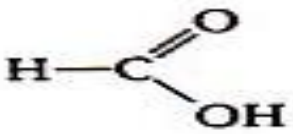
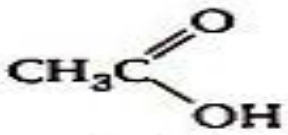
Carboxylic Acids And Their Derivatives

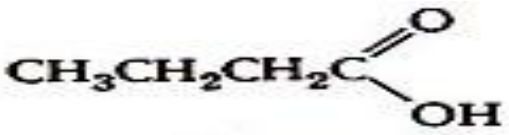
Carboxylic acids are compounds that contain a carboxyl group 



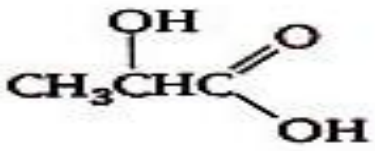
Formic acid



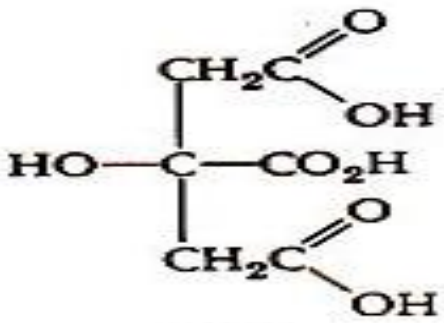
Acetic acid



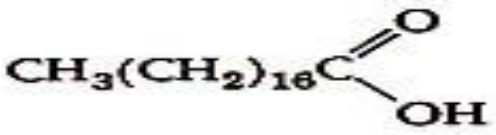
Butyric acid



Lactic acid



Citric acid



Stearic acid

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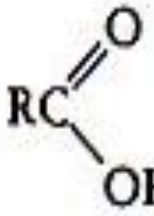
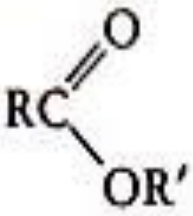
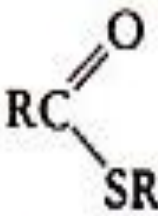
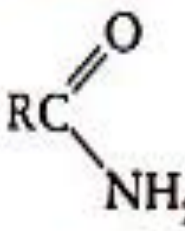
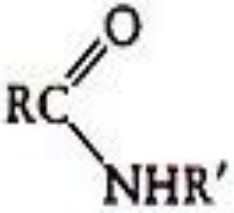
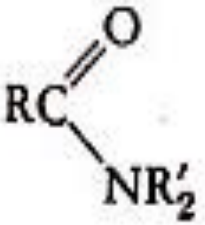
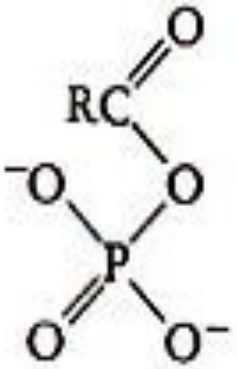
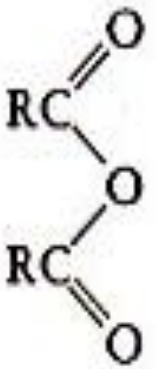
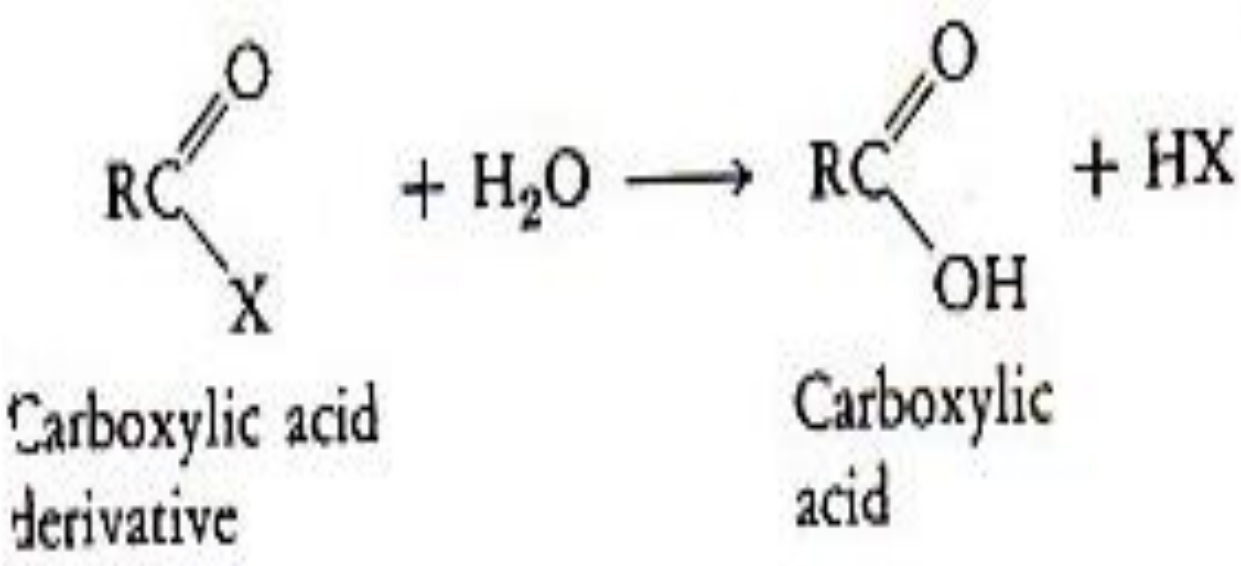
Table 18-1. Structural Formulas of Carboxylic Acids and Their Derivatives

			
Carboxylic acid	Ester	Thioester	Amide
			
N-substituted amide	*N*,*N*-disubstituted amide	Acyl phosphate	Carboxylic acid anhydride

R and R′ can be either alkyl or aryl groups in this table.

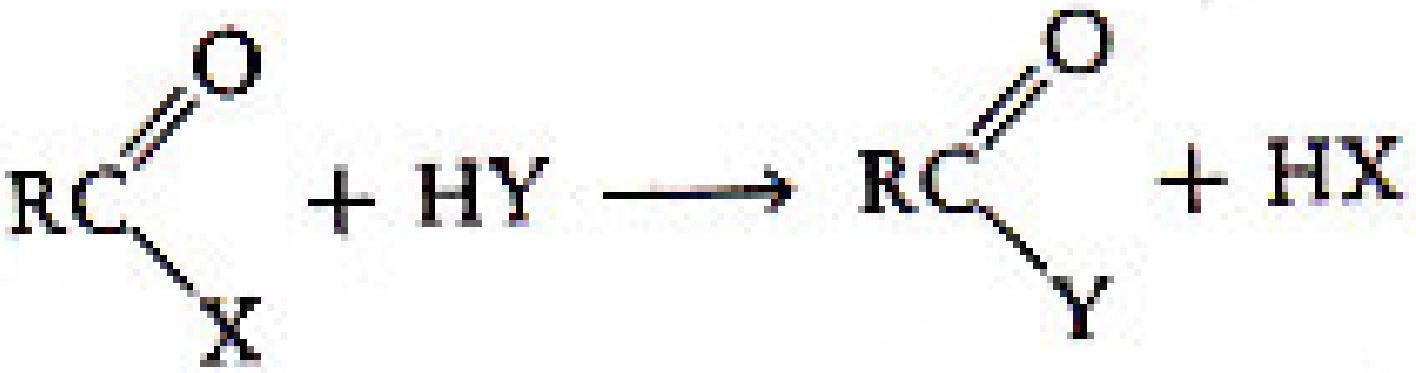
* These compounds are called derivatives of carboxylic acids because **they can hydrolyzed to the carboxylic acid** according to the following equation:



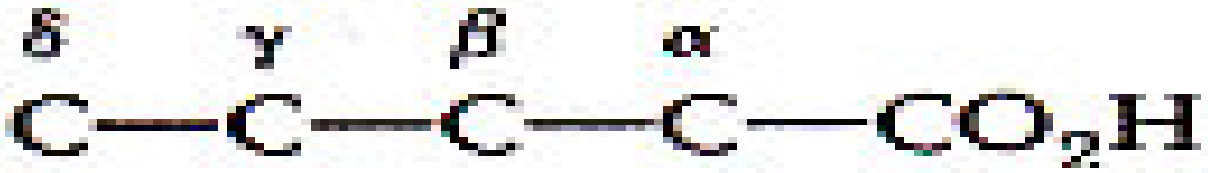
X = OR, OAr, SR, NH_2, NHR′, NR'_2, OPO_3^{-2}, O_2CR

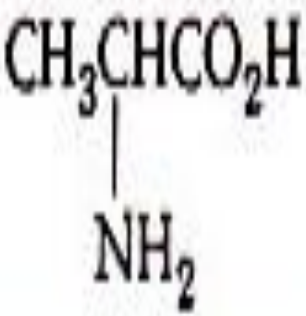
- The major type of reaction that carboxylic acids and their derivatives undergo in living systems is **substitution reaction** .

