# BIOORGANIC CHEMISTRY

**Bio-organic chemistry** studies organization and features of substances taking part in the processes of life, in connection to study of their biological functions.

- The main objects of its study are ***biological polymers (bio-polymers)*** and ***bio-regulators***.
- **Bio-polymers** are high molecular natural compounds, which are structural basis of all living beings, which play a certain role in the processes of life. Bio-polymers include peptides and proteins, polysaccharides (carbohydrates), nucleic acids. This group includes lipids, which are not high molecular combinations by themselves but in the organism they are usually bonded to other bio-polymers.
- **Bio-regulators** are compounds, which chemically regulate the exchange of substances. They comprise vitamins, hormones, many synthetic biologically active compounds, including medicines.

The unity of chemical reactions, going on in the organism, is called the exchange of substances or **metabolism**. Substances, formed in cells, muscles and organs of plants and animals in the process of metabolism, are called **metabolites**.

- **Metabolism** comprises two directions: ***catabolism*** and ***anabolism***.
- **Catabolism** includes reactions of substances decomposition, which come into the organism with food. As a rule, they go hand-in-hand with oxidation of organic compounds and go with the discharge of energy.
- **Anabolism** is a synthesis of complex molecules from more simple, as a result of which formation and renovation of structural elements of a living organism is realized.
- Metabolic processes come with participation of ***enzymes***, i.e. specific proteins, which are in the organism cells, and play the role of catalysts for bio-chemical processes (***bio-catalysts***).

# HOMOLOGOUS SERIES

Rank of similar structured compounds, having similar chemical properties, in which separate members of the rank differ from each other only by the number of -$CH_2$- groups, are called homologues rank (homologous series), and –$CH_2$- group is called homologous diversity.

Reactions with the majority of members of homologous rank go in the same way (the exceptions are only the first members of the rank). Thus, if you know chemical reactions of only one member of the rank, you can state with a high degree of possibility, that the similar transformations take place with the rest members of the homologous rank.

A general formula can be defined for any homologous rank, which reflects the relation between carbon and hydrogen atoms at members of this rank. Such formula is called general formula of the homologous rank. Thus, $C_nH_{2n+2}$ – formula of alkanes, $C_nH_{2n+1}OH$ – is a formula of aliphatic single atom alcohols.

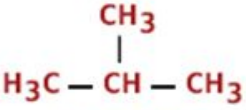
# Isomerism of organic compounds

- If two or more individual substances have the same quantity structure (molecular formula) but are different from each other by the succession of atom bonds or their place in the space, then they are called **isomers**.
- **If their structure differs, then their chemical and physical properties are also different.**
- **Types of isomery** are **structural** (isomers of organization, structure) and **stereo-isomery** (space).
- **Structural isomery** could be of the following types:
- isomery of the hydrocarbon skeleton (chain isomers), for example, butane and 2-methy-l-propane;
- isomery of the place of functional groups (or multiple bonds), for example, 1-butanol and 2-butanol;
- isomers of functional group (interclass), for example, 1-buta-nol and di-ethyl ether.
- **Stereo-isomery** is divided into conformation and configuration.

# Structural isomerism of organic compounds

$H_3C-CH_2-CH_2-CH_3$

butane

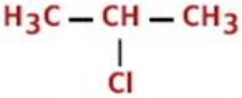


$H_3C-\overset{\overset{\displaystyle CH_3}{|}}{CH}-CH_3$

isobutane
or
2-methylpropane

$H_3C-CH_2-CH_2-Cl$

propyl chloride
or
1-chloropropane

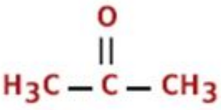


$H_3C-\underset{\underset{\displaystyle Cl}{|}}{CH}-CH_3$

isopropyl chloride
or
2-chloroproppane

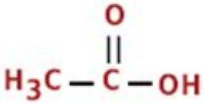
$H_3C-CH_2-CHO$

**propanal**



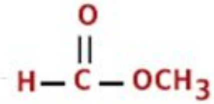
$H_3C-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$

**acetone or**
**2-propanone**



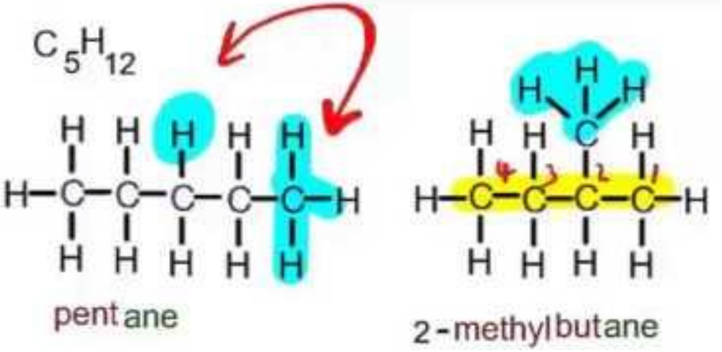
$H_3C-\overset{\overset{\displaystyle O}{\|}}{C}-OH$

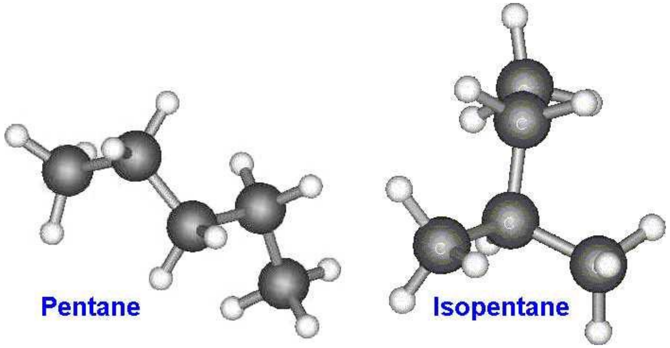
acetic acid

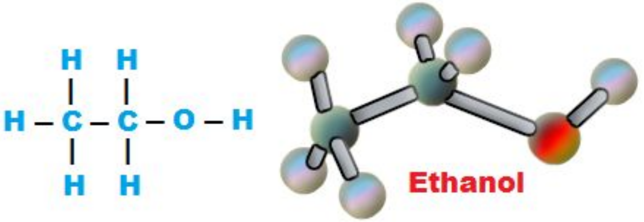


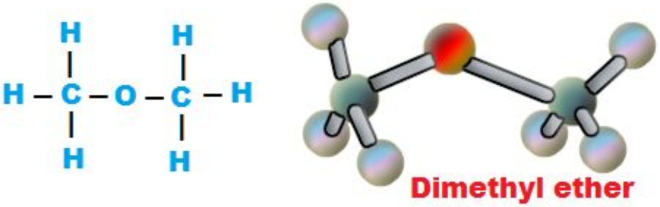
$H-\overset{\overset{\displaystyle O}{\|}}{C}-OCH_3$

