جامعة الزهراء للبنات
Al-Zahraa University for Women

FACULTY OF PHARMACY

Pharmaceutical Chemistry Department

Second Year

Organic Pharmaceutical Chemistry II

Laboratory Course

Semester 2

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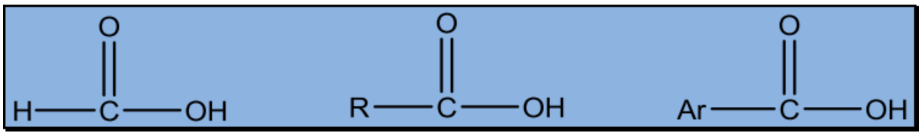
IDENTIFICATION OF CARBOXYLIC ACIDS

Carboxylic acids are organic compounds that have a carboxyl group (-COOH) attached to hydrogen (HCOOH), to an alkyl group (RCOOH), or to an aryl group (ArCOOH).



They may be mono carboxylated such as formic acid and acetic acid, multi carboxylated such as oxalic acid and succinic acid, hydroxylated such as lactic acid and citric acid, or they may be aromatic such as benzoic acid and salicylic acid.
Carboxylic acids that have long, straight-chain hydrocarbon group (with 12 or more C atoms) are commonly classified as **fatty acids,** and several are biological importance. Fatty acids occur in animal or vegetable tissue and nearly always have an even number of C atoms. Those that have only single bonds between C atoms are **saturated fatty acids,** while those with one or more C=C double bond are **unsaturated fatty acids.** The general formula of saturated fatty acid is:

$$C_nH_{2n+1}COOH$$

Stearic acid is saturated fatty acids with 17 C atoms in the hydrocarbon group, R, so general formula is:

$$C_{17}H_{2\,(17)+1}COOH = C_{17}H_{35}COOH$$

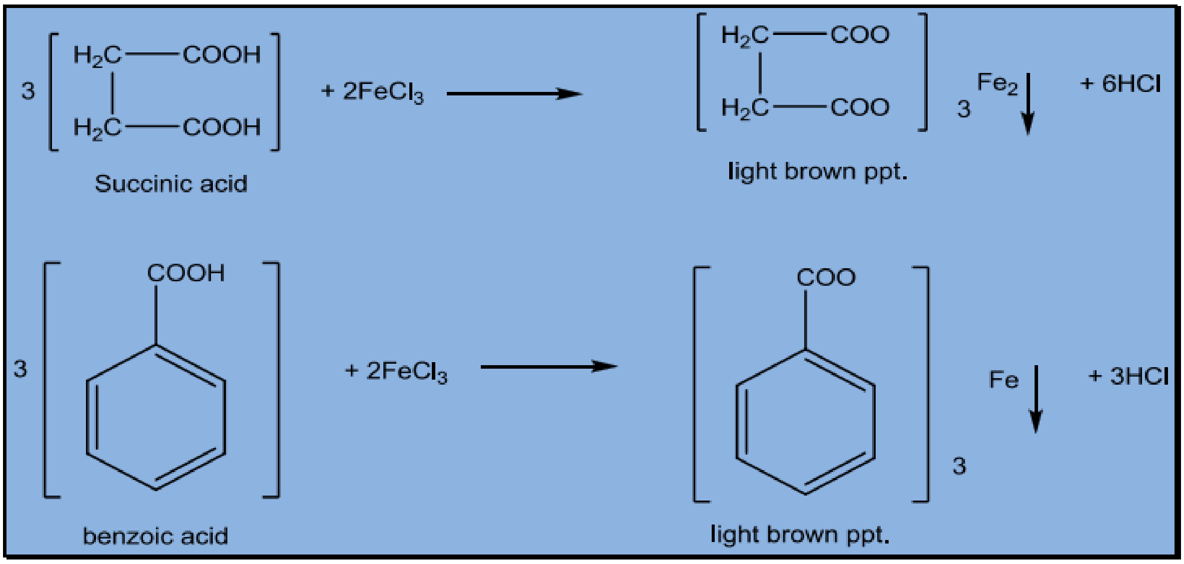
General test (Ferric chloride test).

