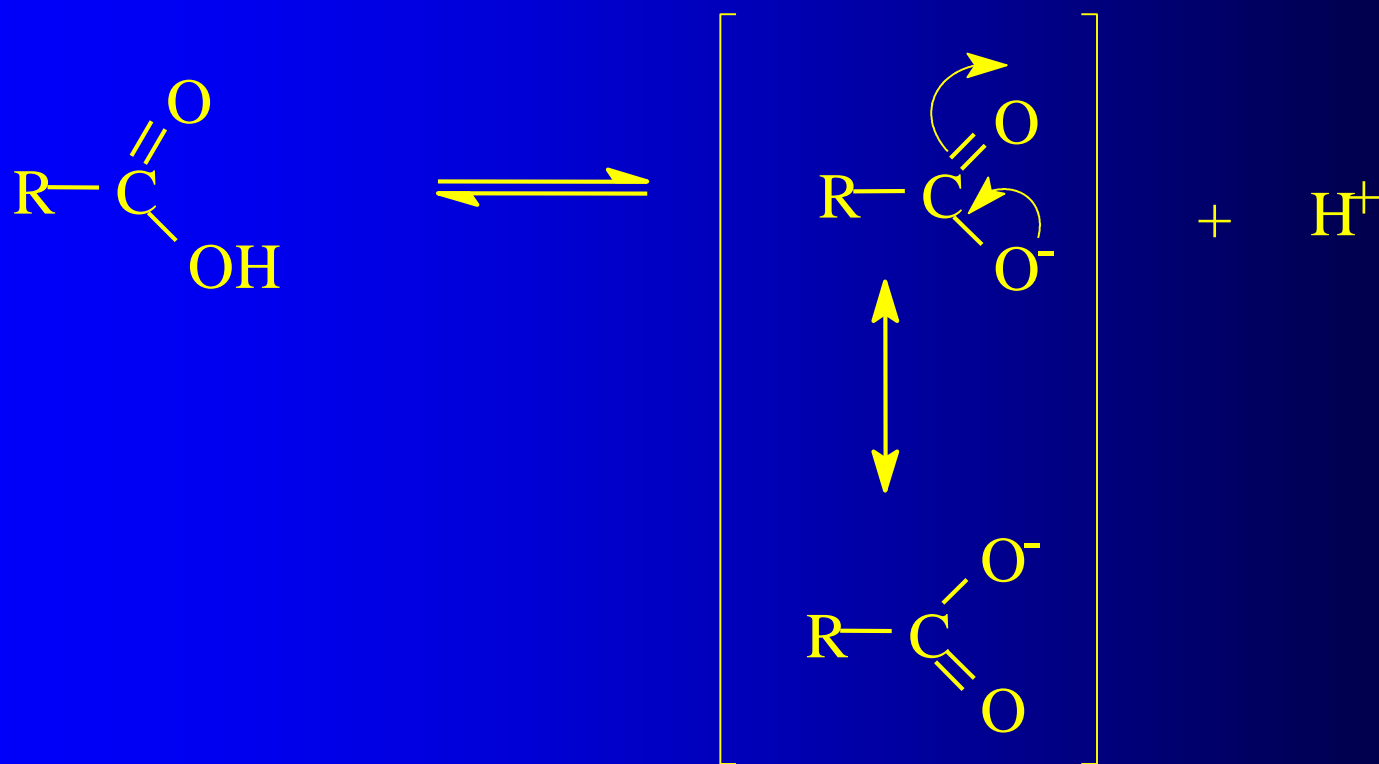
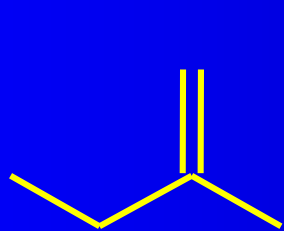


Lecture 18

More Carboxylic Acids

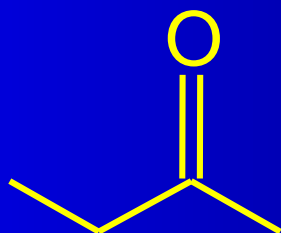


Boiling Points



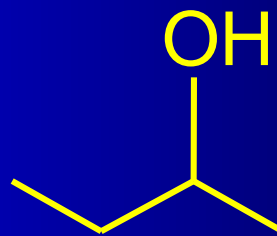
bp (1 atm) 31°C

Molar mass 70



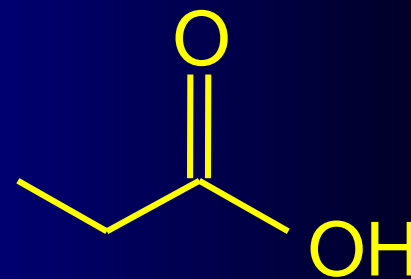
80°C

72



99°C

74



141°C

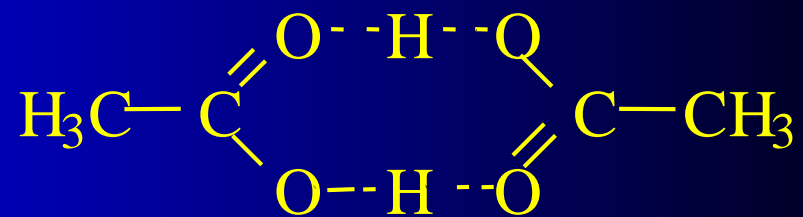
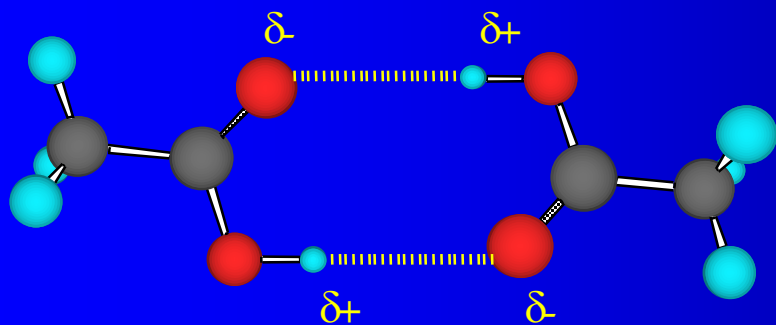
74

- Intermolecular forces, especially hydrogen bonding, are stronger in carboxylic acids than in other compounds of similar shape and molecular weight



Physical Properties

- In the liquid and solid states, carboxylic acids are associated by hydrogen bonding into dimeric structures



Infrared Spectroscopy

- A carboxylic acid is characterized by peaks due to OH and C=O groups in its infrared spectrum.
- C=O stretching gives an intense absorption near 1700 cm^{-1} .
- OH peak is broad and overlaps with C—H absorptions.



