HETEROFUNCTIONAL COMPOUNDS. Hydroxy acids. Oxo acids.

Senior teacher of General chemistry department

PhD in Physical chemistry

Yanovska Anna Olexandrivna

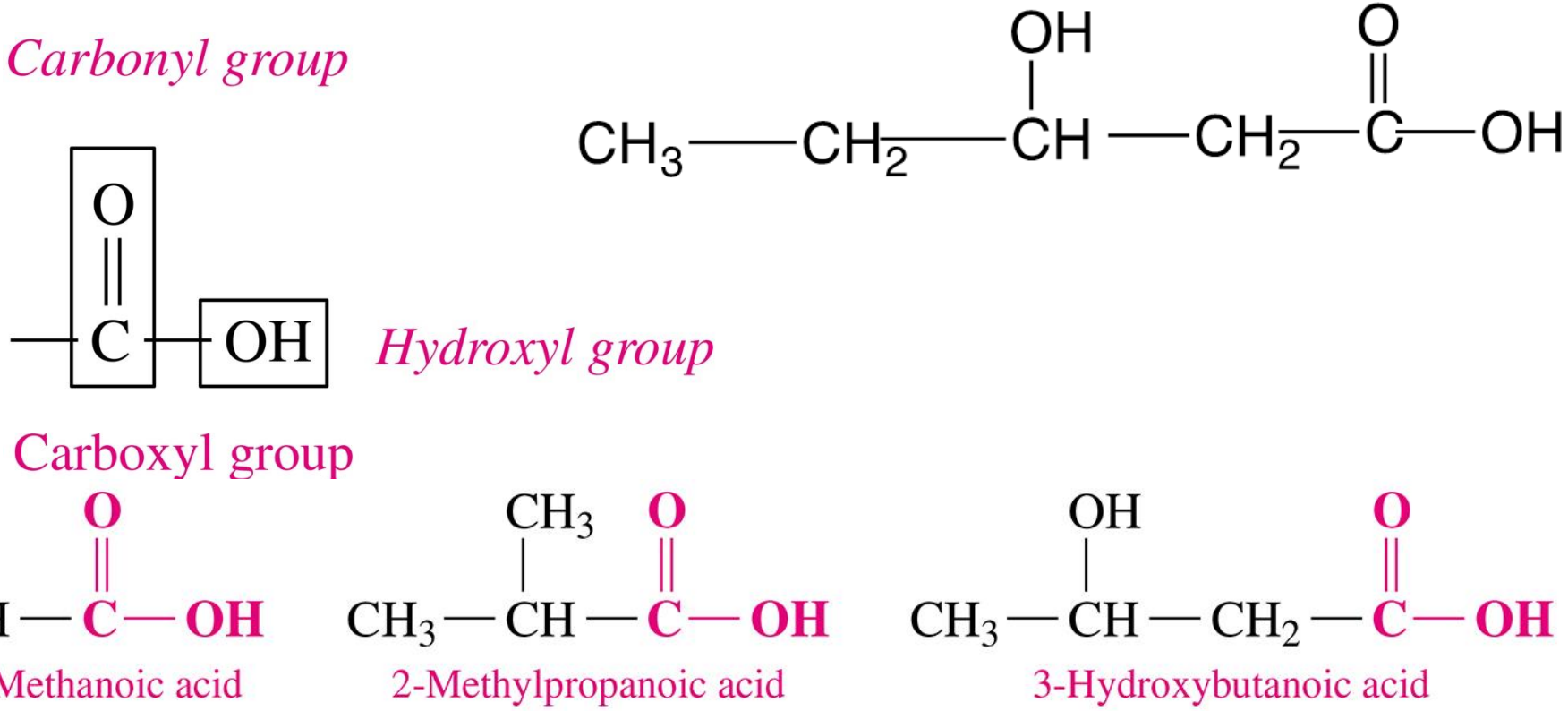
Some types of combining functional groups in heterofunctional compounds

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	$CH_3C(=O)COOH$	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

A carboxylic acid contains a carboxyl group, which consists of a hydroxyl group —OH attached to the carbon in a carbonyl group. Hydroxoacids contain two groups: hydroxyl group and carboxylic group.



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, α-ketoglutaric acid are important in metabolism of carbohydrates.

Several different alpha hydroxy acids may be found in skin care products singly or in combination.

Alpha Hydroxy Acids

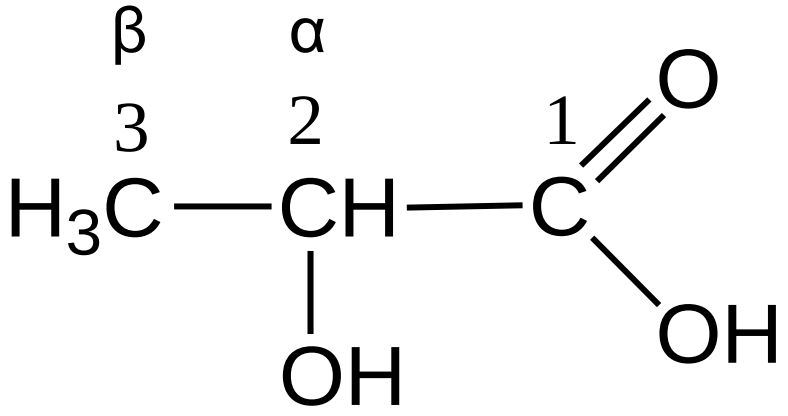
Alpha hydroxy acids (AHAs)

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

Alpha Hydroxy Acid (Source)	Condensed Structural Formula
Glycolic acid (sugar cane)	$HO-CH_2-\overset{\overset{O}{\|\|}}{C}-OH$
Lactic acid (sour milk)	$CH_3-\overset{\overset{OH}{\|}}{CH}-\overset{\overset{O}{\|\|}}{C}-OH$
Tartaric acid (grapes)	$HO-\overset{\overset{O}{\|\|}}{C}-\overset{\overset{OH}{\|}}{CH}-\overset{\overset{OH}{\|}}{CH}-\overset{\overset{O}{\|\|}}{C}-OH$
Malic acid (apples)	$HO-\overset{\overset{O}{\|\|}}{C}-CH_2-\overset{\overset{OH}{\|}}{CH}-\overset{\overset{O}{\|\|}}{C}-OH$
Citric acid (citrus fruits)	$HO-\overset{\overset{CH_2-COOH}{\|}}{\underset{\underset{CH_2-COOH}{\|}}{C}}-COOH$

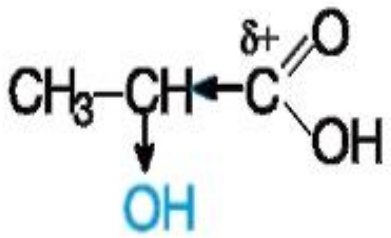
Hydroxy acids

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

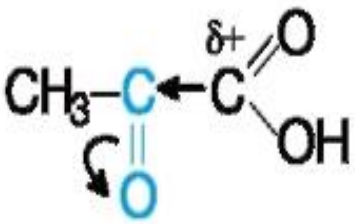


2-hydroxypropanoic acid
α-hydroxypropanoic acid

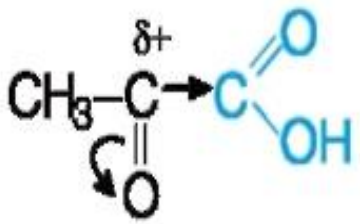
Electronic effects



–*I* effect of the hydroxyl group

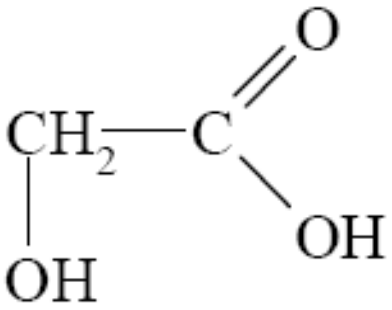


–*I* effect of the oxo group

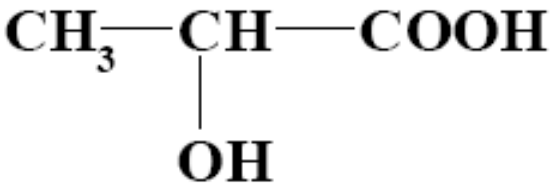


–*I* effect of the carboxyl group

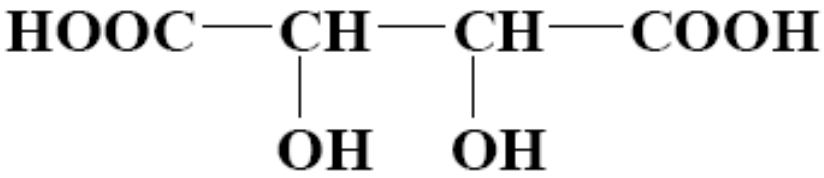
- When the functional groups are close to each other their interaction is more sharply pronounced. This may be illustrated by comparing acidic and electrophilic properties of some heterofunctional carboxylic acids.
- In the aliphatic series, all groups are electron-withdrawing substituents, therefore one group has an influence on another. Thus, lactic and pyruvic acids are stronger (pKa 3.9 and 2.4, respectively) than propionic acid (pKa 4.9) The hydroxyl group in lactic acid and the oxo group in pyruvic acid decrease an electron density on the carboxylic carbon (the leftmost and middle structures below).



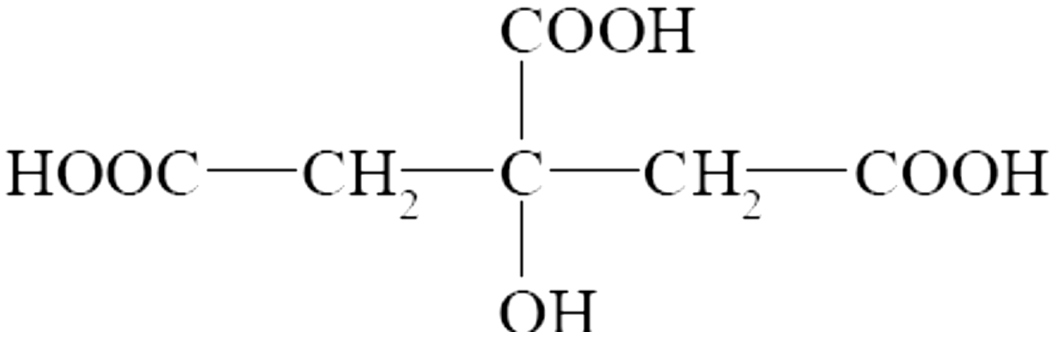
glycolic acid,
hydroxyacetic acid,
hydroxyethanoic acid