In this reaction, the group or atom bonded to the carbonyl carbon is replaced by another group. The general reaction is the following:

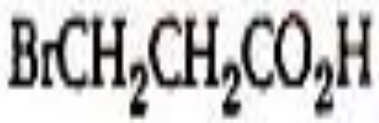


- The location of the substituent on the chain is designated by the letters α, β, γ, or δ , which refer to the following positions:

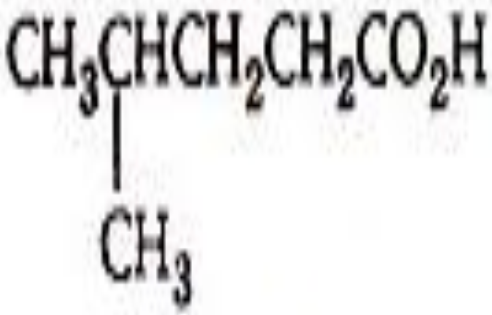




α-Aminopropionic acid



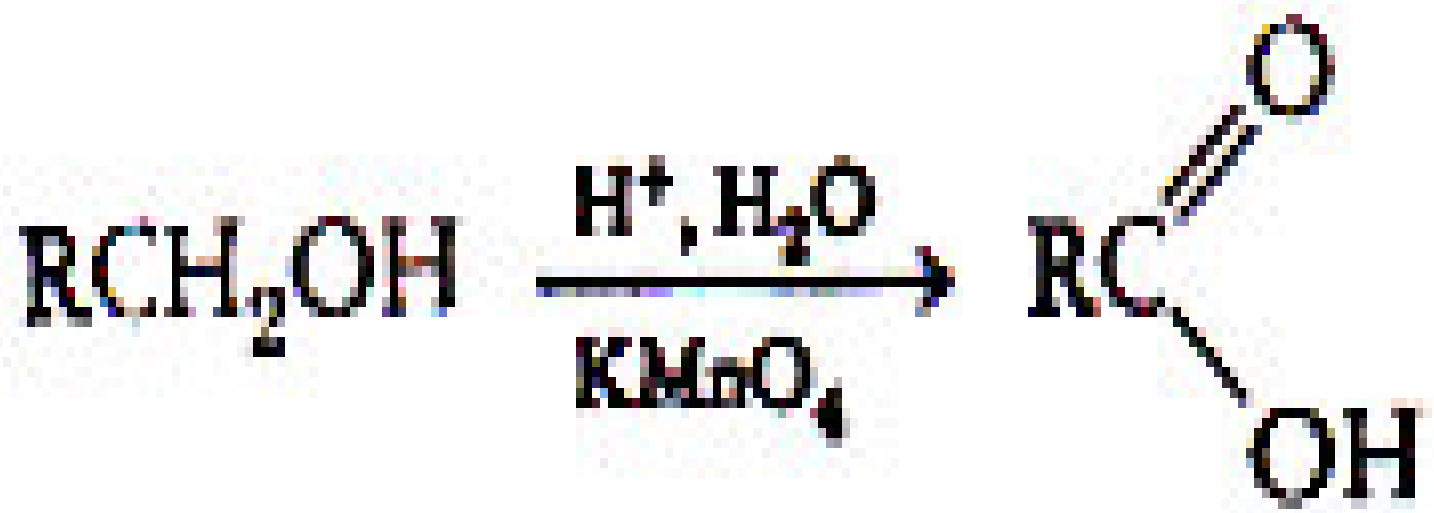
β-Bromopropionic acid



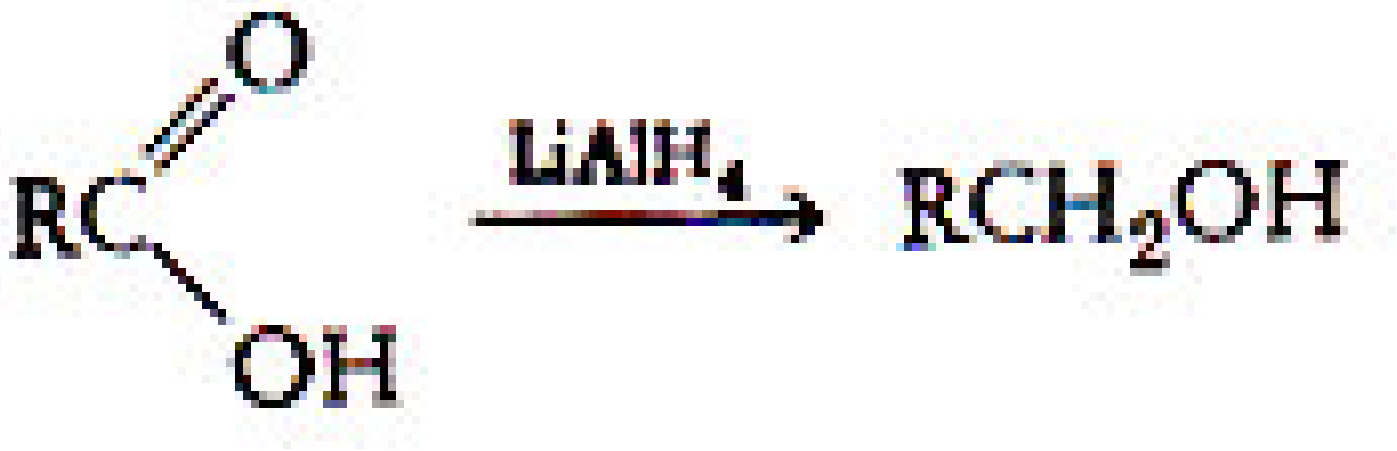
γ-Methylvaleric acid

Preparing Carboxylic Acids

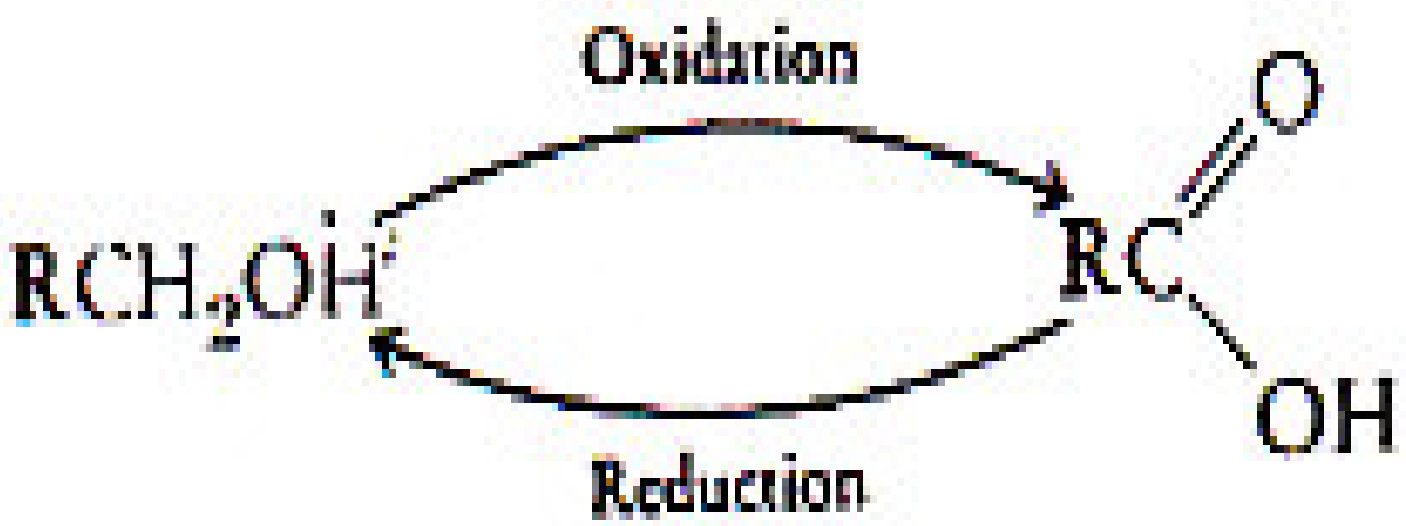
* The oxidation of primary alcohols forms carboxylic acids. For example:



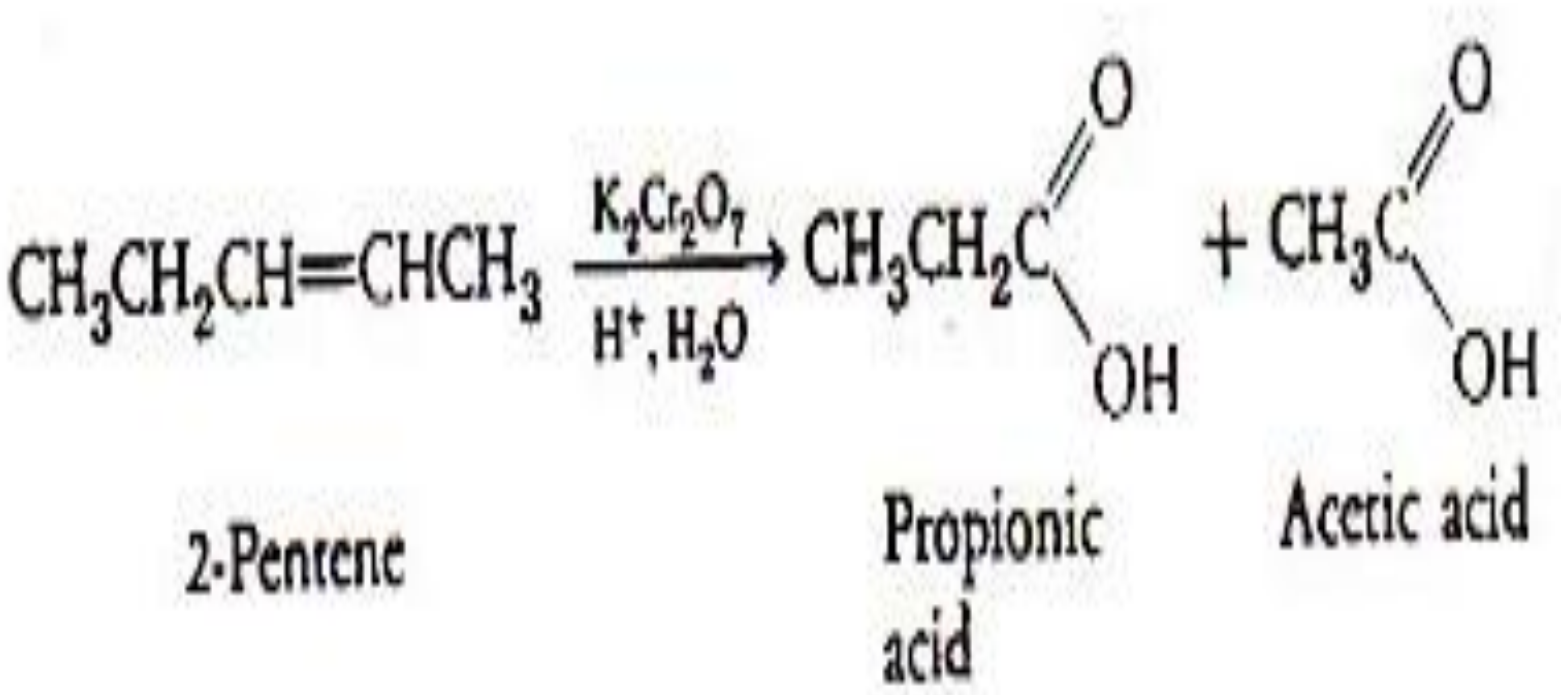
* The reverse of this reaction can be accomplished. Thus, a carboxylic acid can form a primary alcohol by reaction with lithium aluminum hydride, a strong reducing agent. For example:



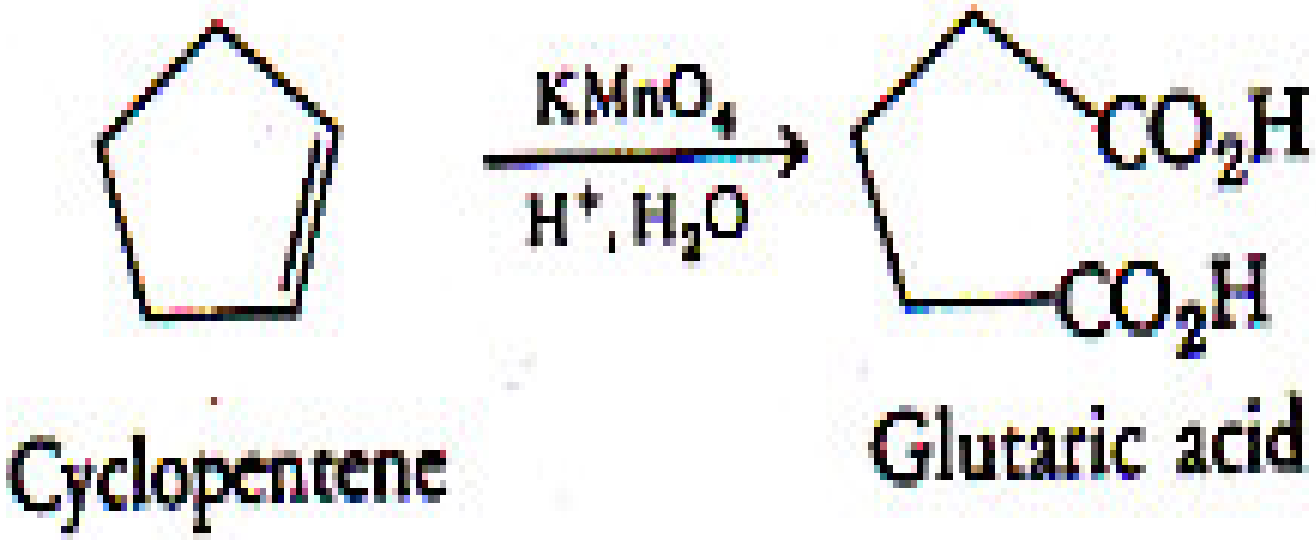
* In this way, primary alcohols and monocarboxylic acids are readily interconverted:



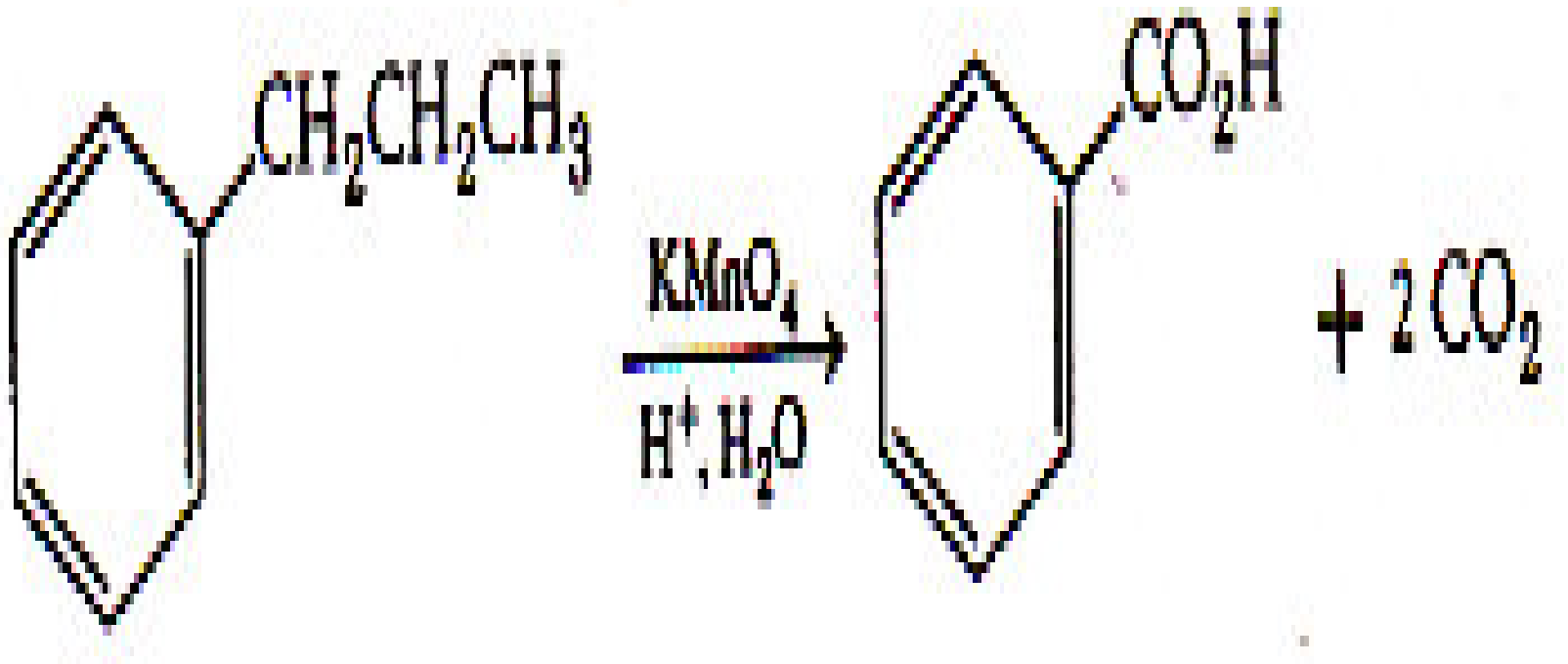
* **Vigorous oxidation of alkenes** results in the breaking of the double bond, for example:



* This reaction is particularly useful for forming dicarboxylic acids from cycloalkenes. For example

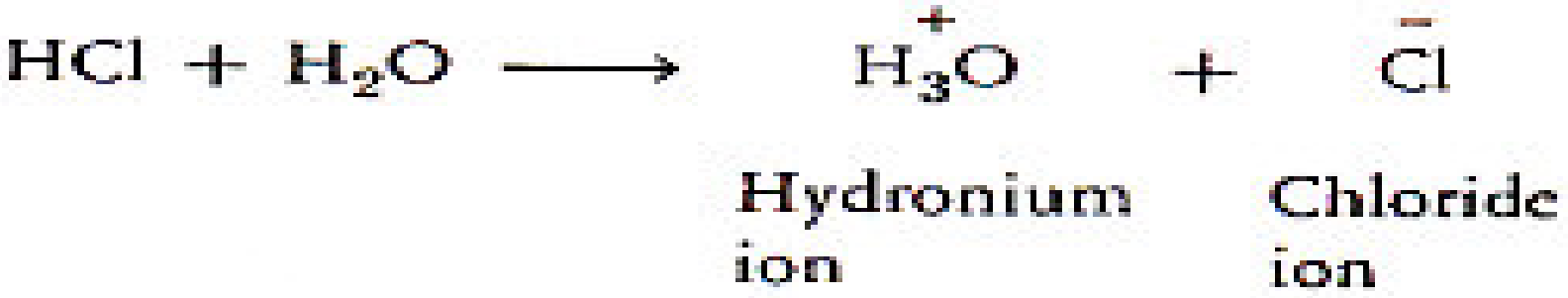


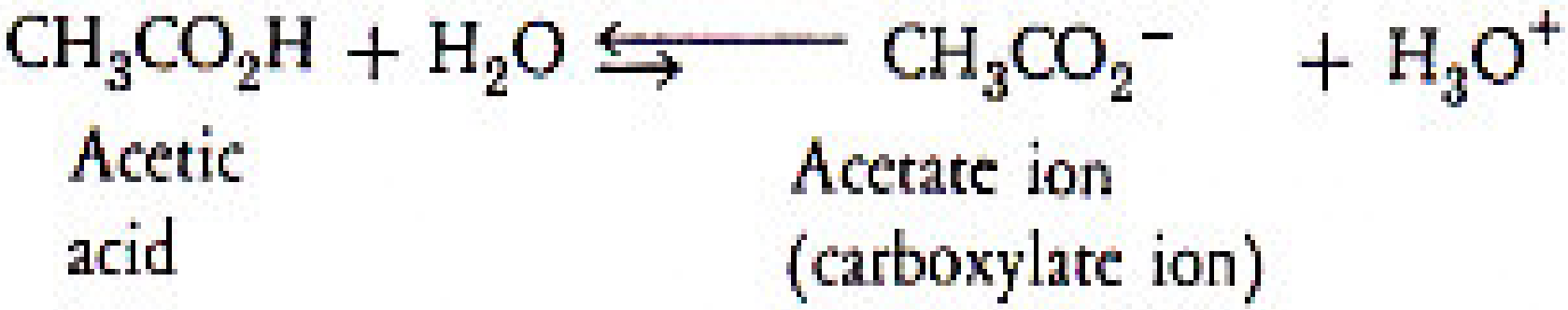
* Aromatic carboxylic acids can be prepared by oxidation of an alkyl side chain on an aromatic ring



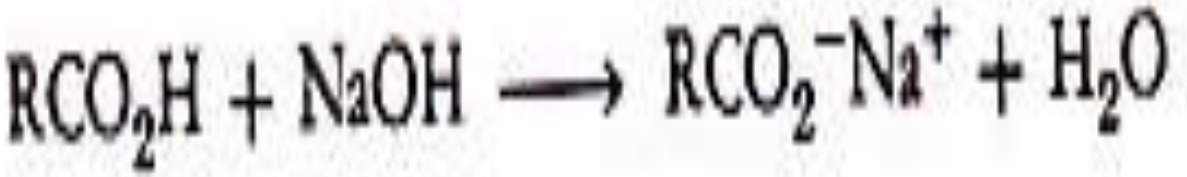
Acidity Of Carboxylic Acids

* Carboxylic acids are weak acids compared to inorganic acids such as hydrochloric acid ,nitric acid ,and sulfuric acid.