Infrared Spectrum of 4-Phenylbutanoic acid

*



O—H and C—H stretch

C=O

monosubstituted benzene

3500

3000

2500

2000

1500

1000

500

Wave number, cm^{-1}

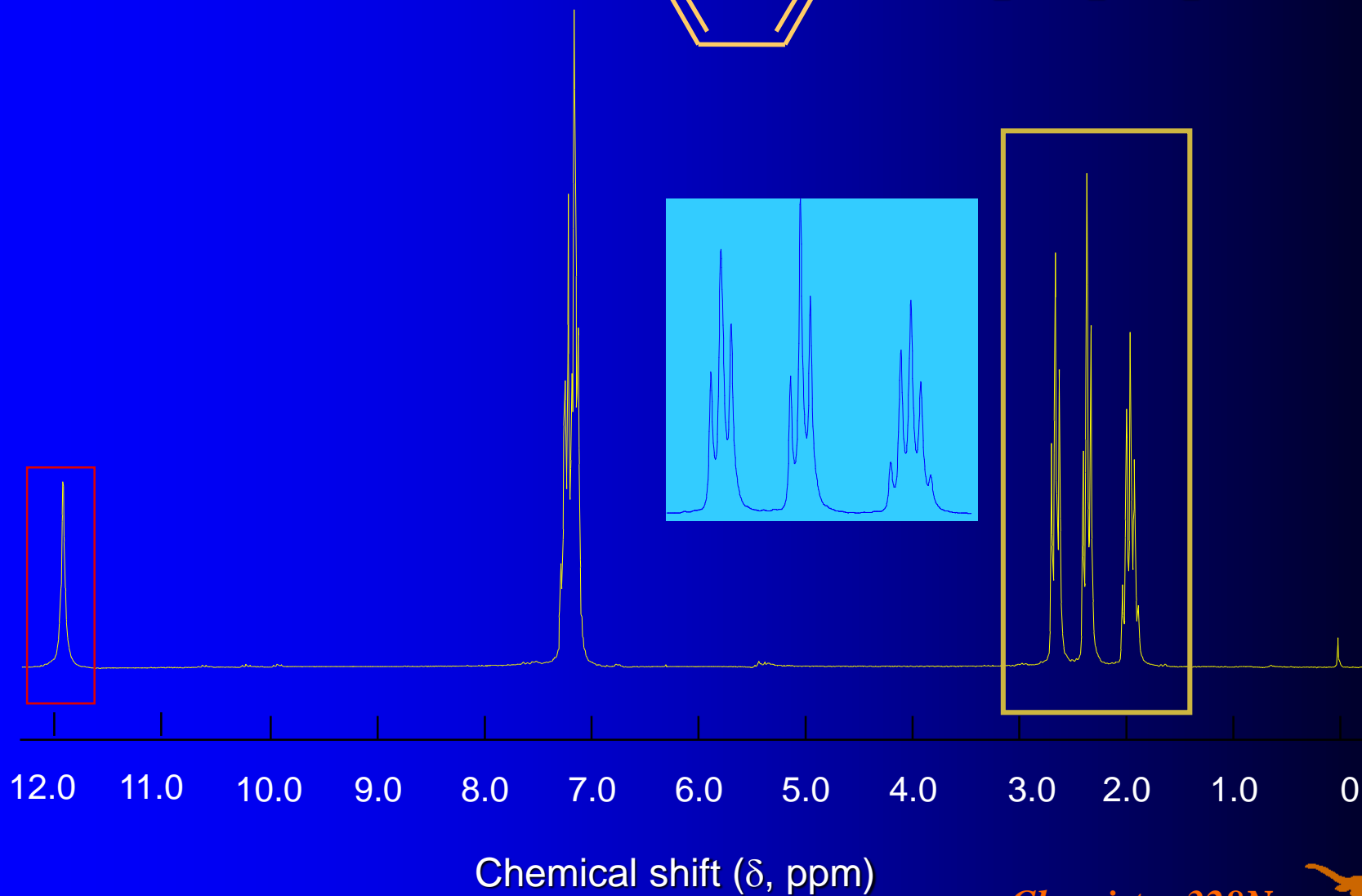
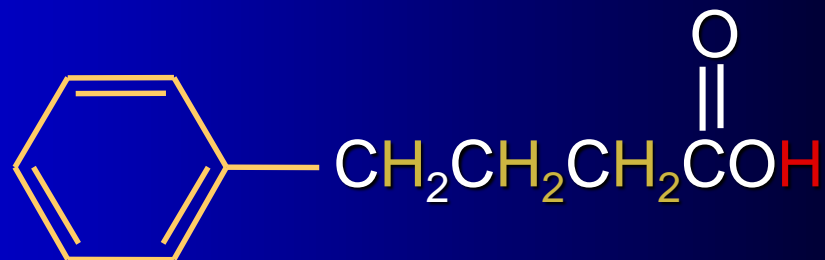


^1H NMR of Carboxylic acids

The acidic proton in the HO- group of a carboxylic acid is normally the least shielded of all protons in a ^1H nmr spectrum: (δ 10-12 ppm; broad). It moves with pH and it is subject to exchange with D_2O .



Proton NMR



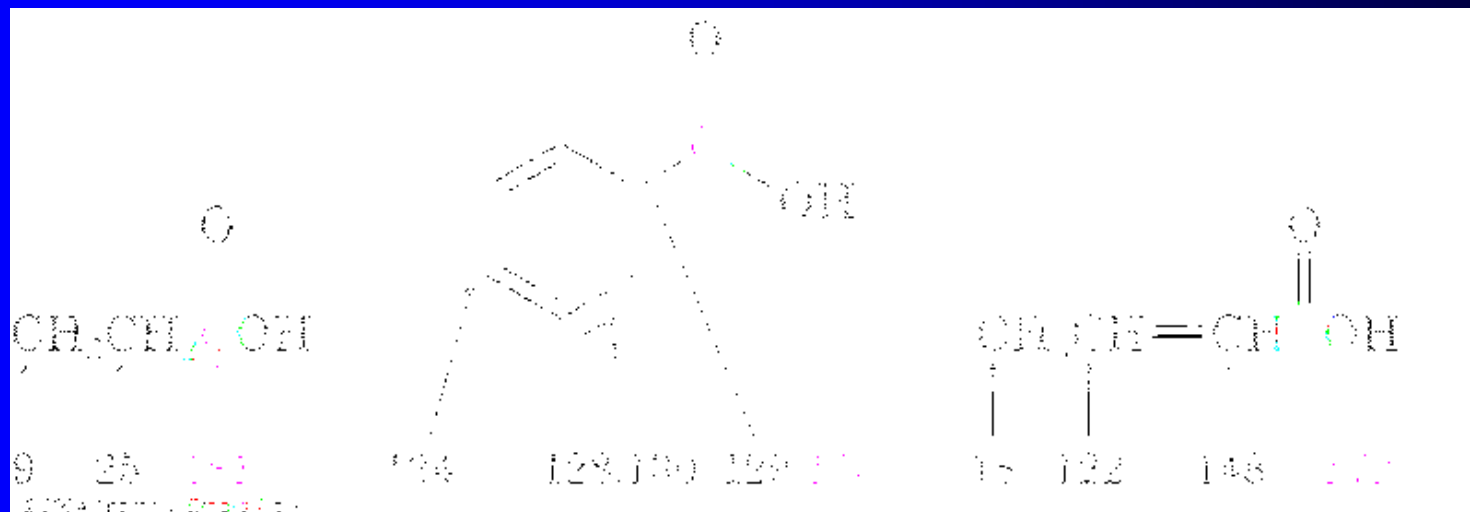
^{13}C NMR of Carboxylic acids

The Carbonyl carbon on the carboxylic acid group is at low field (δ 165-185 ppm), but not quite as deshielded as the carbonyl carbon of an aldehyde or ketone (δ 190-215 ppm).

