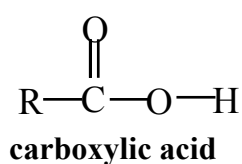
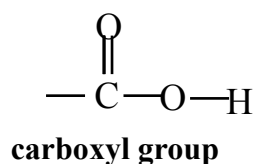


Chapter 12 Carboxylic Acids

Introduction

The combination of a carbonyl group and a hydroxyl on the same carbon atom is called a carboxyl group. Compounds containing the carboxyl group are distinctly acidic and are called carboxylic acids. The carboxyl group is one of the most widely occurring functional groups in chemistry and biochemistry. Not only are carboxylic acids themselves important, but the carboxyl group is the parent group of a large family of related compounds called carboxylic acid derivatives.



12.1. Classification and Nomenclature of carboxylic acids.

12.1.1 Classification of carboxylic acids.

Carboxylic acids are classified according to the substituent bonded to the carboxyl group. An aliphatic acid has an alkyl group bonded to the carboxyl group, while an aromatic acid has an aryl group. The simplest acid is formic acid, with a proton bonded to the carboxyl group. Fatty acids are long-chain aliphatic acids derived from the hydrolysis of fats and oils.

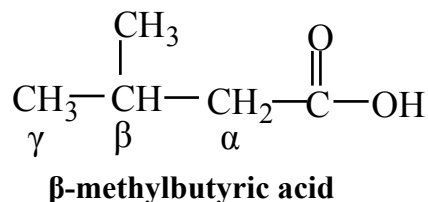
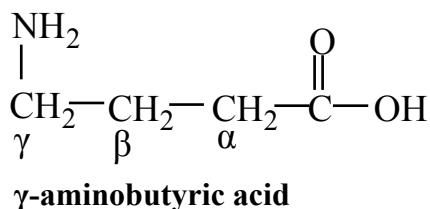
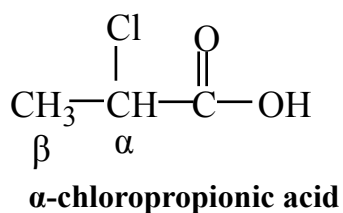
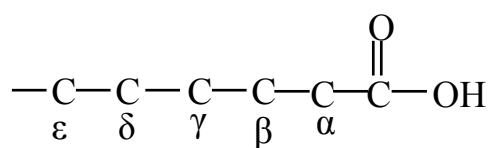
12.1.2 Nomenclature of carboxylic acids.

1. Common Names

Several aliphatic carboxylic acids have been known for hundreds of years, and their common names reflect their historical sources. *Formic acid* was extracted from ants: *formica* in Latin. Acetic acid was isolated from vinegar, called acetum (“sour”) in Latin. Propionic acid was considered to be the first fatty acid, and the name is derived from the Greek protos pion (“first fat”). Butyric acid results from the oxidation of

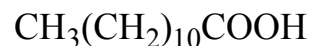
butyl aldehyde, which is found in butter: butyrum in Latin. Caproic($\text{CH}_3(\text{CH}_2)_4\text{COOH}$), caprylic($\text{CH}_3(\text{CH}_2)_6\text{COOH}$), and capric acids ($\text{CH}_3(\text{CH}_2)_8\text{COOH}$) are found in the skin secretions of goats: caper in Latin.

In common names, the positions of substituents are named using Greek letters. Notice that the lettering begins with the carbon atom adjacent to the carboxyl carbon, the α -carbon. With common names, the prefix *iso-* is sometimes used for acids ending in the $-\text{CH}(\text{CH}_3)_2$ grouping.



2. IUPAC Names:

The IUPAC nomenclature for carboxylic acids are obtained by dropping the final *-e* of the name of the alkane corresponding to the longest chain in the acid and by adding *-oic acid* uses the name of the alkane that corresponds to the longest continuous chain of carbon atoms. The carboxyl carbon atom is assigned number 1. The examples as follows:



IUPAC name: methanoic acid

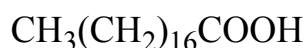
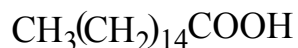
ethanoic acid

dodecanoic acid

Common name: formic acid

acetic acid

lauric acid

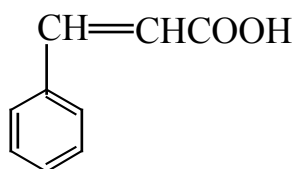


IUPAC name: hexadecanoic acid

octadecanoic acid

Common name: palmitic acid

stearic acid

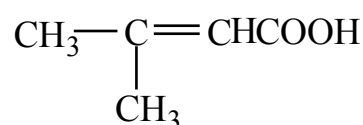
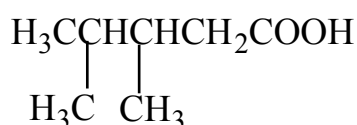


IUPAC name: 3-phenyl-2-propenoic acid

butanoic acid

Common name: cinnamic acid

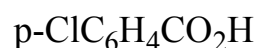
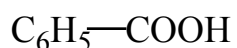
butyric



IUPAC name: 3, 4-dimethylpentanoic acid

3-methyl-2-butenoic acid

Aromatic acids of the form Ar-COOH are named as derivatives of benzoic acid.



Benzoic acid

4-methylbenzoic acid

4-chlorobenzoic acid

Benzoic acid

p-toluic acid

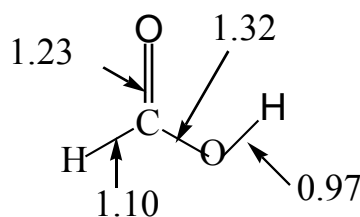
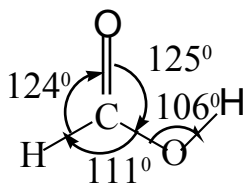
p-chlorobenzoic acid

Nomenclature of Dicarboxylic Acids

A dicarboxylic acid (also called a *diacid*) is a compound with two carboxyl groups. The common names of simple dicarboxylic acids are used more frequently than their systematic names.

12.2 Structure of Carboxyl Group

The structure of the most stable conformation of formic acid is shown below. The entire molecule is approximately planar. The sp^2 hybrid carbonyl carbon atom is planar, with nearly trigonal bond angles. The O-H bond also lies in this plane, eclipsed with the C=O bond.

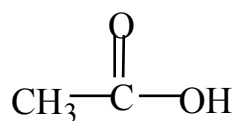


12.3 Physical Properties and Spectroscopy of Carboxylic Acids

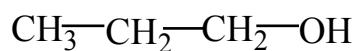
12.3.1 Physical Properties of Carboxylic Acids

1. Boiling Points

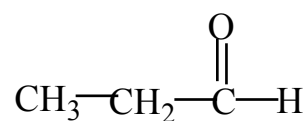
Carboxylic acids boil at considerably higher temperatures than do alcohols, ketones, or aldehydes of similar molecular weights. For example, acetic acid (MW 60) boils at 118 °C, 1-propanol (MW 60) boils at 97 °C, and propionaldehyde (MW 58) boils at 49 °C.



acetic acid, bp 118

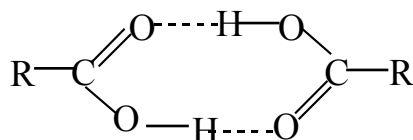


1-propanol, bp 97



propanal, bp 49

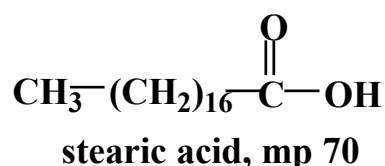
The high boiling points of carboxylic acids result from formation of a stable, hydrogen-bonded dimer. A dimer contains an eight-membered ring joined by two hydrogen bonds, effectively doubling the molecular weight of the molecules leaving the liquid phase.

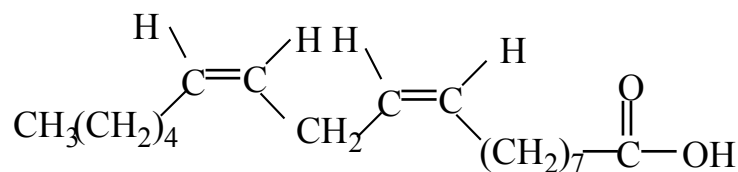


hydrogen-bonded acid dimer

2. Melting Points

Acids containing more than eight carbon atoms are generally solids, unless they contain double bonds. The presence of double bonds (especially cis double bonds) in a long chain impedes formation of a stable crystal lattice, resulting in a lower melting point. For example, both stearic acid (octadecanoic acid) and linoleic acid (cis,cis-9,12-octadecadienoic acid) have 18 carbon atoms, but stearic acid melts at 70 °C and linoleic acid melts at -5 °C.





linoleic acid, mp -5

The melting points of dicarboxylic acids are relatively high. With two carboxyl groups per molecule, the forces of hydrogen bonding are particularly strong in diacids; a high temperature is required to break the lattice of hydrogen bonds in the crystal and melt the diacid.