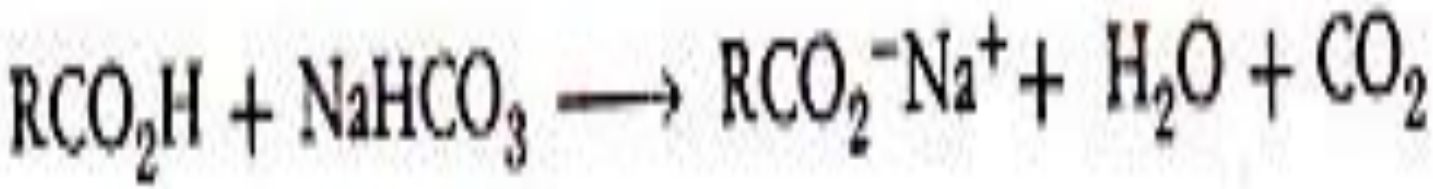




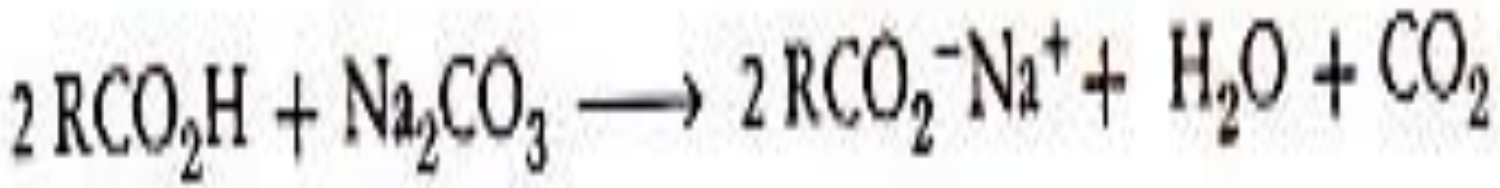
* All carboxylic acids react completely with aqueous solutions of strong bases such as sodium hydroxide to form salts.



$$RCO_2H + NaOH \longrightarrow RCO_2^-Na^+ + H_2O$$

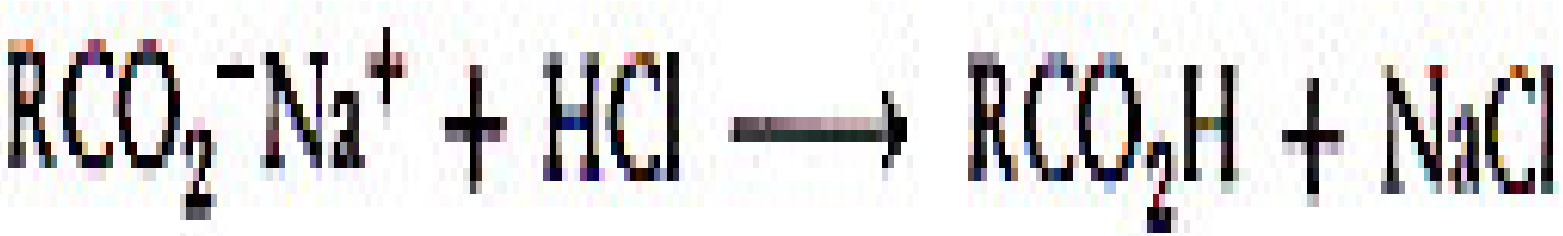


$$RCO_2H + NaHCO_3 \longrightarrow RCO_2^-Na^+ + H_2O + CO_2$$

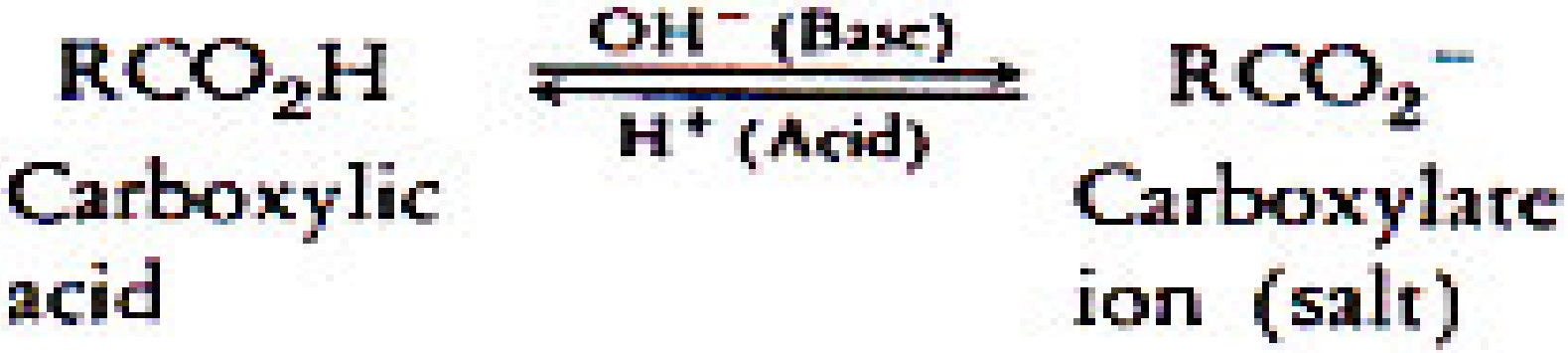


$$2\,RCO_2H + Na_2CO_3 \longrightarrow 2\,RCO_2^-Na^+ + H_2O + CO_2$$

* When the solid formed in this way reacts with strong acids such as HCl, HNO_3 , H_2SO_4 ,the carboxylic acid is reformed:



* Carboxylic acids and their salts are easily interconverted:



Esters

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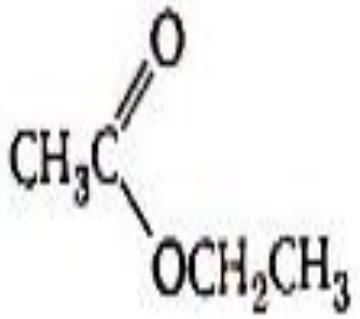
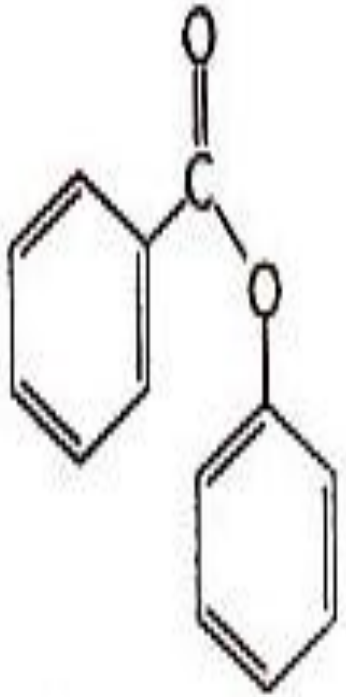
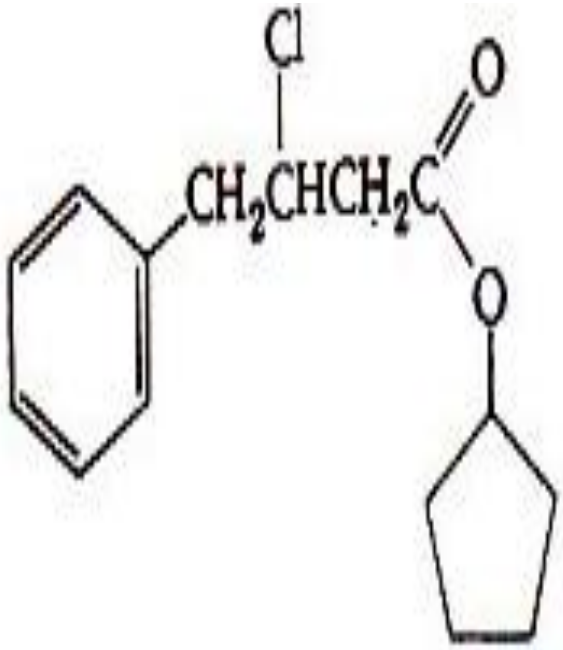


Ethyl acetate
(Ethyl ethanoate)

