Bio-organic chemistry

Lecture #11

Hydroxy and oxoacids. Classification, distribution, application, physiological role of hydroxy and oxoacids, their preparation and chemical properties. Keto-enol tautomerism of oxoacids.

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Some types of combining functional groups in heterofunctional compounds

Heterofunctional classes	*Functional groups*		*Representatives*	
			formula	*trivial name*
Amino alcohols	NH_2	OH	$H_2NCH_2CH_2OH$	Colamine
Hydroxy carbonyl compounds	OH	>C=O	$HOCH_2CHCH{=}O$ OH	Glyceraldehyde
Hydroxy carboxylic acids	OH	COOH	$HOCH_2COOH$	Glycolic acid
Amino acids	NH_2	COOH	H_2NCH_2COOH	Glycine
Oxo acids	=O	COOH	CH_3CCOOH ‖ O	Pyruvic acid

Hydroxyl, amino, oxo, and carboxyl groups are encountered most widely in heterofunctional compounds. A ***combination of different functional groups*** results in the formation of mixed classes of organic compounds, some of them are given in Table (other combinations are possible, of course).

Hydroxy acids are organic compounds that contain a hydroxyl group and a carboxylic group

Hydroxy acids are the derivatives of carboxyl acids that contain –OH group (1 or more)

Methanoic acid   2-Methylpropanoic acid   3-Hydroxybutanoic acid

Biological role:

- Heterofunctional compounds are widespread in the nature. They are in fruits and vegetable leafs. Also they are formed in body.
- So, the lactic acid is product of transformation glucose (glycolysis) in human body.
- A malic and citric acid formed in a cycle of tricarboxylic acids, which is also known as citric acid cycle or Krebs' cycle.
- Hydroxoacids such as: pyruvic acid, acetoacetic acid, oxaloacetic acid, -ketoglutaric acid are important in metabolism of carbohydrates

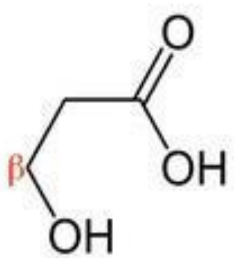
Classification of Hydroxyacids

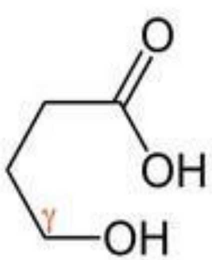
Sign of classification	Class name	
the structure of the carbon radical	aliphatic	Aromatic
atomicity (quantity of –OH group) and basicity (quantity of –COOH group)	monobasic diatomic	monobasic diatomic
	dibasic triatomic	
	dibasic tetratomic	monobasic tetratomic
	tribasic tetratomic	
Position of -OH and -COOH groups	**α-Hydroxyacids**	
	β-Hydroxyacids	
	γ-Hydroxyacids	

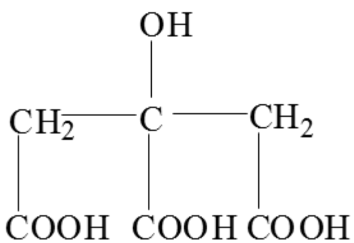
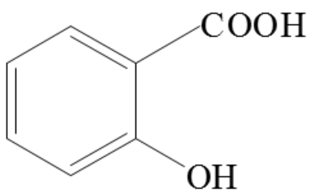
Alpha Hydroxy Acids(AHAs)

Hydroxy acids (HAs) represent a class of compounds which have been widely used in a number of cosmetic and therapeutic formulations in order to achieve a variety of beneficial effects for the skin.