3. Solubilities

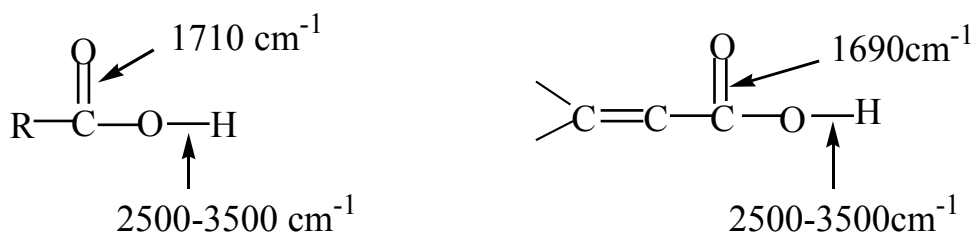
Carboxylic acids form hydrogen bonds with water, and the lower molecular-weight carboxylic acids (up through four carbon atoms) are miscible with water. As the length of the hydrocarbon chain increases, water solubility decreases until acids with more than 10 carbon atoms are essentially insoluble in water.

Carboxylic acids are very soluble in alcohols because acids form hydrogen bonds with alcohols. Also, alcohols are not as polar as water, so the longer-chain acids are more soluble in alcohols than they are in water. Most carboxylic acids are quite soluble in relatively nonpolar solvents such as chloroform because the acid continues to exist in its dimeric form in the nonpolar solvent. Thus, the hydrogen bonds of the cyclic dimer are not disrupted when the acid dissolves in a nonpolar solvent.

12.3.2 Spectroscopy of Carboxylic Acids

1. Infrared Spectroscopy

The most obvious feature in the infrared spectrum of a carboxylic acid is the intense carbonyl stretching absorption. In a saturated acid, this vibration occurs around 1710 cm^{-1} , often broadened by hydrogen bonding involving the carbonyl group. In conjugated acids, the carbonyl stretching frequency is lowered to about 1690 cm^{-1} .

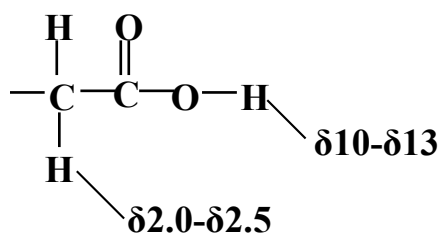


The O—H stretching vibration of a carboxylic acid absorbs in a broad band around 2500-3500 cm^{-1} . This frequency range is lower than the hydroxyl stretching frequencies of water and alcohols, whose O—H groups absorb in a band centered around 3300 cm^{-1} . In the spectrum of a carboxylic acid, the broad hydroxyl band appears right on top of the C—H stretching region. This overlapping of absorptions give the 3000 cm^{-1} region a characteristic appearance of a broad peak (the O—H stretching) with sharp peaks (C—H stretching) superimposed on it.

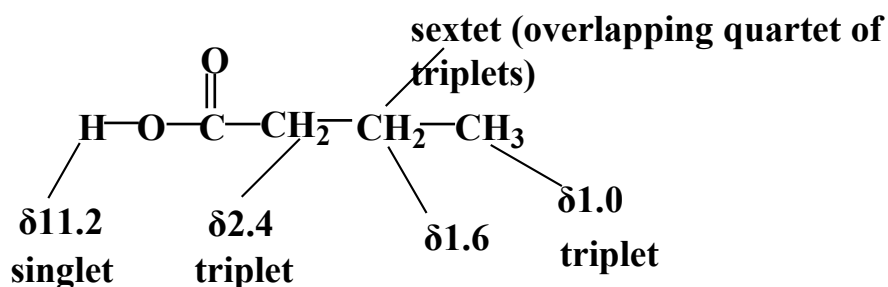
Notice the shift in the position of the carbonyl absorptions, and notice that the conjugated, unsaturated acid has a fairly strong C=C stretching absorption around 1630 cm^{-1} , just to the right of the carbonyl absorption.

2. NMR Spectroscopy

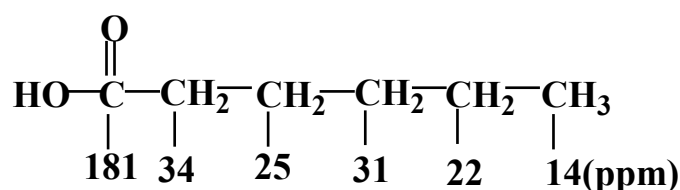
Carboxylic acid protons are the most deshielded protons we have encountered, absorbing between $\delta 10$ and $\delta 13$. Depending on the solvent and the concentration, this acid proton peak may be sharp or broad, but it is always unsplit because of proton exchanges.



The protons on the α -carbon atom absorb between $\delta 2.0$ and $\delta 2.5$, in about the same position as the protons on a carbon atom alpha to a ketone or an aldehyde.



The carbon NMR chemical shifts of carboxylic acids resemble those of ketones and aldehyde. The carbonyl carbon atom absorbs around 180 ppm, and the α -carbon atom absorbs around 30 to 40 ppm. The chemical shifts of the carbon atoms in hexanoic acid are the following:

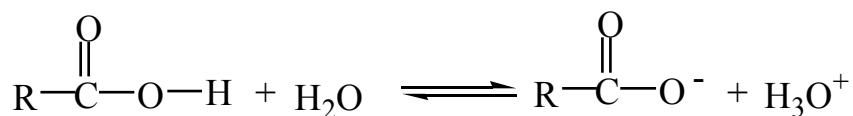


12.4 Chemical Properties of Carboxylic Acids

12.4.1 Acidity of Carboxylic Acids

1. Measurement of Acidity

A carboxylic acid may dissociate in water to give a proton and a carboxylate ion. The equilibrium constant K_a for this reaction is called the *acid-dissociation constant*. The $\text{p}K_a$ of an acid is the negative logarithm of K_a , and we commonly use $\text{p}K_a$ as an indication of the relative acidities of different acids.



$$K_a = \frac{[\text{RCO}_2^-][\text{H}_3\text{O}^+]}{[\text{RCO}_2\text{H}]} \qquad \text{p}K_a = -\log_{10}K_a$$

Values of $\text{p}K_a$ are about 5 ($K_a=10^{-5}$) for simple carboxylic acids. For example, acetic acid has a $\text{p}K_a$ of 4.7 ($K_a=1.8 \times 10^{-5}$). Although carboxylic acids are not as strong as most mineral acids, they are still much more acidic than other functional groups we have studied. For example, alcohols have $\text{p}K_a$ values in the range 16 to 18. Acetic

acid ($\text{pK}_a=4.74$) is about 10^{11} times as acidic as the most acidic alcohols! In fact, concentrated acetic acid causes acid burns when it comes into contact with the skin.

Dissociation of either an acid or an alcohol involves breaking an O-H bond, but dissociation of a carboxylic acid gives a carboxylate ion with the negative charge spread out equally over two oxygen atoms, compared with just one oxygen atom in an alkoxide ion. The delocalized charge makes the carboxylate ion more stable than the alkoxide ion; therefore, dissociation of a carboxylic acid to a carboxylate ion is less endothermic than dissociation of an alcohol to an alkoxide ion.

The carboxylate ion can be visualized either as a resonance hybrid or as a conjugated system of three p orbitals containing four electrons. The carbon atom and the two oxygen atoms are sp^2 hybridized, and each has an unhybridized p orbital. Overlap of these three p orbitals gives a three-center π molecular orbital system. There is half a π bond between the carbon and each oxygen atom, and there is half a negative charge on each oxygen atom.

Diacid has two dissociation constants: K_{a1} is for the first dissociation, and K_{a2} is for the second dissociation, to give a dianion. The second carboxyl group is always less acidic than the first because extra energy is required to create a second negative charge close to another, mutually repulsive, negative charge.

2. Substituent Effects on Acidity

A substituent that stabilizes the negatively charged carboxylate ion enhances dissociation and results in a stronger acid. Electronegative atoms enhance the strength of an acid in this manner. This inductive effect can be quite large if one or more strongly electron-withdrawing groups are present on the α -carbon atom. For example, chloroacetic acid (ClCH_2COOH) has a pK_a of 2.86, indicating that it is stronger acid than acetic acid ($\text{pK}_a=4.74$). Dichloroacetic acid ($\text{Cl}_2\text{CH—COOH}$) is stronger yet, with a pK_a of 1.26. Trichloroacetic acid ($\text{Cl}_3\text{C—COOH}$) has a pK_a of 0.64, comparable in strength to some mineral acids.