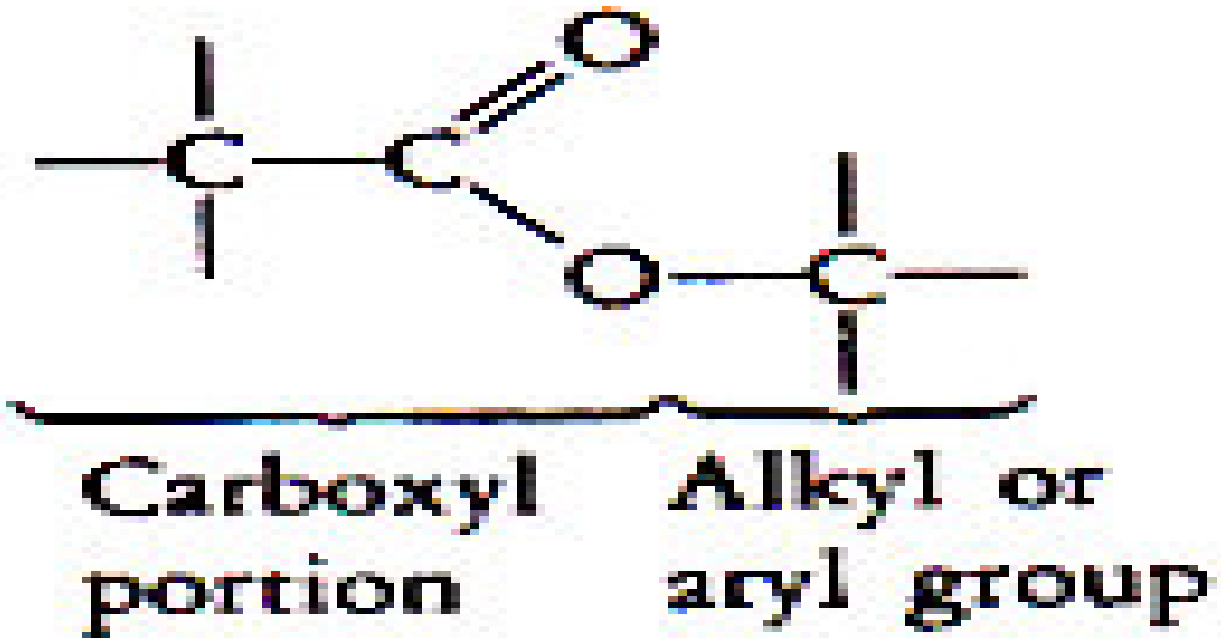


Phenyl benzoate



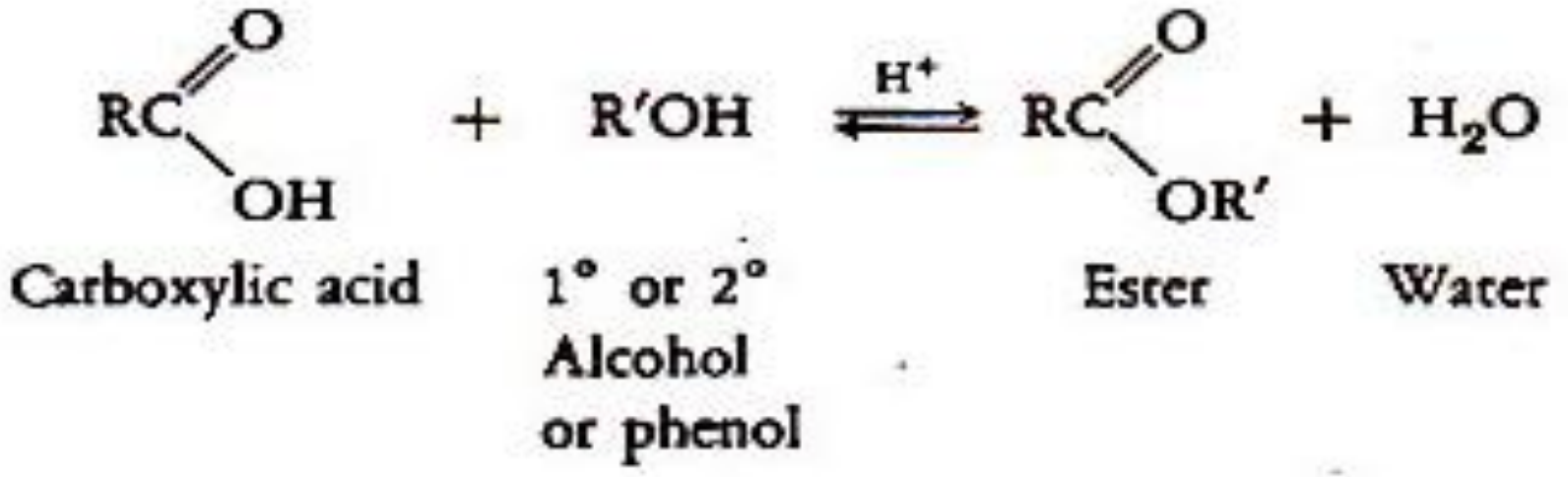
Cyclopentyl 3-chloro-4-phenylbutanoate

* Esters are made of two parts, the carboxyl part and an alkyl or aryl group:



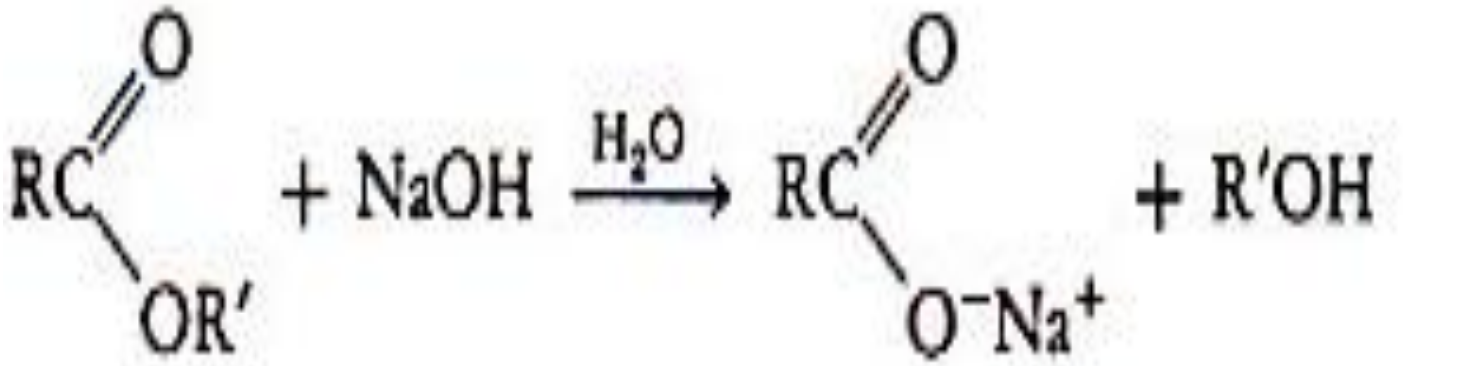
preparation

* When a phenol or a primary or secondary alcohol is heated with a carboxylic acid in the presence of a mineral acid as a catalyst, an equilibrium is established with the ester and water:



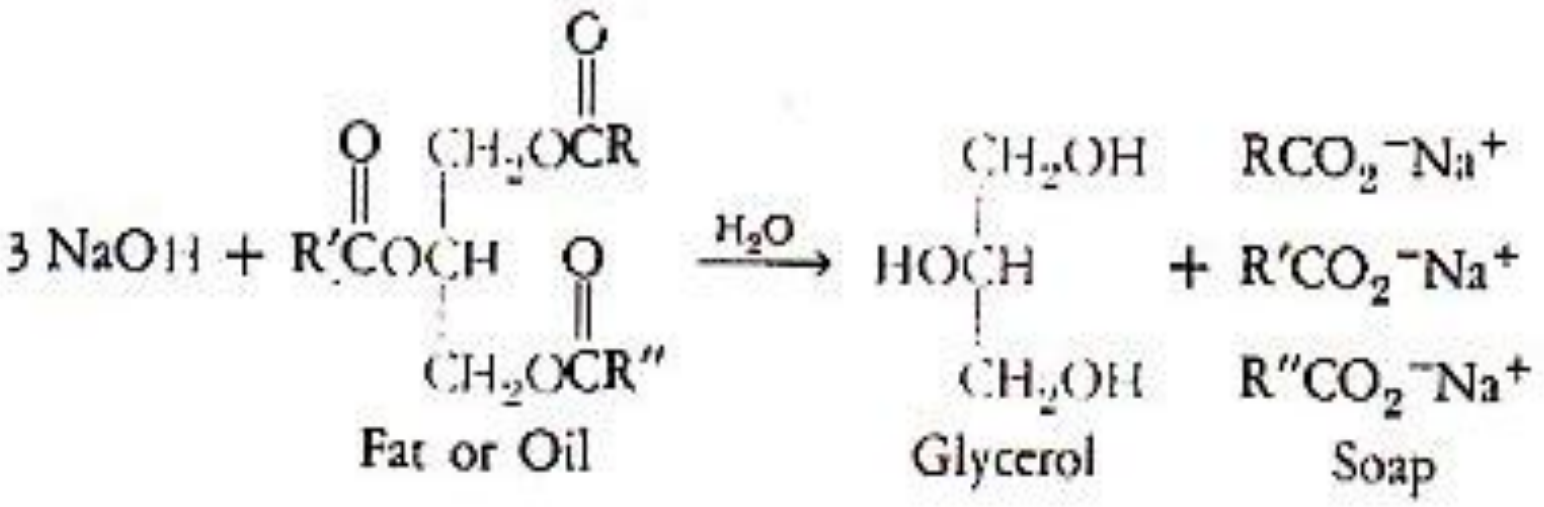
Reactions

* The hydrolysis of an ester in an alkaline solution.

