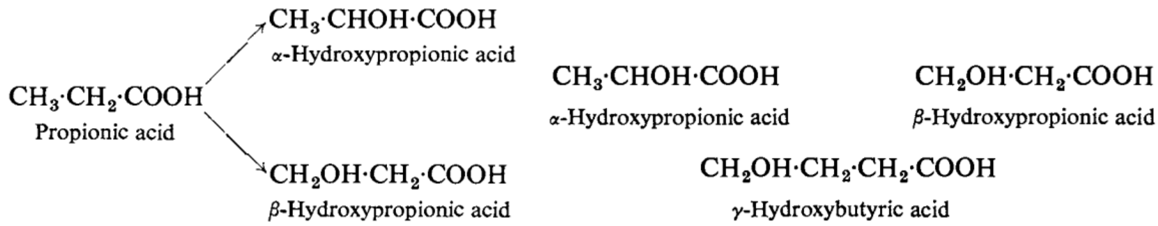
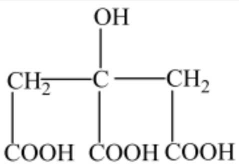
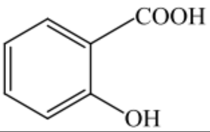
Lesson 4,5. Heterofunctional compounds. Hydroxy Acids, Keto Acids, Aromatic Hydroxy Acids

The hydroxyl (-OH) group in alcohol is polarized due to the electronegativity difference between atoms. The oxygen of the -OH group can react as either a base or a nucleophile in the nucleophilic substitution reactions.

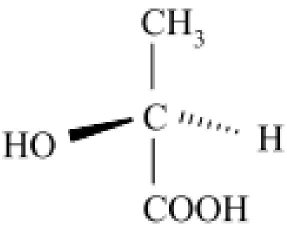
The hydroxy acids possess two functional groups (i.e. the alcohol and the carboxyl groups) and are prepared and react accordingly, e.g. glycollic acid is prepared from a halogen acid by hydrolysis and it gives the reactions of primary alcohols as well as those of acids. The simplest member of the series of hydroxyacids is glycolic acid (CH_2OH-COOH) (hydroxyacetic acid). The next members of the series are derived from propionic acid. Two isomeric acids exist since it is possible to substitute a hydroxyl group in the propionic acid molecule in two different positions thus:



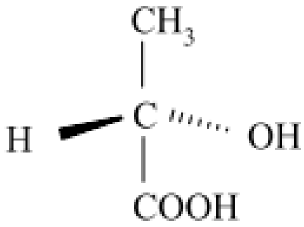
Main representatives

Formula	Name
$HO-CH_2-COOH$	**Glycolic acid**
$CH_3-CH(OH)-COOH$	**Lactic acid**
$HOOC-CHOH-CH_2-COOH$	**Malic acid**
$HOOC-CH(OH)-CH(OH)-COOH$	**Tartaric acid**
	**Citric acid**
	**Salicylic acid**

Optical isomerism

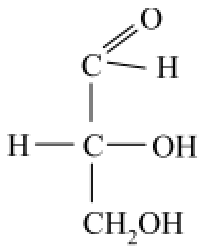


L- lactic acid

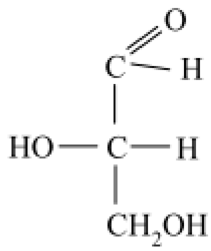


D-lactic acid

The lactic acid molecule have two forms of optical isomers: L- and D-lactic acids respectively. Glyceraldehyde is used as the standard. Thus D–isomer was called a substance, which had group -OH to the right from asymmetric carbon atom.



D-glyceric aldehyde



L- glyceric aldehyde

General methods of Hydroxy Acids preparation

(1) By introducing the hydroxyl group into an acid molecule:

(a) From the halogen substituted acids, by hydrolysis, e.g. with moist silver oxide

$$CH_2Cl{\cdot}COOH + H_2O = CH_2OH{\cdot}COOH + HCl$$

(b) From the amino-acids, by reaction with nitrous acid

$$CH_2NH_2{\cdot}COOH + HNO_2 = CH_2OH{\cdot}COOH + N_2 + H_2O$$

(2) By introducing a carboxyl group into an alcohol.

(a) From aldehyde cyanhydrins, by hydrolysis.

$$CH_3{\cdot}CH(OH)CN + 2H_2O = CH_3{\cdot}CHOH{\cdot}COONH_4$$

(b) From glycols, by partial oxidation.

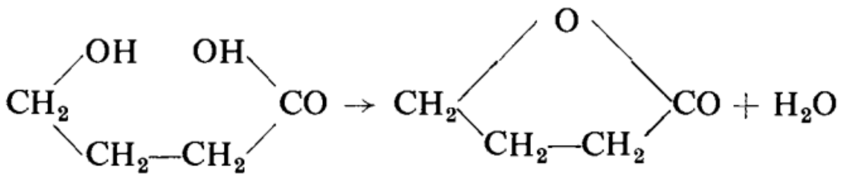
$$CH_2OH{\cdot}CH_2OH \rightarrow CH_2OH{\cdot}COOH$$

The Properties of Hydroxy Acids

1) Oxydation of alcohol grouping and formation of pyruvic acid

$$CH_3{\cdot}CHOH{\cdot}COOH \rightarrow CH_3{\cdot}CO{\cdot}COOH$$

2) Internal dehydration (for γ- and δ-hydroxy acids, the interaction of the alcoholic and acidic groups takes place on heating, and the resulting compound is called a lactone.



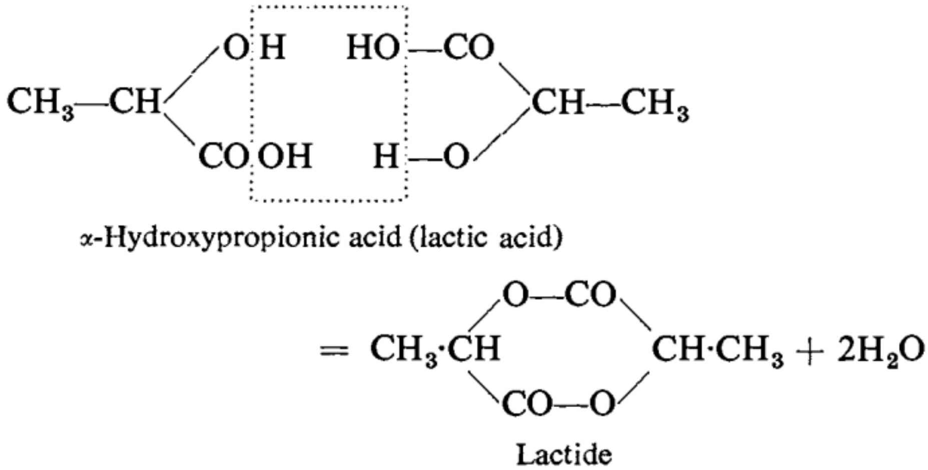
Hydroxybutyric acid Butyrolactone

By dehydration of β-hydroxy acids unsaturated acids are formed

$$CH_2OH{\cdot}CH_2{\cdot}COOH = CH_2{:}CH{\cdot}COOH + H_2O$$

β-Hydroxypropionic acid (Hydracrylic acid) Acrylic acid

By dehydration of α-hydroxy acids lactides are formed



Main representatives

<u>*Lactic acid*</u>

Ordinary lactic acid is the inactive (or racemic) form. The dextrorotatory acid (sarcolactic acid) occurs in meat juices and is obtainable from meat extract. The laevorotatory does not occur naturally but may be obtained by removing the dextrorotatory fraction of the inactive mixture.

Ordinary or fermentation lactic acid is formed during the souring of milk, as the result of the "lactic fermentation" of lactose by the lactic bacillus. It is manufactured from sour milk or by the lactic fermentation of sugars other than lactose (e.g. sucrose in sugar molasses or the sugars formed by the hydrolysis of wood shavings).

$$C_{12}H_{22}O_{11} + H_2O = 4CH_3{\cdot}CHOH{\cdot}COOH$$

It can be oxidized in the presence of potassium permanganate to acetaldehyde. Milder oxidation gives pyruvic acid.