The acid solution should be made neutral before performing the test with ferric chloride solution. This is achieved by adding dilute ammonia solution drop by drop with shaking to a solution of about 0.5 gm of the acid in water until the medium becomes basic as indicated by changing the color of litmus paper to blue or changing the color of phenolphthalein indicator from colorless to pink, in which case the characteristic odor of ammonia is predominant.
As mentioned above the solution should be neutral and the excess ammonia should be removed by heating the test tube until the odor of ammonia disappears.
(*Note:* In case of oxalic acid keep part of its neutral solution to be used in its special test as will be seen later).
Cool the solution, and then add few drops of ferric chloride solution to get different colors of solutions or precipitates as follows:

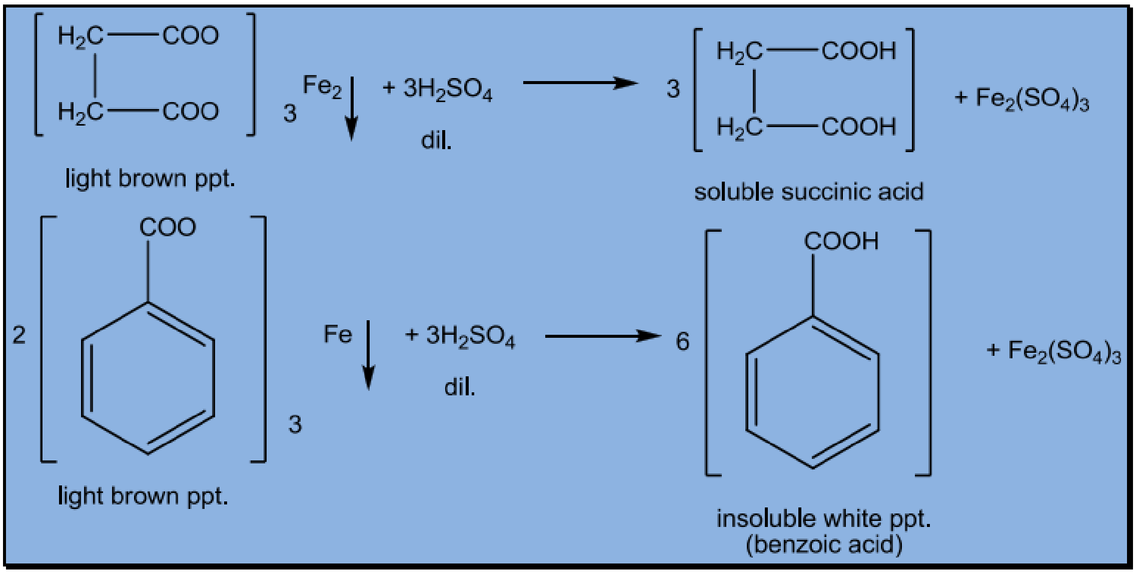
Formic acid and acetic acid give a red colored solution:

$$3HCOOH + FeCl_3 \longrightarrow \underset{\text{red color}}{(HCOO)_3Fe + 3HCl}$$

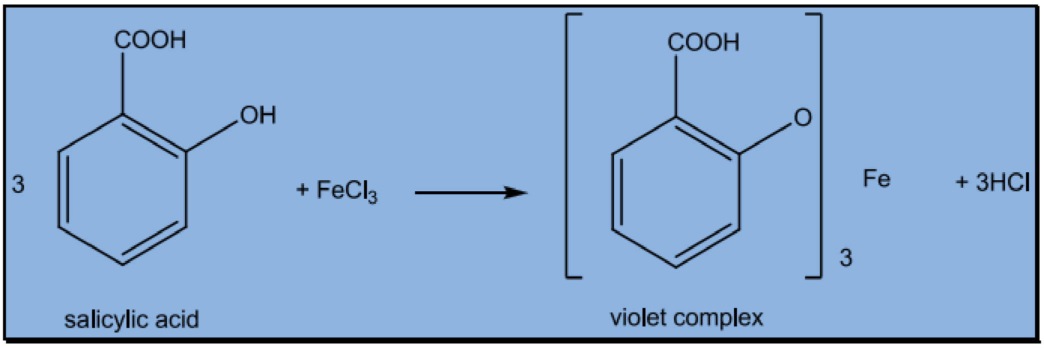
Succinic acid and benzoic acid give a light brown precipitate.



