CH 318 N LECTURE 14

Textbook Assignment: Chapter 18

Homework (for credit): POW 7 posted

Today's Topics:

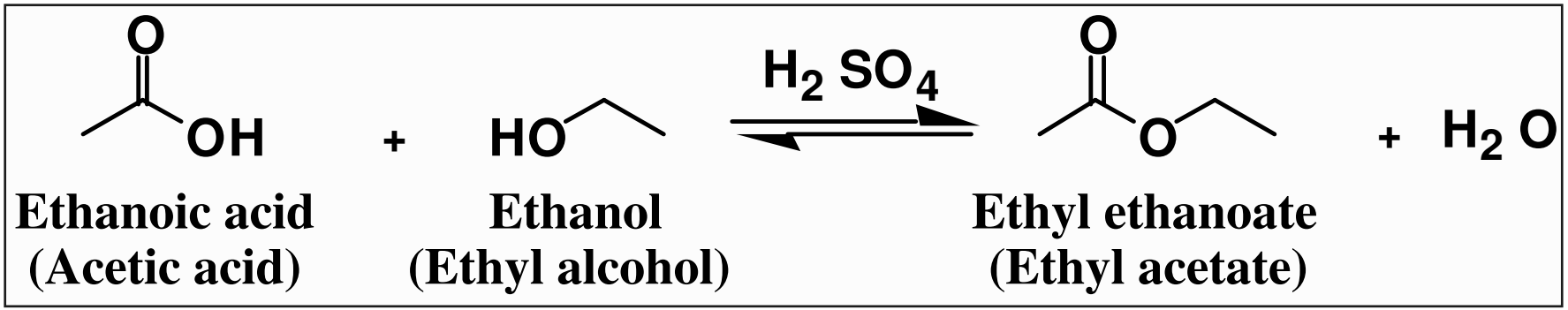
Functional Derivatives of Carboxylic Acids

Notice & Announcements:

Carboxylic Acids

Fischer Esterification

- Esters can be prepared by treating a carboxylic acid with an alcohol in the presence of an acid catalyst, commonly H_2SO_4, $ArSO_3H$*, or gaseous HCl



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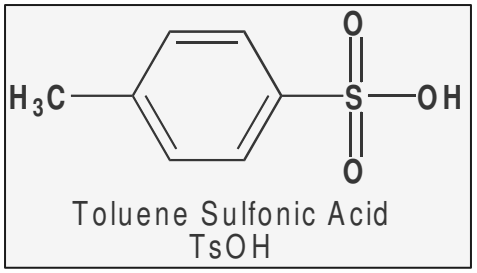


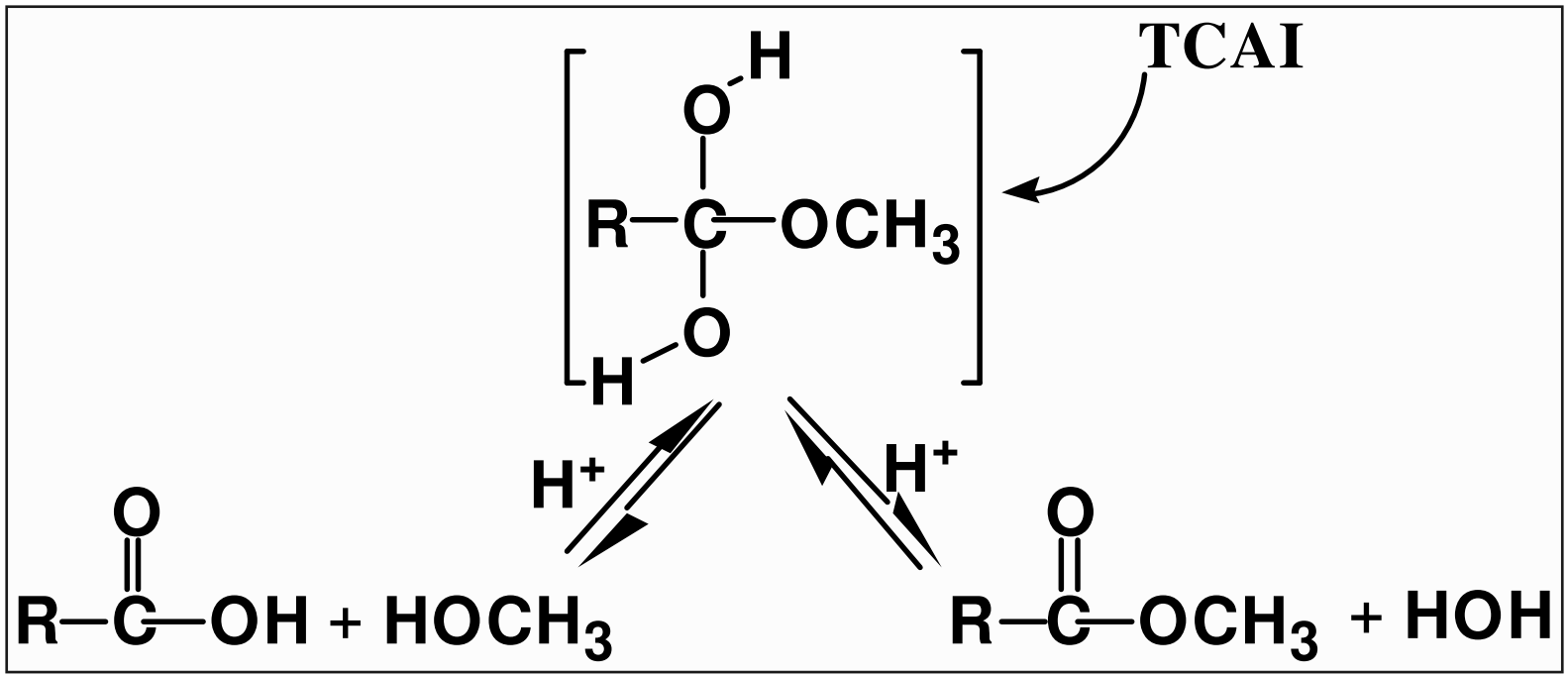
Fischer Esterification

Fischer esterification is an equilibrium reaction

- by careful control of experimental conditions, it is possible to prepare esters in high yield
- if the alcohol is inexpensive relative to the carboxylic acid, it can be used in excess to drive the equilibrium to the right
- alternatively, water can be removed by azeotropic distillation and a Dean-Stark trap

Fischer Esterification

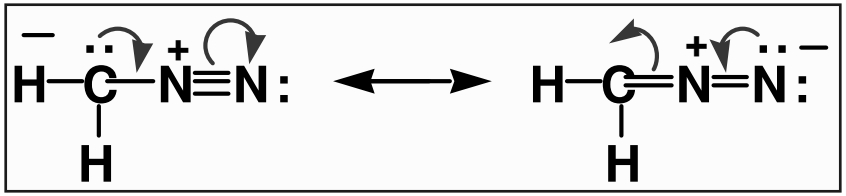
– a key intermediate in Fischer esterification is the tetrahedral carbonyl addition intermediate formed by addition of ROH to the C=O group



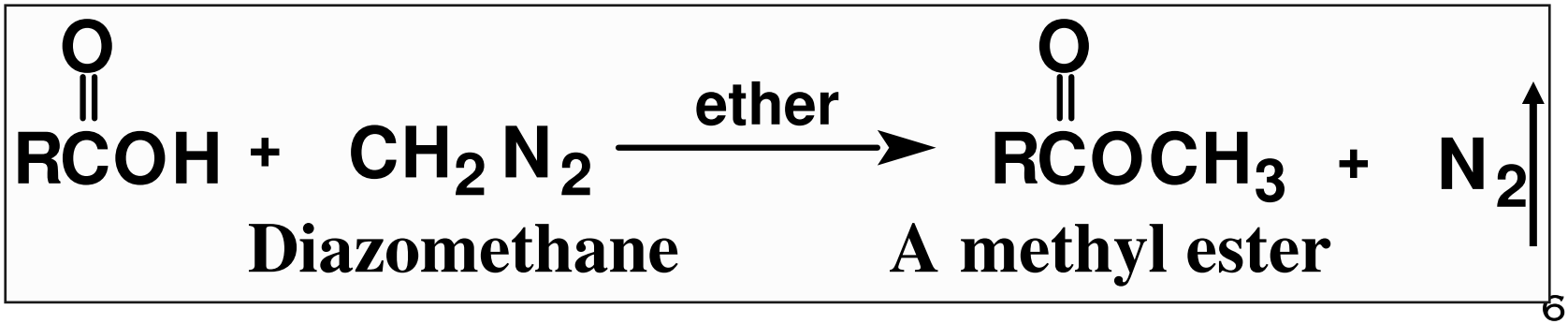
(refer to mechanism worksheet)