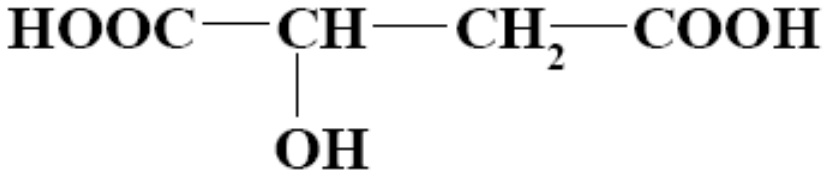
lactic acid,
α- hydroxypropanoic acid,
2- hydroxypropanoic acid



tartaric acid
α,α'-dihydroxysuccinic acid,
2,3-dihydroxybutanedioic acid,



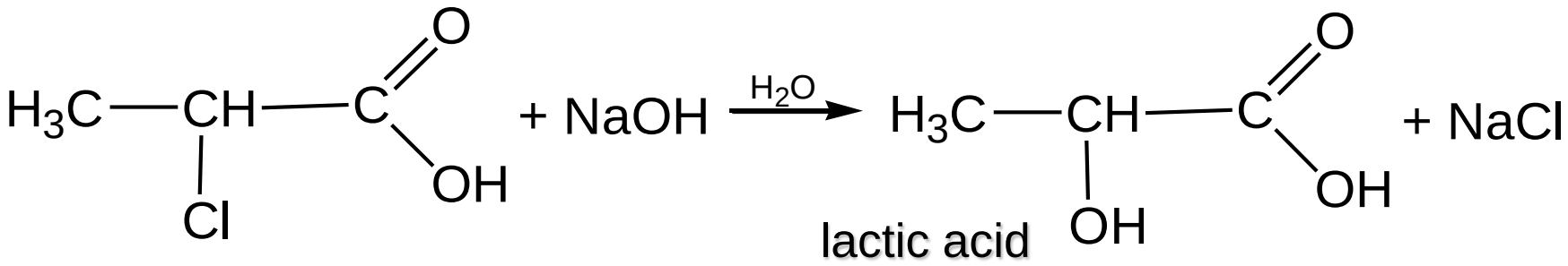
citric acid,
3-carboxy-3-hydroxy-pentanedioic acid



malic acid,
hydroxysuccinic acid
hydroxybutanedioic acid

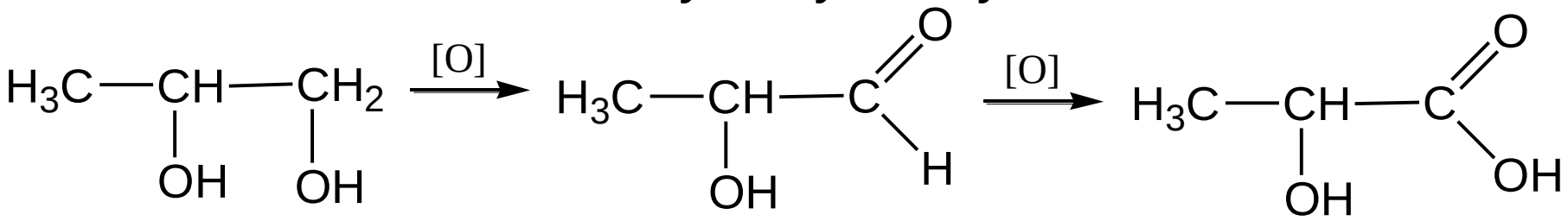
Methods of preparation of hydroxyacids:

1. Hydrolysis of α-halogenoacids

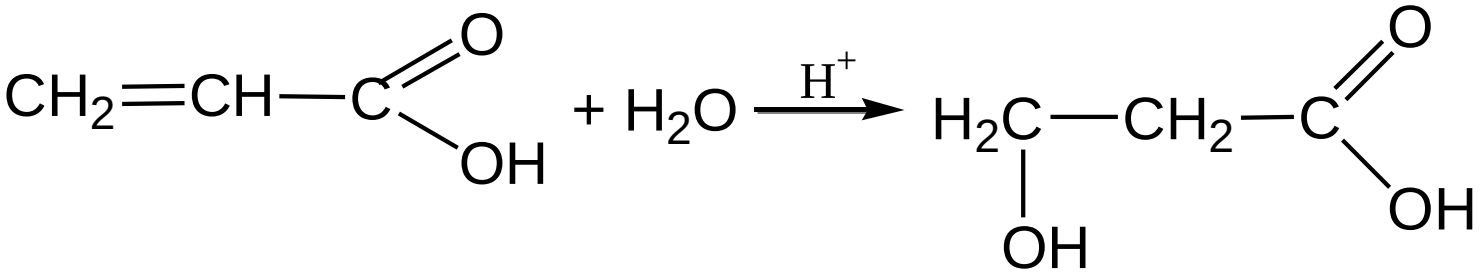


lactic acid

2. Oxidations of diols and hydroxyaldehydes

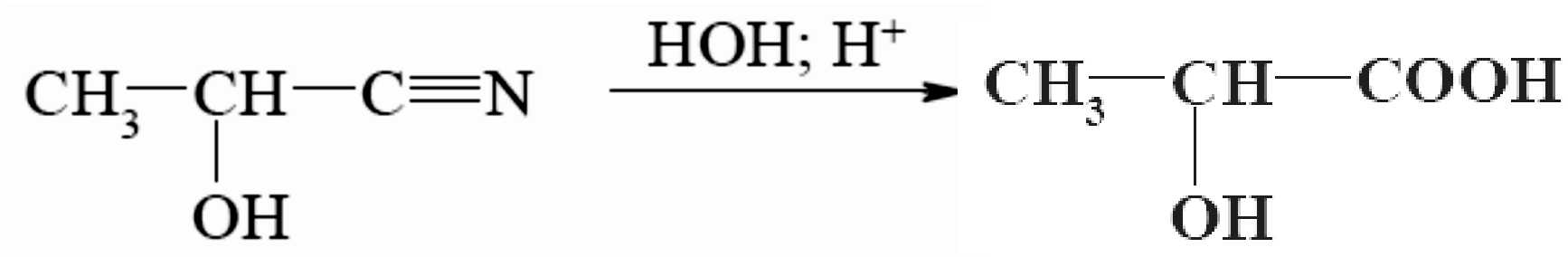


3. Hydration of α,β-unsaturated carboxylic acids



β-hydroxypropanoic acid

4. Hydrolysis of hydroxynitriles (cyanohydrins)



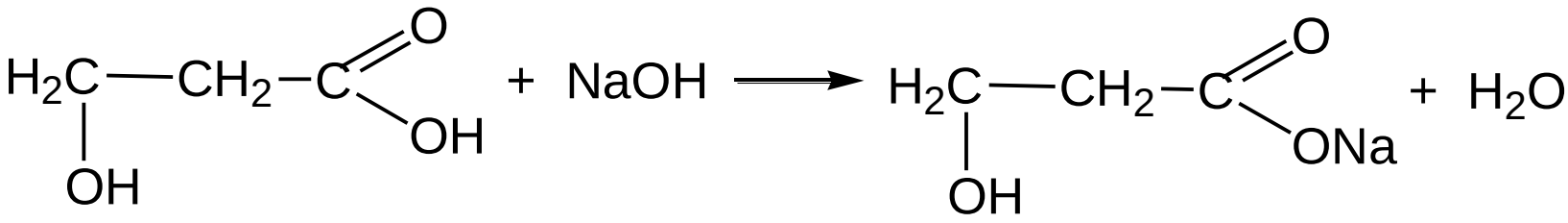
Physical and chemical properties of hydroxycarboxylic acid

For <u>physical properties</u> of hydroxycarboxylic acids are colorless liquids or crystalline substance, soluble in water.

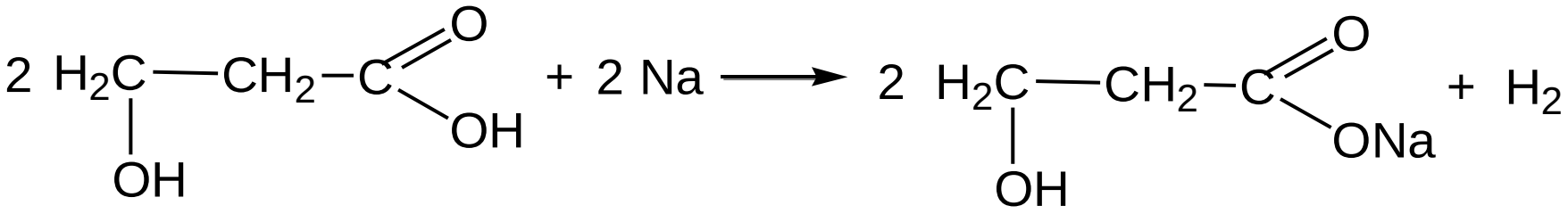
<u>Chemical properties:</u> in the molecule of hydroxyacids ether – OH group or carboxyl group can react.

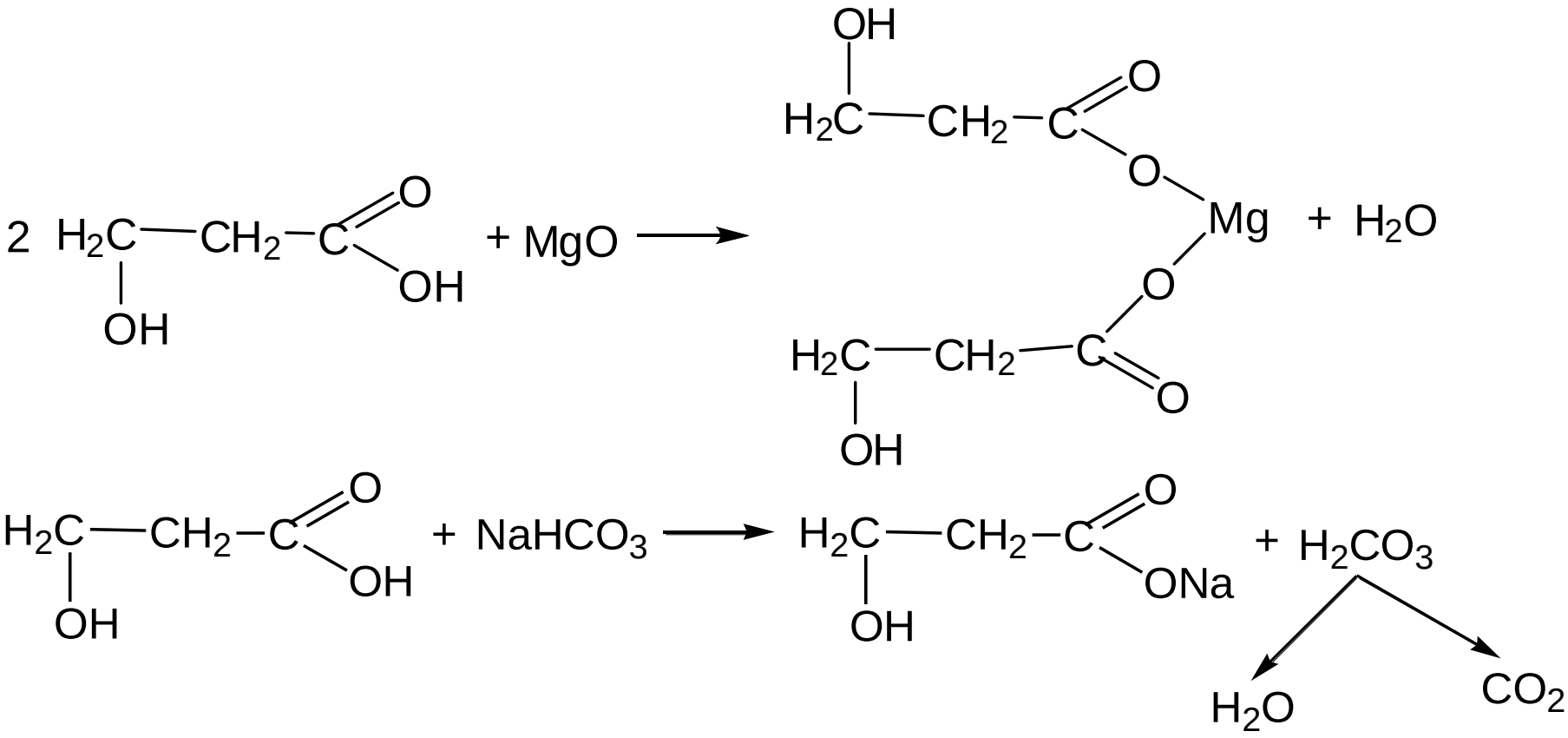
Carboxyl group can react forming:

a) salts:

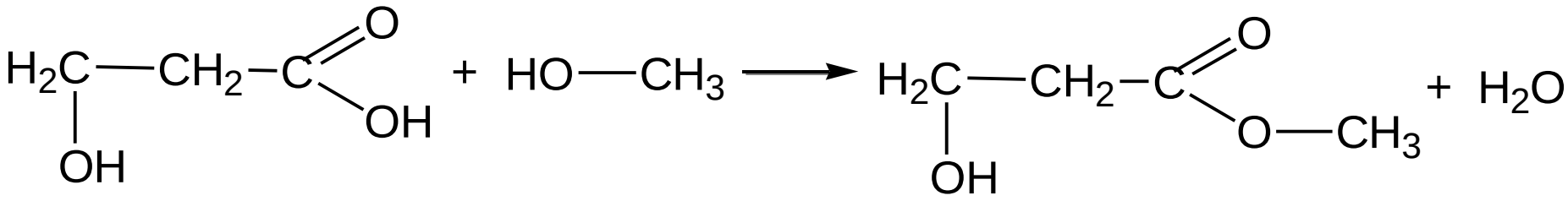


sodium β-hydroxypropanoic acid



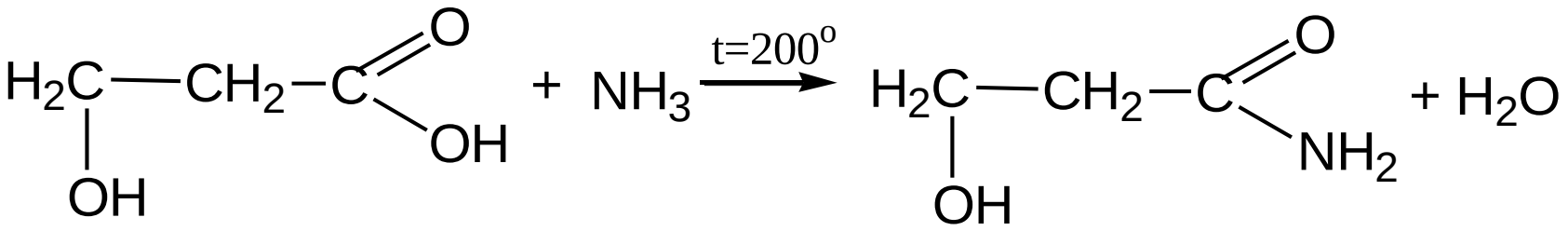


b) Ester formation:



Methyl-β-hydroxypropanoate

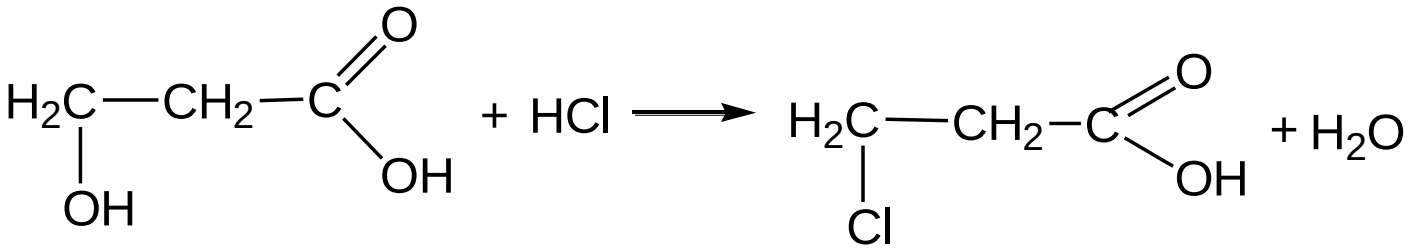
c) Amides formation:



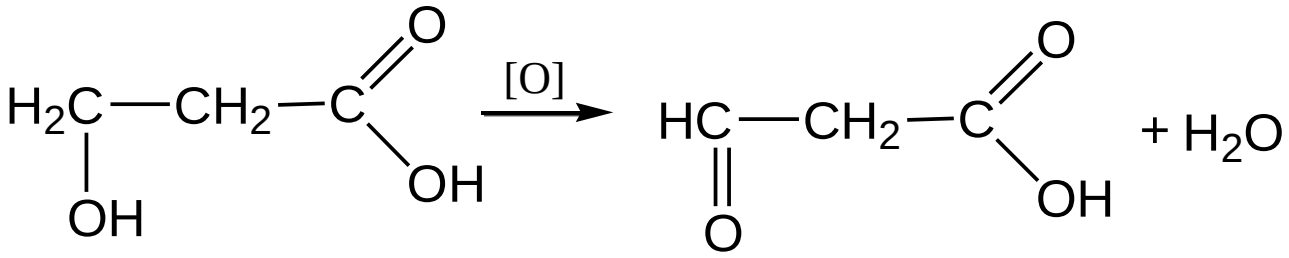
amide of β-hydroxypropanoic acid

II. –OH group reaction:

a) hydrohalogens (HCl, HBr, HI, HF)



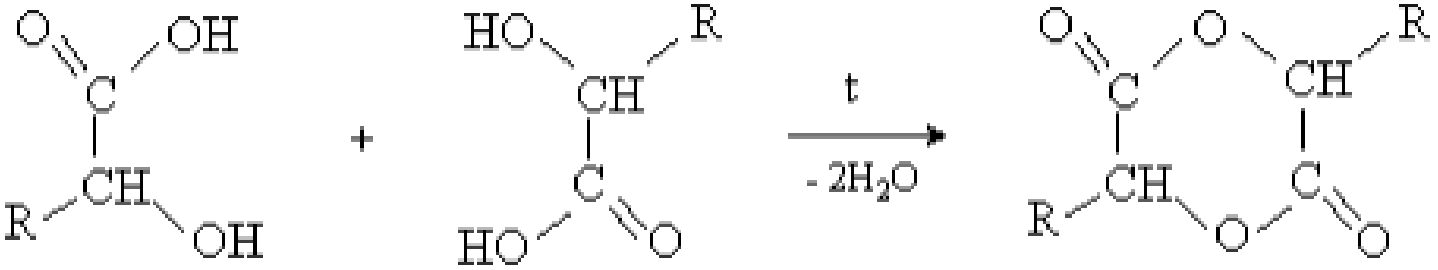
b) can oxidize



β-oxopropanoic acid

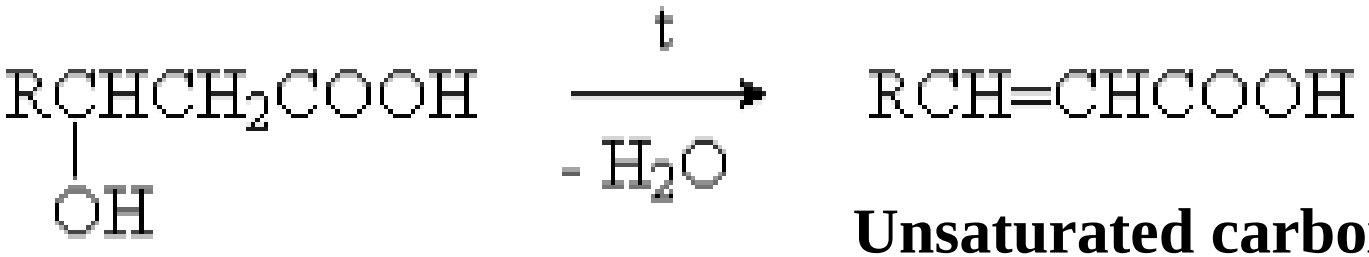
Related to heat of:

1. α-hydroxyacids



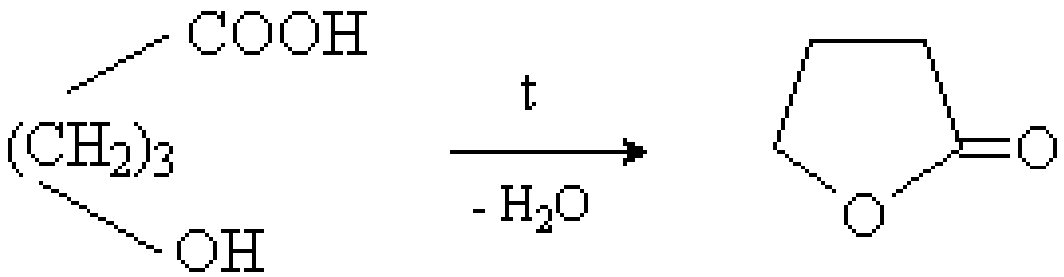
lactic acid if R-CH_3 **lactide**

2. β-hydroxyacids



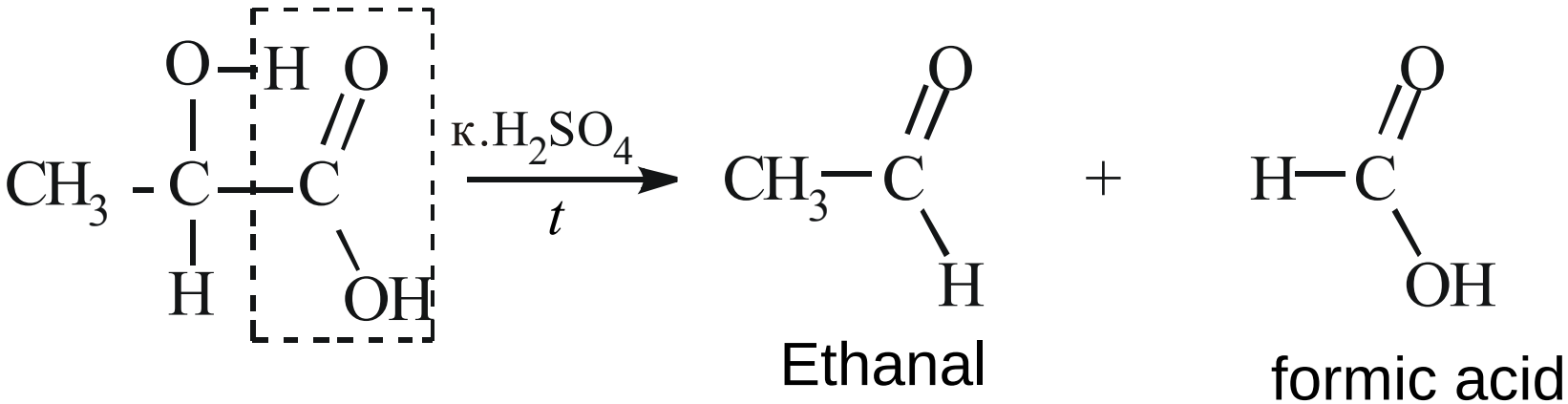
Unsaturated carboxylic acids

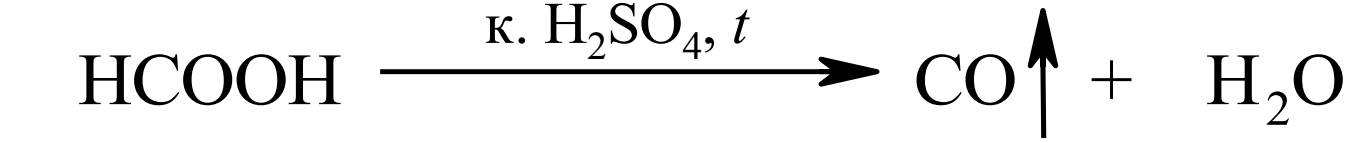
3. γ-hydroxyacids

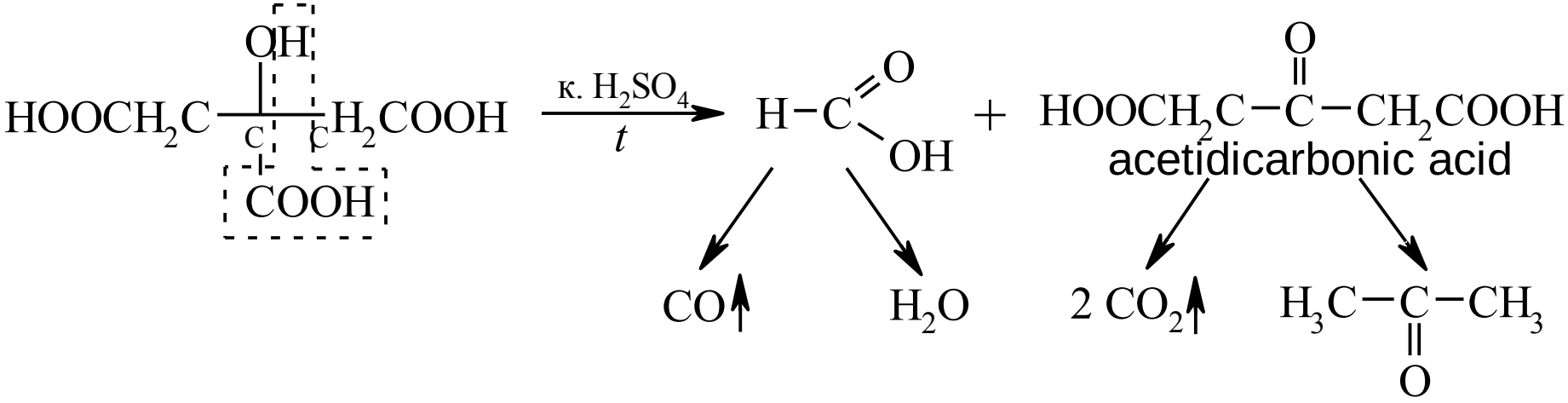


butyrolactone

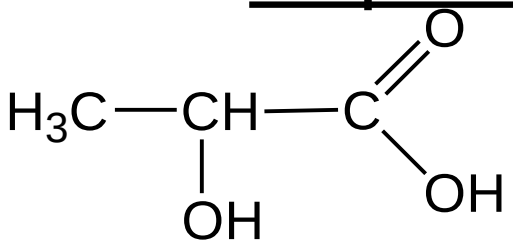
Decomposition α-hydroxyacids



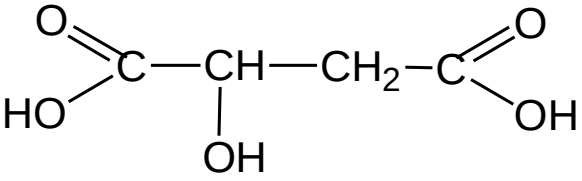




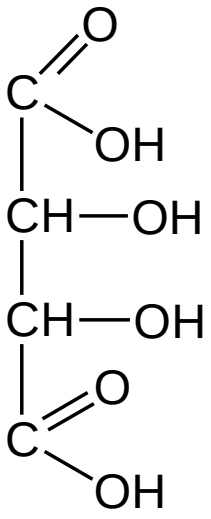
Representatives of hydroxyacids:



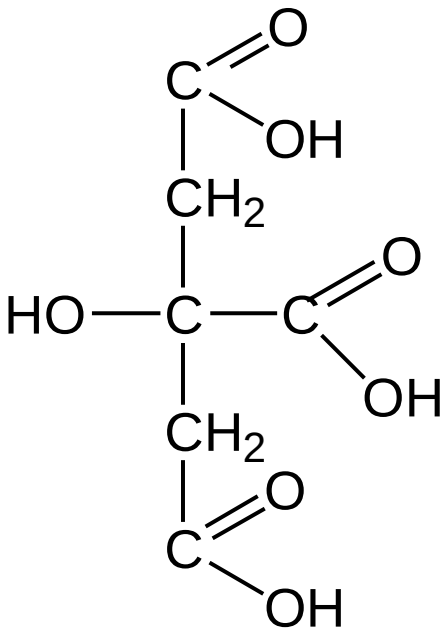
lactic acid. lactic acid is a trivial name because at first it was extracted from milk. It is present in yogurt, sour milk and other milk products. It can form in muscles during hard and prolonged work. Salts of milk acid are used in medicine.



Malic acid. It is present in green apples and some berries. It takes part in biological processes in human organisms and organisms of other alive creatures. It is used medicine for synthesis of some medical preparations.



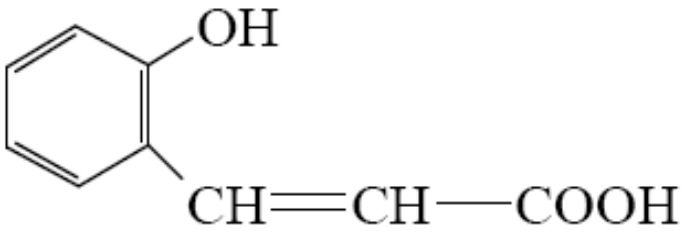
Tartaric acid . It is present in grape. It is used in medicine for synthesis of some medical preparations.



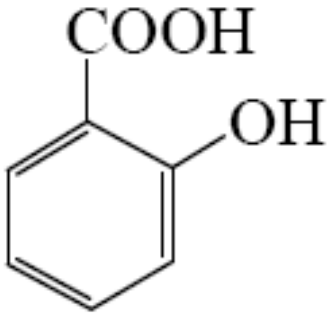
Citric acid . It is present in orange, lemon and other citric fruits. It takes part in biological processes in human organism.

Aromatic hydroxy acids.

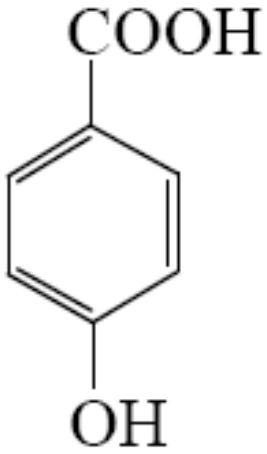
Phenolacids are the derivatives of aromatic carboxyl acids that contain –OH group (1 or more).



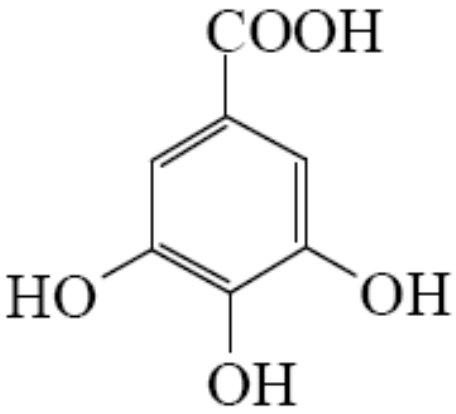
o-hydroxycinnamic acid



salicylic acid,
2-hydroxybenzoic acid



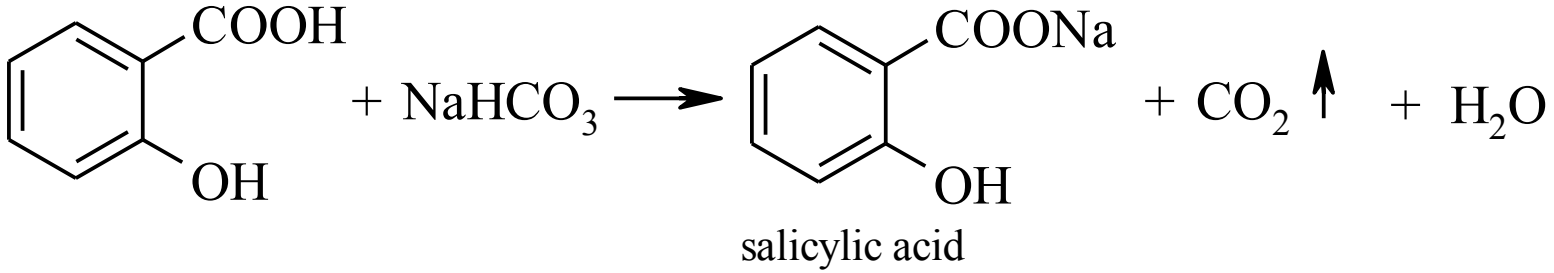
4-hydroxybenzoic acid



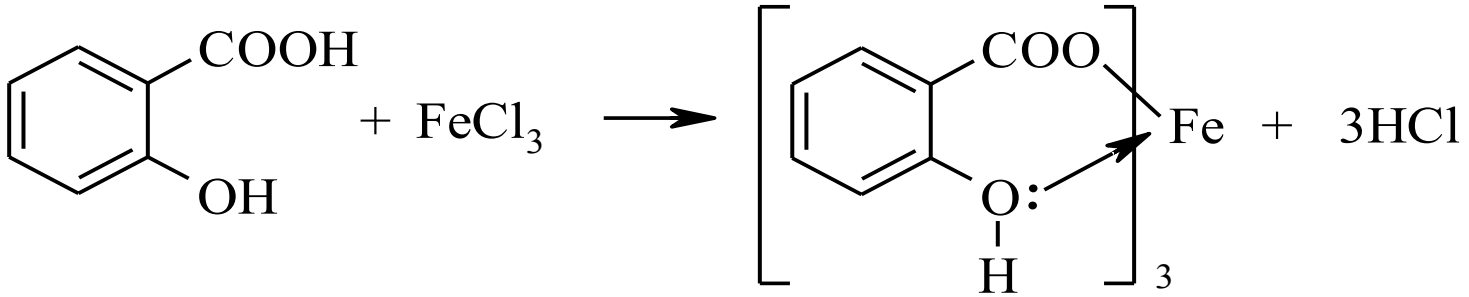
3,4,5-trihydroxybenzoic acid,
gallic acid

Chemical properties of phenolacids:

Chemical properties of phenolacids due to the presence in their structure of carboxyl group, phenolic hydroxyl and the aromatic nucleus.

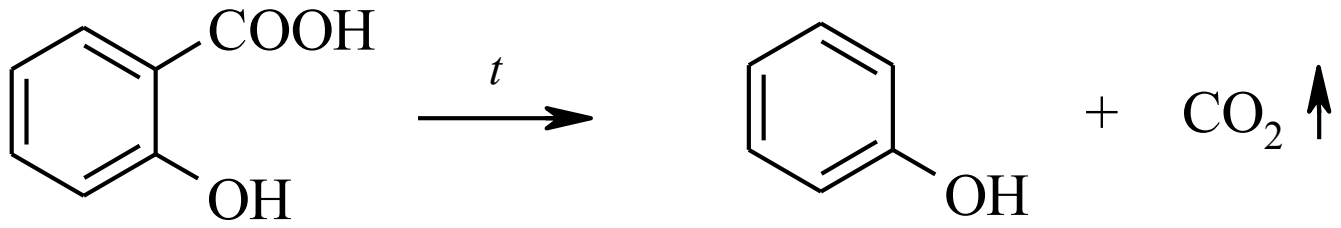


salicylic acid



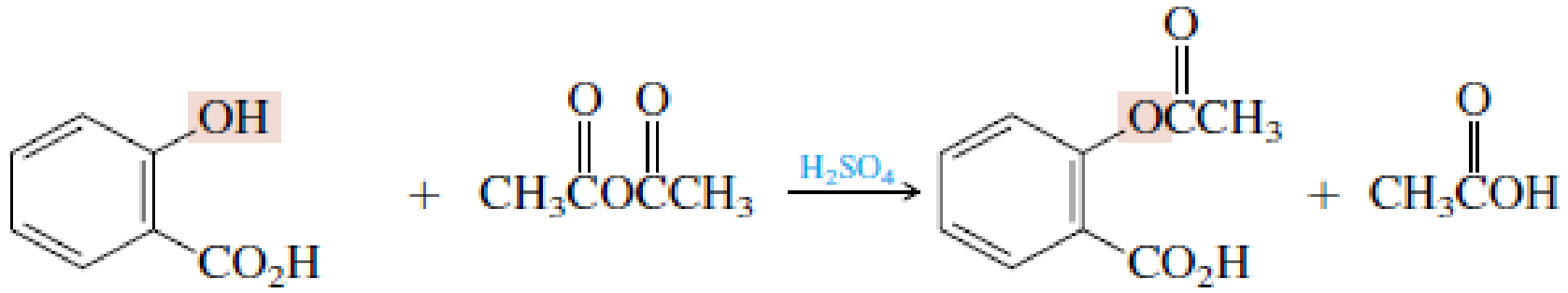
complex helatic salt of salicylic acid (violet colour)