methylformate

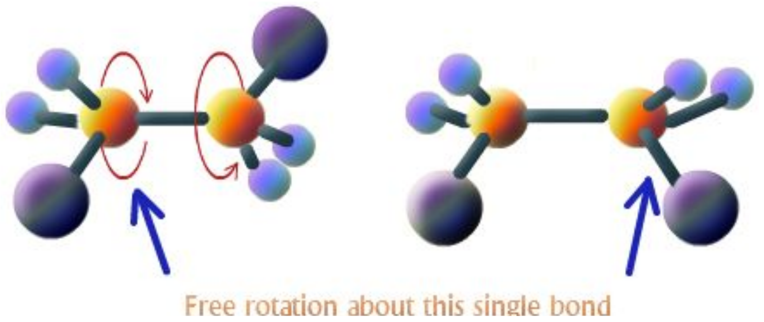


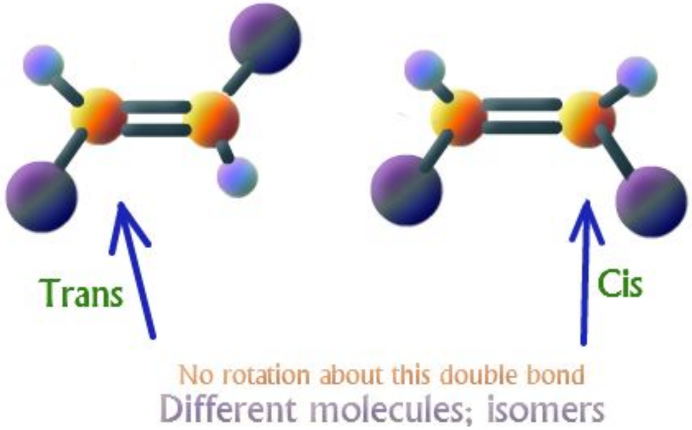






# Geometric isomerism of organic compounds





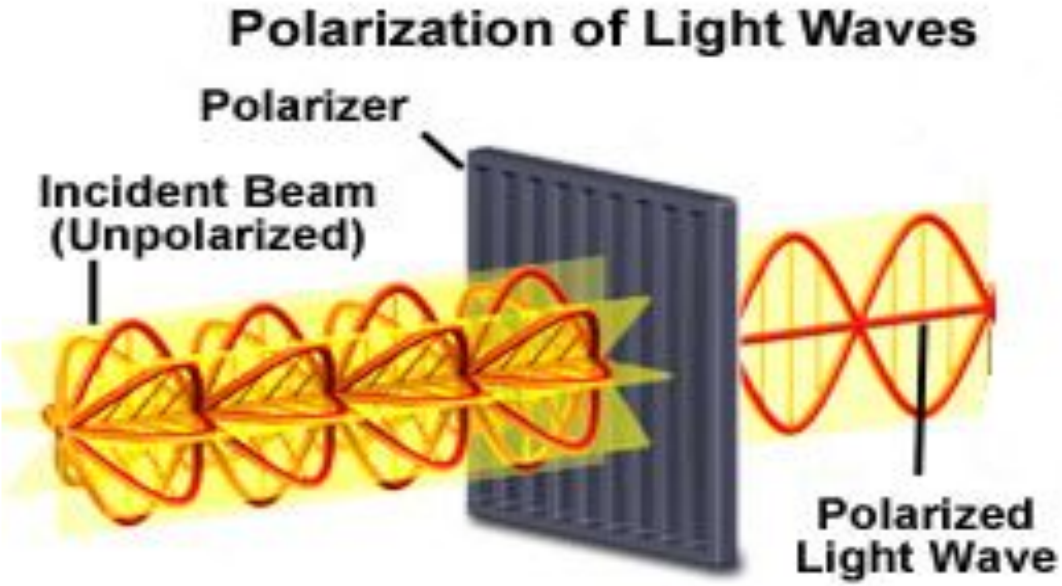
**If you swap the chlorine and hydrogen atoms on the first carbon atom, the new arrangement has a different relative positioning of the atoms in space.**

**GEOMETRICAL ISOMERS**

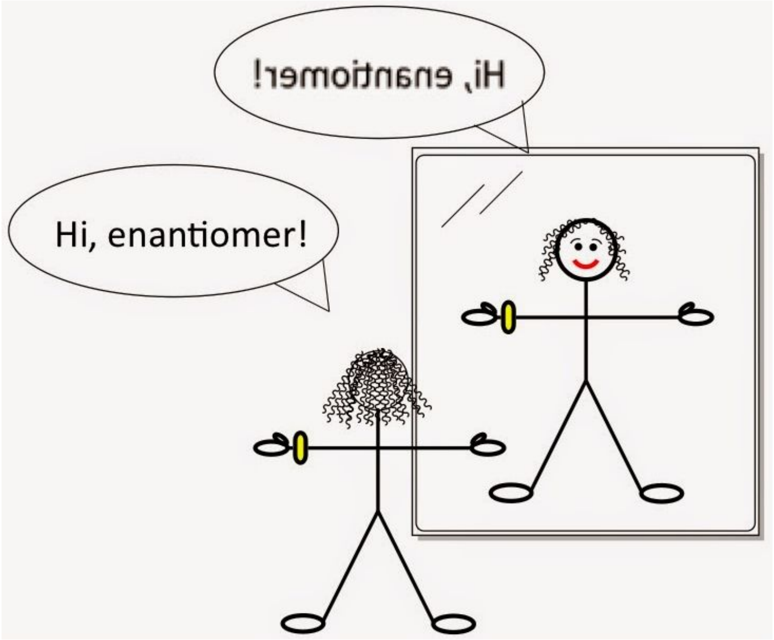
**If you swap the chlorine and hydrogen atoms on the first carbon atom, the new arrangement has the same relative positioning of the atoms in space.**

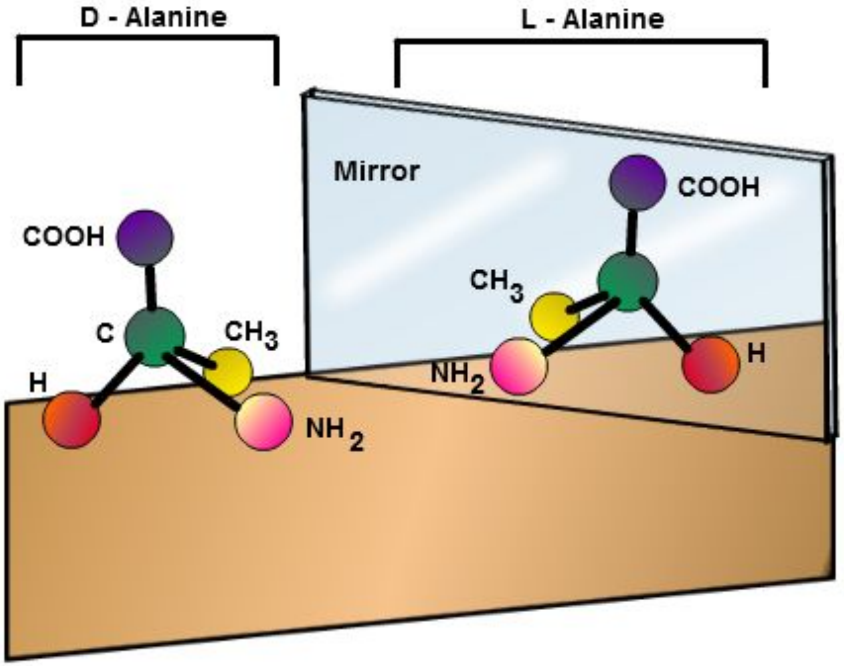
**NO GEOMETRICAL ISOMERISM**

# Enantiomerism (optical or mirror reflection isomerism)



Optically active compounds form two special isomers which are each other’s mirror reflections (**enantiomers**).