- occur naturally in fruit, milk, and sugarcane
- are used in skin care products





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**

Physical and chemical properties of hydroxy carboxylic acid

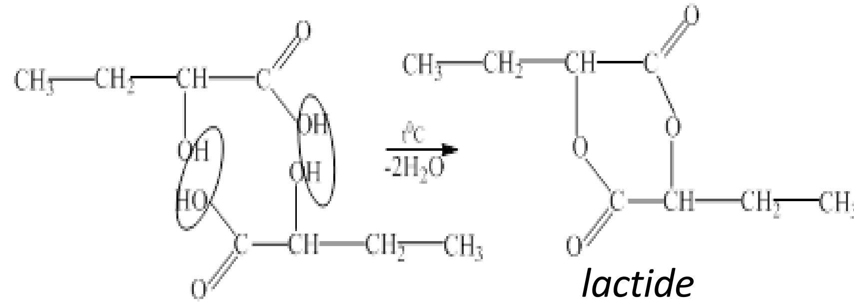
- For physical properties of hydroxy carboxylic acids are colorless liquids or crystalline substance, soluble in water.
- Chemical properties: in the molecule of hydroxy acids ether –OH group or carboxyl group can react.

Chemical properties of aliphatic hydroxy acids (on an example of glycolic acid)

CH_2OH-COOH	**reaction of –COOH group**
	1 *neutralization* $+ NaOH \xrightarrow[-H_2O]{} CH_2OH - COONa + H_2O$ sodium glycollate
	2 $+ Na_2CO_3 \xrightarrow[-H_2O\ -CO_2\uparrow]{} CH_2OH - COONa$ sodium glycollate
	3 *esterification* $+ CH_3 - OH \xrightarrow{H^+} CH_2OH - CO - O - CH_3 + H_2O$
	4 *amide formation* $+ NH_3 \xrightarrow{t^o} CH_2OH - CONH_2 + H_2O$
	5 *oxidation* $\xrightarrow{[O]} HOC - COOH \xrightarrow{[O]} HOOC - COOH$ $- H_2O$ glyoxalic acid oxalic acid
	reaction of -OH
	1 *acetilation* $+ H_3C - COCl \xrightarrow[-HCl]{} CH_3 - CO - O - CH_2 - COOH$
	2 $+ HBr \xrightarrow[-H_2O]{} CH_2Br - COOH$

Specific properties

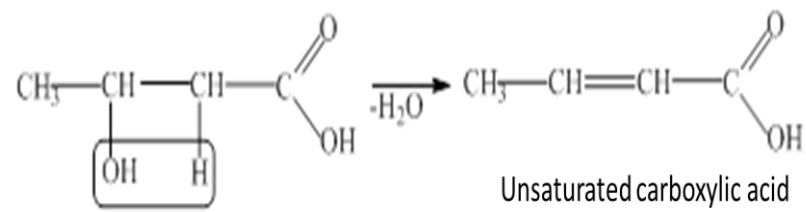
Intermolecular dehydration (for α-Hydroxy acids)