To distinguish between these two acids add to the precipitate few drops of dilute sulphuric acid to liberate the free carboxylic acid again. In one case the liberated acid is water soluble and it is succinic acid which is aliphatic. On the other hand benzoic acid is liberated as a white precipitate because it is insoluble in water since it is aromatic.



Salicylic acid gives a violet color.



Oxalic, tartaric, citric, and lactic acids don't give a special change. Again the details of the general reaction are:

$$NH_4OH + RCOOH \longrightarrow \underset{\text{ammonium salt of the acid (neutral solution)}}{RCOONH_4} + H_2O$$

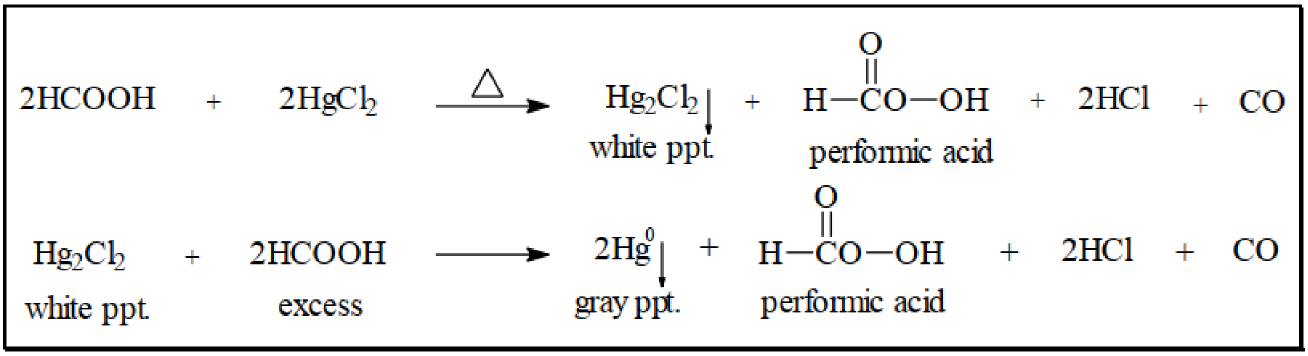
$$\underset{\text{neutral salt}}{3\,RCOONH_4} + FeCl_3 \longrightarrow \underset{\text{ferric salt of the acid}}{(RCOO)_3Fe} + 3NH_4Cl$$

Special tests for formic acid:

Formic acid has the group (HC=O) so it can reduce certain compounds while being oxidized:

A. $HgCl_2$ test.

Formic acid reduces mercuric chloride to mercurous chloride (white precipitate) and, in the presence of excess acid, to mercury element (gray precipitate).



$$2HCOOH + 2HgCl_2 \xrightarrow{\Delta} \underset{\text{white ppt.}}{Hg_2Cl_2\downarrow} + \underset{\text{performic acid}}{H-\overset{\overset{\displaystyle O}{\|}}{C}O-OH} + 2HCl + CO$$

$$\underset{\text{white ppt}}{Hg_2Cl_2} + \underset{\text{excess}}{2HCOOH} \longrightarrow \underset{\text{gray ppt.}}{2Hg^0\downarrow} + \underset{\text{performic acid}}{H-\overset{\overset{\displaystyle O}{\|}}{C}O-OH} + 2HCl + CO$$

To few drops of the acid add few drops of mercuric chloride solution, and Then heat to get a white precipitate. Add excess of the acid with heating to get the gray precipitate of elemental mercury.

B. Tollen's test.

For procedure and preparation of Tollen's reagent refer to this test (page 18).

$$HCOOH + Ag(NH_3)_2OH \xrightarrow{\triangle} \underset{\text{silver mirror}}{Ag^0\downarrow} + \underset{\text{ammonium performate}}{NH_4COO{-}OH}$$

C. Alkaline $KMnO_4$ test.

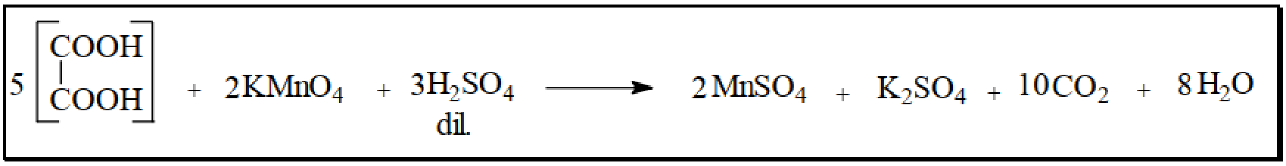
Formic acid reacts with potassium permanganate solution, a strong oxidizing agent, in alkaline medium causing decolourization of the reagent.
Mix 2 - 3 drops of the acid with 5 ml of sodium bicarbonate solution, and then add 1% potassium permanganate solution drop by drop and observe the disappearance of a brown precipitate of manganese oxide.