Decarboxylation



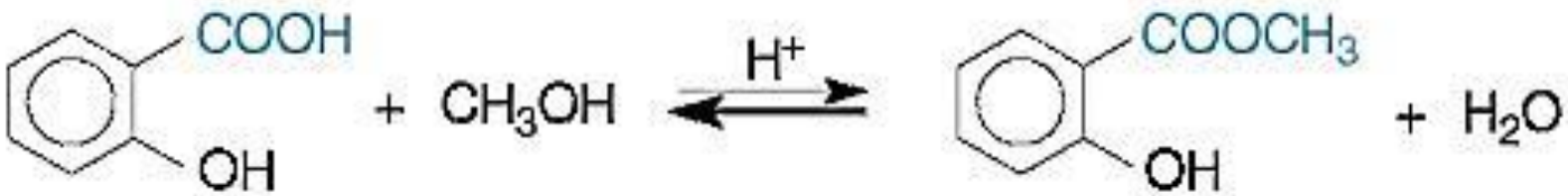
salicylic acid — phenol

O-acetylsalicylic acid, better known as aspirin. It is prepared by acetylation of the phenolic hydroxyl group of salicylic acid:



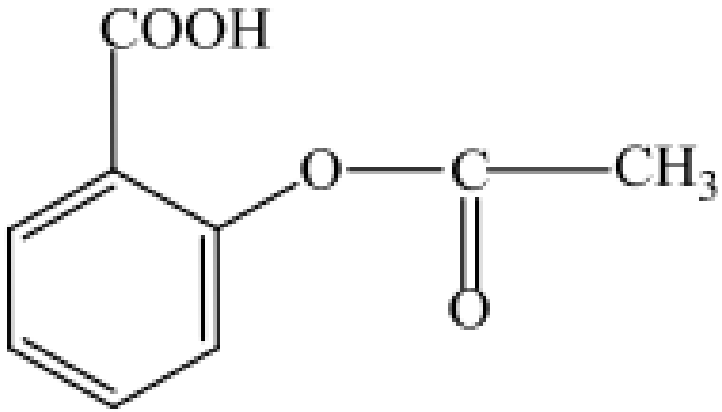
Salicylic acid (*o*-hydroxybenzoic acid) | Acetic anhydride | *O*-Acetylsalicylic acid (aspirin) | Acetic acid

often-recommended drug. It is an analgesic, effective in relieving headache pain. It is also an antiinflammatory agent, providing some relief from the swelling associated with arthritis and minor injuries. Aspirin is an antipyretic compound; that is, it reduces fever. Each year, more than 40 million lb of aspirin is produced in the United States, a rate equal to 300 tablets per year for every man, woman, and child.

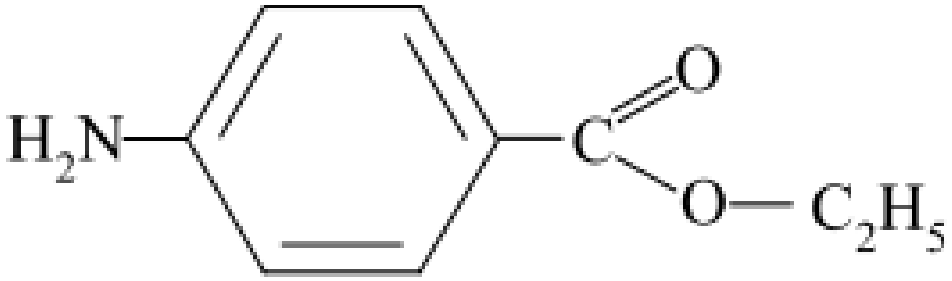


salicylic acid | methyl salicylate

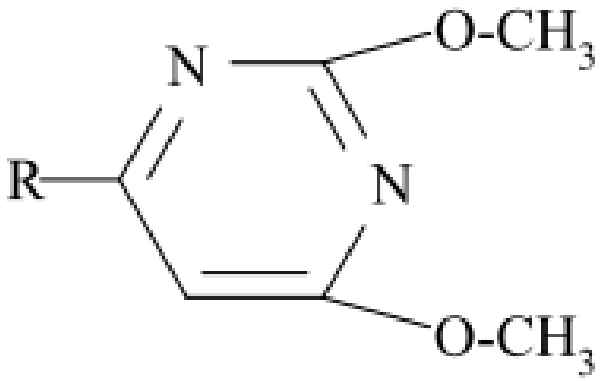
Important in medicine



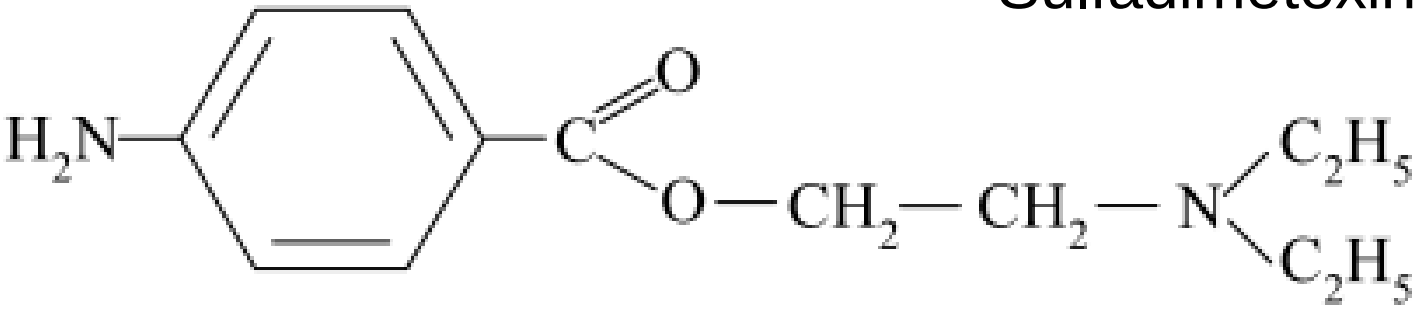
Aspirine



Anesthesin



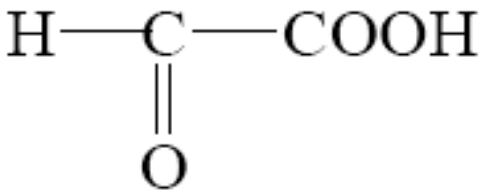
Sulfadimetoxine



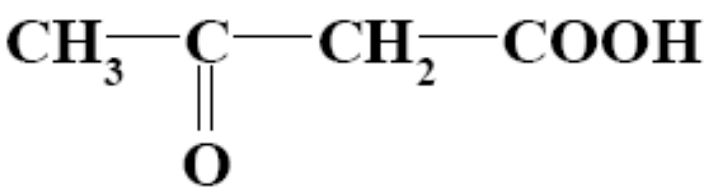
Novocaine

Oxoacids

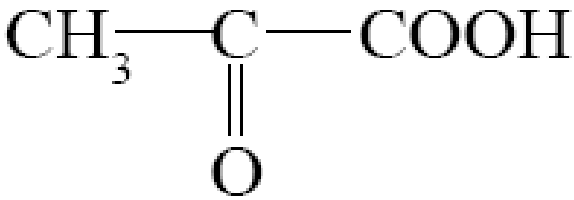
To oxoacids include aldehydo- and ketonoacids. These compounds include in the structure of the carboxyl group, aldehyde functional group or ketone functional group.



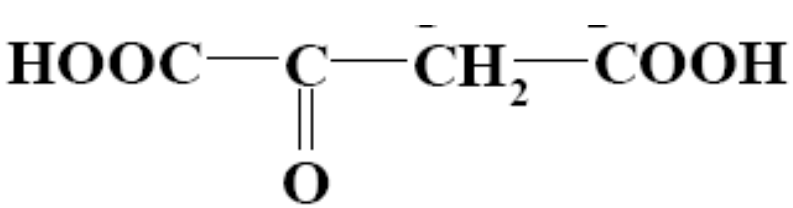
glyoxylic acid, oxoethanoic acid



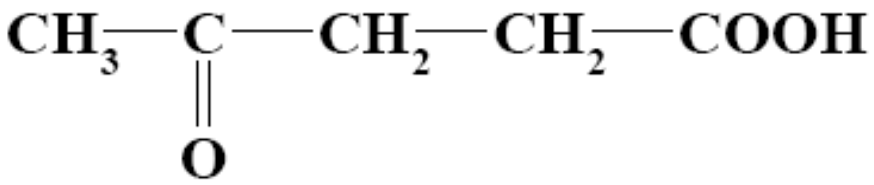
acetoacetic acid, 3-oxobutanoic acid, *β*-ketobutyric acid



pyroracemic acid, 2-oxopropanoic acid

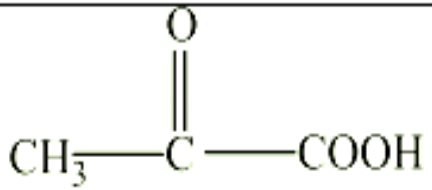
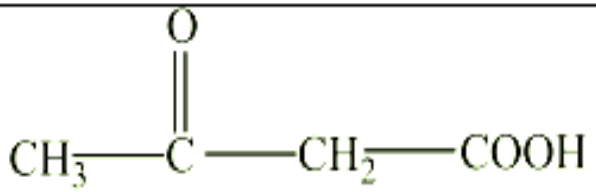
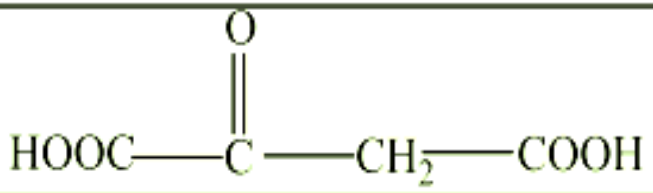
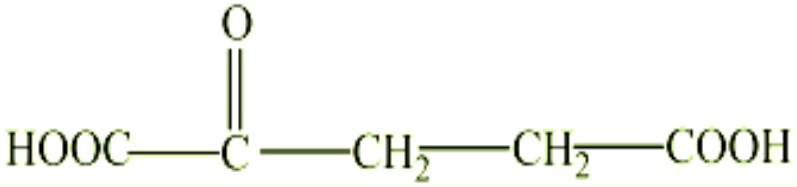


oxalacetic acid, oxobutanedioic acid, ketosuccinic acid



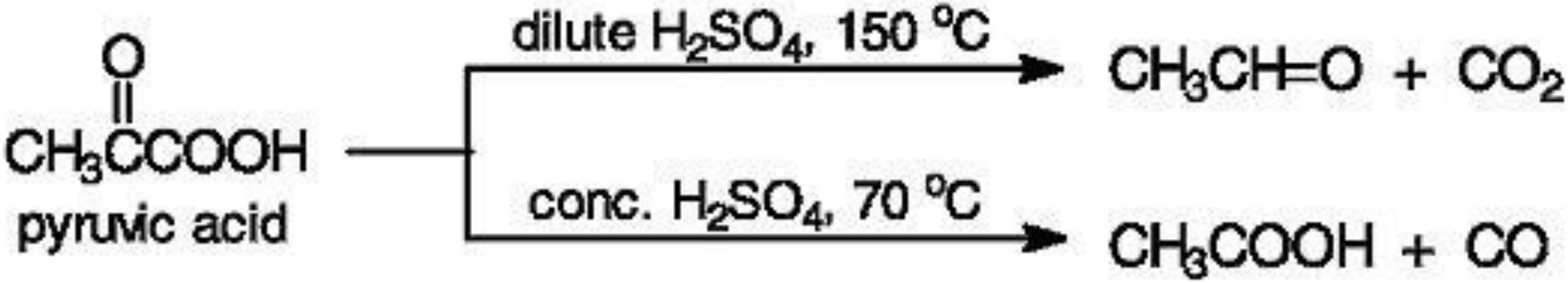
γ-ketovaleric acid, 4-oxopentanoic acid, levulinic acid