lactide

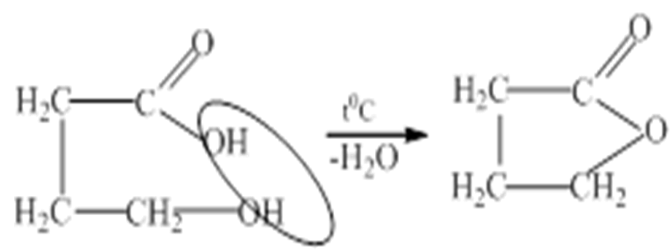
Intramolecular dehydration

β-Hydroxy acids



Unsaturated carboxylic acid

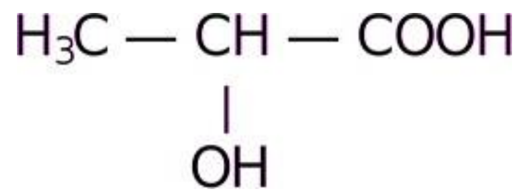
γ-hydroxy acids

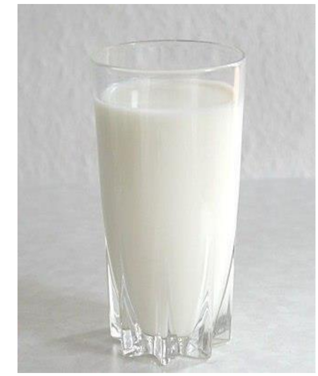


lactone

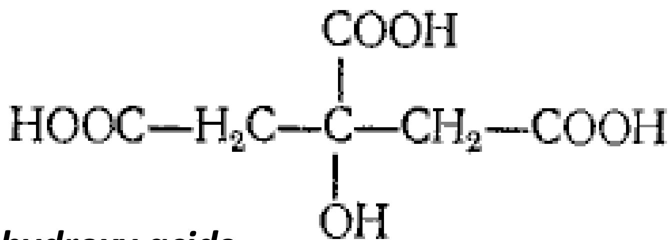
Representatives of hydroxy acids:

Lactic acid. lactic acid is a trivial name because at first it was extracted from milk. It is present in yogurt, sour milk and other milk products. It can form in muscles during hard and prolonged work. Salts of milk acid are used in medicine. Lactic acid is produced industrially by bacterial fermentation of carbohydrates (sugar, starch) or by chemical synthesis from acetaldehyde



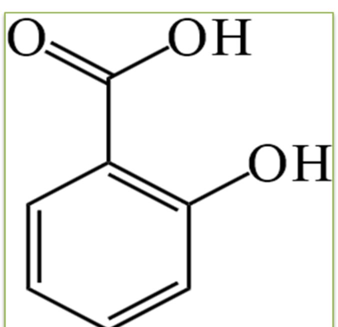


Citric acid . It is present in orange, lemon and other citric fruits. It takes part in biological processes in human organism



Aromatic hydroxy acids

Or phenolacids are the derivatives of aromatic carboxyl acids that contain –OH group (1 or more).

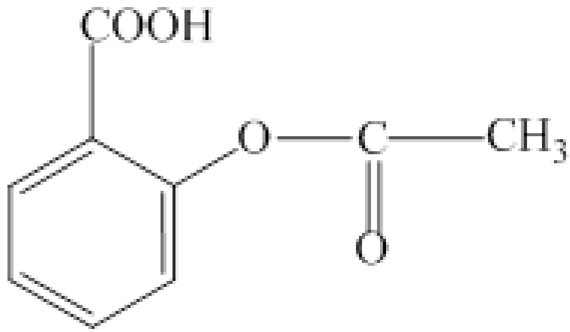


salicylic acid

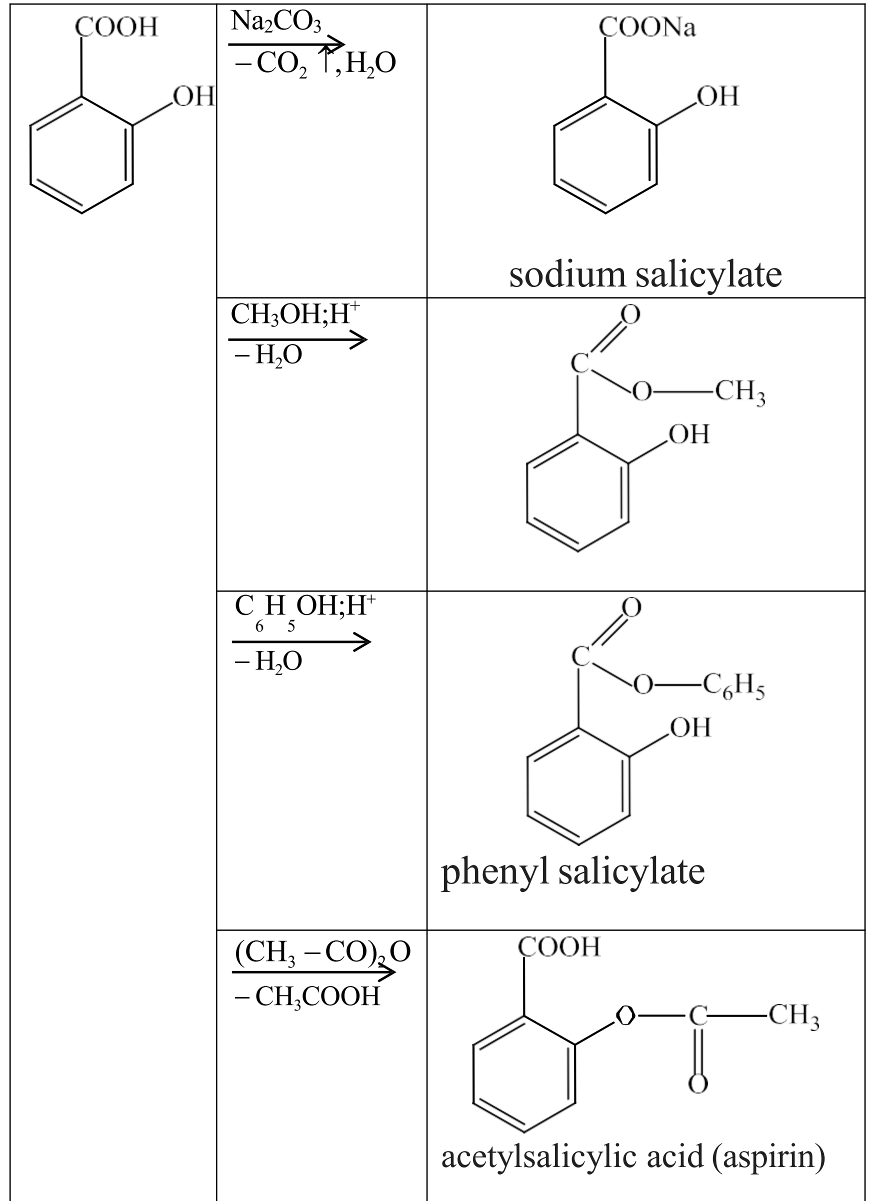
o-hydroxybenzoic acid

Occurs in natural products, usually in the form of methyl salicylate. Is used in medicine, in analytical chemistry and food industry .

Chemical properties of phenol acids:

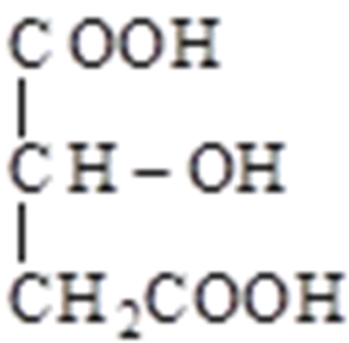


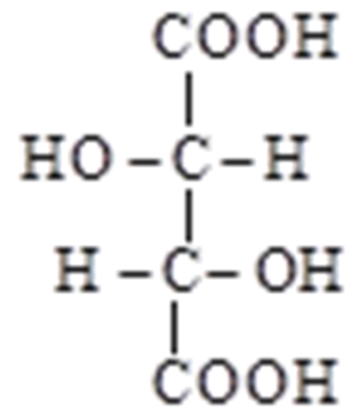
Aspirin, also known as *acetylsalicylic* acid (ASA), is a medication used to treat pain, fever, or inflammation



Poly heterofunctional compounds are the compounds that contain more than two different functional groups

- **The malic acid** is a dicarboxylic acid that is made by all living organisms, contributes to the sour taste of fruits, and is used as a food additive. The malic acid was first isolated from apples. The name "malic" derives from Latin, with "malus" meaning "apple",
- **Tartaric acid** is a white, crystalline organic acid that occurs naturally in many fruits, most notably in grapes, but also in bananas, tamarinds, and citrus. Its salt, potassium bitartrate, commonly known as cream of tartar, develops naturally in the process of winemaking.





Oxoacids

Oxo acids include aldehydo- and ketono acids. These compounds include in the structure the carboxyl group, aldehyde functional group or ketone functional group.

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

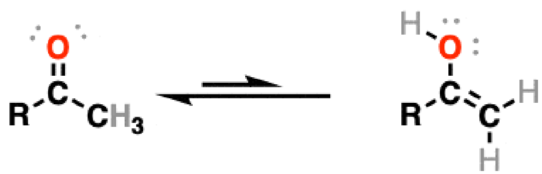
Keto-Enol Tautomerism

Many ketones and aldehydes have an alter-ego “enol” form with completely different chemical properties than the familiar “keto” form. In this article we’ll explore the structure and properties of this “enol” form, go through the mechanism for the keto-enol transformation, and describe some of the key factors that can affect the keto-enol equilibrium.

Summary - Keto-Enol Tautomerism

Keto-enol tautomerism is an equilibrium between an aldehyde or ketone and a structural isomer, called the **enol** form.

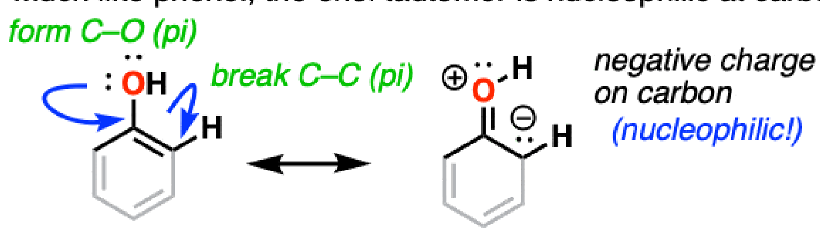
Keto-enol tautomerism



“Keto” tautomer **“enol” tautomer**

Bonds Formed	Bonds Broken
C–C (pi)	C–O (pi)
O–H	C–H

This is equilibrium, **not** resonance. Keto-enol tautomerism can’t occur if a proton on the alpha carbon cannot be removed.
Much like phenol, the enol tautomer is nucleophilic at carbon.



resonance form

- Equilibrium generally favors the keto tautomer
- Keto-enol tautomerism is catalyzed by acid or base.
- Several factors can increase the stability of the enol tautomer, such as substitution, resonance, hydrogen bonding and aromaticity.

Hydroxy and oxoacids play significant biological roles in various metabolic processes and therapeutic applications. Here are some key points regarding their biological functions:

1. **Receptor Interaction**: Hydroxy-carboxylic acids have been identified as endogenous ligands for specific G protein-coupled receptors (GPR81, GPR109A, and GPR109B). These receptors are part of a novel family known as hydroxy-carboxylic acid (HCA) receptors, which are involved in various physiological processes, including energy metabolism and inflammation regulation.
2. **Metabolic Functions**: Oxoacids, particularly 2-oxoacids (also known as α-ketoacids), are crucial intermediates in central metabolism. Compounds like pyruvate, oxaloacetate, and 2-oxoglutarate serve as metabolic hubs, connecting various biochemical pathways involving amino acids, carbohydrates, and coenzymes. This interconnectedness is vital for maintaining metabolic homeostasis.
3. **Therapeutic Applications**: Hydroxy acids, such as alpha-hydroxy acids (AHAs) and beta-hydroxy acids (BHAs), are widely used in cosmetic and therapeutic formulations. They are known for their beneficial effects on the skin, including exfoliation, improving skin texture, and treating conditions like acne and hyperpigmentation. Their applications extend to pharmaceutical products aimed at various skin conditions.
4. **Biological Activities of Phenolic Acids**: Among the diverse range of naturally occurring phenolic acids, many hydroxy- and polyhydroxybenzoic acids exhibit significant biological activities. These compounds have been studied for their antioxidant properties and potential health benefits, including anti-inflammatory and anticancer effects.