The magnitude of a substituent effect depends on its distance from the carboxyl group. Substituents on the α -carbon atom are most effective in increasing acid

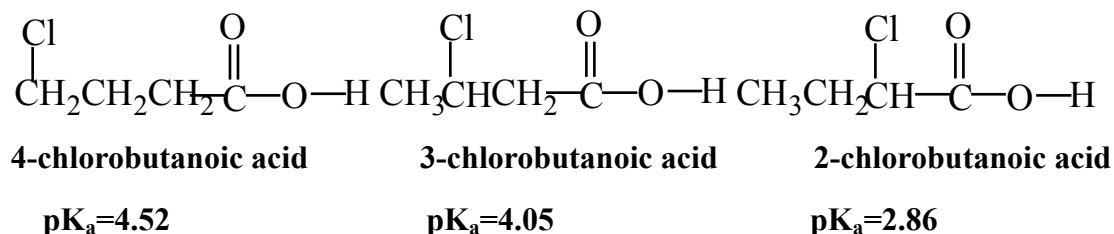
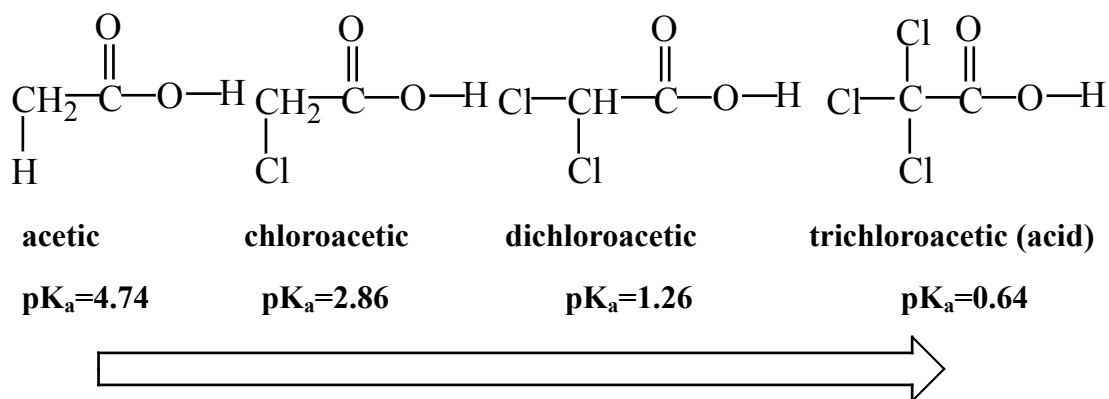
strength. More distant substituents have smaller effects on acidity, showing that inductive effects decrease rapidly with distance.

electronic effect:

-I effect:



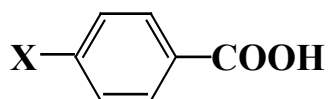
X=	F	Cl	Br	I	CHO	NO ₂	N ⁺ (CH ₃) ₃
pK _a	2.66	2.86	2.90	3.18	3.53	1.68	1.83



+I effect:

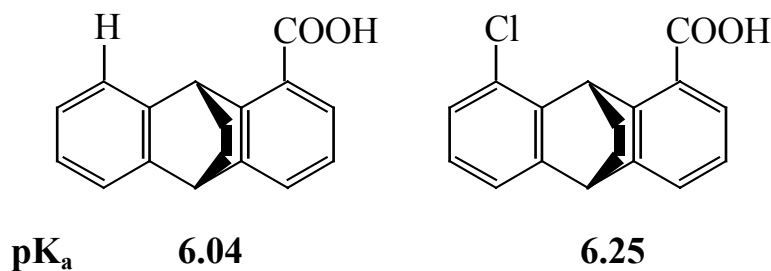
	HCOOH	CH ₃ COOH	(CH ₃) ₂ CHCOOH	(CH ₃) ₃ CCOOH
pK _a	3.75	4.76	4.86	5.05

Conjugate effect:

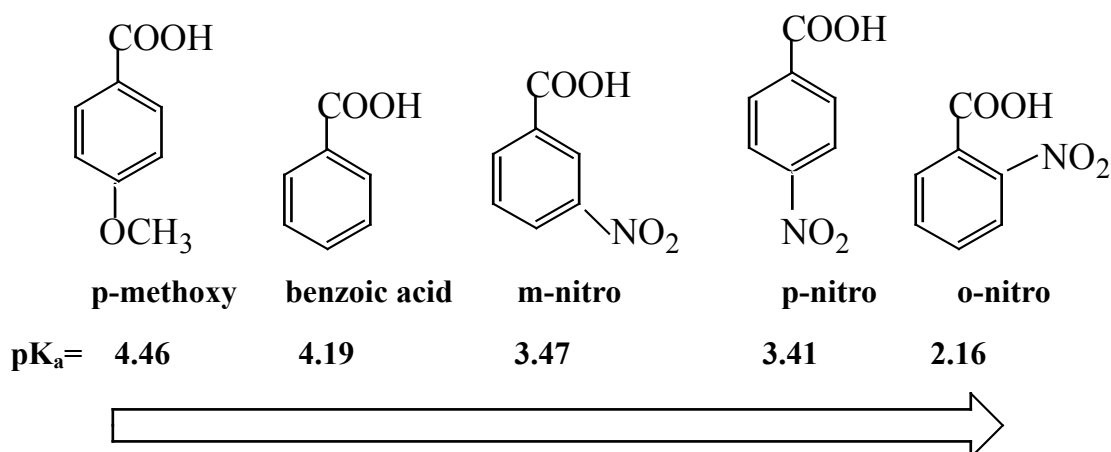


X=	OH	OCH ₃	CH ₃	H	Cl	NO ₂
pK _a	4.57	4.47	4.38	4.20	3.97	3.42

Field effect:



Substituted benzoic acids show similar trends in acidity, with electron-withdrawing groups enhancing the acid strength and electron-donating groups decreasing the acid strength. These effects are strongest for substituents in the ortho and para positions. In the examples shown below, notice that a nitro substituent (electron-withdrawing) increases the strength of the acid, while a methoxyl substituent (electron-donating) decreases the acid strength. The nitro group has a larger effect in the ortho and para positions than in the meta position.

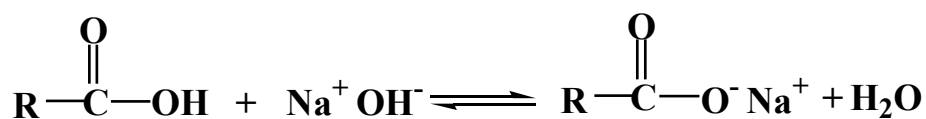


12.4.2 Main Reactions

1. Salts of carboxylic acids

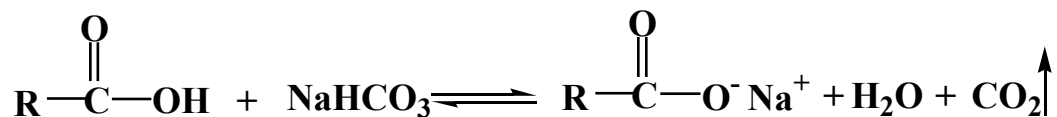
Strong base can completely deprotonate a carboxylic acid. The products are a carboxylate ion, the cation remaining from the base, and water. The combination of a carboxylate ion and a cation is a salt of a carboxylic acid.

For example:



Salt formation can be used to identify and purify acids. Carboxylic acids are deprotonated by the weak base sodium bicarbonate, forming the sodium salt of the

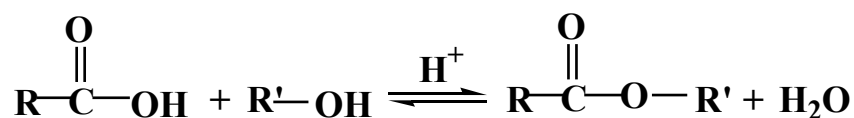
acid, carbon dioxide, and water. An unknown compound that is insoluble in water, but dissolves in a sodium bicarbonate solution with a release of bubbles of carbon dioxide, is almost certainly a carboxylic acid.



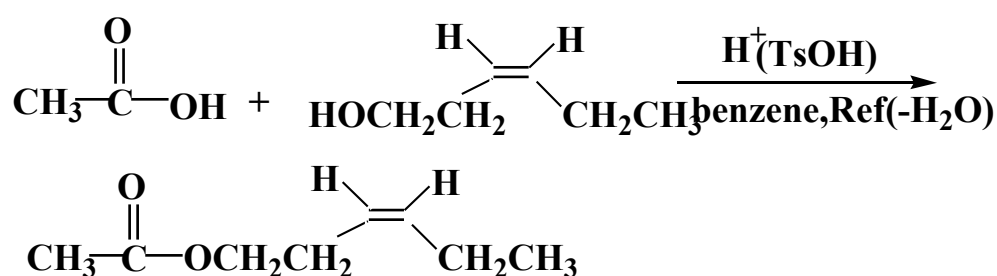
2. Esterification (Condensation of acids with alcohols)

The Fischer esterification converts carboxylic acids and alcohols directly to esters by an acid-catalyzed nucleophilic acyl substitution. The net reaction is replacement of the acid -OH group by the -OR group of the alcohol.