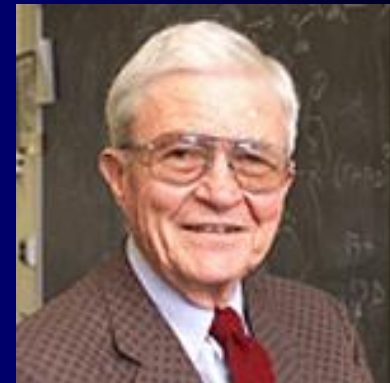


^{13}C NMR of Carboxylic acids

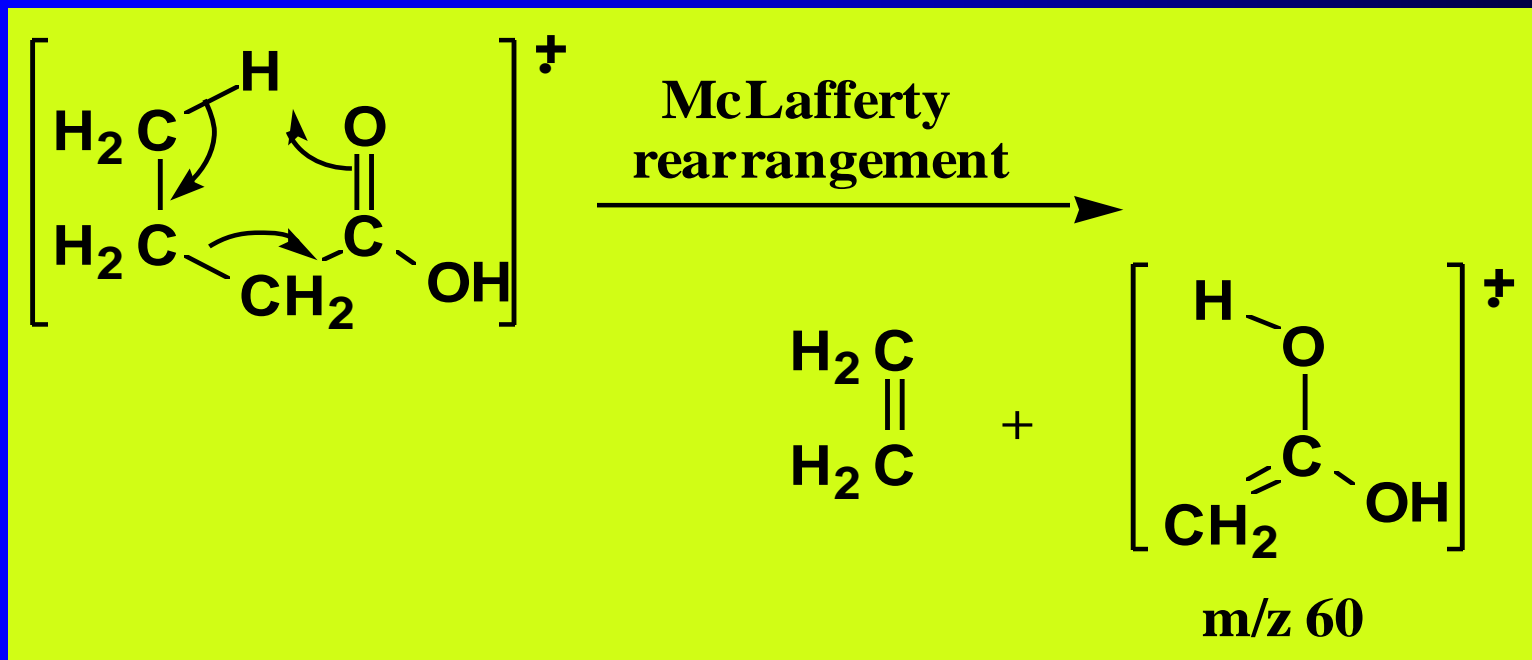
- Carboxyl $^{13}\text{COOH}$ signals are at $\delta 165$ to $\delta 185$
- Aromatic and α,β -unsaturated acids are near $\delta 165$ and saturated aliphatic acids are near $\delta 185$



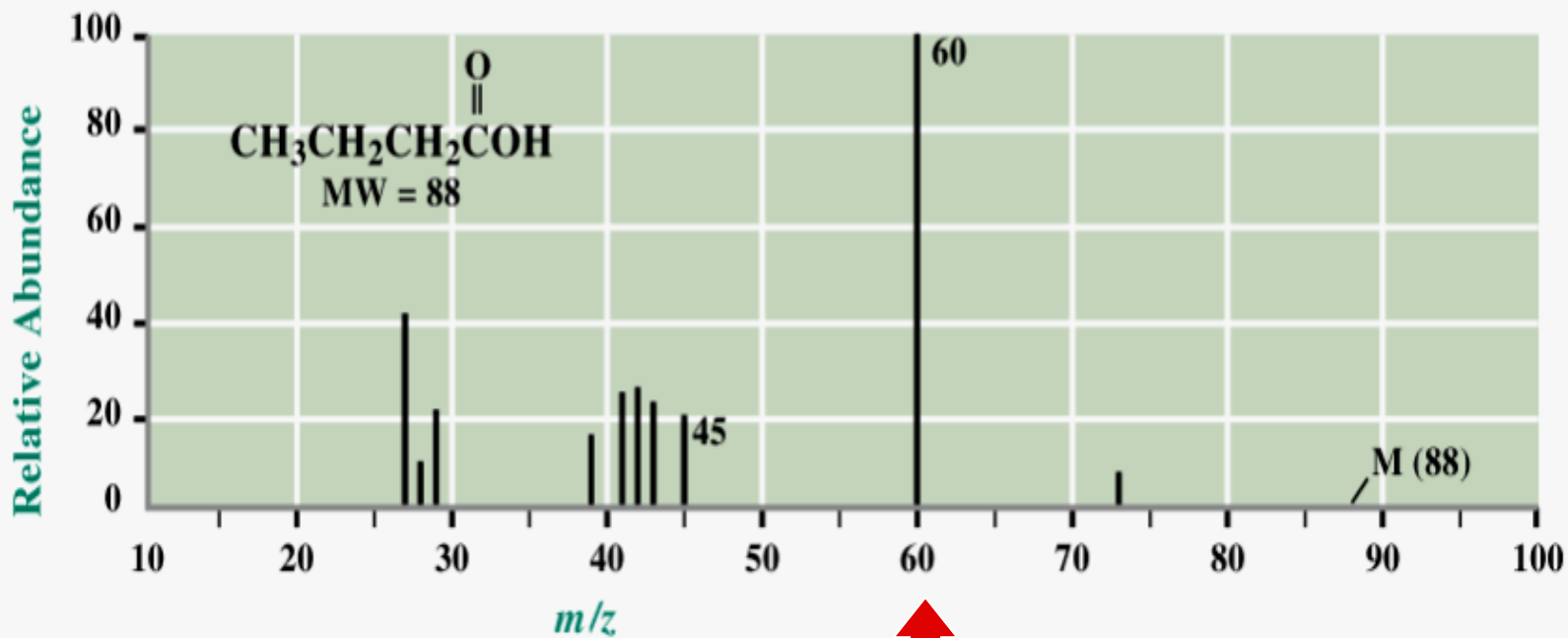
Mass Spectrometry



- The McLafferty rearrangement gives a characteristic peak at $m/z = 60$



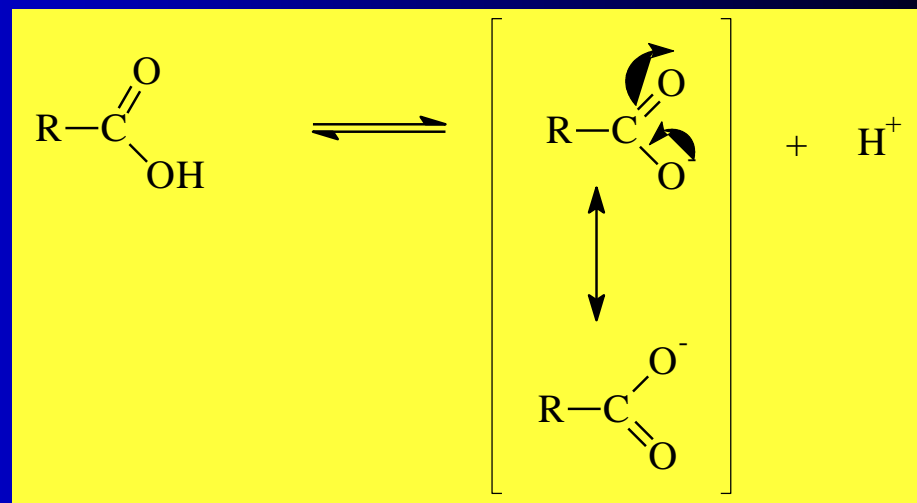
Mass spectrum of butanoic acid



Acidity

- Carboxylic acids are weak acids
 - The pK_a of typical aliphatic and aromatic carboxylic acids falls within the range 4 to 5