Aldehydic and ketonic acids

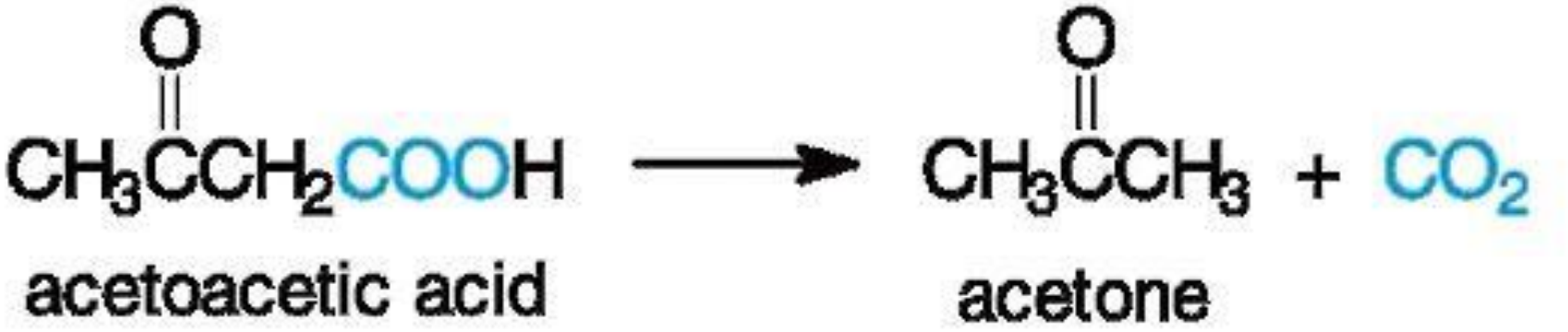
Formula	Name
	**Pyruvic acid**
	**Acetoacetic acid**
	**Oxaloacetic acid**
	α- ketoglutaric acid

Chemical properties of oxoacids

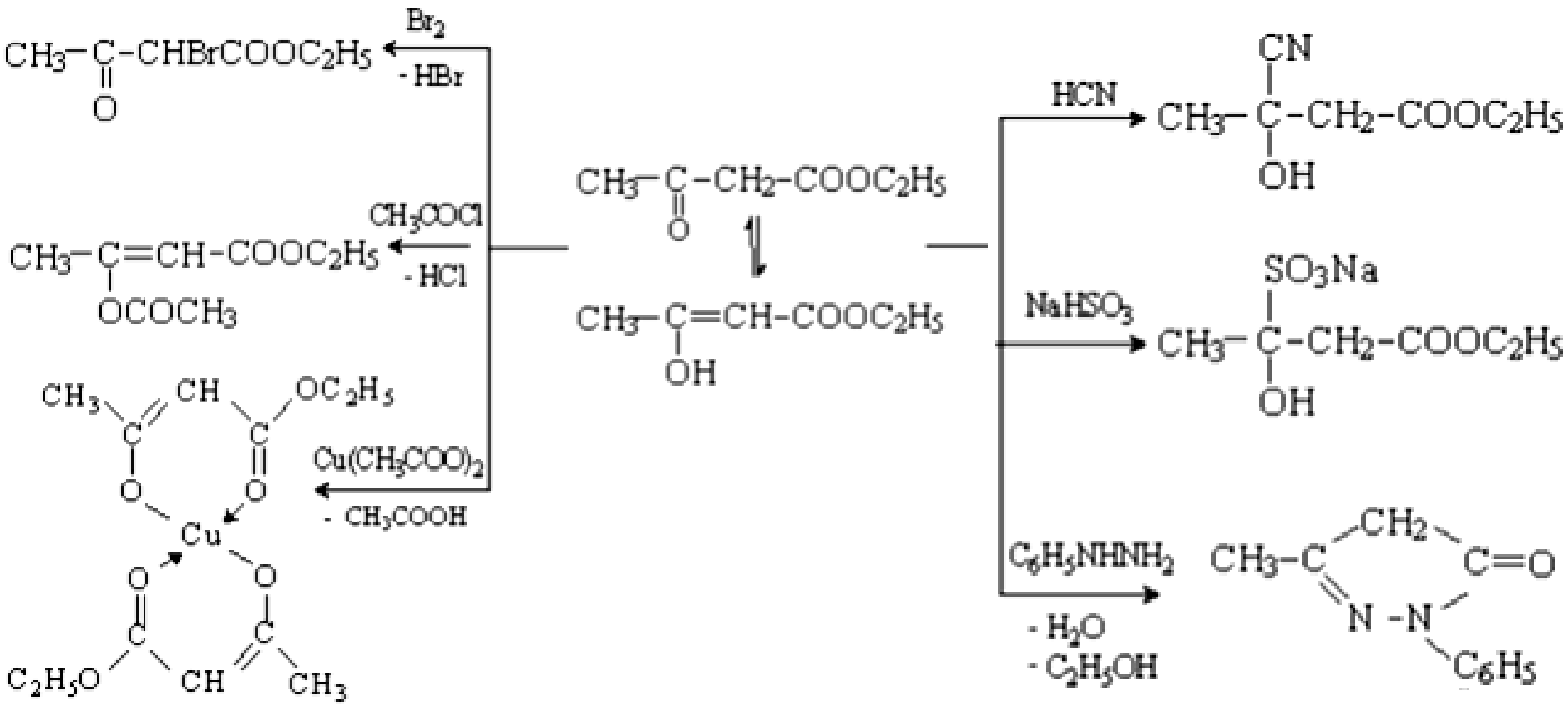
1. Decarboxylation of α-oxoacids

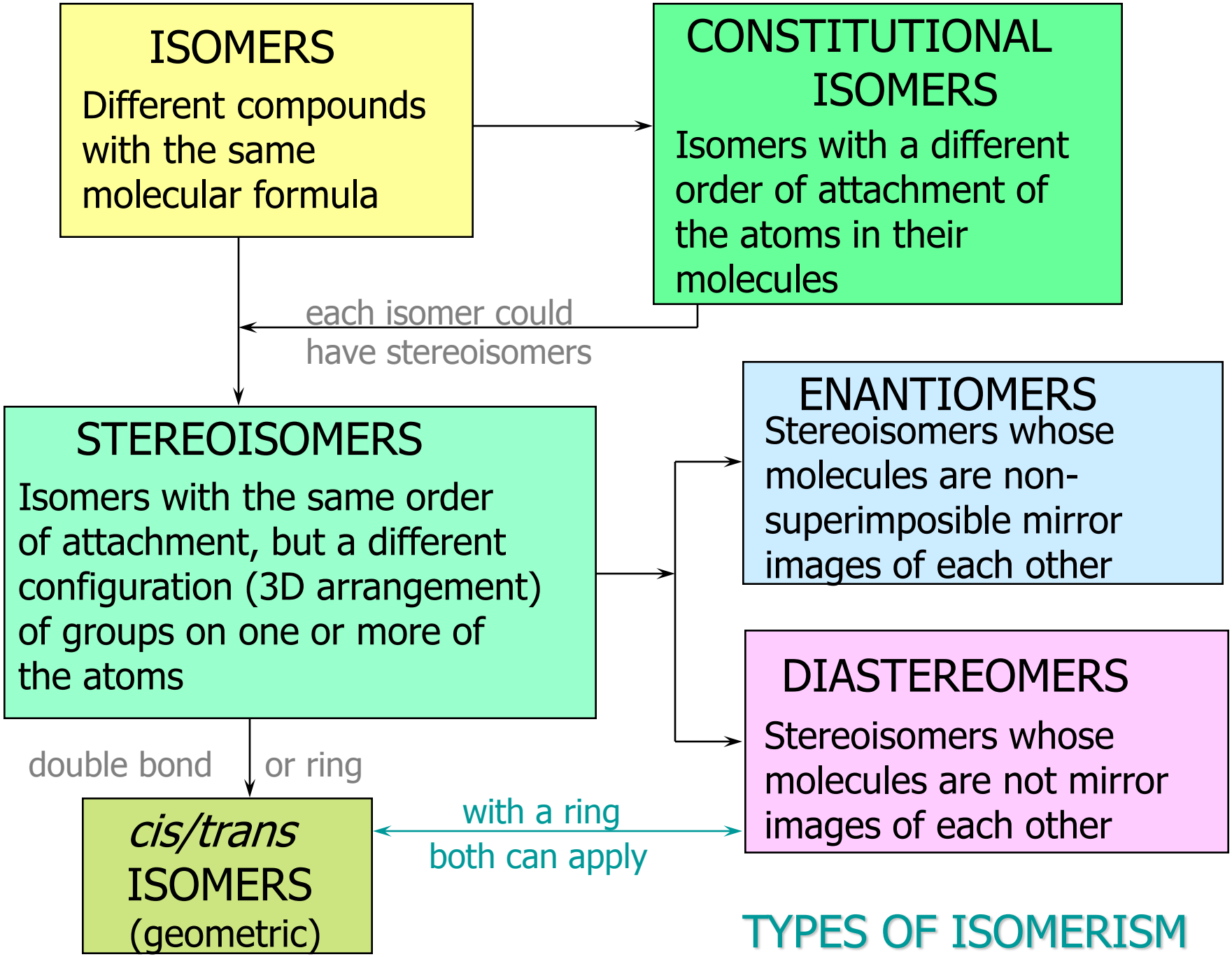


2. Decarboxylation of β-oxoacids



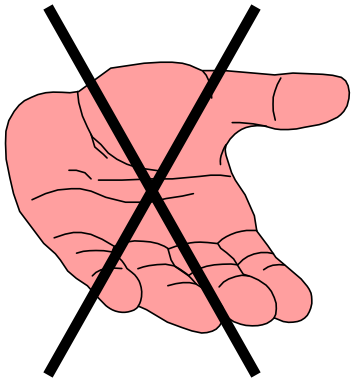
Aldehydic and ketonic acids chemical properties



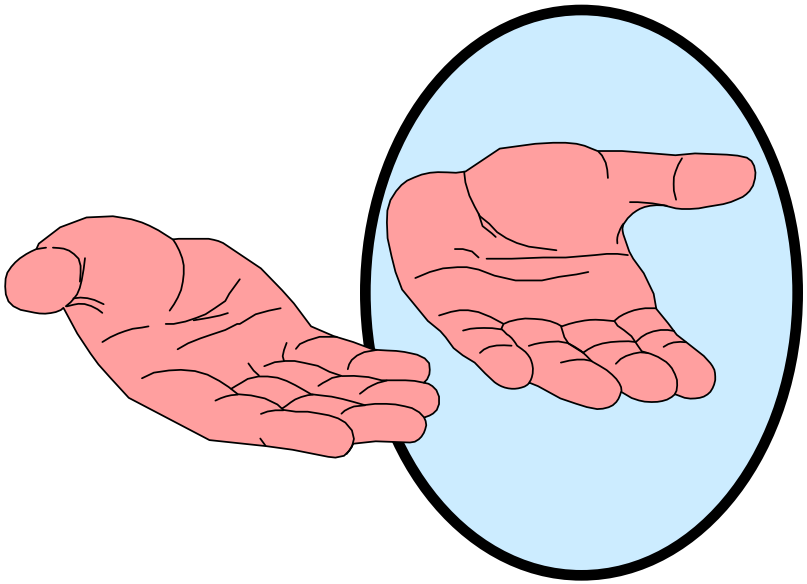

ISOMERS
Different compounds with the same molecular formula
CONSTITUTIONAL ISOMERS
Isomers with a different order of attachment of the atoms in their molecules
each isomer could have stereoisomers
STEREOISOMERS
Isomers with the same order of attachment, but a different configuration (3D arrangement) of groups on one or more of the atoms
ENANTIOMERS
Stereoisomers whose molecules are non-superimposible mirror images of each other
DIASTEREOMERS
Stereoisomers whose molecules are not mirror images of each other
double bond
or ring
cis/trans ISOMERS (geometric)
with a ring
both can apply
TYPES OF ISOMERISM

- Any organic molecule containing a single carbon atom with four different groups attached to it exhibits chirality.
- A **chiral center** is an atom in a molecule that has four different groups tetrahedrally bonded to it. It is **asymmetric** atom.
- **Enantiomers** are stereoisomers whose molecules are nonsuperimposable mirror images of each other.