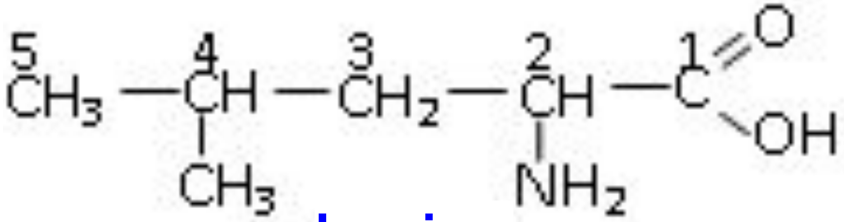


# Principles of optical activity of organic compounds

– ***there is chiral carbon atom;***

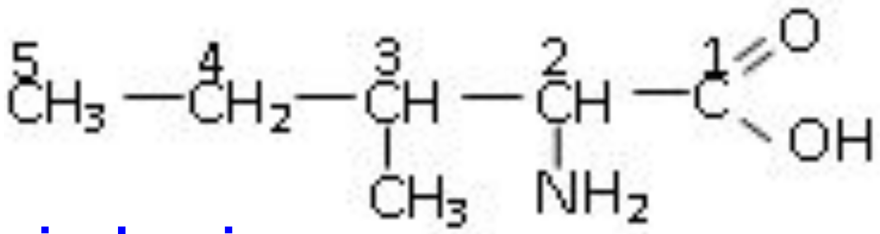
– ***there are no elements of symmetry in the molecule.***

**Chiral carbon atom** is atoms which has bonds with four different atoms or groups.



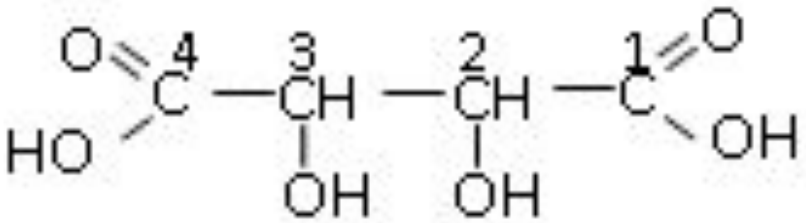
$\overset{5}{C}H_3-\overset{4}{C}H(CH_3)-\overset{3}{C}H_2-\overset{2}{C}H(NH_2)-\overset{1}{C}OOH$

**leucine**



$\overset{5}{C}H_3-\overset{4}{C}H_2-\overset{3}{C}H(CH_3)-\overset{2}{C}H(NH_2)-\overset{1}{C}OOH$

**isoleucine**

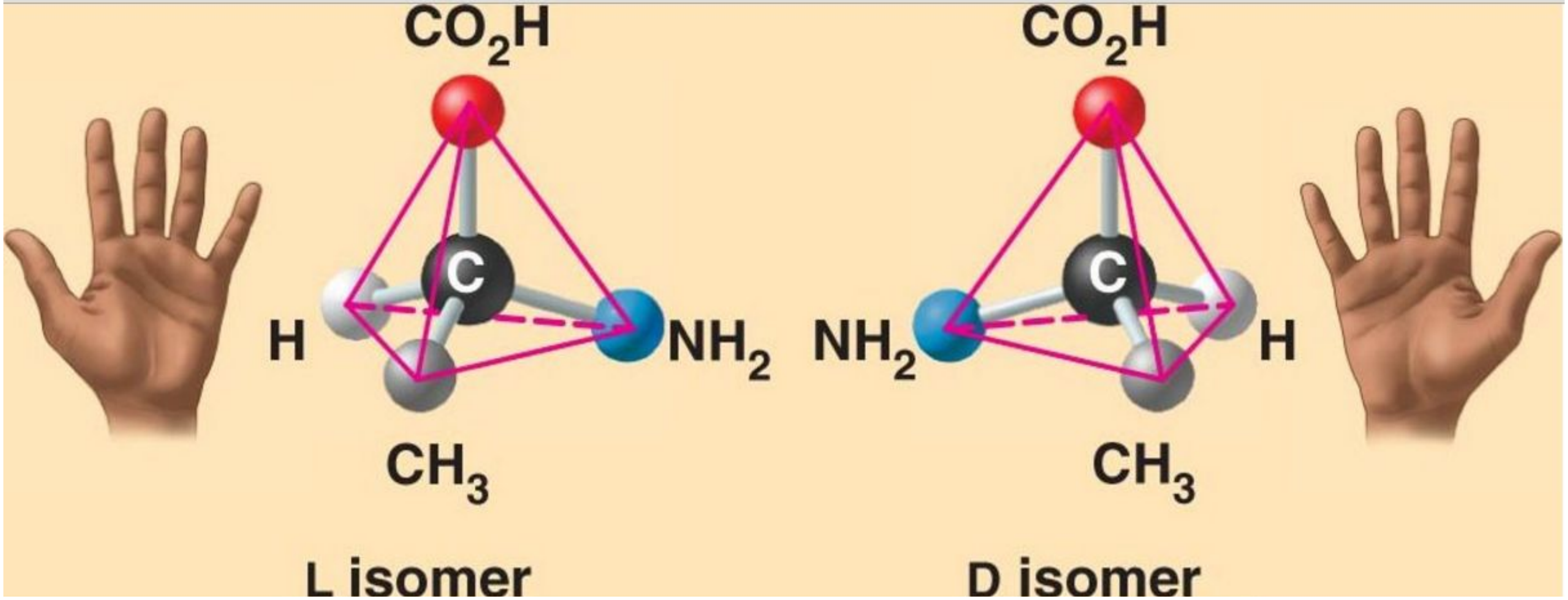


$HOO\overset{4}{C}-\overset{3}{C}H(OH)-\overset{2}{C}H(OH)-\overset{1}{C}OOH$

**tartaric acid**

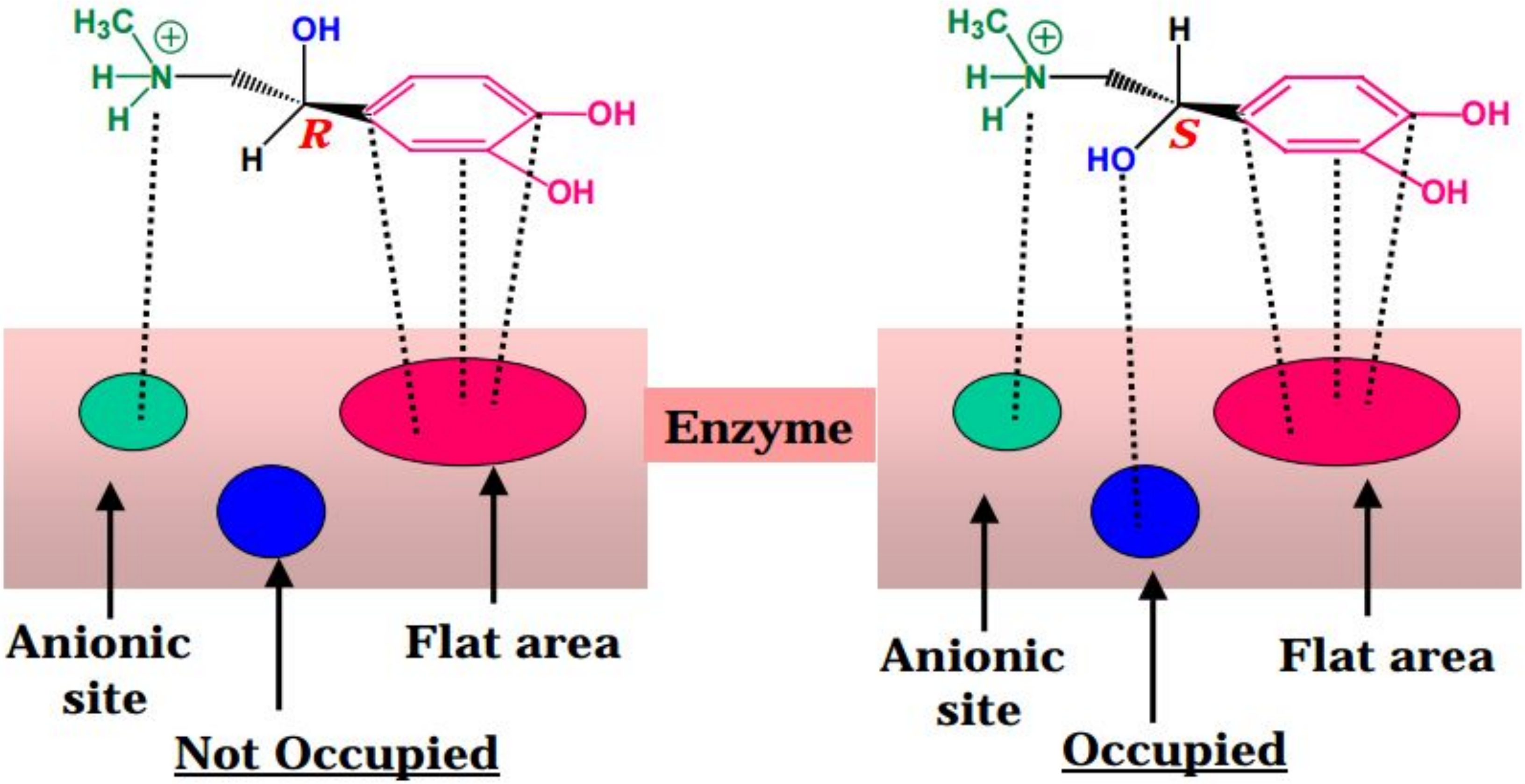
# Properties and nomenclature of enantiomers

