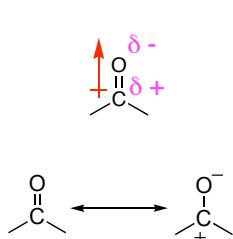


Chapter 17: Aldehydes and Ketones: Nucleophilic Addition to the Carbonyl Group

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.

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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

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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 (H_2NNH_2 , KOH, Δ)

100

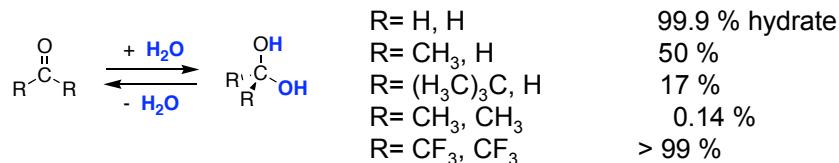
2. Reduction to 1° and 2° alcohols (15.2)

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 catalysts affect ΔG° , ΔG^\ddagger , both, or neither

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17.7: Cyanohydrin Formation

Addition of H-CN adds to the aldehydes and unhindered ketones.

(related to the hydration reaction)

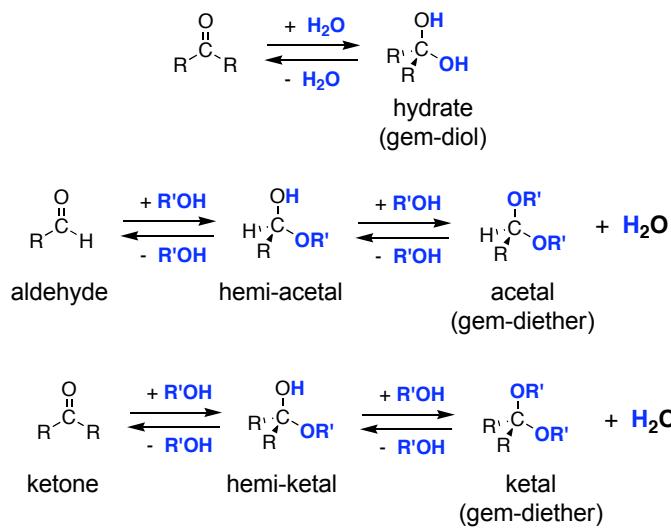
The equilibrium favors cyanohydrin formation

Mechanism of cyanohydrin formation (Fig. 17.3)

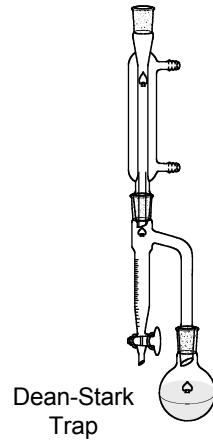
104

17.8: Acetal Formation

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



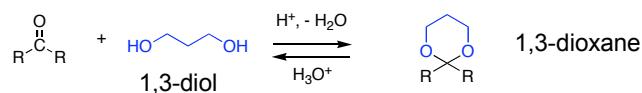
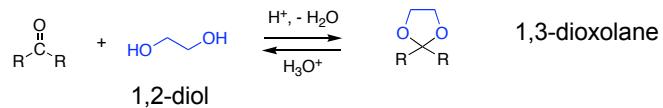
Mechanism of acetal (ketal) formation is acid-catalyzed (Fig 17.4)



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

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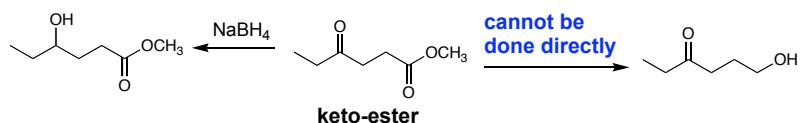
Dioxolanes and dioxanes: cyclic acetal (ketals) from 1,2- and 1,3-diols



107

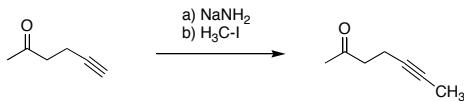
17.9: Acetals (Ketals) as Protecting Groups

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).