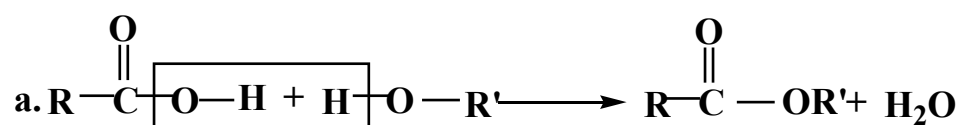
General Reaction:

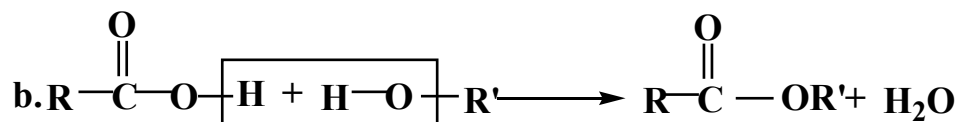


Special Examples:

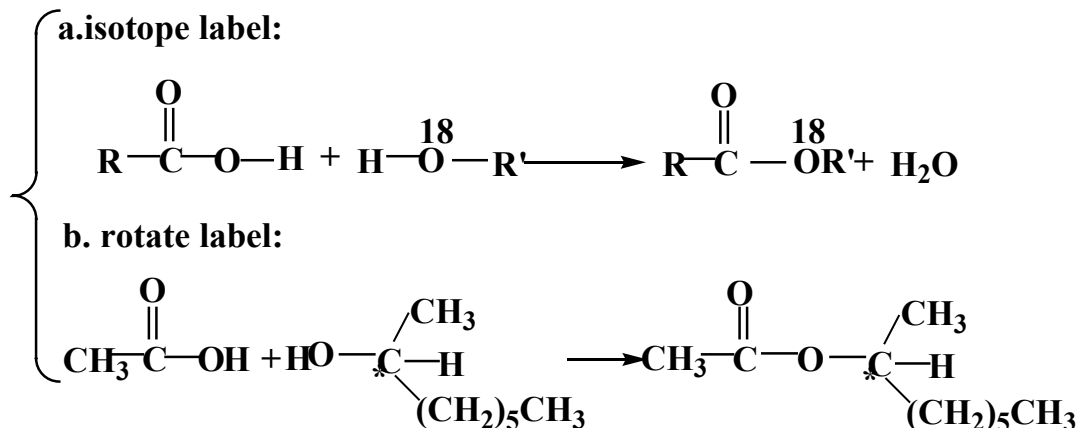


There are two possible ways to form ester:





Experiment:

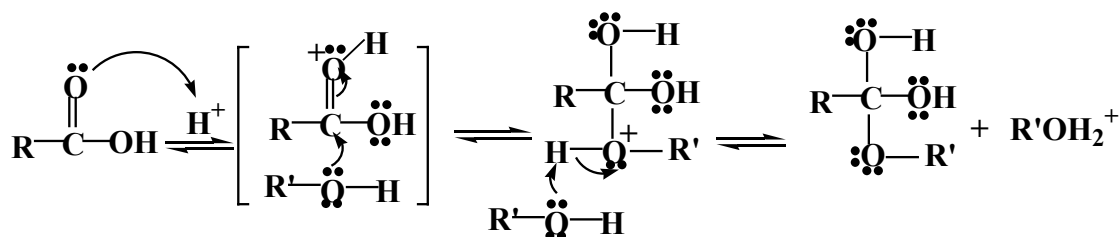


When benzoic acid reacts with methanol that has been labeled with ^{18}O , the labeled oxygen appears in the ester. This result reveals just which bonds break in the esterification (a).

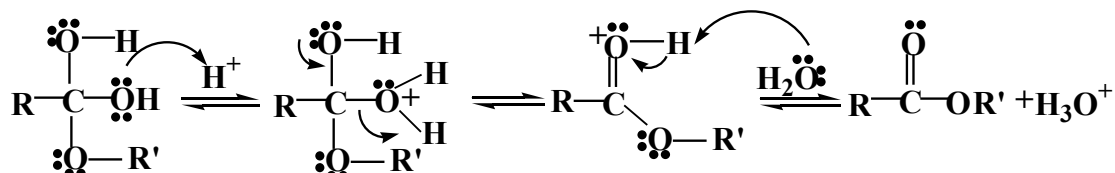
The esterification mechanism is an acid-catalyzed nucleophilic acyl substitution. The carbonyl group of a carboxylic acid is not sufficiently electrophilic to be attacked by an alcohol. The acid catalyst protonates the carbonyl group and activates it toward nucleophilic attack. Loss of a proton gives the hydrate of an ester. Loss of water from the hydrate of the ester occurs by the same mechanism as loss of water from the hydrate of a ketone. Protonation of either one of the hydroxyl groups allows it to leave as water, forming a resonance-stabilized cation. Loss of a proton from the second hydroxyl group gives the ester.

The mechanism of the esterification may seem long and complicated at first, but it is simplified by breaking it down into two stages: (1) acid-catalyzed addition of the alcohol to the carbonyl and (2) acid-catalyzed dehydration.

(1) Acid-catalyzed addition of the alcohol to the carbonyl.

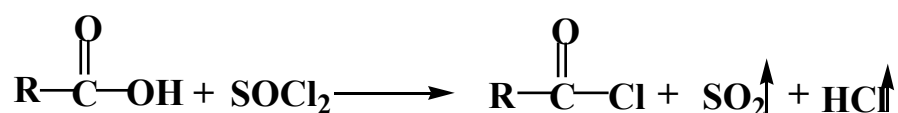
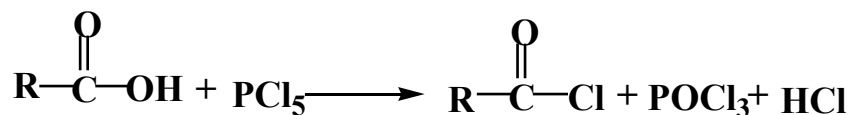
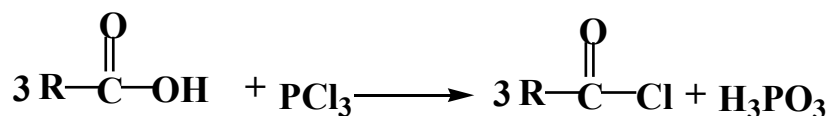


(2) Acid-catalyzed dehydration.



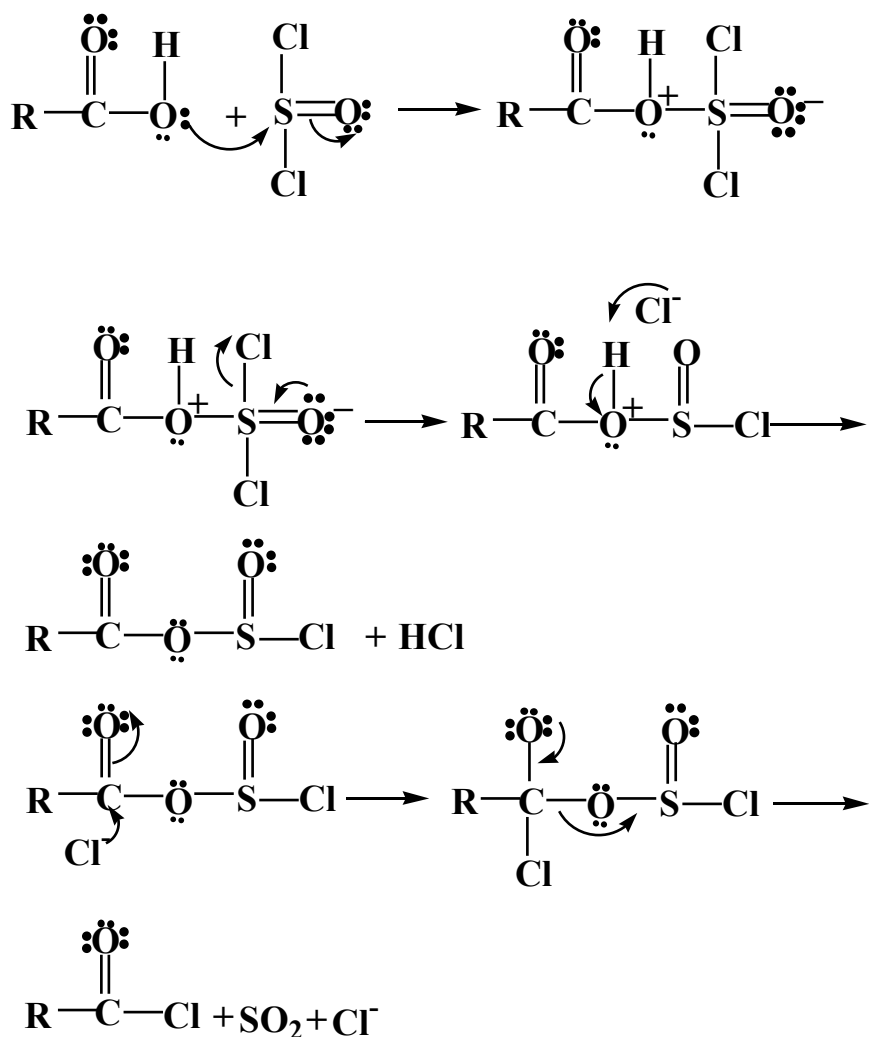
3. Synthesis of Acyl Chlorides

We use PCl_5 (an acid chloride of phosphoric acid), PCl_3 (an acid chloride of phosphorous acid), and SOCl_2 (an acid chloride of sulfurous acid). All of these reagents react with carboxylic acids to give acyl chlorides in good yields:



The best reagents for converting carboxylic acids to acyl chlorides are thionyl chloride (SOCl_2) and oxalyl chloride (COCl_2) because they form gaseous by-products that do not contaminate the product. Oxalyl chloride is particularly easy to use because it boils at 62°C and any excess is easily evaporated from the reaction mixture.

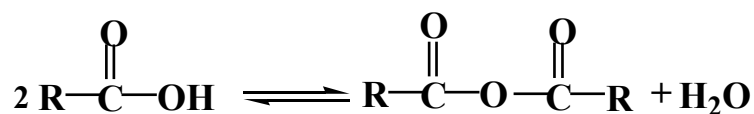
The mechanisms of the reaction begin like the reaction of an alcohol with thionyl chloride. Either oxygen atom of the acid can attack sulfur, replacing chloride by a mechanism that looks like sulfur's version of nucleophilic acyl substitution. The product is an interesting, reactive chlorosulfite anhydride. This reactive anhydride undergoes nucleophilic acyl substitution by chloride ion to give the acid chloride.