Diazomethane

- Diazomethane, CH_2N_2
  - a potentially explosive, toxic, yellow gas, is best represented as a hybrid of two contributing structures



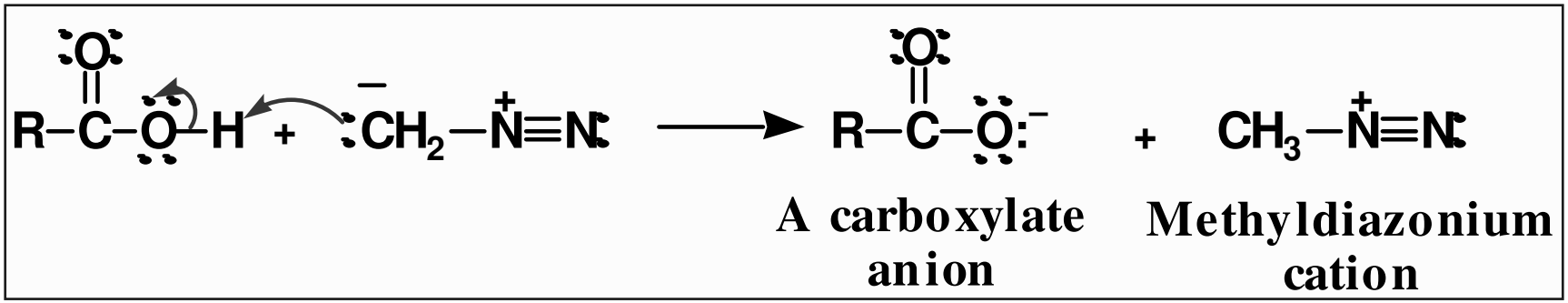
  - treating a carboxylic acid with diazomethane gives a **methyl ester**



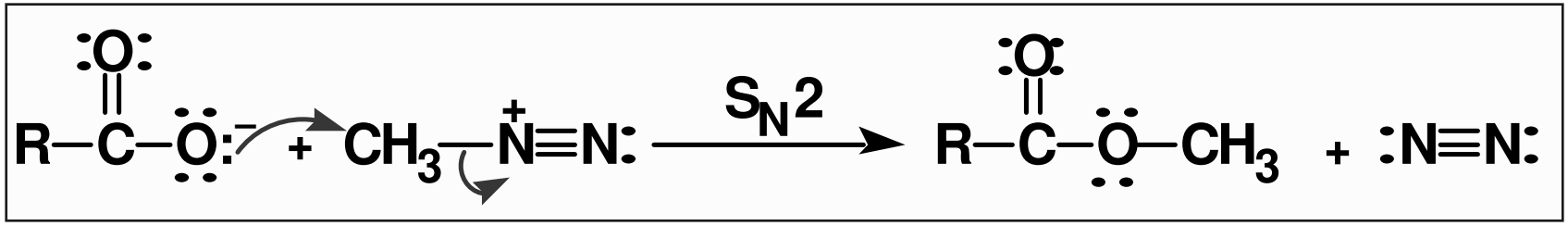
Diazomethane

- Esterification occurs in two steps

  Step 1: proton transfer to diazomethane

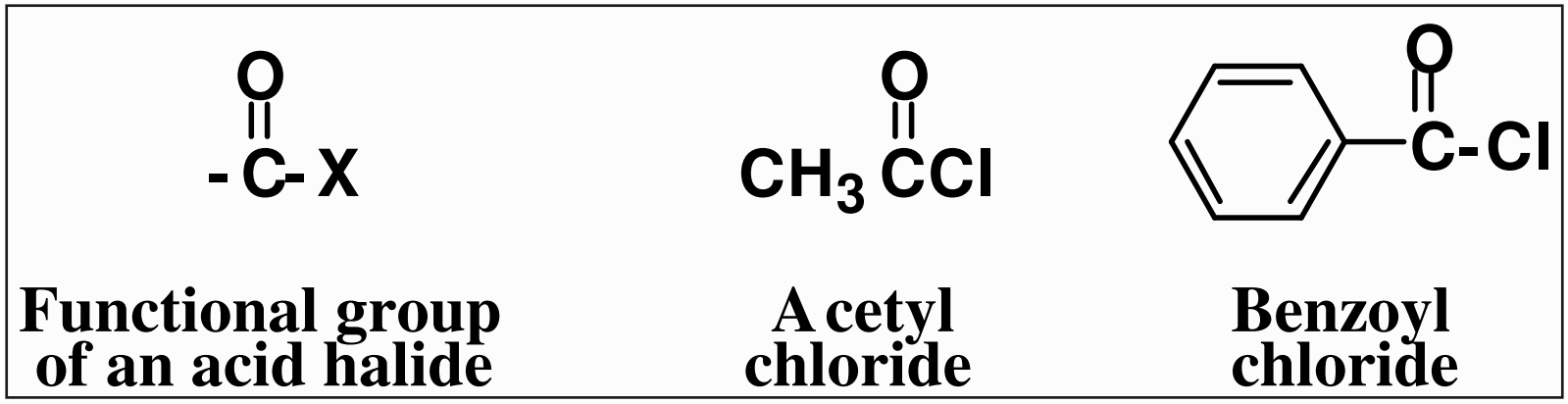


  Step 2: nucleophilic displacement of N_2



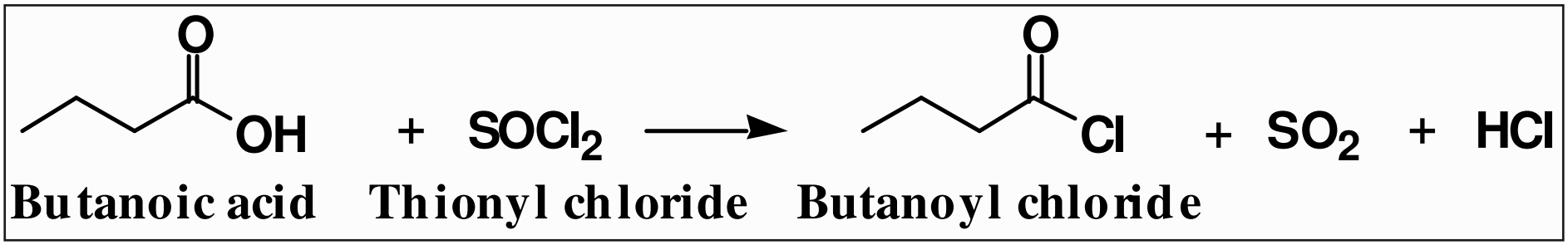
Acid Chlorides

- The functional group of an acid halide is a carbonyl group bonded to a halogen atom
  - among the acid halides, acid chlorides are by far the most common and the most widely used



Acid Chlorides

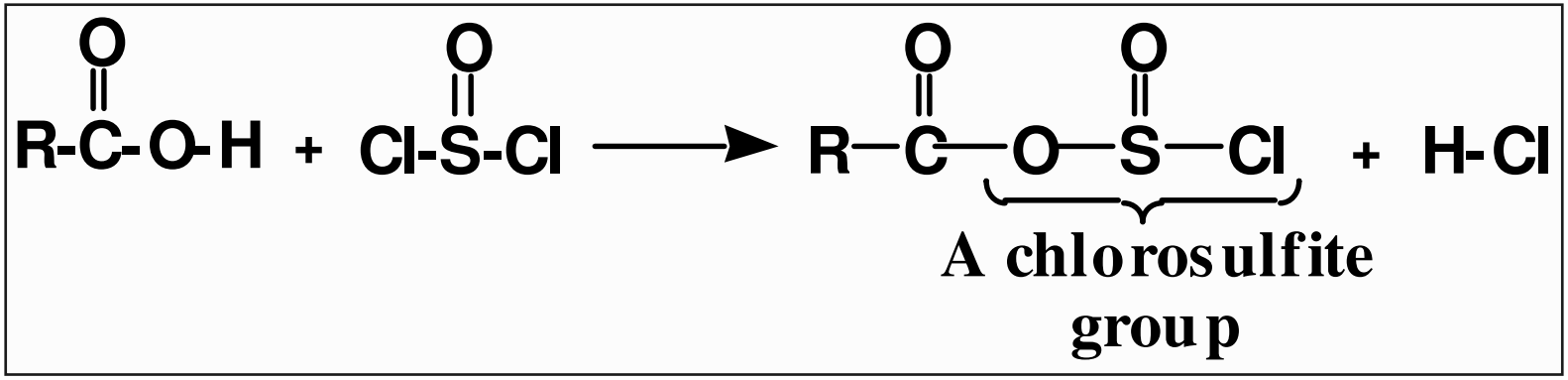
– acid chlorides are most often prepared by treating a carboxylic acid with **thionyl chloride**



