

Lecture 20



Herman Emil Fischer 1852 -1919

Nobel Prize 1902

Sugars, Esters and Purines

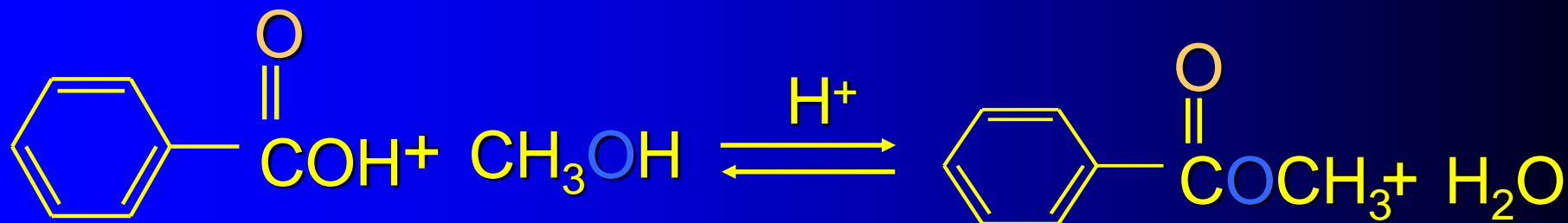
April 4, 2019

Chemistry 328N



Acid-catalyzed Esterification

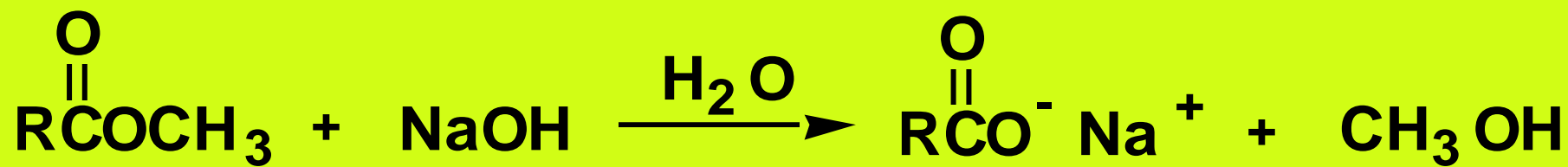
(also called Fischer esterification)



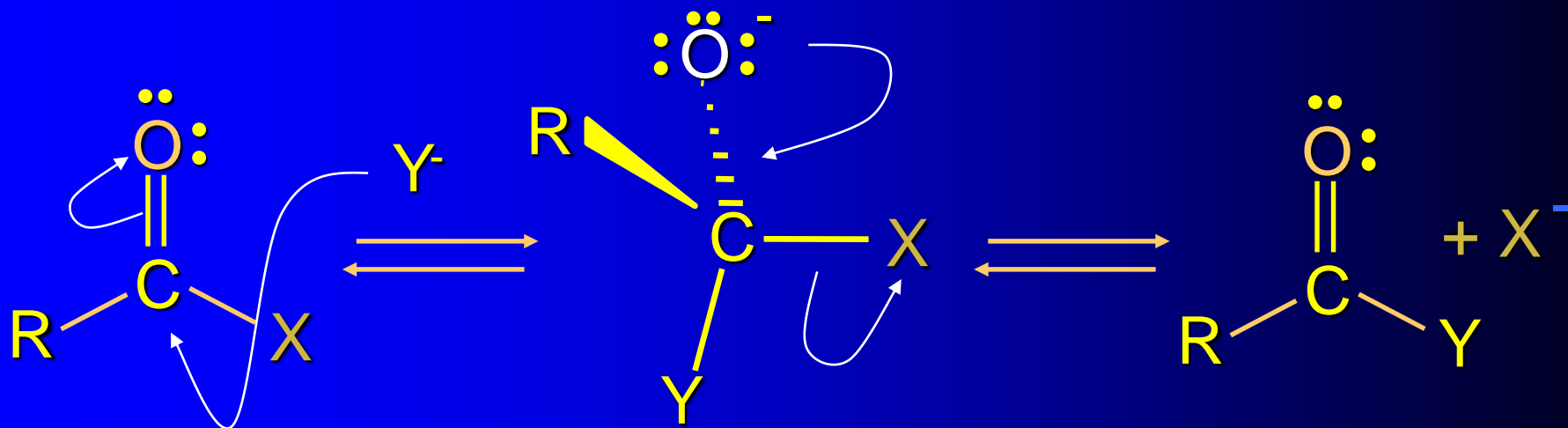
Please study the mechanism



Reaction of Esters with Grignard Reagents

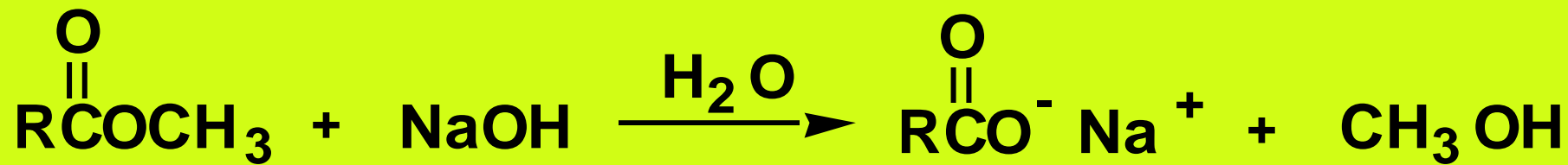


Nucleophilic Acyl Substitution



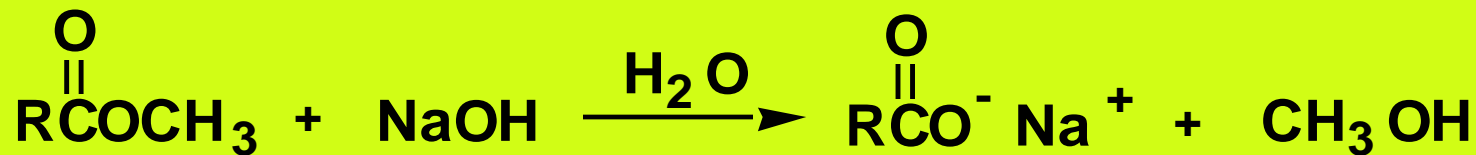
Reaction of Esters with OH^-

- Saponification



Saponification of Esters

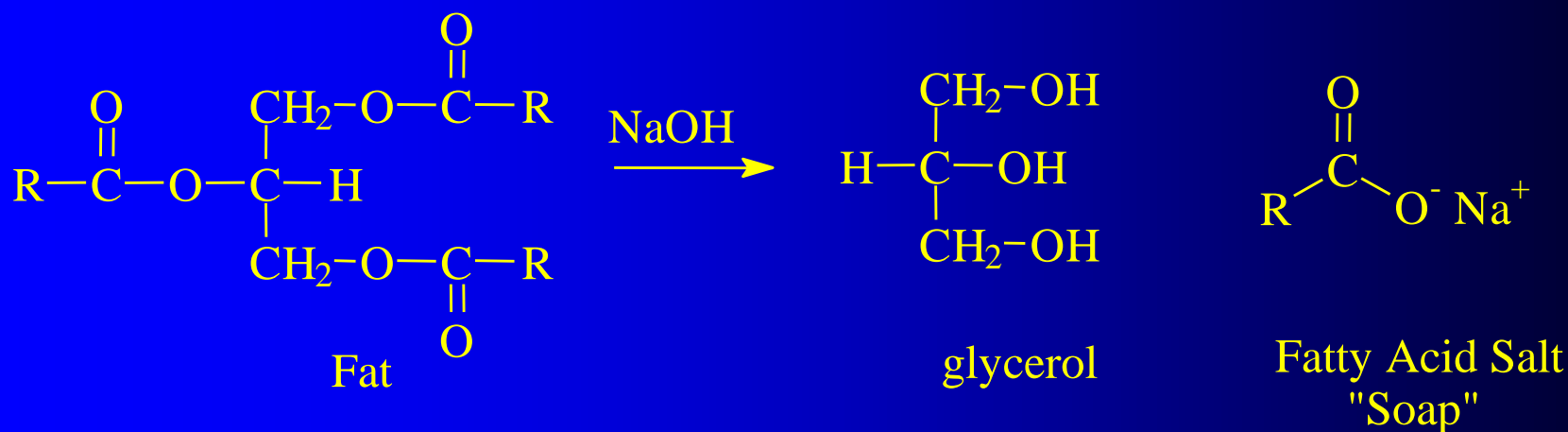
- Hydrolysis of an esters is aqueous base is called **saponification**
- Each mol of ester hydrolyzed requires 1 mol of base; for this reason, ester hydrolysis in aqueous base is said to be “base-promoted” (not catalyzed)



