

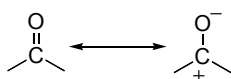
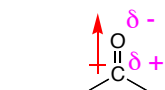
Chapter 17: Aldehydes and Ketones: Nucleophilic Addition to the Carbonyl Group

17.1: Nomenclature (please read)

suffix: -al for aldehydes

-one for ketone

17.2: Structure and Bonding: The Carbonyl Group: 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. 115

17.3: Physical Properties (please read)

17.4: Sources of Aldehydes and Ketones (Table 17.1, p. 693)

1. Oxidation of Alcohols

a. Oxidation of 1° and 2° alcohols (Chapter 15.9)

b. From carboxylic acids and esters (Chapter 15.3)

c. Ketones from aldehydes

2. Ozonolysis of alkenes (Chapter 6.12)

3. Hydration of alkynes (Chapter 9.12)

4. Friedel-Crafts Acylation – aryl ketones (Chapter 12.7)

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

Reactions of aldehydes and ketones (Table 17.2, p. 695)- Review:

1. Reduction to hydrocarbons (Chapter 12.8)
 - a. Clemmenson reduction (Zn-Hg, HCl)
 - b. Wolff-Kishner (H_2NNH_2 , KOH, Δ)

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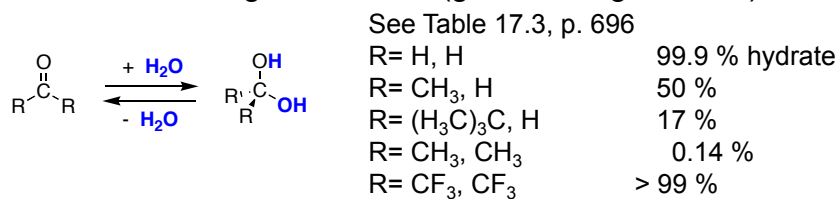
2. Reduction to 1° and 2° alcohols (Chapter 15.2)

3. Addition of Grignard Reagents (Chapters 14.5-14.6)

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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 or acid catalyzed

Base-catalyzed mechanism (p. 699):

hydroxide is a better nucleophile than water

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Acid-catalyzed mechanism (p. 700):
protonated carbonyl is a better electrophile

The hydration reaction is reversible

Does adding acid or base change the amount of hydrate?
Does a catalyst affect ΔG° , ΔG^\ddagger , both, or neither? ¹²¹

17.7: Cyanohydrin Formation

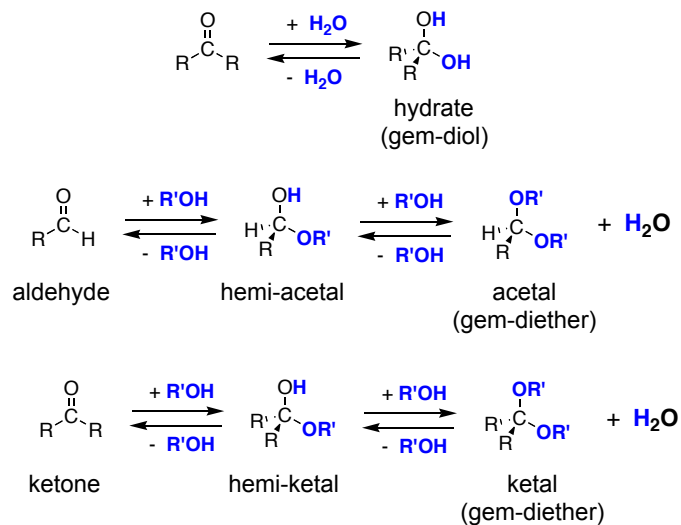
Addition of H-CN to the aldehydes and unhindered ketones.
(related to the hydration reaction)

The equilibrium favors cyanohydrin formation

Mechanism of cyanohydrin formation (p. 701)

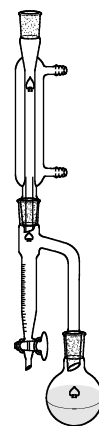
17.8: Reaction with Alcohols: Acetals and Ketals

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



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Mechanism of acetal (ketal) formation is acid-catalyzed (p. 705)

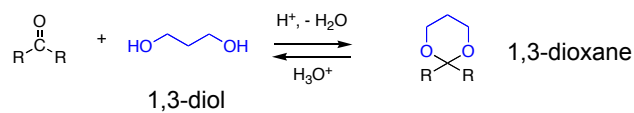
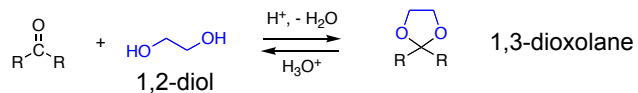


Dean-Stark
Trap

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

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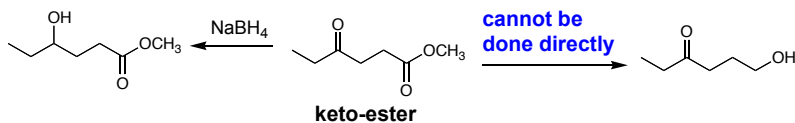
Dioxolanes and dioxanes: cyclic acetal (ketals) from 1,2- and 1,3-diols



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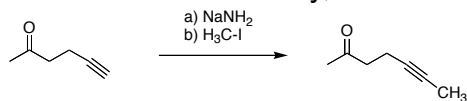
17.9: Acetals and Ketals as Protecting Groups

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).

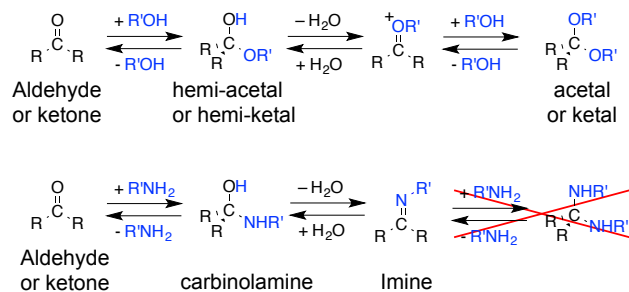


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The reaction cannot be done directly, as shown. Why?



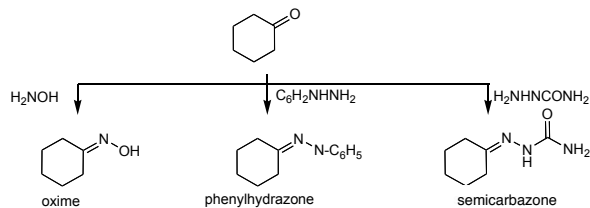
17.10: Reaction with Primary Amines: Imines (Schiff base)



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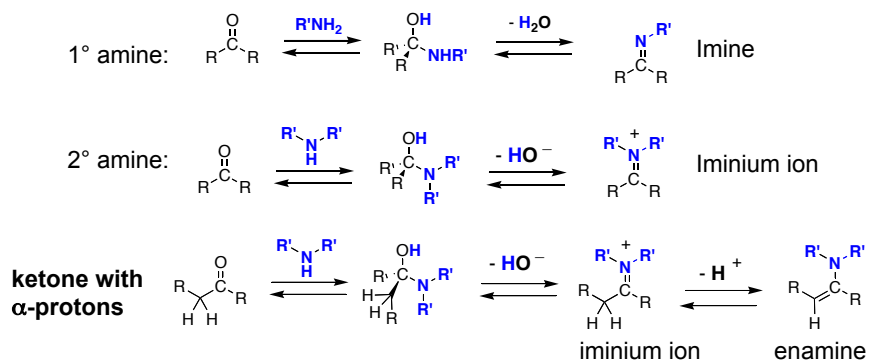
Mechanism of imine formation (p. 709):

See Table 17.4 (p. 712) for the related carbonyl derivative, oximes, hydrazone and semicarbazones (please read)



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17.11: Reaction with Secondary Amines: Enamines



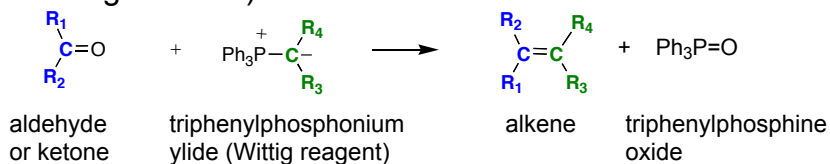
Mechanism of enamine formation (p. 713)

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17.12: The Wittig Reaction

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

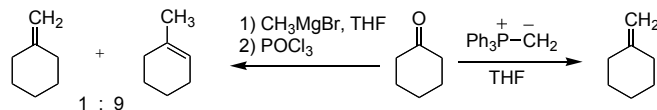
The synthesis of an alkene from the reaction of an aldehyde or ketone and a phosphorus *ylide* (Wittig reagent), a dipolar intermediate with formal opposite charges on adjacent atoms (overall charge neutral).



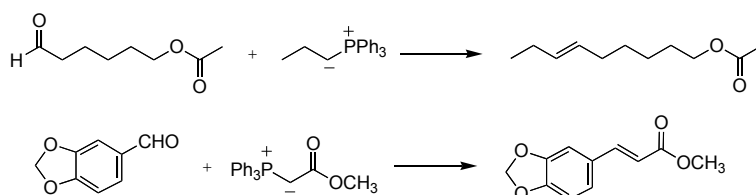
Accepted mechanism (p. 716)

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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.

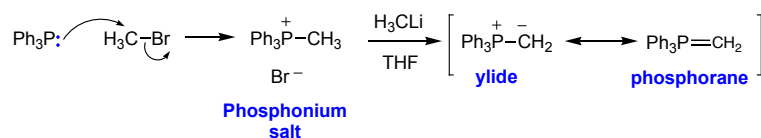


Predicting the geometry (*E/Z*) of the alkene product is complex and is dependent upon the nature of the ylide.

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Alkene Synthesis via the Wittig Reaction:

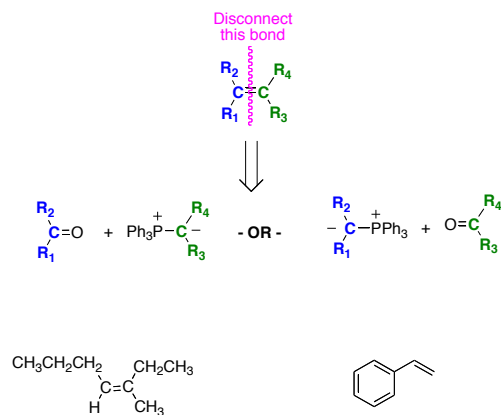
A Wittig reagent is prepared from the reaction of an alkyl halide with triphenylphosphine ($\text{Ph}_3\text{P}:$) to give a phosphonium salt. The protons on the carbon adjacent to phosphorous are acidic.



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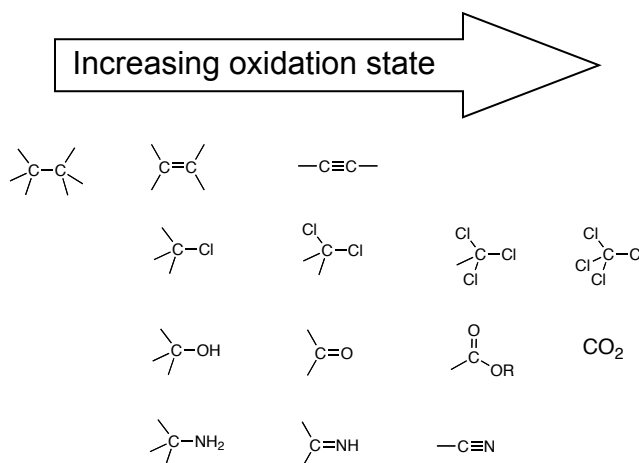
- There will be two possible Wittig routes to an alkene.
- Analyze the structure *retrosynthetically*, i.e., work the synthesis out backwards.
- *Disconnect* (break the bond of the target that can be formed by a known reaction) the doubly bonded carbons. One becomes the aldehyde or ketone, the other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



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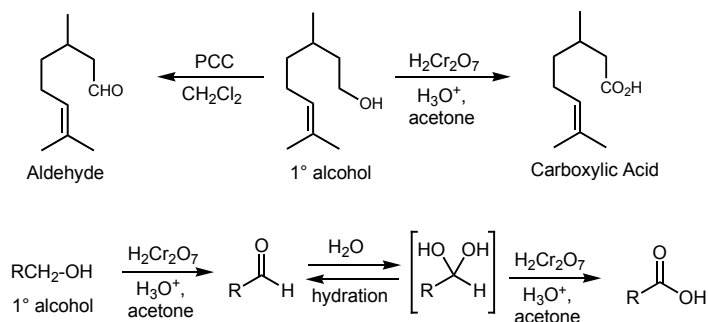
17.13: Stereoselective Addition to Carbonyl Groups (please read)

17.14: Oxidation of Aldehydes



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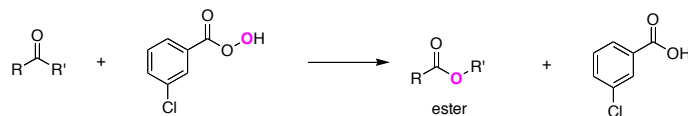
See Chapter 15.9



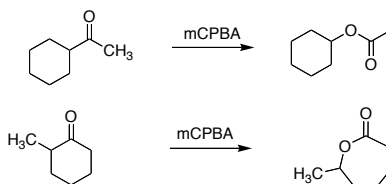
Aldehydes are oxidized by Cr(VI) reagents to carboxylic acids in aqueous acid. The reaction proceeds through the hydrate

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Baeyer-Villiger Oxidation of Ketones. Oxidation of ketones with a peroxy acid to give as esters (p. 732)



Oxygen insertion occurs between the carbonyl carbon and the more substituted α -carbon



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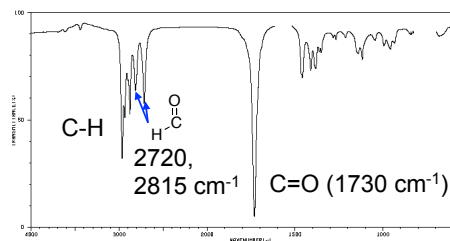
17.15: Spectroscopic Analysis of Aldehydes and Ketones

Infrared Spectroscopy: highly diagnostic for carbonyl groups

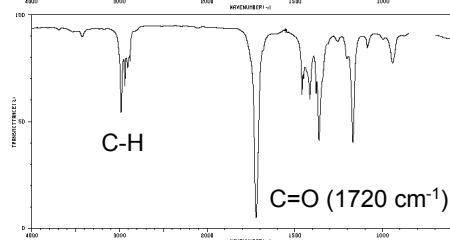
Carbonyls have a strong C=O absorption peak between
1660 - 1770 cm^{-1}

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

Butanal

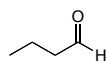


2-Butanone

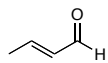


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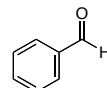
C=O stretches of aliphatic, conjugated, aryl and cyclic carbonyls:



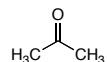
aliphatic aldehyde
1730 cm^{-1}



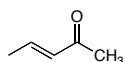
conjugated aldehyde
1705 cm^{-1}



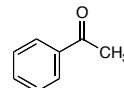
aromatic aldehyde
1705 cm^{-1}



aliphatic ketone
1715 cm^{-1}



conjugated ketone
1690 cm^{-1}



aromatic ketone
1690 cm^{-1}



1715 cm^{-1}



1750 cm^{-1}



1780 cm^{-1}



1815 cm^{-1}

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

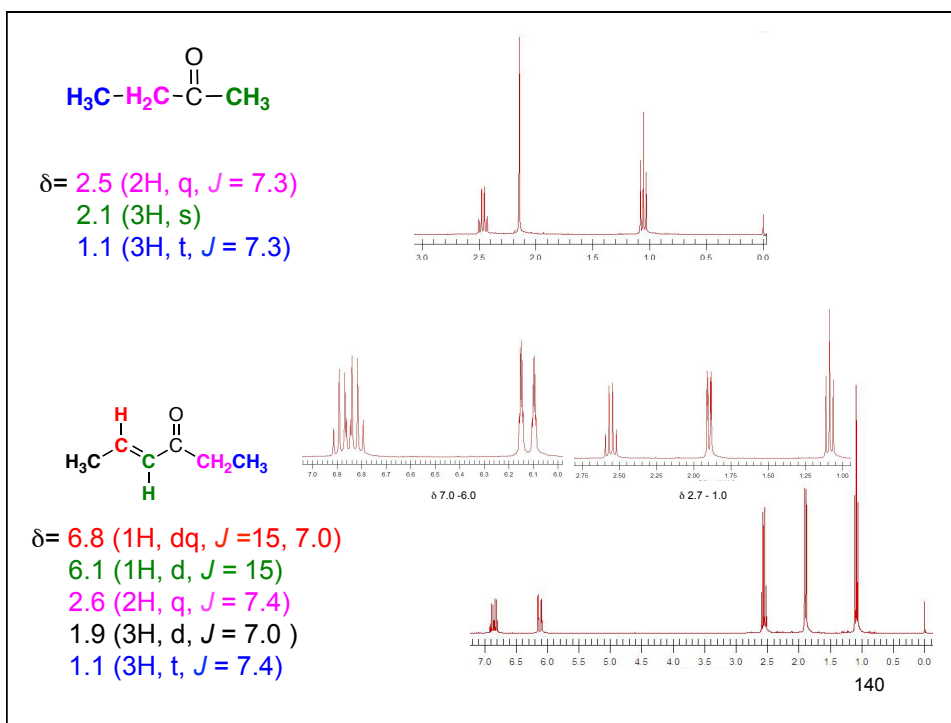
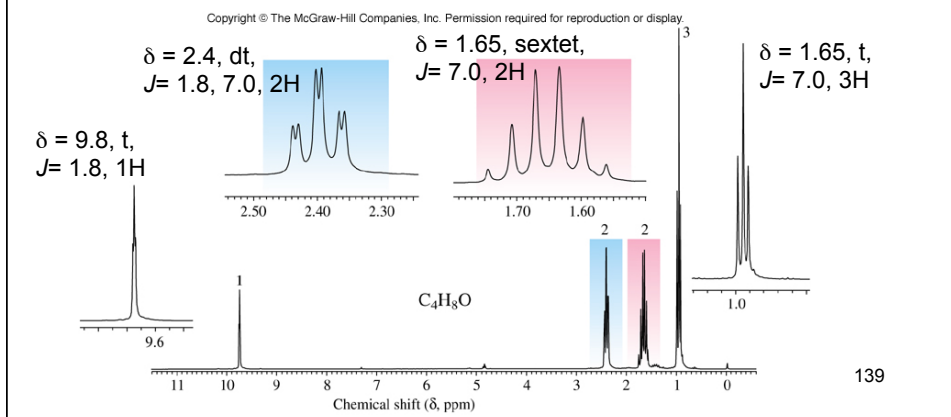
*Ring (angle) strain moves the C=O stretch to higher energy
(left, higher cm^{-1})*

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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

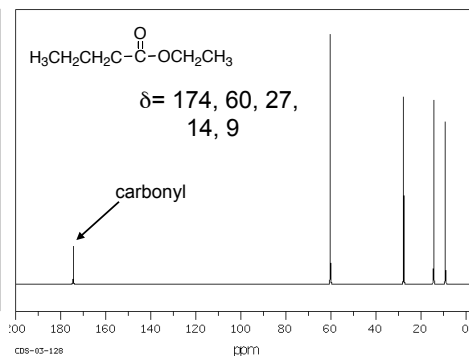
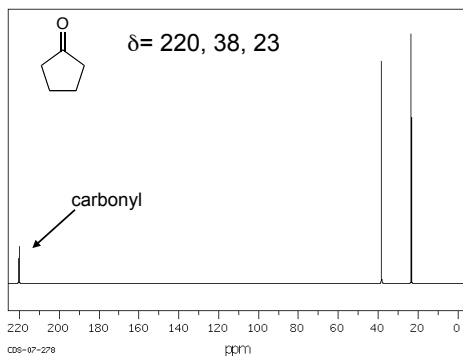


¹³C NMR:

The intensity of the carbonyl resonance in the ¹³C 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



C₉H₁₀O₂

IR: 1695 cm⁻¹

¹³C NMR: 191

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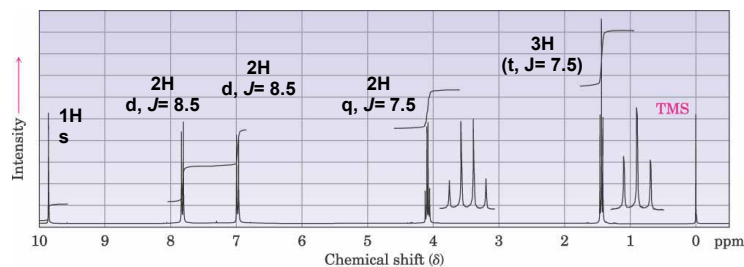
130

128

115

65

15



C₁₀H₁₂O

IR: 1710 cm⁻¹

¹³C NMR: 207

134

130

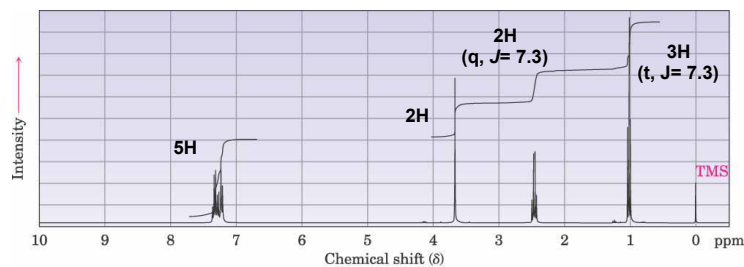
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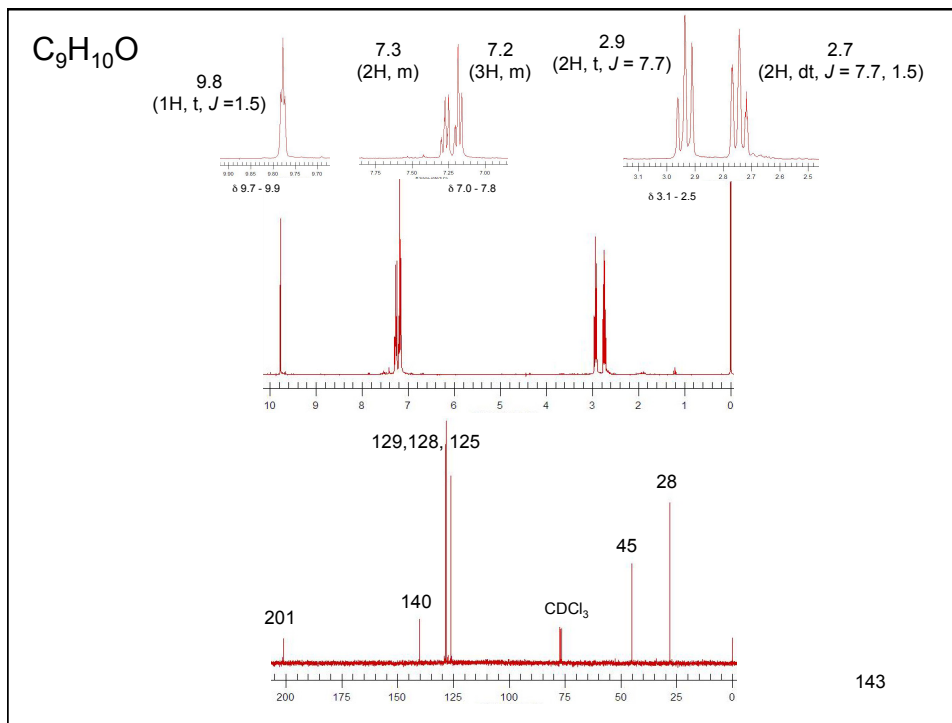
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10





Chapter 18: Carboxylic Acids

18.1: Carboxylic Acid Nomenclature (please read)

suffix: -oic acid

18.2: Structure and Bonding (please read)

18.3: Physical Properties. The carboxylic acid functional group contains both a hydrogen bond donor (-OH) and a hydrogen bond acceptor (C=O).

Carboxylic acids exist as hydrogen bonded dimers.