**Enantiomers** have the same physical and chemical properties but they rotate polarization plane of plane polarized light to opposite sides, in space they cannot be superposed. Example of impossibility of superposition of an object and its mirror reflection is impossibility to wear right glove on the left hand which corresponds right hand space location.



# Biological activity of enantiomers

## Enantiomers of Epinephrine



**Enzyme**

**Anionic site**

**Flat area**

**Not Occupied**

**Anionic site**

**Flat area**

**Occupied**

**(+)-Epinephrine**

***Poorer Fit*** ➡ ***Less Active***

**(-)-Epinephrine**

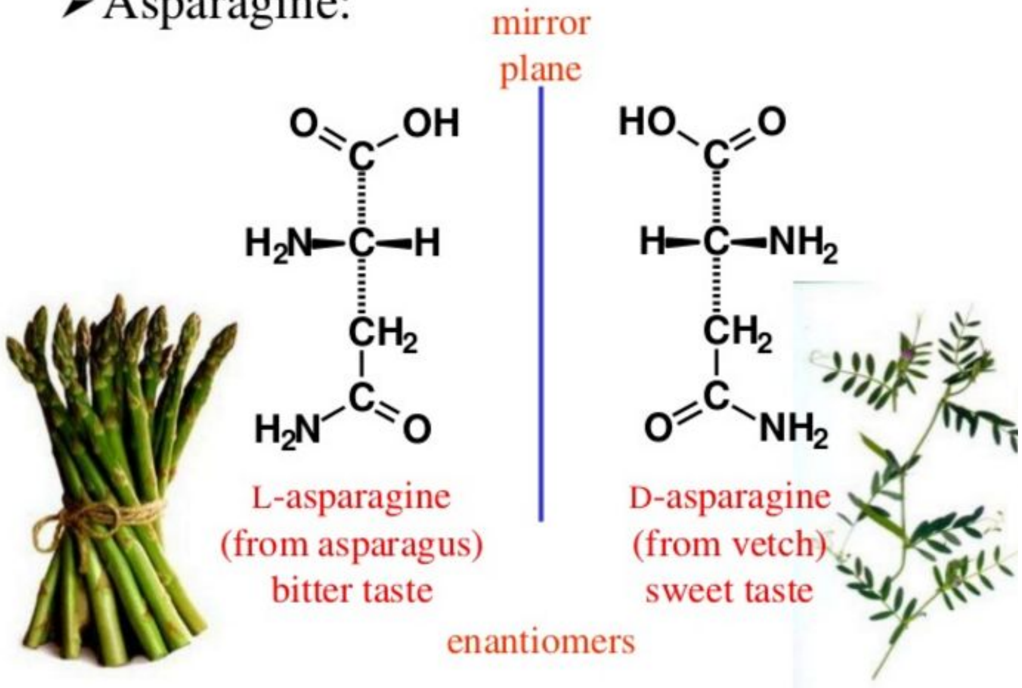
***Better Fit*** ➡ ***More Active***

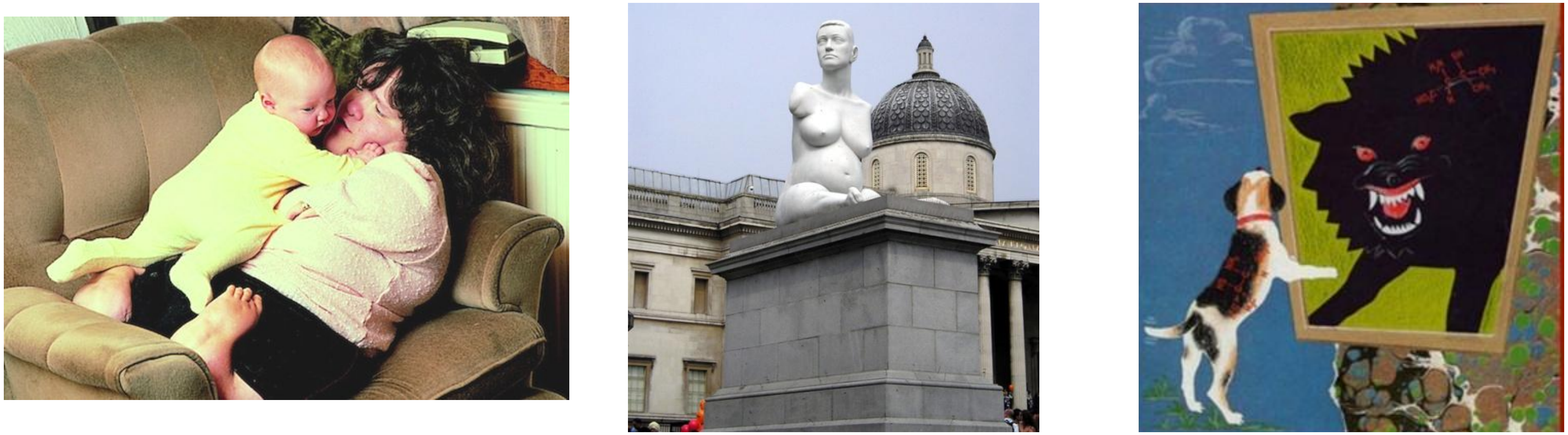
# Biological activity of enantiomers

**DARVON** **analgesic**

**NOVRAD** **antitussive**

- Asparagine:





The consequences of the medicinal product "Thalidomide"

# Acidity and basicity of organic compounds

- Bronsted’s acids (proton acids) are neutral molecules or ions, which are able to donate proton (proton donors).

- Bronsted’s bases are neutral molecules or ions, which are able to accept proton (proton acceptors).