- Hydrolysis of an ester in aqueous base involves **Nucleophilic acyl substitution**



Saponification of Fat



Stearic Acid



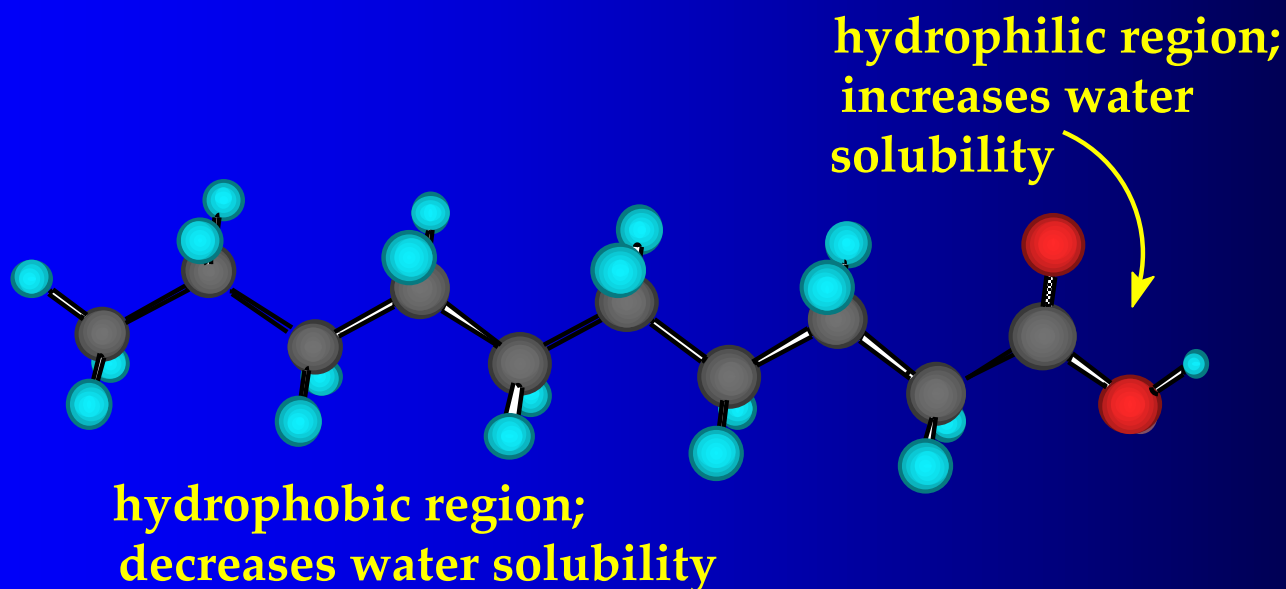
Oleic acid

etc.



Physical Properties

- Water solubility decreases as the relative size of the hydrophobic portion of the molecule increases

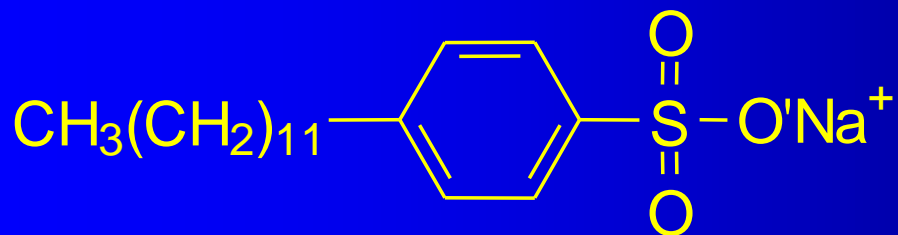


Soaps and Detergents

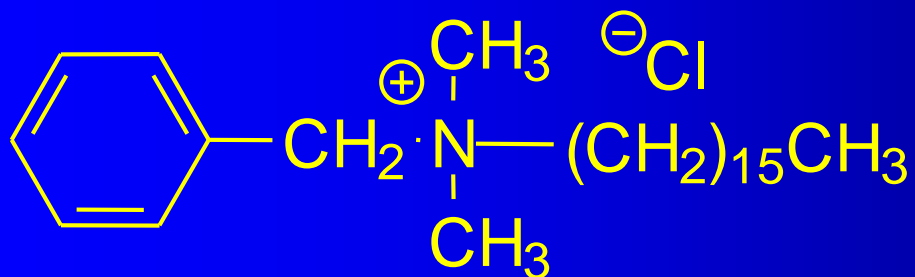
Surface Active Agents = surfactants



Soap



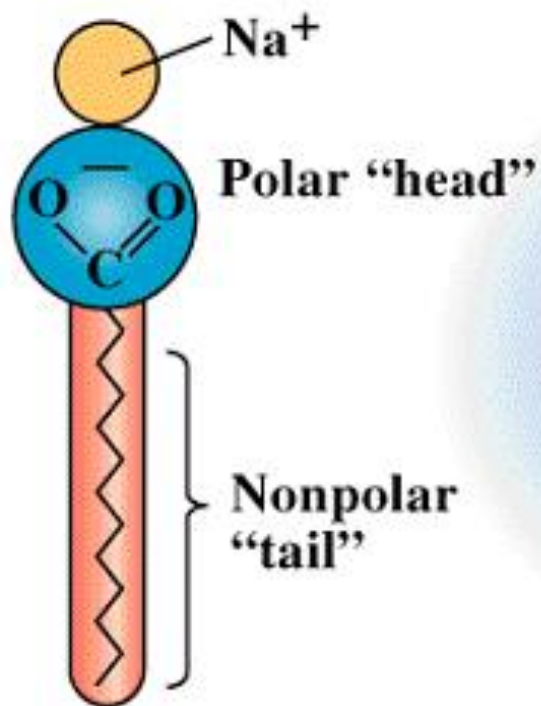
Anionic detergent



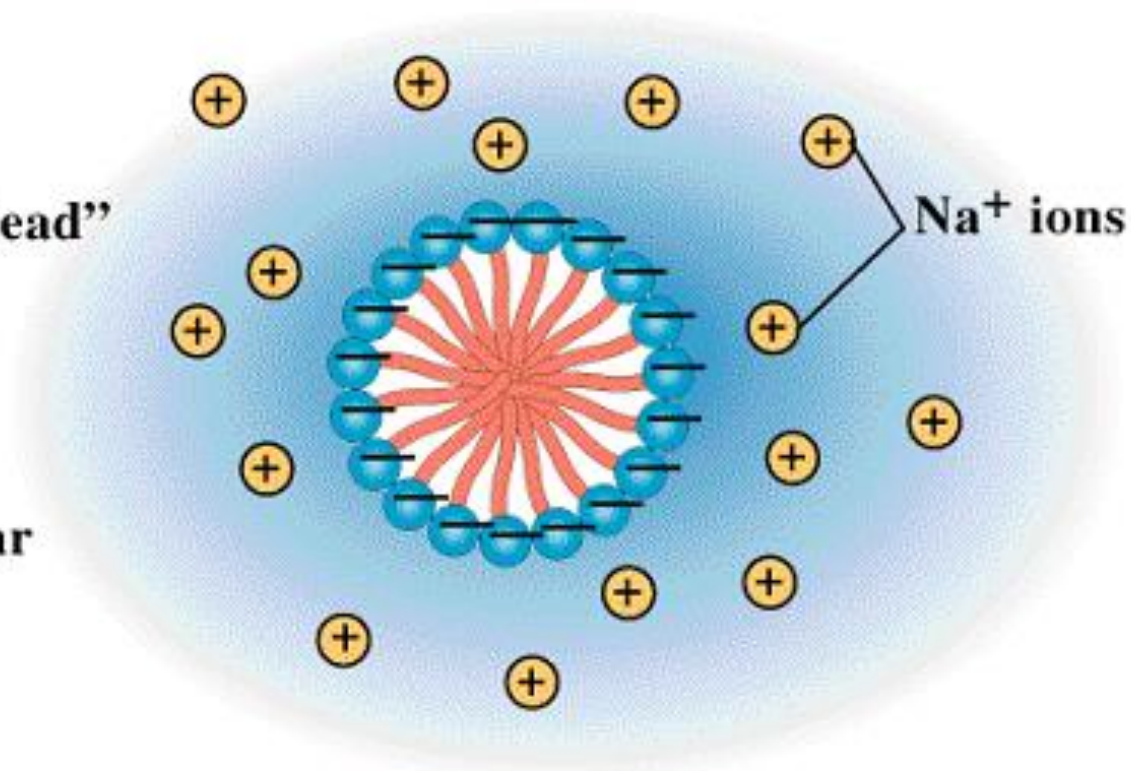
Cationic Detergent



Soap micelle



A soap

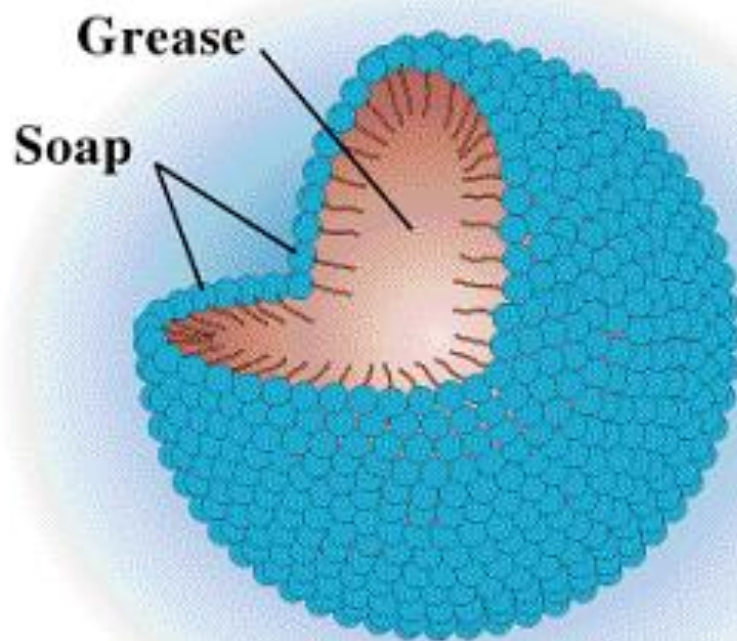


Cross section of a soap micelle in water



Soap micelle with a dissolved grease droplet

Soap micelle with
“dissolved” grease



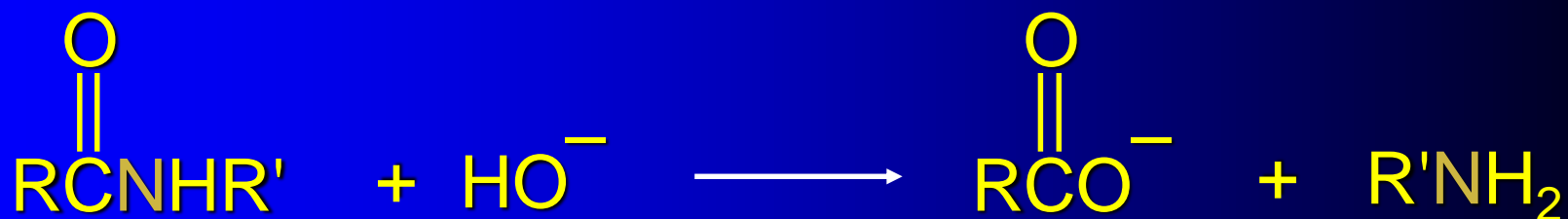
Hydrolysis of Amides

Hydrolysis of amides is also irreversible. In acid solution the amine product is protonated to give an ammonium salt.



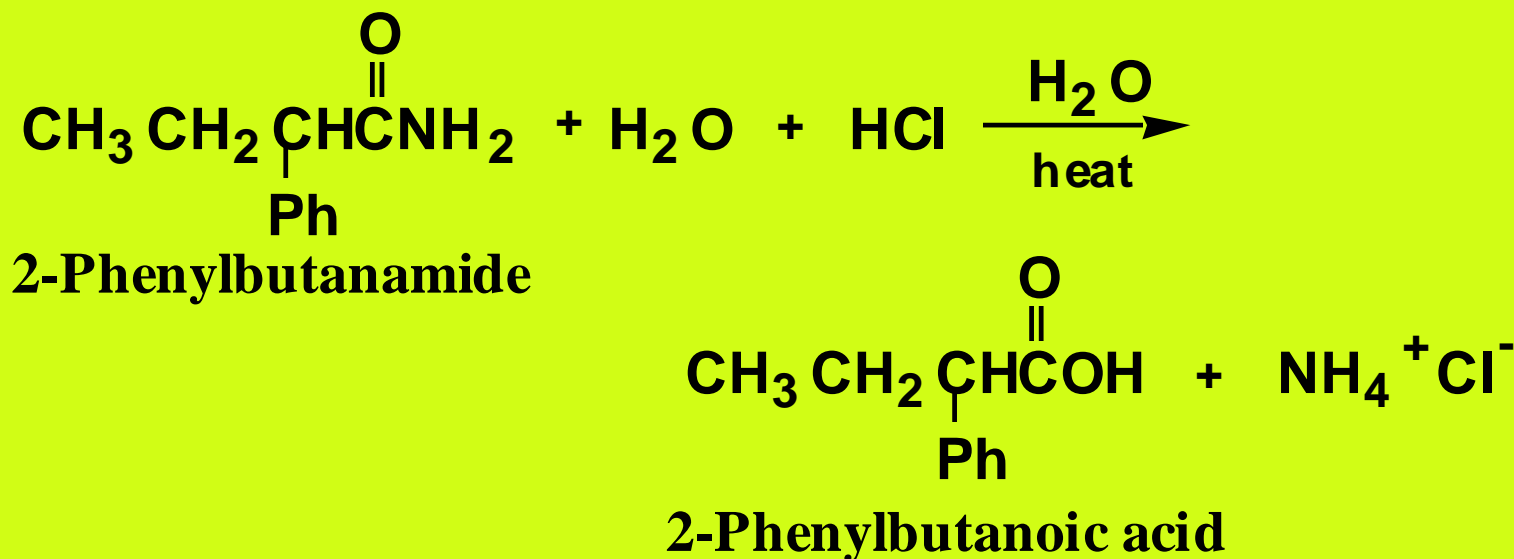
Hydrolysis of Amides

- In basic solution the carboxylic acid product is deprotonated to give a carboxylate ion.
- This makes the reaction irreversible!



Hydrolysis of Amides in Acid

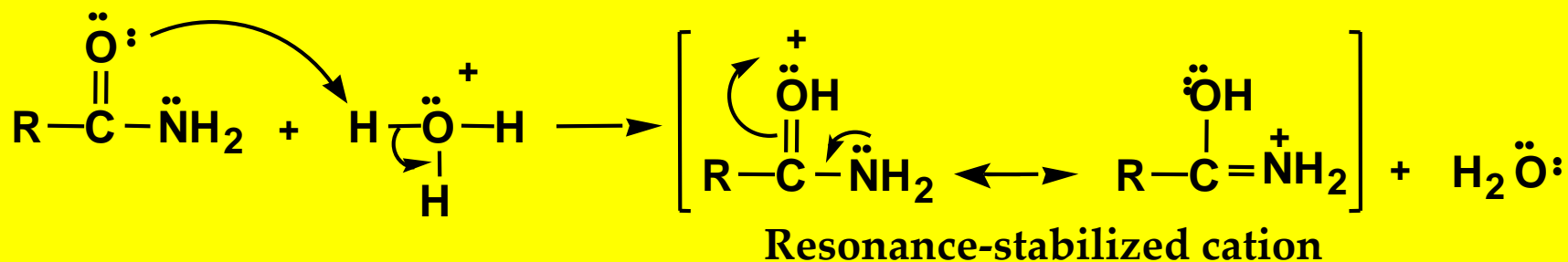
- Hydrolysis of amides in aqueous acid requires 1 mol of acid per mol of amide



Hydrolysis of Amides in Acid

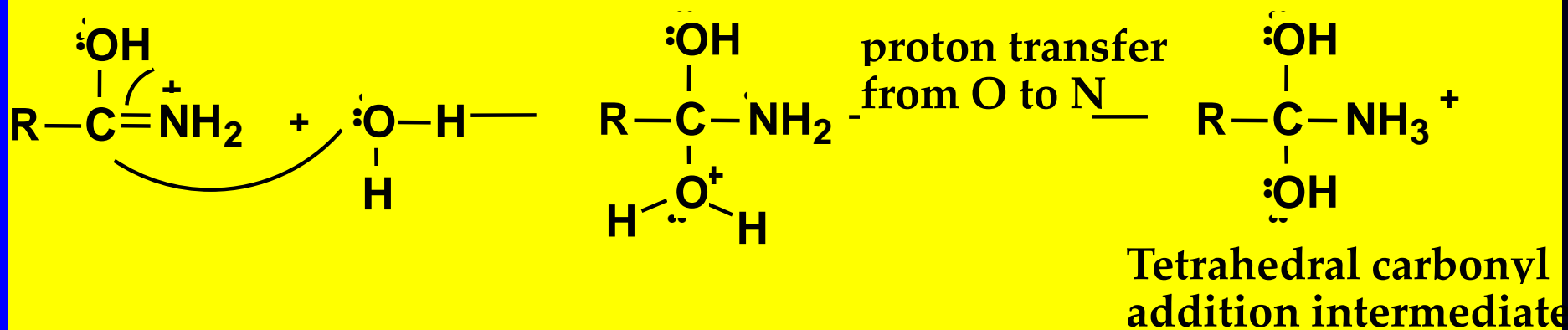
- Acid-catalyzed hydrolysis of an amide is divided into three steps

Step 1: protonation of the carbonyl oxygen



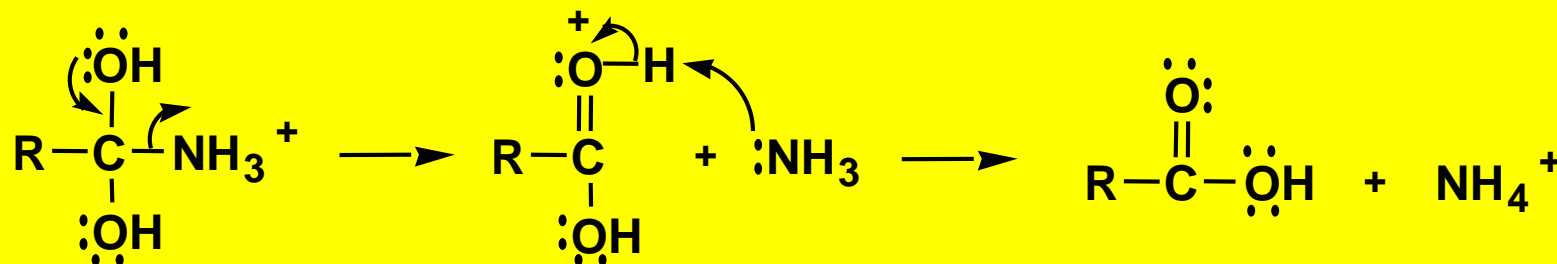
Hydrolysis of Amides in Acid

Step 2: addition of H₂O to the carbonyl carbon followed by proton transfer



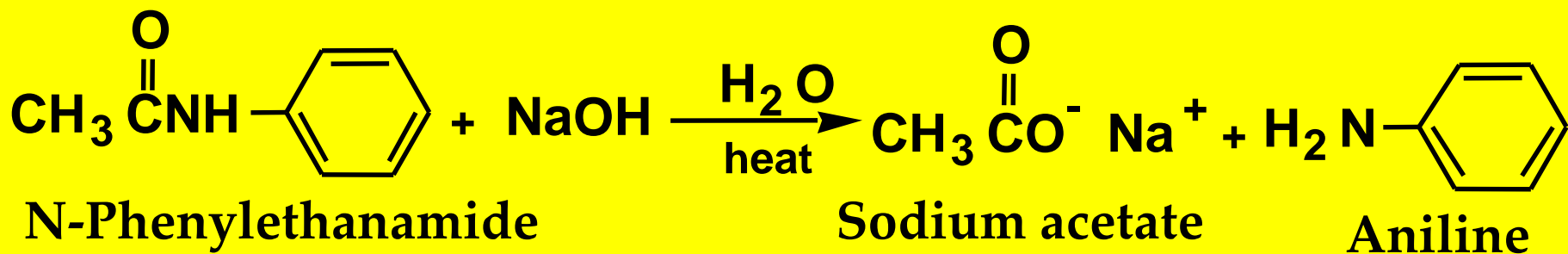
Hydrolysis of Amides in Acid

Step 3: collapse of the intermediate coupled with proton transfer to give the carboxylic acid and ammonium ion



Hydrolysis of Amides in Base

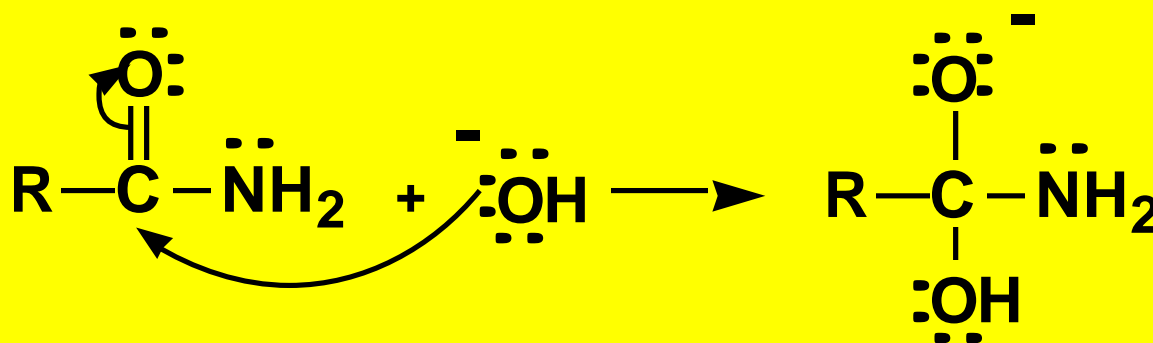
- Hydrolysis of an amide in aqueous base requires 1 mole of base per mole of amide



Hydrolysis of Amides in Base

- Hydrolysis of an amide in aqueous base is divided into three steps

Step 1: addition of hydroxide ion to the carbonyl carbon

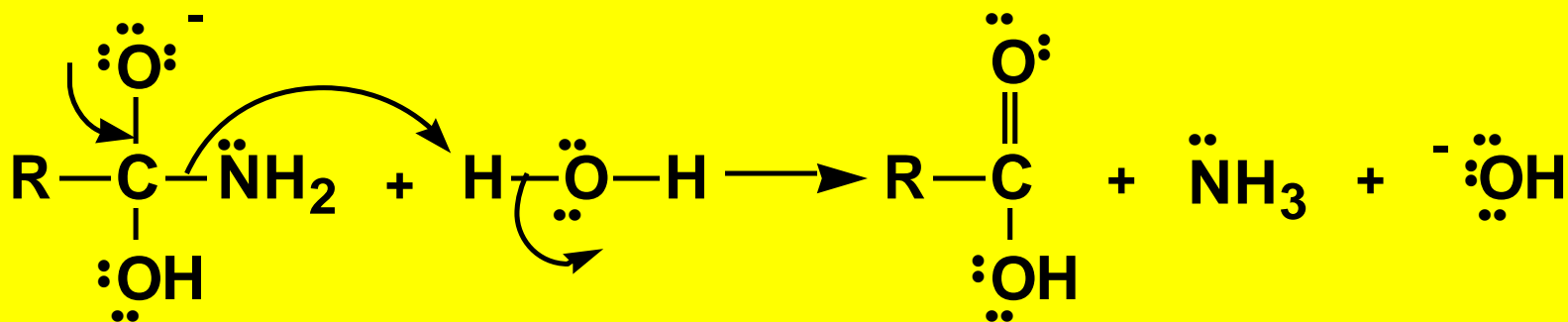


**Tetrahedral carbonyl
addition intermediate**



Hydrolysis of Amides in Base

Step 2: collapse of the intermediate to form a carboxylic acid and ammonia



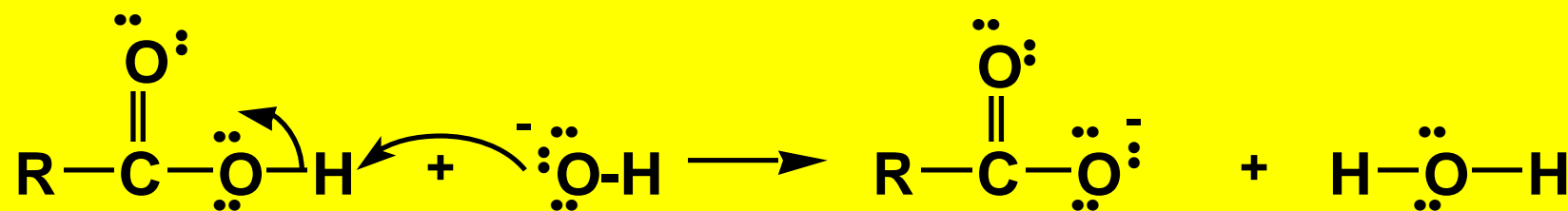
**Tetrahedral carbonyl
addition intermediate**

A very rare event... Why???



Hydrolysis of Amides in Base

Step 3: proton transfer to form the carboxylate anion and water. Hydrolysis is driven to completion by this acid-base reaction



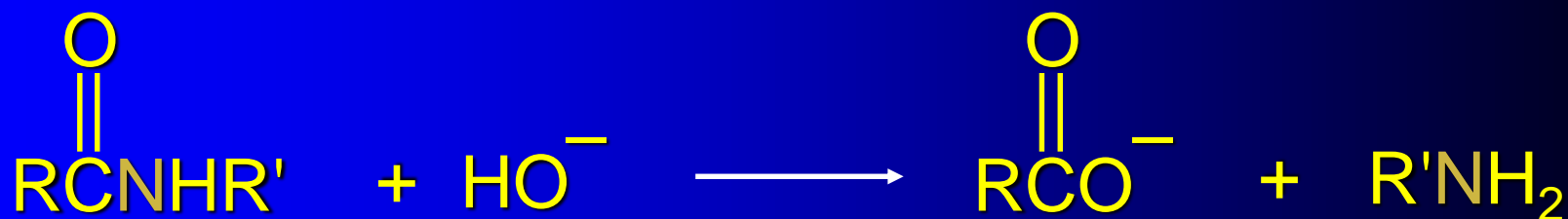
Hydrolysis of Amides

Hydrolysis of amides is irreversible. In acid solution the amine product is protonated to give an ammonium salt.



Hydrolysis of Amides

- In basic solution the carboxylic acid product is deprotonated to give a carboxylate ion.
- This makes the reaction irreversible!

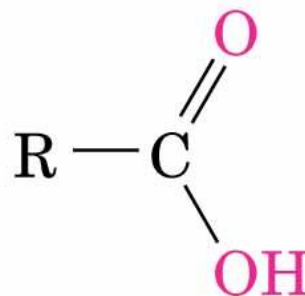


Chemistry of Nitriles

- Nitriles and carboxylic acids both have a carbon atom with three bonds to an electronegative atom, and both contain a π bond
- Both both are electrophiles



Nitrile

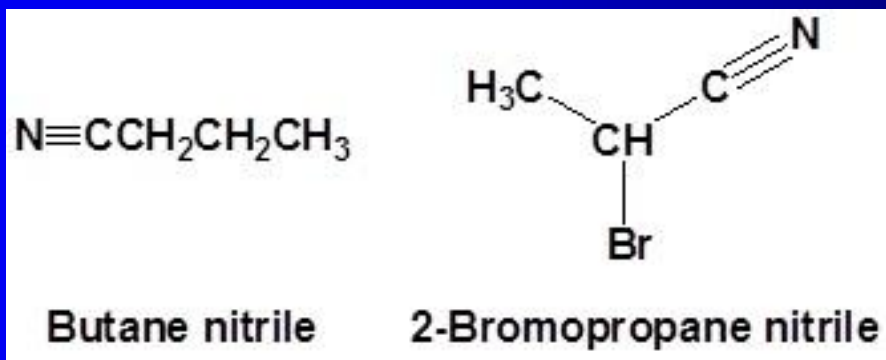


Carboxylic Acid

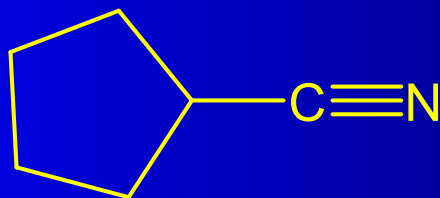


Naming Nitriles

Name the parent alkane (include the carbon atom of the nitrile as part of the parent) followed with the word -nitrile. The carbon in the nitrile is given the #1 location position. It is not necessary to include the location number in the name because it is assumed that the functional group will be on the end of the parent chain.



Cycloalkanes are followed by the word -carbonitrile.



Cyclopentane carbonitrile



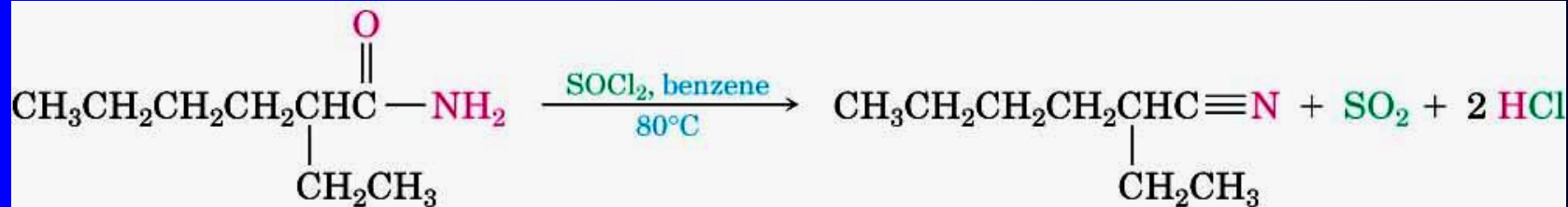
Preparation of Nitriles

- Sandmeyer reaction of diazonium salts
- S_N2 reactions with Cyanide anion
- Cyanohydrin formation
- Dehydration of Amides
- There are many more....



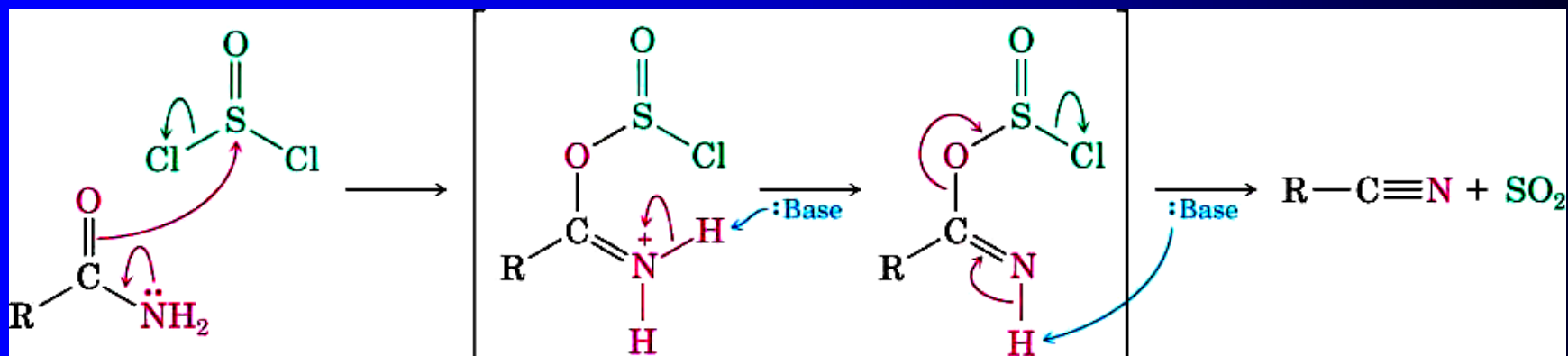
Preparation of Nitriles by Dehydration

- Reaction of primary amides RCONH_2 with SOCl_2 (or other dehydrating agents)
- Not limited by steric hindrance or side reactions (as is the reaction of alkyl halides with NaCN)



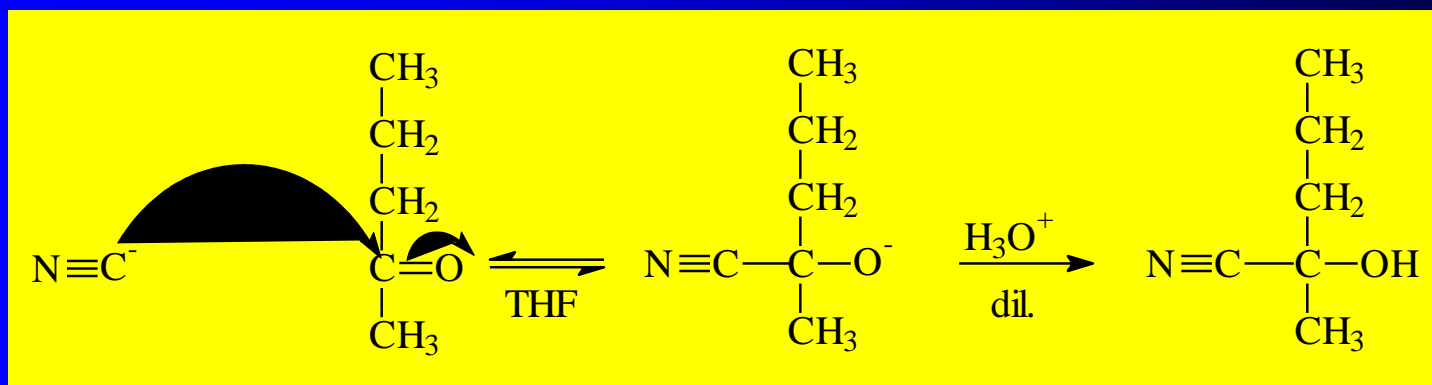
Mechanism of Dehydration of Amides

- Nucleophilic amide oxygen atom attacks SOCl_2 followed by deprotonation and elimination



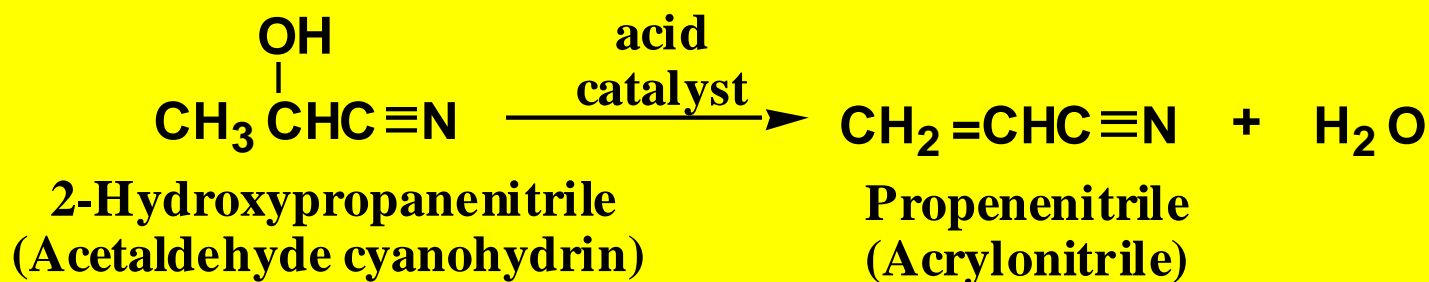
Addition of HCN to Carbonyls

- Mechanism of cyanohydrin formation



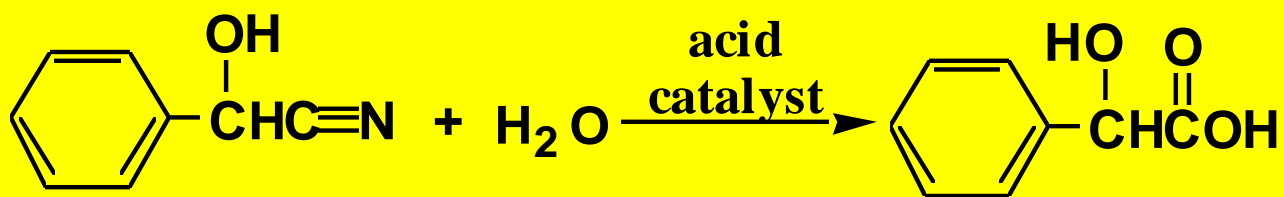
Cyanohydrins

- The value of cyanohydrins is for the new functional groups into which they can be converted
 - acid-catalyzed dehydration of the 2° alcohol gives a valuable monomer



Cyanohydrins

- acid-catalyzed hydrolysis of the cyano group gives an α -hydroxycarboxylic acid



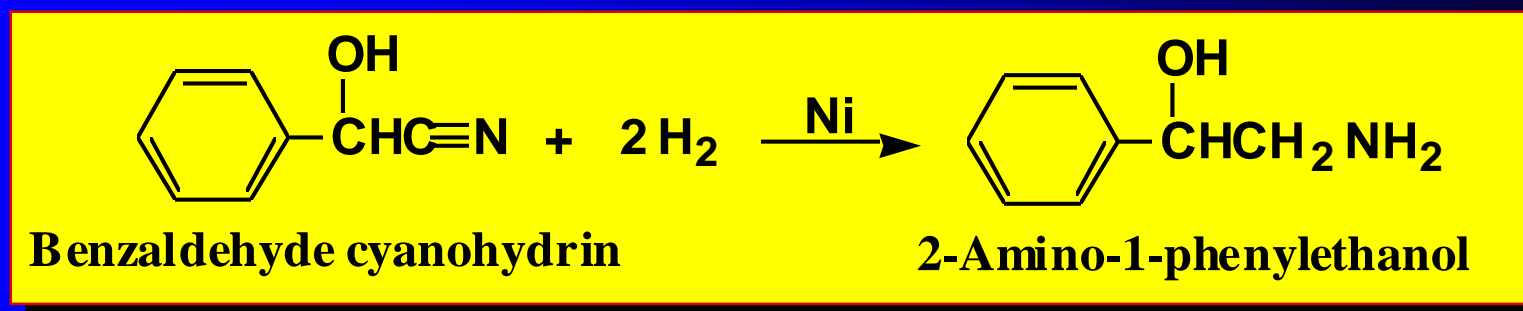
Benzaldehyde cyanohydrin
(Mandelonitrile)

2-Hydroxy-2-phenyl-ethanoic acid
(Mandelic acid)



Cyanohydrins

- catalytic reduction of the carbon-nitrogen triple bond converts the cyano group to a 1° amine



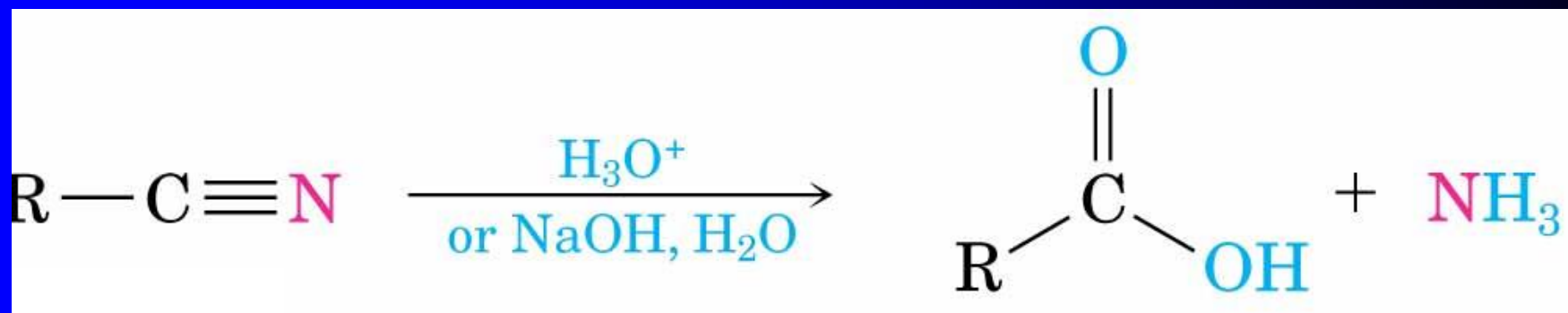
LiAlH₄ also works well...

But...what about Pd/C and H₂



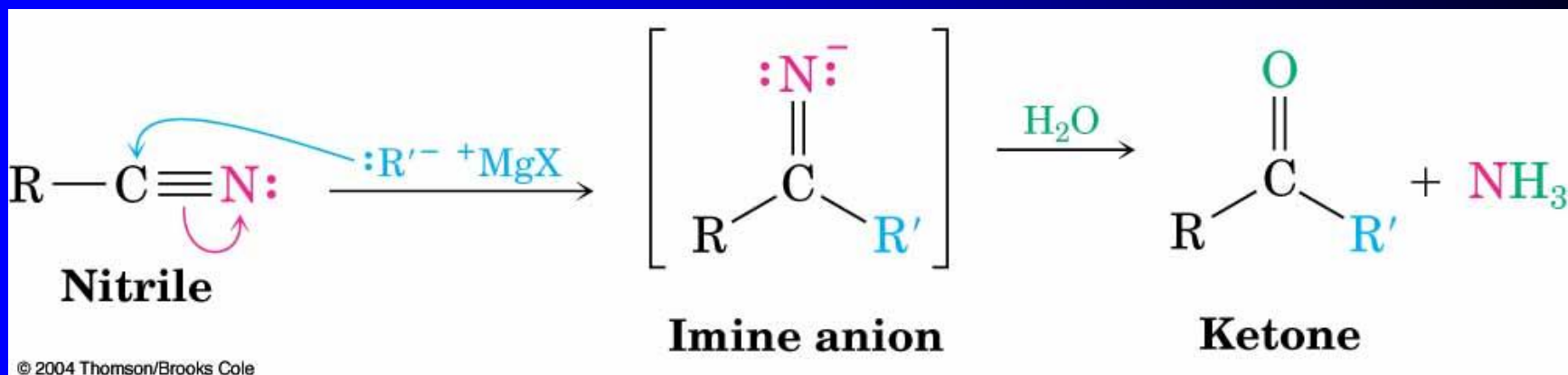
Hydrolysis: Conversion of Nitriles into Carboxylic Acids

- Hydrolyzed in with acid or base gives a carboxylic acid and ammonia



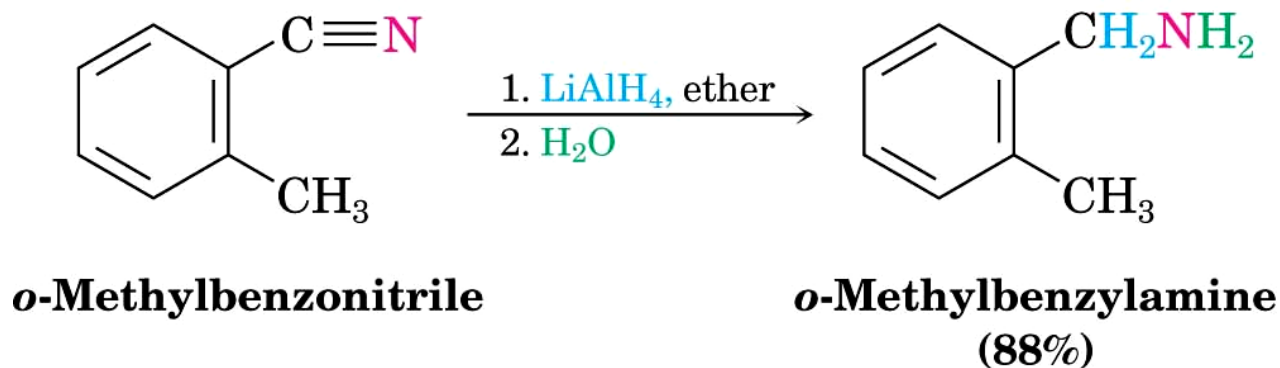
Reaction of Nitriles with Organometallic Reagents

- Grignard reagents add to give an intermediate imine anion that is hydrolyzed by addition of water to yield a ketone



Reduction: Conversion of Nitriles into Amines

- Reduction of a nitrile with LiAlH_4 gives a primary amine



Some “loose ends” before we go on

- Spectroscopy of acid derivatives
- A selective reduction for your tool box



Reduction of Acid Derivatives

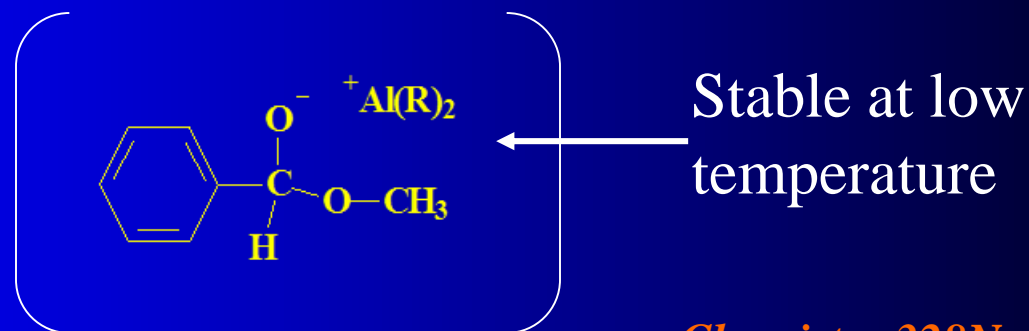
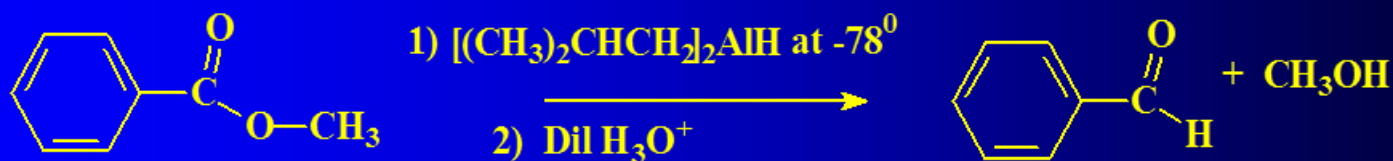
- Acids (page 736-738)
- Esters (page 796-798)
- Please work through the example in section 18.9
- Amides (page 798-799)
- Nitriles (page 800)
- Selective reductions with NaBH_4
- Esters to aldehydes by DIBALH (page 797-798)



DIBALH

Diisobutylaluminum hydride (DIBALH) at -78°C selectively reduces esters to aldehydes

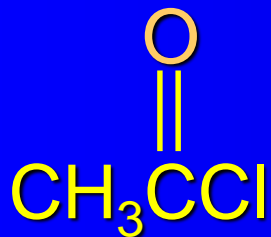
- at -78°C , the tetrahedral intermediate does not collapse and it is not until hydrolysis in aqueous acid that the carbonyl group of the aldehyde is liberated



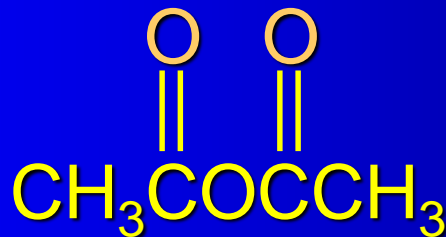
Infrared Spectroscopy

C=O stretching frequency depends on whether the compound is an acyl chloride, anhydride, ester, or amide.

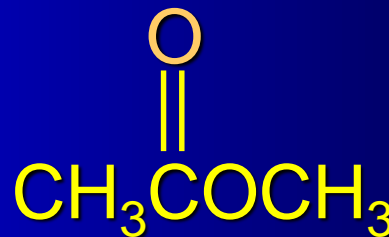
C=O stretching frequency ν



1822 cm^{-1}



1748
and
1815 cm^{-1}



1736 cm^{-1}



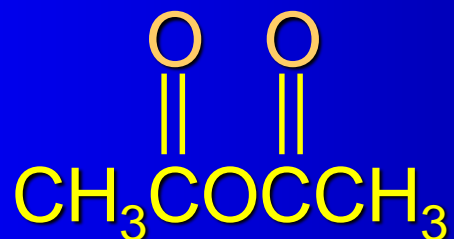
1694 cm^{-1}



Infrared Spectroscopy

Anhydrides have two peaks due to C=O stretching. One from symmetrical stretching of the C=O and the other from an antisymmetrical stretch.

C=O stretching frequency ν



1748 and 1815 cm⁻¹

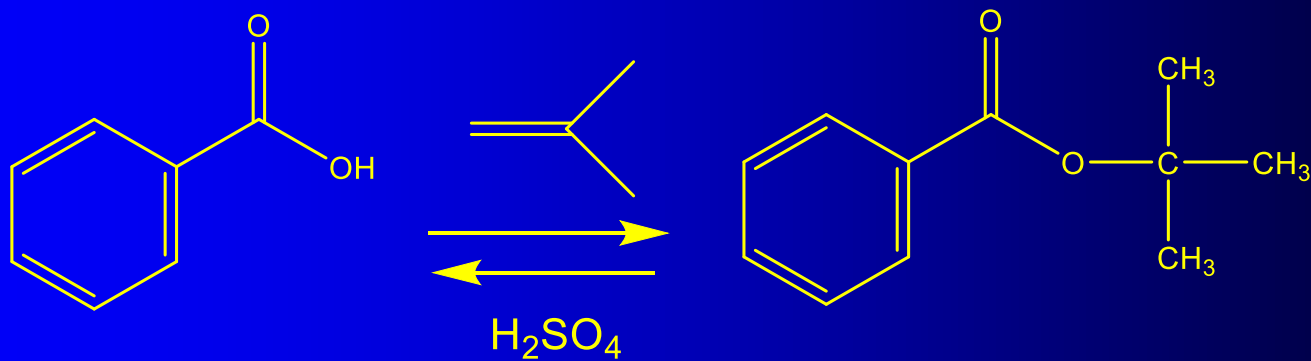


Infrared Spectroscopy

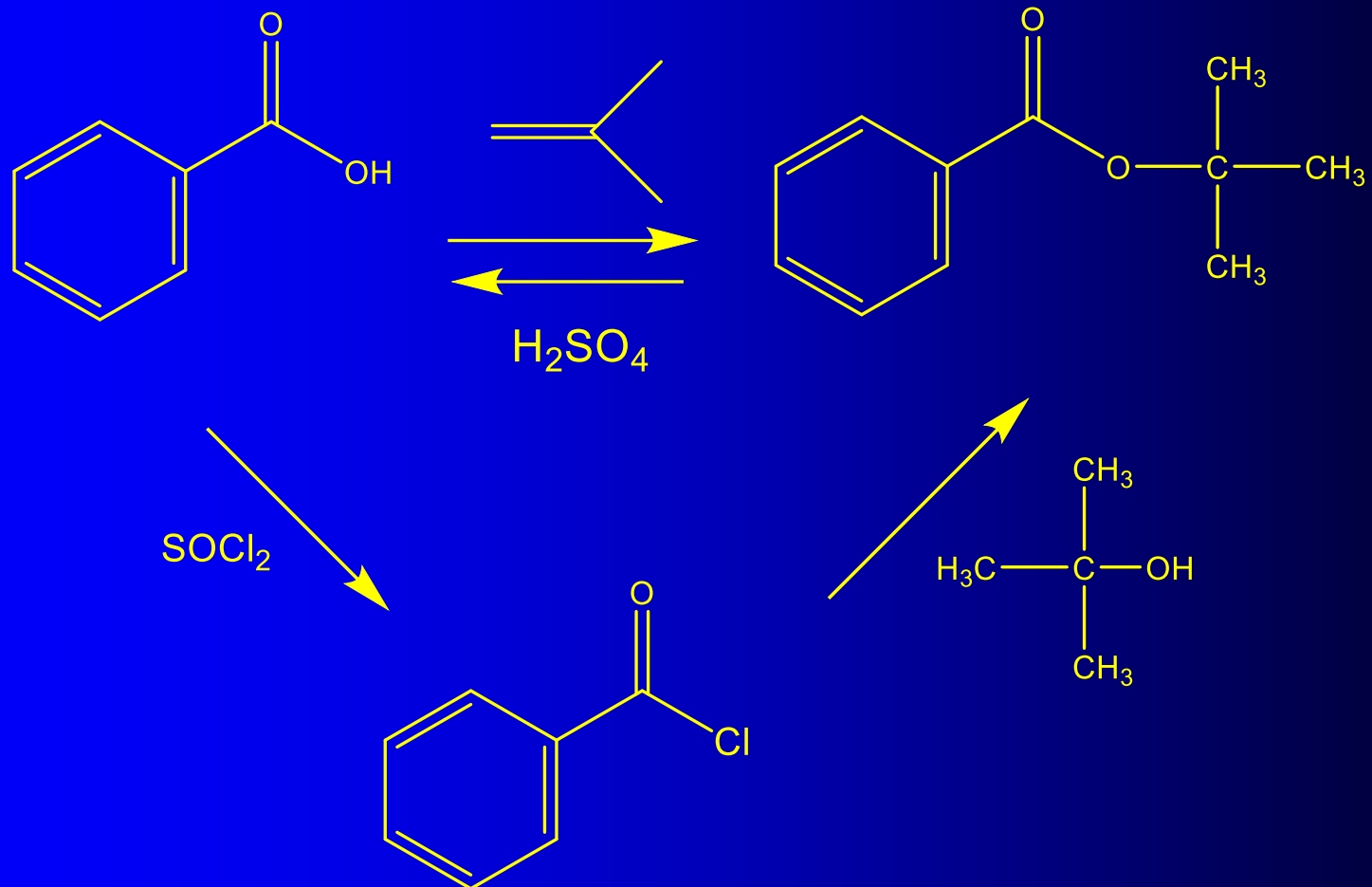
Nitriles are readily identified by absorption due to carbon-nitrogen triple bond stretching that is “all alone” in the 2210-2260 cm^{-1} region.



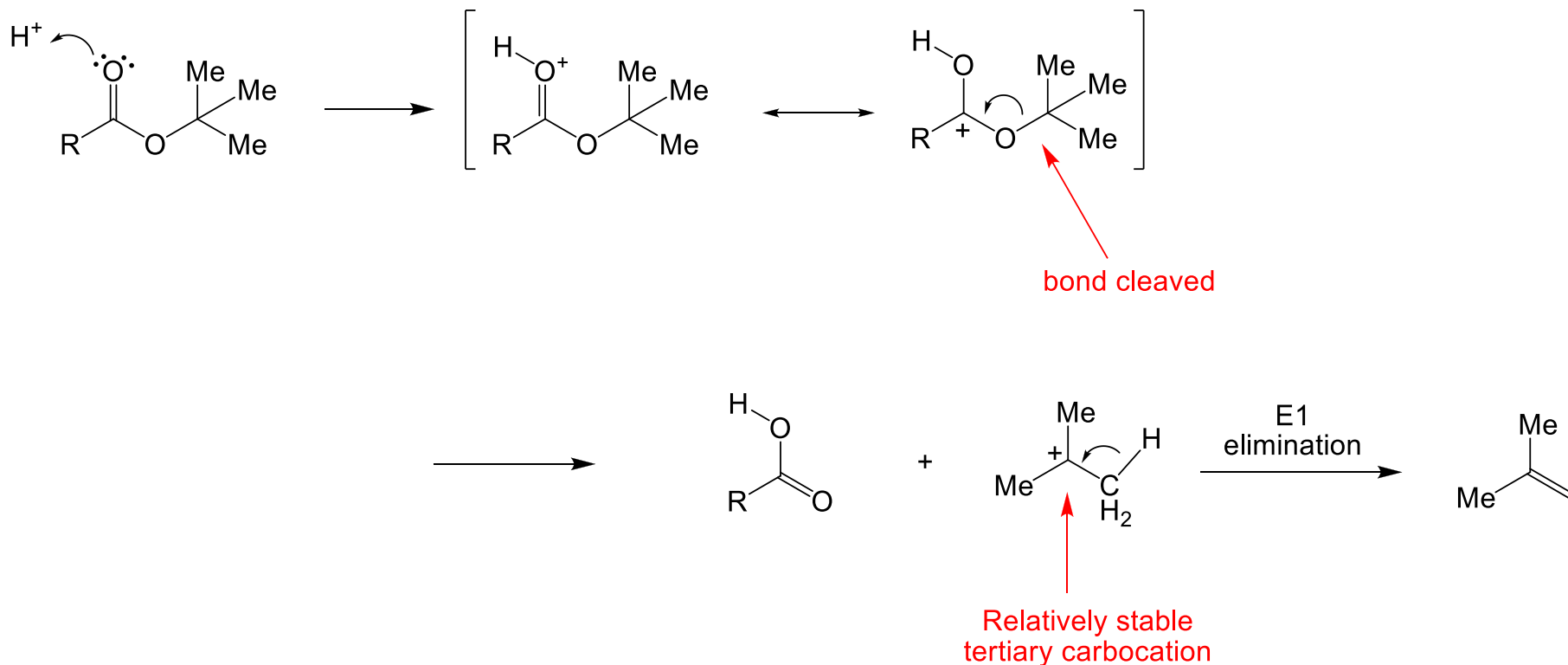
t-Butyl esters



t-Butyl esters



t-Butyl ester hydrolysis



Note which bond is broken in this hydrolysis !!