Chirality

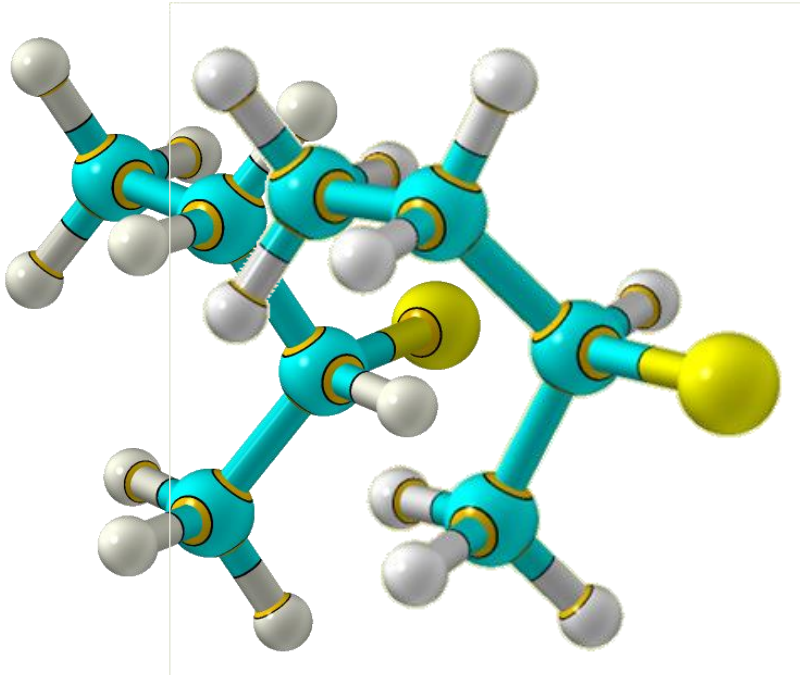


The mirror image of a chiral object is different and will not superimpose on the original object.



Objects which are chiral have a sense of "handedness" and exist in two forms.

Stereoisomers



enantiomers

Stereoisomers that are nonidentical mirror images are called *enantiomers.*

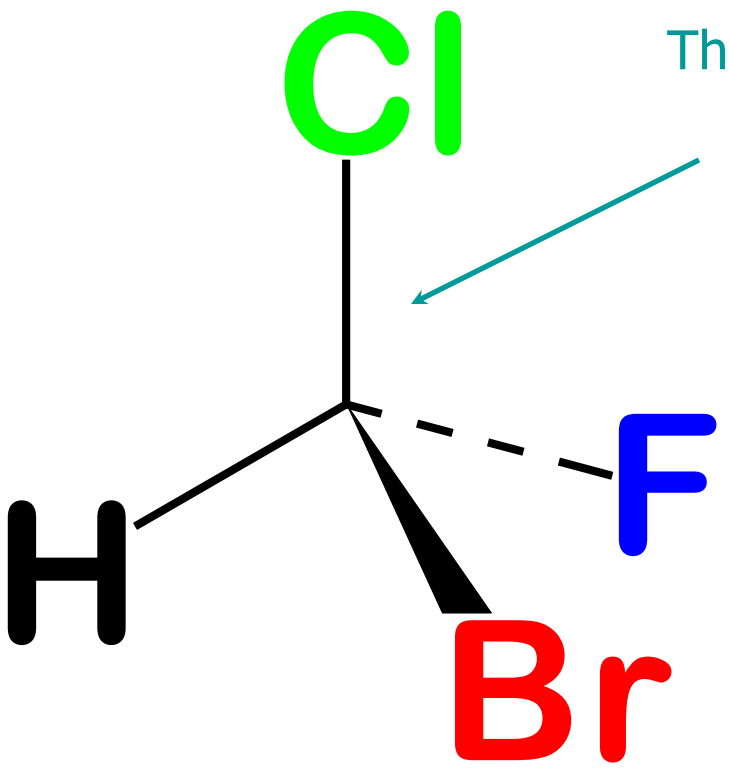
Isomers

- Isomers: different compounds with the same molecular formula
- Constitutional isomers: isomers with a different connectivity
- Stereoisomers: isomers with the same molecular formula, the same connectivity but a different orientation of their atoms in space that cannot be interconverted by rotation about a single bond

Chirality

- A plane of symmetry is a plane that cuts through an object in such a way that one half of the object is an exact mirror image of the other half.
- A molecule that has a plane of symmetry must be identical to its mirror image and therefore must be nonchiral, or achiral.

Stereogenic Carbons



This is one type of ....

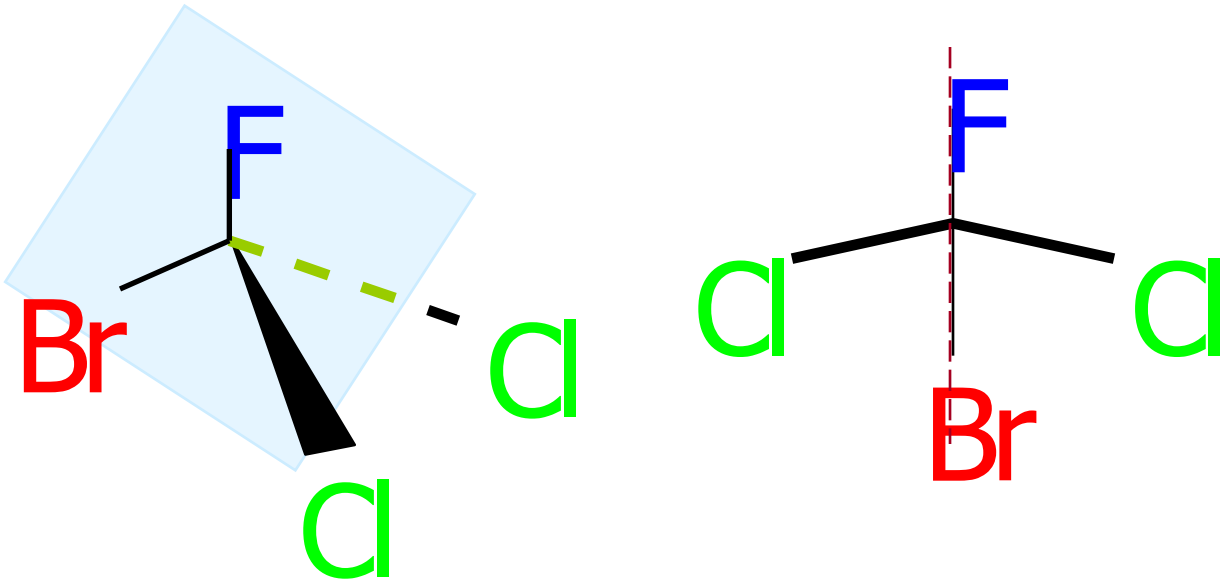
stereocenter

.... others are possible

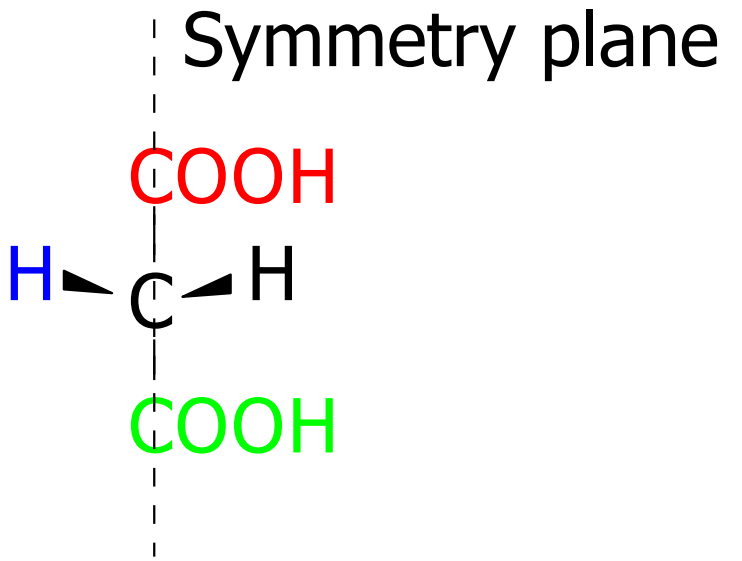
A stereogenic carbon is tetrahedral and has four different groups attached.

Elements of Symmetry

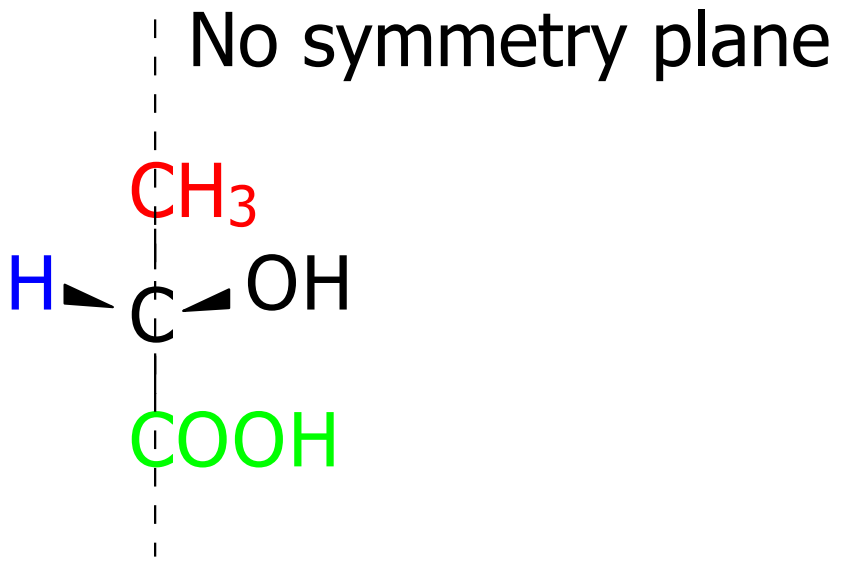
- Plane of symmetry: an imaginary plane passing through an object dividing it such that one half is the mirror image of the other half