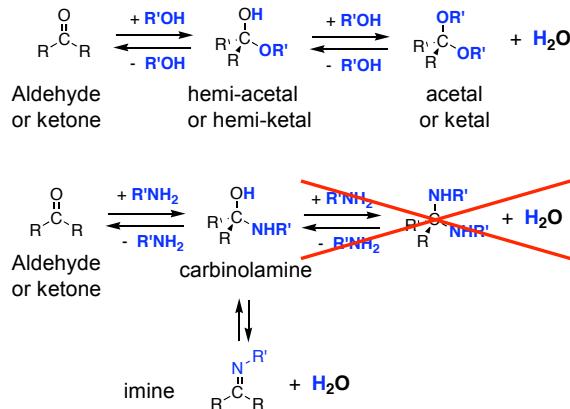


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The reaction cannot be done directly, as shown. Why?

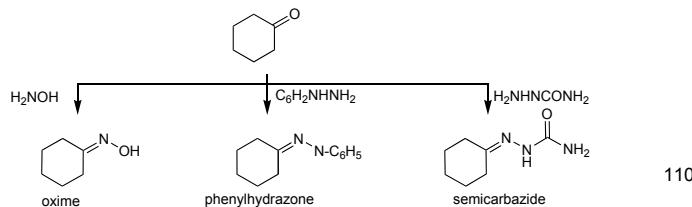


17.10: Reaction with Primary Amines: Imines (Schiff base)

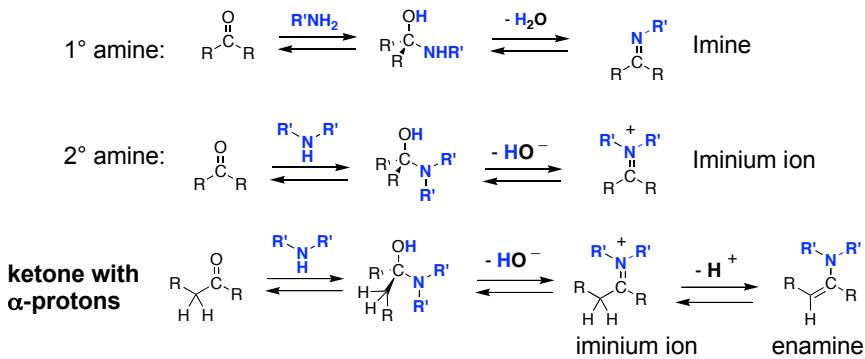


Mechanism of imine formation (Fig. 17.5):

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



17.11: Reaction with Secondary Amines: Enamines



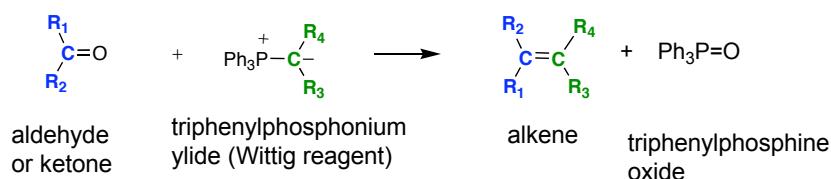
Mechanism of enamine formation (Fig 17.6)

111

17.12: The Wittig Reaction

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

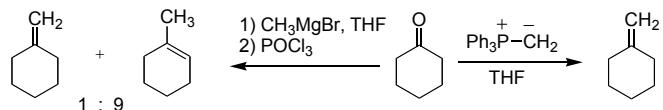
The synthesis of an alkene from the reaction of an aldehyde or ketone and a phosphorus *ylide* (Wittig reagent), a dipolar intermediate with formal opposite charges on adjacent atoms (overall charge neutral).



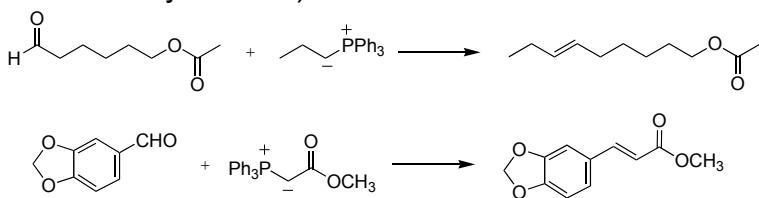
Accepted mechanism (Fig. 17.7) (please read)

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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.