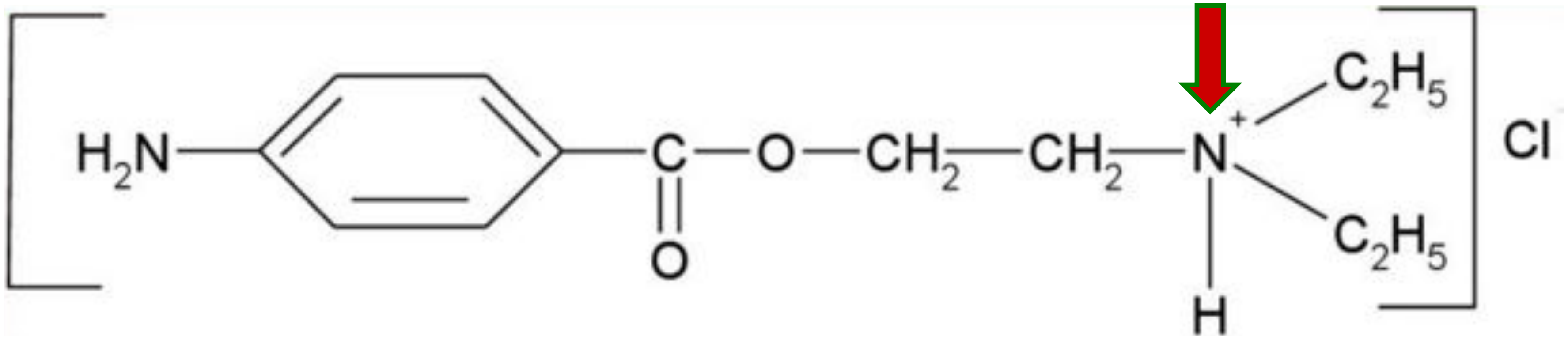
- Acid and base features are not absolute but relative features of compounds: acid features appear only in the presence of base; and base features appear only in the presence of acid. As a solvent at studying acid-base balance water is usually used.

# Using basic properties to get water soluble forms of medicines

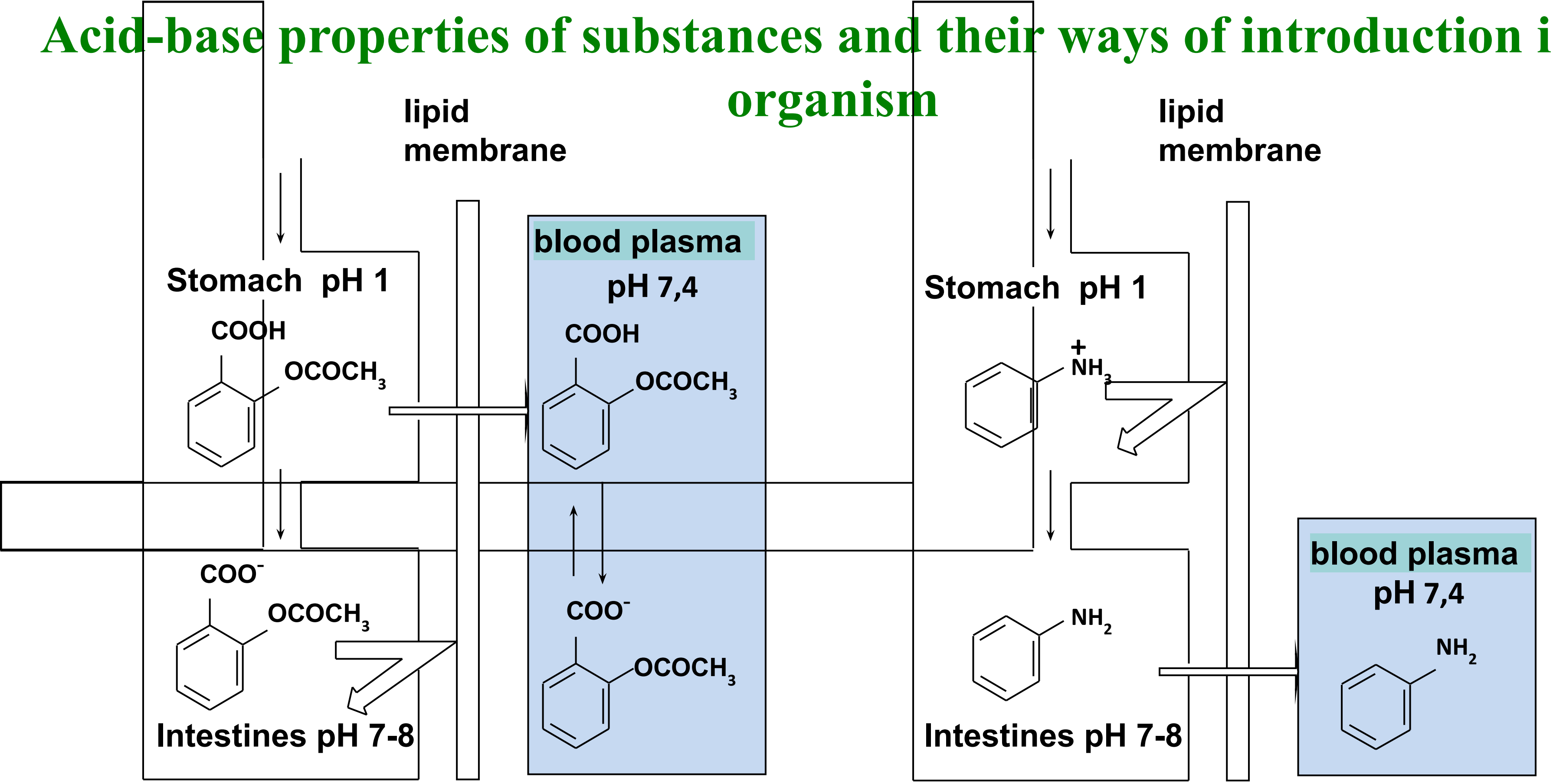
Basic properties of medicines are used to get their water soluble forms. Interacting with acids compounds with ionic bonds are formed, which are salts well-soluble in water.

For example, novocaine for injections is used in the form of hydrochloride.

**The strongest basic centre which attaches proton**



# Acid-base properties of substances and their ways of introduction into organism



lipid membrane

Stomach pH 1

blood plasma pH 7,4

Intestines pH 7-8

lipid membrane

Stomach pH 1

Intestines pH 7-8

blood plasma pH 7,4

Acid medicines are better absorbed from stomach (pH 1-3), and absorption of medicines or xenobiotics-bases is done only after they come to intestines from stomach (pH 7-8). During one hour from stomach of rats about 60% of acetylsalicylic acid and only 6% of aniline are absorbed from initial dose. In the intestines of rats about 56% of aniline are absorbed. Such weak base as cofein ($pK_{BH+}$ 0,8), is absorbed better for the same period of time (36%), as even at strong acid medium in stomach cofein is mainly in non-ionised state.

# Types of reactions in Organic chemistry

Organic reactions are classified according to the following principles:

1. Electron nature of reagents.
2. Number of particle change due to reaction.
3. Panial (additional) principles
4. Mechanism of elementary

reaction stage.