Symmetry Plane

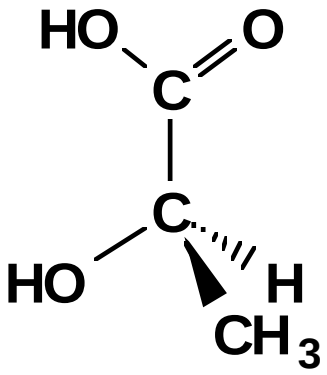


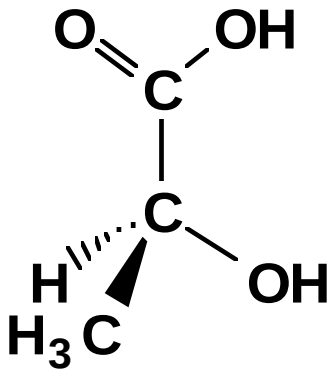
achiral

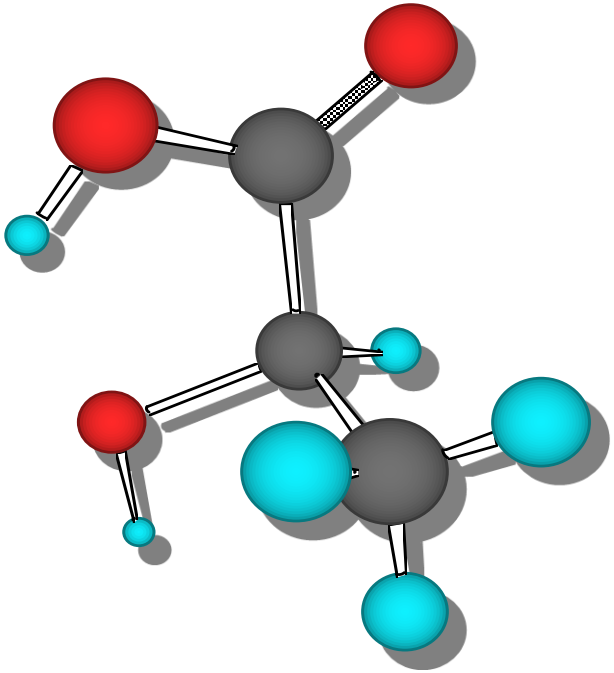


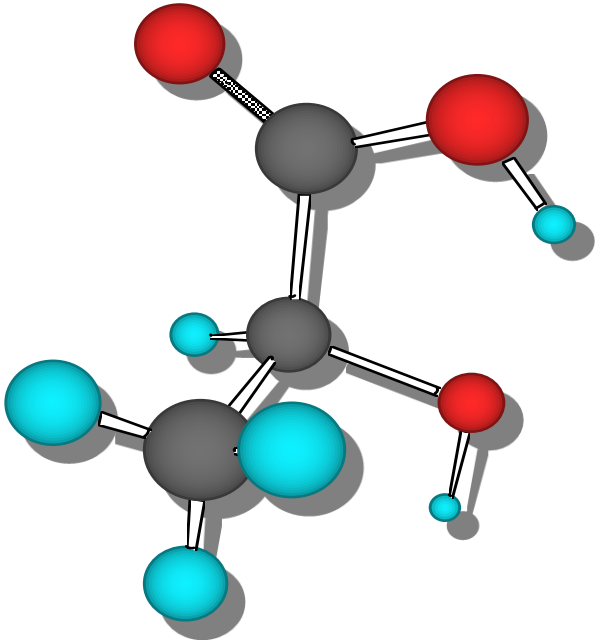
chiral

Enantiomers. Lactic acid



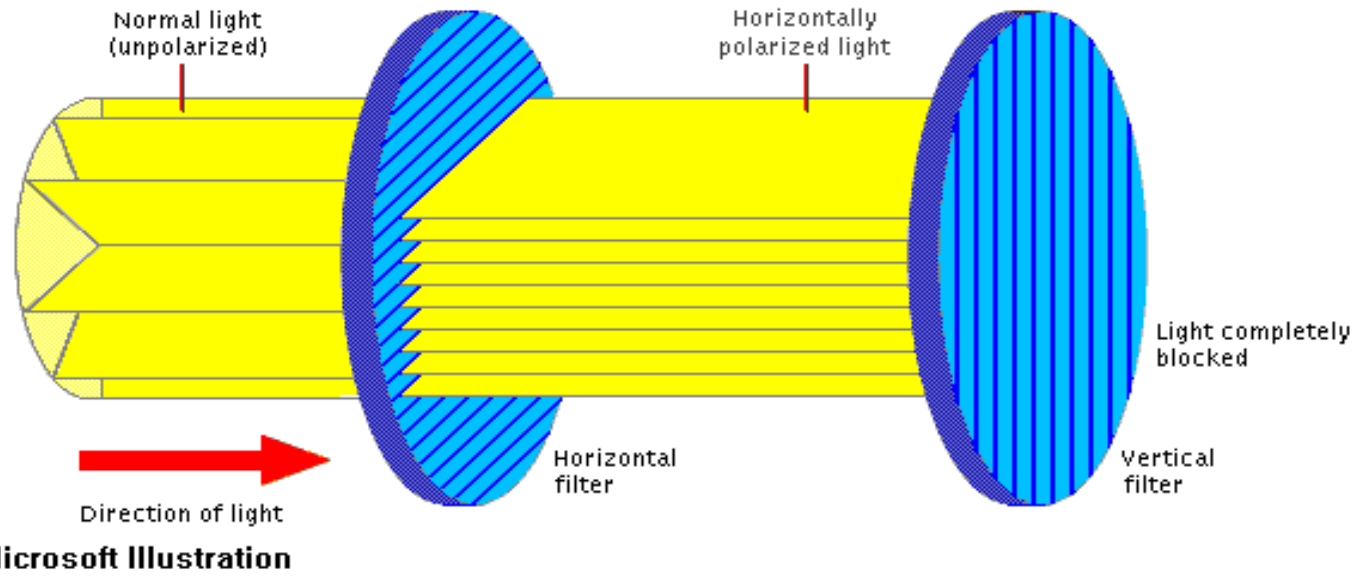






Optical Activity

- optical activity - ability of certain molecules to rotate plane polarized light



- detected using a polarimeter

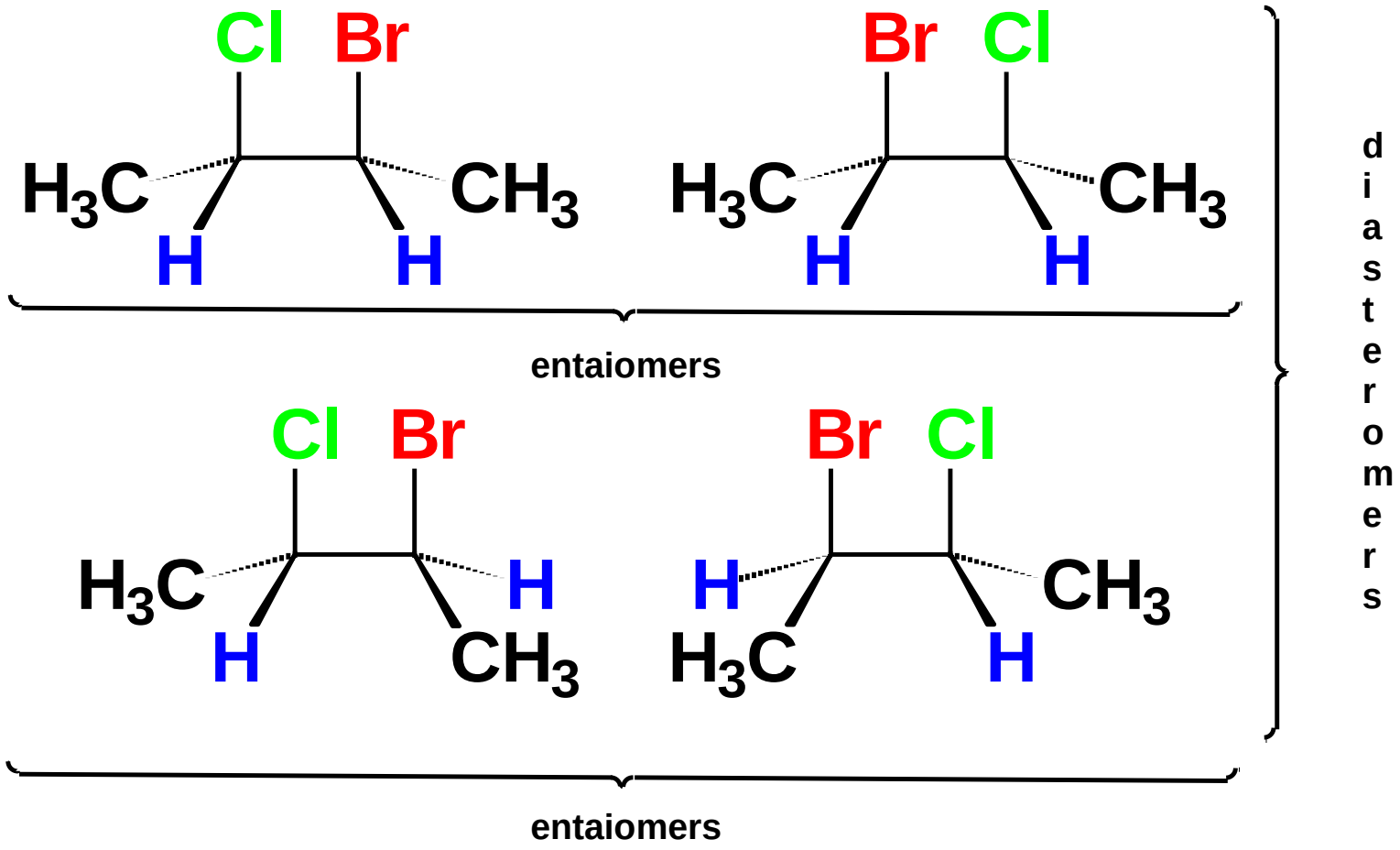
Optical Activity

- Observed rotation: the number of degrees, α, through which a compound rotates the plane of polarized light
- Dextrorotatory (+): rotation of the plane of polarized light to the right
- Levorotatory (-): rotation of the plane of polarized light to the left

Diastereoisomer

- Enantiomers: opposite configurations at all stereogenic centers.
- Diastereomers: Stereoisomers that are not mirror images of each other. Different configuration at some locations.

Two Stereocenters



Enantiomers & Diastereomers

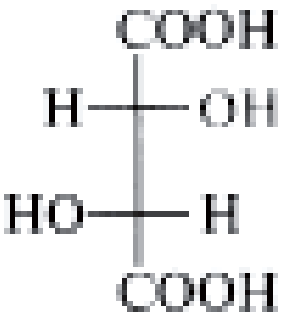
- For a molecule with 1 stereocenter, 2 stereoisomers are possible
- For a molecule with 2 stereocenters, a maximum of 4 stereoisomers are possible
- For a molecule with n stereocenters, a maximum of 2^n stereoisomers are possible
- 2^{n-1} pairs of enantiomers

Racemic Mixture

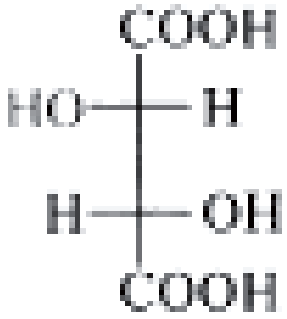
- Racemic mixture (d,l;±): an equimolar mixture (50:50) of two enantiomers
  - because a racemic mixture contains equal numbers of dextrorotatory and levorotatory molecules, its specific activity is zero.

Properties of Stereoisomers

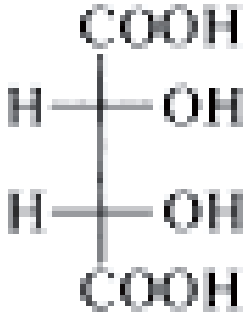
- Enantiomers have identical physical (except for α) and chemical properties.
- Diastereomers are different compounds and have different physical and chemical properties
- Meso-tartaric acid, for example, has different physical and chemical properties from its enantiomers



D-tartaric acid

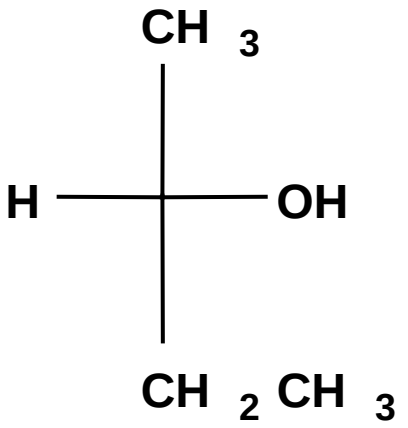


L-tartaric acid



mezo-tartaric acid

Fischer Projections



- Fischer projection: a two-dimensional representation showing the configuration of a stereocenter
  - horizontal lines represent bonds projecting forward
  - vertical lines represent bonds projecting to the rear
  - the only atom in the plane of the paper is the stereocenter

Fischer Projections