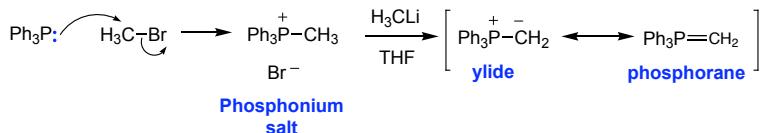


Predicting the geometry (*E*/*Z*) of the alkene product is complex and is dependent upon the nature of the ylide.

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17.13: Planning an Alkene Synthesis via the Wittig Reaction

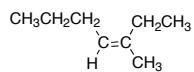
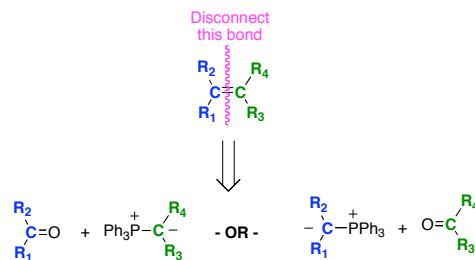
A Wittig reagent is prepared from the reaction of an alkyl halide with triphenylphosphine ($\text{Ph}_3\text{P}:$) to give a phosphonium salt. The protons on the carbon adjacent to phosphorous are acidic.



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

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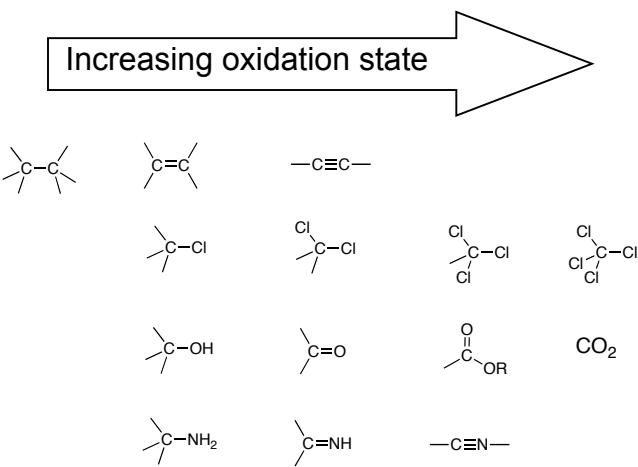
- There will be two possible Wittig routes to an alkene.
- Analyze the structure *retrosynthetically*, i.e., work the synthesis out backwards
- *Disconnect* (break the bond of the target that can be formed by a known reaction) the doubly bonded carbons. One becomes the aldehyde or ketone, the other the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



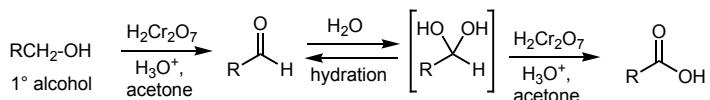
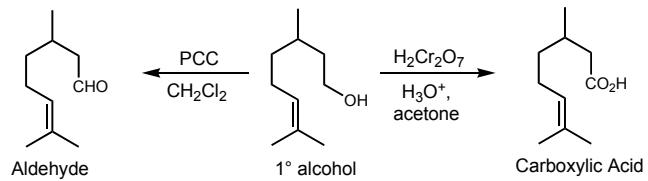
115

17.14: Stereoselective Addition to Carbonyl Groups (please read)

17.15: Oxidation of Aldehydes



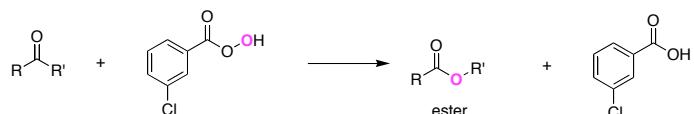
116



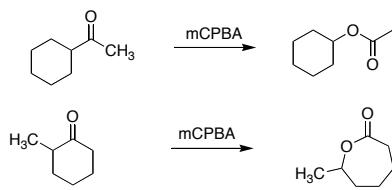
Aldehydes are oxidized by Cr(VI) reagents to carboxylic acids in aqueous acid. The reactions proceeds through the hydrate