Acid Chlorides

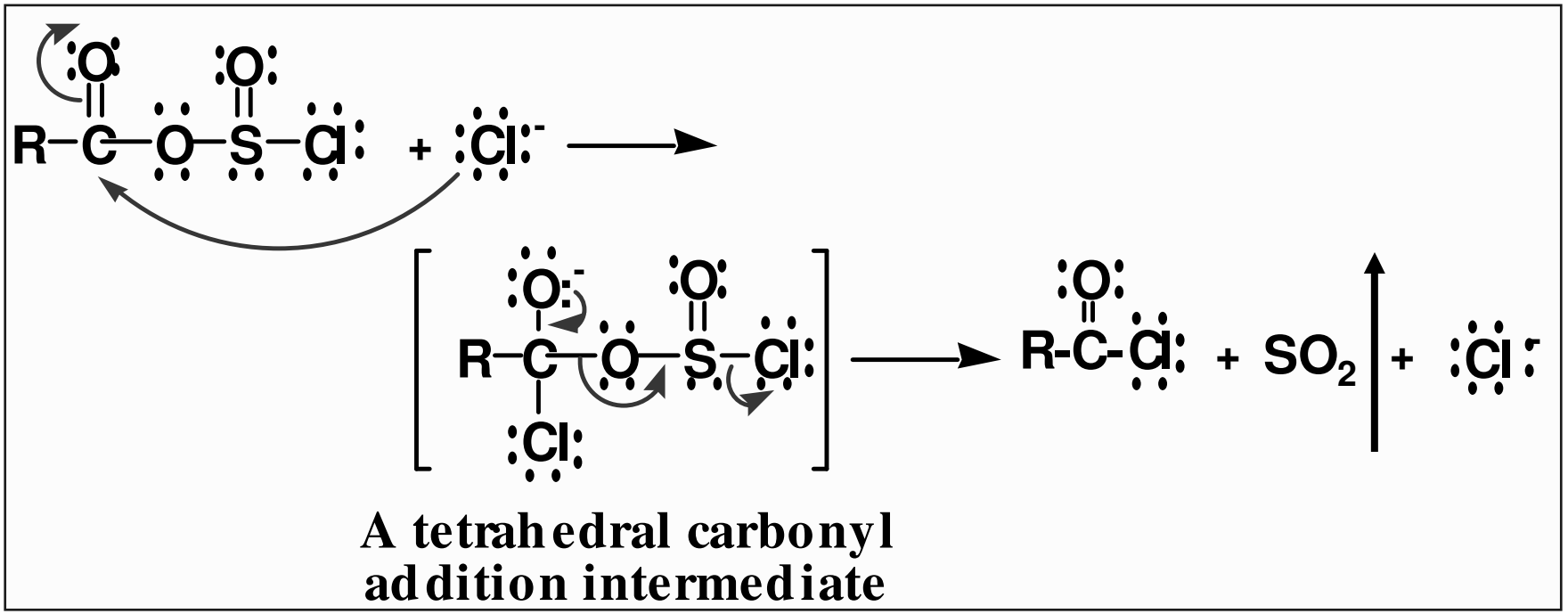
- The mechanism for this reaction is divided into two steps.

  Step 1: reaction with $SOCl_2$ transforms OH, a poor leaving group, into a chlorosulfite group, a good leaving group



Acid Chlorides

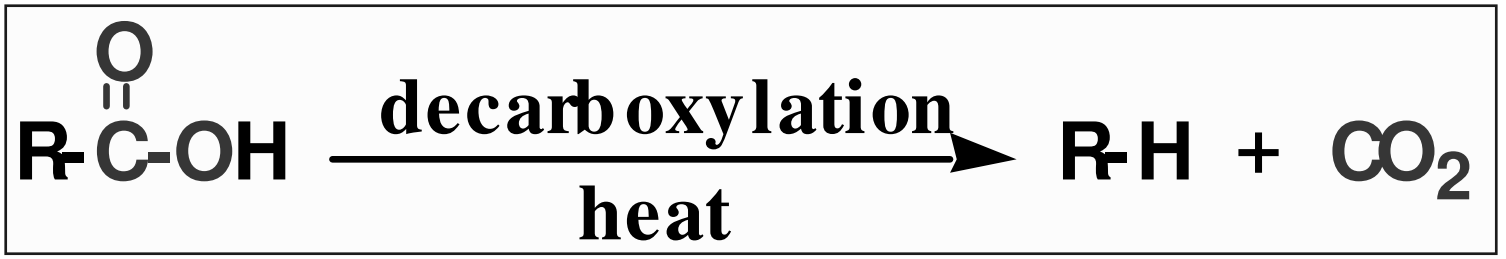
Step 2: attack of chloride ion gives a tetrahedral carbonyl addition intermediate, which collapses to give the acid chloride



Note: the reaction is irreversible

Decarboxylation

- Decarboxylation: loss of CO_2 from a carboxyl group
  - carboxylic acids, *if heated to a very high temperature*, undergo thermal decarboxylation

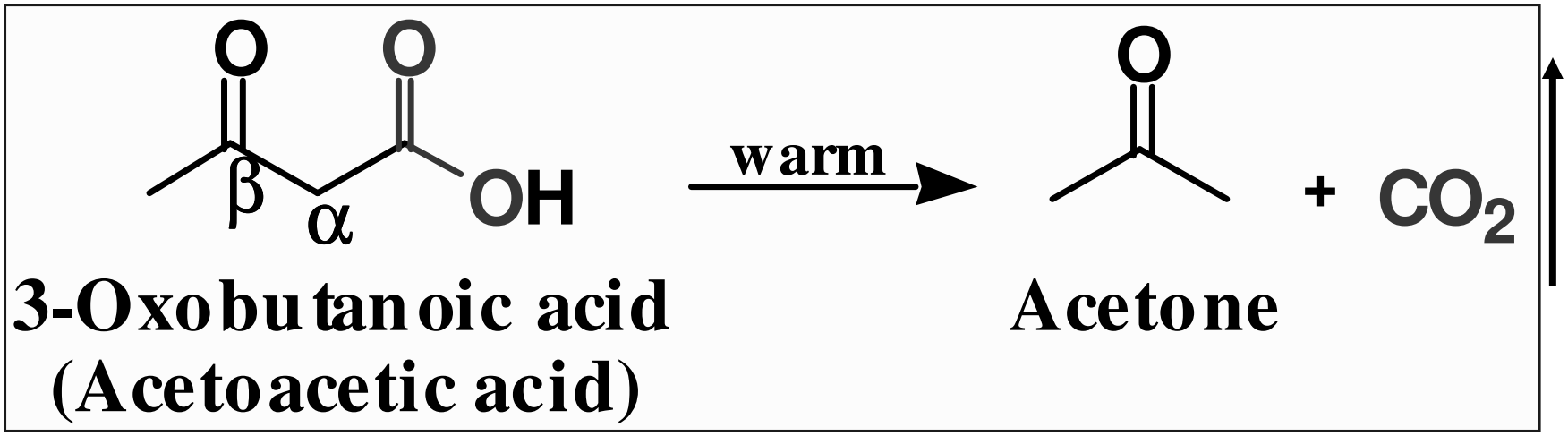


  - most carboxylic acids, however, are quite resistant to moderate heat and melt or even boil without decarboxylation