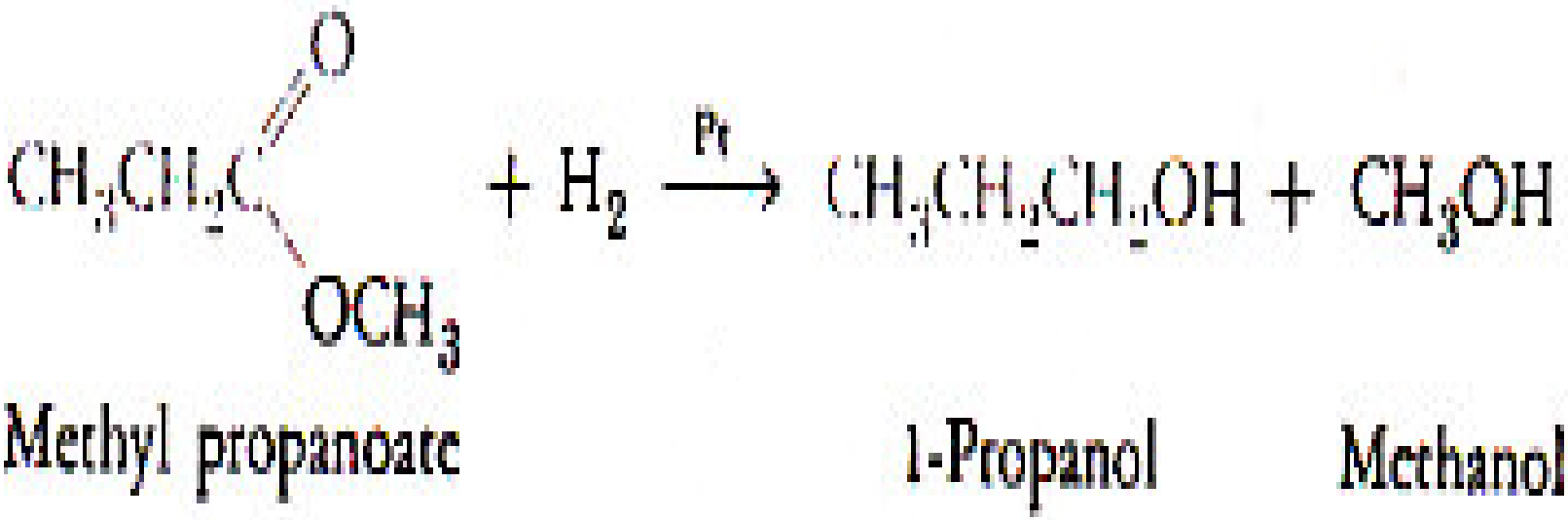


- The conversation of an ester to an alcohol and the salt of a carboxylic acid by an aqueous base is called **saponification**.

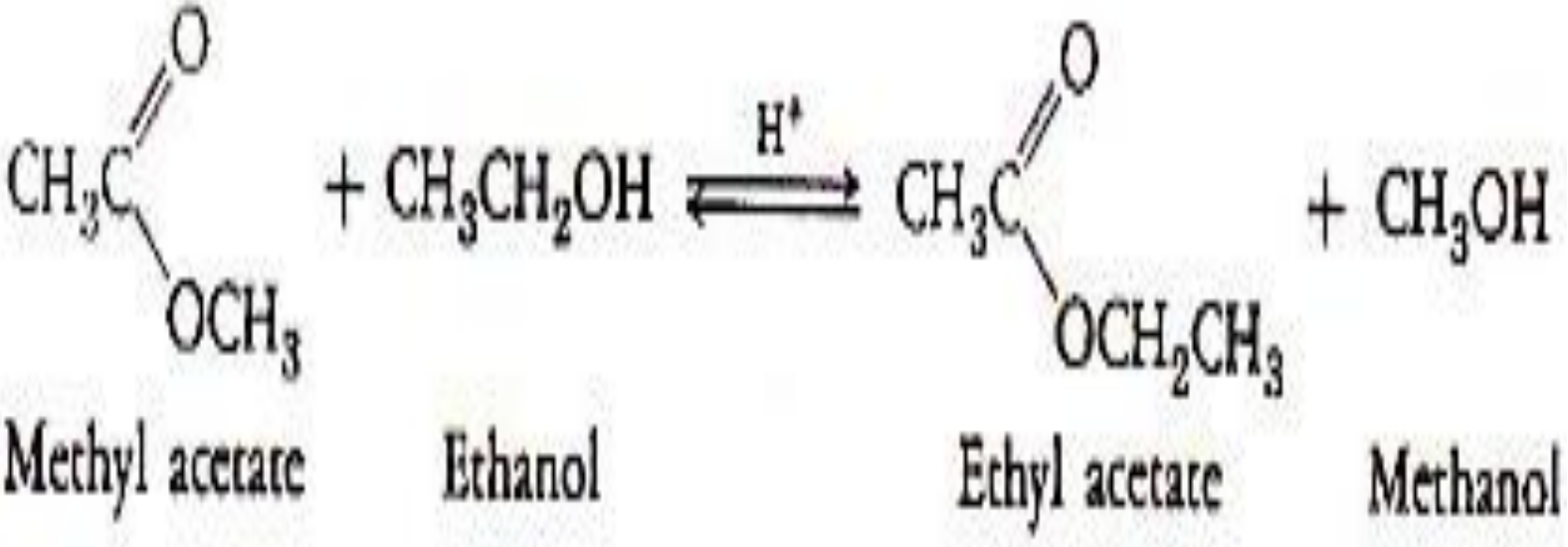
The name refer to the fact that soaps are formed by the alkaline hydrolysis of naturally occuring fats and oils,for example



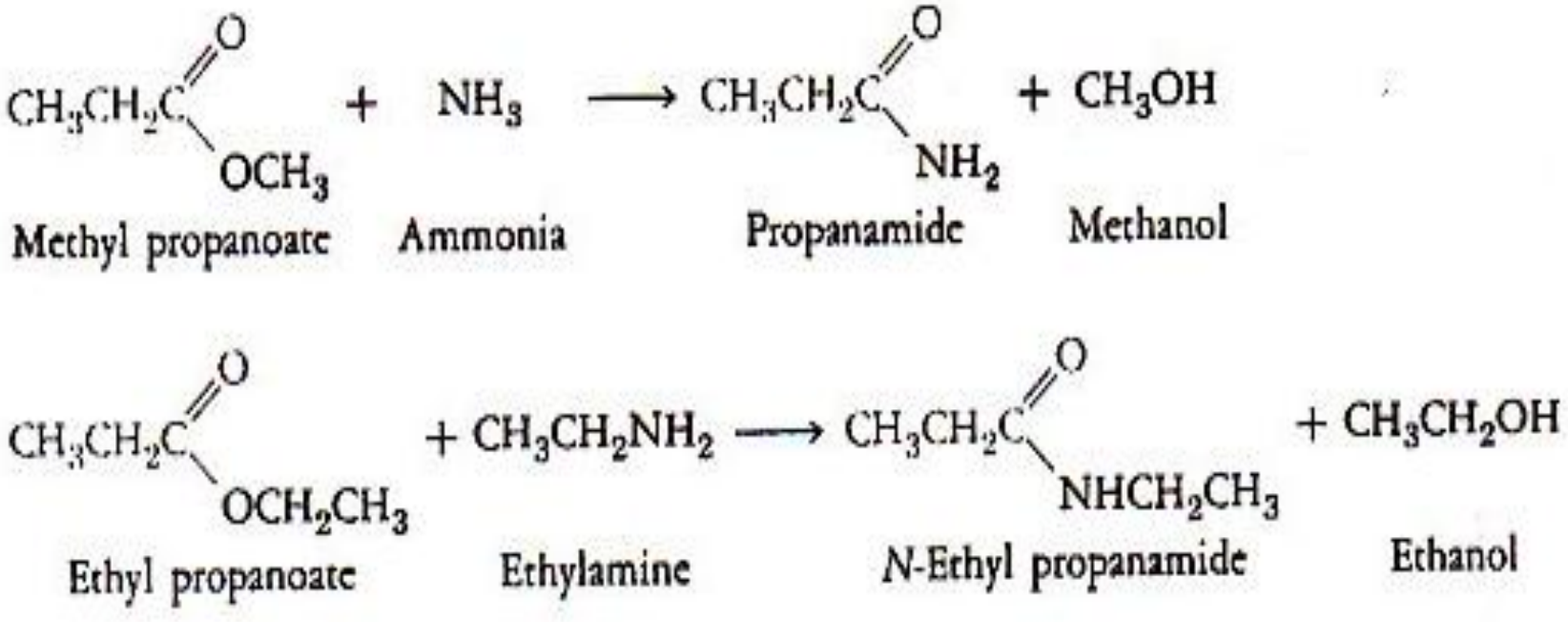
* Esters,like carboxylic acids,can be reduced to alcohols by reducing agents such as lithium aluminum hydride or hydrogen and a metal catalyst. For example:



* There are a number of reactions in which the alkoxy group of the ester is replaced by another group. One such reaction , called **transesterification**, is the acid-catalyzed reaction of an ester and an alcohol. For example:

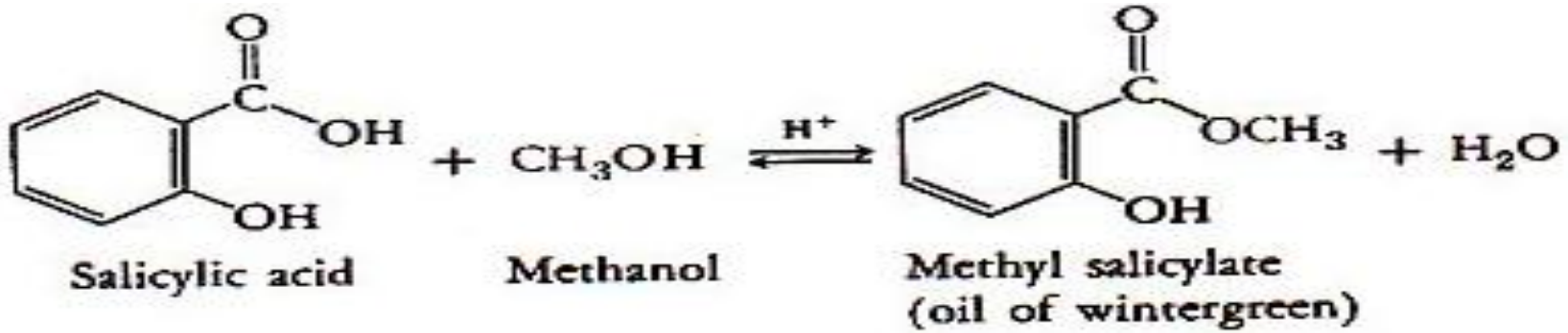


* A related reaction occurs by treating an **ester with ammonia or an amine**. This called an **ammonolysis reaction**. In this case, **an amide or an N-substituted amide** is the product. For example:

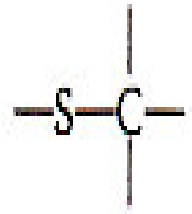


Esters Of Salicylic Acid

Salicylic acid contains both a **carboxyl group** and a **phenol group**. Both of these functional groups can form esters.