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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 α -carbon



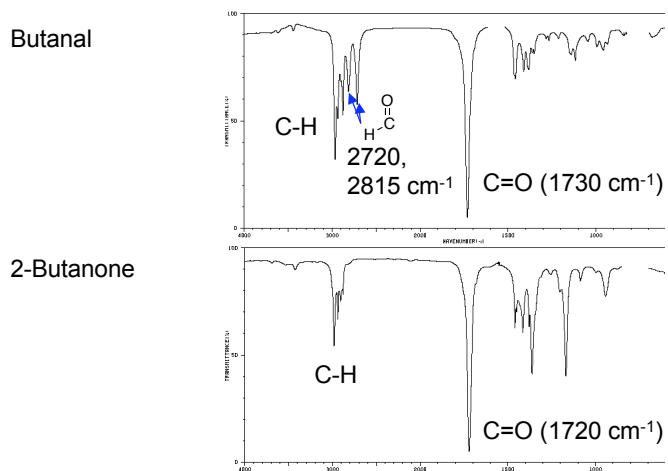
118

19.17: Spectroscopic Analysis of Aldehydes and Ketones

Infrared Spectroscopy: highly diagnostic for carbonyl groups

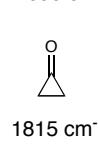
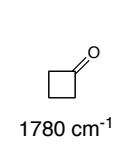
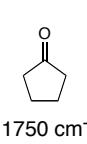
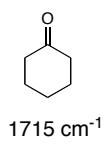
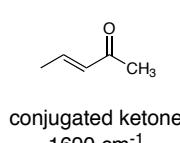
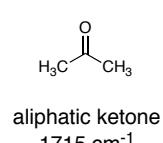
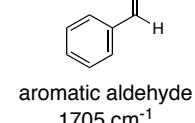
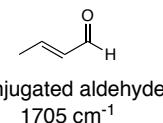
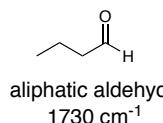
Carbonyls have a strong C=O absorption peak between
 $1660 - 1770 \text{ cm}^{-1}$

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



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

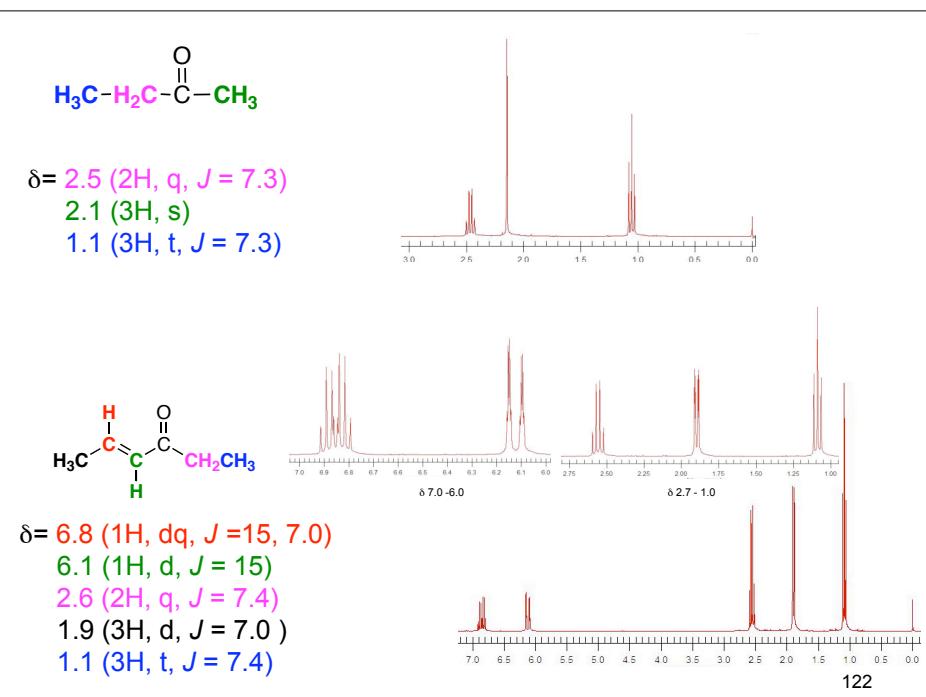
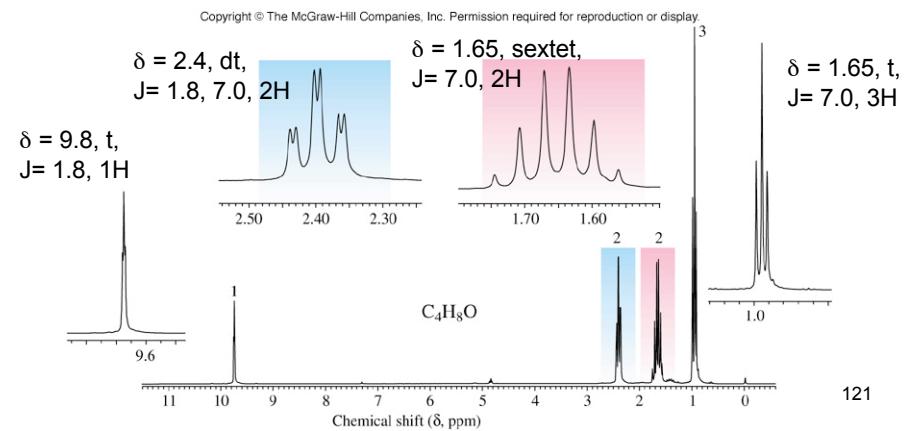