• The greater acidity of carboxylic acids relative to alcohols, both of which have oxyanions conjugate bases is because:

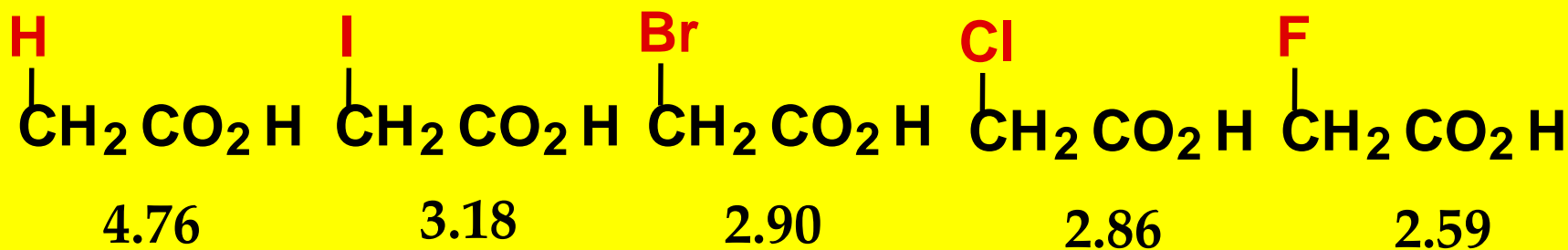


- *the carboxylate anion is stabilized by resonance*



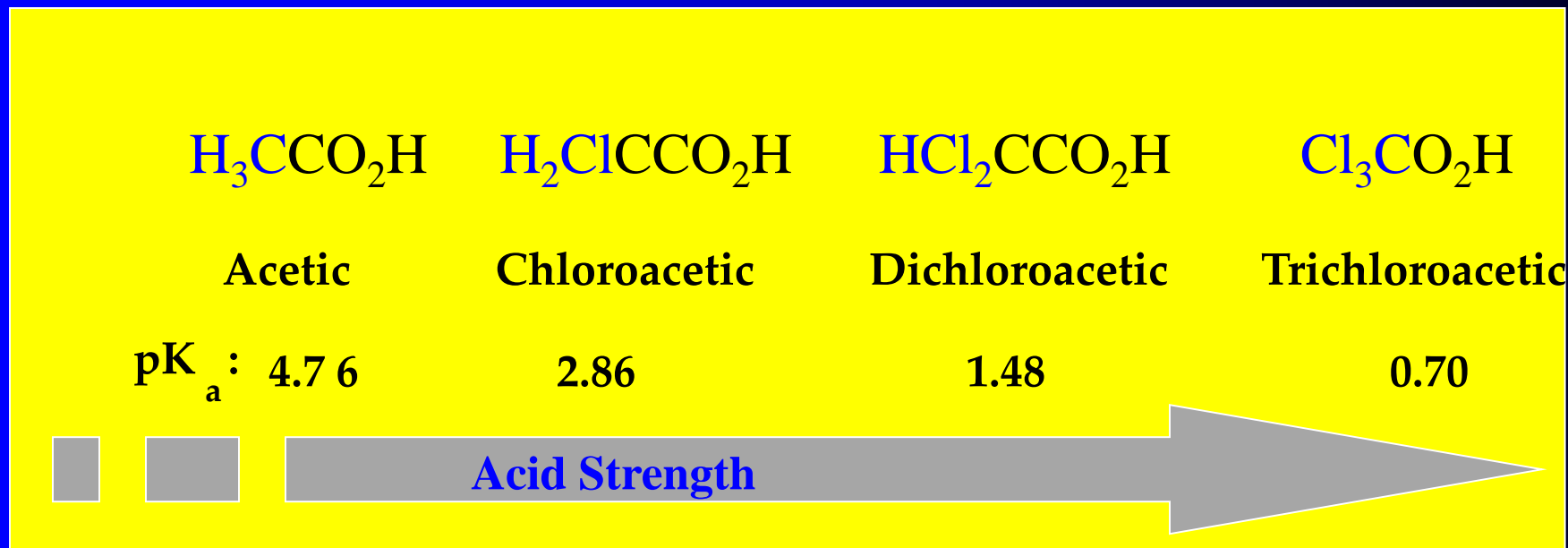
Acidity

- Electron-withdrawing substituents near the carboxyl group increase acidity through their inductive effect



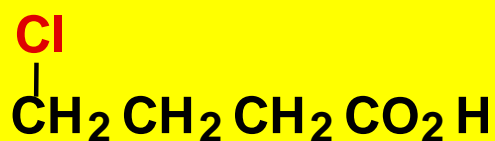
Acidity

- Substitution by multiple electron-withdrawing groups further increases acidity



Acidity

- The inductive effect of an electron-withdrawing substituent falls off rapidly with its distance from the carboxyl group



4-Chlorobutanoic

pK_a: 4.52



3-Chlorobutanoic

3.98



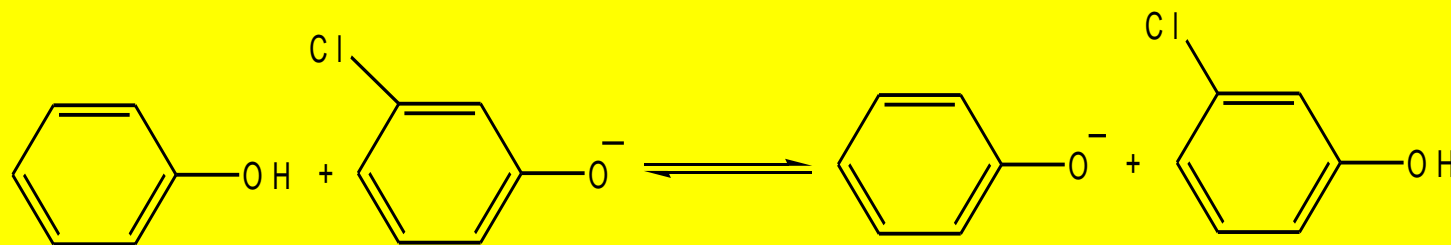
2-Chlorobutanoic

2.83

Acid Strength



Be Sure to Study Trends in Acid Strength

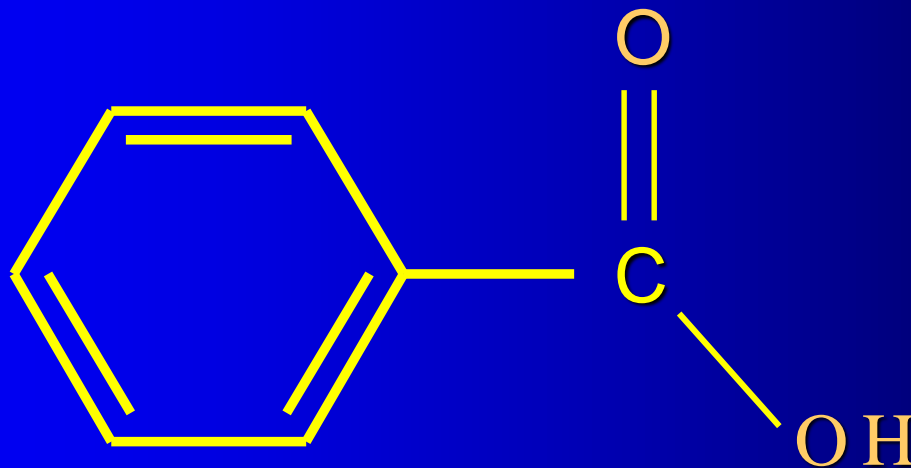


Which way does the equilibrium lie??