Decarboxylation

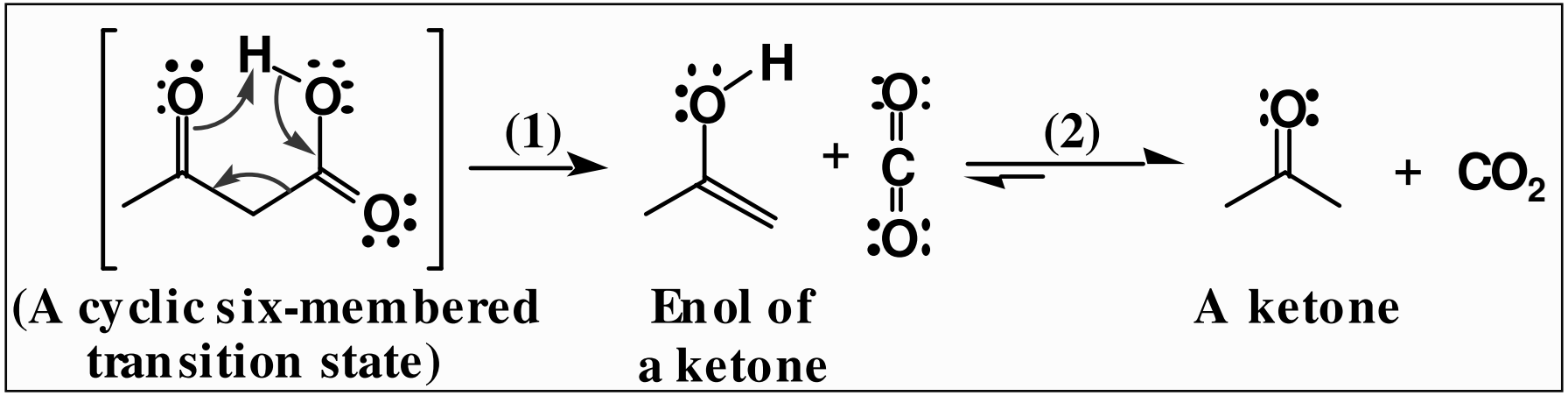
The most importan exceptions are carboxylic acids that have a carbonyl group beta to the carboxyl group **i.e.- β keto-acids**

–this type of carboxylic acid undergoes decarboxylation on mild heating



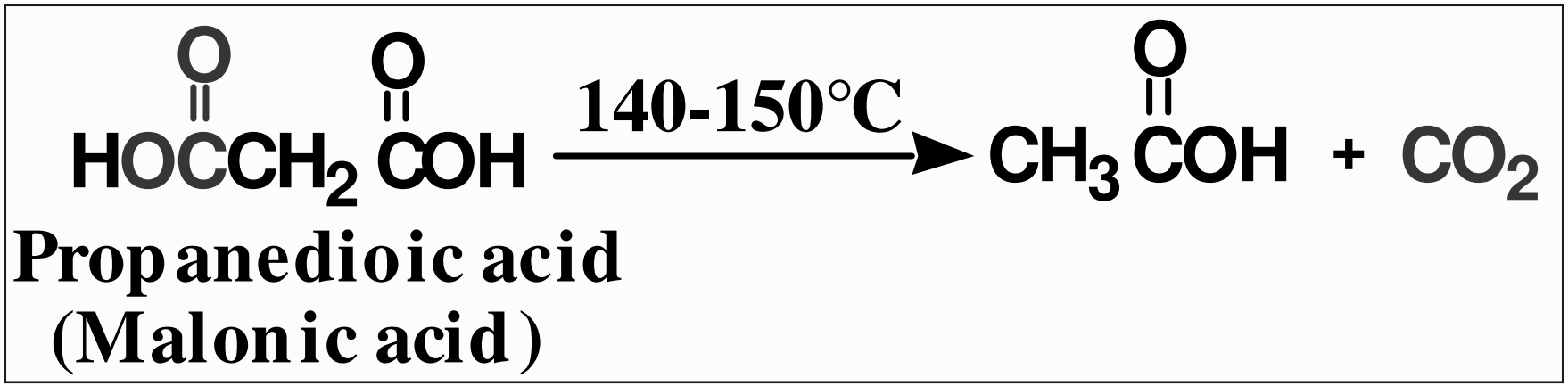
Decarboxylation

– thermal decarboxylation of a β-ketoacid involves rearrangement of six electrons in a cyclic six-membered transition state

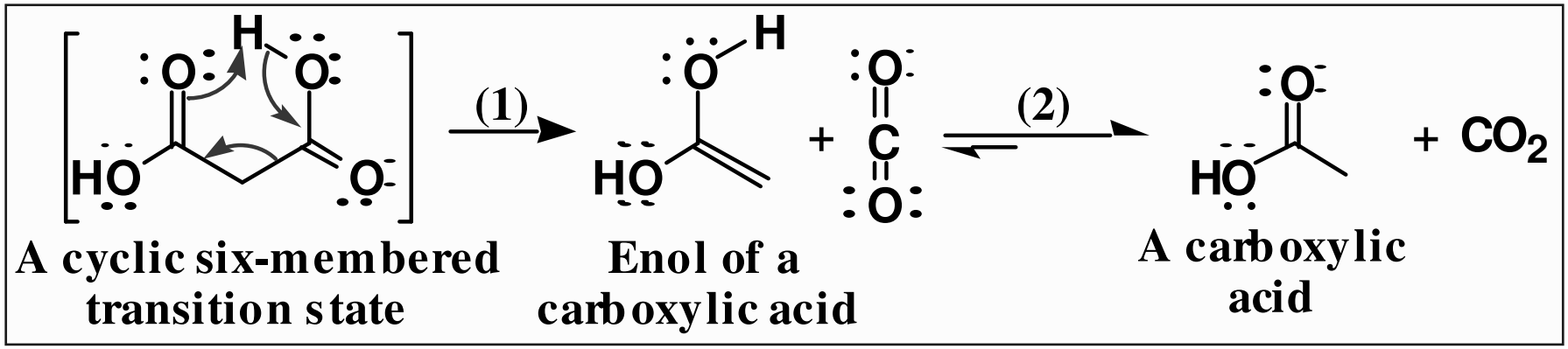


Decarboxylation

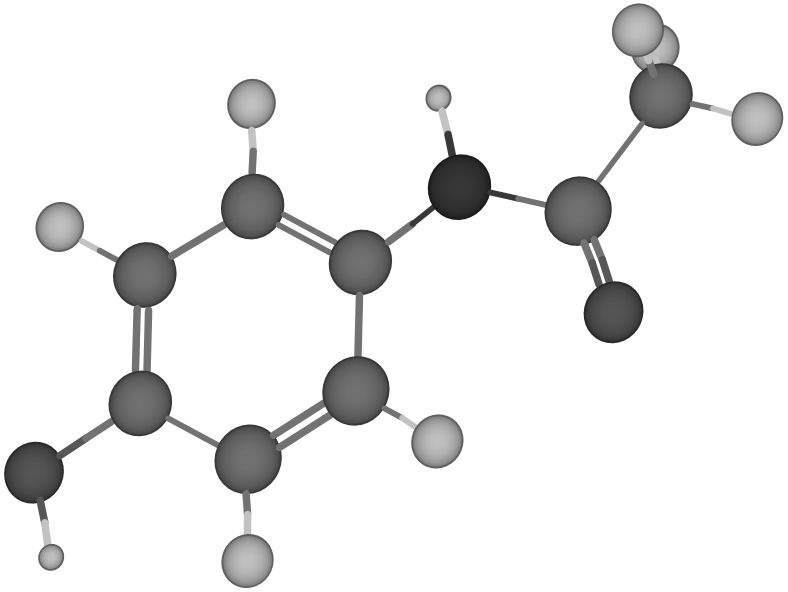
- decarboxylation occurs if there is any carbonyl group beta to the carboxyl
- malonic acid and substituted malonic acids, for example, also undergo thermal decarboxylation

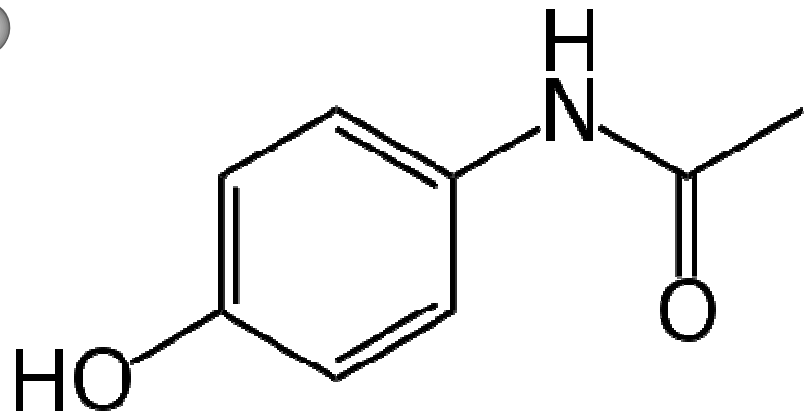


– thermal decarboxylation of malonic acids also involves rearrangement of six electrons in a cyclic six-membered transition state



