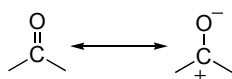
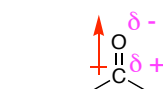


## Chapter 17: Aldehydes and Ketones: Nucleophilic Addition to the Carbonyl Group

### 17.1: Nomenclature (please read)

**17.2: Structure and Bonding:** Carbonyl groups have a significant dipole moment



Aldehyde	2.72 D
Ketone	2.88
Carboxylic acid	1.74
Acid chloride	2.72
Ester	1.72
Amide	3.76
Nitrile	3.90
Water	1.85

Carbonyl carbons are electrophilic sites and can be attacked by nucleophiles. The carbonyl oxygen is a basic site.

97

### 17.3: Physical Properties (please read)

### 17.4: Sources of Aldehydes and Ketones (Table 17.1, p. 708)

1a. Oxidation of 1° and 2° alcohols (**15.10**)

1b. From carboxylic acids

1c. Ketones from aldehydes

98

2. Ozonolysis of alkenes (**6.20**)
  
3. Hydration of alkynes (**9.12**)
  
4. Friedel-Craft Acylation (**12.7**) -aryl ketones
  
5. Hydroformylation of alkenes (please read)

99

### **17.5: Reactions of Aldehydes and Ketones: A Review and a Preview**

Reactions of aldehydes and ketones: Review:

1. Reduction to hydrocarbons
  - a. Clemmenson reduction (Zn-Hg, HCl)
  - b. Wolff-Kishner ( $\text{H}_2\text{NNH}_2$ , KOH,  $\Delta$ )

100

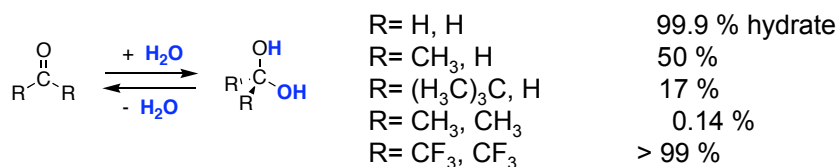
2. Reduction to 1° and 2° alcohols (15.2)

3. Addition of Grignard Reagents (14.6-14.7)

101

### 17.6: Principles of Nucleophilic Addition: Hydration of Aldehydes and Ketones

Water can reversibly add to the carbonyl carbon of aldehydes and ketones to give 1,1-diols (geminal or gem-diols)



The hydration reaction is base and acid catalyzed

Base-catalyzed mechanism (Fig. 17.1): hydroxide is a better nucleophile than water

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Acid-catalyzed mechanism (Fig. 17.2): protonated carbonyl is a better electrophile

The hydration is reversible

Does adding acid or base change the amount of hydrate?

Does a catalyst affect  $\Delta G^\circ$ ,  $\Delta G^\ddagger$ , both, or neither

103

### 17.7: Cyanohydrin Formation

Addition of H-CN adds to the aldehydes and unhindered ketones.  
(related to the hydration reaction)

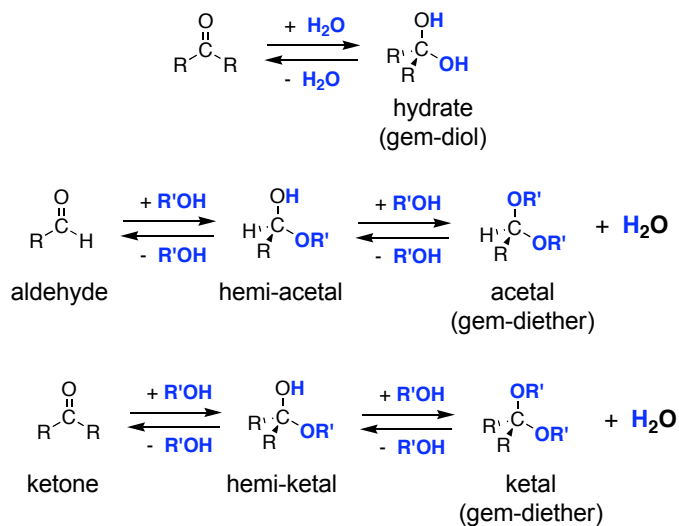
The equilibrium favors cyanohydrin formation

Mechanism of cyanohydrin formation (Fig. 17.3)

104

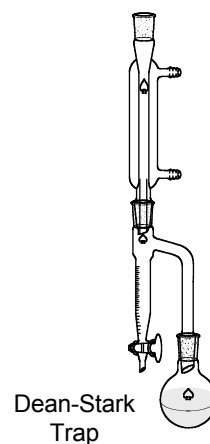
### 17.8: Acetal Formation

Acetals are geminal diethers- structurally related to hydrates, which are geminal diols.



105

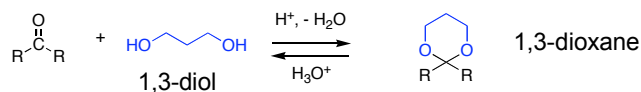
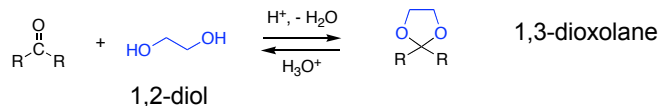
Mechanism of acetal (ketal) formation is acid-catalyzed (Fig 17.4)



The mechanism for acetal/ketal formation is reversible  
How is the direction of the reaction controlled?

106

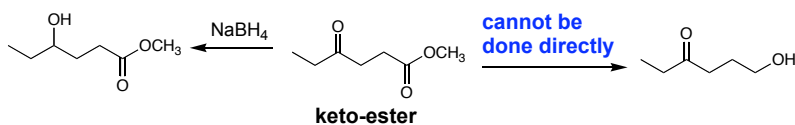
### Dioxolanes and dioxanes: cyclic acetal (ketals) from 1,2- and 1,3-diols



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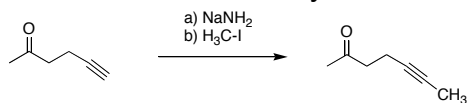
### 17.9: Acetals (Ketals) as Protecting Groups

*Protecting group:* Temporarily convert a functional group that is incompatible with a set of reaction conditions into a new functional group (with the protecting group) that is compatible with the reaction. The protecting group is then removed giving the original functional group (deprotection).

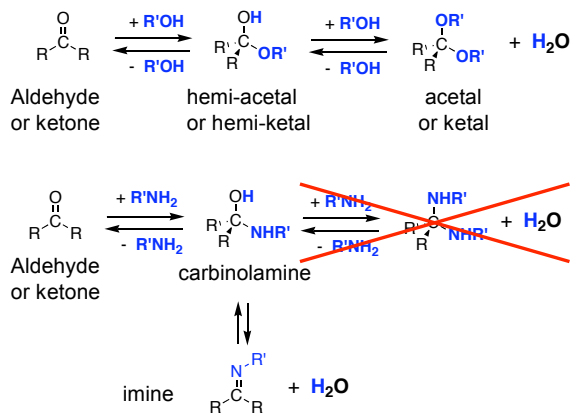


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The reaction cannot be done directly, as shown. Why?



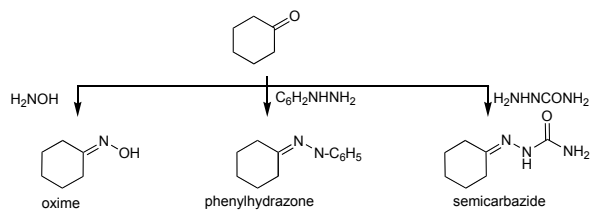
### 17.10: Reaction with Primary Amines: Imines (Schiff base)



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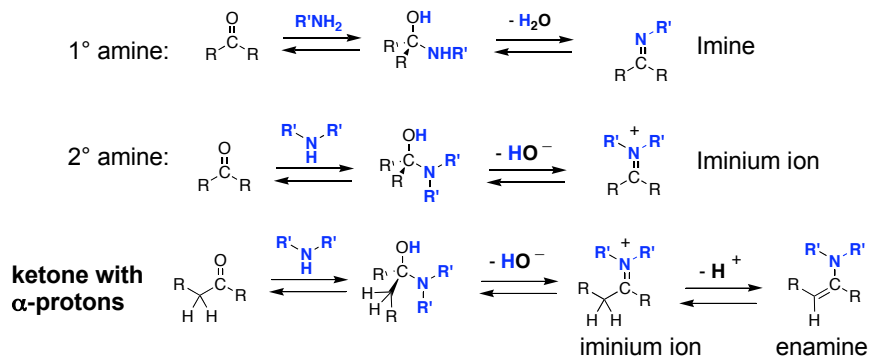
Mechanism of imine formation (Fig. 17.5):

See Table 17.4 for the related carbonyl derivative, oximes, hydrazone and semicarbazides (please read)



110

### 17.11: Reaction with Secondary Amines: Enamines



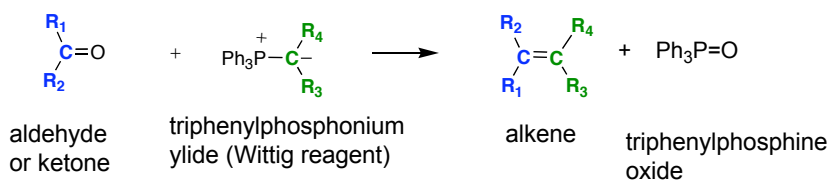
Mechanism of enamine formation (Fig 17.6)

111

### 17.12: The Wittig Reaction

1979 Nobel Prize in Chemistry: Georg Wittig (Wittig Reaction) and H.C. Brown (Hydroboration)

The synthesis of an alkene from the reaction of an aldehyde or ketone and a phosphorus *ylide* (Wittig reagent), a dipolar intermediate with formal opposite charges on adjacent atoms (overall charge neutral).

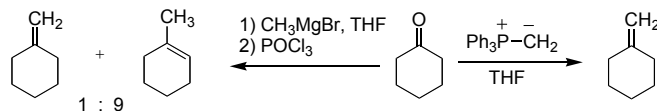


Accepted mechanism (Fig. 17.7) (please read)

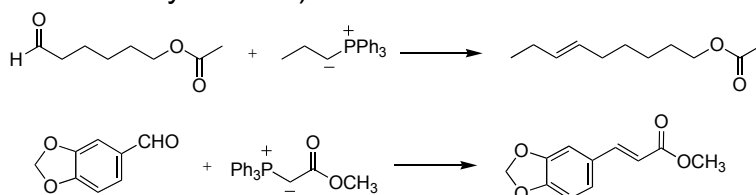
112



The Wittig reaction gives C=C in a defined location, based on the location of the carbonyl group (C=O)



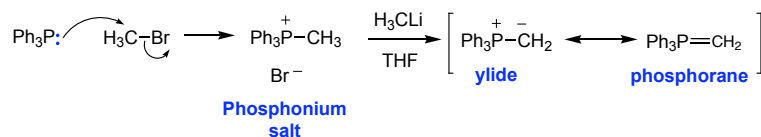
The Wittig reaction is highly selective for ketones and aldehydes; esters, lactones, nitriles and amides will not react but are tolerated in the substrate. Acidic groups (alcohols, amine and carboxylic acids) are not tolerated.



Predicting the geometry (*E/Z*) of the alkene product is complex and is dependent upon the nature of the ylide. 113

### 17.13: Planning an Alkene Synthesis via the Wittig Reaction

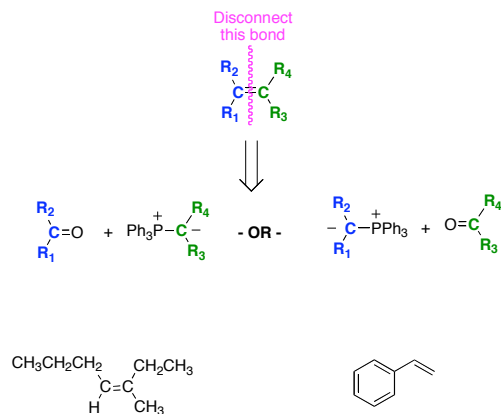
A Wittig reagent is prepared from the reaction of an alkyl halide with triphenylphosphine ( $\text{Ph}_3\text{P}:$ ) to give a phosphonium salt. The protons on the carbon adjacent to phosphorous are acidic.



Deprotonation of the phosphonium salt with a strong base gives the *ylide*. A *phosphorane* is a neutral resonance structure of the ylide.

114

- There will be two possible Wittig routes to an alkene.
- Analyze the structure *retrosynthetically*, i.e., work the synthesis out backwards
- *Disconnect* (break the bond of the target that can be formed by a known reaction) the doubly bonded carbons. One becomes the aldehyde or ketone, the other the ylide

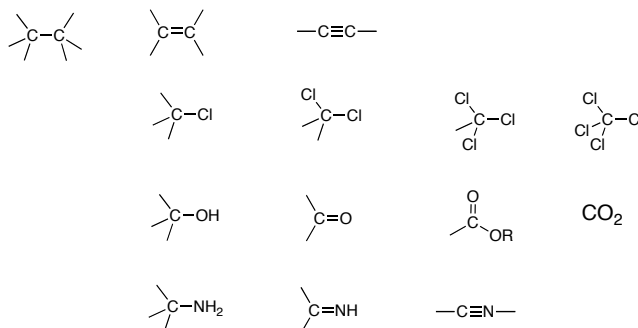


115

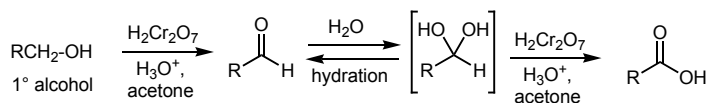
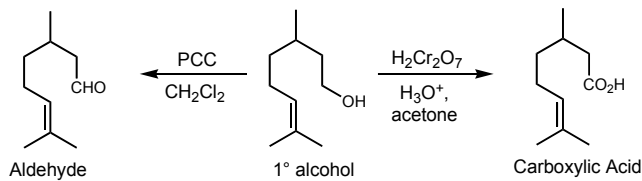
### 17.14: Stereoselective Addition to Carbonyl Groups (please read)

### 17.15: Oxidation of Aldehydes

Increasing oxidation state



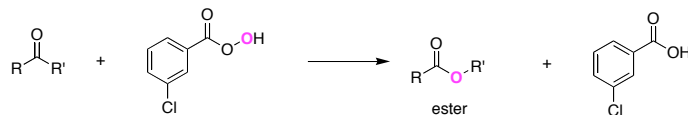
116



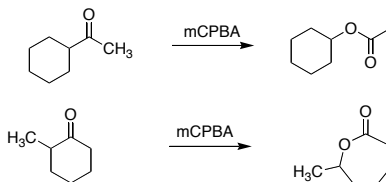
Aldehydes are oxidized by Cr(VI) reagents to carboxylic acids in aqueous acid. The reaction proceeds through the hydrate

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**17.16: Baeyer-Villiger Oxidation of Ketones.** Oxidation of ketones with a peroxy acid (mCPBA) to give as esters



Oxygen insertion occurs between carbonyl carbon and more the substituted  $\alpha$ -carbon



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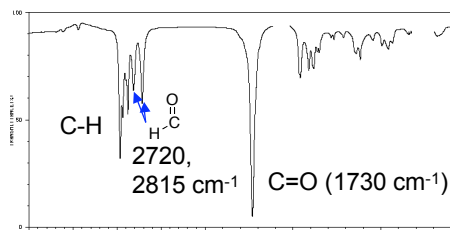
### 19.17: Spectroscopic Analysis of Aldehydes and Ketones

*Infrared Spectroscopy*: highly diagnostic for carbonyl groups

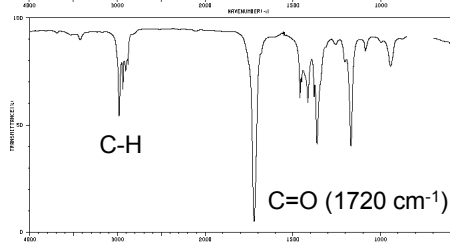
Carbonyls have a strong C=O absorption peak between 1660 - 1770  $\text{cm}^{-1}$

Aldehydes also have two characteristic C-H absorptions around 2720 - 2820  $\text{cm}^{-1}$