Thioesters

Thioesters are compounds containing an  group bonded to the carbonyl carbon.

- The reactions of thioesters are similar to those of esters,but they occur more rapidly.
- The general equations for the reactions of thioesters with water,alcohols,amines,and other thiols are as follows:

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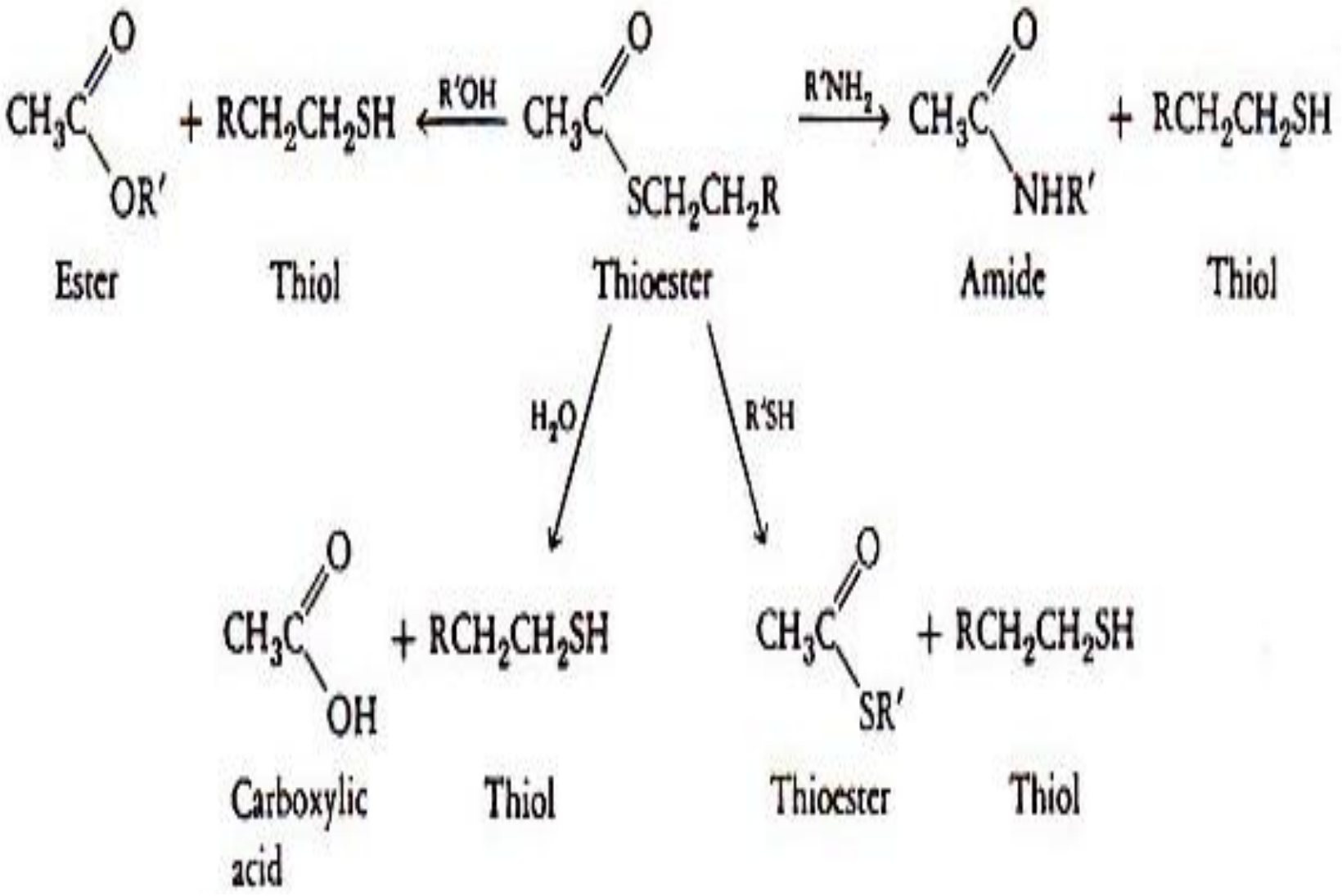
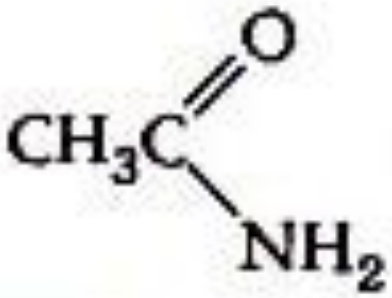
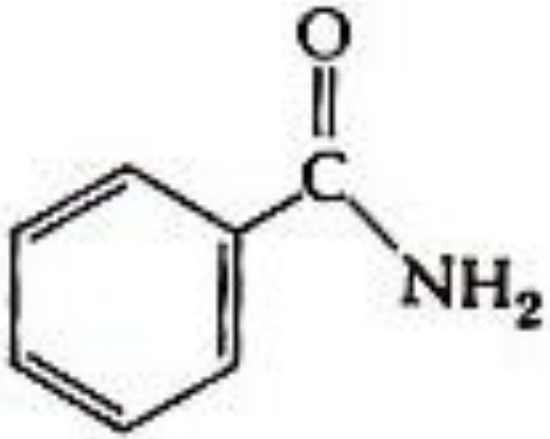

CH3C(=O)OR'
+ RCH2CH2SH
R'OH
CH3C(=O)SCH2CH2R
R'NH2
CH3C(=O)NHR'
+ RCH2CH2SH
Ester
Thiol
Thioester
Amide
Thiol
H2O
R'SH
CH3C(=O)OH
+ RCH2CH2SH
CH3C(=O)SR'
+ RCH2CH2SH
Carboxylic acid
Thiol
Thioester
Thiol

Amides

Amides can be regarded as carboxylic acids in which the hydroxy group is replaced by an $-NH_2$,-NHR ,or $-NR_2$ group. For example:



Acetamide
(related to acetic acid)



Benzamide
(related to benzoic acid)

- The bond between the carbonyl carbon and the nitrogen **called an amide bond**.

When it joins amino acids. it is called a **peptide bond**

* Amides are prepared by the reaction of ammonia or amines with a variety of acid derivatives such as esters and acid anhydrides. Their major reaction of biological interest is **hydrolysis** to a carboxylic acid and an amine or ammonia.

  For example:

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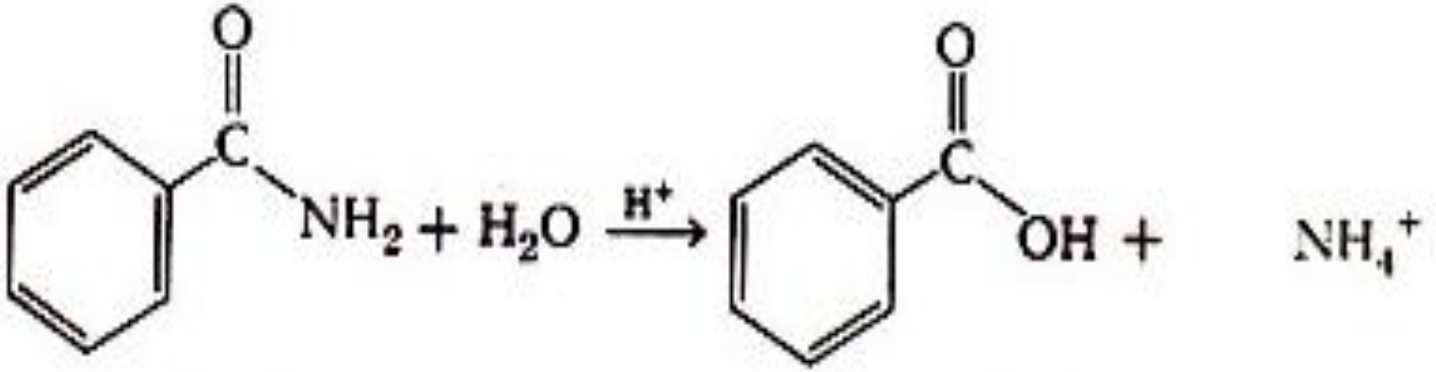
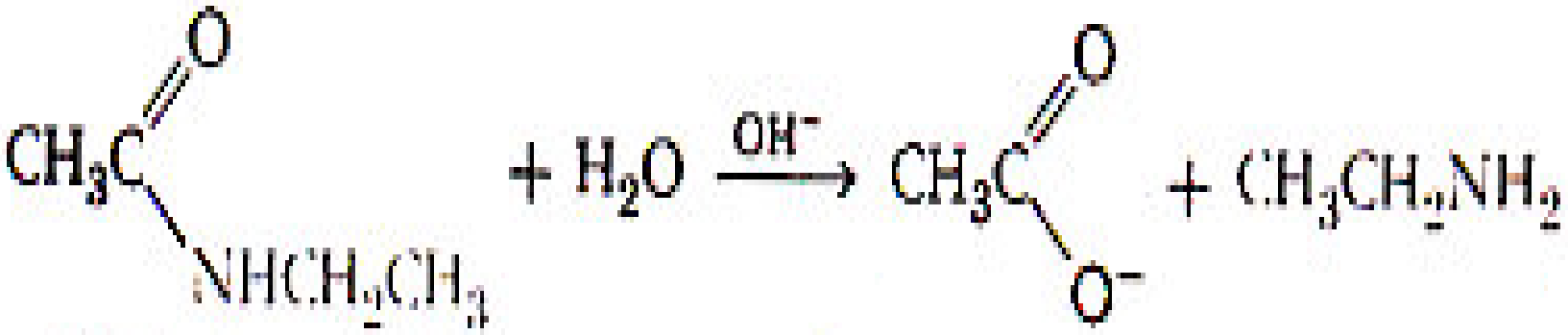