Functional Derivatives of Carboxylic Acids

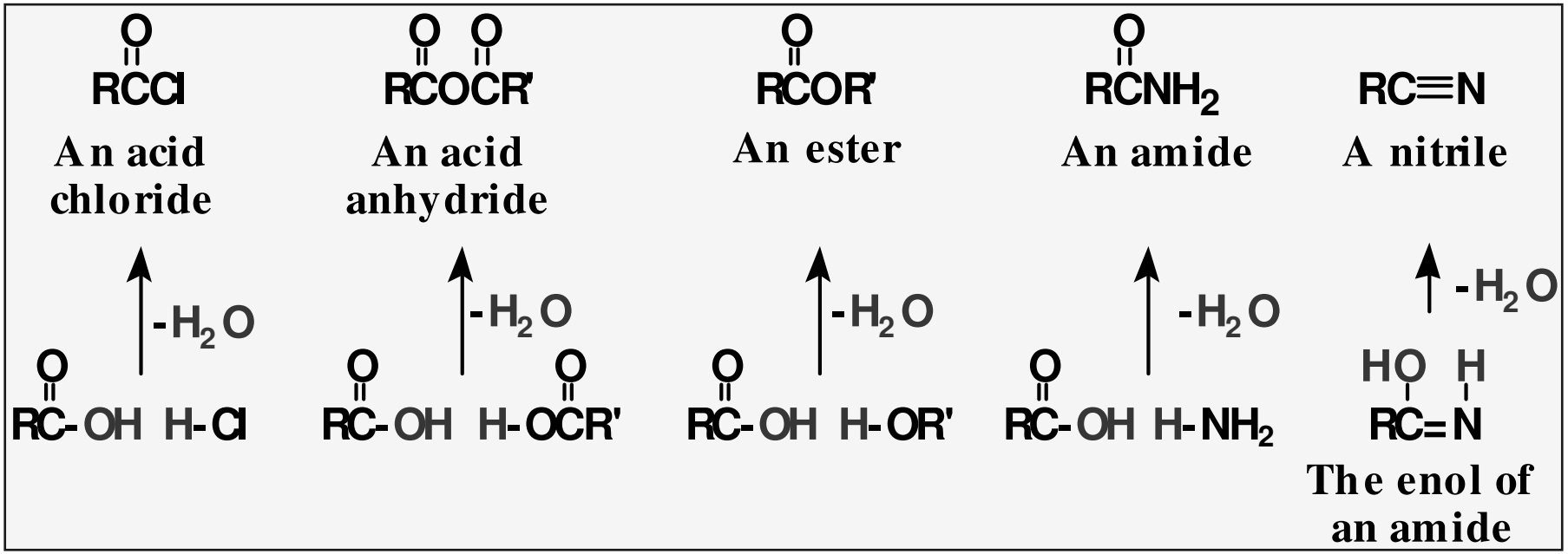




acetaminophen

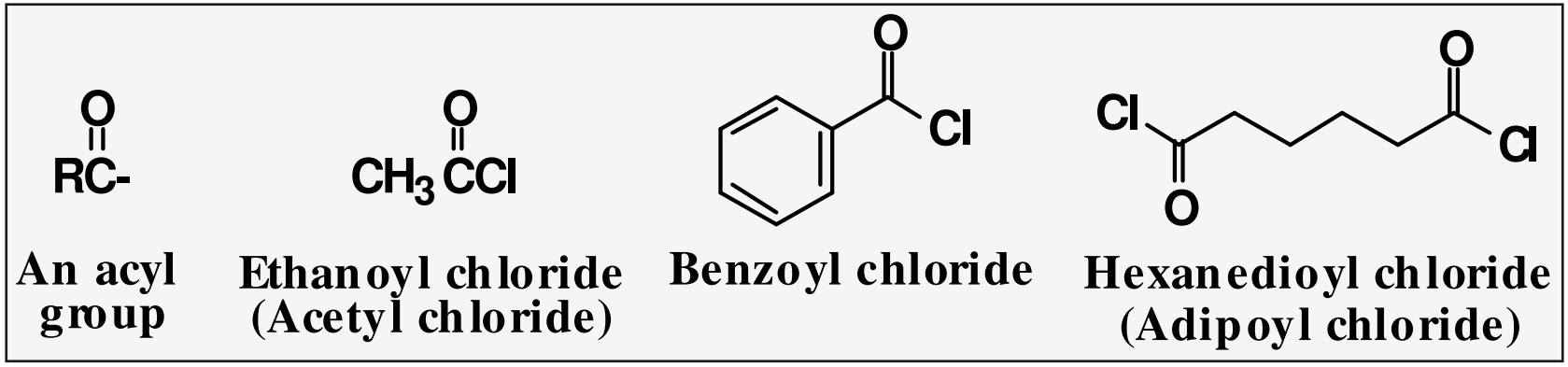
Organic acid derivatives

- There are five classes of organic acid derivatives
- Each arises from a dehydration reaction, usually a **condensation**
- Therefore, each derivative can also be hydrolyzed



Acid halides

- The functional group of an acid halide is an acyl group bonded to a halogen
  - the most common are the acid chlorides
  - to name, change the suffix -ic acid to -yl halide



An acyl group

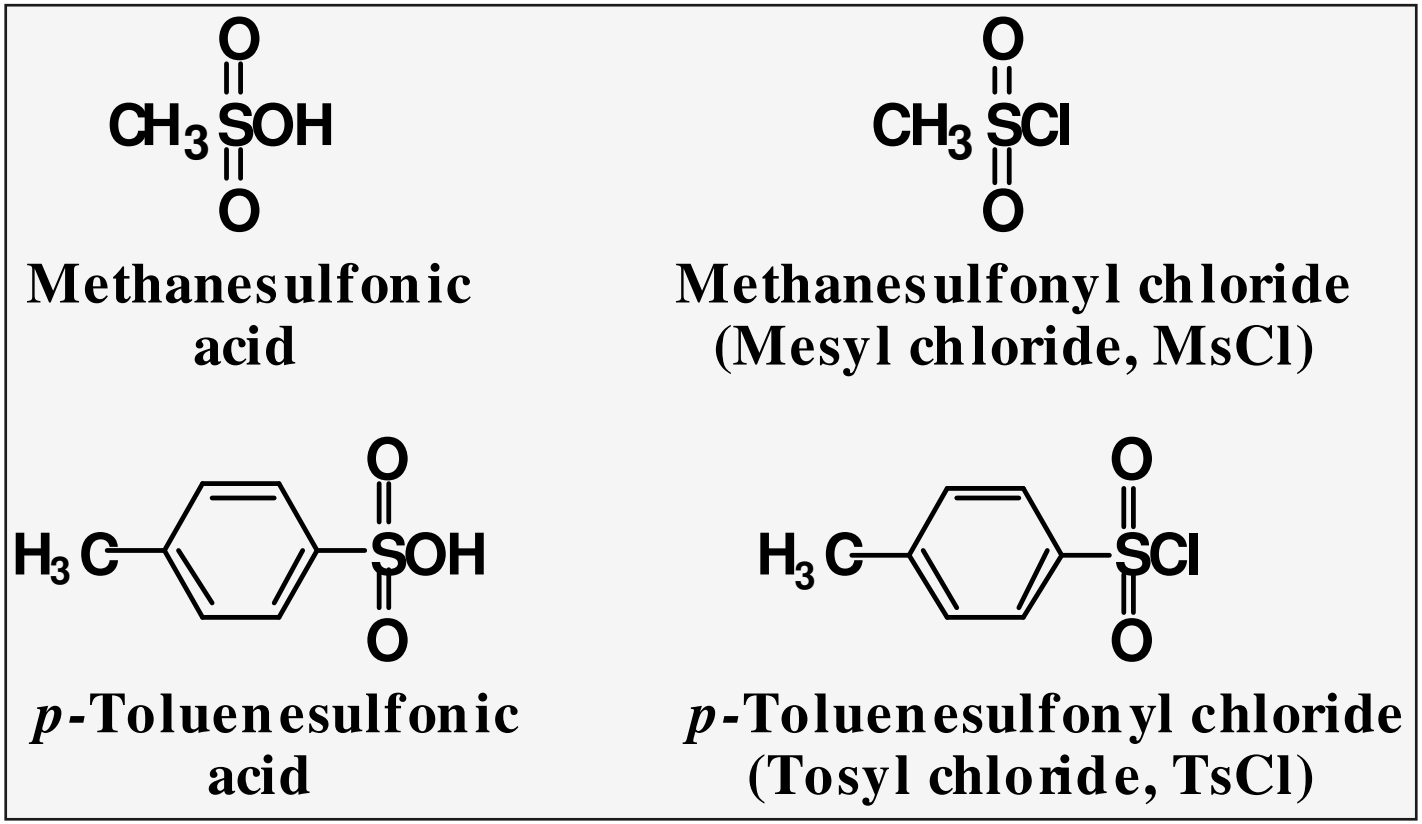
Ethanoyl chloride (Acetyl chloride)