In particular, acid chlorides (acyl chlorides) are easily made and are commonly used as an activated form of a carboxylic acid. Both the carbonyl oxygen and the chlorine atom withdraw electron density from the acyl carbon atom, making it is strongly electrophilic. Acid chlorides react with a wide range of nucleophiles, generally through the addition-elimination mechanism of nucleophilic acyl substitution.

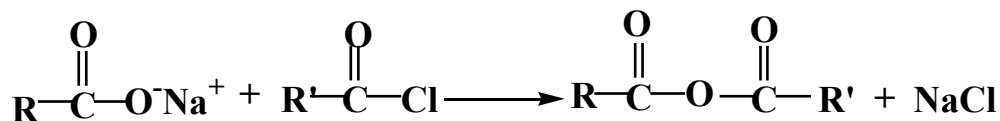
4. Synthesis of Anhydrides

Two carboxylic acid molecules react in the presence of phosphorous pentoxide to give carboxylic acid anhydrides:



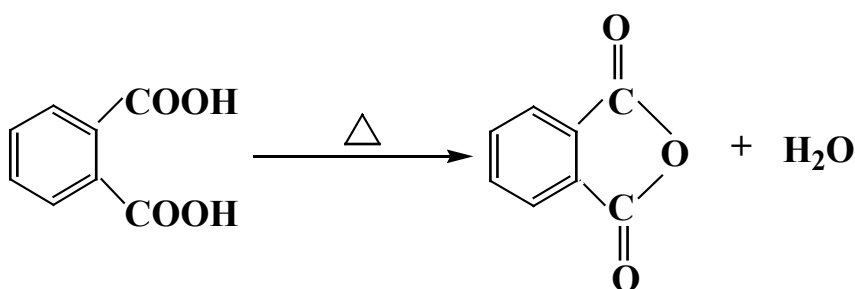
The best method of preparing acid anhydrides is by a nucleophilic acyl substitution

reaction of an acid chloride with a carboxylic acid anion. Both symmetrical and unsymmetrical acid anhydrides can be prepared in this way.



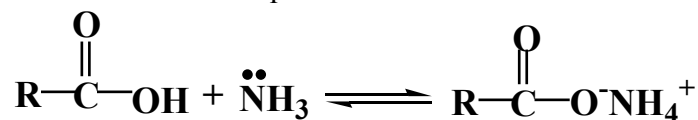
In the reaction a carboxylate anion acts as a nucleophile and brings about a nucleophilic substitution reaction at the acyl carbon of the acyl chloride.

Cyclic anhydrides can sometimes be prepared simply by heating the appropriate decarboxylic acid. This method succeeds, however, only when anhydride formation leads to a five- or six-membered ring:



5. Synthesis of Acyl Amides

Carboxylic acids react with aqueous ammonia to form ammonium salts:



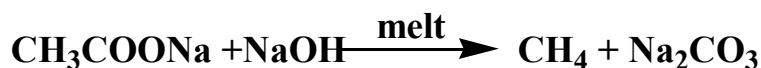
Because of the low reactivity of the carboxylate ion toward nucleophilic addition-elimination, further reaction does not usually take place in aqueous solution. However, if we evaporate the water and subsequently heat the dry salt, dehydration produces an amide:



6. Decarboxylation of Carboxylic Acids

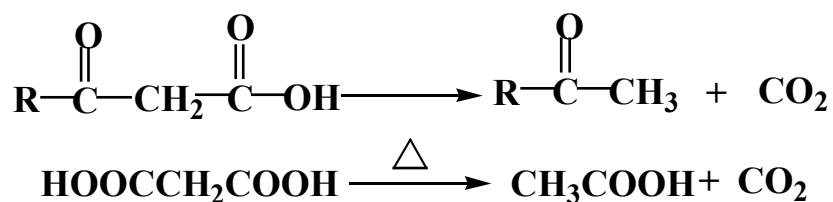
The reaction whereby a carboxylic acid loses CO₂ is called a decarboxylation:





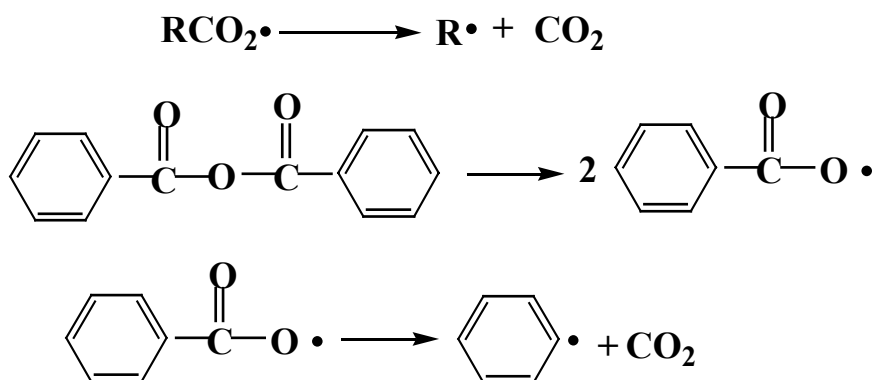
Although the unusual stability of carbon dioxide means that decarboxylation of most acids is exothermic, in practice the reaction is not always easy to carry out because the reaction is very slow. Special groups usually have to be present in the molecule for decarboxylation to be rapid enough to be synthetically useful.

Acids whose molecules have a carbonyl group one carbon removed from the carboxylic acid group, called β -keto acids, decarboxylate readily when they are heated to 100-150 °C. Some β -keto acids even decarboxylate slowly at room temperature.

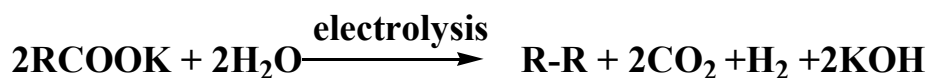


Decarboxylation of Carboxyl Radicals

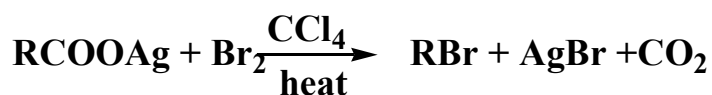
Although the carboxylate ions (RCO_2^-) of simple aliphatic acids do not decarboxylate readily, carboxyl radicals ($\text{RCO}_2\cdot$) do. They decarboxylate by losing CO_2 and producing alkyl radicals:



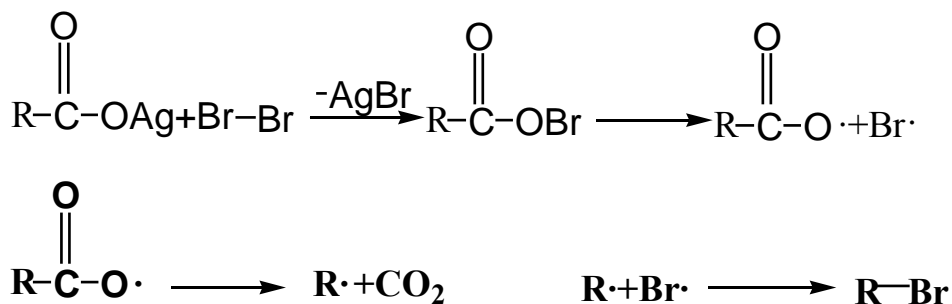
(1) Kolbe electrolysis:



(2) Hunsdiecker reaction:

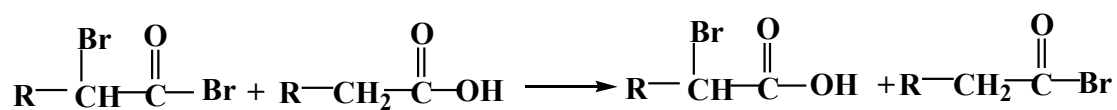
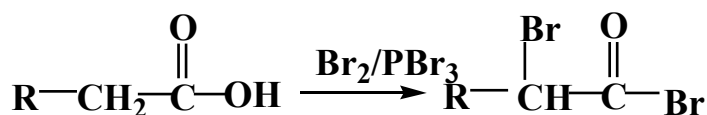


Mechanism:



7. α -H Substituent by Halogen

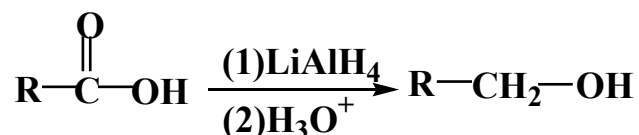
The reaction replaces a hydrogen atom with a bromine atom on the α -carbon of a carboxylic acid. The carboxylic acid is treated with bromine and phosphorous tribromide, followed by water to hydrolyze the intermediate α -bromoacyl bromide.



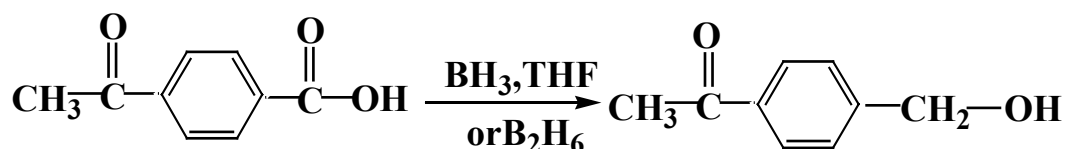
8. Reduction of Carboxylic Acids

(1). Reduction to alcohols

Lithium aluminum hydride (LiAlH_4 or LAH) reduces carboxylic acids to primary alcohols. The aldehyde is an intermediate in this reduction, but it cannot be isolated because it is reduced more easily than the original acid.