Butanal

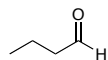


2-Butanone

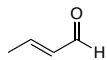


119

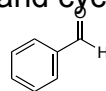
C=O stretches of aliphatic, conjugated, aryl and cyclic carbonyls:



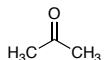
aliphatic aldehyde  
1730  $\text{cm}^{-1}$



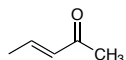
conjugated aldehyde  
1705  $\text{cm}^{-1}$



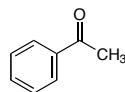
aromatic aldehyde  
1705  $\text{cm}^{-1}$



aliphatic ketone  
1715  $\text{cm}^{-1}$



conjugated ketone  
1690  $\text{cm}^{-1}$



aromatic ketone  
1690  $\text{cm}^{-1}$



1715  $\text{cm}^{-1}$



1750  $\text{cm}^{-1}$



1780  $\text{cm}^{-1}$



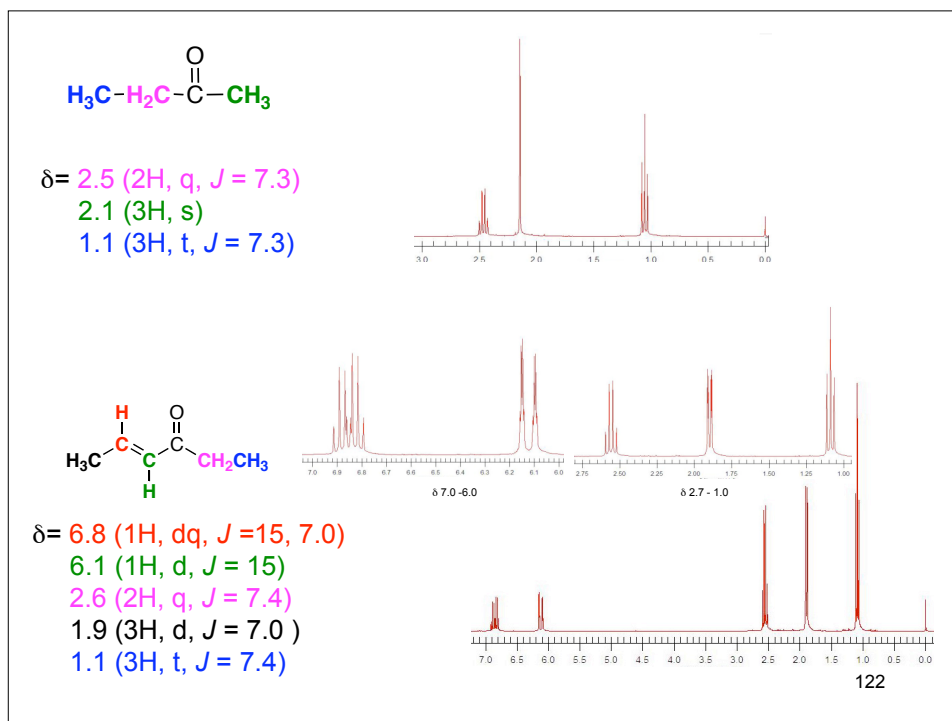
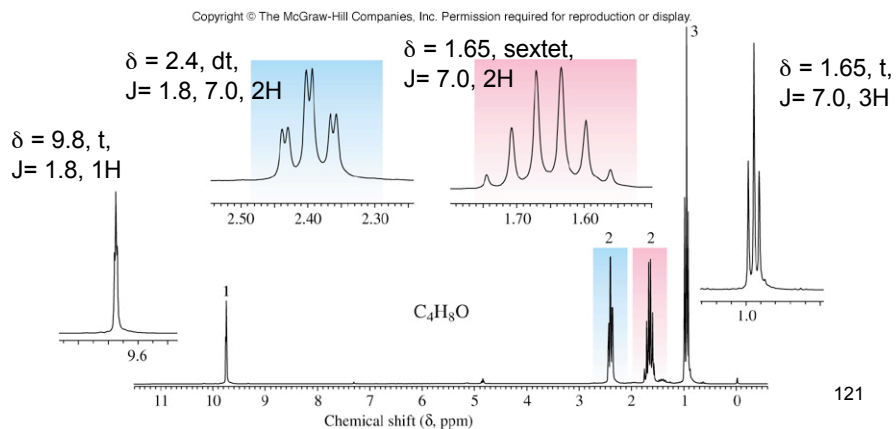
1815  $\text{cm}^{-1}$

*Conjugation moves the C=O stretch to lower energy (right, lower  $\text{cm}^{-1}$ )*

*Ring (angle) strain moves the C=O stretch to higher energy (left, higher  $\text{cm}^{-1}$ )*

120

$^1\text{H}$  NMR Spectra of Aldehydes and Ketones: The  $^1\text{H}$  chemical shift range for the aldehyde proton is  $\delta$  9-10 ppm  
 The aldehyde proton will couple to the protons on the  $\alpha$ -carbon with a typical coupling constant of  $J \approx 2$  Hz  
 A carbonyl will slightly deshield the protons on the  $\alpha$ -carbon; typical chemical shift range is  $\delta$  2.0 - 2.5 ppm



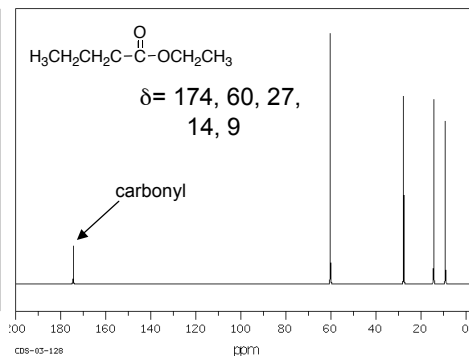
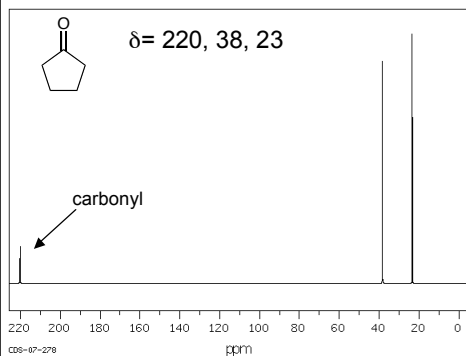
### <sup>13</sup>C NMR:

The intensity of the carbonyl resonance in the <sup>13</sup>C spectrum usually weak and sometimes not observed.

The chemical shift range is diagnostic for the type of carbonyl

ketones & aldehydes:  $\delta = \sim 190 - 220$  ppm

carboxylic acids, esters,  
and amides  $\delta = \sim 165 - 185$  ppm



### $C_9H_{10}O_2$

IR:  $1695\text{ cm}^{-1}$

<sup>13</sup>C NMR: 191

163

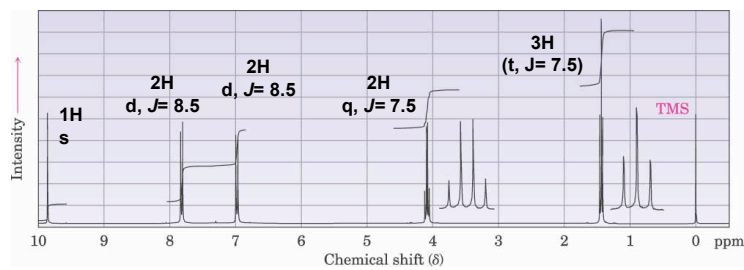
130

128

115

65

15



### $C_{10}H_{12}O$

IR:  $1710\text{ cm}^{-1}$

<sup>13</sup>C NMR: 207

134

130

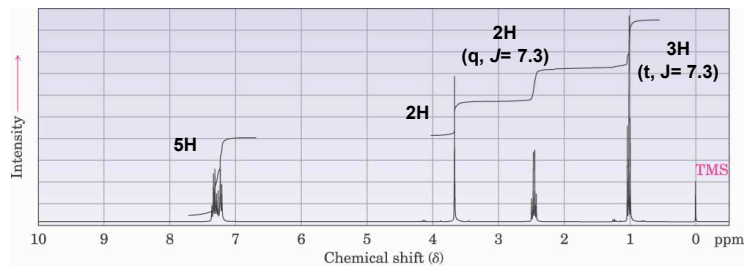
128

126

52

37

10



124