$$HCOOH + KMnO_4 \xrightarrow{NaHCO_3} \underset{\text{brown ppt.}}{MnO\downarrow} + H_2O + CO_2$$

Special tests for oxalic acid.

A. Acidic $KMnO_4$ test.

Oxalic acid doesn't react with alkaline potassium permanganate solution. With acidic potassium permanganate solution it reacts causing decolourization of the reagent:

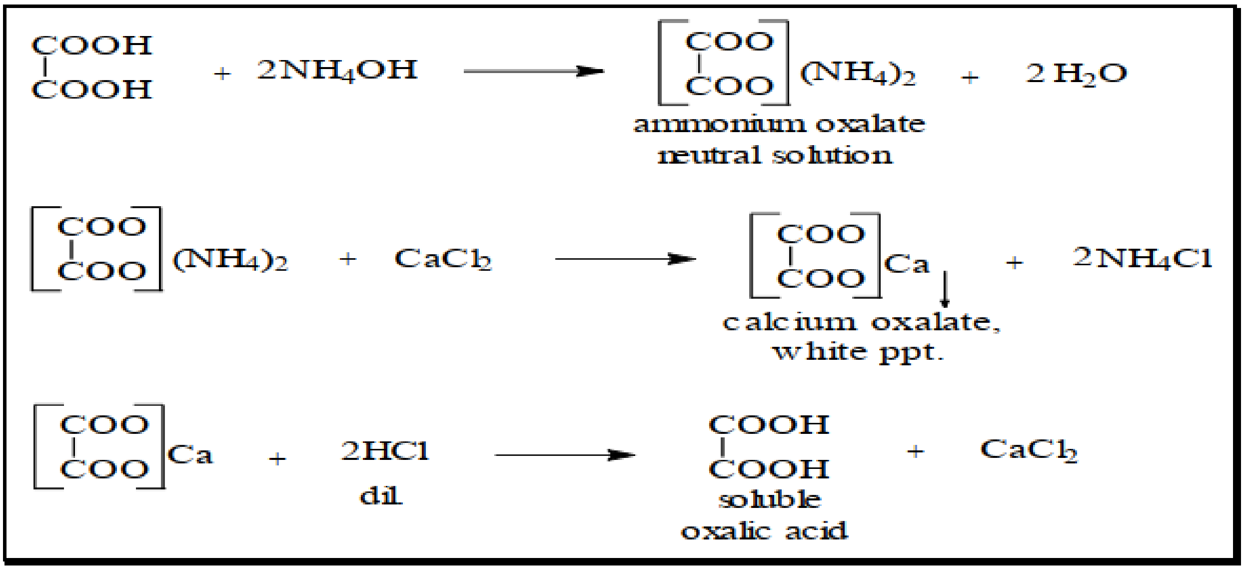


$$5\begin{bmatrix}COOH\\ |\\ COOH\end{bmatrix} + 2KMnO_4 + \underset{\text{dil.}}{3H_2SO_4} \longrightarrow 2MnSO_4 + K_2SO_4 + 10CO_2 + 8H_2O$$

Dissolve 0.5 gm of the acid in 2 - 3 ml of distilled water and add 2 - 3 ml of dilute sulfuric acid. Heat gently (water bath), and then add potassium permanganate solution drop by drop and observe the disappearance of the violet color of the reagent.

B. $CaCl_2$ test.

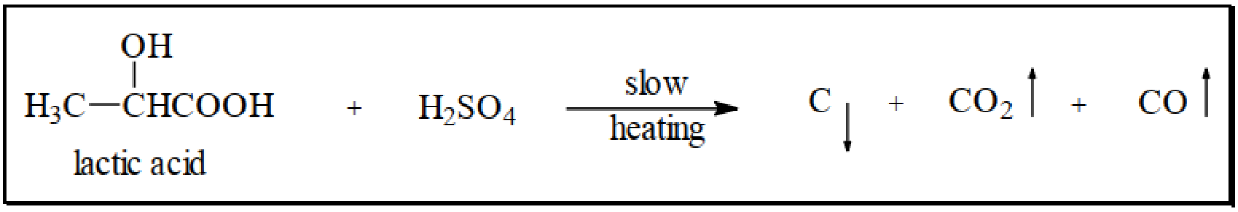
To the neutral solution of the acid (see the general test) add few drops of calcium chloride solution; a white precipitate of calcium oxalate is formed. This precipitate dissolves in dilute hydrochloric acid and not in dilute acetic acid



Special test for lactic acid.

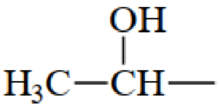
A. H_2SO_4 test.

Add 1 ml of concentrated sulfuric acid to 0.5 ml of the acid and heat slowly to get bubbles of carbon dioxide and then a black color is produced.

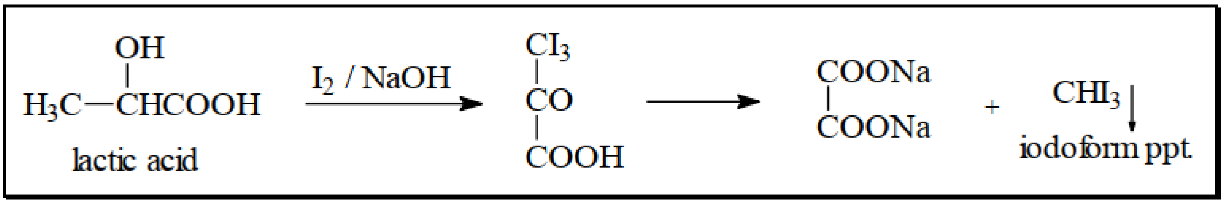


B. Iodoform test.

Lactic acid can undergo Iodoform formation reaction since it contains a terminal methyl group;

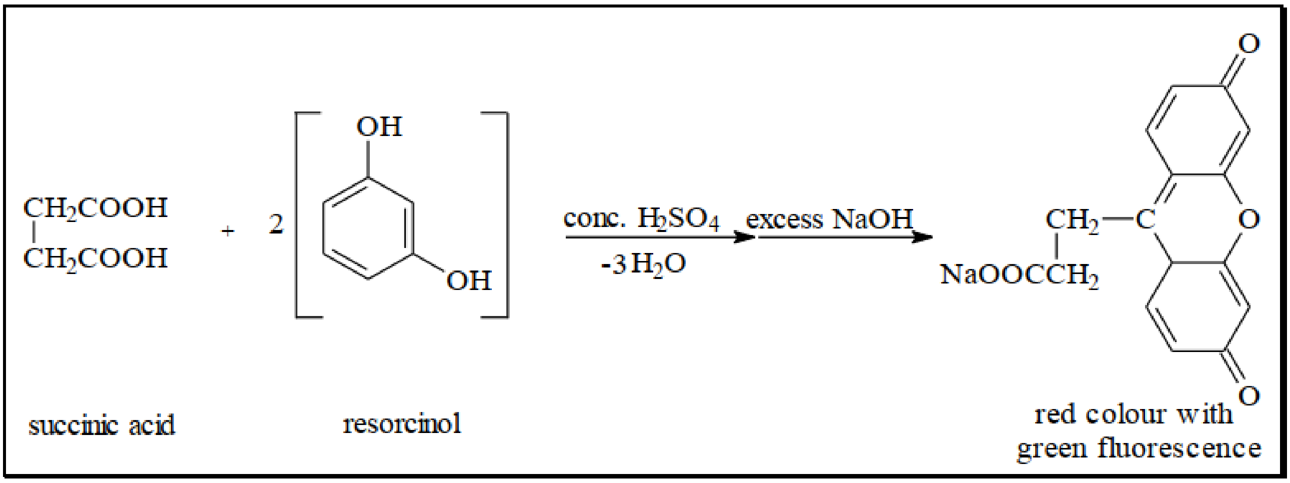


$$H_3C-\overset{OH}{\overset{|}{CH}}-$$



Fluorescence test for succinic acid.

In a test tube mix equal quantities of succinic acid and resorcinol with 2 drops of concentrated sulfuric acid. Heat the mixture on direct flame for 1 minute until the mixture melts. Cool and add excess of 10% sodium hydroxide solution to get a red color with green fluorescence. If the color is not so clear dilute with water.



succinic acid

resorcinol

red colour with green fluorescence

THE PROPERTIES AND PREPARATION OF ESTERS AND SOAP

In this experiment we are going to prepare several esters and not their characteristic aromas. We will also prepare soap a carboxylic acid salt

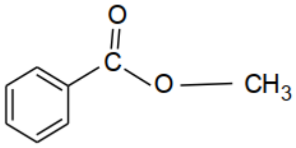
Esters:

The general formula for an ester is RCOOR‘. An ester can be prepared by reacting an alcohol with carboxylic acid. The R group in the general formula was part of the acid. The other group, symbolized R‘was part of the alcohol. Sulfuric acid catalyzes the reaction.

$$\begin{array}{cccc} RCOOH + & R'OH & \xrightarrow{H_2SO_4} & RCOOR' + H_2O \\ \text{Carboxylic acid} & \text{alcohol} & & \text{ester} \end{array}$$

The names of esters are similar in form to those of the salt of carboxylic acids.

$HCOOCH_3$	CH_3COOCH_3	$CH_3COOCH_2CH_3$
Methyl formate	methyl acetate	ethyl acetate

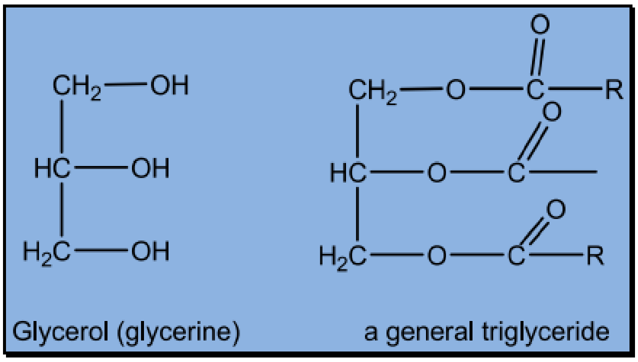


Methyl benzoate

Many esters are colorless liquids with pleasant, fruity aromas. The aroma and flavor of many foods are due to the presence of esters.

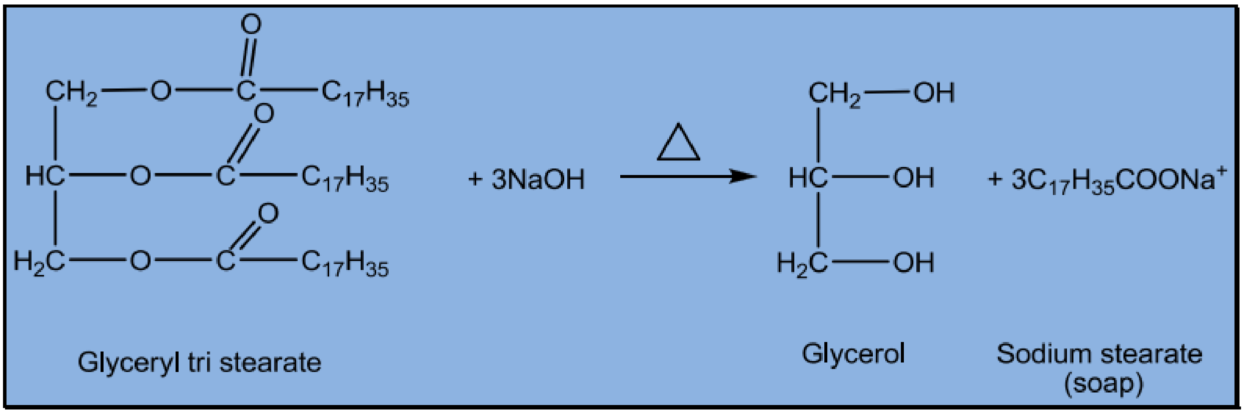
Triglycerides:

Triglycerides are triesters, containing three ester functional groups per molecule. They are large molecules that can be considered the products of the reaction of glycerol (an alcohol containing three –OH groups that is also called glycerine) with three fatty acids. Fats and oils are triglycerides.



The preparation of soap - Saponification

Soap is prepared by the hydrolysis of triglycerides in the presence of strong base like NaOH or KOH. Instead of obtaining a fatty acids as products of the hydrolysis. The Na or K salt of the fatty acids is obtained. If a fatty acid did form in the hydrolysis, it would quickly be neutralized by the NaOH or KOH to form the soap.
The soluble salt of a fatty acid is soap. The reaction that produces soap is called **Saponification** and it is of great industrial importance. Sodium stearate is produce when glyceryl tri stearate, from animal fat, is heated in the presence of aqueous NaOH. Sodium stearate is the primary component of Ivory soap.



Procedure:

A. Preparation of some esters

1. Place the following reagents in the labeled test tubes:
- Test tube A: 20 drops of ethanol + 20 drops of glacial acetic acid + 10 drops of concentrated H2SO4.
- Test tube B: 20 drops of pentanol + 20 drops of glacial acetic acid + 10 drops of concentrated H2SO4.
- Test tube C: 20 drops of benzoic acid + 20 drops of ethanol + 10 drops of concentrated H2SO4.

2. Stir the contents of each test tube. When the water bath has reached 85o C, turn off the burner and place stoppered test tube in the hot water.
3. After 10 min. removes the stopper from each tube and notes the odor should product. You be able to detect the aroma of banana, butter rum, fingernail and minty

scent of wintergreen. Record the aroma of each mixture on the report sheet, then complete the equation and name the ester.

B. Preparation of soap

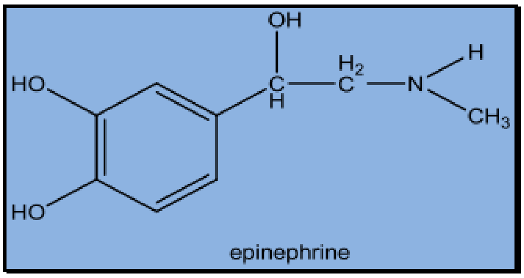
1. In an evaporating dish, mix 2 ml of vegetable oil and 3 ml of ethanol, this is a good solvent for both triglyceride (the vegetable oil) and NaOH. Add 20 drops of 50 % NaOH.
2. Heat the mixture, while stirring, with a moderate, almost luminous flame until it becomes a thick paste. Allow the evaporating dish to cool. Note the appearance of the product on the report sheet, then complete the equation and name the products of the saponification reaction.

IDENTIFICATION OF AMINES

Amines are organic compounds and functional groups that contain a basic nitrogen atom with lone pair. Amines are derivatives of ammonia, wherein one or more hydrogen atoms have been replaced a subsistent such as an alkyl or aryl group. Important amines including amino acids, biogenic amines, trimethyl amine and aniline. For aliphatic amines name groups attached to N; use suffix -amine.

Biological Activity:

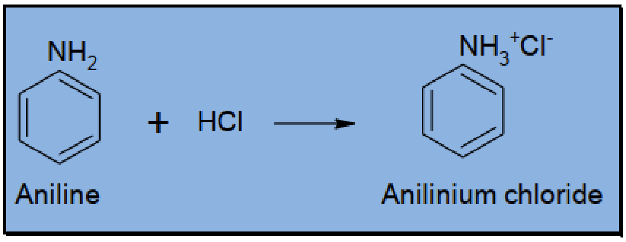
Amines have strong, characteristic odors, and are toxic. The smells of ammonia, old fish, urine, rotting flesh, and semen are mainly composed of amines. Many kinds of biological activity produce amines by breakdown of amino acids. Many hormones like epinephrine, nor epinephrine, and dopamine, are amines.



Chemical Reactions:

1. General test (The hydrochloric acid test).

Amines are characterized chiefly through their basicity. A water insoluble compound that dissolves in cold dilute hydrochloric acid or a water-soluble compound whose aqueous turn litmus blue.



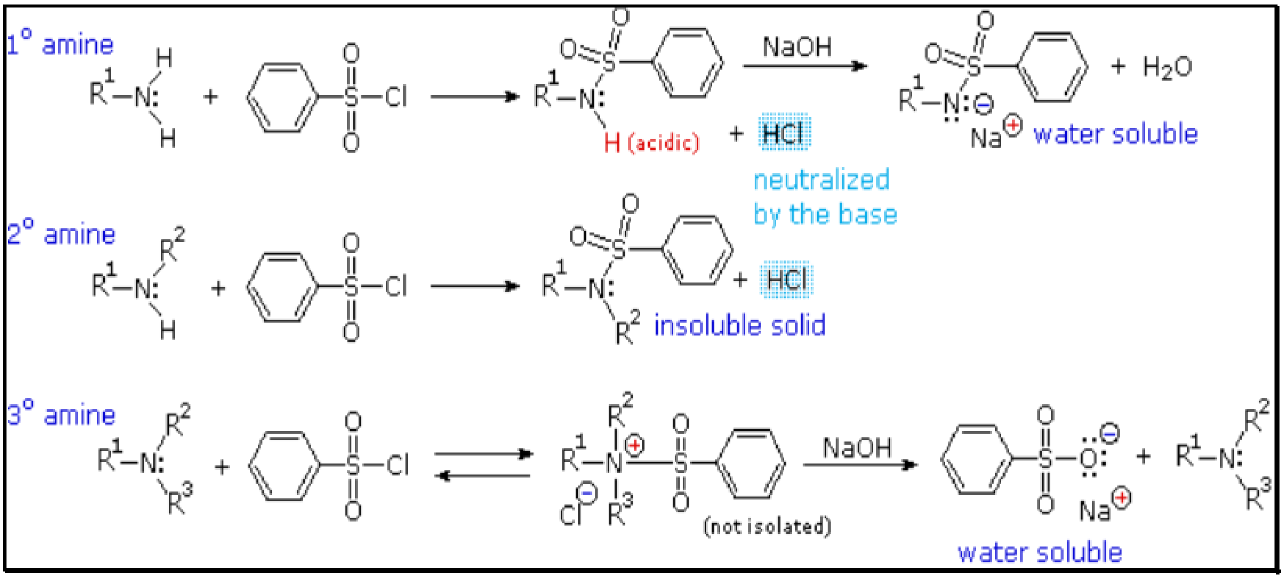
Procedure:

Place 3 ml of water in a clean test tube. Add one drop or a spatula tip of your unknown. Swirl the mixture. If your unknown is soluble, test the pH of the solution. An alkaline pH is indicative of an amine. If your unknown is not soluble in water, add 3 ml of 5% HCl solution. If your unknown dissolves in the acid solution, an amine is indicated.

2. Tests for differentiation between Primary and secondary amines:

The Hinsberg Test:

An electrophilic reagent, benzenesulfonyl chloride, reacts with amines in a fashion that provides a useful test for distinguishing primary, secondary and tertiary amines (the Hinsberg test). As shown in the following equations, 1° and 2°-amines react to give sulfonamide derivatives with loss of HCl, whereas 3°-amines do not give any isolable products other than the starting amine. In the latter case a quaternary "onium" salt may be formed as an intermediate, but this rapidly breaks down in water to liberate the original 3°-amine (lower right equation).



The **Hinsberg test** is conducted in aqueous base (NaOH or KOH), and the benzenesulfonyl chloride reagent is present as an insoluble oil. The amine dissolves in the reagent phase, and immediately reacts (if it is 1° or 2°), with the resulting HCl being neutralized by the base. The sulfonamide derivative from 2°-amines is usually an insoluble solid. However, the sulfonamide derivative from1°-amines are acidic and dissolve in the aqueous base. Acidification of this solution then precipitates the sulfonamide of the 1°-amine. Benzenesulphonyl chloride reacts with primary and secondary but not with tertiary amines to yield substituted sulphonamides. The substituted sulphonamide formed from a primary amine dissolves in the alkali medium while that produced from a secondary amine is insoluble in alkali.

Procedure:

Place 0.5 mL (or 0.5 g) of the compound, 15 - 10 mL of 5% NaOH and 1 mL of benzenesulphonyl chloride in a test tube, stopper the tube and shake until the odor of the sulphonyl chloride has disappeared. The solution must be kept alkaline (if no reaction has occurred, the substance is probably a tertiary amine).

If a precipitate appears in the alkaline solution, dilute with about 10 mL of water and shake; if the precipitate does not dissolve, a secondary amine is indicated.

If there is no precipitate, acidify it cautiously to congo red with concentrated hydrochloric acid (added drop wise): a precipitate is indicative of a primary amine.