Borane also reduces carboxylic acids to primary alcohols. Borne (complex with THF) reacts with the carboxyl group faster than with any other carbonyl function. It often gives excellent selectivity, as shown by the following example, where a carboxylic acid is reduced while a ketone is unaffected. (LiAlH₄ would also reduce the ketone.)

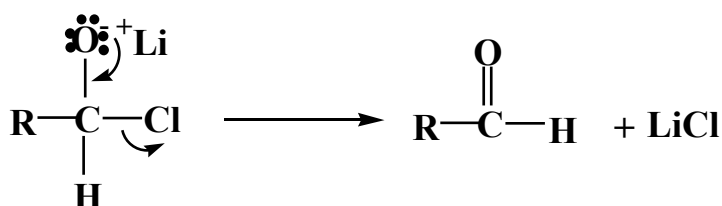
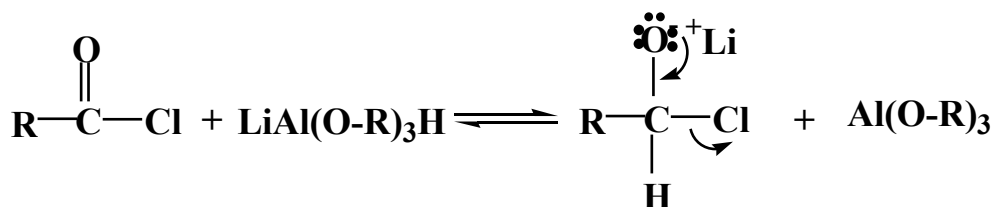


(2). Reduction to Aldehydes

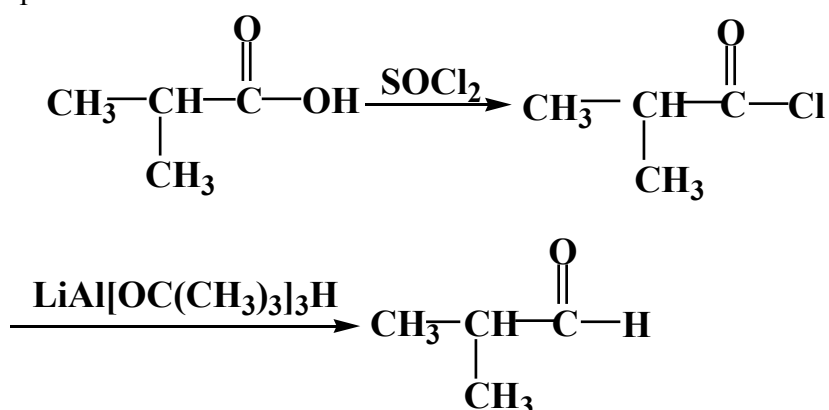
Reduction of carboxylic acids to aldehydes is difficult because aldehydes are more reactive than carboxylic acids toward most reducing agents. Almost any reagent that reduces acids to aldehydes also reduce aldehydes to primary alcohols. What is needed is a derivative of the acids that is more reactive than the aldehyde. As you might guess, the reactive acid derivative is the acid chloride.

Lithium aluminum tri(*t*-butoxy), LiAl[OC(CH₃)₃]₃H, is a weaker reducing agent than lithium hydride. It reduces acid chlorides because they are strongly activated toward nucleophilic addition of a hydride ion. Under these conditions, the aldehyde reduces more slowly and is easily isolated.

Example 1:



Example 2:



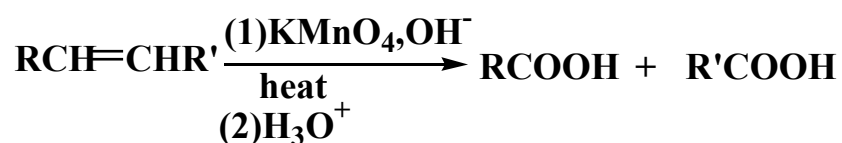
Li-methylamine also can reduce carboxylic acids. For example:



12.5. Preparation of carboxylic acids.

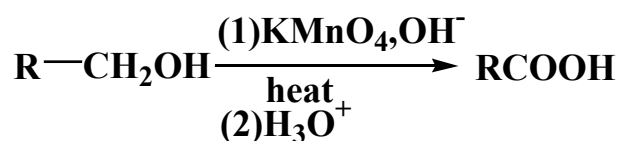
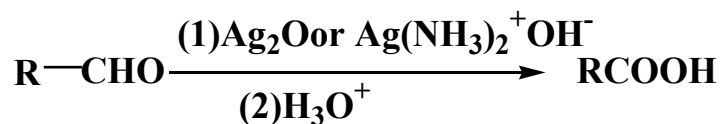
1. Oxidation of alkenes

Alkenes can be oxidized to carboxylic acids with hot alkaline KMnO_4 :



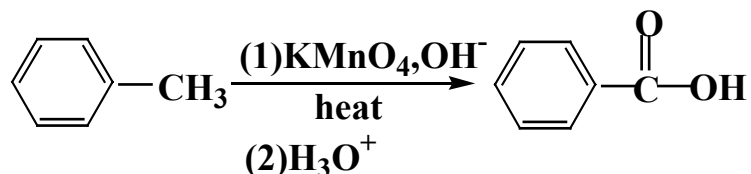
2. Oxidation of aldehydes and primary alcohols

Aldehydes can be oxidized to carboxylic acids with mild oxidizing agents such as $\text{Ag}(\text{NH}_3)_2\text{OH}^-$. Primary alcohols can be oxidized with KMnO_4 . Aldehydes and primary alcohols are oxidized to carboxylic acids with chromic acid (H_2CrO_4) in aqueous acetone .



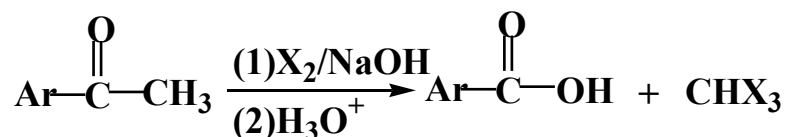
3. Oxidation of alkylbenzenes

Primary and secondary alkyl groups (but not 3° groups) directly attached to a benzene ring are oxidized by KMnO_4 to a $-\text{COOH}$ group.



4. Oxidation of methyl ketones

Methyl ketones can be converted to carboxylic acids via the haloform reaction.



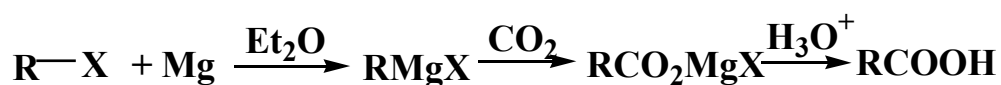
5. Hydrolysis of cyanogen

In the hydrolysis the $-\text{CN}$ group is converted to a $-\text{CO}_2\text{H}$ group.

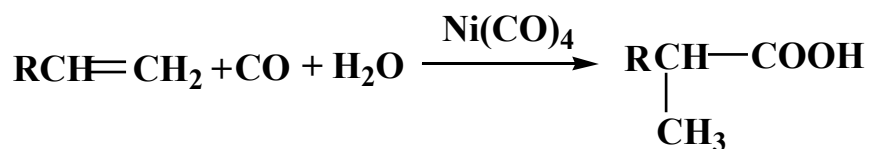


6. Carbonation of Grignard reagents

Grignard reagents react with carbon dioxide to yield magnesium carboxylates. Acidification produces carboxylic acids:



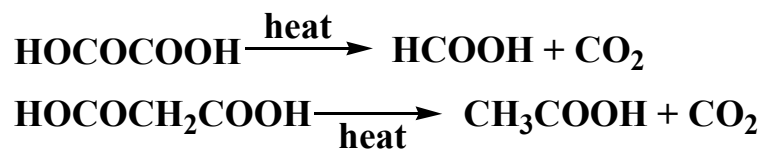
7. Reppe reaction



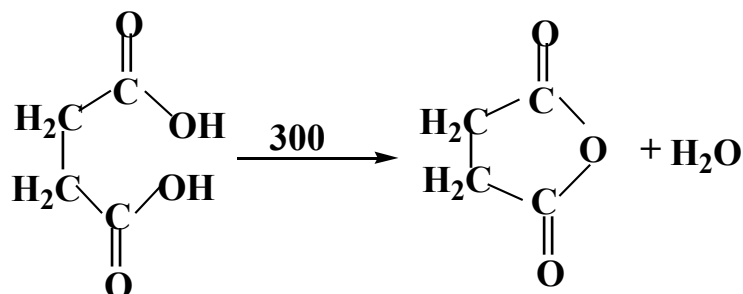
12.6 Important Carboxylic acids (self-study)

12.7 Dicarboxylic acids

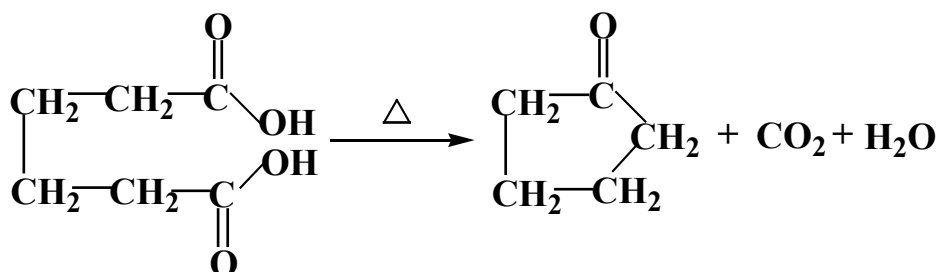
1. decarboxylation



2. Dehydration



3. Decarboxylation and dehydration



Some cyclic anhydrides and ketones are made simply by heating the corresponding diacid. Because five- and six-membered cyclic anhydrides and ketones are particularly stable.