Benzoyl chloride

Hexanedioyl chloride (Adipoyl chloride)

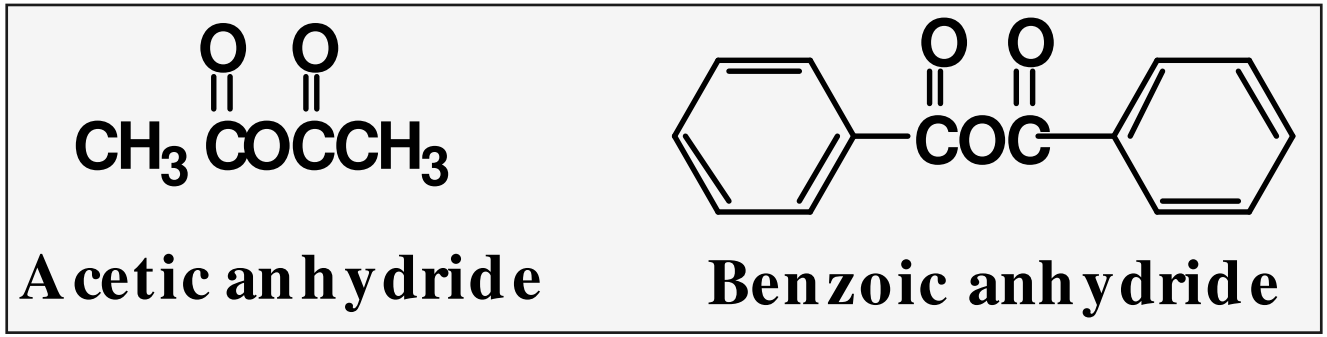
Sulfonyl Chlorides

– replacement of -OH in a sulfonic acid by -Cl gives a **sulfonyl chloride**



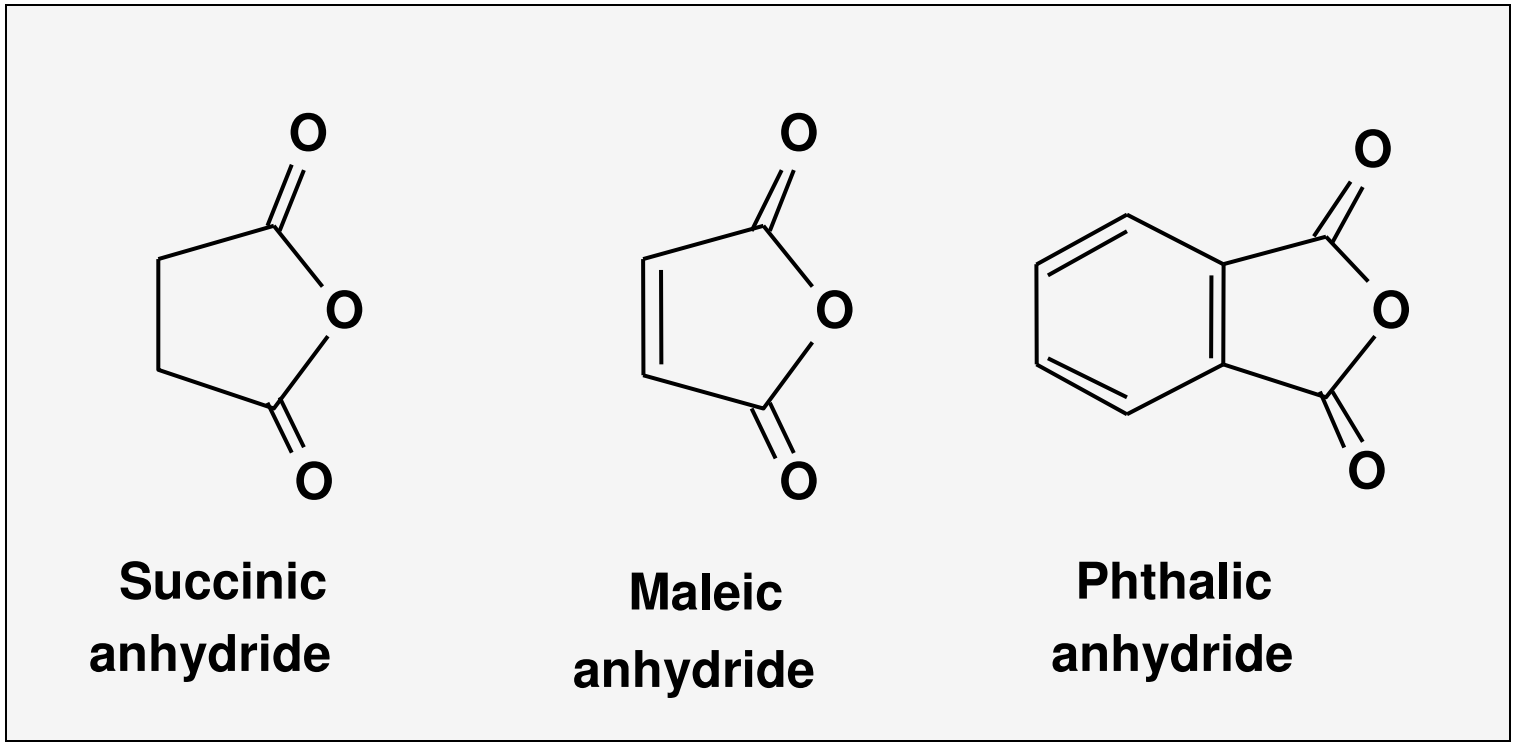
Acid Anhydrides

- The functional group of an acid anhydride is two acyl groups bonded to an oxygen atom
  - the anhydride may be symmetrical (two identical acyl groups) or mixed (two different acyl groups)
  - to name, replace acid of the parent acid by anhydride



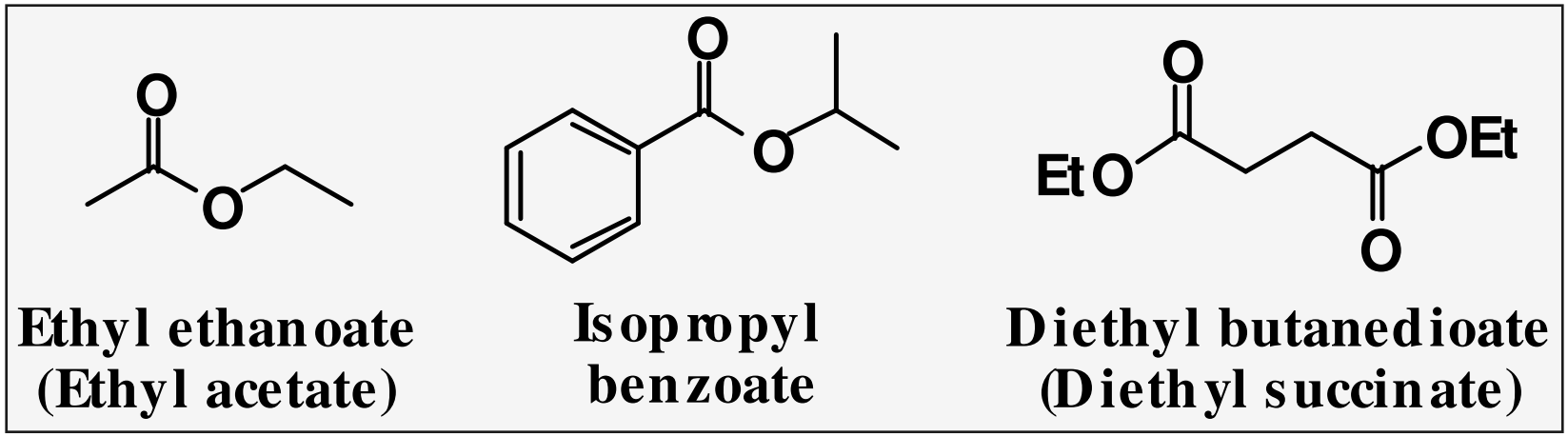
Acid Anhydrides

- Cyclic anhydrides are named from the dicarboxylic acids from which they are derived



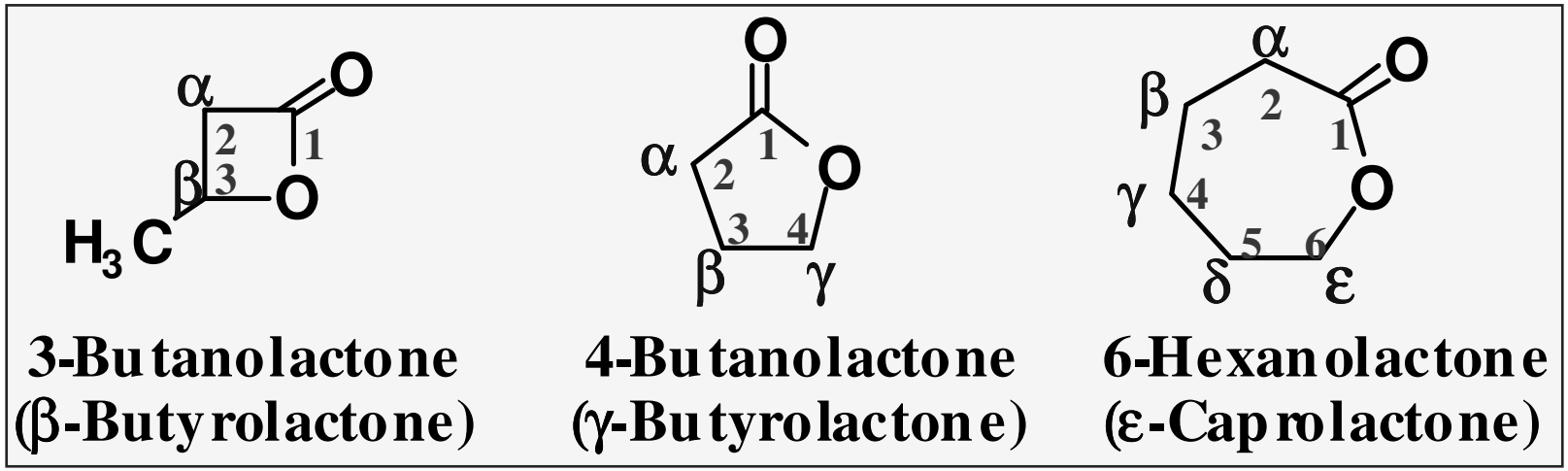
Esters

- The functional group of an ester is an acyl group bonded to -OR or -OAr
  - name the alkyl or aryl group bonded to oxygen followed by the name of the **acid**
  - change the suffix -ic acid to -ate



Esters

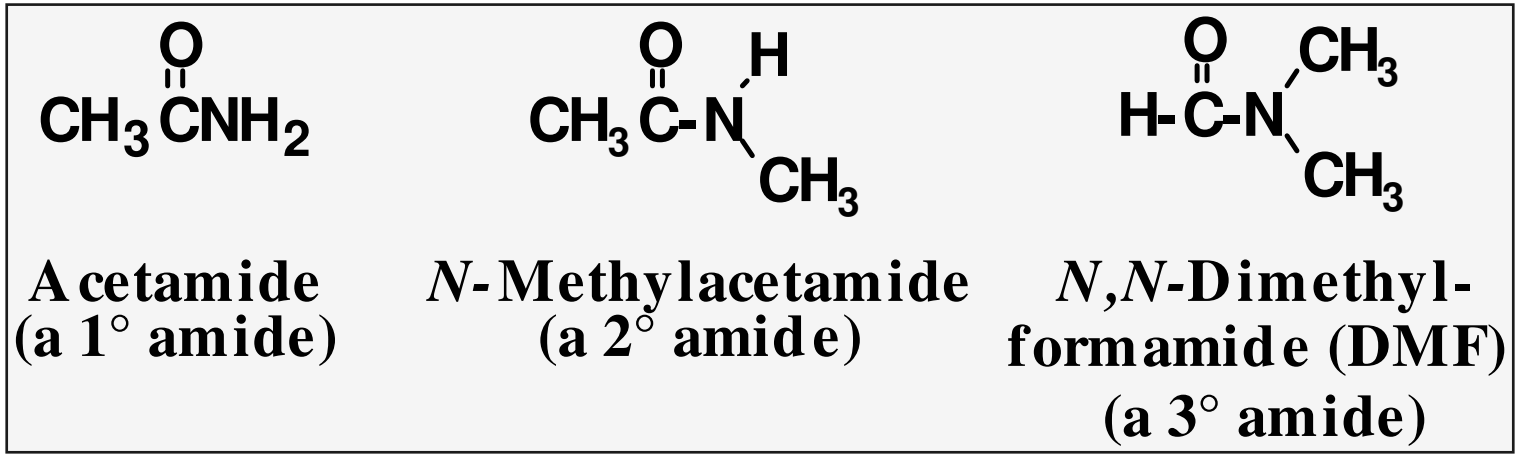
- Cyclic esters are called **lactones**
  - name the parent carboxylic acid, drop the suffix -ic acid and add -olactone



3-Butanolactone (β-Butyrolactone) **4-Butanolactone (γ-Butyrolactone)** **6-Hexanolactone (ε-Caprolactone)**

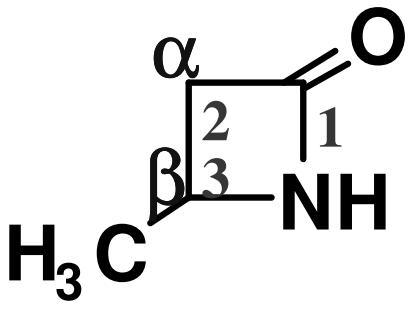
Amides

- The functional group of an amide is an acyl group bonded to a nitrogen atom
  - IUPAC: drop -oic acid from the name of the parent acid and add -amide
  - if the amide nitrogen is bonded to an alkyl or aryl group, name the group and show its location on nitrogen by *N*-

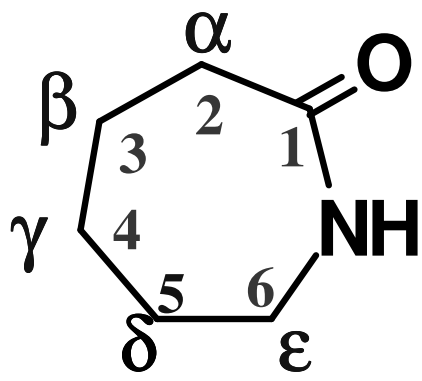


Amides

- Cyclic amides are called **lactams**
  - name the parent carboxylic acid, drop the suffix -ic acid and add -lactam



3-Butanolactam
(β-Butyrolactam)



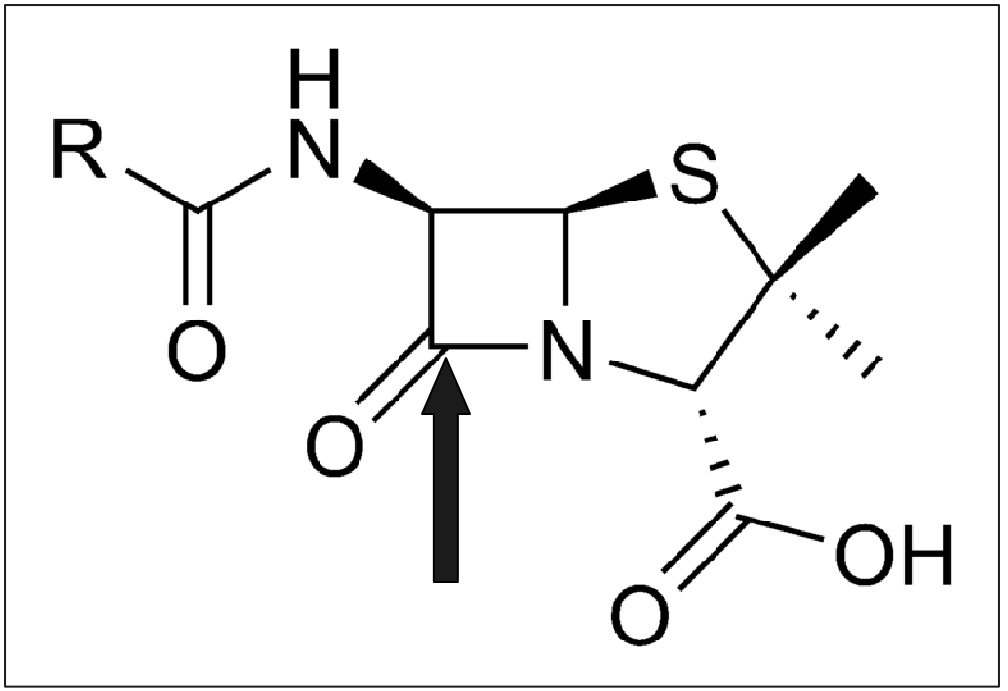
6-Hexanolactam
(ε-Caprolactam)