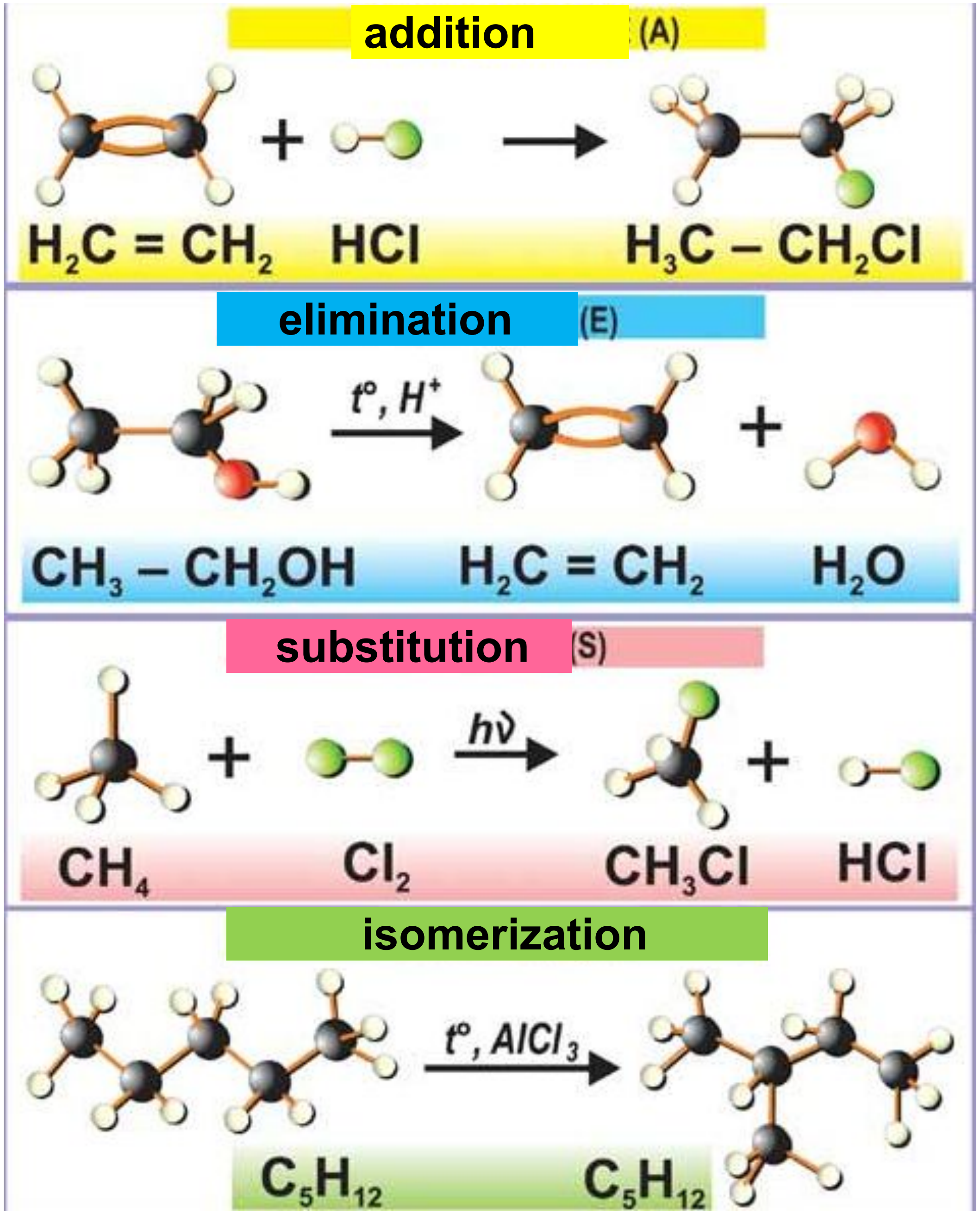
# According to electron nature of reagents reactions are subdivided into: nucleophilic, electrophilic and free radical

- ***Free radicals*** are electroneutral particles which have non-shared electron, for example, Cl·, ·$NO_2$. Free radical reactions are typical of alkanes.
- ***Electrophilic reagents*** are cations or molecules which in itself or in the presence of catalyst have high affinity to electron pair or negatively charged molecule centres. They include cations $H^+$, $Cl^+$, $^+NO_2$, $^+SO_3H$, $R^+$ and molecules with free orbitals $AlCl_3$, $ZnCl_2$ и т.п.

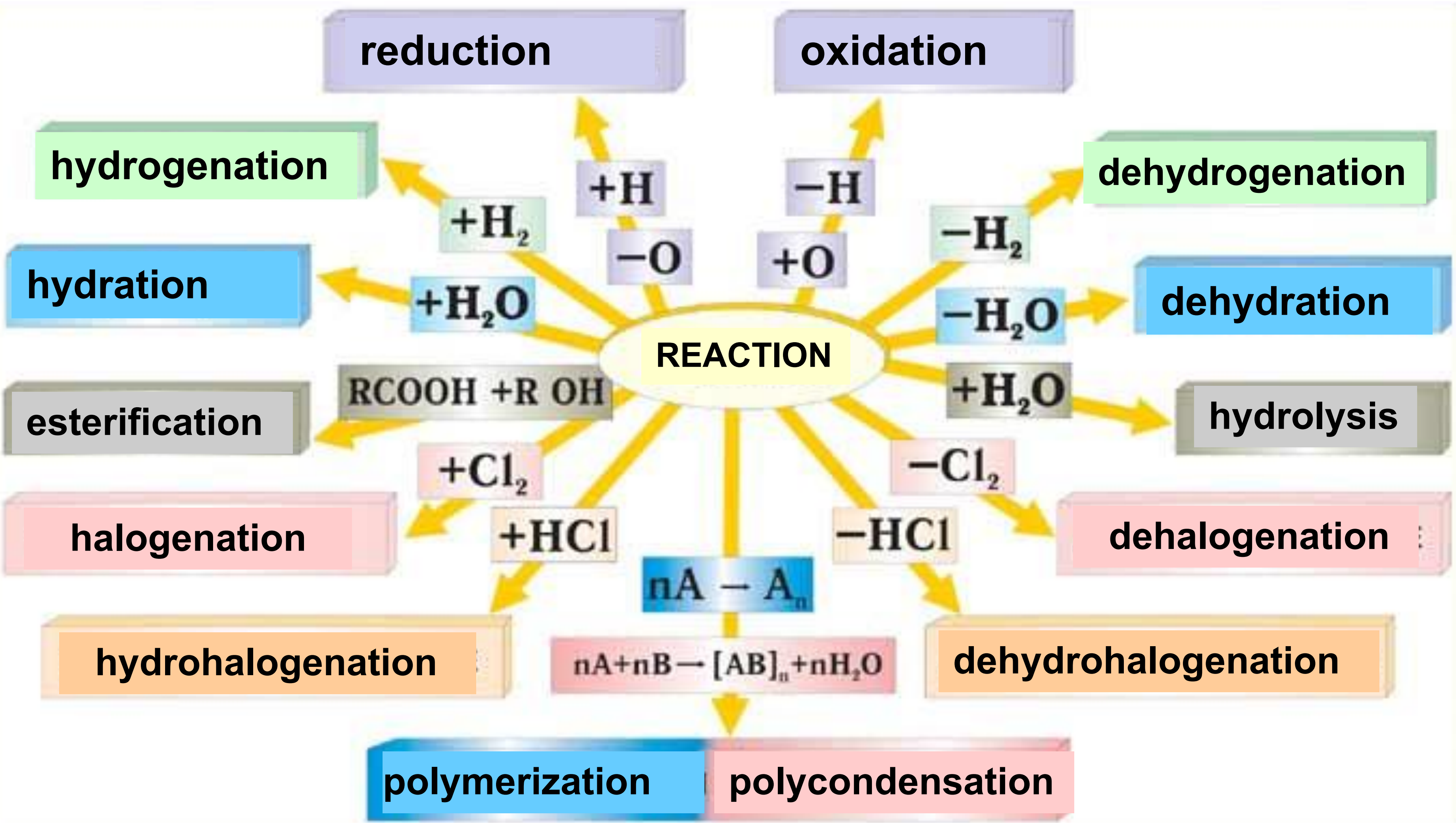
Electrophilic reactions are typical of alkenes, alkanynes, aromatic compounds (addition on the place of the double bond, proton substitution).

- ***Nucleophilic reagents*** are anions or molecules which have centres of higher electron density. They include anions and moleculs as $HO^-$, $RO^-$, $Cl^-$, $Br^-$, $RCOO^-$, $CN^-$, $R^-$, $NH_3$, $C_2H_5OH$, etc.

- According to number of particle change there are substitution, addition, elimination and degradation, isomerization



# Reaction classification according to panial principles



reduction

$+H$

$-O$

oxidation

$-H$

$+O$

hydrogenation

$+H_2$

dehydrogenation

$-H_2$

hydration

$+H_2O$

dehydration

$-H_2O$

REACTION

esterification

RCOOH +R OH

hydrolysis

$+H_2O$

halogenation

$+Cl_2$

dehalogenation

$-Cl_2$

hydrohalogenation

$+HCl$

dehydrohalogenation

$-HCl$

$nA \rightarrow A_n$

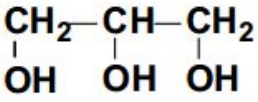
$nA+nB \rightarrow [AB]_n+nH_2O$

polymerization

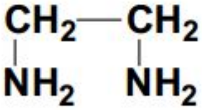
polycondensation

- **Poly-functional compounds contain several same functional groups.**

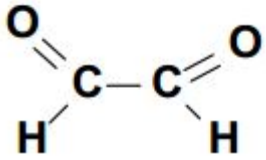
$Cl-CH_2-CH_2-Cl$ $HO-CH_2-CH_2-OH$



$CH_2(OH)-CH(OH)-CH_2(OH)$



$CH_2(NH_2)-CH_2(NH_2)$

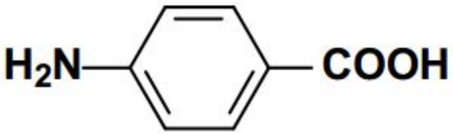


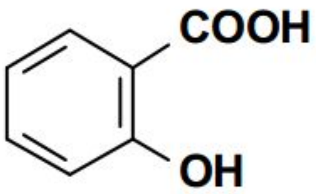
$HOOC-COOH$

- **Hetero-functional compounds contain several different functional groups.**

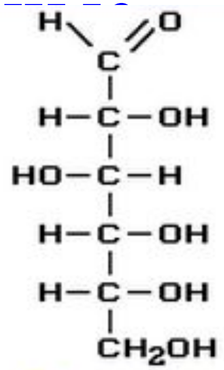
$CH_2=CHCOOH$ $CH_3C(O)COOH$ $HOCH_2CH_2NH_2$

$HOCH_2COOH$ $CH_3CH(NH_2)COOH$

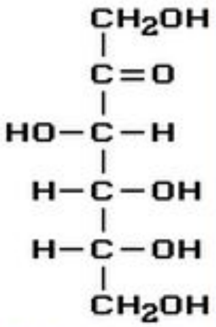




- **Hetero-poly-functional compounds contain same and different functional groups.**

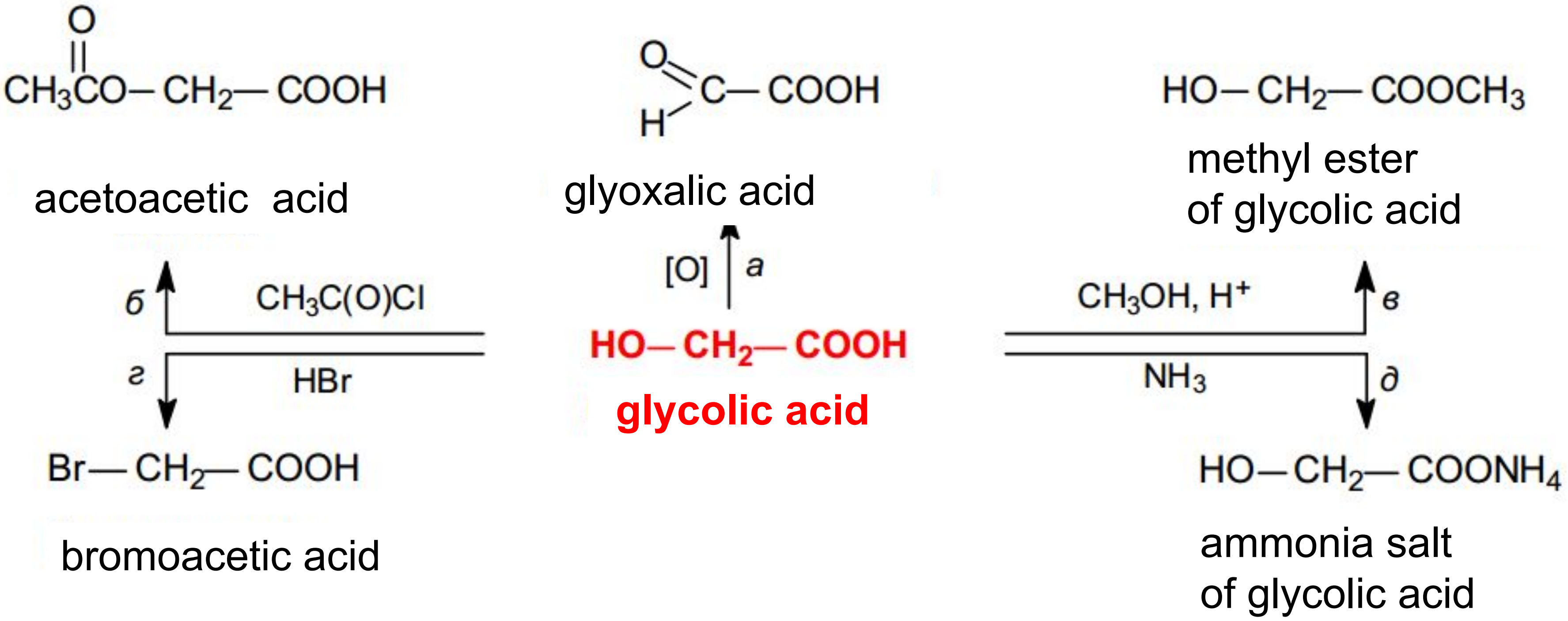


glucose



fructose

- Each group at poly- and hetero-functional compounds can participate at the same reactions as well as corresponding group at mono-functional compounds



acetoacetic acid

glyoxalic acid

methyl ester
of glycolic acid

**glycolic acid**

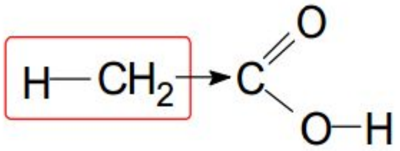
bromoacetic acid

ammonia salt
of glycolic acid

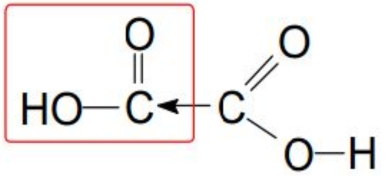
# Characteristic properties of poly- and hetero-functional compounds

- A lot of properties (amphoteric character)
- Increase or decrease of some properties in comparison to mono-functional compounds (if OH, SH, COOH groups are at the structure of the molecule then it leads to acidic property increase if amino groups are at the molecule $NH_2$, NH, it lea to basic property increase.