$$CH_3{\cdot}CHOH{\cdot}COOH \xrightarrow{O} CH_3{\cdot}CHO + CO_2 + H_2O$$

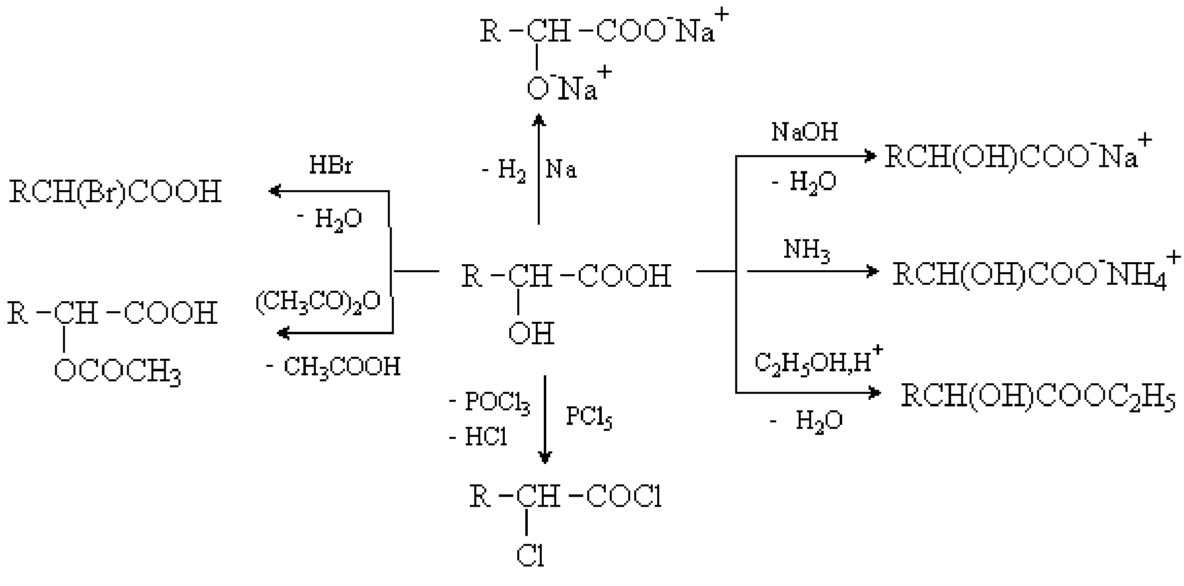
$$CH_3{\cdot}CHOH{\cdot}COOH \xrightarrow{O} CH_3{\cdot}CO{\cdot}COOH + H_2O$$

Oxy-Acids can be reduced in the organism into Hydroxy-Acids

$CH_3COCOOH + NAD{\cdot}H + H^+ \rightarrow CH_3CH(OH)COOH + NAD^+$

Pyruvic acid D- Lactic Acid

Main reactions of Hydroxy Acids



Aldehydic and ketonic acids

The most important aldehydic acid is glyoxalic acid OHC-COOH (a product of the oxidation of glycol), and the chief ketonic acids are pyruvic acid (CH_3-CO-COOH - an intermediate product in the fermentation of sugar).

Isomerism

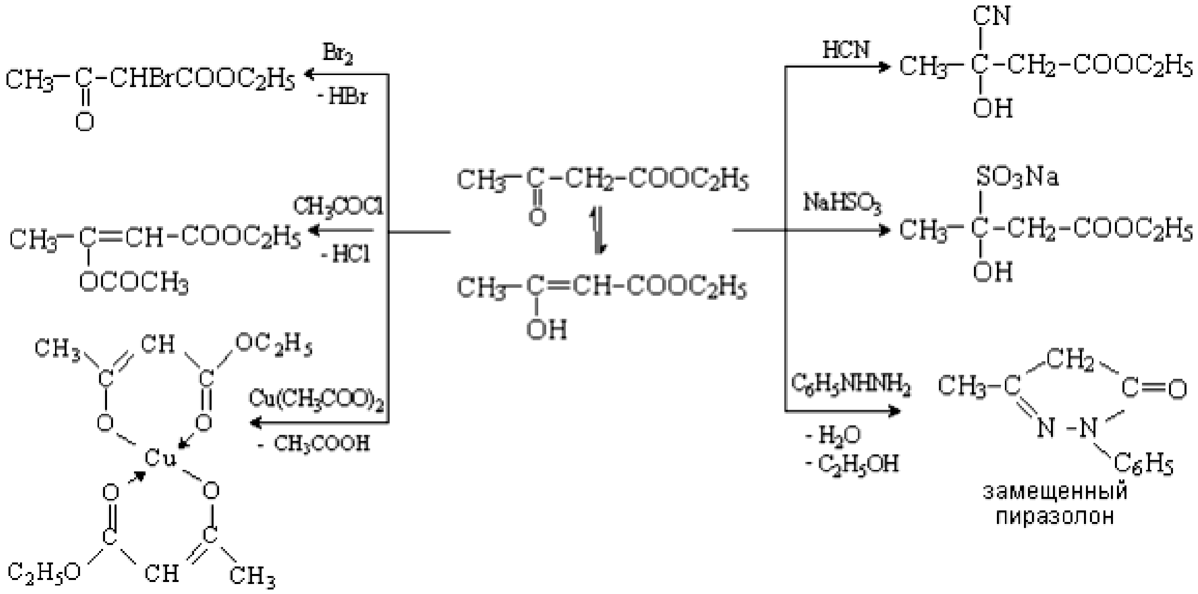
Keto-enol tautomerism

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}COOC_2H_5 \rightleftarrows CH_3{\cdot}C(OH){:}CH{\cdot}COOC_2H_5$$

Ketonic form　　　　Enolic form

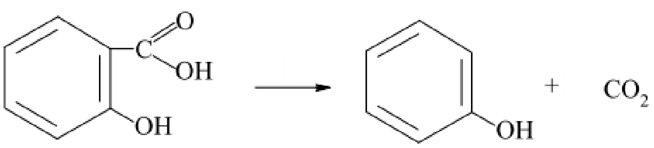
Formula	Name
$CH_3-C(=O)-COOH$	**Pyruvic acid**
$CH_3-C(=O)-CH_2-COOH$	**Acetoacetic acid**
$HOOC-C(=O)-CH_2-COOH$	**Oxaloacetic acid**
$HOOC-C(=O)-CH_2-CH_2-COOH$	α- ketoglutaric acid

Main chemical reactions of acetacetic ester

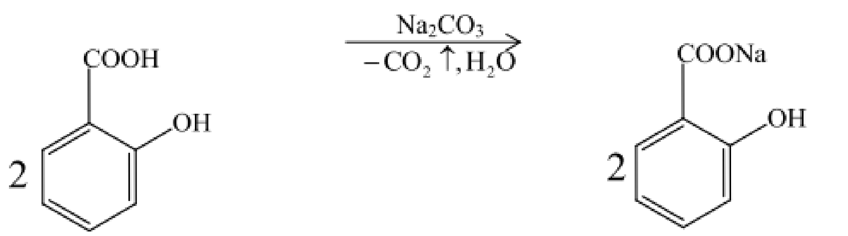


Main reactions of o-hydroxybenzoic (Salicylic) acid

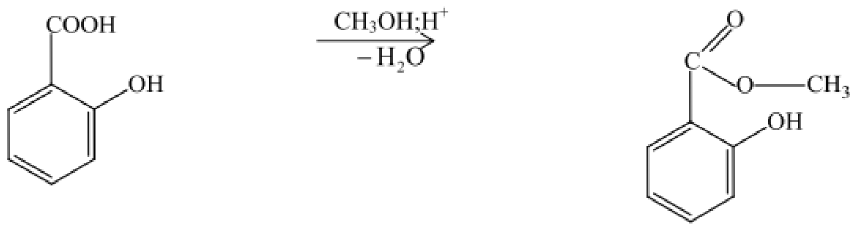
It can be decarboxylated with phenol formation:



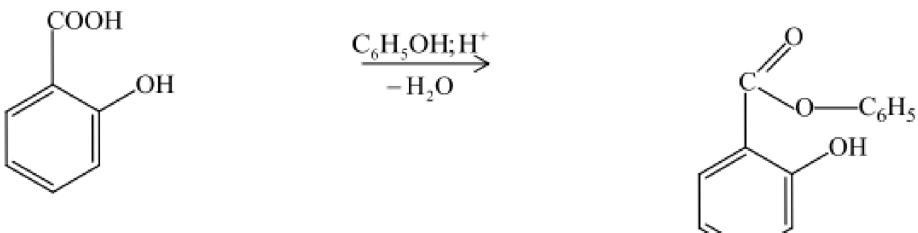
<u>Reactions of carboxylic group</u>



Sodium salicylate

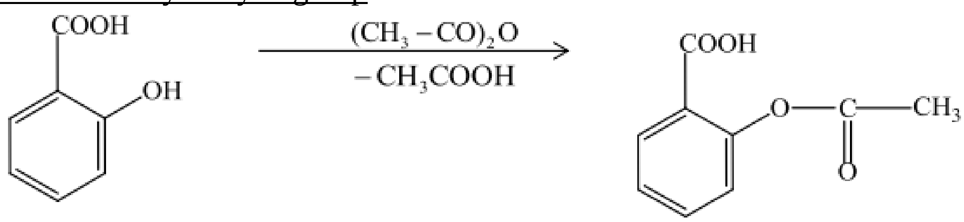


Methyl salicylate



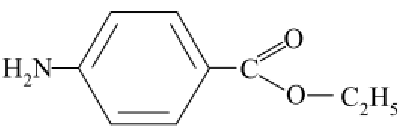
Phenyl salicylate

<u>Reaction of hydroxylic group</u>

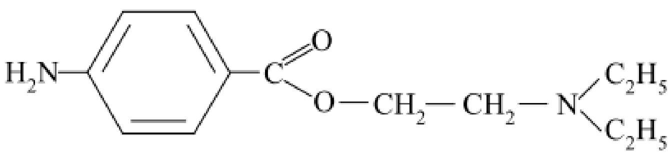


Acetyl salicylate (acetylsalicylic acid)
(aspirin)

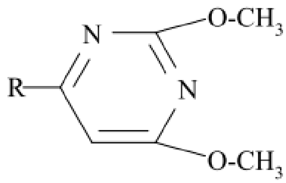
<u>**Important in medicine**</u>



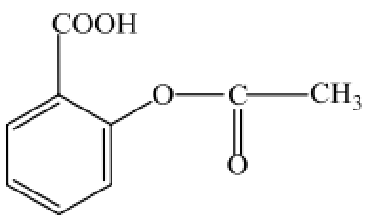
Anesthesin



Novocaine



Sulfadimetoxine



Aspirine