Please Practice This Game

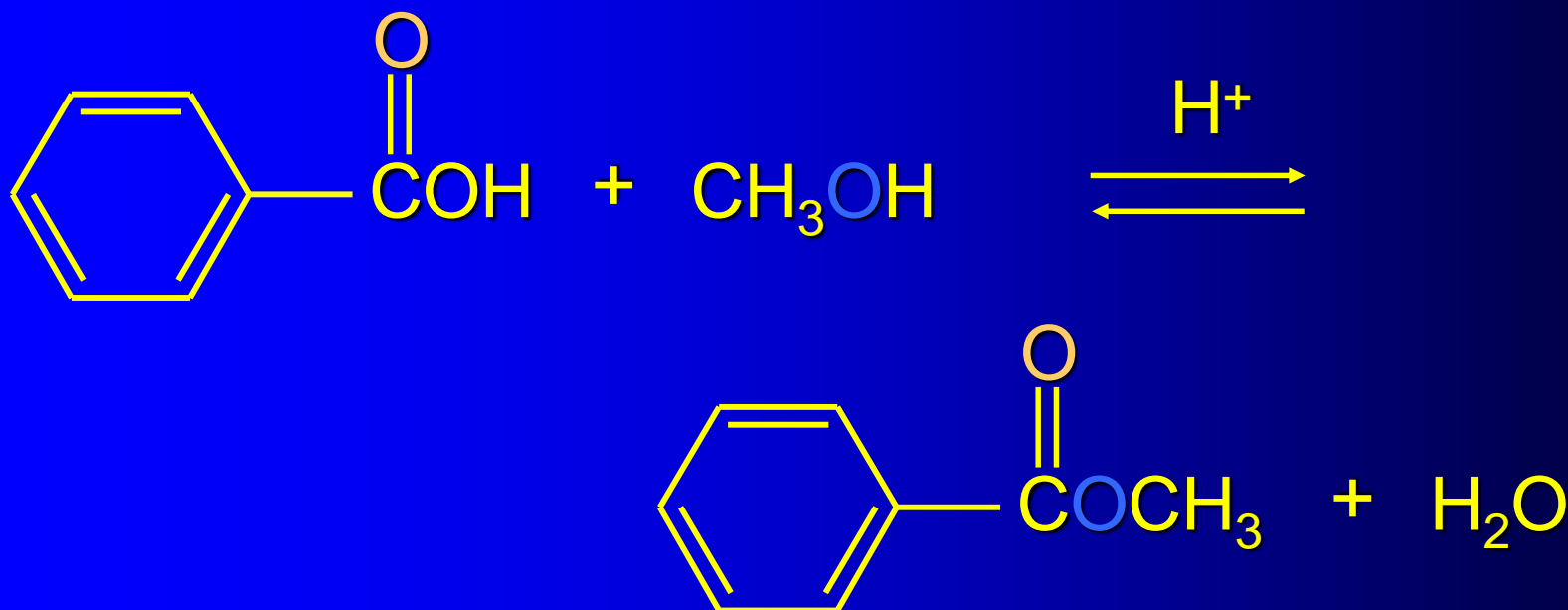


Reactions of Carboxylic acids



Acid-catalyzed Esterification

(also called Fischer esterification)

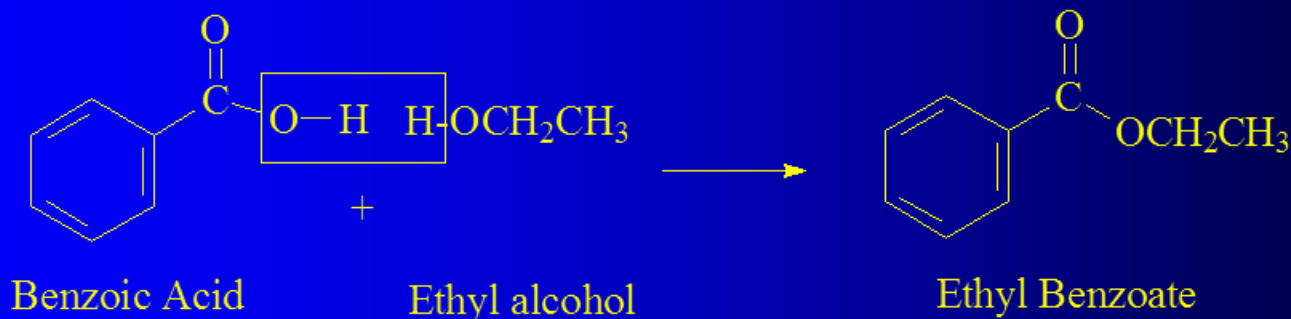


- Important fact: the oxygen of the alcohol is incorporated into the ester as shown.



Nomenclature of Esters

The IUPAC name for esters is derived from the names of the parent carboxylic acids. The alkyl group bonded to oxygen is named first followed by the name of the acid in which the suffix **-ic** is replaced by the suffix **-ate**



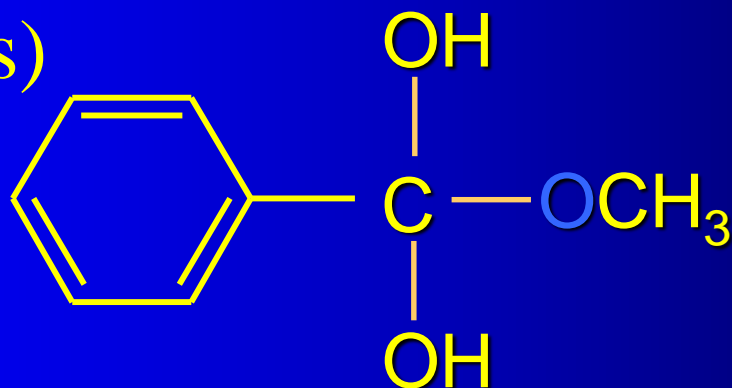
Mechanism of Fischer Esterification

- The mechanism involves two stages:
 - 1) formation of tetrahedral intermediate
(3 steps)
 - 2) dissociation of tetrahedral intermediate
(3 steps)