  If there is additional electron acceptor group near acid centre then acid property is increased;



**acetic acid** , $pK_a$ 4.7



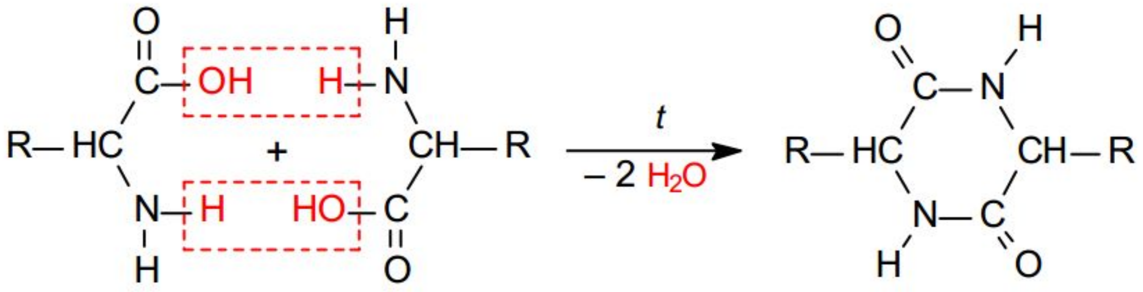
**oxalic acid** , $pK_a$ 2.3

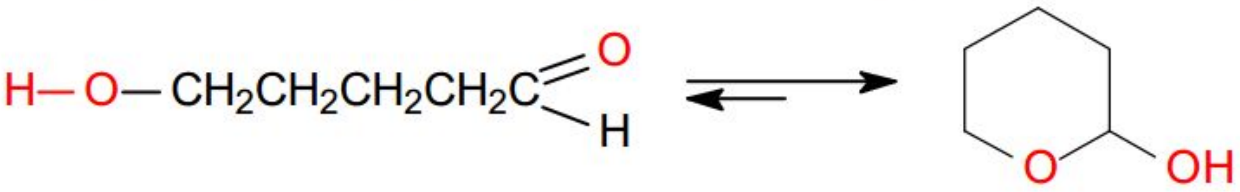
  If there is electron acceptor substitute then nucleophilic reactions are facilitated and electrophilic reaction rate is slower

- New specific properties appear

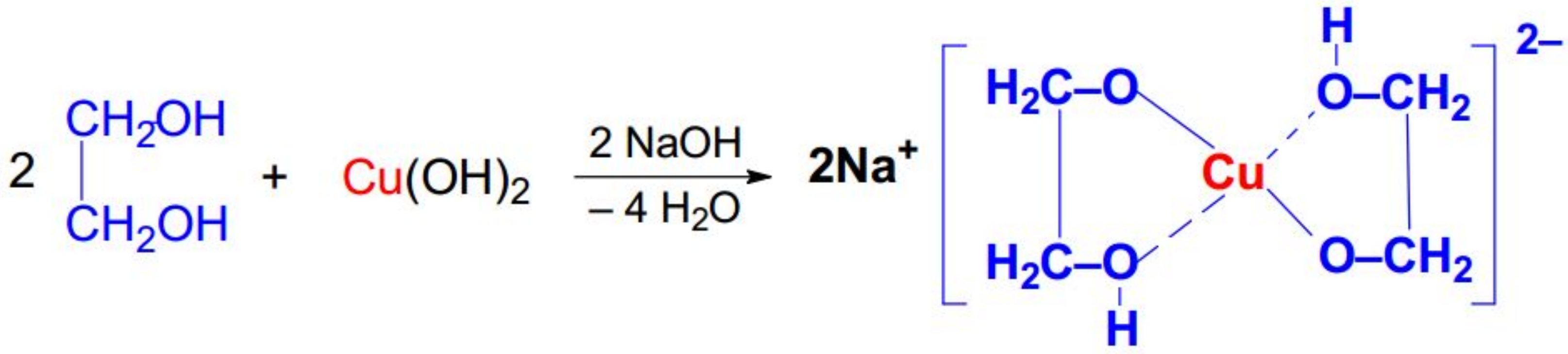
# Specific properties of poly- and hetero-functional compounds

- **Cycle formation reaction**

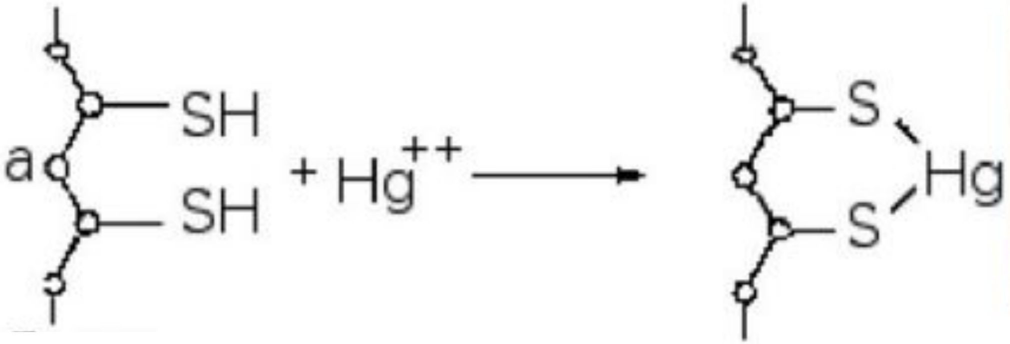




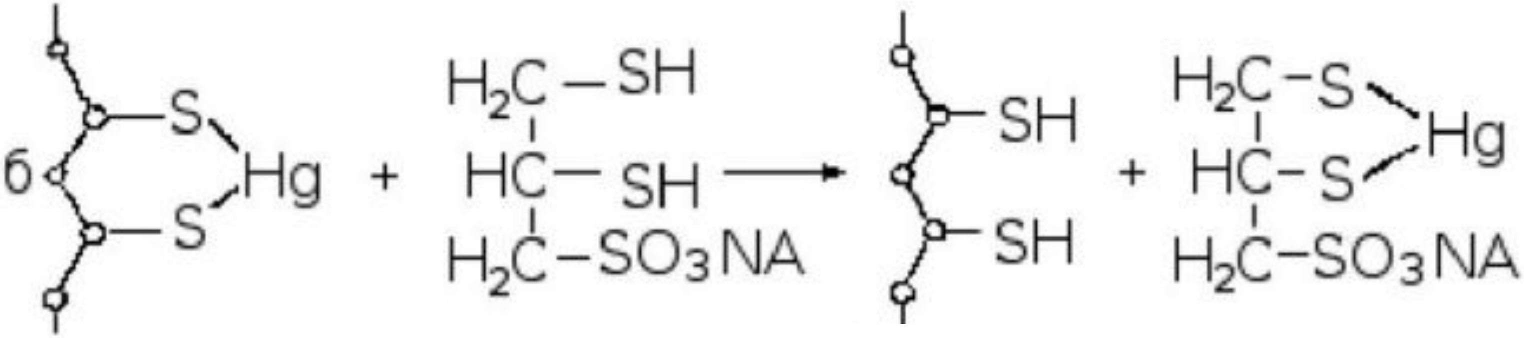
- **Chelate complex formation**



# Polyfunctional compounds as an antidotes



**protein**



**unitiol** **protein**

Bioorganic chemistry