penam –old term for β-lactam

Penicillins

the penicillins are a family of β-**lactam antibiotics**

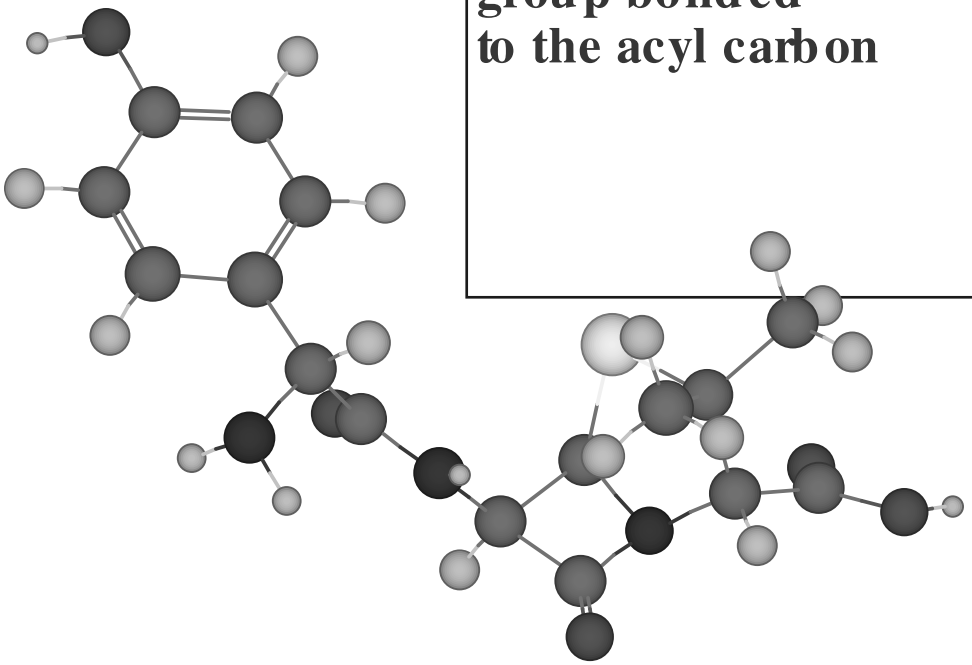
The compound is an exceptional "acylating" agent because of the ring strain of the lactam.

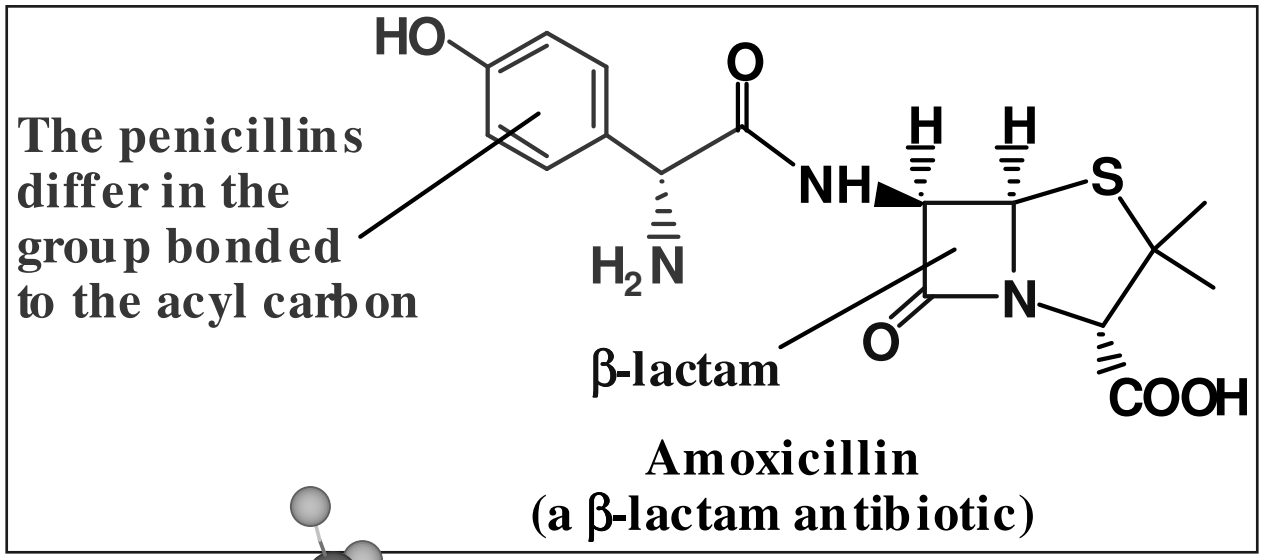


Inhibit cell wall synthesis by acylating and de-activating the required enzymes.

Penicillins

the penicillins are a family of **β-lactam antibiotics**

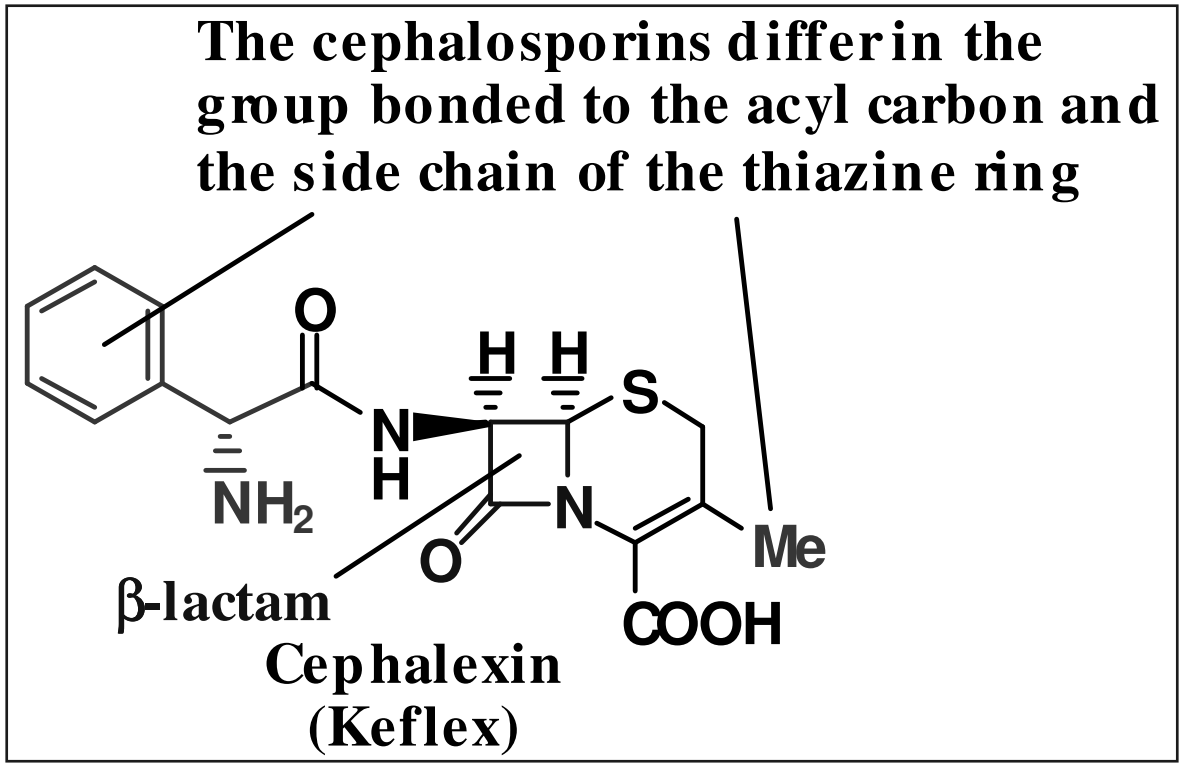




Pharmacophore-substructure responsible for the biological activity

Cephalosporins

the cephalosporins are also β-**lactam antibiotics**



Bacteria develop resistance by producing β-**lactamases-**enzymes, which can hydrolyze the lactam before it can inhibit cell wall synthesis.