Mechanism of Fischer Esterification

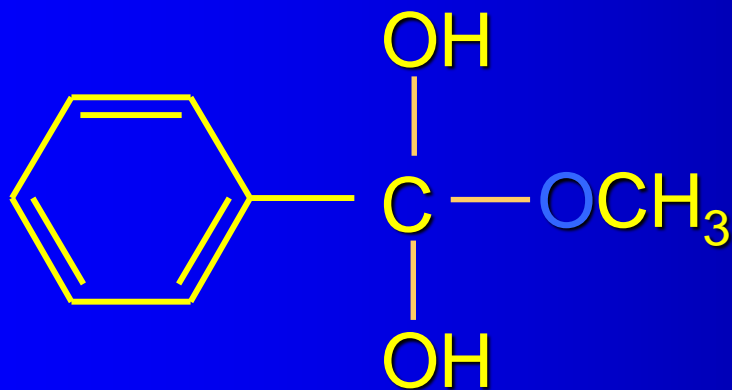
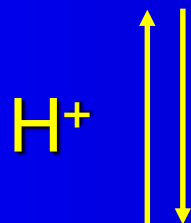
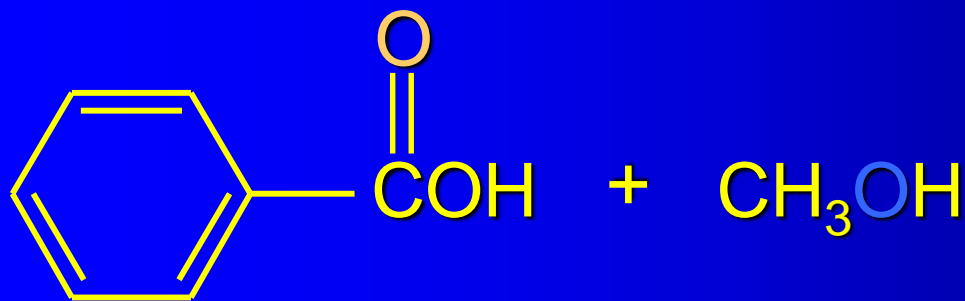
- The mechanism involves two stages:
- 1) formation of tetrahedral intermediate (3 steps)
- 2) dissociation of tetrahedral intermediate (3 steps)



tetrahedral intermediate



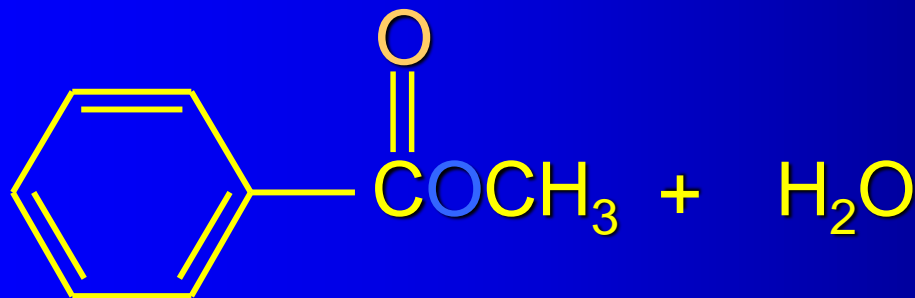
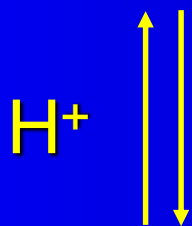
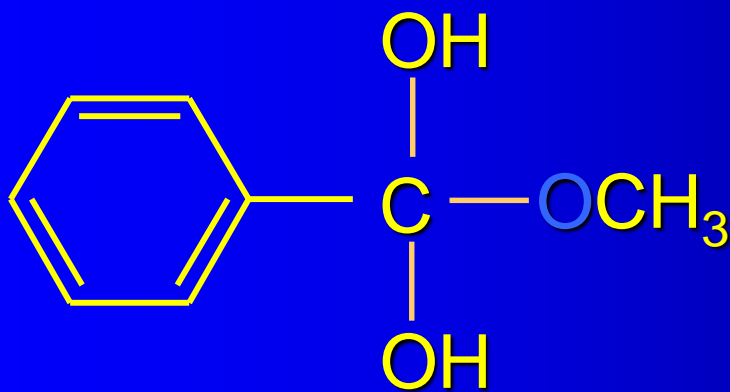
First stage: formation of tetrahedral intermediate



- methanol adds to the carbonyl group of the carboxylic acid
- the tetrahedral intermediate is analogous to a hemiacetal



Second stage: conversion of tetrahedral intermediate to ester



- this stage corresponds to an acid-catalyzed dehydration



Mechanism of Fischer esterification

1 Proton transfer from the acid catalyst to the carbonyl oxygen increases the electrophilicity of the carbonyl carbon...

2 which is then attacked by the nucleophilic oxygen atom of the alcohol...

3 to form an oxonium ion.

4 Proton transfer from the oxonium ion to a second molecule of alcohol...

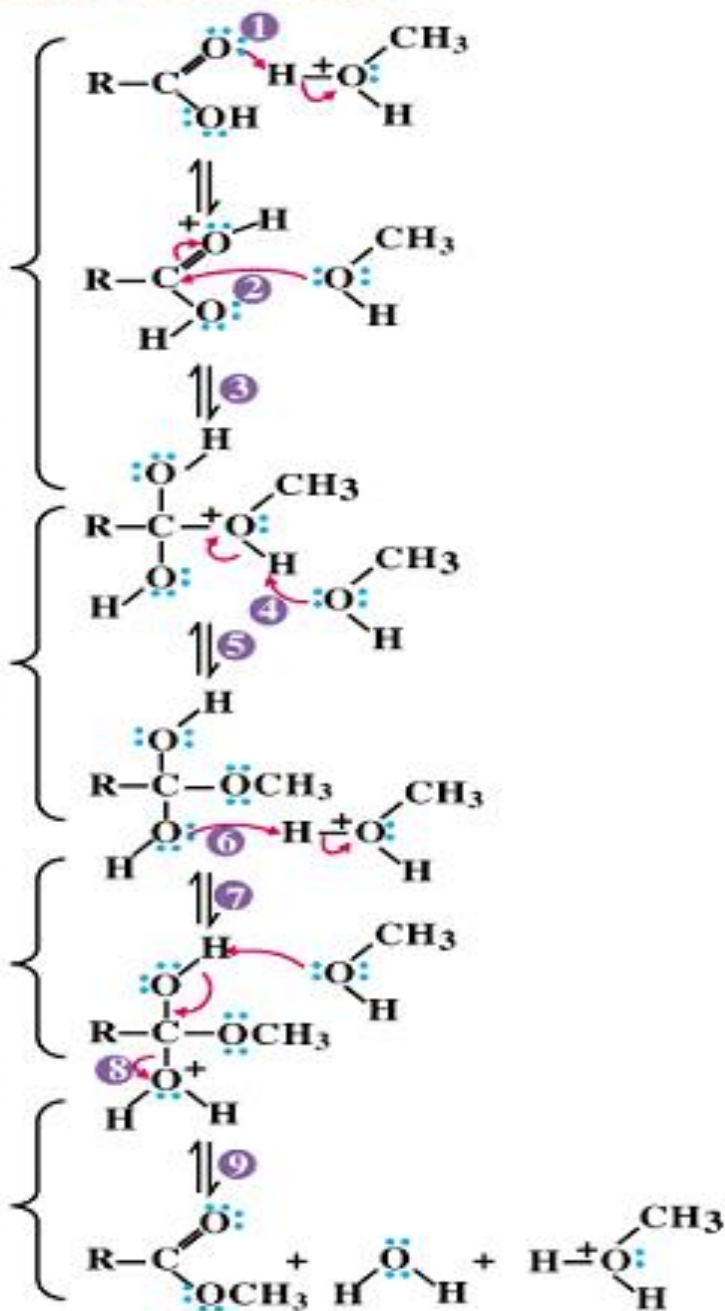
5 gives a tetrahedral carbonyl addition intermediate (TCAI).

6 Proton transfer to one of the —OH groups of the TCAI...

7 gives a new oxonium ion.

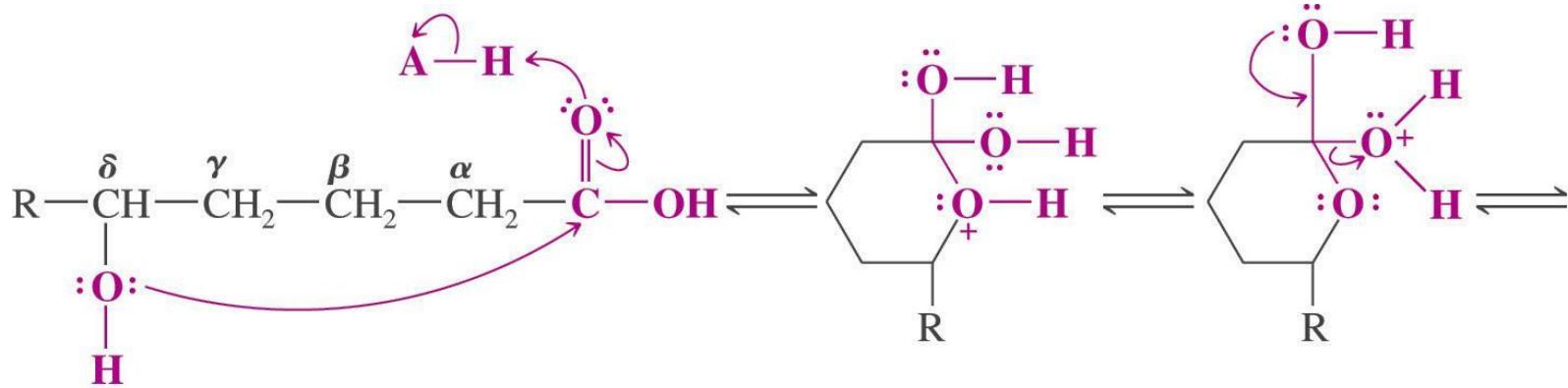
8 Loss of water from this oxonium ion...

9 gives the ester and water.

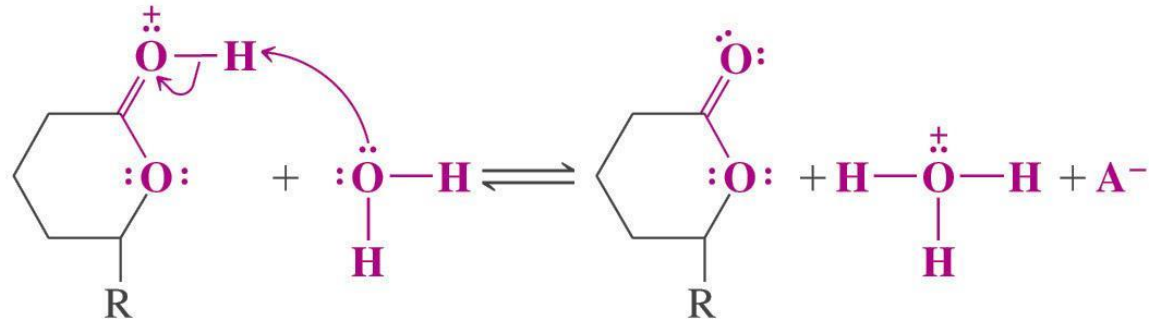


– Lactones

- γ - or δ -Hydroxyacids undergo acid catalyzed reaction to give cyclic esters known as γ - or δ -lactones, respectively



