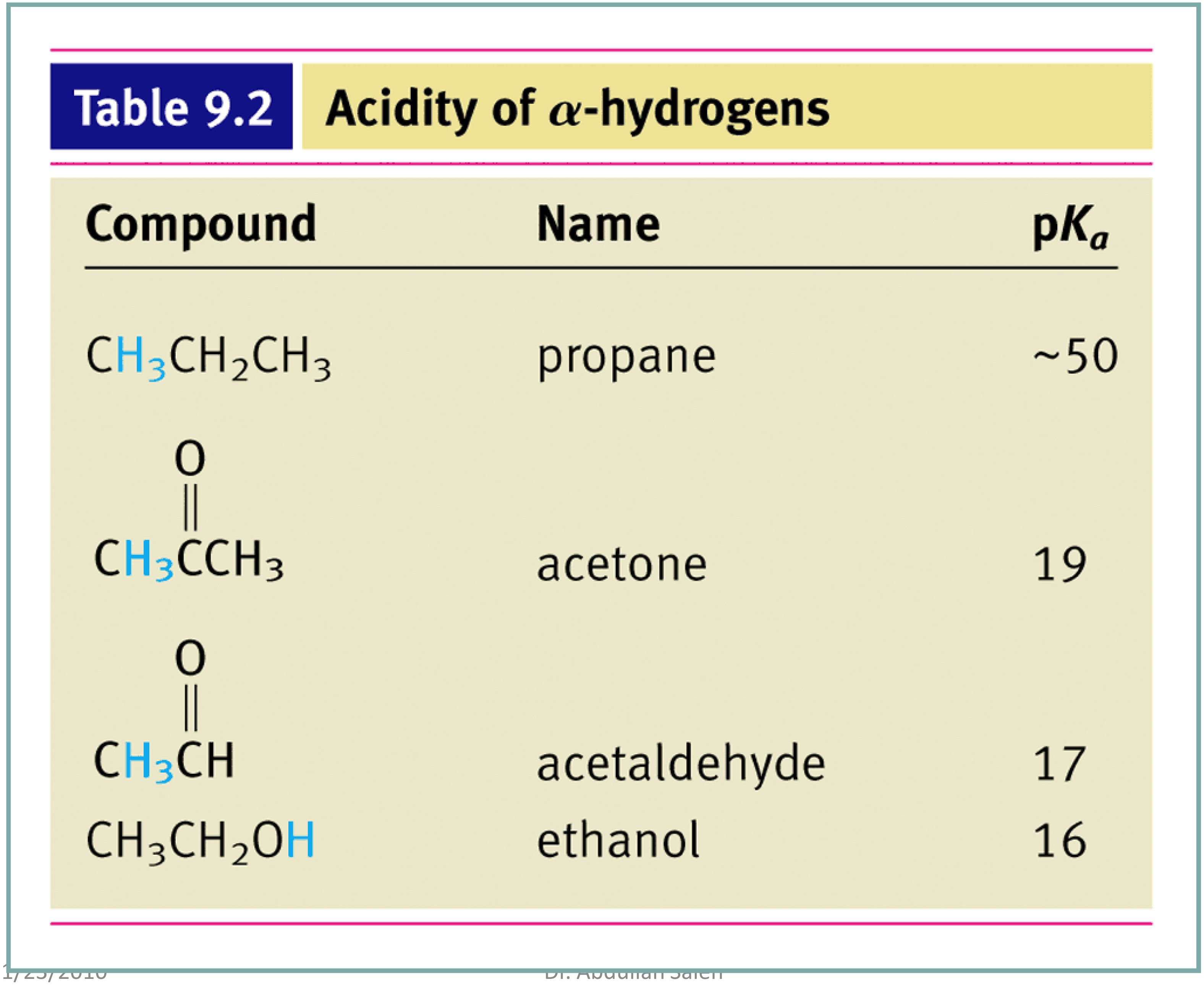
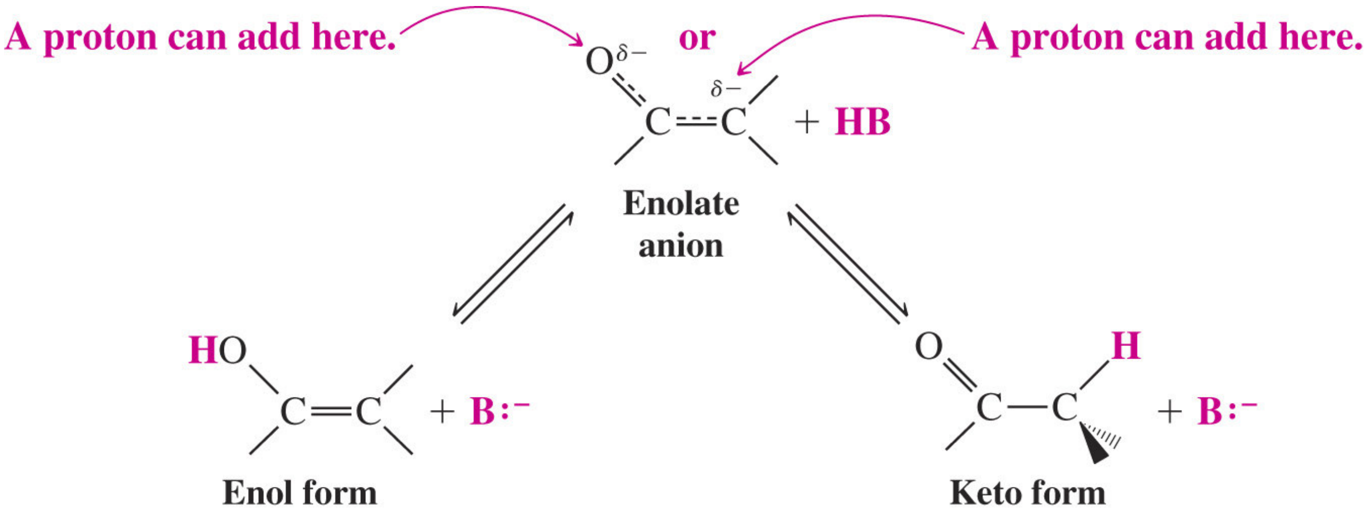


Table 9.2 **Acidity of α-hydrogens**

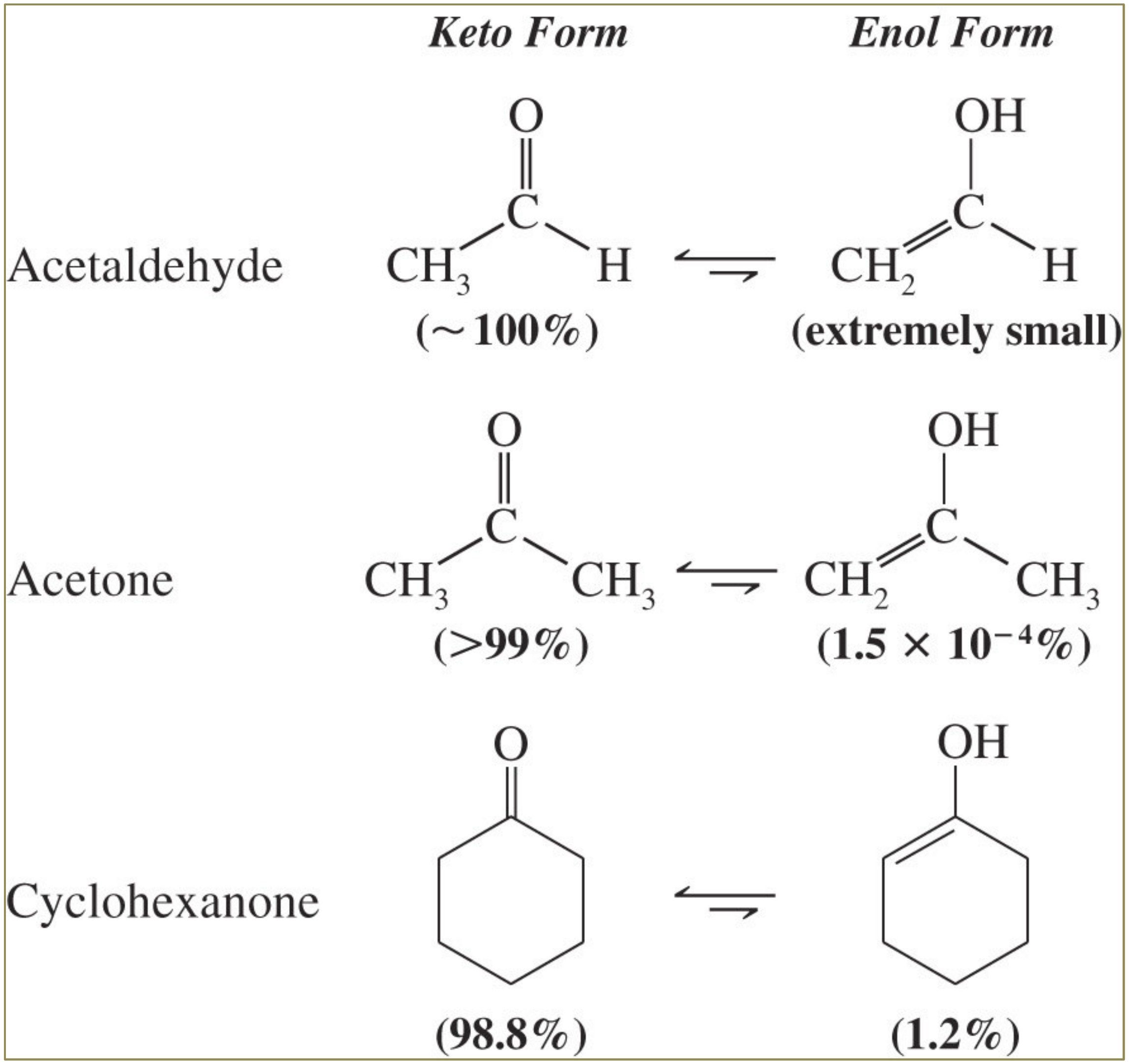
Compound	Name	pK_a
$CH_3CH_2CH_3$	propane	~50
$CH_3\overset{\overset{O}{\|}}{C}CH_3$	acetone	19
$CH_3\overset{\overset{O}{\|}}{C}H$	acetaldehyde	17
CH_3CH_2OH	ethanol	16

- The enolate anion can be protonated at the carbon or the oxygen
  - The resultant enol and keto forms of the carbonyl are formed reversibly and are interconvertible

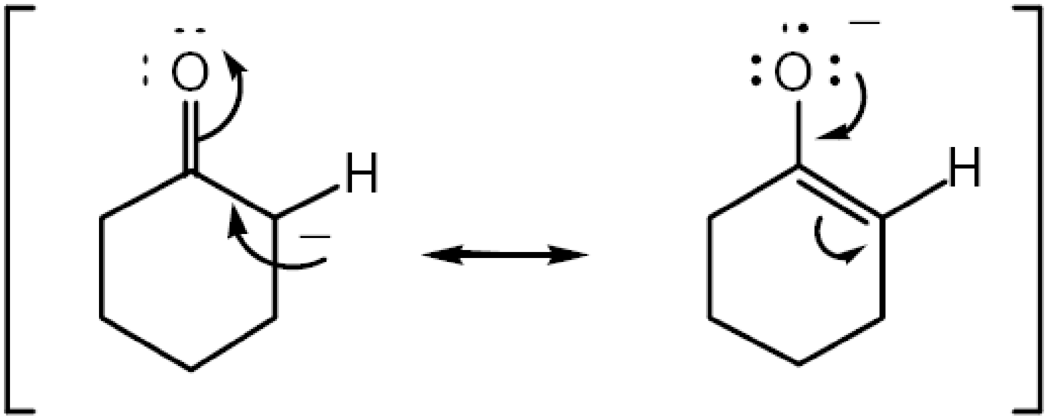


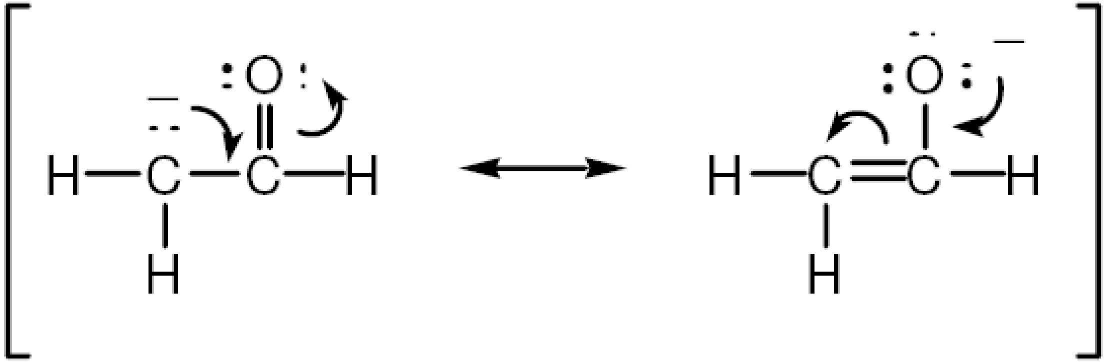
- Enol-keto tautomers are constitutional isomers that are easily interconverted by a trace of acid or base
    - Most aldehydes and ketones exist primarily in the keto form because of the greater strength of the carbon-oxygen double bond relative to the carbon-carbon double bond

- Keto and Enol Tautomers



Resonance contributors to the enolate anion of cyclohexanone & acetaldehyde





End of Chapter 9

Dr.
Abdullah
I. Saleh