Conjugation moves the C=O stretch to lower energy (right, lower cm^{-1})

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

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

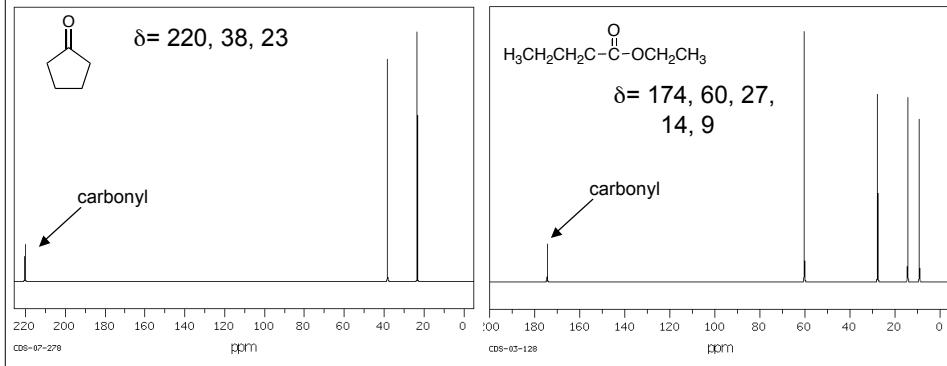


^{13}C NMR:

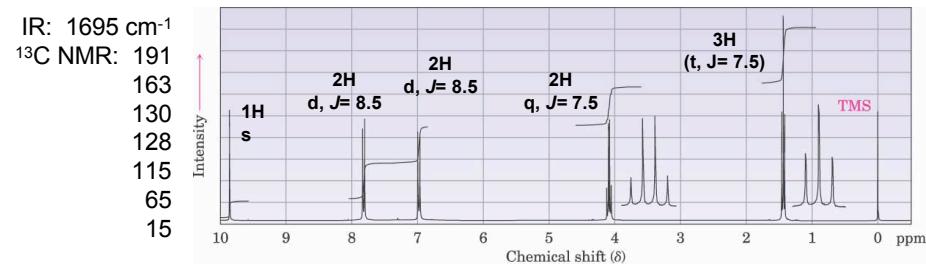
The intensity of the carbonyl resonance in the ^{13}C spectrum usually weak and sometimes not observed.

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



$\text{C}_9\text{H}_{10}\text{O}_2$



$\text{C}_{10}\text{H}_{12}\text{O}$