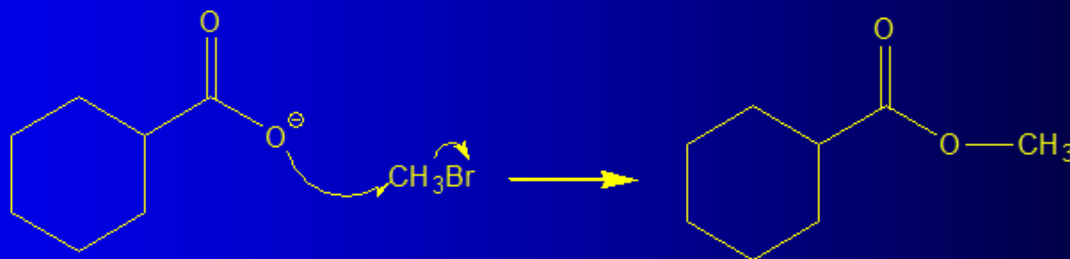
A δ -hydroxy acid



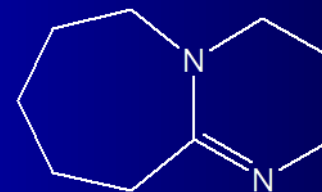
A δ -lactone

Synthesis of Esters

- S_N2



- Fischer Esterification
- Diazomethane
- Via Acyl chloride

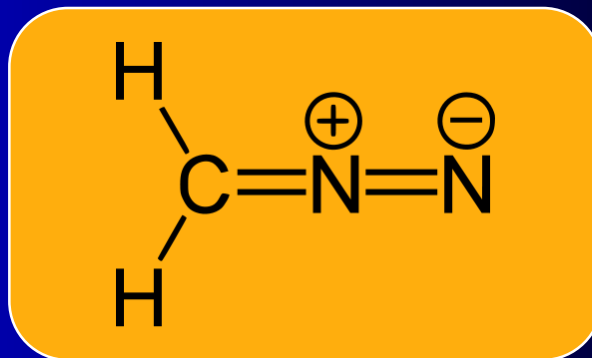


1,8-Diazabicyclo[5.4.0]undec-7-ene

DBU

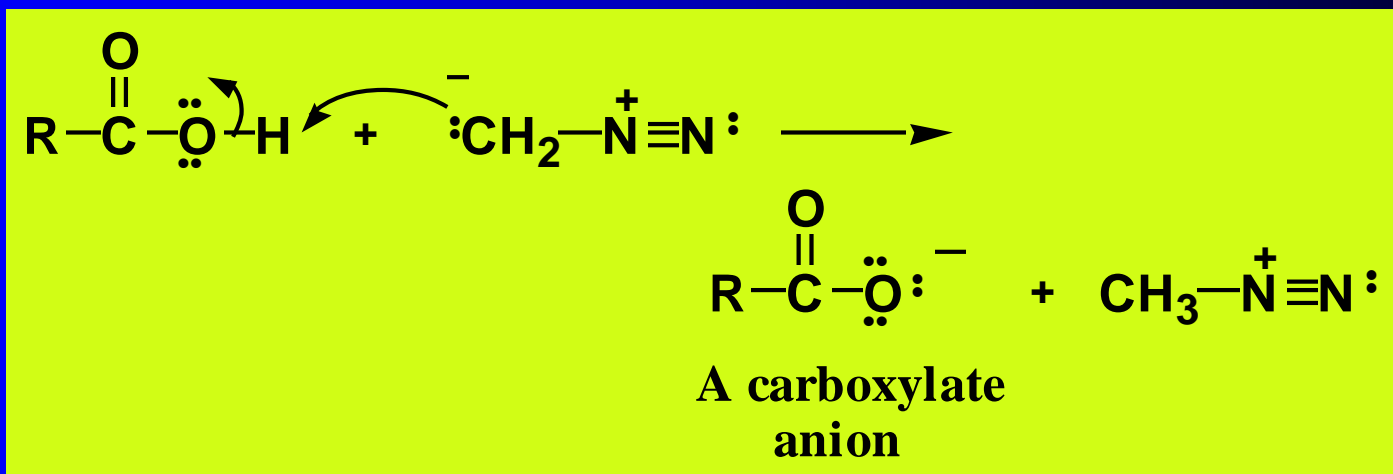


Diazomethane



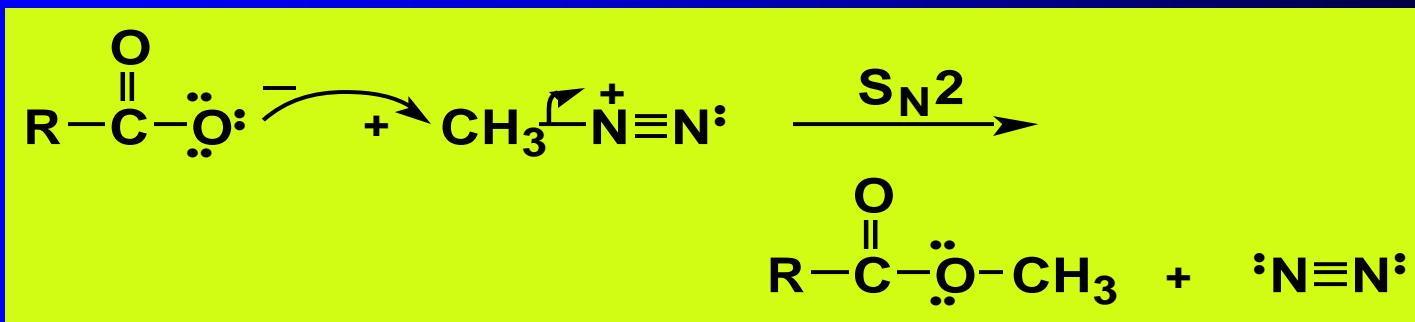
- Esterification occurs in two steps

Step 1: proton transfer from the carboxyl group to diazomethane



Diazomethane

Step 2: nucleophilic displacement (S_N2) of N_2 , an extraordinarily good leaving group, by the carboxylate anion



Diazomethane

Diazomethane is toxic by inhalation or by contact with the skin. Symptoms include chest discomfort, headache, weakness and, in severe cases, collapse. Symptoms may be delayed. In one instance a laboratory worker consumed a hamburger near a fumehood where he was generating a large quantity of diazomethane, and died four days later from fulminating pneumonia. Like any other alkylating agents it is expected to be carcinogenic, but such concerns are overshadowed by its serious acute toxicity.

CH₂N₂ may explode in contact with sharp edges, such as ground-glass joints, even scratches in glassware¹ Glassware should be inspected before use and preparation should take place behind a blast shield. Specialized kits to prepare diazomethane with flame-polished joints are commercially available. ***The compound explodes when heated beyond 100 °C, exposed to intense light, alkali metals, or calcium sulfate. Use of a blast shield is highly recommended while using this compound.***



Explosive response to safer chemistry

Chemists in Switzerland have devised a neat chemical trick that allows them to use the highly explosive reagent, diazomethane, in their reactions without risk to life or limb. Bill Morandi and Erick Carreira at ETH Zurich have shown that it is possible to use a precursor and a simple iron porphyrin catalyst to carry out cyclopropanations of styrenes, enynes and dienes in strong aqueous potassium hydroxide solution. Diazomethane can be used in aziridination, carbonyl homologation, cyclopropanation, dipolar cycloaddition, epoxidation, esterification reactions and more but its toxicity and explosive nature often precludes its use. Carreira's work opens up a new approach in which the gas is generated and consumed by the reaction in situ.



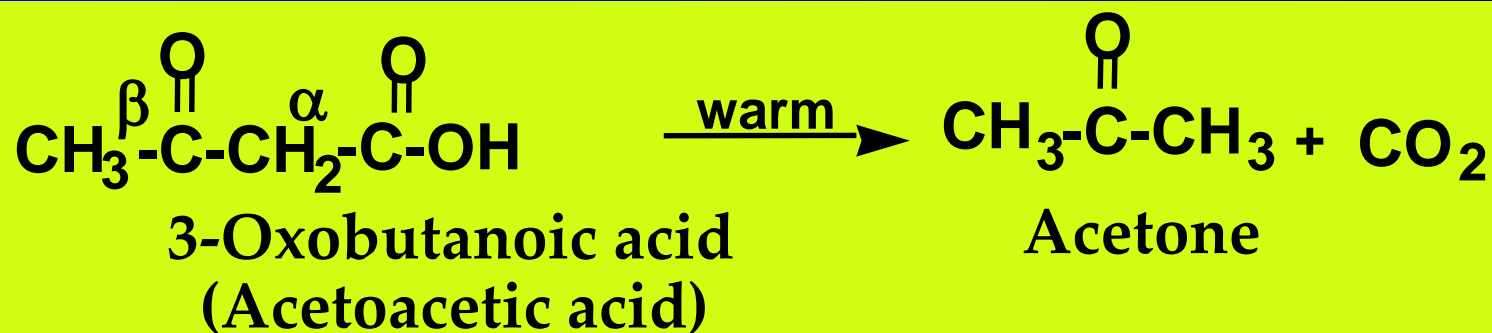
Decarboxylation

- Decarboxylation: loss of CO_2 from a carboxyl group
- Most carboxylic acids, if heated to a very high temperature (fried), undergo thermal decarboxylation
- Most carboxylic acids, however, are quite resistant to reasonable heat and melt or even boil without decarboxylation



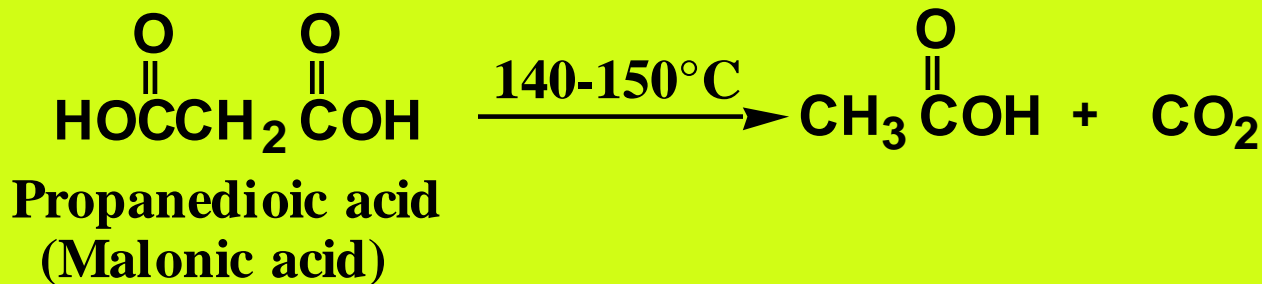
Decarboxylation

- Exceptions are carboxylic acids that have a carbonyl group beta to the carboxyl group
 - this type of β -ketocarboxylic acid undergoes decarboxylation on mild heating



Decarboxylation

- Decarboxylation occurs readily if there is any carbonyl group beta to the carboxyl
- Malonic acid and substituted malonic acids, for example, also undergo thermal decarboxylation



Decarboxylation

- Thermal decarboxylation of β -ketoacids involves rearrangement of six electrons in a cyclic six-membered transition state
- This class of compounds undergoes decarboxylation at relatively low temperatures