12.8 Substituted Carboxylic acids

12.8.1. Hydroxyl-acid

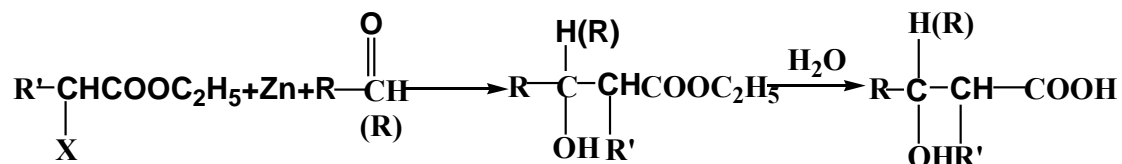
1. Preparation:

(1) Hydrolysis of halocarboxylic acid

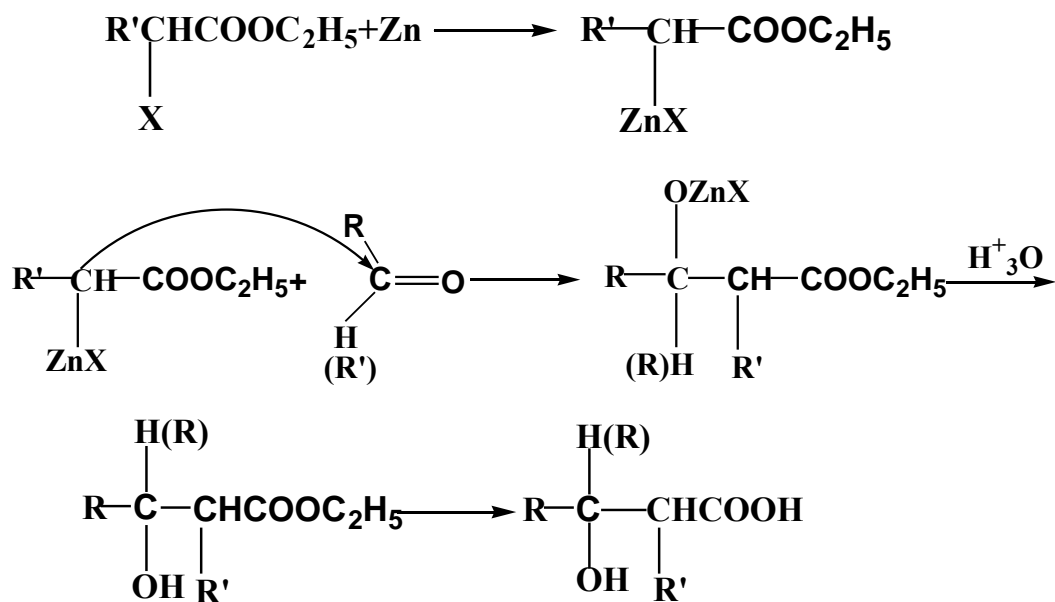


(2) Hydrolysis of cyanohydrins

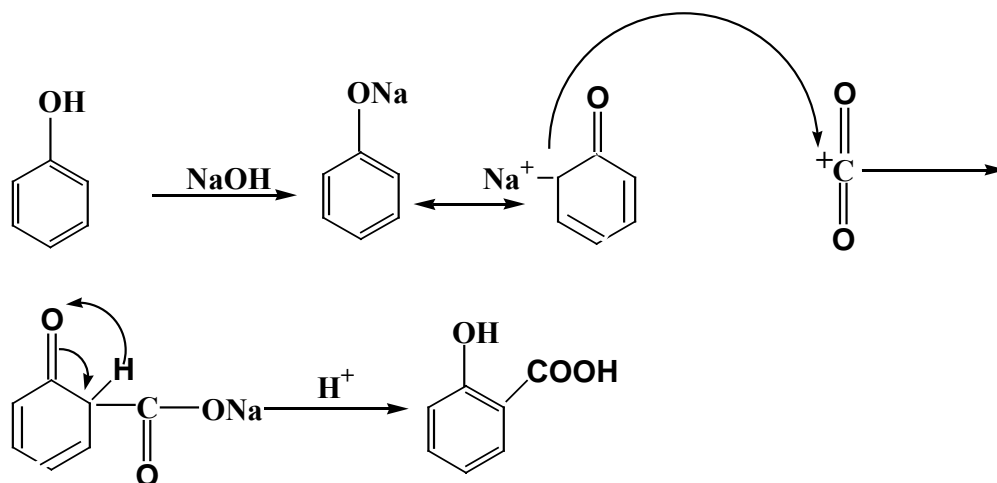
(3) Reformatsky reaction



Mechanism:



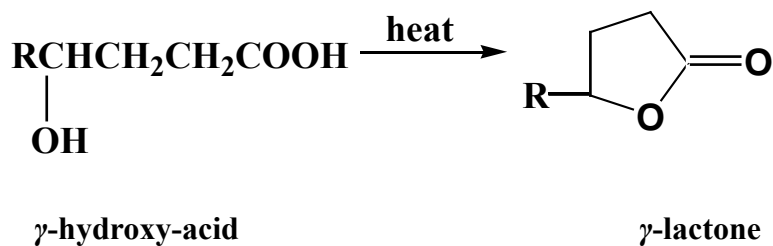
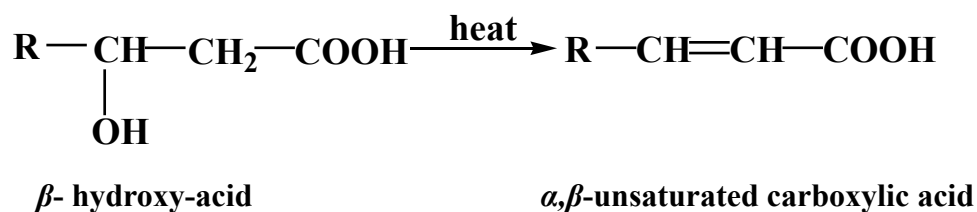
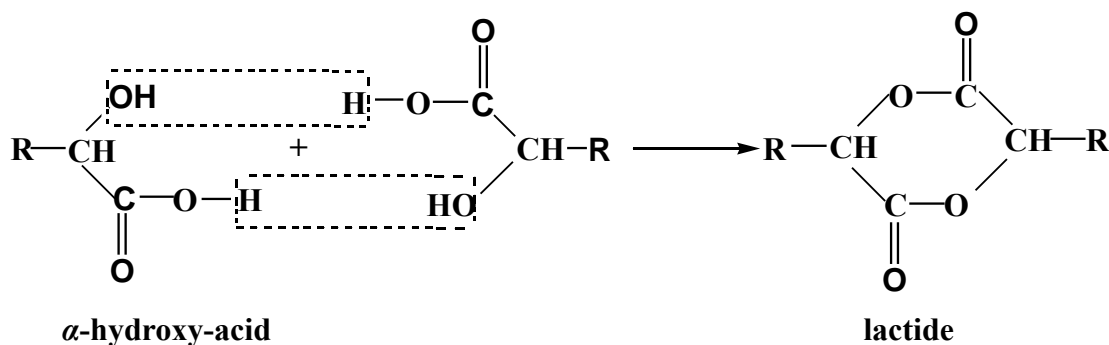
(4) Kolbe reaction to synthesis of salicylic acid



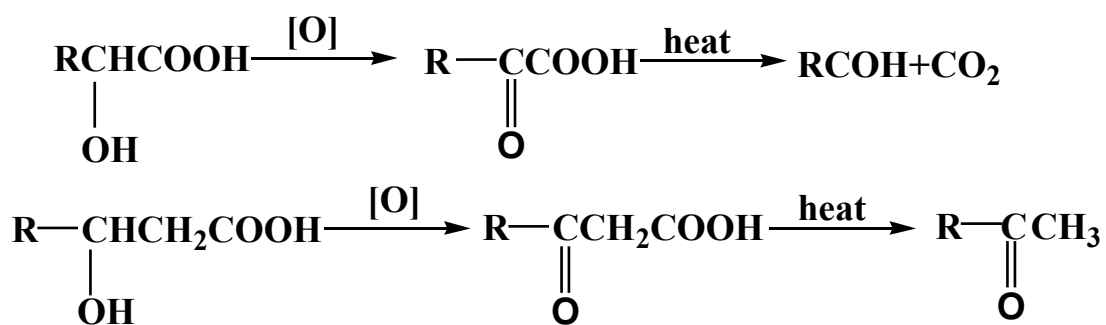
2. Properties

(1). Dehydration

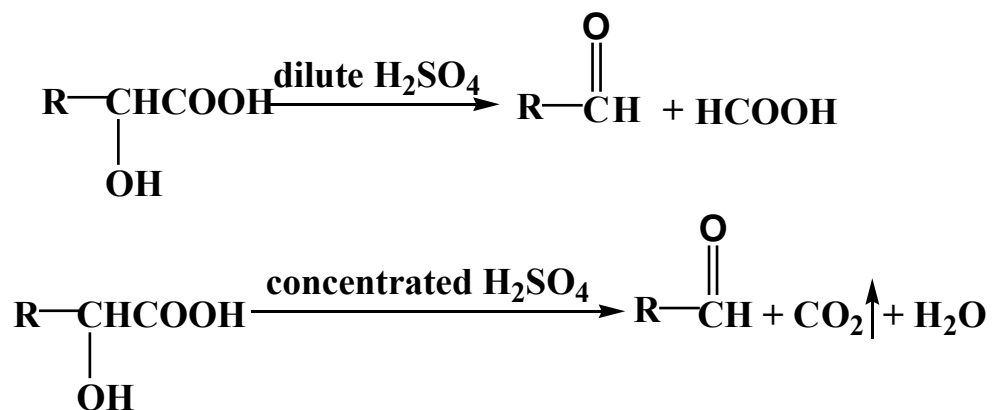
When heated, α -hydroxy-acid can dehydrate to form lactide, β -hydroxy-acid can form α,β -unsaturated carboxylic acid, while γ -hydroxy-acid can form γ -lactone, depending on the positions of the hydroxyl group of hydroxyl acid.



(2). Oxidation



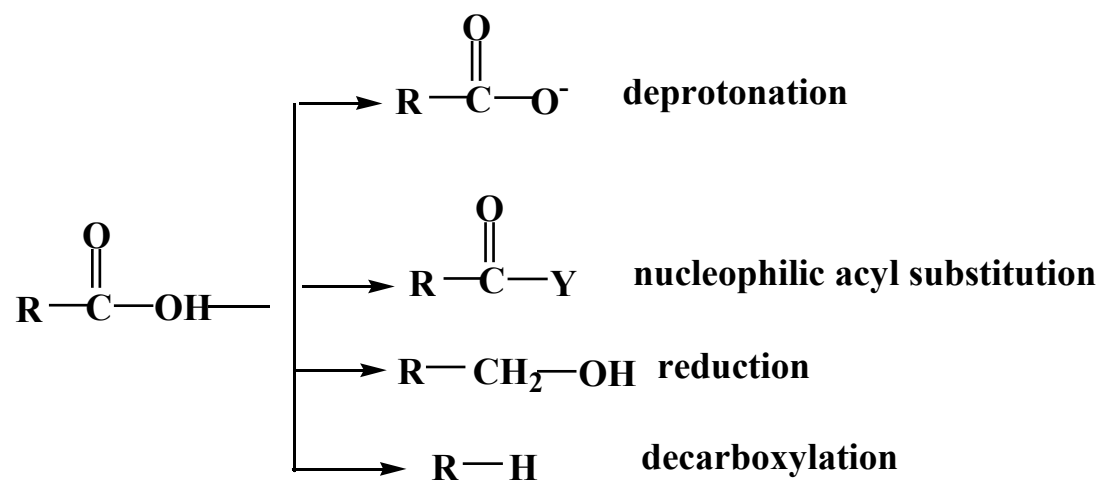
(3). Decomposition



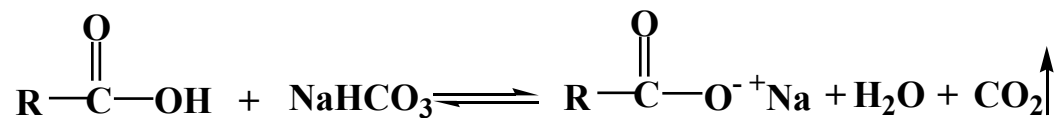
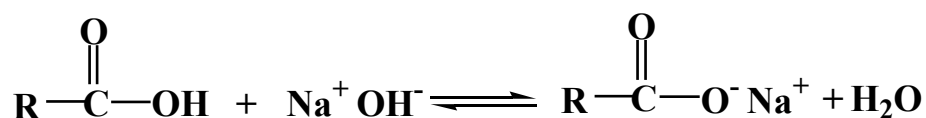
12.9 Theory of Acids and Bases (self-study)

Summary: Reaction of carboxylic acids

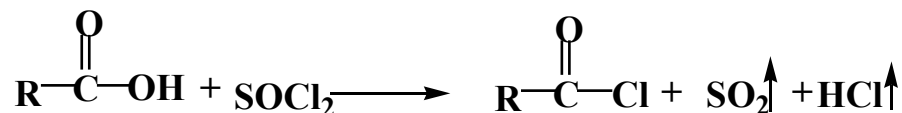
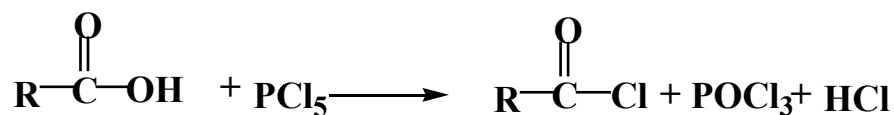
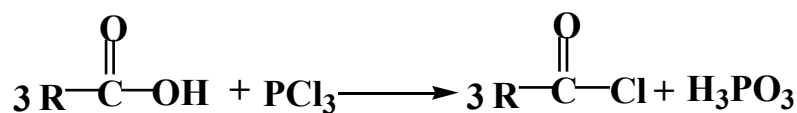
General types of reaction:



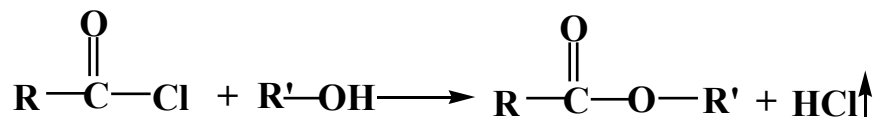
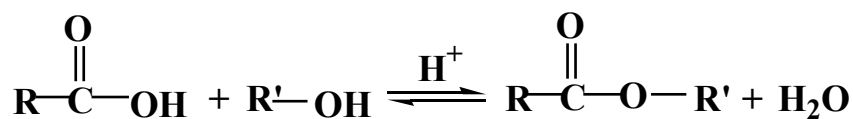
1. Salt formation



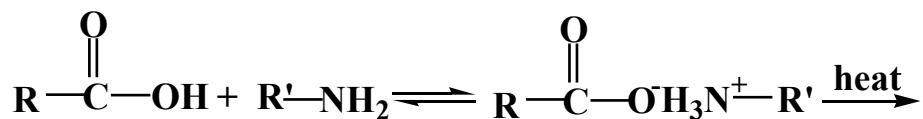
2. Conversion to acid chlorides



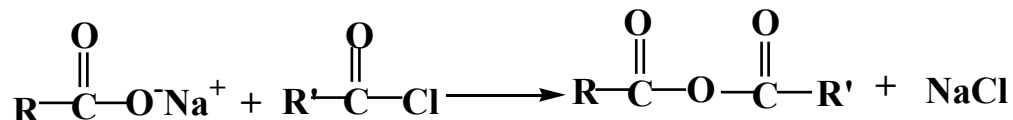
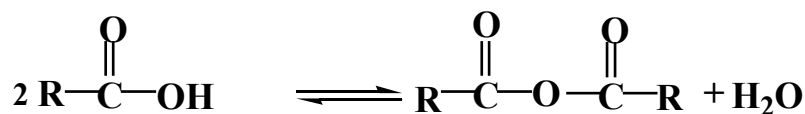
3. Conversion to esters



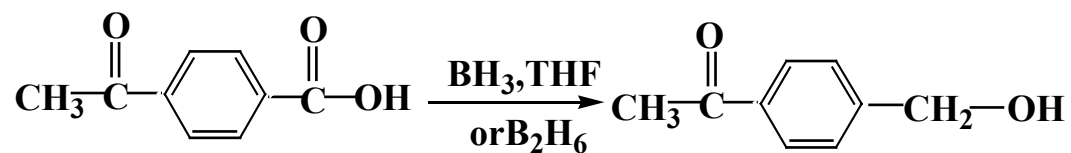
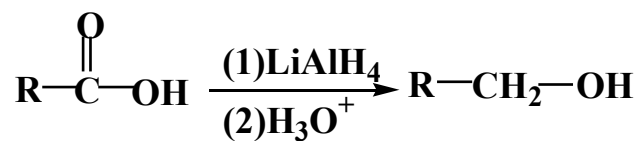
4. Conversion to amides



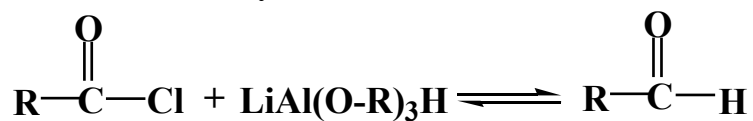
5. Conversion to anhydrides



6. Reduction to primary alcohols



7. Reduction to aldehydes



8. Side-chain halogenation