Benzamide Benzoic acid Ammonium ion

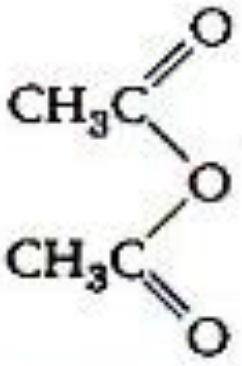


N-Ethylacetamide Acetate ion Ethanamine

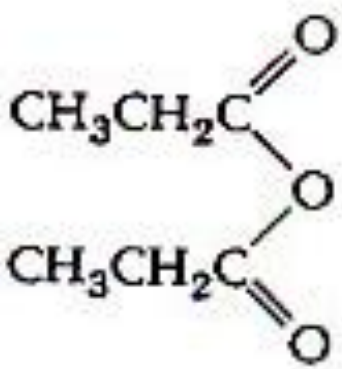
Carboxylic Acid Anhydrides

A carboxylic acid anhydride can be regarded as a carboxylic acid whose –OH group has been substituted by a carboxylate group.

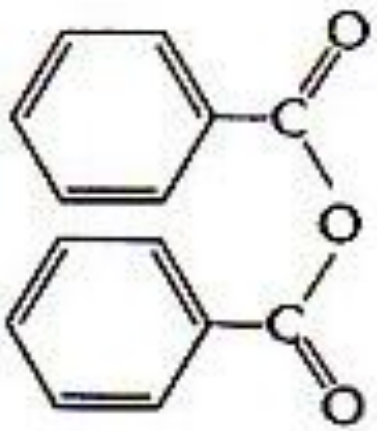
For example:



Acetic anhydride
(Ethanoic anhydride)



Propionic anhydride
(Propanoic anhydride)



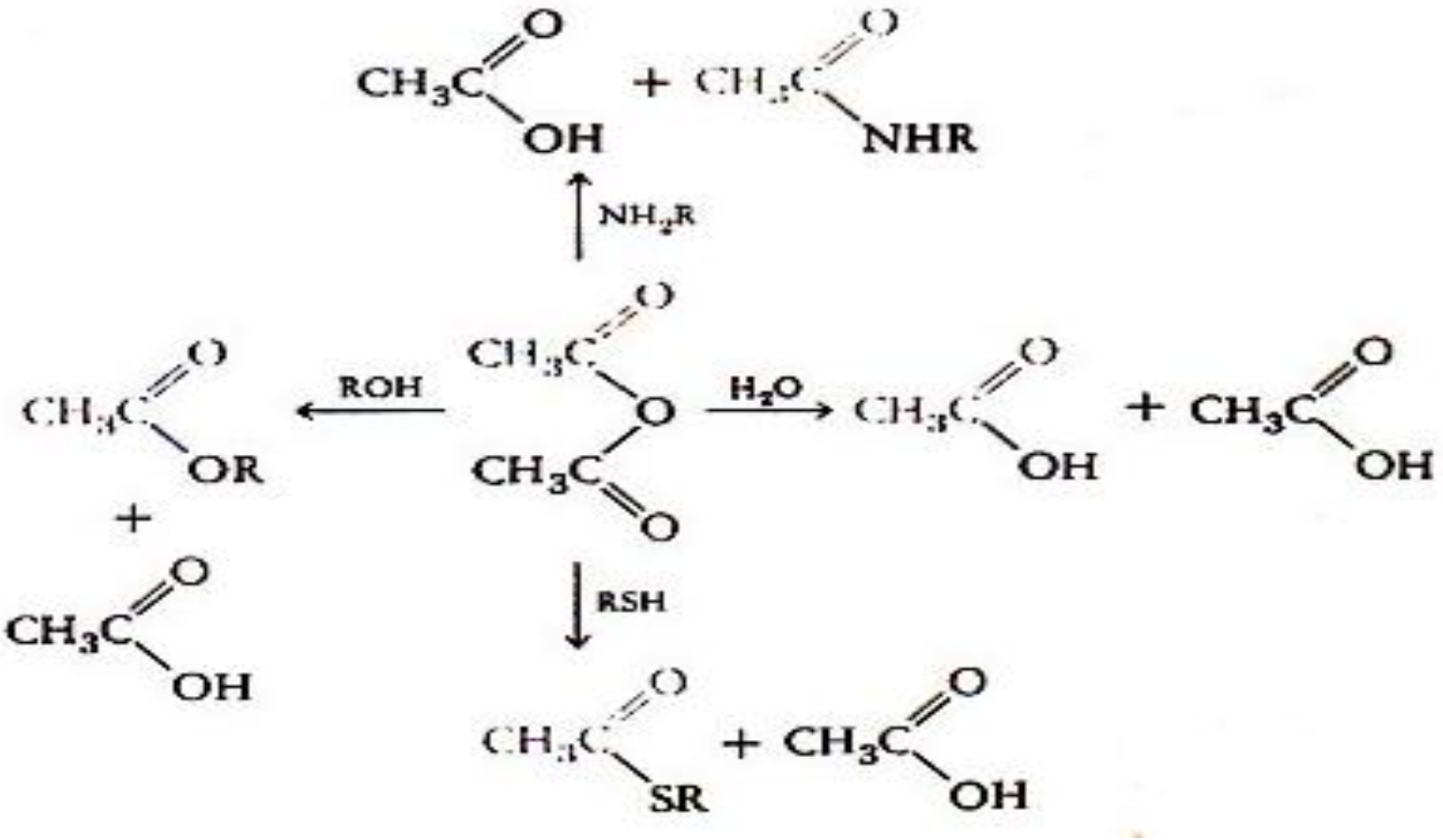
Benzoic anhydride

Anhydride react with water,amines,alcohols, and thiols.All of these reactions involve

substituting an –OH , -NHR, -OR, or –SR

group for the  group,

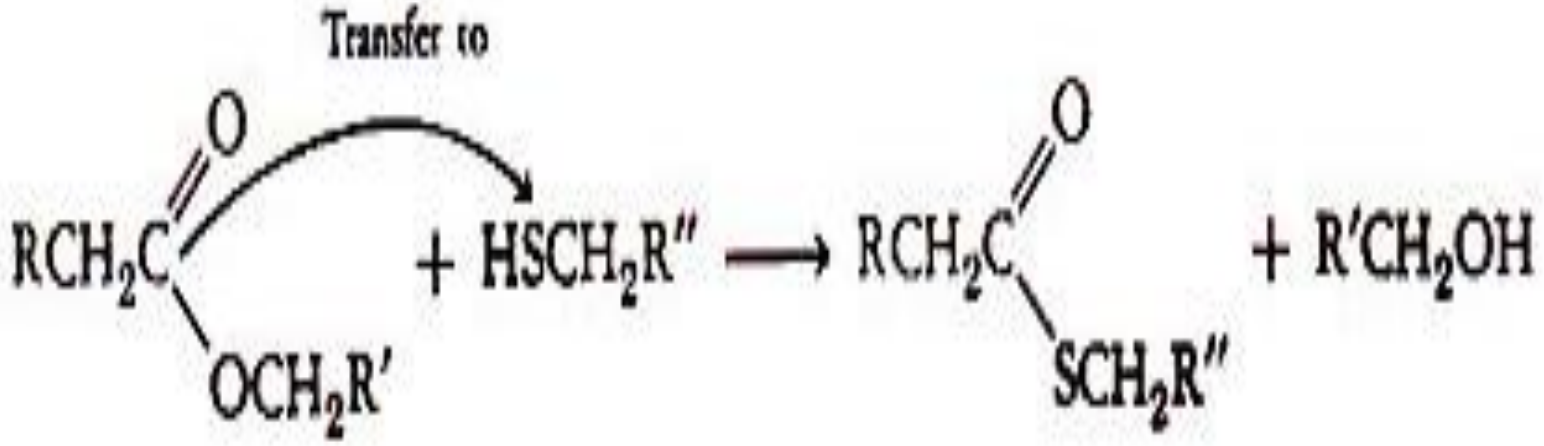
As shown by the following reactions :



*most of the reactions of carboxylic acids and their derivatives are substitution reaction.

Acyl Transfer Reactions

Many of the **substitution reactions** of carboxylic acids and their derivatives in living systems are called **acyl transfer reaction**. The following is the general equation:



In most carboxylic acid derivatives in living systems, the group bonded to the carbonyl carbon is much larger and more complex than the acyl group. A typical example is the reaction of acetyl coenzyme A with an acyl carrier protein (ACP). The equation for this reaction is as follows: