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СМІРНОВА О.В., ШУНКОВ В.С.

Basis of the Structure and Reactivity of Biologically Active Compounds

НАВЧАЛЬНИЙ ПОСІБНИК ІЗ БІООРГАНІЧНОЇ ХІМІЇ

Вінниця
Нілан-ЛТД
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Рекомендовано
Міністерством освіти і науки України
як навчальний посібник для англомовних студентів
вищих медичних закладів IV рівнів акредитації

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Навчальний посібник складається з двох частин, в яких висвітлюються основні теоретичні поняття органічної хімії та розглянуто основи реакційної здатності біологічно активних сполук, використовуючи механізми перебігу хімічних реакцій.

В першій частині посібника даються теоретичні поняття та механізми реакцій, в яких беруть участь біологічно активні сполуки, коротко пояснюється роль в організмі людини.

В другій частині посібника розглянуто методичні розробки до практичних занять: тестові завдання для перевірки знань, словник-мінімум основних формул органічних сполук та їх номенклатура.

Посібник відповідає програмі «Біоорганічна хімія» для студентів вищих медичних закладів освіти III – IV рівнів акредитації, 5.05.2005р., м.Київ.

Рекомендовано Міністерством освіти і науки України як навчальний посібник для англомовних студентів вищих медичних закладів IV рівнів акредитації.

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Preface

The teaching of bioorganic chemistry at higher medical schools is carried out without a previous study of the organic chemistry course. In some countries, where students come from, general chemistry is not studied in schools before educational establishments.

Therefore, there was a requirement to create a manual on bioorganic chemistry, where theoretical bases of structure and reactionary ability of organic compounds would be expanded.

The manual, which is offered, answers the program from bioorganic chemistry for medical universities and requirements of the balance process.

In the manual, the concepts of electronic and spatial structure of organic compounds and their influence are shortly laid out on reactionary ability.

Material engulfs all classes of organic compounds from alkanes to hydrocarboxylic acids.

In every section of the manual, questions are given for self-control, examples of control tests and method of implementation of laboratory works. This helps us to understand the motion of processes, which take place in the organism of man.

For the preparation of the manual, teaching of bioorganic chemistry is in the department of biological and general chemistry of the Vinnitsa National Pirogov Memorial Medical University.

This manual is recommended for foreign students of medical and dental faculties, who study in English.

Plan of Practical lessons
For I-st Year Foreign Students of the Medical Faculty
(Bioorganic Chemistry) Semester II

№	Theme of the practical lessons	Hours
	Module 1	
1	Nomenclature, isomerization, electronic structure of chemical bonds.	**2**
2	Reactivity of alkanes, alkenes, arenes.	**2**
3	Reactivity of alcohols, phenols and amines.	**2**
4	Reactivity of aldehydes and ketones.	**2**
5	Reactivity and biological significance of carboxylic acids and their derivatives.	**2**
6	HFA. Lipids. Phosphoglyceride.	**2**
7	Reactivity and biological significance of heterofunctional compounds (hydroxy acids, oxoacids, phenolic acids)	**2**
	Module 2	
8	Structure and chemical properties of α-amino acids.	**2**
9	Structure and physical-chemical properties of proteins.	**2**
	Module 3	
10	Monosaccharides, structure and chemical properties.	**2**
11	Oligo- and Polysaccharides, structure and chemical properties.	**2**
	Module 4	
12	Heterocyclic compounds, classification, structure and chemical properties.	**2**
13	Nucleic acids: structure, classification and application in medicine.	**2**
14	Practical skills: “Theoretical essential principles of structure and reactivity of bioorganic compounds”.	**2**
15	Module (biologically important classes of organic compounds, biopolymers).	**2**

Plan of Practical lessons
For I-st Year Foreign Students of the Dental Faculty
(Bioorganic Chemistry) Semester II

№	Theme of the practical lessons	Hours
	Content module 1	
1	Classification of organic compounds. Nomenclature.	**2**
2	Spatial structure of biological active compounds. Enantiomerism and conformation isomerism.	**2**
3	Electronic structure of carbon atom, the nature of chemical bond. Conjugation and aromaticity of biological active compounds.	**2**
4	Electronic effects in biological active compounds.	**2**
5	Acidity and basicity of biological active compounds.	
6	Reactivity of alkanes and halogen containing alkanes.	**2**
7	Reactivity of alkenes.	**2**
8	Reactivity of arenes.	**2**
9	Nucleophilic addition reaction of oxocompounds.	**2**
10	Nucleophilic substitution reaction of carboxylic acids and their biological active derivatives.	**2**
11	Lipids.	**2**
12	Heterofunctional biological active compounds.	**2**
	Content module 2	
13	Amino acids: structural units of peptides and proteins.	**2**
14	Peptides and proteins.	**2**
	Content module 3	
15	Monosaccharides such as structural units of complex carbohydrates.	**2**
16	Complex carbohydrates: oligo - and polysaccharides	**2**
	Content module 4	
17	Biologically active heterocyclic compounds.	**2**
18	Nucleic acids.	**2**
19	Practical skills of situational problems and solutions.	**2**
20	The final module of Bioorganic chemistry	**2**

TOPIC 1

BIOORGANIC CHEMISTRY STUDIES THE STRUCTURE, PHYSIO-CHEMICAL PROPERTIES AND MECHANISMS OF REACTIONS, WHICH INVOLVE THE BIOLOGICALLY ACTIVE COMPOUNDS.

1.1. Bioorganic Chemistry - As a Subject

Biologically active compounds are synthesized in the human body or enter the body and are involved in biochemical processes. They are:

Biopolymers	***Low-molecular Substances***
↓	↓
- Proteins - Nucleic acids - Polysaccharides and their derivatives which contain lipids	- Vitamins - Hormones - Alkaloids - Drugs and other substances

Although, bioorganic chemistry emerged at the boundary of organic and biological chemistry, it uses the theoretical and physical concepts, which are chemical methods of classical organic chemistry.

Bioorganic chemistry is a separate chapter of the 70s in the last century, based on chemistry of natural compounds.

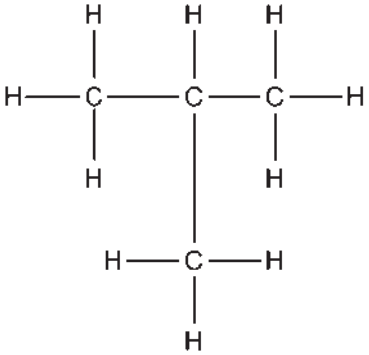
Although bioorganic chemistry emerged at the turn of the organic and biological chemistry, it is based on the material of classical organic chemistry, using its theoretical concepts and the whole vast arsenal of physical and chemical methods.

Scientific basis of Organic Chemistry is the Butlerov theory, which explains the large number and varieties of organic compounds.

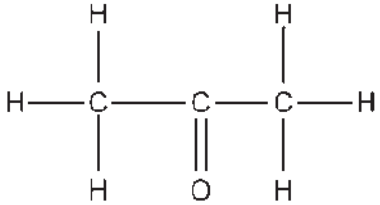
1.2. Basics of the A. Butlerov Theory

Basics of the theory of the structure of organic compounds A. Butlerov formulated in 1858-1861, were confirmed by further development of organic chemistry:

a) The atoms that make up the molecules of organic compounds are linked together according to their valence. The order relation is called chemical structure of atoms. A carbon atom in organic compounds is always **tetravalent**:



Isobutane



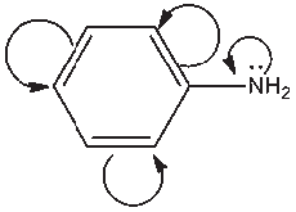
Acetone

b) Properties of materials depend not only on the qualitative and quantitative composition, but also on the order in which the atoms are combined in the molecule, i.e the chemical structure of the molecule:

$C_4H_{10}O$	**$C_4H_{10}O$**
$H_3C—CH_2—O—CH_2—CH_3$	$H_3C—CH_2—CH_2—CH_2—OH$
Diethyl ether	*1-Butanol*
Volatile Fluid, t_{boil} = 34,6 °C	Fluid, t_{boil} = 117,4 °C
Does not react with Me	Reacts with Me

c) Atoms or groups of atoms that form the molecule, mutually influence each other, which determine the reactivity of the molecule.

In the molecule of aniline benzene, nucleus increases the acidic properties of oxide, and oxy-group increases the reactivity of the benzene nucleus in the substitution reaction.



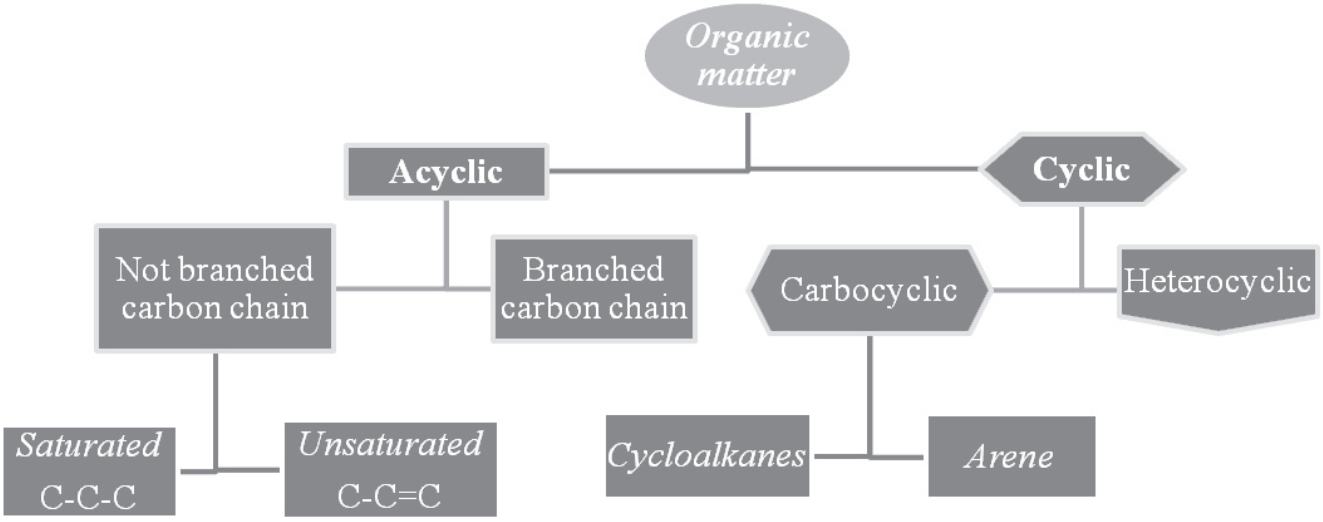
Aniline

d) Studying the reactivity of a substance, you can set its structure, and vice versa. The structure of matter can be judged on its properties.

1.3. Classification of Organic Compounds

Currently there are more than 20 million organic compounds. The study of the structure and properties of such a large number of organic compounds is due to the classification system. Organic compounds are classified according to various criteria.

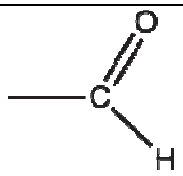
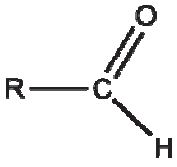
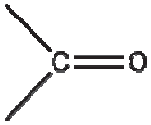
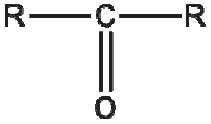
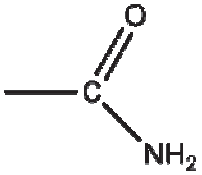
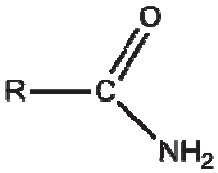
1. By building a carbon skeleton:



2. By the nature of the functional groups:

Table 1.

Classification of organic compounds by natural functional groups

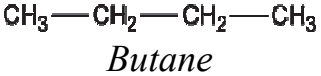
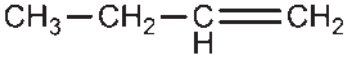
Name of the class of substances	*Functional group*	*The general formula of class*
Halogenalkanes	-F, -Cl, -Br, -I	R-Hal
Alcohols, phenols	-OH	R-OH
Tioalcohols, thiophenols	-SH	R-SH
Ethers (ethers)	-OR*	R-O-R*
Aldehydes		
Ketones		
Carboxylic acids	-COOH	R-COOH
Sulfonic	$-SO_3H$	$R-SO_3H$
Esther (esters)	-COOR*	R-COOR*
Amides		
Amines	$-NH_2$	$R-NH_2$
Nitro compounds	$-NO_2$	$R-NO_2$
Nitriles	-CN	R-CN

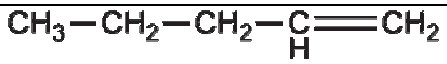
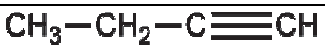
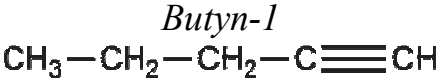
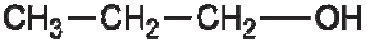
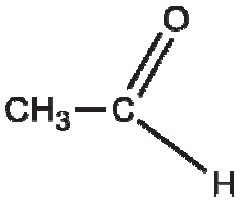
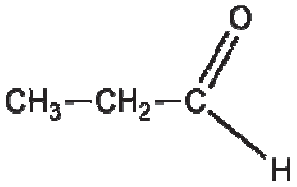
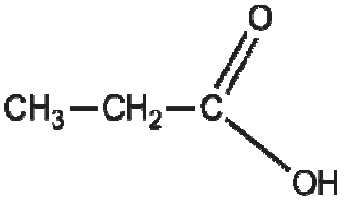
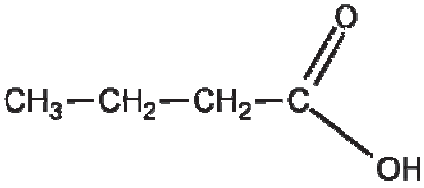
1.4. Homologous Series of Organic Compounds

Homologous series – a sequence of compounds that have the same type of structure and similar properties. Each successive member differs from the previous homologous - CH_2. The compounds of each class are placed in the homologous series having the general formula.

Table 2.

Classification of Classes of Organic Compounds

Name of the class	*The general formula of class*	*Examples*
Alkanes	$\mathbf{C_nH_{2n+2}}$	 *Propane*  *Butane*
Alkenes	$\mathbf{C_nH_{2n}}$	 *Butene-1*

		 *Penten-1*
Alkynes	**C_nH_{2n-2}**	 *Butyn-1*  *Pentyn*-1
Arene	**C_nH_{2n-6}**	 *Toluene*  *Dimethylbenzene*
Saturated monohydric alcohols	**$C_nH_{2n+1}OH$**	 *Propanol*  *Butanol*
Aldehydes	**$C_nH_{2n}O$**	 *Ethanal*  *Propanal*
Saturated monobasic carboxylic acids	**$C_nH_{2n+1}COOH$**	 *Propanoic acid*  *Butanoic acid*

1.5. Nomenclature of Organic Compounds

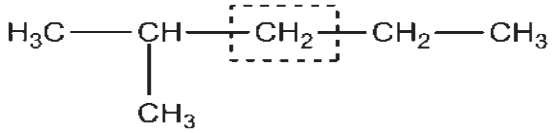
Nomenclature - a system of rules that allows us to define a compound.

1. Trivial nomenclature.

The names of substances under this nomenclature historically, by chance, do not reflect the structure of matter, and may indicate its origin, special features and others. Trivial names of organic compounds are firmly rooted and many of them are still recognized. They are especially used in the chemistry of natural and heterocyclic compounds.

2. Rational nomenclature.

Considers compounds as a derivative of the first member of the homologous series, which includes similar compounds. For example, alkanes are considered as derivatives of methane.



Ethyl isopropyl methane

Now this nomenclature comes from consumption, so as not to permit a substance with a complex structure.

3. International Nomenclature (IUPAC).

Principles of naming on the international nomenclature:

1) Determine the **primary (main) structure** - a structural fragment molecule underlies its name. Acyclic compounds are the longest carbon chains that contain the largest number of multiple bonds, substituents, and cyclic - cycle.

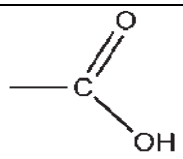
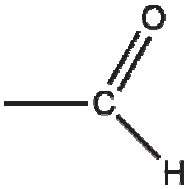
2) Enumerate the main chain, starting with the oldest functional group called the main chain

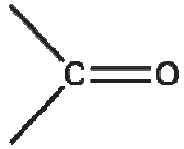
3) Determine the number of carbon atoms, some of which are substituents (radical's functional groups).

4) Arrange substituents alphabetically: functional groups (Table 3) and radicals.

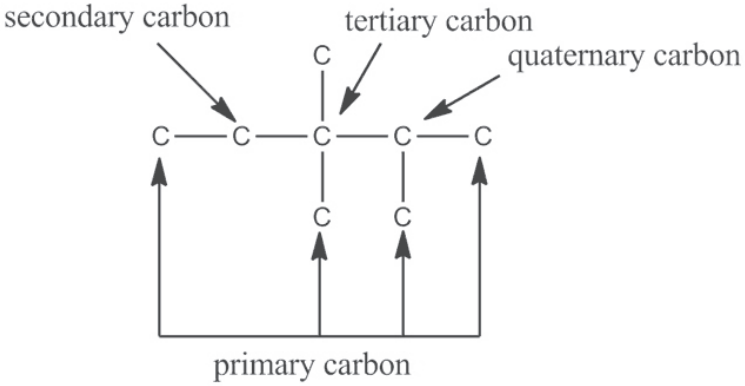
Table 3.

Functional groups

Functional group	*Name of prefix*	*Name in the end(suffix)*
	carboxy-	*- oic acid*
	al-	*- al*

	oxo-	*- on*
-OH	oxy- (hydroxy-)	*- ol*
-SH	mercapto-	*- thiol*
$-NH_2$	amino-	*- amine*
$-NO_2$	nitro-	–
$-SO_3H$	sulfonic-	–
Halogens	chlorine, bromine, iodine	–

Since propane is more radical for each alkane, the carbon atoms are unequal:



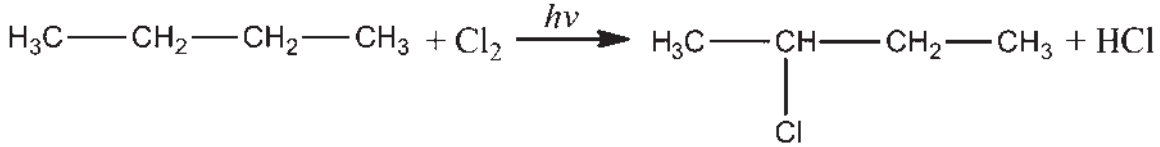
5) End of the compound causes **older functional group**.

1.6. General Regularities of Organic Reactions

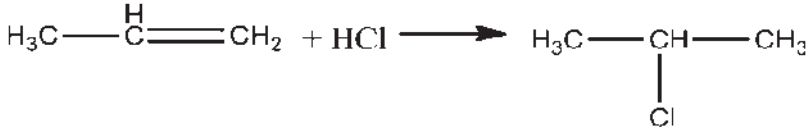
In organic chemistry reactions;
substrate is a molecule of large complex structures and
reagent is a particle of a smaller and less complex structure.
Substrate and reagent react

1. By **direction,** organic reactions are divided into:

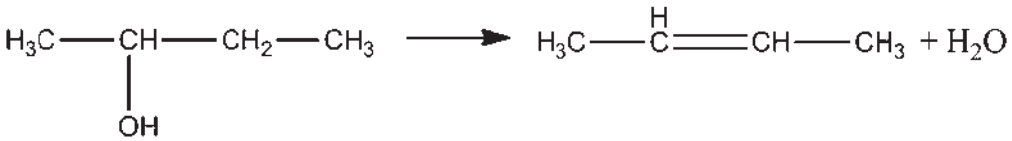
a) Substitution reaction:



b) Addition reaction:

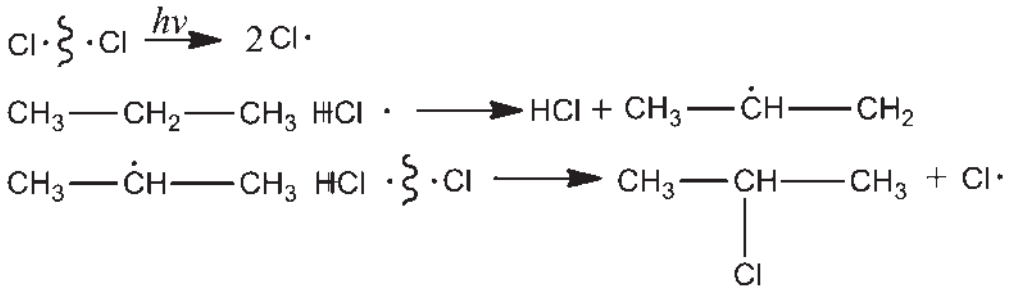


c) Elimination reaction:



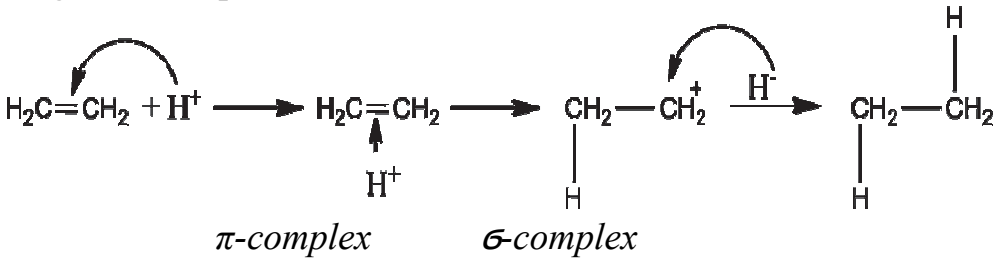
2. By **the nature** of the organic reagent, reactions are divided into:

a) Free radical reactions (or homolytic), which act as a free radical reagent, for example, free radical substitution in alkanes:



Free radicals are particles Cl*.

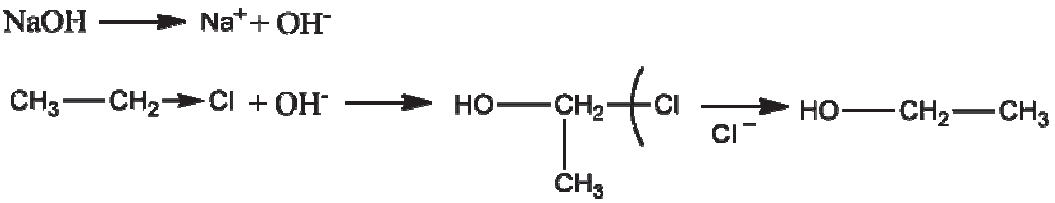
b) Electrophilic (or heterolytic, or ionic) where the electrophile is a reagent. For example, joining in electrophilic alkenes:



π-complex *σ-complex*

Electrophile is a piece of H^+.

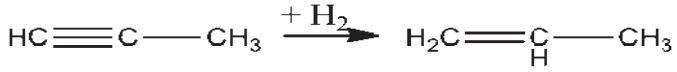
c) Nucleophilic (or heterolytic, or ionic) where the nucleophile is a reagent. For example, nucleophilic substitution of alcohols:



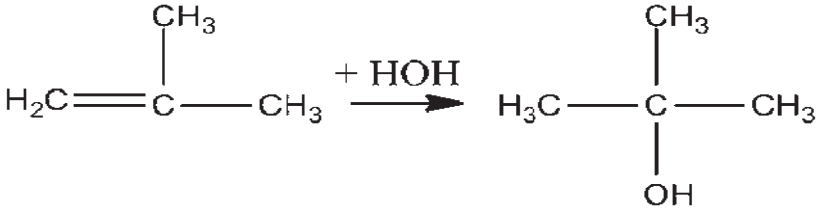
Nucleophile is a group of OH^-.

3. By **the nature of what is introduced into the molecule**, or split off:

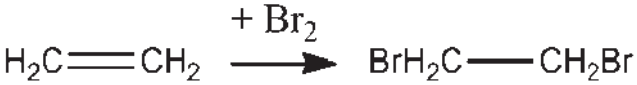
a) Hydrogenation - addition of hydrogen:



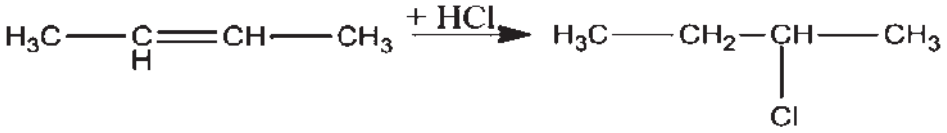
b) Hydration - addition of water:



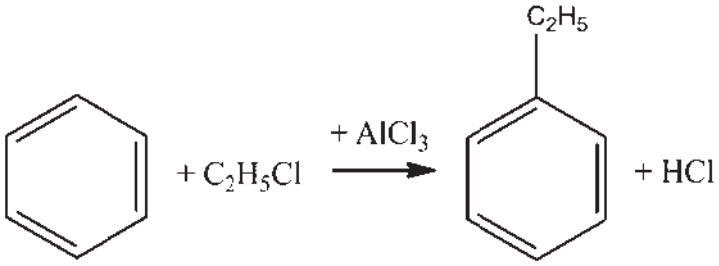
c) Halogenation - addition of halogens:



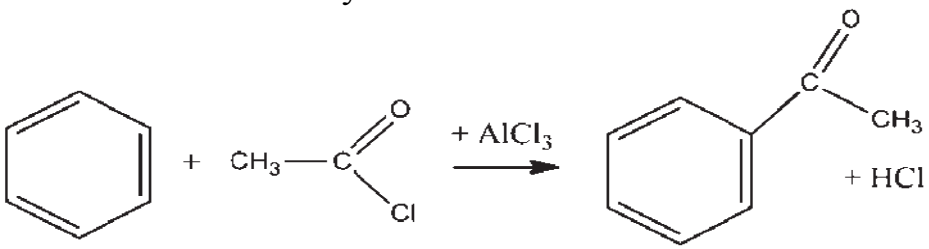
d) Hydrohalogenation - join of hydrohalohens:



d) Alkylation - alkyl input (radicals):

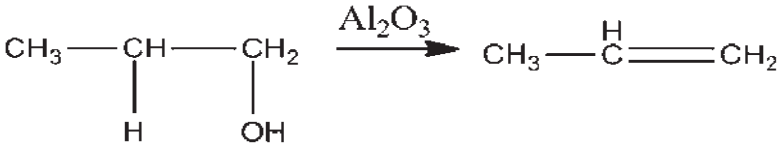


e) Acylation - introduction of acyl:



g) Dehydrogenation - cleavage of hydrogen:

i) Dehydration – splitting of water:



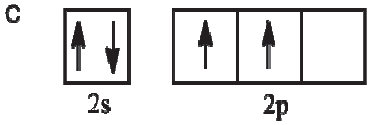
TOPIC 2

ELECTRONIC STRUCTURE OF A CARBON ATOM AND ITS CHEMICAL COMMUNICATIONS

2.1.Electronic Structure of a Carbon Atom and its Chemical Bonds

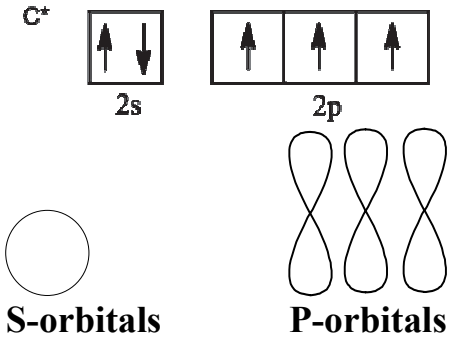
One reason for the large number and variety of organic compounds lies in the peculiarities of the structure of the carbon atom.

Electron-graphic formula of the carbon atom in the ground state is given by:



With the two unpaired electrons of carbon atoms they can form two covalent bonds. However, organic compounds and carbon atoms, in accordance with the theory of Butlerov, are always tetravalent, that is, excitation occurs at all times in the electron.

A graphic formula in this case is as follows:



Formation of Orbitals

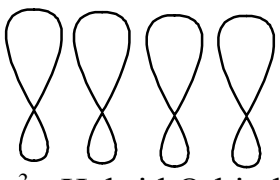
Such carbon atom forms four covalent bonds, which are unequal because S-orbital and P-orbital have different energy and shape of forms.

It also goes for alkane molecules, which are all equally linked. This is achieved by hybridisation.

Hybridisation - is the alignment of the orbitals in the energy and shape.

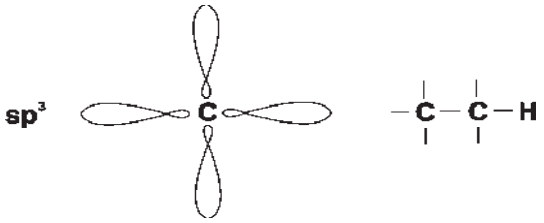
Depending on the conditions in which there is a formation of a chemical bond, the carbon atom is in a different hybridisation period.

1. If the condition of bond formation is such that the S-orbital and the P-orbitals are hybridized, the formation of four equivalent $s\rho^3$- hybrids orbital is produced. They have the same energy and shape. In this case we say that a carbon atom is in **$s\rho^3$-hybridisation**.



$s\rho^3$ - Hybrid Orbitals

This gives the carbon atom the formation of chemical bonds of four equivalent $s\rho^3$ - hybrid orbitals. Able sp^3 - hybridisation of carbon is in alkanes group

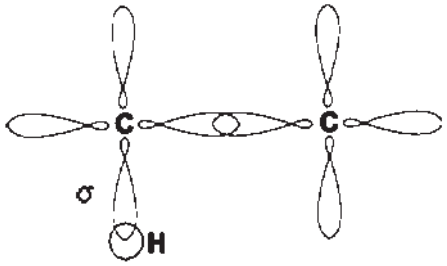


If $s\rho^3$, which is a hybrid carbon atom, forms a chemical bond with another $s\rho^3$, this will cause another hybrid carbon atom and due to this, there will be an overlap of hybrid orbitals and σ – bonds, which will be formed.

Schematically, this can be written as:

$$\overset{\sigma}{C - C} \rightarrow s\rho^3 - s\rho^3$$
$$(C) \quad (C)$$

C-H bond in alkanes is a σ-bond and is formed by the overlaping of sp^3- hybrid orbitals of carbon and s-orbital of the hydrogen atom.

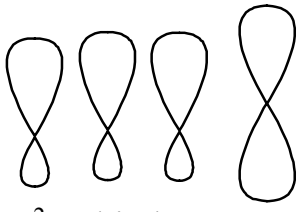


Schematically, this can be written as:

$$\overset{\sigma}{C - H} \rightarrow s\rho^3 - s$$
$$(C) \quad (H)$$

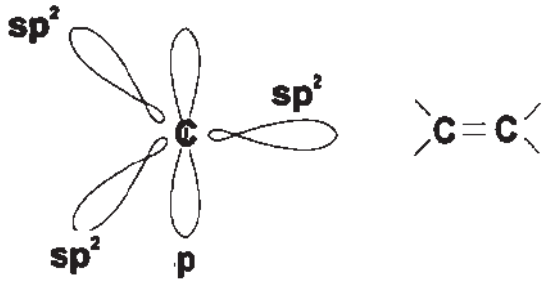
$S\rho^3$-hybrid orbitals are directed at an angle of 109°28' and determine the spatial configuration of the molecule.

2. Under other conditions the formation of chemical bonds hybridize one s-orbital and two p-orbitals, resulting in formation of three **sp^2-**hybrid orbitals and left remaining one free p-orbital. In this case, we can say that the carbon atom is in a state of sp^2-hybridisation

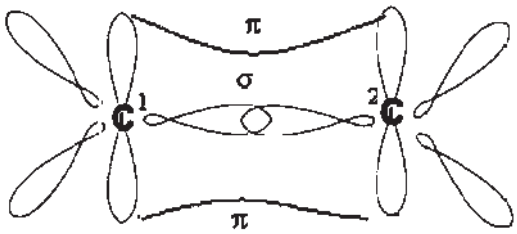


$s\rho^2$–orbitals ρ –orbital

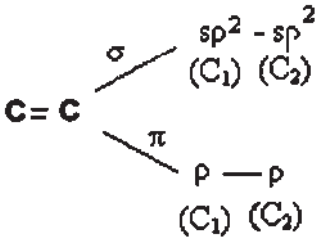
In the state of $s\rho^2$- hybridisation, carbon atom is in alkenes:



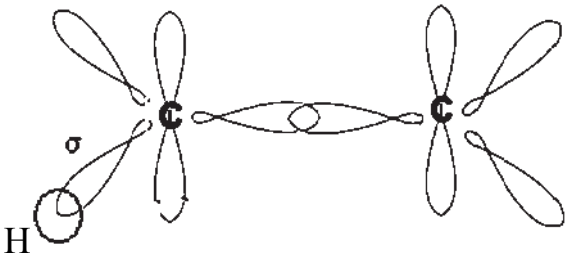
Double bond between carbon atoms in alkenes consist of σ-due and π-communication. The overlapping of sp^2- orbitals form σ-bond and the overlapping of free ρ-orbitals form π-bond.



Schematically, this can be written as:



C-H bond in alkenes is an σ-bond and is formed by the overlapping of sp^2- hybrid orbitals of carbon and s-orbital of the hydrogen atom.

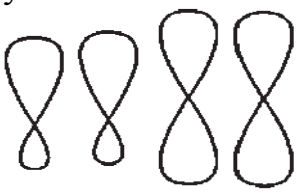


Schematically, this can be written as:

$$C - H \rightarrow sp^2 - s$$
$$(C) \quad (H)$$

sp^2- hybrid orbitals are directed at an angle of 120°, the molecule is located in plane.

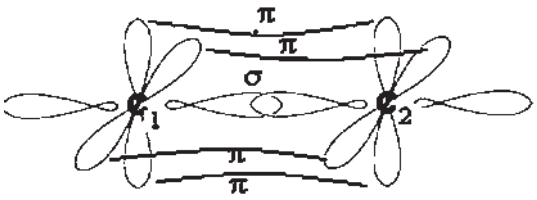
3. Conditions of formation of chemical bonds may be such that hybridizing one s-orbital and one p-orbital leads to the formation of two **sp-hybrid** orbitals and two free p-orbitals. In this case, we can say that the carbon atom is in a state of sp-hybridisation.



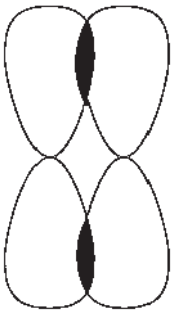
sρ- orbitals P-orbitals

In the state of sρ-hybridisation carbon atom is in alkyne HC≡CH.

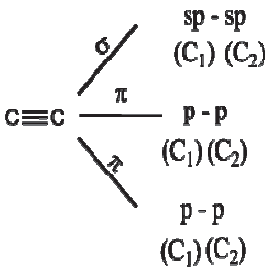
In the alkyne between the carbon atoms a triple bond is formed. One of them is a σ-bond and is formed by overlapping of sρ-hybrid orbitals.



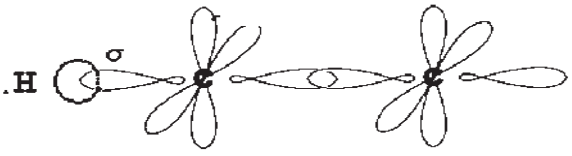
The remaining two bonds are π-bonds, which are formed by the overlapping of the free ρ - orbitals.



Schematically, this can be written as:



C-H bond in the alkyne is the σ-bond that is formed by the overlapping of sρ-hybrid orbitals of carbon and s-orbitals of the hydrogen atom.



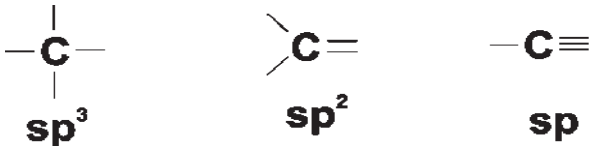
Schematically, this can be written as:

$$\overset{\sigma}{C - H} \rightarrow sp - s$$
$$(C)(H)$$

sρ- hybrid orbitals are directed at an angle of 180°,i.e.,the molecule has a linear configuration.

Thus, if a carbon atom forms four simple σ-communications it is in the **sρ^3**-hybridisation phase. If a carbon atom forms a double bond with another atom,it is in **sρ^2**-

hybridisation phase. If a carbon atom forms a triple bond with other atoms, It is in **sρ**-hybridisation period.



In biologically active compounds, carbon is mainly located in the $s\rho^3$- hybridisation and $s\rho^2$– hybridisation periods.

2.2. Isomerism of Biologically Active Compounds

Another reason for the large number and variety of organic compounds are isomers.

Isomerism - is the existence of organic compounds with the same qualitative and quantheative composition, but different properties due to the different structure of organic compounds.

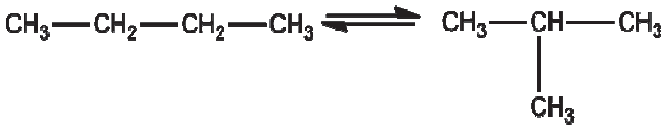
For Bioorganic and Biological Chemistry, isomerism is the cause of different biological activities. That is, only certain isomers exhibit biological activity, which may disappear in the process of isomerization and this may cause pathological changes in the human body.

There are two fundamentally different types of isomerism: structural and spatial.

2.2.1. Structural Isomerism

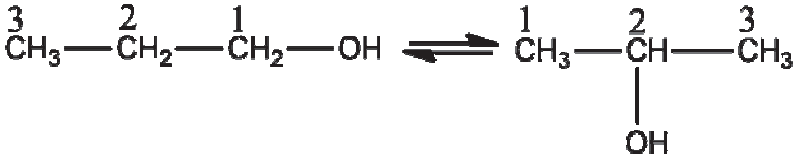
Structural isomers are caused by various factors:

1. **Isomerism of carbon skeleton** is due to the different order of linkages between the carbon atoms and this causes a different structure of the carbon skeleton:

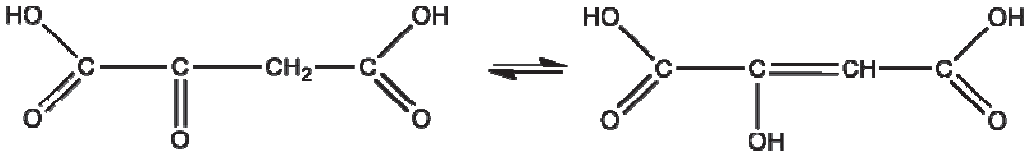


2. **Isomerism location of the multiple bond:**

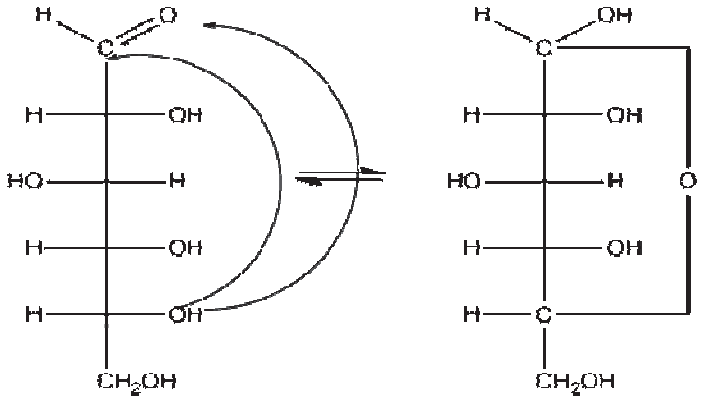
3. **Isomerism arrangement of the functional groups:**



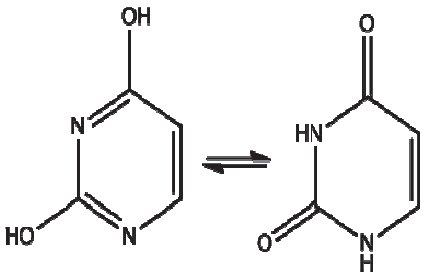
4. **Tautomerism** - a type of isomerism, which is caused by migration of a hydrogen atom between other atoms in one molecule. For example, acet-oxalic acidis characterizes the typical keto-enol tautomerism:



For glucose, the typical characterization is the cyclo-chain or oxy-oxo tautomerism:



For nitrogenous bases, the typical is the lacto-lactam tautomerism. For example, uracil tautomers can be written as:



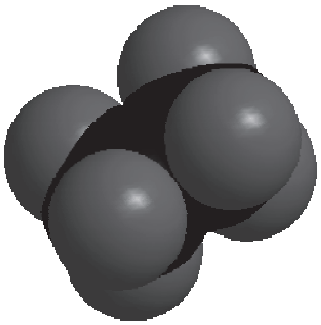
2.2.2. The Spatial Structure of Biologically Active Compounds

One type of isomerism is called the spatial isomerism. The molecules of organic compounds can be arranged differently in space.

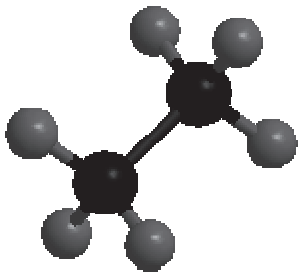
The spatial arrangement of molecules is called **configuration**.

For the spatial images of molecules we can use:

A) Stewart model, in which the atoms are represented in the form of a hemisphere:

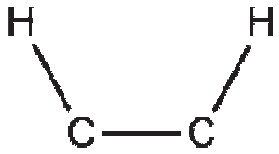


B) Ball-rod model in which the atoms are shown as spitres connected by rods that link them together:



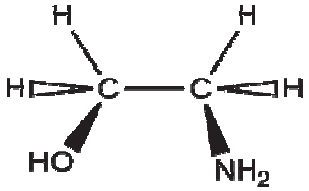
The plane of the spatial arrangement of the molecules is written with the help of the **stereo-chemical formulas** and **configurations**.

For example, to write the configuration of the molecule **colamine** HO-CH_2-CH_2-NH_2 (produced in the human body as a result of decarboxylation of the amino acid serine), you must create a model of the molecule and look at it so that you can see two carbon atoms and two hydrogen atoms that are directed upwards and are coplanar with the carbon atoms. The relationship between them is written as usual, in the structural formula, i.e. a single line:



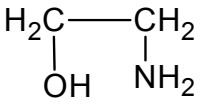
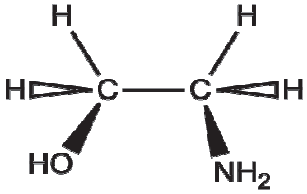
The other two hydrogen atoms are directed away from the observer in space.

Functional groups HO-and -NH_2 are sent to the observer in space.



Configuration

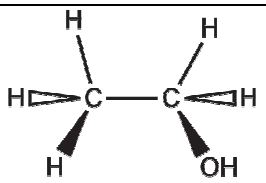
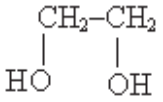
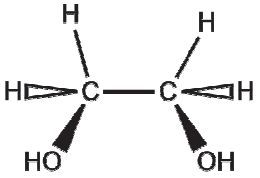
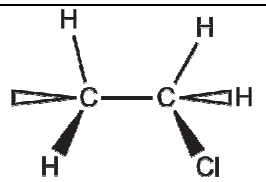
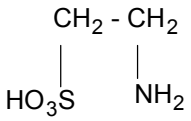
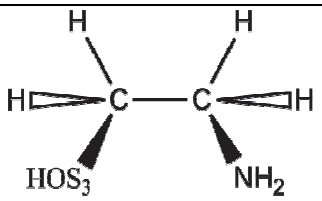
Thus, to characterize colamine we can write the following formula:

C_2H_7ON		
Molecular Formula	*Structural Formula*	*Configuration*

Characteristics of some biologically active compounds are given in table number 4.

Table4

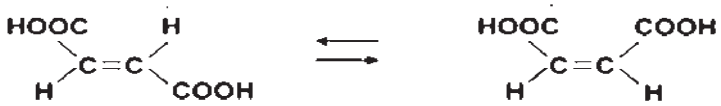
Table of the Structure of Biologically Active Compounds

The biologically active agent	*Molecular formula*	*Structural formula*	*Configuration*
Ethanol - antiseptic, causes toxic effects on the human body:	C_2H_6O	$CH_3–CH_2 – OH$	
Ethylene glycol - antifreeze, causes toxic effects on the human body:	$C_2H_6O_2$		
Chloroethane – anesthetic:	C_2H_5Cl	$CH_3 - CH_2 - Cl$	
Taurine - an intermediate in the synthesis of bile acids:	$C_2H_7O_3SN$		

Types of Spatial Isomerism

1. **Cis-trans-isomerism -** is due to the different arrangement of atoms, which are relative to the double bond.

A classic example of cis-trans isomerism is fumaric-maleic acid:

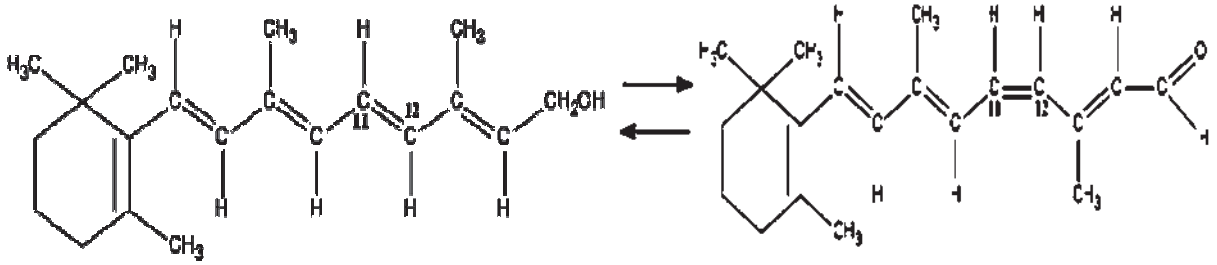


Isomerization is a gap in communication.

The biological significance of cis-trans isomerism:

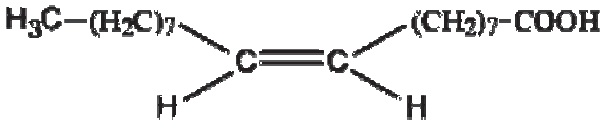
Fumaric acid is normally formed in the body of the Krebs cycle. Since metabolic disorders can occur because of isomerization of **maleic** fumaric acid, a known skin disease, named psoriasis can happen due to this.

Retinol (vitamin A) has a **trans**-configuration. In humans, it gets isomerized with the cis-configuration, which participates in the process of vision.



Trans – Retinol *Cis – Retinol*

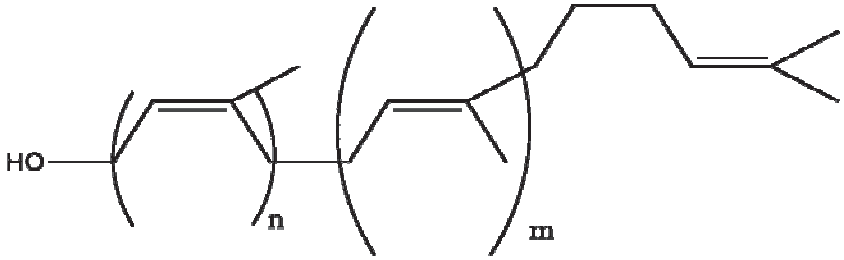
High-unsaturated fatty acids in the lipid composition have cis-configuration. For example:



Oleic Acid

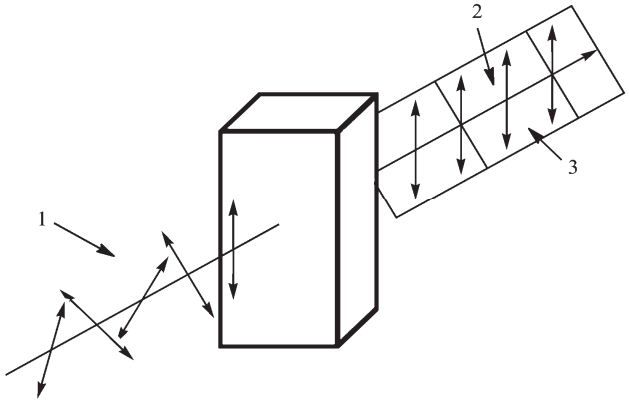
This makes them bent and shortened in form, which is important for maintaining the structure of cell membranes.

Natural compounds polyprenols that transport carbohydrates in the human body have a cis configuration.



2. Enantiomers – this kind of isomerism is due to the ability of substances to rotate the plane of polarization.

The plane of polarization (4) is perpendicular to the plane of polarized beams (pic.1). Passing an ordinary light beam, in which the oscillations occur in different planes, produces the polarized beam (1). Through the prism of spare passes the next beam (2). As a result of electromagnetic waves in a polarized beam they occur in the same plane (3).



If the path of the polarized beam is to be put in a tube with a solution of an organic compound, the plane of polarization (4) will rotate to the right or to the left.

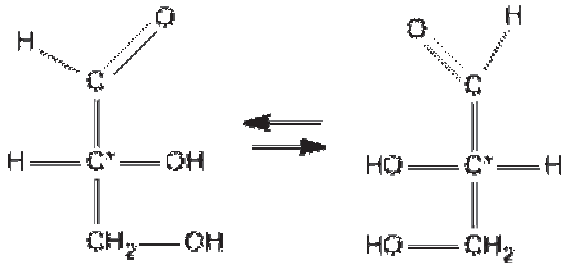
The ability of certain substances to rotate the plane of polarization is called optical activity.

Only asymmetric molecules can exhibit the optical activity. **Asymmetry - one of the main signs of wild life:** aminoacids, monosaccharides, polysaccharides, DNA – these are asymmetrical molecules. The assymetrical body point, points out the human hand. Hand in Greek − **Hiroshi**. This is the term used in surgery and palmistry. The term, which is used in organic chemistry, is **chirality.**

Chirality –is a property of a substance to exist as a pair of incompatible specular reflections.

The formulas of chiral molecules are usually written in the Fischer projection, that is, they have a carbon chain vertically and at the top of the carbon atom the senior functional group is written.

An example of a chiral molecule can be glyceraldehyde:



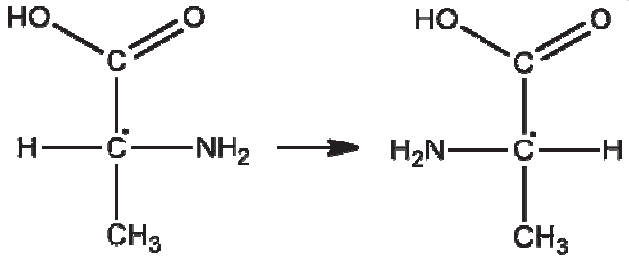
D – Glyceraldehyde *L – Glyceraldehyde*

These molecules are asymmetric because they have an asymmetric carbon atom C* and chiral center.

Chiral center - is a carbon atom, which is in the sρ^3- hybridisation phase and is associated with four different substituents.

These two molecules have a different configuration of the chiral center. The first molecule is a functional group and is located on the right, which means the molecule has D-configuration. The second functional group of the molecule is located on the left, which means the molecule is L-configuration. D-configuration and L-configuration are called the **re1ative** configurations.

For example, to write enantiomers of alanine (CH_3-CH (NH_2)-COOH), we need to find the chiral center: In the molecule of alanine it is the second carbon atom. We write the vertical carbon chain and the amino group NH_2 to the right place relative to a chiral center like in the molecule of glyceraldehyde. This enantiomer has the D-configuration. If amino group is at the left chiral center, such enantiomer is called L-configuration.



These two molecules are optical isomers:

Both molecules are called optical isomers, since they do not differ from each other in their basic chemical and physical properties. Though, the plane of polarization is rotated by the same angle, but in opposite directions.

Rotation to the right is indicated by the sign "+" and rotation to the left by "-".

"+" And"-" is the **absolute** configuration, which we can determine only by doing an experiment, using a **polarimeter**.

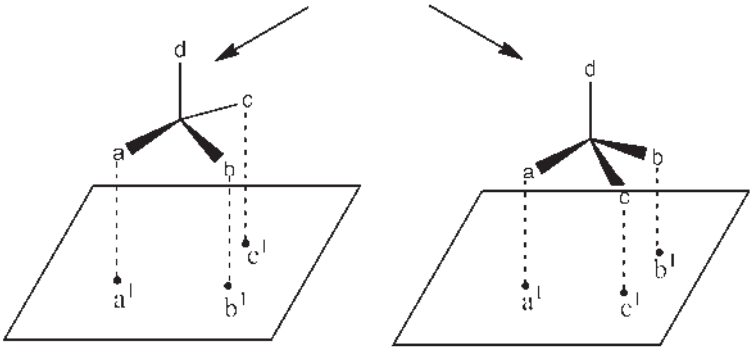
Enantiomers – are isomers, which are related to each other as an object and its mirror image. A mixture of enantiomers is a **racemate**. The racemate is optically inactive.

Diastereomers - isomers, which do not relate to each other as an object and its mirror image.

The biological significance of the enantiomers:

In humans, the substrate and the active sites of enzymes are optical antipodes, that is, they fit together like a lock and key. Only in this way can they interact.

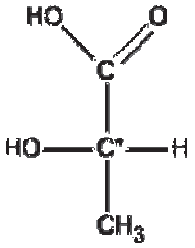
Substratum



Surface Enzyme

Interaction occurs *Interaction does not occur*

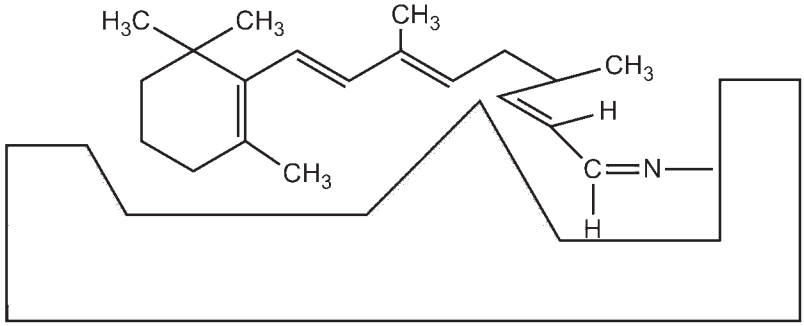
Lactic acid in the human body has a configuration of L (+).



L (+) - Lactic Acid

If as a result of metabolism, the body produced D-lactic acid, a reaction will occur with the respective centers of the enzyme as L-lactic and this will cause a biochemicall reaction.

Cis-retinal and **opsin protein** are optical antipodes. In this case, they interact and form a complex of rhodopsin, which is involved in the process of vision.



If this complex falls on a quantum of light, the isomerization of cis-retinal to trans-retinal will be detached from opsin. This is the nerve impulse in the view. Thus, this example shows the importance of two kinds of isomerisms for the process view.

Antigen and **antibody** interact with each other because they are optical antipodes and fit together like a lock and key.

L-thyroxine - is a natural hormone of the thyroid gland.

D-thyroxine - reduces blood pressure.

Antiarrhythmic agent, **L-acting propranolol** is 100 times stronger than the D-isomer.

L-levamisole is used as an anthelmintic agent and the D-isomer causes nausea.

Acetylsalicylic acid and **prostaglandinsyntetase** are optical antipodes. As a result of this, the interaction suppresses pain, decreasing of temperature, relieving of the inflammatory effect and reduction for the risk of blood clots.

3. **The conformational isomer is due to the rotation of atomic groups with respect to carbon-carbon σ -communication**.

Isomers, which are formed at the same time, are called **conformers**. Process of isomerism happens without the breaking of ties. Conformers have one molecule, but different geometric shapes.

Cause of rotation–is due to the repulsion of the atoms when they are at a distance, which is approximately equal to the sum of the radii of the atoms.

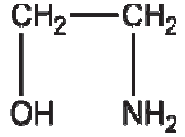
The Conformation of the Compounds with an Open Carbon Chain:

During the rotation of the atoms with respect to σ-bonds there may be two extreme positions:

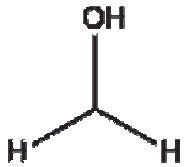
a) In which the atoms are too close to each other and obscure one another;

b) In which the atoms are located at maximum distance from each other.

To use the image conformed by Newman projection; you need to look at the model along with the carbon – carbon σ-communication.



The carbon atom that is closer to the observer represents a point; from it at an angle of 109°28' there is conductivity of communication and records of the atoms and atomic groups, which are connected to this atom.



The carbon atom, which is located behind the first atom and is invisible to the observer, depicts a circle. Since this bond is also not visible, the image of a little shift constrains the first atom. This is called **eclipsed conformation** (a).

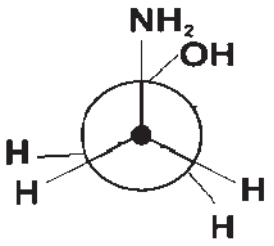
In the eclipsed conformation of the minimum distance between the atoms, their electron sitlls interact with each other, which creates additional energy in the system.

This is a disadvantage for the system and it is thermodynamically unstable, since it raises **torsional stress**.

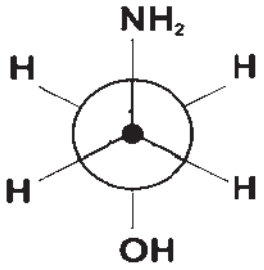
Torsional stress - is the increase of the energy of the system due to the conformation of the shaded.

Therefore, the atoms repel each other and take more extreme position, which is the **inhibited conformation**. In this case, the atoms are at maximum distance from each other, their electron shell do not interact with each other and the energy of the system is minimal. This conformation of the molecule is delayed or inhibited; in this case, the conformation is **inhibited** (b).

Occlusion and inhibited conformation in the Newman projection for colamine can be written as:



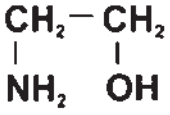
a



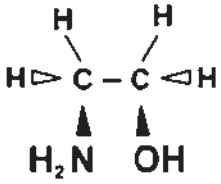
b

Thus, for a complete description of colamine we can write the following formula:

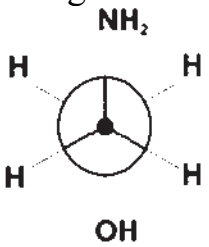
Moleculer Formula



Structural Formula



Configuration

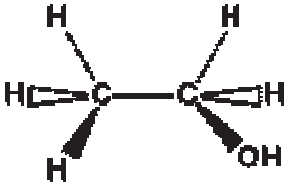
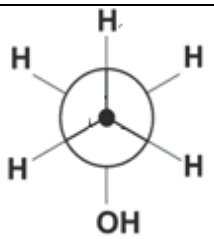
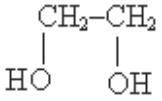
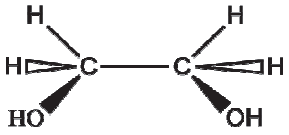
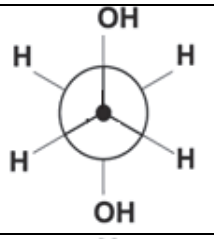
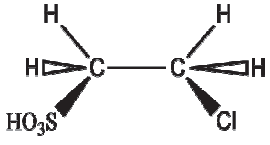


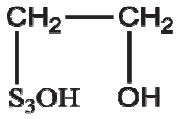
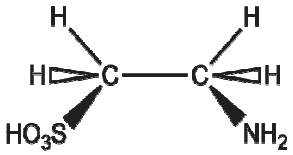
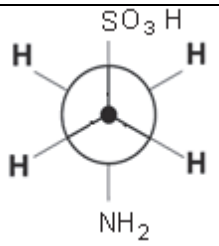
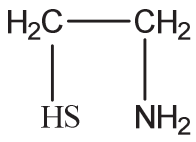
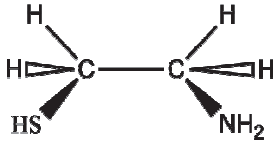
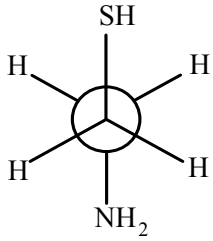
Inhibited Conformation

Full characterisation of some of the biologically active compounds is given in table 5.

Table 5

Structure of Biologically Active Compounds with an Open Carbon Chain

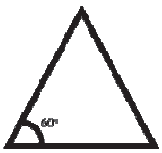
The Biologically Active Substance	***The Molecular Formula***	***Structural Formula***	***Configuration***	***Inhibited Conformation***
Ethanol -antiseptic, a toxic effect on the human body	C_2H_6O	CH_3-CH_2-OH		
Ethylene glycol- antifreeze, toxic effects on the human body	$C_2H_6O_2$			
Chloromethane – an aesthetic tool, the body is decomposed with formation of free radicals	C_2H_5Cl	CH_3-CH_2-Cl		

Taurine-an intermediate in the synthesis of bile acids	$C_2H_7O_3SN$			
Mercaptoethylamine–radioprotective agent	C_2H_7SN			

Closed Conformation of the Compounds with the Carbon Chain

If the carbon atom forms a long chain, the result of rotation of atomic groups with respect to the C-C σ-communication, causes a flexible chain. The size of the angle between σ-bonds is 109°28'.

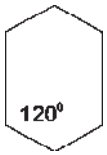
As a result, the flexible carbon chain can form loops. Three carbon atoms form the smallest loop.



This is cyclopropane, in which the angle between the σ-bonds is 60°, which is significantly different from the normal value of 109°28'. As a result, the system generates surplus energy, which is called the angular strain.

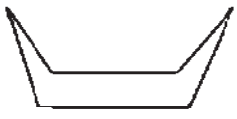
The angular power – is the excess energy due to the deviation of angle from the normal value.

Most importantly, is the six-membered ring, as it contains many biologically active compounds.

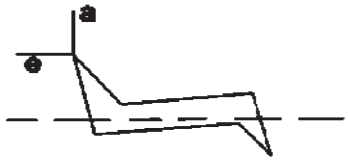


Cyclohexane

The angle of 120°in cyclohexane is also different from the normal value, so it appears as the angular strain. Consequently, this cycle cannot be located in the plane. As a result, the rotation of atomic groups with respect to σ-connection, cyclohexanes are located in space and form the two extreme conformations.



Bath

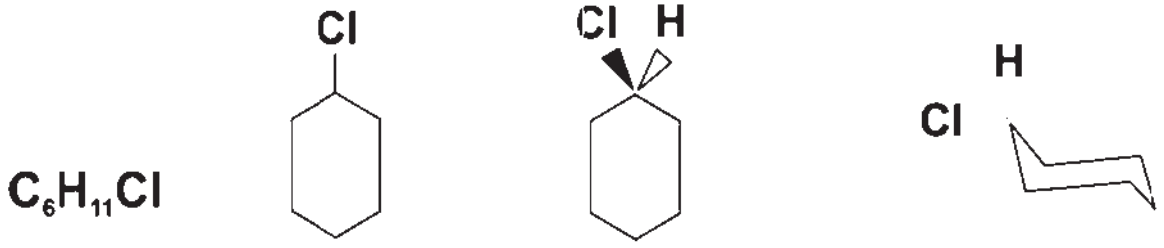


Chair

Chair conformation is energetically more favorable, since it is the one that does not have any torsional and angular strain.

Of great importance is an oriented carbon bond: **equatorial (e)** and **axial (a)**. Equatorial communications are directed parallel to the equator. The axial bond is perpendicular to the equator. Bulky substituents are located on the equatorial since they are known as energetically more favorable.

For example, a complete characterisation of chlorocyclohexane can be written as:

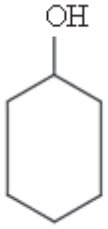
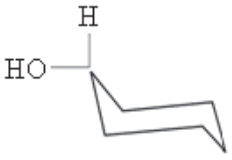
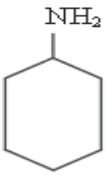
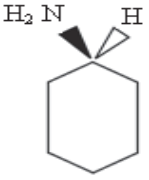
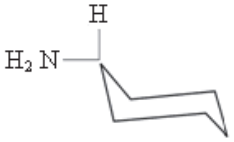
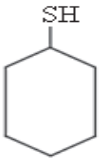
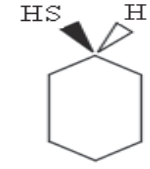
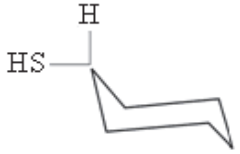
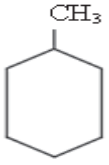
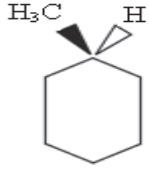
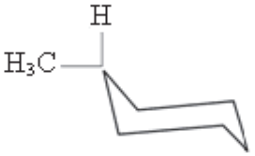


Molecular Formula | *Structural Formula* | *Configuration* | *Conformation*

A Complete Characterization of Some Derivatives of Cyclohexane Is Given in Table 6.

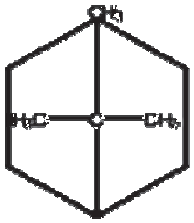
Table 6

The Structure of Cyclohexane Derivatives

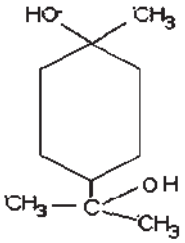
Substance	***The molecular formula***	***Structural formula***	***Configuration***	***Conformation***
Cyclohexane -solvent, starting material for the preparation of adipic acid for the synthesis of Dacron.	$C_6H_{12}O$			
Aminocyclohexane	$C_6H_{13}N$			
Mercaptocyclohexane	$C_6H_{12}S$			
Methylcyclohexane	C_7H_{14}			

The Biological Significance of Conformational Isomerism:

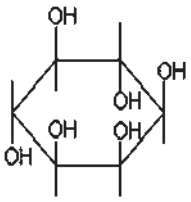
Drugs on the basis of cyclohexane:



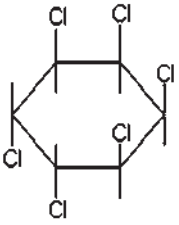
Camphor



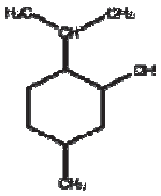
Terpin hydrate



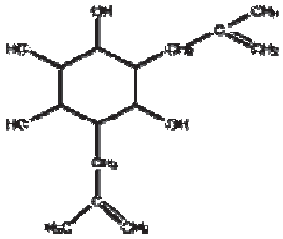
Myoinositol



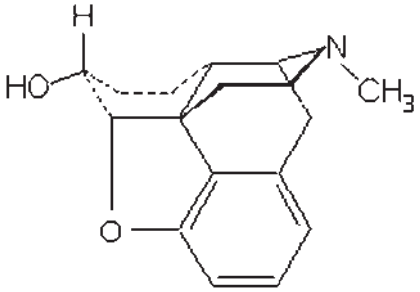
Chlorocyclohexane



Methyl (Antiseptic calming action, sedative effect)



Streptidine (An antibiotic)



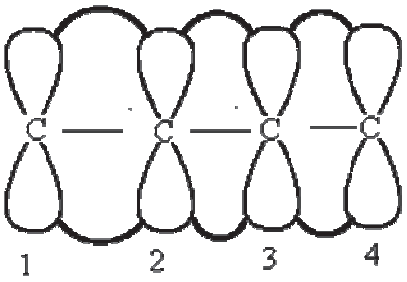
Morphine (An analgesic)

2.3. Conjugation and Aromaticity of Biologically Active Compounds

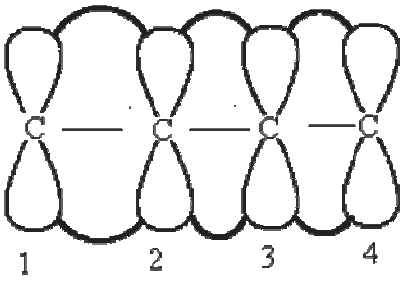
Another factor that affects the activity of biologically active compounds is the phenomena of **conjugation and aromaticity** called a conjugated system, in which the alternating double and simple communication is formed.

Conjugate systems with open-chain coupling:

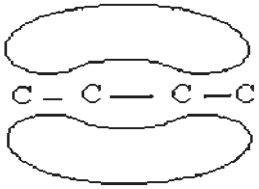
A classic example of such systems is a butadiene-1, 3 or simply butadiene (CH_2═$CH-CH$═CH_2). The carbon atom in butadiene is in sp^2-hybridisation; the molecule is in the plane. A double bond consists of σ-bond that is formed by the overlapping of sp^2-hybrid orbitals of carbon atoms and π-bond formed with the free ρ-orbitals, which overlap between the C_1-C_2 andC_3-C_4 atoms, i.e. **isolated** double bonds:



P-orbitals, which form a π-bond, are also called π-orbitals or π-electron density; π-electron density is located in space, so it is very mobile and is over lapped between the C_2 -C_3



That is, the electron density is not centered between two adjacent carbon atoms and is **delocalized** over the whole system (i.e. molecule) and formed by a single dual of four central clouds that cover all carbon atoms:



System with a continuous electron density is thermodynamically more stable than those with isolated bonds.

This redistribution of electron density in the π-bonds that lead to stabilization of the molecule is called conjugation.

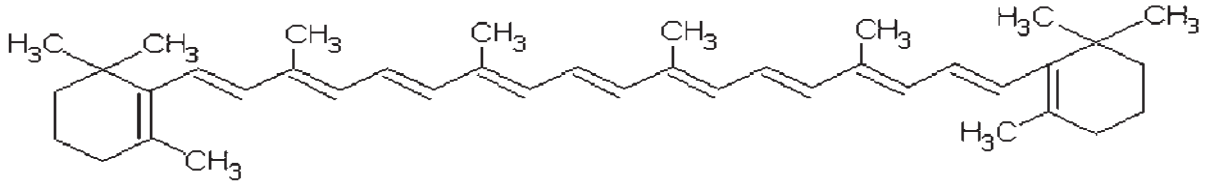
Since the pair only takes the π-orbital, this type of interface is called **π, π-conjugation**.

The degree of stability and stabilization of the system is characterized by the **delocalization of energy**.

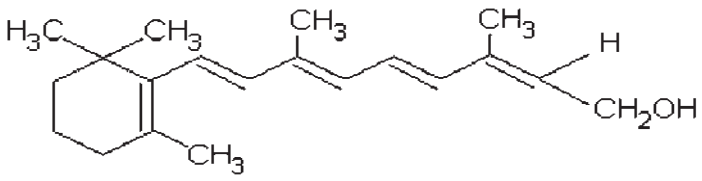
Energy of delocalization means decreasing of energy. For example, for adiene the delocalization energy is 15kj/mol^{-1}.

The biological significance of conjugate systems with open-chain coupling

Examples of biologically active compounds with open chain pairing are carotene and retinol:



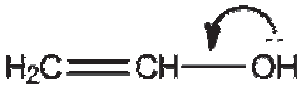
ß-carotene



Retinol (vitamin A)

The longer the chain of conjugation, the more stable the system, which has implications for the functioning of biological systems.

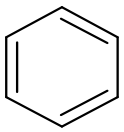
There is another kind of coupling in systems in which there is an alternating double bond, simple bond and electron pair, such as vinyl alcohol:



Electron pair of the oxygen atom enters into conjugation with the π-electron density of the radical. Graphically an arrow that starts from the electron pair and is aimed at the middle of the σ-communication shows this. This kind of pairing is called **ρ, π-conjugation**, and has the greatest value in itterocyclic compounds.

Paired with a closed circuit system inter face

A classic example of such a system is **benzene**.



The carbon atom in benzene is in the sp^2-hybridisation; the molecule is in the plane. A double bond consists of an σ-bond that is formed by the overlapping of sp^2-hybrid orbitals of carbon atoms and a π-bond is formed with the free ρ-orbitals because of the high mobility of the overlapping between all carbon atoms that are delocalized over the whole system. The result is a continuous dual of the electron cloud that covers all carbon atoms. Graphically, it shows a circle inside the loop:

Continuous closed electron density results in a high-energy delocalization -227.8 kJ/mol.

This high stability of the system with a high degree of unsaturation is the key criteria for aromaticity.

Aromaticity – is unusually low energy of the unexcited state, which is due to delocalization of π-electrons.

There are **three signs of aromaticity**:

1. Planar skeleton of the molecule (due to sp^2- hybridisation of the atom carbon);

2. A continuous circuit (due to the presence of π,π or ρ,π-conjugation);

3. The number of delocalized electrons must comply with the rule Huckel (the number of delocalized electrons N= 4n +2, witre n must be an integer).

We find these three characteristics of aromaticity in the **benzene** molecule:

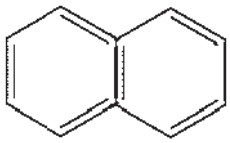
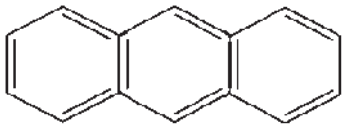
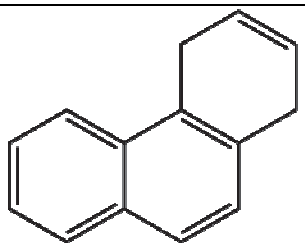
1. The benzene molecule has a planar skeleton, since the carbon atoms are in sp^2-hybridisation phase.

2. In the benzene molecule, as a result of a continuous chain of conjugation, π,π-conjugation is formed.

3. The number of delocalized electrons in benzene is 6, i.e. each carbon atom gives a pair of one π-electron. Hence, 6=4n+2, hence n=1. Consequently, the Huckel's rule is confirmed. Signs of aromaticity of benzene derivatives are given in **table 7**.

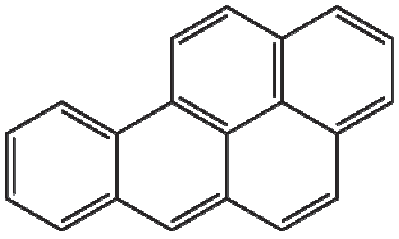
Table 7

Aromaticity of Benzene Derivatives

Connection	*Signs of Aromaticity*
 **Naphthalene** (used for the synthesis of drugs, solvents)	**a)** The skeleton of a planar molecule, since the carbon atoms are in sp^2-hybridisation; **b)** An unbroken chain of conjugation due to π,π-conjugation; **c)** The number of delocalized electrons in the molecule of naphthalene is equal to10. Means that, 10=4n+2, hence then=2. Consequently, the Huckel's rule is confirmed.
 **Anthracene** (used for the synthesis of dyes, part of the medical substances)	**a)** The skeleton of a planar molecule, since the carbon atoms are in sp^2- hybridisation; **b)** An unbroken chain of conjugation due to π,π-conjugation; **c)** The number of delocalized electrons in a molecule is equal to 14. Means that, 14=4n+2, hence then=3. Consequently, the Huckel's rule is confirmed.
 **Phenanthrene** (basis of alkaloids)	**a)** The skeleton of a planar molecule, since the carbon atoms are in sp^2- hybridisation; **b)** An unbroken chain of conjugation due to π,π - conjugation; **c)** The number of delocalized electrons in a molecule is equal to 14. Means that, 14=4n+2, hence then=3. Consequently, the Huckel's rule is confirmed.

The Biological Significance of Conjugate Systems of the Benzene Series

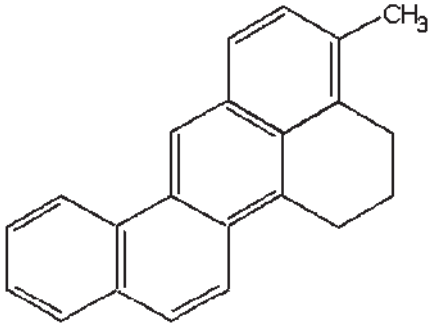
Benzene and its derivatives are carcinogenic substance. Compound carcinogens benzene rings or **polycyclic aromatic hydrocarbons** are the sort of a variety of industries: metallurgy, petrochemical, coking and thermal power plants. With the amount of exhausted gases in the air, the air gets a lot of carcinogens. Even in cities where there are no enterprises in the industries; the air contains high concentrations of the substances. They are the primary source of vehicle exhaustion, once they are out; they contain one of the strongest carcinogens–**benzpyrene.**



The maximum permit table concentration of 10^{-9}g in 1 m^3 is in the air. In some cities, this concentration is 3-8 times higher. There is high concentrations of benzpyrene in tobacco smoke, hence every smoker receives a portion of this carcinogen.

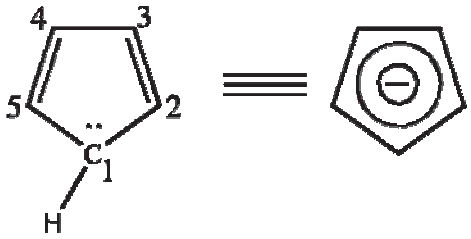
Benzpyrene is also in smoked foods, in sunflower oil, which is obtained at high temperature.

In humans with metabolic disorders of cholesterol, a formation of a very powerful carcinogen –**methylcholanthrene** is formed.



Related nonbenzoic systems

A large number of compounds that do not contain a benzene nucleus possess aromaticity. These include: **cyclopentadienyl-anion**, which are formed by deprotonation (cleavage of H^+) cyclopentadiene:



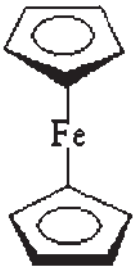
Cyclopentadienyl–anion

This anion is aromatic because:

a) The skeleton of a planar molecule is flat, because of the carbon atoms in sp^2-hybridisation;

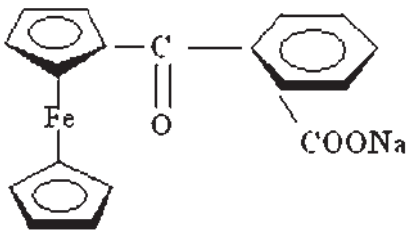
b) An unbroken chain of conjugation by ρ, π-conjugation, and electron pair of carbon C_1 overlaps with the π-electrons of the carbon atoms C_2 and C_5;

c) The conjunction of participation in electron 6 (2,3,4,5 carbon atoms give a conjugated system of 1 electron and the first carbon gives two electrons). Hence, 6=4n+2, hence n=1. Cyclo pentadienyl–anion with cations of itavy metals makes the bond with the so-called**"sandwich"**structure-**metallocenes**. If the complex contains an iron atom, it is called **ferrocene**

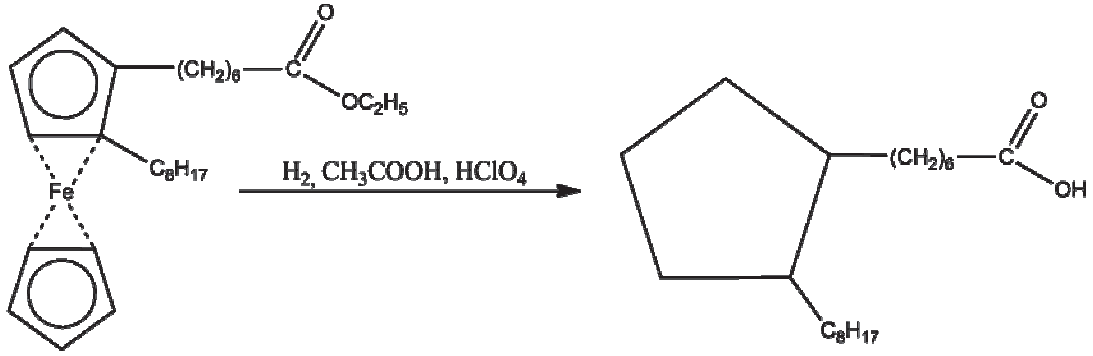


The biological significance of ferrocene derivatives:

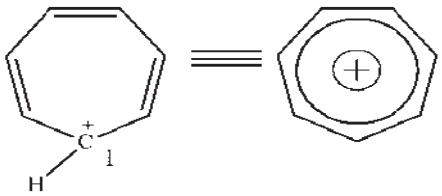
a) Organic iron medication is used to treat iron deficiency anemia:



b) Ferrocene derivatives are using intermediates for synthesis of biogically active substances, such as a **simple acid**:



c) Another system is non benzoic **cyclopentadienyl-ortropylium cation**-cation which is formed by the cleavage of hydride-anion H^- from cyclo itptatriene:



Cycloheptatriene–cation

This cation is aromatic because:

a) The skeleton of the molecule duet of the flat sp^2-hybridisation of carbon atoms;

b) An unbroken chain of conjugation by π, π- conjugation (π-electron density is redistributed to the free orbital of C_1);

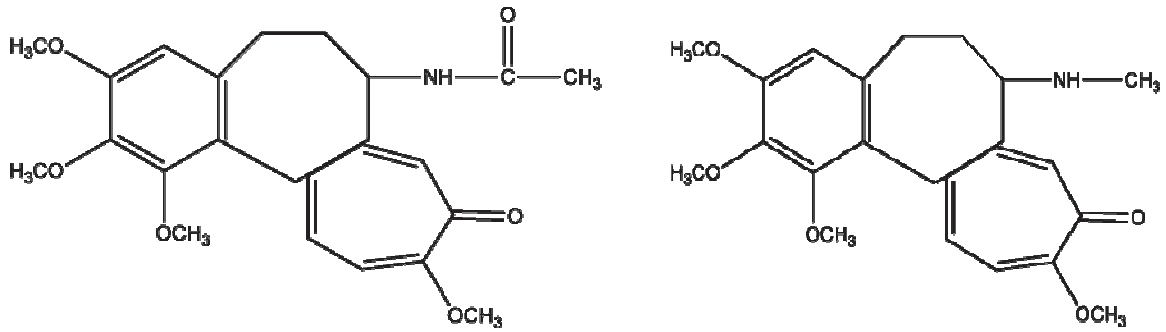
c) In conjunction of the participation of electron 6 all carbon atoms except the first are sent to a dual system of 1 electron. Hence, 6=4n+2, hence n=1.

The biological significance of tropylium derivative is the cation:

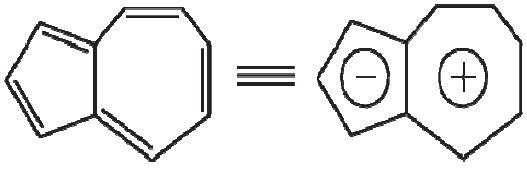
a) Antibiotics that inhibit rotting wood, for example: **tuaplisine**.

b) Colamine is used to treat skin cancer;

c) Colchicine causes the division of chromosomes, so it is used to study the genetics of plants .



Condensed core, consisting of cyclopentadienyl–anion and tropylium–cation is called **azulene**:



This is also an aromatic system because:

a) The skeleton of the molecule duet of the flat sp^2- hybridisation of carbon atoms;
b) An unbroken chain of conjugation is caused because of π,π-conjugation;
c) In the conjugation, 10 electrons take part hence, 10= 4n+2, hence n =2.

In nature there is no azulene. It is obtained synthetically.

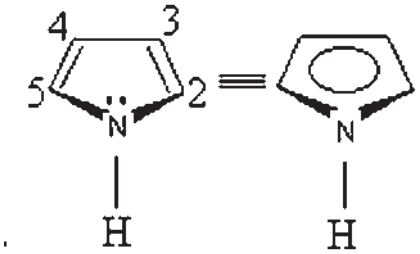
The biological significance is alkyl- substituted azulene contained in essential oils of medicinal plants- Roman chamomile, eucalyptus, and worm wood- which explain their anti-inflammatory effect.

Aromatic heterocyclic compounds

Aromatic characteristics of heterocyclic compounds are the basis of many biologically active compounds; their stability is the duet of aromaticity.

Aromaticity of five-membered cycles

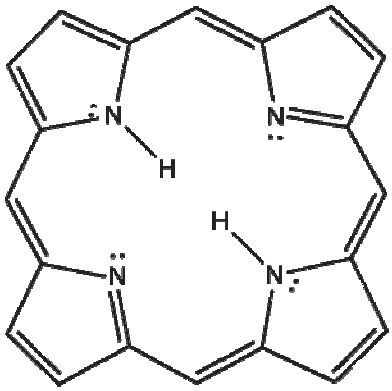
An example of five-membered **pyrrole** cycle is:



The pyrrole molecule has three features of aromaticity:
a) The skeleton of the molecule duet of the flat sp^2- hybridisation of the atoms;
b) An unbroken chain of conjugation by ρ, π- conjugation (nitrogen gives a pair of electrons);
c) In conjunction the participation of electron 6 takes place (2,3,4,5 carbon atoms give a conjugated system of 1electron and the nitrogen atom gives unshared electron pair).
hence, 6=4n+2, hence n=1. Consequently, the pyrrole is an aromatic ring.

The nitrogen atom, which commends to the lone pair of the electron pair, is called the pyrrole nitrogen.

Nuclei pyrrole and products that are contained in the recovery are important bioactive compounds as **chlorophyll, hemoglobin** and **vitamin B_{12}**, which are based heterocyclic system - **porfin**:



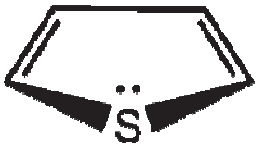
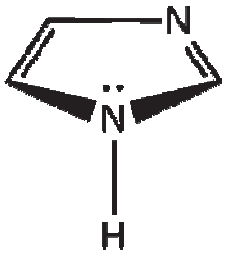
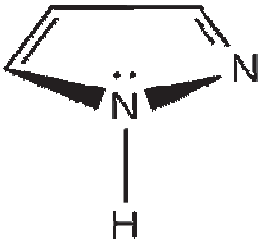
The conjunction is a porfin system and consists of 26 p-electrons. Energy delocalization of nucleus: 840 kJ / mol.

Long chain coupling in condensed heterocycle causing high stability of these molecules is important to perform important functions in the human body.

Five-membered aromatic nucleus with different hetero atoms and their derivatives are the basis of many biologically active compounds (table 8).

Table 8

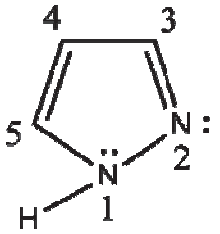
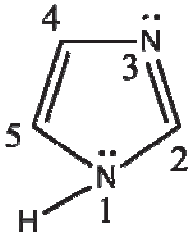
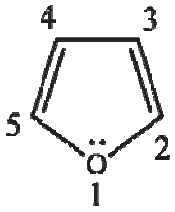
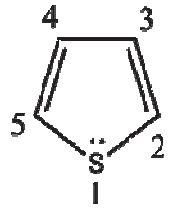
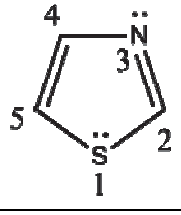
Biologically active compounds containing five-membered itterocycles

Heterocycle	*Biologically active compounds*
 Furan	Furatsillin, furazolidone
 Thiophene	Vitamin H (biotin), ichthyol
 Thiazole	Streptocid, norsulfazol, etalazol, penicillin, vitamin B_1, enzyme cocarboxylase
 Imidazole	Histidine, histamine, pilocarpine, dibasol
 Pyrazol	Amidopyrine, proteins, phenylbutazone
 Oxazole	Derivatives have antipyretic, analgesic, antibacterial, hypnotic effects

Signs of aromaticity of five-membered heterocycles (tab. 9)

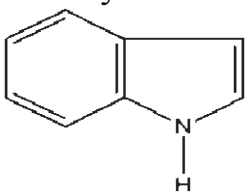
Table 9

Aromaticity of five-membered heterocycles

Connection	*Signs of aromaticity*
 **Pyrazole** (basic drugs: amidopyrine, analginum, phenyl butazone)	**a)** The skeleton of the molecule is flat due to sp^2-hybridisation of atoms; **b)** Continuous chain conjugation by p, π-conjugation (N_1 gives to conjugation electron pair); **c)** Involved in conjugation of 6 electrons ($C_{3,\ 4,5}$ and N_2 in favor with the conjugation system 1 electron and atom N_1 provides an unshared electron pair). Means that, 6=4n+2, hence the n=1. Consequently, the Huckel's rule is confirmed.
 **Imidazole** (in purines, histidine, alkaloids)	**a)**The skeleton of the molecule is flat due to sp^2-hybridisation of atoms; **b)**Continuous chain of conjugation by p, π-conjugation (N_1 gives to conjugation electron pair); **c)**Involved in conjugation of 6 electrons ($C_{2,\ 4,\ 5}$ and N_3 in favor of the conjugation system 1 electron and atom N_1 provides an unshared electron pair). Means that, 6=4n+2, hence the n=1. Consequently, Huckel's rule is confirmed.
 **Furan** (consisting of furfural, furatsilin)	**a)**The skeleton of the molecule is flat due to sp^2-hybridisation of atoms; **b)**Continuous chain of conjugation by p, π-conjugation (O gives rise to conjugation of the electron pair); **c)**Involved in conjugation of 6 electrons ($C_{2,\ 3,4,5}$ in favor of the conjugation system 1 electron and atom O provides an unshared electron pair). Means that, 6=4n+2, hence the n=1. Consequently, Huckel's rule is confirmed.
 **Thiophene** (in ihtiole)	**a)** The skeleton of the molecule is flat due to sp^2-hybridisation of atoms; **b)** Continuous chain of conjugation by p,π-conjugation (S gives conjugation to the electron pair); **c)** Involved in conjugation of 6 electrons ($C_{2,3,4,5}$ in favor of the conjugation system 1 electron and atom S provides an unshared electron pair). Means that, 6=4n+2, hence the n=1. Consequently, the Huckel's rule is confirmed.
	**a)** The skeleton of the molecule is flat due to sp^2-hybridisation of atoms; **b)** Continuous chain of conjugation by p, π-conjugation (S gives conjugation to the electron pair); **c)** Involved in conjugation of 6 electrons ($C_{2,\ 4,5}$ and N_3 in

Thiazole (in norsulfazole, penicillin)	favor of the conjugation system 1 electron and atom S provides an unshared electron pair). Means that, 6=4n+2, hence the n=1. Consequently, Huckel's rule is confirmed.

Also belonging to the aromatic heterocycle condensed with benzene, for example:



Indol

Indole is aromatic because:

a) The skeleton of the molecule is flat due to sp^2- hybridisation of atoms;

b) Continuous chain of conjugation by p, π-conjugation (N gives to the conjugation electron pair);

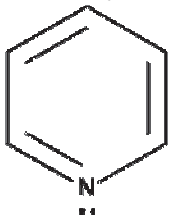
c) Involved in conjugation the 10 electrons (carbons give to the conjugate system 1 electron and nitrogen atom 2 electrons).

Means that, 10=4n+2, hence the n=2. Consequently, the rule of Huckel is confirmed.

Indole is a member of tryptophan, serotonin, skatole, indomethacin and other biologically active compounds.

Aromaticity of six -membered cycles

An example of six -membered **pyridine** cycles is:



In the molecule of pyridine aromaticity has three features:

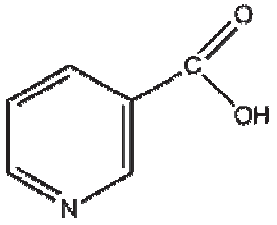
a) The skeleton of the molecule duet of the flat sp^2-hybridisation of carbon atoms and nitrogen;

b) A non broken chain of conjugation by π, π-conjugation;

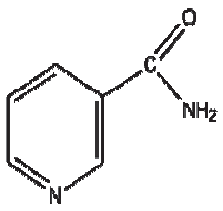
c) In conjunction of participatation of the electron 6 (each of the five carbon atoms in the conjugated system gives to the nitrogen atom and 1 electron gives an electron).hence, 6=4n+2, hence n=1. Consequently, this pyridine contains aromatic rings.

The nitrogen atom, which does not give a non shared electron pair to pair, is called the pyridine nitrogen.

Examples of **biologically active compounds** based on pyridine nucleus are vitamins which are PP, B_6, niacin, folic acid, barbiturates, etc.

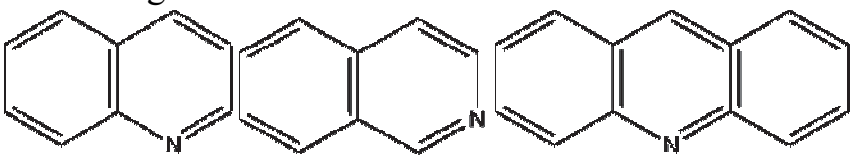


Nicotinicacid



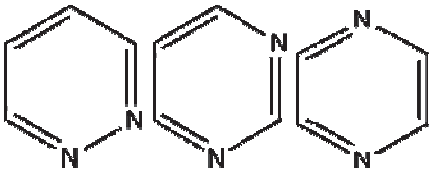
VitaminPP

By the six-membered aromatic nuclei with pyridine nitrogen atom are condensed by heterocyclic with one nitrogen atom:



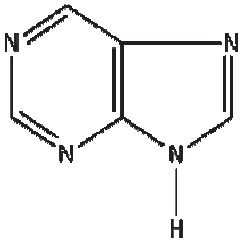
Quinoline *Isoquinoline* *Acridine*

With two nitrogen atoms:



Pyridazine *Pyrimidine* *Pyrazine*

Condensed systems with pyrrole and pyridine nitrogen atoms, the most important of which is a purine:



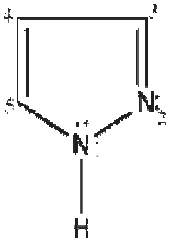
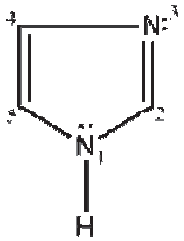
Purine

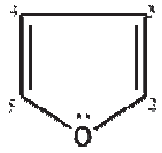
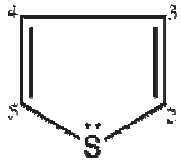
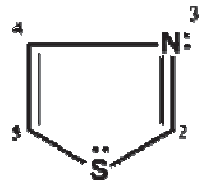
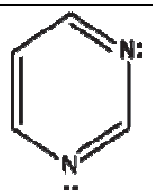
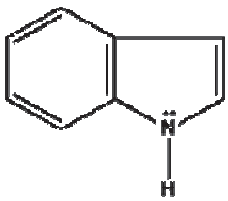
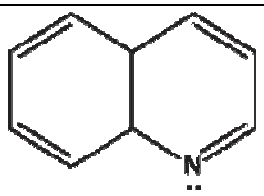
It is a very important biologically active compound containing heterocycles with pyrrole and pyridine nitrogen atoms which are chlorophyll, haemoglobin, and vitamin B_{12}. A long chain of conjugation in these compounds results in high stability of these molecules, this is of great importance to carry out important functions in the human body.

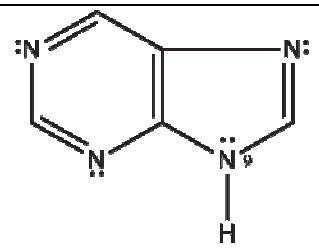
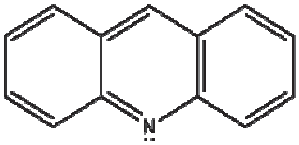
We find signs of aromaticity of heterocyclic compounds (tab. 10)

Table 10

Aromaticity of heterocycles

Connection	***Signs of aromaticity***
 **Pyrazole** (the basis of drugs: aminopyrine, analgine, pitnyl butazone)	**a)** The skeleton of the molecule duet of the flat sp^2 – hybridisation of the atoms; **b)** An unbroken chain of conjugation by ρ, π-conjugation (nitrogen gives an electron pair in the pair); **c)** In conjunction participate 6 electrons (3,4,5 atoms of carbon and nitrogen in the two give the conjugated system of 1 electron and the nitrogen atom gives a non shared electron pair). Hence, 6=4n+2, hence n=1.
 **Imidazole** (in purines, histidine, alkaloids)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by ρ,π-conjugation (nitrogen gives an electron pair in the pair); **c)** In conjunction participates 6 electron (2,4,5 atoms of carbon and nitrogen in the three give the conjugated system of 1 electron, and the nitrogen atom gives a no n shared electron air). Hence, 6=4n+2, hence n=1.

 **Furan** (consisting of furfural, furacilini)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by ρ, π-conjugation (oxygen gives a pair of an electron pair); **c)** In conjunction participates 6 electrons (2,3,4,5 carbon atoms give a conjugated system of 1 electron, and an oxygen atom gives a non shared electron pair). Hence, 6=4n+2; hence n=1.
 **Thiophene** (in the ichthyolum)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by ρ, π-conjugation (sulfur gives a pair of an electron pair); **c)** In conjunction of the participation of 6 electrons (2,3,4,5 carbon atoms give a conjugated system of 1 electron, and a sulfur atom gives a non shared electron pair). Hence, 6=4n+2, hence n=1.
 **Thiazole** (in the norsulfazole, penicillin)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by ρ,π-conjugation (sulfur gives a pair of an electron pair); **c)** In conjunction, 6 electrons participate (2,4,5 atoms of carbon and nitrogen in the three give the conjugated system of 1 electron, and a sulfur atom gives an unshared electron pair). Hence, 6=4n+2, hence n=1.
 **Pyrimidine** (the basis of nitrogenous bases: uracil, thymine, cytosine)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by π,π-conjugation; **c)** In conjunction, 6 electrons participate (all carbon and nitrogen atoms to give the conjugated system of an electron). Hence, 6=4n+2, hence n=1.
 **Indole** (consisting of tryptophan, serotonin, indigo)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by ρ,π-conjugation (nitrogen gives an electron pair in the pair); **c)** In conjunction, 10 electrons participate (all the carbon atoms to give the conjugated system of 1 electron and the nitrogen atom gives an unshared electron pair). Hence, 10=4n+2, hence n=2.
 **Quinoline** (consisting of alkaloids, drugs-cinhofen - for the treatment of gout)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by π,π-conjugation; **c)** In conjunction participates 10 electrons (all the atoms of carbon and nitrogen to give a conjugated system of an electron). Hence, 10=4n+2, hence n=2.

 **Purine** (composed of nitrogenous bases – adenine, guanine, alkaloids-theophylline, the o-bromine, caffeine, uric acid)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by ρ,π-conjugation (nitrogen gives an electron pair in the pair); **c)** In conjunction participates 10 electrons (C_9 gives the nitrogen atom lone electron pair, all other carbon and nitrogen atoms give a conjugated system of 1electron). Hence, 10=4n+2, hence n=2.
 **Acridine** (consisting of quinacrine-anantimalarial drugs)	**a)** The skeleton of the molecule duet of the flat sp^2-hybridisation of the atoms; **b)** An unbroken chain of conjugation by π,π-conjugation; **c)** In conjunction 14 electrons participate (all the atoms of carbon and nitrogen to give a conjugated system of an electron). Hence, 14=4n+2, hence n=3.

2.4. Electronic effects in biologically active compounds

The electronic effect – a shift of electron density in the system (molecule). This shift which occurs within the molecule is different in electronegativity of the atoms. Among the electronegativity elements are as follows:

$$F>O>N,\ Cl>Br>Csp>Csp^2>Csp^3>S>H$$

There are two types of electronic effects: inductive and mesomeric.

1. Inductive effect (I) – is the off set of the electron density to the more electronegative atom of σ-communication.

The inductive effect is manifested in any system (molecule), where there are different electro-negativities of the atoms.

For example:

a) In the molecule of chloroethane, the more electronegative element is chlorine, so it pulls over the electron density from the carbon; graphically this is shown by the arrow, which goes to σ-communications:

$$\overset{\delta+}{CH_3\text{—}CH_2}\rightarrow Cl$$
$$-I$$

On the carbon atom a partial positive charge arises, the one that is in the (radical) decreases the electron density. In this case, we say that **the inductive effect is manifested negatively - -I.**

b) In the propene molecule, the atom of carbon in the sp^2-hybridisation is more electronegative because it pulls over the electron density from the carbon in the sp^3-hybridisation:

$$CH_3 \longrightarrow \overset{\delta^-}{HC}=CH_2$$
$$sp^3 \quad sp^2 \quad sp^2$$
$$+I$$

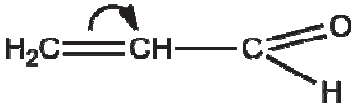
In the carbon atom a partial negative charge occurs, i.e. in the radical with a double bond, the increasing of electron density happens. In this case, it shows **a positive inductive effect +I**. (It should be noted that the methyl group is always pushing it to the electron density as well as carbon, which is in the sp^3-hybridisation and has a low electronegativity).

A characteristic feature of the inductive effect is the rapid decrease in its chain of σ-bonds.

2. Mesomeric Effect (M) or the effect of conjugation of the shift of electron density on the conjugated system.

In the conjugated systems, there can be alternative double and single bonds :=—=(for example: CH_2=CH—CH=CH_2), i.e. π,π–conjugation or a double bond – a simple communication-e-pair : =—**:**(e.g., CH2=CH-ÖH), i.e. ρ,π-conjugation.

For example, acrylic aldehyde in the molecule, which is observed **π,π-conjugation** to an electronegative oxygen atom, the electron density is shifted from the carbon π-communication, because it is more mobile than the electron density σ-communications; graphically this can be shown by a curved arrow that starts from the middle of the double bond and is directed towards an oxygen atom.

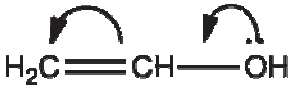


–M

Acrylicaldehyde

But in the dual system, there is a shift of the entire system of π-bonds, graphically shown by a curved arrow that starts from them idle of the double bond between carbon atoms and is directed to the adjacent carbon atom toward the oxygen. As a result, the in fluence of the aldehyde group of the electron density in the system, i.e.in the radical is reduced, and then **the negative mesomeric effect is manifested -M**.

In a system with **ρ,π-conjugation**, such as **vinylalcohol**



+M

Electron pair of the oxygen atom is at the interface with π-orbitals of carbon atoms. Graphically, it shows a curved arrow that starts from the electron pair and is aimed at the middle of the C-O. Since the dual system is the shift of electron density throughout the molecule, then the next shift of π-electron density of the double bond shows a curved arrow from the middle of the double bond in the carbon atom. As a result, the system increases the electron density, that is, they say show **a positive mesomeric effect+M.**

Mesomeric effect of conjugated chain extends without attenuation. Substituents that increase the electron density in the system are called the electron donors.

Substituents, which reduce the electron density in the system, are called electron acceptors.

The same substituent may be in a single molecule electron donor, and in the other as an electron acceptor.

Electronic effects are very important for the reactivity of organic compounds.

2.5. Acidic and basic biologically active compounds

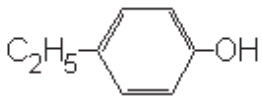
In inorganic chemistry of acid-base properties explain the theory of electrolytic dissociation Arritnius, according to which the acid dissociation of the proton yield of H^+ and reason -OH^- anion. But the organic compounds do not dissociate to explain their acid-base properties of the two theories are used-Bronsted and Lewis.

1. According to the theory of proton Bronsted acid-donor protons and the foundation - is the proton acceptors.

That is any substance that contains hydrogen, may leave it in the form of a proton, thus exhibiting acidic properties (tab.11).

Table 11

The acidity of different classes of organic compounds

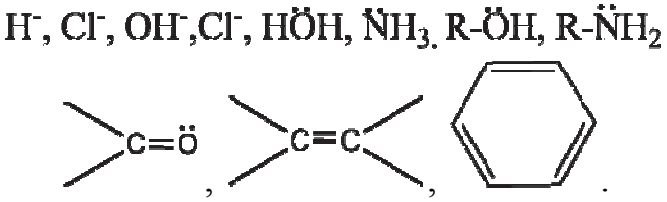
Acid	***pKa***
$C_2H_5CH_3$	48-60
$C_2H_5NH_2$	30
C_2H_5OH	18
H_2O	14
	12
CH_3COOH	4,7
HCl	1

2. according to the electron theory of Lewis, acids-are acceptors of an electron pair and the reason-is an electron pair is a donor.

Acids have a free orbital, which is they accept electron pair from the base.

Examples of Lewis acids: $AlCl_3$, $AlBr_3$, $FeCl_3$, $ZnCl_2$ and others in which metal atoms are free orbital.

Examples of Lewis bases:



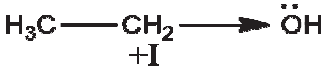
Consider the acid-base properties of some classes of compounds.

2.5.1. Acidity of alcohols

Acidic properties of alcohols depend on the strength of the attraction of a proton to an oxygen atom, this in turn depends on the electron density on the oxygen atom, which is due to the presence of an unshared electron pair of oxygen and the electronic effect of the radical.

Alcohol exhibits acidic properties of the resulting hydroxyl proton separation. But this weak acid, since the oxygen atom creates a high electron density due to the presence of an unshared electron pair and the positive inductive effect of the radical.

Such oxygen is strongly attracted to the positively charged proton

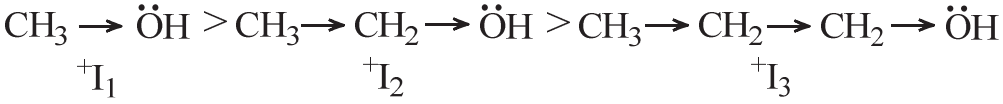


Therefore, alcohols give **alcoholates** salts only with strong bases, for example, with alkali metals:

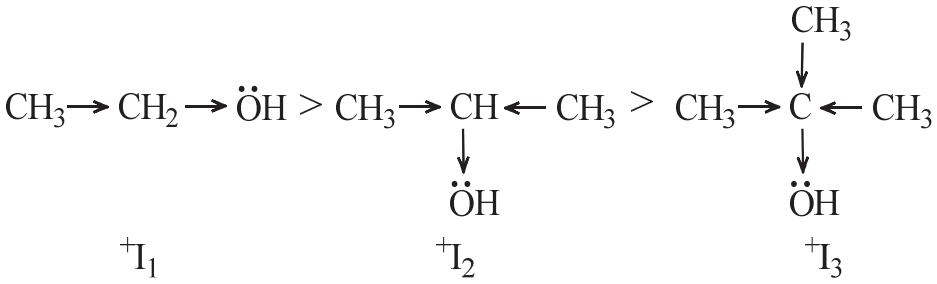
$$2CH_3\text{-}CH_2\text{-}OH+2Na\rightarrow 2CH_3\text{-}CH_2\text{-}ONa+H_2\uparrow$$

The presence of structural fragments and substituents in the radical influence on the acidic properties of alcohols:

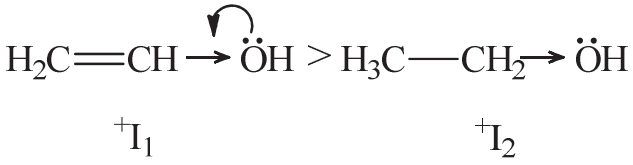
a) In a homologous series, the acidity decreases, as it increases the positive inductive effect of the long radical, electron density on the oxygen becomes more and more attracted to a proton such as oxygen:



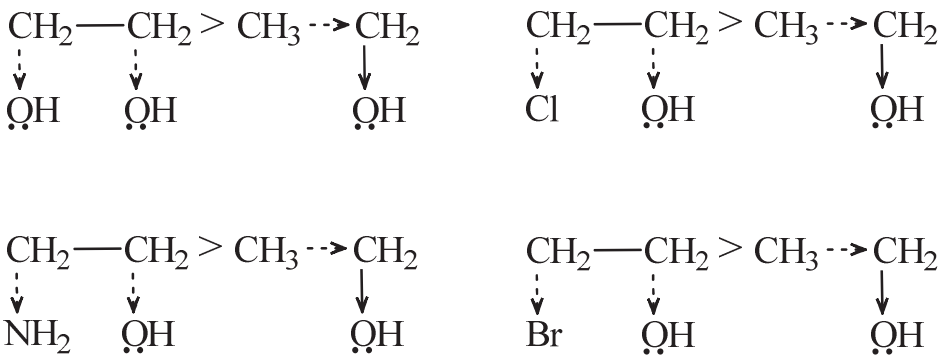
b) Primary alcohols(1) more acidic than secondary(2) and tertiary(3), as it increases the positive inductive effect of neighboring radicals, the electron density at the oxygen becomes more and more attracted to a proton to this oxygen:



c) Unsaturated alcohols are more acidic than the rich, as a positive inductive effect of the radical with sp^2-carbon hybrid is less than radical with sp^3-a hybrid of carbon and the lone electron pair of oxygen goes to the ρ,π-conjugation, resulting in electron density on oxygen decreases and the proton is split off easily

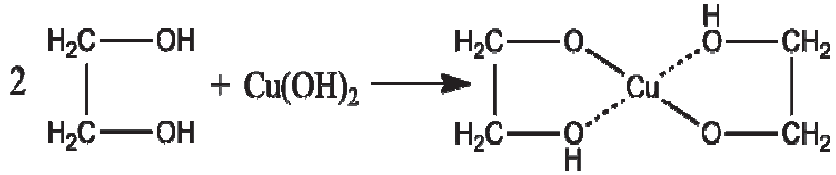


d) Electron accept or substituents in the radical (-OH,Cl-,and NH_2-) increase the acidic properties, as they pull together a part of the electron density from the radical, resulting in electron density on oxygen decreases and the proton is split off more easily:



→ Electronic effect is stronger)
⇢ Electronic effect is weaker)

As a result of increased acidity of the polyols, they may interact with cuprum (II) hydroxide. The products of this reaction are **chelates** - a blue solution.



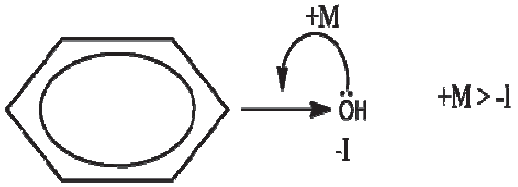
Ethylene glycol *Chelate*

In chelates there are two types of communication-ions (1) and by covalent donor-acceptor mechanism (2).

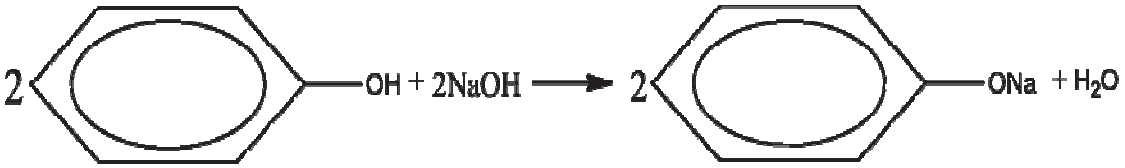
The formation of chelates used as a **qualitative response** to the polyhydric alcohols, and **in clinical analysis for the detection of sugars in biological fluids.**

2.5.2. Acidity phenols.

Phenols exhibit stronger acidic properties than alcohols because hydroxyl group shows a strong positive mesomeric effect (an unshared electron pair of oxygen goes to the ρ,π-conjugation), resulting in electron density on oxygen decreases and the proton is split off easily.



Phenols give salt **phenolates** in the interaction with metals, metal oxides, bases:



The biological significance of the acidity of phenol is that due to the high acidic properties of phenol, carbolic acid is used as an antiseptic.

The presence of substituents in the benzene ring affects the acidic properties of phenols (tab. 12).

Table 12

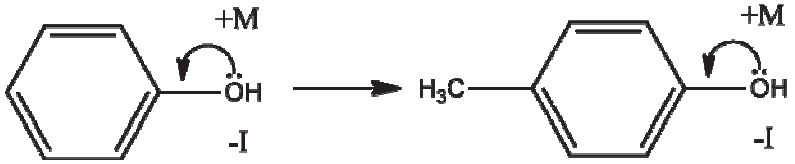
Acidity of phenol derivatives

Formula of compound	***pKa***
o-CH_3-C_6H_4-OH	10,28
p-CH_3-C_6H_4-OH	10,19
m-CH_3-C_6H_4-OH	10,08
C_6H_4-OH	9,95
m-NO_2-C_6H_4-OH	8,35
o-NO_2-C_6H_4-OH	7,20
p-NO_2-C_6H_4-OH	7,14
2,4-$(NO_2)_2$-C_6H_3-OH	4,01
2,4,6-$(NO_2)_3$-C_6H_2-OH	1,02

Effect of substituents on the acidity of the phenol

Electron substituents decrease the acidity of phenols:

a) Radical - in a pair of methyl - methyl phenol increases the electron density in the benzene ring, so the electron pair of oxygen is slightly shifted to the pair(M+ decreases), resulting in the oxygen atom remaining a relatively high electron density and the proton more strongly attracted to it. Therefore, phenol is a stronger acid than steam - methylphenol:

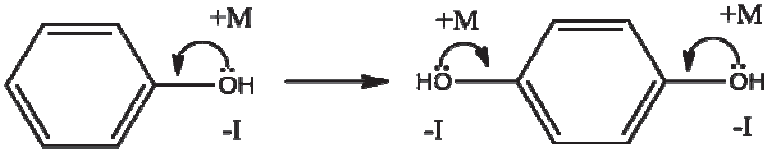


phenol vapor – methylphenol

(⟶ - mesomeric effect is stronger)

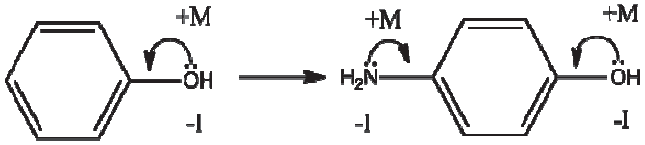
(⇢ - mesomeric effect is weaker)

b) In the molecule pair - because dioxybenzene +M effect of the second hydroxyl groups decreased +M first hydroxyl group, resulting in atom oxygen remains relatively high electron density and the proton strongly attracted to it. Therefore, phenol is stronger acid than steam – dioxyphenol:



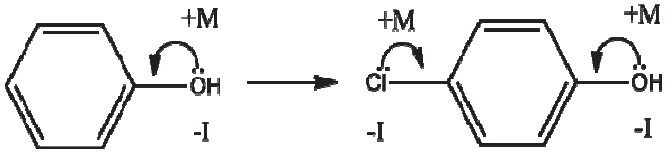
phenol vapor – dioxybenzenes

c) In the molecule pair - +M aminophenol due to the effect of amino decreases +M hydroxyl, resulting in an atom of oxygen maintained a fairly high electrondensity and the proton strongly attracted to it. Therefore, phenol is a stronger acid than p - aminophenol:



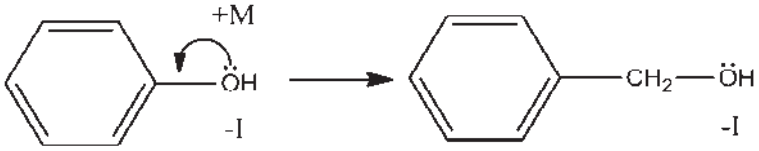
phenol vapor – aminophenol

d) In the molecule pair - chlorophenol by +M effect of the chlorine atom decreases +M hydroxyl, resulting in an atom of oxygen maintained a fairly high electron density and the proton strongly attracted to it. Therefore, phenol is a stronger acid than p - chlorophenol:



Phenol vapor – chlorophenol

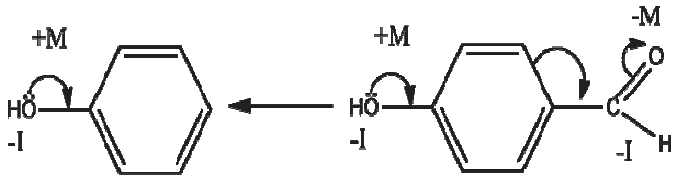
e) In a molecule of benzyl alcohol is manifested only -I (as in alcohols fatty), resulting in the oxygen atom remains quite high electron density and the proton more strongly attracted to it. Therefore, phenol is a stronger acid than the benzyl alcohol:



Phenol, benzyl alcohol

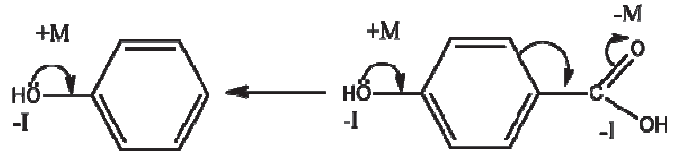
Electron substituents increase the acidity of phenols:

a) In the molecule of p – hydroxybenzaldehyde, aldehyde − group by a negative inductive and mesomeric effects reduces the electron density in the benzene ring, resulting in increased hydroxyl +M, and decreases the density at the oxygen electronic hydroxyl groups, therefore, the proton is easily cleaved, hence, the pair – hydroxybenzaldehyde is a stronger acid than phenol:



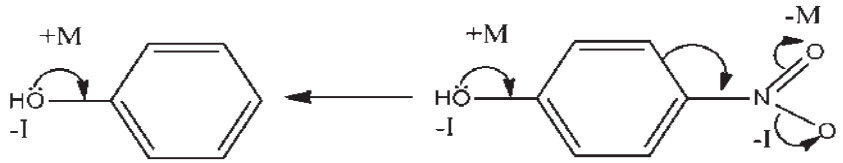
Phenol, p – hydroxybenzaldehyde

b) In the molecule of p - hydroxybenzoic acid, carboxyl – a group of negative inductive and mesomeric effects reduce the electron density in the benzene ring, resulting in increased M+ and hydroxyl groups decreases the electron density at the hydroxy oxygen, so it is easy to split off a proton, then p -hydroxybenzoic acid is a stronger acid than phenol:



Phenol, p - hydroxybenzoic acid

c) In the molecule pair – nitrophenol, nitro - a group of negative inductive and mesomeric effects reduces the electron density in the benzene ring, resulting in increased hydroxyl +M, and decreases the density at the oxygen electronic hydroxyl groups, so it is easy to split off a proton, then p - nitrophenol is a stronger acid than phenol:



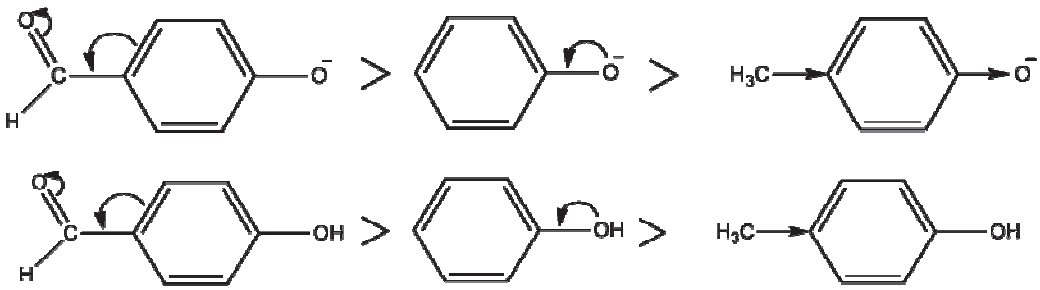
Phenol, p – nitrophenol

Thus, the substituents alter the electron density (delocalization) in the benzene nucleus, affecting the acidic properties of phenol.

Acidity of phenols is defined as stability of phenoxy-ion $C_6H_5O^-$.

Electron substituents reduce the electron density in the nucleus and promote delocalization of the negative charge (electron density) pitnoxy-ion, stabilizing it. There by increasing the acidity of phenols.

Substituents hinder electron delocalization of the negative charge phenoxy-anion, the stability decreases and its acidity is also reduced.



2.5.3. The acidity of thiols

Thiols exhibit stronger acidic properties than alcohols because the sulfur atom is less electronegative than oxygen, and smaller contacts over the electron density from the radical. Therefore, the sulfur atom created does not have a very high electron density, and the proton is not strongly associated with it:

Due to the low electronegativity, sulfur atom negative charge mercaptide -anion RS^- delocalized to a greater extent than aloxyd-anions RO^-, so RS^--anion stable and higher acidity of the thiols.

Thiols react with metals, alkalis and salts give **a thiolate**:

$$2CH_3 – SH + 2\ Na \rightarrow 2CH_3 – SNa + H_2$$

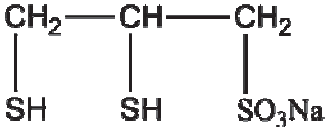
$$2CH_3 – SH + 2NaOH \rightarrow 2CH_3 – SNa + 2H_2O$$

Methylmercaptide sodium

Thiols form salts with itavy metals, which is of **great biological significance**:

a) Heavy metals (Pb, Hg, Bi), which are called thiol poisons, bind SH - groups of proteins -enzymes and destroy their catalytic activity;

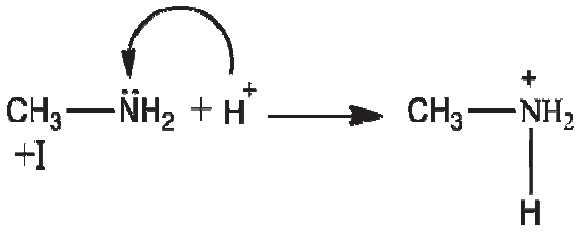
b) Thiols are used as an antidote (antidote) poisoning heavy metals, such as **unitiol.**



Unitiol

2.5.4. Basic properties of amines

Amines are organic bases. **Basic properties** of amines are dependent on the presence of an unshared electron pair on the nitrogen atom and the electronic effects of the radicals and substituents. Fatty amines exhibit a fairly strong basic properties (in comparison with ammonia), as Lewis is the donor lone pair (on the nitrogen atom) and, furthermore, the electron density on the nitrogen atom is increased by the positive inductive effect of the radical. Therefore, the nitrogen atom creates a high electron density and it easily attracts the proton (i.e., is the basis of Bronsted):



Amine salt

Amines react with water, acids:

(Hydroxide anion can be detected in solution using phenolphthalein)

(Chloride - anion can be detected in solution by Silver nitrate).

The presence of structural fragments and substituents in the radical influence on the basicity of amines:

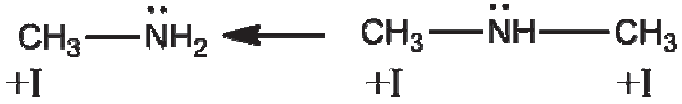
a) Amines are stronger bases than ammonia, as a result of the positive inductive effect of the radical on the nitrogen atom increases the electron density and it easily attracts the proton

+I

b) In the homologous series of amine basicity increases, as it increases the positive inductive effect of the longer radical, the electron density on the nitrogen becomes more and more active as amino acid interacts with a proton

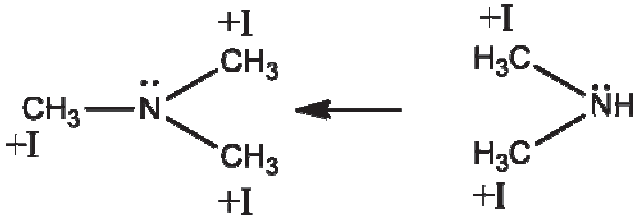
+I +I

c) The secondary amines are stronger bases than the primary, as it increases the positive inductive effect of the two radicals, the electron density on the nitrogen becomes more and more active as secondary amine reacts with the proton acid



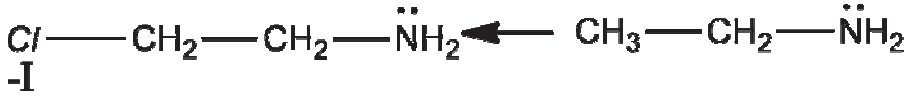
Methylamine dimethyl amine
(Primary) (Secondary)

Tertiary amines are less basic than the secondary as well as the three methyl groups hinder the approach of the proton (spatial factor):

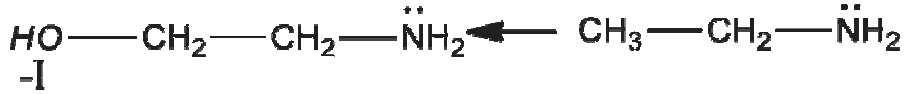


Trimethyl amine dimethyl amine
(Tertiary) (Secondary)

c)Electron acceptor substituents (OH^-, Cl^-) reduces the basicity of amines, as part of the electron density from the radical tightening on itself, resulting in the nitrogen atom decreases the electron density and the proton is not actively attacking it:

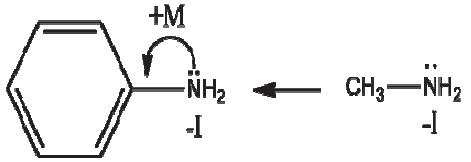


2 – chlorethylamine ethylamine



Oxymethylamine (coalmine) ethylamine

d) **Aromatic amines** (aniline) exhibit weak basic properties, because the electron pair of the nitrogen atom is in the ρ,π-conjugation (a lone electron pair of nitrogen in the aliphatic amines is free, there is no mesomeric effect) and is easily attacked by a proton:

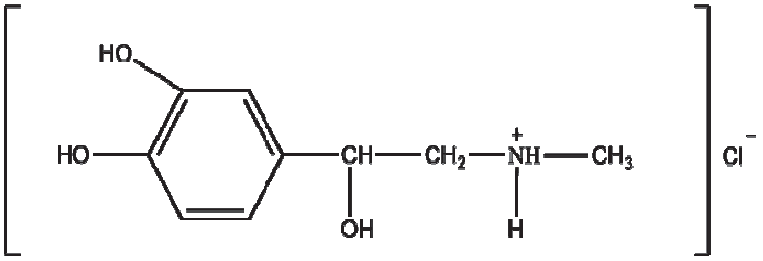


Aniline Methylamine

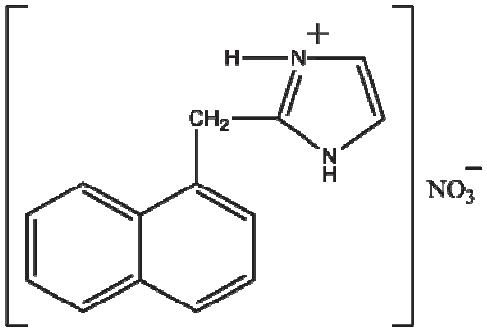
The biological significance of the basicity of amines

Basicity amines are of great importance for the absorption of pharmaceutical substances - amines. They are used in the form of salts of inorganic and organic acids. This increases their solubility in water and the rate of absorption.

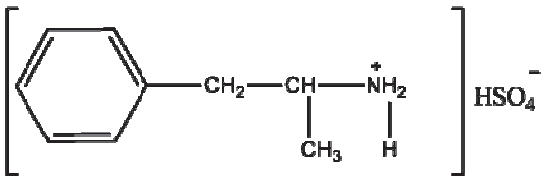
Amines as drugs



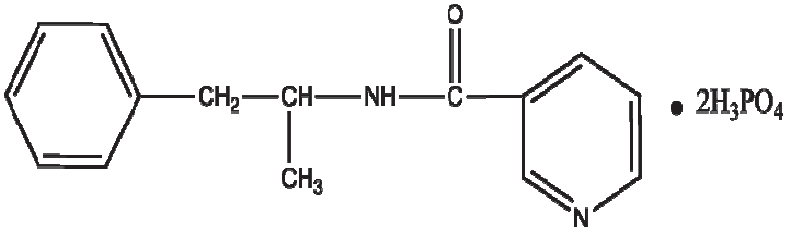
Adrenaline hydrochloride



Naphazoline nitrate



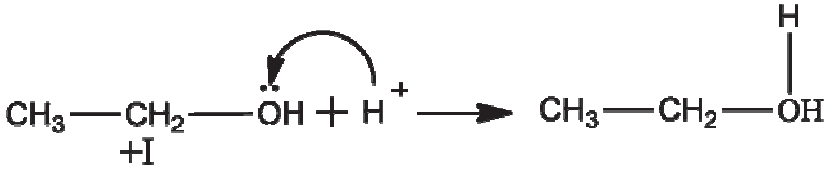
Ampittamine sulphate



Pitnatine diphosphate

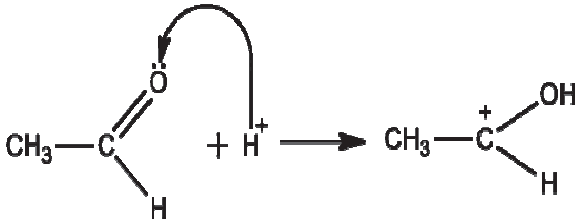
The basicity of the individual atoms in a variety of organic compounds:

a) Alcohols may be due to the basic properties of the lone pair of electrons of the oxygen atom. This can be attacked by a proton that is **to protonate**:



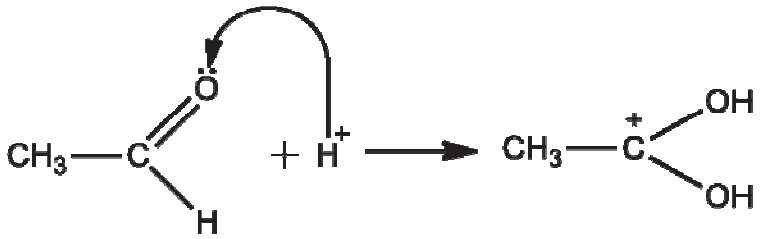
This process can go in the reactions of nucleophilic substitution or elimination (removal) oxy-group.

b) Aldehydes protonated oxygen atom of the aldehyde group, which shows basic properties due to the unshared electron pair and the oxygen of the aldehyde group, which shows basic properties due to the unshared electron pair:



This process occurs in the reactions of nucleophilic addition to aldehydes.

c) In carboxylic acids protonated oxygen atom – oxo-group:



This process occurs in the reactions of nucleophilic substitution in carboxylic acids and their derivatives.

Thus, the above described theoretical concepts are used to explain the mechanisms of reactions involving biologically active substances.

TOPIC 3
REACTIVITY OF HYDROCARBONS AND THEIR FUNCTIONAL BIOACTIVE DERIVATIVES.

3.1. Ways to break the chemical bonds

Organic reactions occur with the rupture of chemical bonds that can go different ways.

1. Homolytic bond breaking, in which the particles are formed on the same electronic structure:

Each particle that has emerged has one unpaired electron.

Particles with one or more unpaired electrons are called free radicals.

2. Heterolytic rupture bond at which the particles are formed in different electronic structure:

Particle is called the A^+**electrophile (EI) - a particle with a lack of electron density**.

Examples of electrophiles are such particles:

H +, Cl +, NO_2 +, SO_3 +, C + (carbocation).

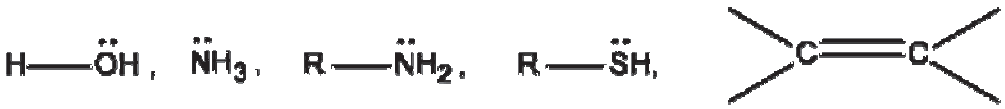
"+" Sign means a free orbital, which electrophile may accept electron pair of the nucleophile.

Particle B -called **nucleophile (Nu) - a particle with an excess of electron density.**

Examples of nucleophiles are:

H–, OH–, Cl– , RO–, RCOO–, C– (carbocation).

It may also be a neutral molecule, in which an atom of oxygen, nitrogen or sulfur is the lone pair of electrons, alkenes, arenes, which have an excess of electron density due to electron π - due, for example:



The particles that we examined - free radicals, electrophiles, and nucleophiles - have a simple structure and are called **agents**, they interact or **attack** the more complex molecules, called **substrates**.

It should be noted that the principle of interaction between an inorganic and organic compounds similar to each other that attract particles with different charges. But if the inorganic compounds of charged particles (ions) resulting from dissociation, the organic - as a result of electronic effects, because most organic molecules do not dissociate.

In the reaction schemes that serves as a further example, not always specified by-products.

3.2. Radical substitution reactions S_r in alkanes

Alkanes - is saturated hydrocarbons with a simple σ-bond between carbon atoms. Carbon in the alkanes is in the sp^3-hybridisation.

For example:

$$CH_3 - CH_2 - CH_3$$

Propane

Why is it that in the alkanes there is **substitution** reaction and why the **radical** substitution?

1. In the alkanes all the bonds are saturated, so there is only a possible replacement (not joining).

2. In the alkanes all the carbon atoms are in state sp^3- hybridisation. Electronegativity of the same, so in the molecule there can be no displacement of the electron density, ie, electronic effects does not occur. This means that centers can not occur with an excess or a deficiency of electron density, so the only possible attack is by free radicals.

The mechanism of radical substitution by the example of bromination of butane:

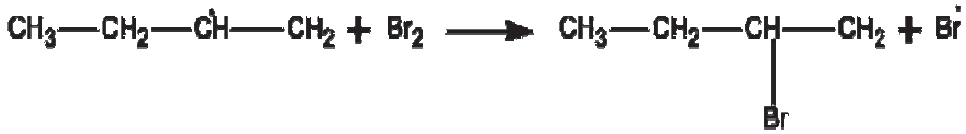
1. The stage of initiation: the action of ultraviolet homolytic bromine molecule is split into two free radicals:

$$Br_2 \xrightarrow{h\nu} Br \cdot + Br \cdot;$$

2. A free radical reacts with bromine molecule of butane and butane is formed by free radical and forms a secondary radical, because it is a more evenly distributed electron density and it is thermodynamically more stable than the primary radical

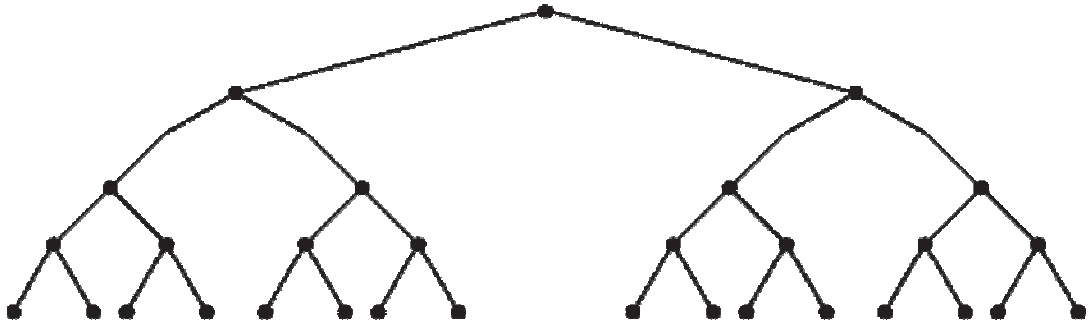
$$CH_3 - CH_2 - CH_2 - CH_3 + Br \cdot \rightarrow CH_3 - CH_2 - C \cdot H - CH_3 + HBr$$

3. A secondary radical of butane reacts with a molecule of bromine and radical substitution product is formed and a new free radical bromine



Free radical reactions are very fast. If the third stage of free radical butane reacted with the second free radical bromine (see the first stage), the radical reaction to this would be broken, but often such reactions go in the chain process. The theory of the chain process was developed by a Russian scientist, academic Nikolay Nikolayevich Semyonov, for which he was awarded with the Nobel Prize in 1956.

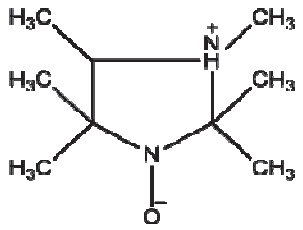
The scheme of the chain process



The biological significance of free radicals

Free radicals are of great biological significance.

1. In general, they are very reactive particles and their active reaction in the Free State does not exist. But there are some free radicals that are quite stable due to delocalization of electron density. For example:



Nitroxyl radical is used to determine the pH of cells. This radical is introduced into a cell, and then remove the EPR spectrum, which depends on the pH of the cell.

2. In humans, free radicals are formed as a result of radiation, ultraviolet radiation, ozone, oxides of nitrogen. They are the products of biochemical reactions, for example, the participation of iron in free radical reactions in the human body:

$$Fe^{2+} + \dot{O}\text{-}\dot{O} + H^{+} \rightarrow Fe^{3+} + HO\text{-}\dot{O}$$

In humans, these free radicals are formed:

H, OH, HO_2, O_2, CH_3, RO.

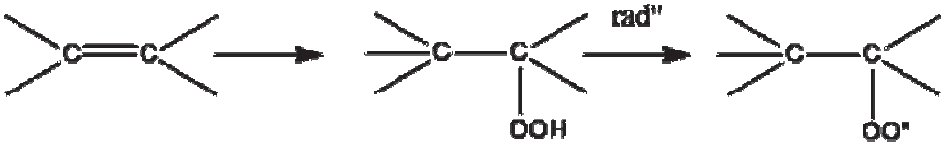
3. Normally, free radicals are involved in these processes:

a) Lipid peroxidation of membranes, which promotes cell growth;

b) The synthesis of prostaglandins - biologically active substances with a broad spectrum of activity in the human body.

But if many free radicals are formed, they exhibit **toxic effects**:

a) Increased lipid peroxidation of membranes, which leads to their destruction. The scheme of this process can be shown as follows:



Hydroperoxide peroxide

This process occurs during **radiation sickness**

b) Reduced levels of amino acids, methionine and tryptophan, which leads to a slowing down of protein synthesis;

c) Break the disulfide bonds -S-S- in proteins;

d) Very sensitive to radiation is the process of oxidative phosphorylation, ie, **impaired synthesis of ATP**;

e) Disrupted the structure of DNA and proteins by alkylation of the nitrogen bases of DNA and proteins of benzene rings (alkylation - is the reaction of the introduction of alkyl, ie, the balance of alkane);

f) Free radicals are one of the factors of aging, particularly of **skin aging**. Under the action of free radicals is free-radical polymerization of the protein elastin, it becomes hydrophobic, rigid, leading to wrinkles. This also contributes to oxygen in the air, because it is biradicale;

g) Excess iron in the body leads to disease called **hemachromatose** as iron provokes the appearance of free radicals which destroy liver cells, heart, pancreas:

$$Fe^{2+} + \dot{O}\text{—}\dot{O} + H^{+} \longrightarrow Fe^{3+} + HO\text{—}\dot{O}$$

h) Appearance of free radicals in the body contributes to **fullerenes**. They are used as additives for lubricating oils as components of batteries in cars. With the exhaust fullerenes into the air, plants, and the human body;

i) Free radicals play a role in the pathogenesis of gastric ulcer, diabetes;

j) Food azo dyes (E-122, E-124) triggers free-radical oxidation of lipids, which gives structure and membrane permeability.

Binding of free radicals in the human body

The body is protected from free radicals **with antioxidants - substances that bind free radicals.** In humans, this is the role of enzymes - **catalase, glutathione peroxidase, superoxide dismutase.** Outside the body it is the role of certain vitamins such as **retinol (vitamin), ascorbic acid (vitamin C), α - tocopitrol (vitamin E)**, which is currently the most powerful antioxidant. The composition of vitamin E is a phenolic hydroxyl group, which binds free radicals.

Scheme of the binding of free radicals:

$$ArOH + RCOO^{\cdot} \longrightarrow ArO^{\cdot} + RCOOH$$

$$ArO^{\cdot} + GSH \longrightarrow ArOH + GS^{\cdot}$$

$$GS^{\cdot} + GS^{\cdot} \longrightarrow GS{-}{-}GS$$

$$GS{-}{-}GS + HADH_2 \longrightarrow 2GSH + HAD$$

(GSH – glutathione - is a tripeptide that reacts with free radicals; NAD - a coenzyme that carries hydrogen atoms).

At the present time there is the search for new antioxidants such as dibunol, derivatives oxypyridine, dextramine etc.

3.3. Electrophilic addition reaction A_e in alkenes

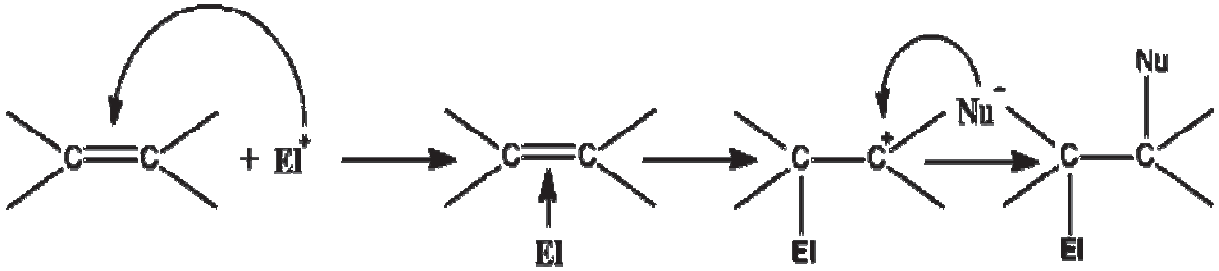
Alkenes - is unsaturated hydrocarbons with a double bond between carbon atoms. The simplest representative - ethene $CH_2=CH_2$.

Why is it that there are addition reactions in alkenes, and why is there **electrophile attack**:

1. An unsaturated double bond, so there is addition reaction;

2. Due to π - electron density of the double bond of alkenes are electrosaturation so they are attacked by electrophiles, i.e. particles with a lack of electron density.

The scheme of the mechanism of electrophilic addition:



π - a set σ - complex or carb - cation

(1) (2) (3) (4)

(Arrows must have the exact start and end)

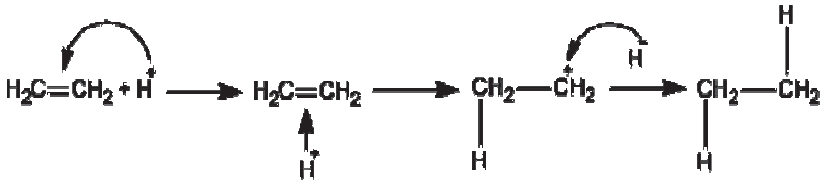
In step (1) the electrophile attacks the double bond, comes to an alkene double bond and forms a π - complex (2). Further, the double bond is broken, electrophile attach at the other carbon atom occurs a full positive charge (ie free orbital) and forms σ - complex (3). The positive charge on the carbon atom is neutralized by a nucleophile - a particle with an excess of electron density - and the final product forms electrophilic addition (4).

Consider the specific reactions that occur with alkenes, and indicate their **biological significance**.

1. The hydrogenation of alkenes (addition of hydrogen).

In vitro reaction proceeds in the presence of a catalyst Pt, Pd or Ni, which splits the molecule of hydrogen electorophile H^+ and H^-nucleophile:

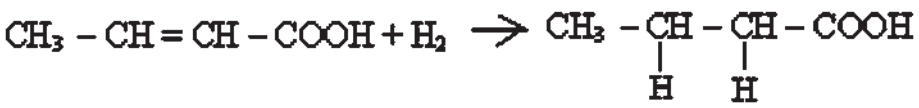
In the case of hydrogenation ethene reaction mechanism can be written graphically as follows:



π - a set σ – complex

The biological significance of the hydrogenation of alkenes:

a)in the synthesis at hydrogenation of crotonic acidis:

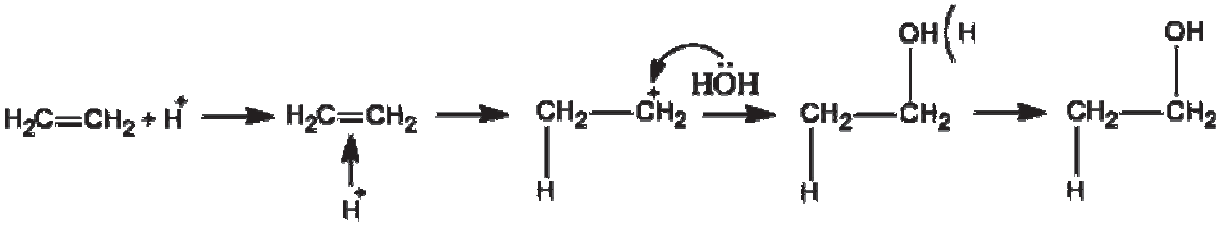


Crotonic acid butyric acid

2. The hydration of alkenes (addition of water).

Water - a weak electrolyte. It does not provide a sufficient number of protons as the electrophile, so the reaction proceeds in vitro in the presence of a catalyst for H^+, which is formed by the dissociation of H_2SO_4 conc.:

In the case of hydrogenation ethene reaction mechanism can be written graphically as follows:

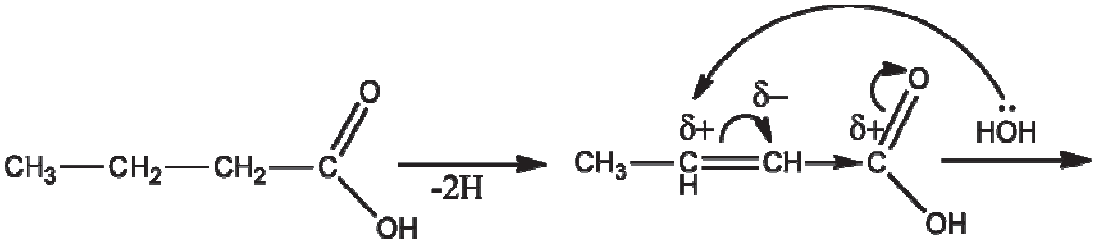


π-complex σ-complex

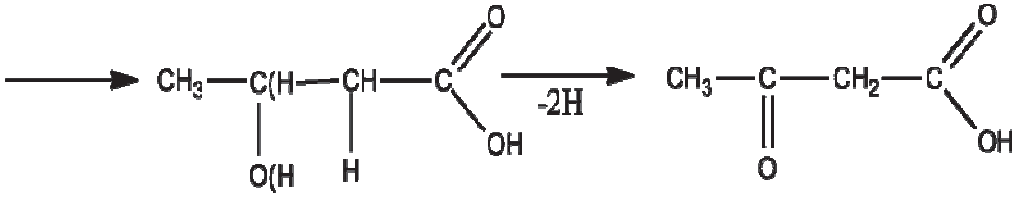
The biological significance of hydration of alkenes:

a) hydration of alkenes in human body - one of the main reactions of the process **of tissue respiration and biological oxidation**.

An example would be a chain of reaction

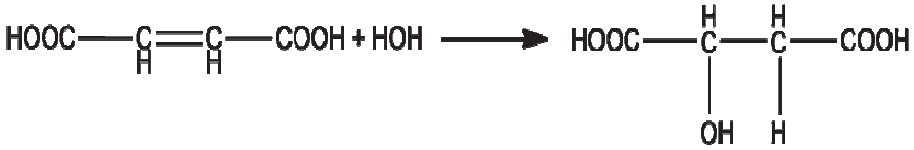


Butyric acid Crotonic acid



β - hydroxybutyric acid β - ketobutyric acid

b) In the Krebs cycle there is the hydration of fumaric acid to malic:



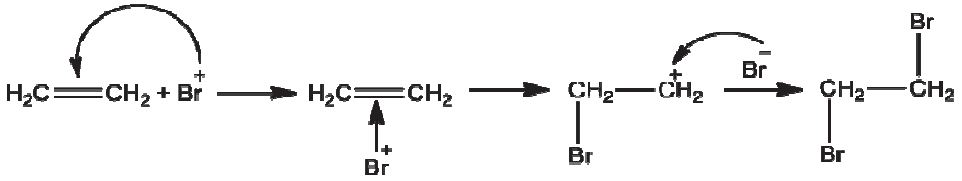
Fumaric acid Malic acid

c) Hydration of alkenes occurs in the b-oxidation of saturated fatty acids

3. Halogenation of alkenes (addition of halogens).

Under the action of π-electron density of the double bond of the molecule splits into heterolytically bromine electrophile and nucleophile Br^+ Br^-:

In the example with ethane, bromination reaction mechanism can be written graphically as follows:



π -a set σ – complex

The reaction is **discoloration of bromine water**. Therefore, this reaction is used as a **quality to the unsaturation**.

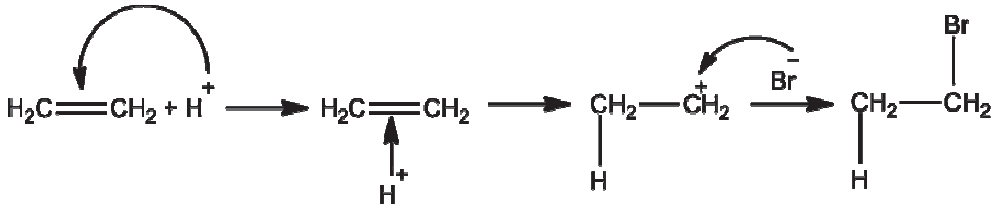
Halogenation of alkenes used for the synthesis of drugs. Since the halo is easily split off, it can be replaced by other functional groups.

4. Hydrohalogenization alkenes (addition of hydrogen halides).

Under the action of π-electron density of the double bond of the molecule breaks down into hydrogen bromide heterolytically electrophile nucleophile H^+ and Br^-:

$$HBr \rightarrow H+ + Br^-$$

In the example, hydrobromination ethene reaction mechanism can be written graphically as follows:



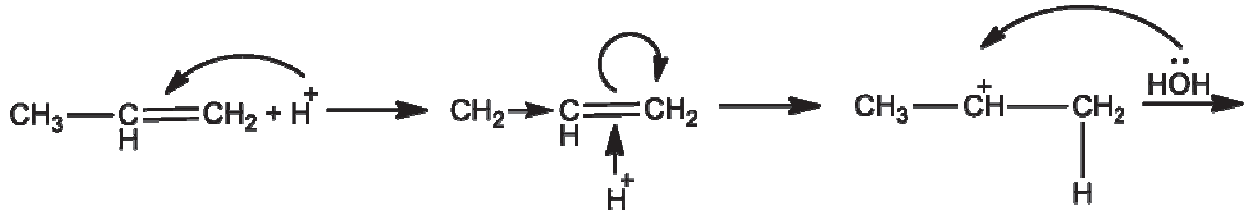
π - a set σ – complex

The reaction of alkenes hydrohalogenation used in the synthesis of drugs.

Hydrohalogenation asymmetric hydration of alkenes and goes onto Markovnikov's rule, that is, hydrogen is added to a hydrogenated carbon atom. This can be explained by δ electron effects.

For example:

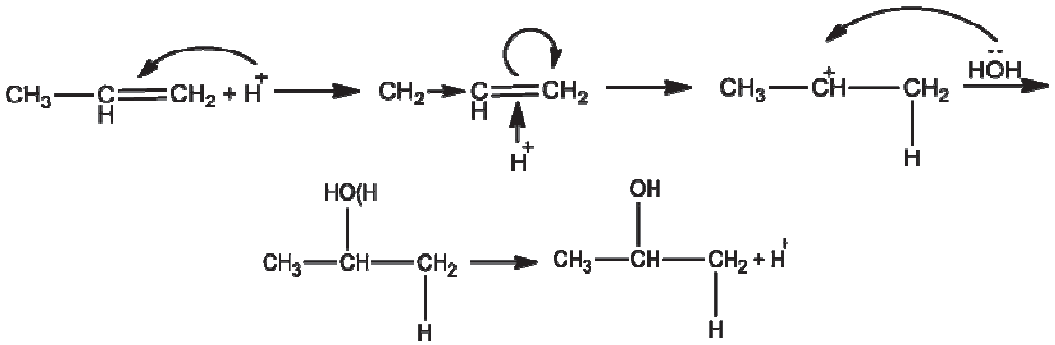
a) The mechanism of hydrobromination of propene can be written as follows:



π -a set σ– complex

In the π-complex (1) is the redistribution of electron density in this way: the inductive effect of electron density from C_3 (sp^3 - a hybrid carbon) is shifted to the more electronegative carbon C_2 (sp^2 - a hybrid of carbon), from which it repels π-electron density of the double bond at C_1. In the first carbon atom creates an excess of electron density, so the proton as a particle with a lack of electron density attached to it (2). In the second carbon atom occurs positively charged, and it attacked bromide - anion as a nucleophile. The result is a finished product (3).

b) The mechanism of hydration of propene can be written as follows:



(See explanation in paragraph A)

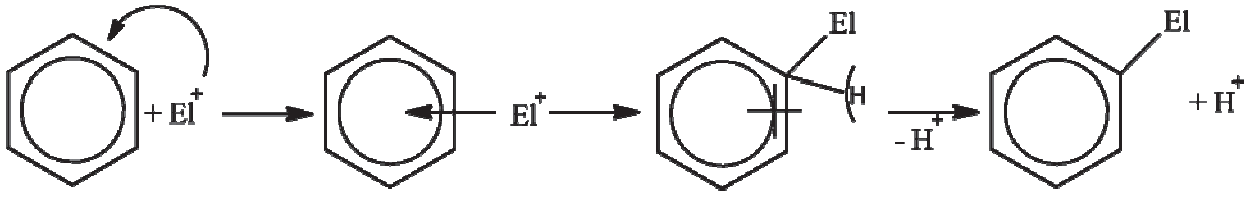
3.4. Electrophilic substitution reactions in the arenes S_e

Arenes – this is benzene and its derivatives. In the arenes are reactions on the mechanism of electrophilic substitution as:

a) Due to the electronic structure of benzene as the aromatic compound is only possible substitution reaction, so as to break single dual clouds that need more power;

b) Benzene has a surplus of electron density due to the presence of π-conjugated electron cloud, so the attack is only a possible electrophile.

The scheme of the mechanism of electrophilic substitution:



π -complex σ - complex

(1) (2) (3) (4)

In (1) step, the electrophile attacks the benzene ring. Then, comes to the electronic system and the conjugate forms the π-complex (2). Further, the dual cloud bursts, electrophile attach to one carbon atom and forms an σ-complex (3). It is unstable, since broken aromaticity. To get rid of the positive charge in the core of the system, the proton is pushed and the reaction product is formed by substitution of (4).

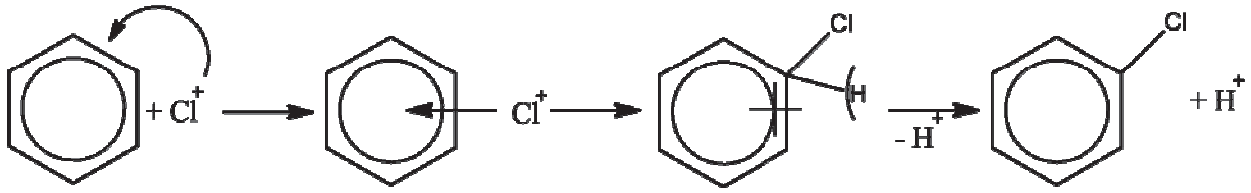
Consider the specific reactions that occur with arenes, and indicate their **biological significance**.

1. Halogenation of arenes.

Because aromaticity is halogenation in the presence of a catalyst, by which an electrophile is formed. Lewis acid catalysts are:

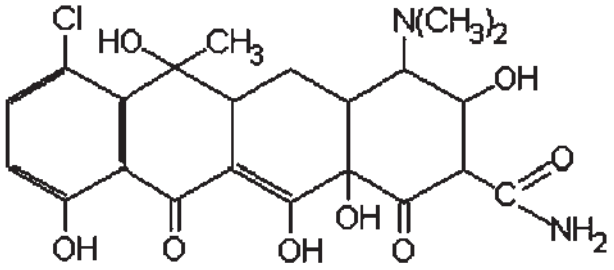
$$Cl_2 + FeCl_3 \rightarrow Cl^+ + FeCl_4^-.$$

The mechanism of halogenation can be written graphically as follows:

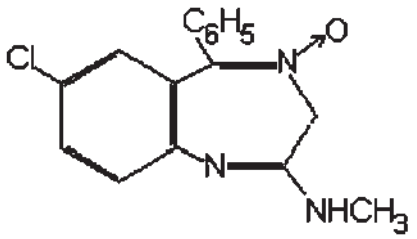


π-complex σ –complex

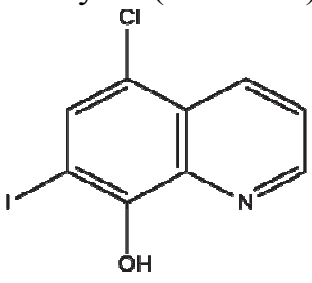
Halogenation of arenes used for the synthesis of drugs:



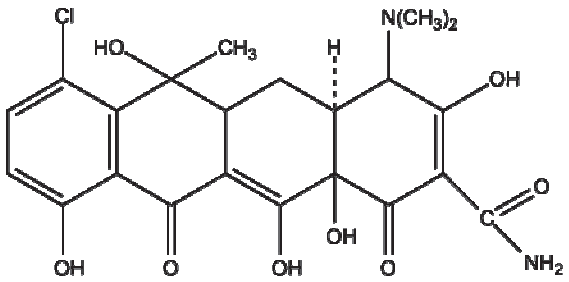
Biomycin (antibiotic)



Elenium (sleeping pill)

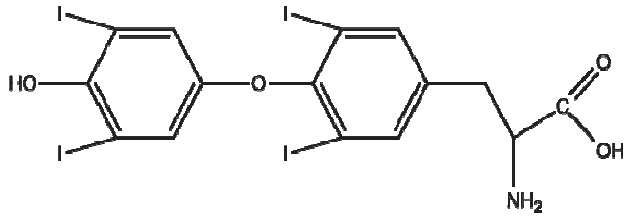


Chlortetracycline (antibiotic)
(Intestinal diseases)



Enteroseptol

The human body is the product of the halogenation of arenes thyroid hormone - **thyroxine**:



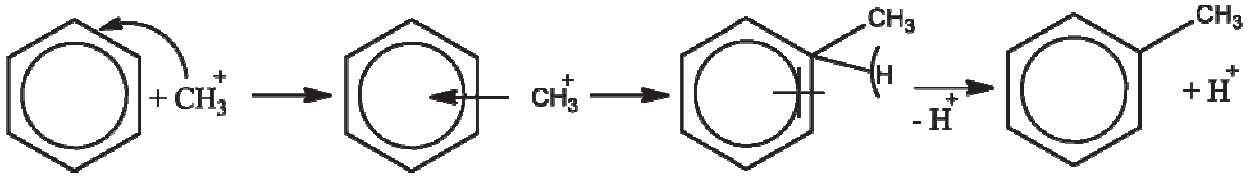
Thyroxine

2. Alkylation of arenes (the introduction of alkyl).

The reaction proceeds in the presence of a catalyst-a Lewis acid.

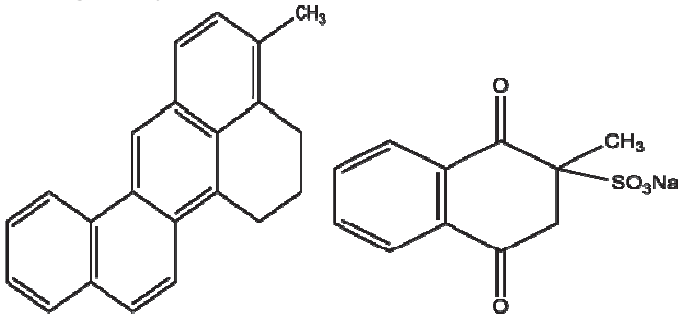
The mechanism of alkylation can be written graphically as follows:

$$CH_3I + AlI_3 \rightarrow CH_3 + + AlI_4^-$$



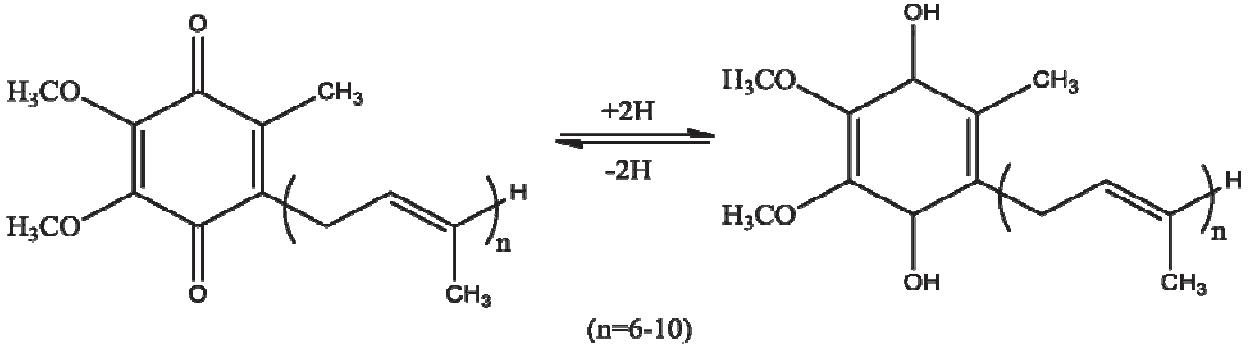
π-complex σ – complex

Alkyl part of the biologically active substances:



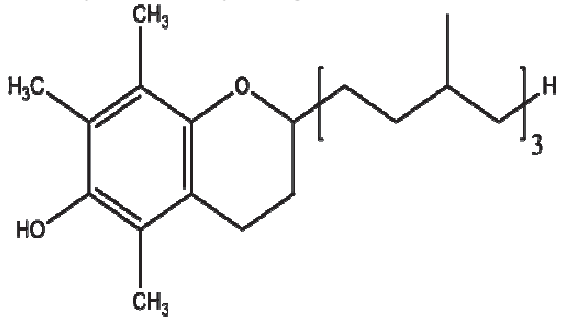
Methylcholanthrene Menadione (increases blood clotting)

(Formed in the body from cholesterol)

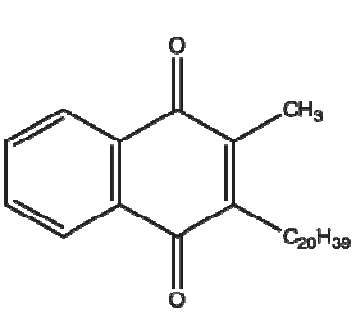


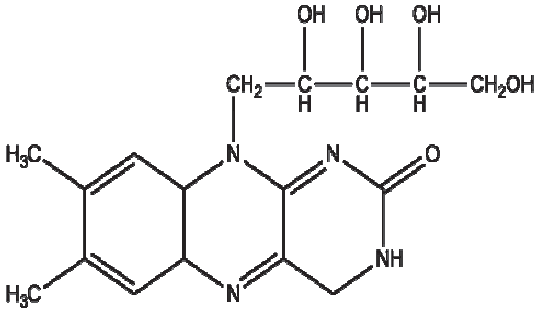
(n=6-10)

Ubiquinone (coenzyme Q, hydrogen transfer in the human body)



Vitamin E (α -tocopitrol, an antioxidant)





Vitamin K (Anti hemorrhagic action)

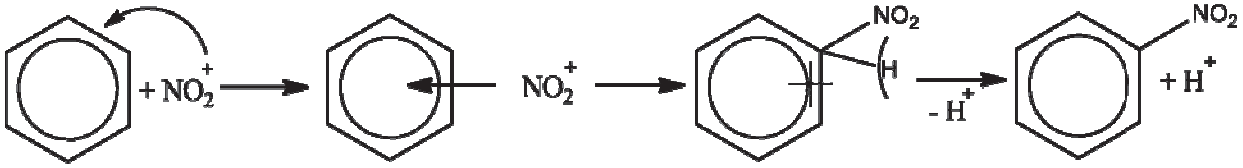
Riboflavin (vitamin B2, the lack of it causes growth retardation)

3. Nitration of arenes (the introduction of nitro-NO_2).

Nitration is carried out using nitrating mixture. It is a mixture of concentrated acids, nitrate and sulfate. In the presence of acid, sulphate nitrate acid dissociates to form anitronium ion, NO_2^+, which is the electrophile:

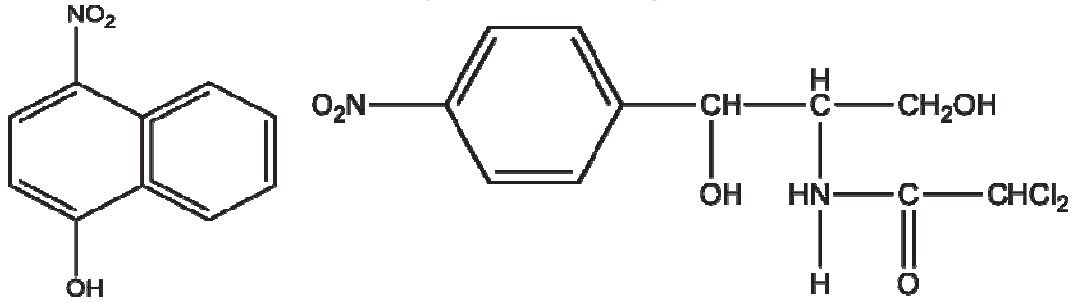
$$HNO_3 + H_2SO_4 \rightarrow NO_2^+ + HSO_4^- + H_2O$$

The mechanism of nitration can be written graphically as follows:



π-complex σ – complex

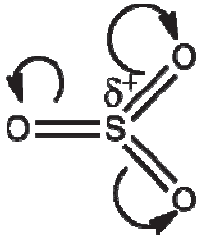
Nitration of arenes used for the synthesis of drugs:



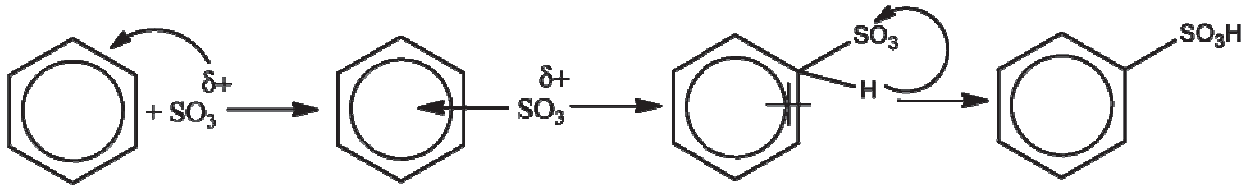
Nitroxoline (5-NOC, germicide) Chloramphenicol(synthetic antibiotic)

4. Sulfonation of arenes (the introduction of sulfonic-SO_3H).

Sulfonation is carried out with the help of sulphur(VI) oxide, which is as a result of the displacement of electronic density electronegative to more oxygen to the sulfur atom arises up excess positive charge. This particle will electrophile and attack the benzene ring.

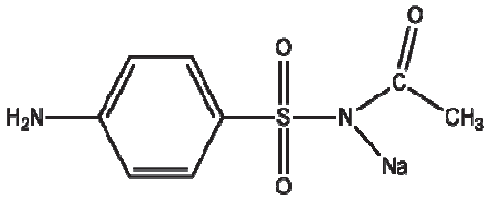


The mechanism of sulfonation can be written graphically as follows:

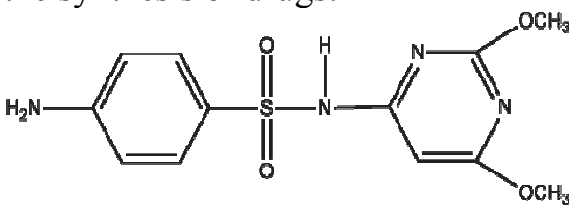


π-complex σ– complex

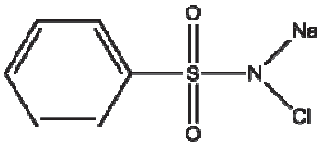
Sulfonation of arenes used for the synthesis of drugs:



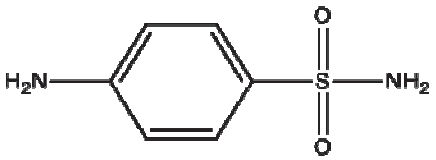
Sulfacyl sodium



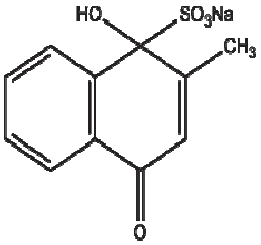
Sulfadimethoxinum



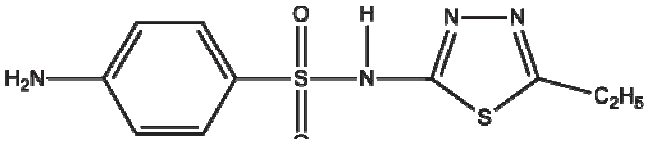
Chloramine



Streptocid



Vicasol



Etazol

3.4.1. The electron and electron-substituents

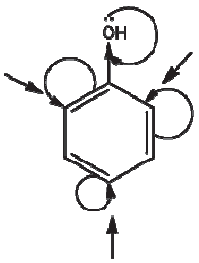
Electron-donating substituents are known to increase the electron density in the system.

Electron-with drawing substituents are known to reduce the electron density in the system.

The effect of these substituents is particularly evident in the reactions of electrophilic substitution in arenes.

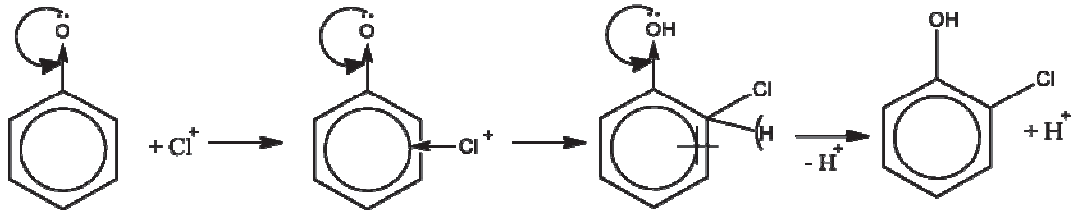
If the benzene ring has substituents-electron donor and electron acceptor, they send another substituent (halogen, alkyl, nitro or sulfo) in a certain position.

Electronsubstituents: -OH,-NH_2,-SH, alkyl – send another subgroup in the **ortho** or **para** position.



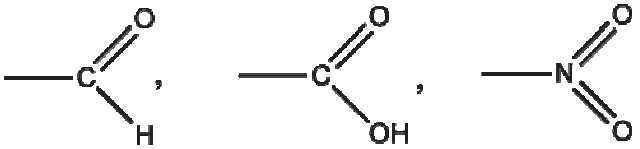
para

For example:

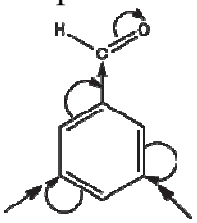


π-complex σ - complex

Electron alternates:

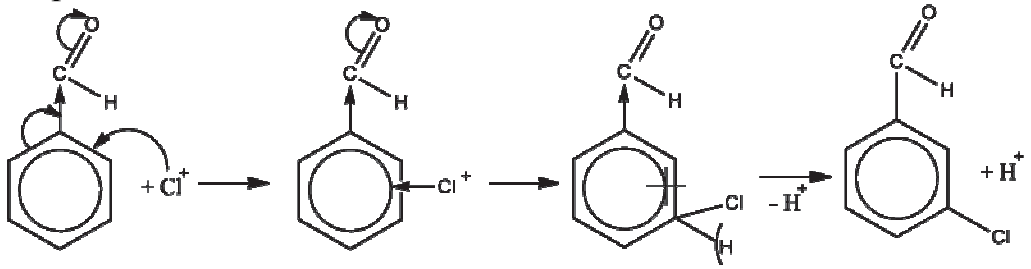


Send another subgroup in the Meta - position.



Meta Meta

For example:



π-complex σ – complex

3.5. Nucleophilic substitution reactions of Sn in halogenation

Halogenalkane - is derived alkanes in which one or more hydrogen atoms substituted by halogen atoms.

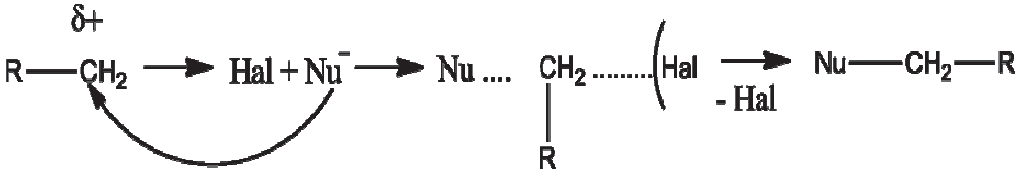
Presence of strongly electronegative halogen atom leads to a redistribution of electron density in the system (molecule). In halogenation there is nucleophilic substitution at sp^3 - hybrid carbon atom, because:

a) All links are saturated, so it is the only possible replacement;

b) As a result of displacement of the electron density to the atom of halogen, that is a result of the negative inductive effect of halogen on the carbon atom there is a partial positive charge. This carbon atom is attacked by a nucleophile, i.e. the particle with an excess of electron density:

$$R - \overset{\delta +}{CH_2} \rightarrow Hal$$

Scheme mechanism of nucleophilic substitution S_N in halogenation:



(2) Active complex (3)

Or the transition state

For the formation of active complex nucleophile approaches from the opposite side of the halogen (1), that is saying that the attack comes from the rear. Next nucleophile begins to form a relationship with carbon, and communication with halogen weakens and forms an active complex or transition state (2). Halogen is easy leaving group is cleaved from the active complex is formed and the replacement of the product (3).

Halogenations are used as intermediates in the synthesis of many organic substances, since halogen is easily replaced by other functional groups.

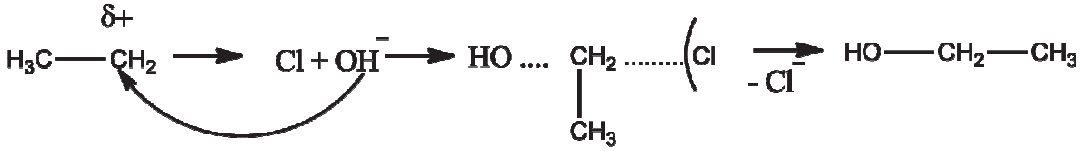
Consider the specific reactions that occur with halogenation, and indicate their **biological significance**.

a) Interaction with alkali:

Dissociation of the alkali hydroxide is formed - the anion OH^-, which is the nucleophile.

Mechanism can be written graphically as follows:

$$NaOH \rightarrow Na^+ + OH^-;$$

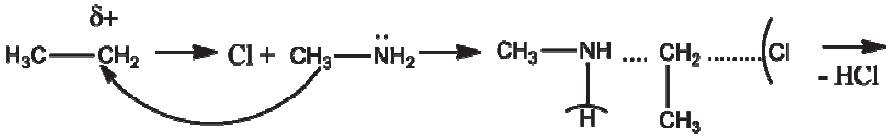


This reaction is used in the synthesis of drugs for the introduction of oxy - group.

b) The interaction with ammonia and amines:

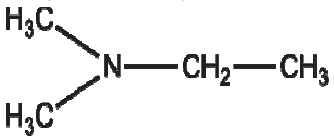
Ammonia and amines by nucleophile is a lone pair of electrons of the nitrogen atom.

Mechanism can be written graphically as follows:



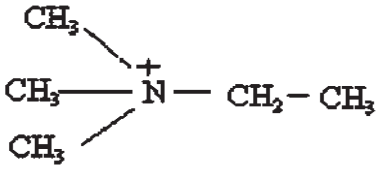
Ethylmethylamin

The result is **alkylation** of nitrogen. If you take even one molecule of amine, it is replaced by hydrogen and formed ethyldimethyliamin:



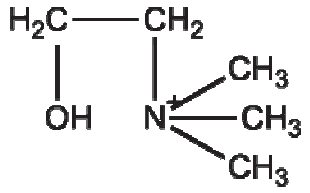
Ethyldimethylamin

By the nitrogen lone pair, there can be an attachment of another alkyl group and formation of the **quaternary base:**

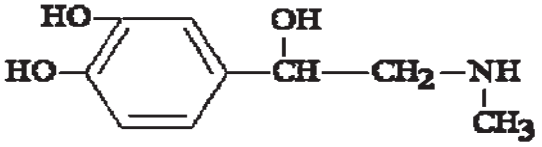


Ethyltrimethylamin

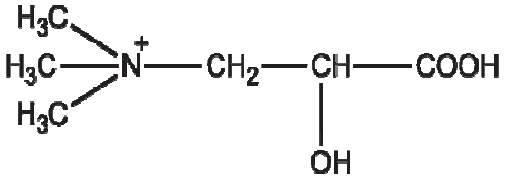
In humans, synthesized by choline is methylation, epinephrine, carnitine, creatine, etc.



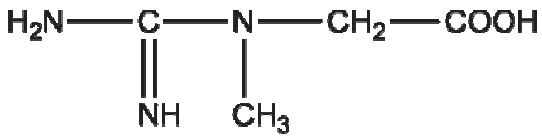
Choline
(Regulates fat metabolism)



Adrenaline
(Constricts blood vessels)

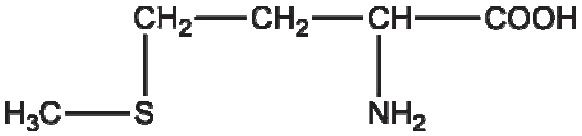


Carnitine
(Transports fatty acids)



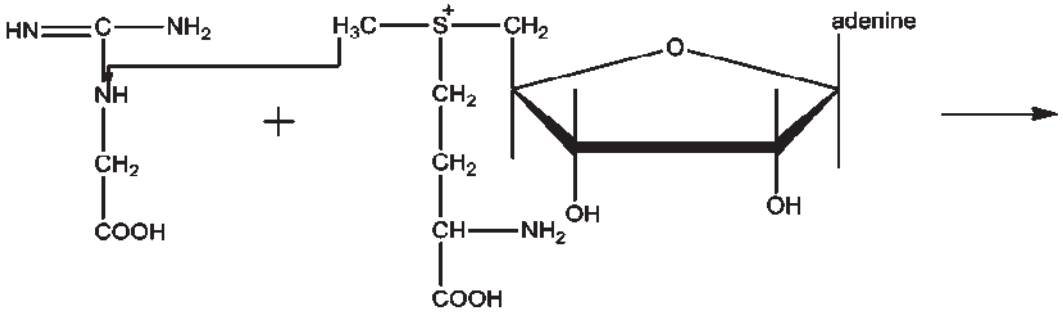
Creatine
(Involved in muscle contraction)

The main methylating agent in the human body is an amino acid - methionine:

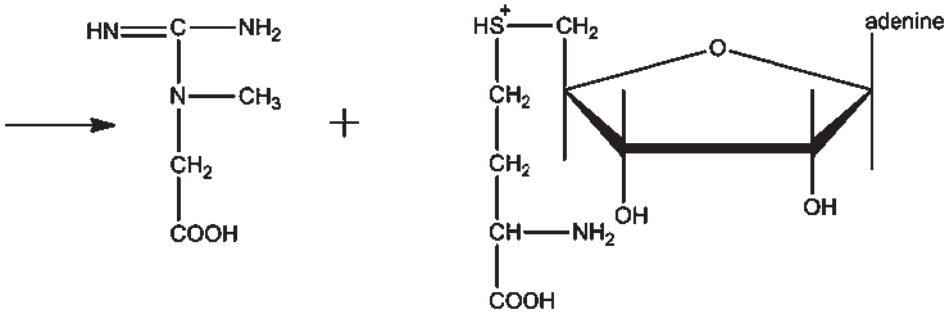


Methionine

The scheme of **methylation in the human body:**



Glyco cyanine S - adenosylmethionine



Creatine Adenosylhomocysteine

3.6. Nucleophilic substitution S_n in alcohol

Alcohols - are derivatives of alkanes, in which one or more hydrogen atoms are substituted by hydroxyl - groups.

Presence of strongly electronegative oxygen atom leads to a redistribution of electron density in the system (molecule).

In alcohols, there are **nucleophilic substitutions** at sp^3 - hybrid carbon atom, because:

a) All links are saturated, so the only possible replacement;

b) As a result of displacement of the electron density to the oxygen atom, that is, the negative inductive effect of oxygen on the carbon atom there is a partial positive charge. This carbon atom is attacked by a nucleophile, i.e. the particle with an excess of electron density:

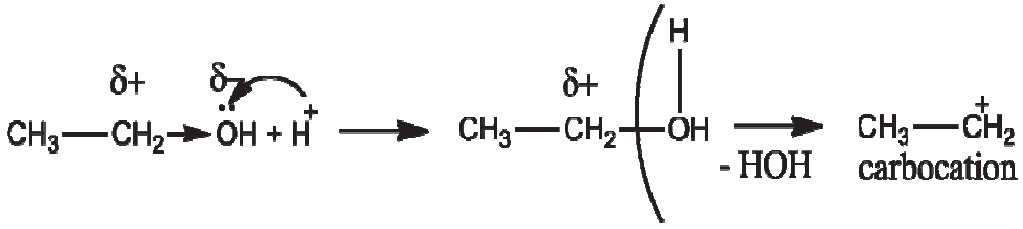
$$\delta +$$
$$R - CH_2 OH \rightarrow$$

Hydroxyl - is a group that is difficult to split off as a strong base. In the Free State it cannot exist. To split an OH^- - group, you should use a catalyst - a proton H^+, which gives the H_2SO_4 conc. The alcohol in this case reacts as a base, since the oxygen atom has an unshared electron pair.

Mechanism can be written graphically as follows:

Step 1:

$$H_2SO_4 \rightarrow H^+ + HSO_4^-;$$



(1) (2) (3)

In step (1) the proton attacks the oxygen of hydroxyl group. Further, the proton attached to oxygen, forms the intermediate particle (2), in which oxygen was trivalent, so the water molecule is split off and forms carbocation (3).

Step 2:

Chloromethane

In the second step carb-cation is attacked by a nucleophile Cl^- and formed the final reaction product - chloromethane.

Humans, in substitution of OH^- - groups go through a stage of formation of phosphorus - esters, since it is easy to split off the phosphate residues:

$$R\text{-}OH + H_3PO_4 \rightarrow R - O - PO_3H_2 \rightarrow R^+ + OPO_3H_2.$$

3.7. Elimination reaction in alcohol

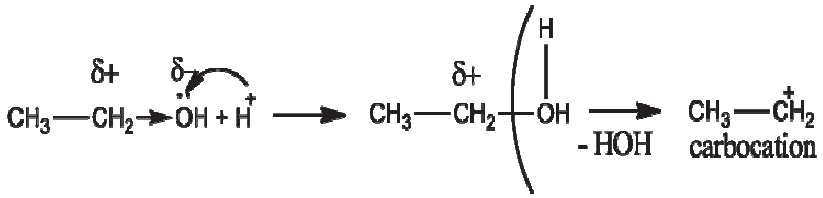
Many reactions between organic compounds are accompanied by competing reactions. Such a reaction for nucleophilic substitution in alcohols is the reaction of **elimination E** (cleavage). In this case, alcohol splits off the water molecule, which is **dehydration**.

Since oxy - the group is split off is difficult, it requires a catalyst for H^+.

Mechanism can be written graphically as follows:

Step 1:

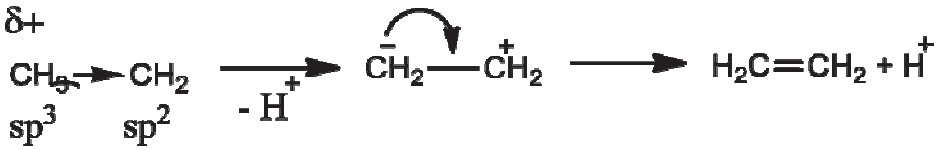
$$H_2SO_4 \rightarrow H^+ + HSO_4^-;$$



In (1) step the proton attacks the oxygen of hydroxyl group. Further, the proton attached to oxygen, forms the intermediate particle (2), in which oxygen was trivalent, so the water molecule is split off and formed carbo-cation (3). That is, the first step of the reaction proceeds as a nucleophilic substitution reaction. Next, the reaction proceeds in a different way.

Step 2:

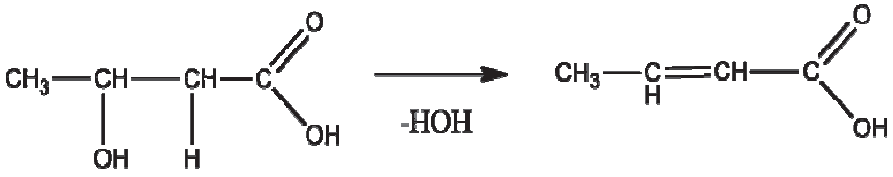
In the formed carb - cation (3) is the redistribution of electron density:



sp^2 - a hybrid carbon atom in the cation-carb (3) contracts over the electron density of the sp^3 - hybrid carbon. In the sp^3 - hybrid carbon occurs as a partial positive charge (δ+), and from it can repel the proton H^+, that is, in this carbon there arises the CH- acidic center. After removal of the proton forms a particle with positive and negative charges on different atoms of carbon (4). As a result of redistribution of electron density between the carbon atoms of the double bond occurs, and the formed product of elimination - the unsaturated hydrocarbon (5).

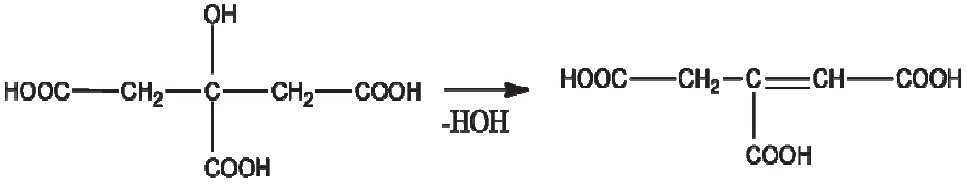
Biological significance of the reactions of dehydration of hydroxyl compounds:

a) The formation of crotonic acid:



β - hydroxybutyric acid Crotonic acid

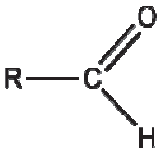
b) The formation of cis-aconitic acid:



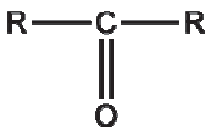
Citric acid cis - aconitic acid

3.8. Nucleophilic addition in oxocompound

Oxo-compounds are those organic compounds, which contain oxo-group >C = O. If the oxo-group is connected to a hydrogen atom, these compounds belong to a class of aldehydes. If oxo-group is connected with the radical, these compounds belong to a class of ketones:

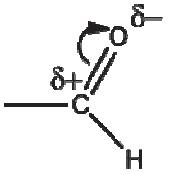


Aldehyde



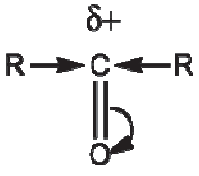
Ketone

Aldehydes are very reactive, since there is a high carbon atom and a partial positive charge due to the shift in π-electron density of the double bond to an oxygen atom:



This carbon atom is attacked by a nucleophile.

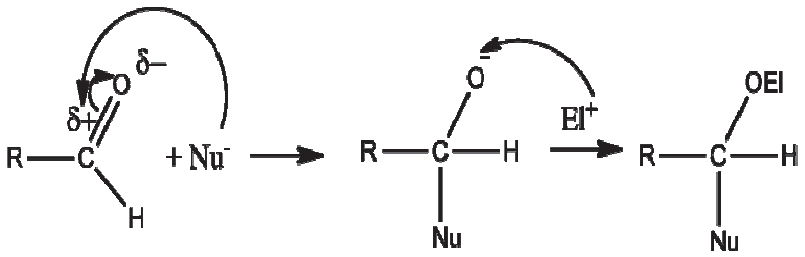
Ketones are less reactive, as the second radical is, that forms a result of the positive inductive effect and reduces the partial positive charge on the carbon atom of an oxo group.



;

The mechanism of nucleophilic addition by the example of aldehydes:

Scheme of the mechanism of nucleophilic addition:



(1) (2) (3)

In step (1) the nucleophile attacks the carbon atom due to the lack of electron density. As a result of the attack, it breaks the double bond, nucleophile attached to the carbon and forms the intermediate particle (2). The negative charge on oxygen in the particle (2) neutralizes the electrophile (usually a proton H^+), and produces the final product of the reaction (3).

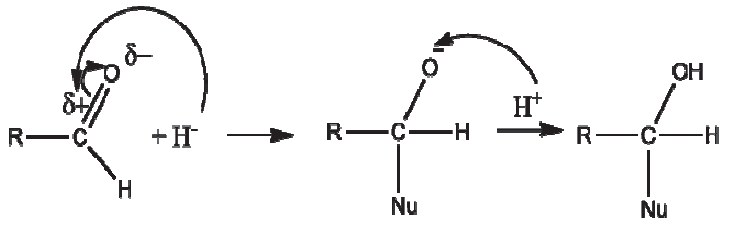
If the nucleophile is weak, the use of catalysis is by acid or alkaline.

Consider the specific reactions that go with aldehydes in vitro as well as in the human body.

1. **Hydrogenation of aldehydes** (recovery).

Hydrogenation of aldehydes in vitro in the presence of a catalyst is platinum or nickel, with which the hydrogen molecule heterolytically decays into a proton and a hydride anion, which is the nucleophile.

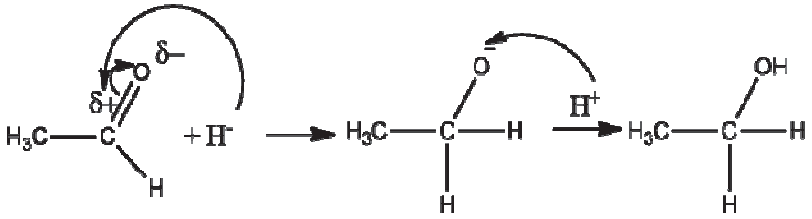
Graphically, the mechanism can be written as follows:



(2) (3)

In step (1) hydride - anion, which was formed in the heterolytic decomposition of the hydrogen molecule, attacks the carbon of the aldehyde group. Double bond C = O is broken and the hydrogen atom attached to carbon and oxygen occurs on the negative charge (2). Then, a proton, which was formed in the heterolytic decomposition of the hydrogen molecule, neutralizes the negative charge of oxygen, and the final product is obtained (3).

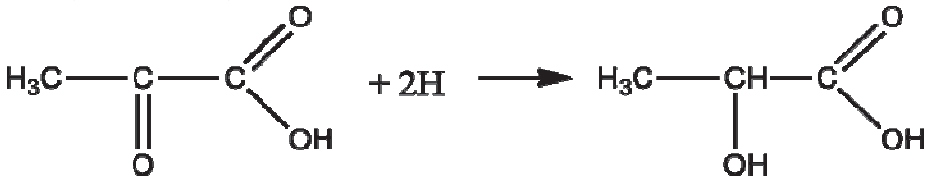
For example, the mechanism of hydrogenation of acetaldehyde can be shown graphically, such as in the scheme:



Acetaldehyde Ethanol

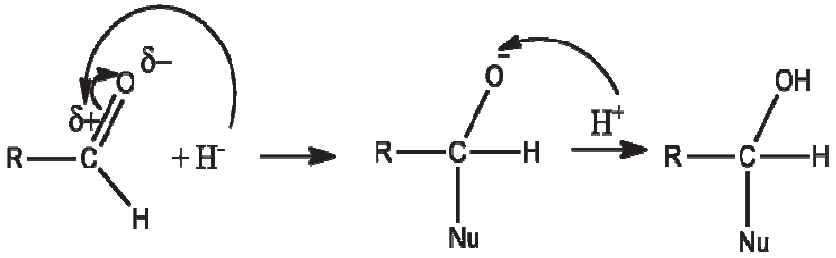
The biological significance of hydrogenation of Oxo compounds:

a)In the process of anaerobic glycolysis, the reduction reaction of pyruvate (pyruvic acid - PVC) to lactate (lactic acid) is:



STC milk

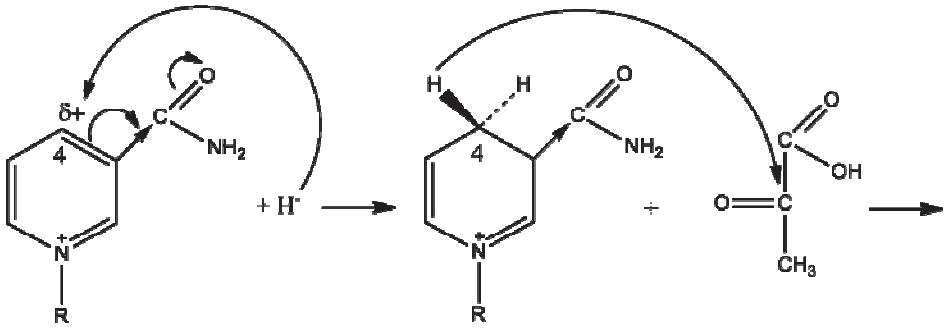
b)In the process of fat synthesis, the reduction reaction of glyceraldehyde to glycerol is:



Glyceraldehydes Glycerin

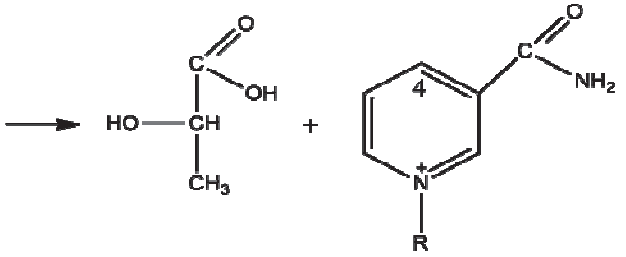
Hydrogen and electrons are transferred into the body by **coenzymes** NAD, NADP, Ubiquinone.

The chemistry of the NAD:



NAD NADH STC

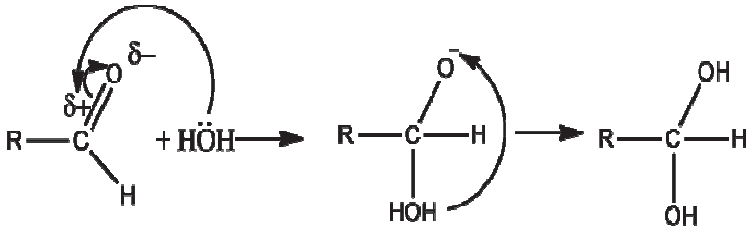
($SubH_2$ → Sub + H^- + H^+→ is dehydrogenation of the substrate, resulting in N^- is a molecule of NAD and H^+ into the solution, which then goes into oxygen STC).



Lactic acid NAD

2. Hydration of aldehydes (can go without a catalyst).

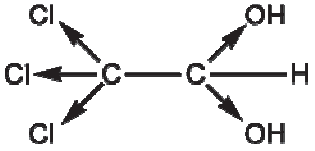
Graphically, the reaction mechanism can be written as follows:



(1) (2) (3)

The first is the attack of a water molecule as the nucleophile (1), and to form an intermediate compound (2), in which the oxygen in the aldehyde of the negative charge arises, and in the water molecule appears trivalent oxygen, which is impossible. Therefore, water molecules are split off from the proton and move to the negatively charged oxygen (2). This is a finished product result (3).

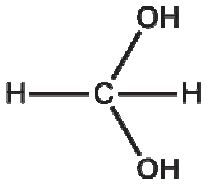
However, compounds with two hydroxyl groups at one carbon atom are unstable, because each oxygen atom pulls the electron density to itself. As a result of the uneven distribution of electron density in the system there is an excess of energy, and it splits the water molecule, but if the radical is electron-substituents, which tightens a part of the electron density, the electron density is distributed uniformly, and the system becomes stable. An example would be chloral hydrate, which is used as a hypnotic



Chloral hydrate

The presence of hydroxyl groups reduces the toxic effects of chlorine atoms.

Formaldehyde in solution is always hydrated



40% solution of **formaldehyde** is called formalin, which is used for the storage of anatomical specimens. The action of formaldehyde is due to irreversible denaturation of proteins, but with the concentration of an aqueous solution of formaldehyde is 0.75 - 1% of the observed reversible denaturation, it is used to store tissue and organ transplantation, followed by their patients and in this case decreases graft rejection.

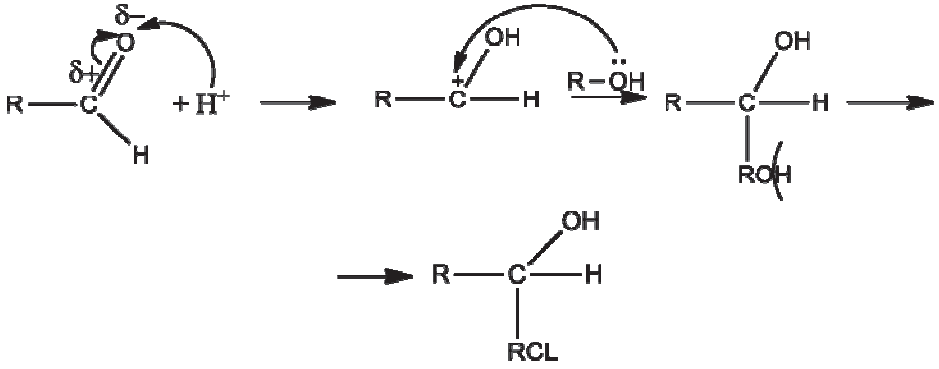
3. Reaction with alcohols.

Alcohols, which are nucleophilic, give pairs of electrons of oxygen, but are weak nucleophiles as oxygen, due to the high electronegativity strongly attracts an unshared electron pair, and this molecule cannot attack the carbon with a partial positive charge, so you need a catalyst.

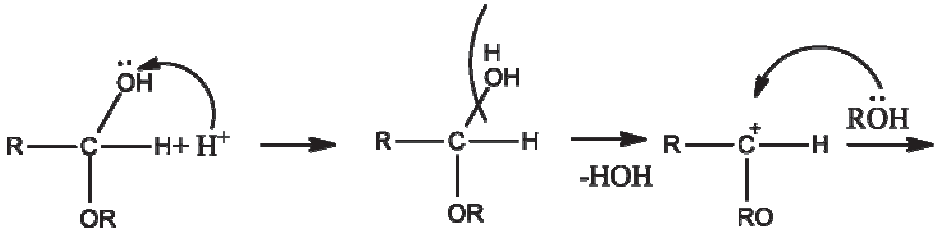
The catalyst used a proton, which gave the H_2SO_4.

Mechanism of the reaction graph can be written as:

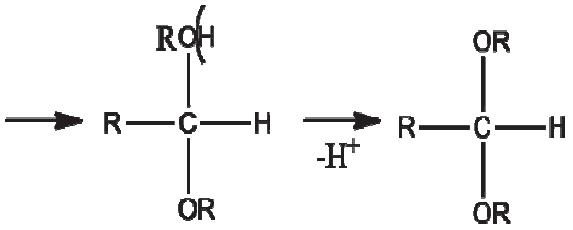
$$H_2SO_4 \rightarrow H^+ + HSO_4^-$$



In step (1) the proton attacks the oxygen (protonation process) in which there is a partial negative charge due to the inductive effect. Formed intermediates (2) with a positive charge on the carbon atom, ie carbocation: This compound was attacked by a molecule of alcohol as a nucleophile, alcohol joins and forms an intermediate compound (3), in which oxygen is trivalent, so the proton is split off from it, and produces the final product (4). The final product is called a hemiacetal. These compounds are unstable, since the carbon atom is bonded to two oxygen atoms, each of which pulls the electron density to itself. Therefore, it is easy to split them off from the hemiacetal molecule of water. Hemiacetal interaction with a second molecule of alcohol is acetal formed, but the reaction proceeds by the mechanism of nucleophilic substitution S_N from sp^3 - hybrid carbon atom. Catalysts also serve as a proton. Graphically, acetal formation mechanism can be described as follows:



(2) (3)

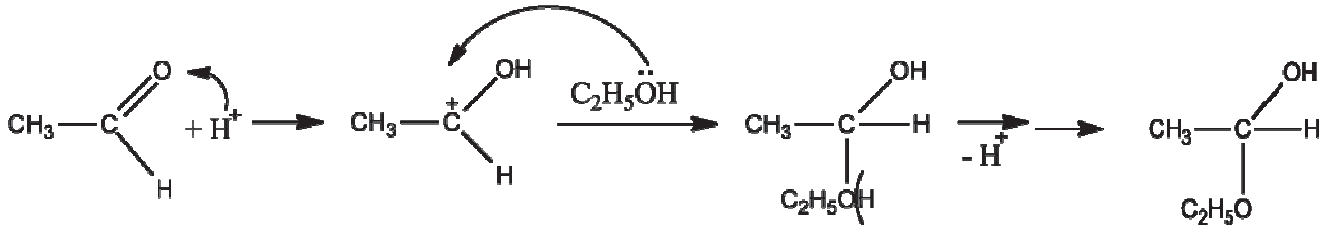


(4) (5)

In step (1) it is protonated hydroxyl oxygen. Proton joins and forms an intermediate compound (2), in which oxygen is trivalent, which is not typical for it. Therefore, the water molecule is split off and forms carbocation (3). It was attacked by a second molecule of alcohol. Forms intermediate (4) with trivalent oxygen, from which the proton is split off. The final product (5) is an acetal.

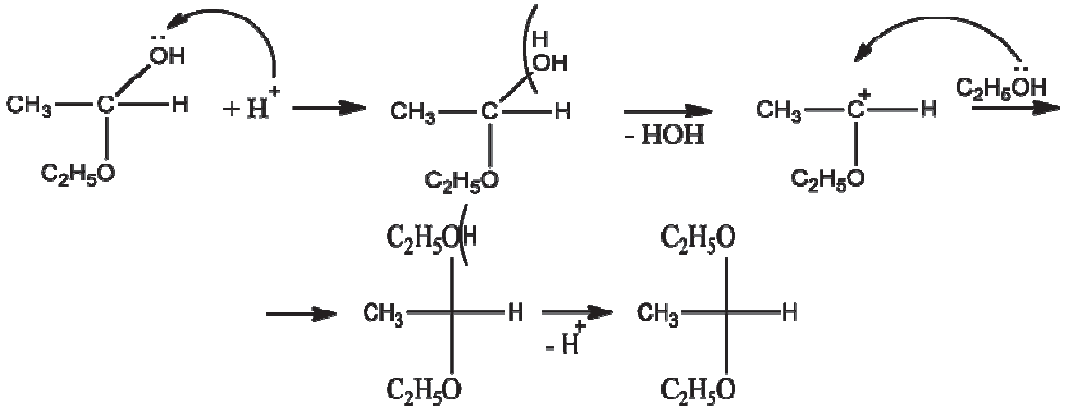
For example, the interaction of acetaldehyde and 1st ethanol: stage - the formation of hemiacetal:

Step 1 -Hemiacetal Formation:



Hemiacetal

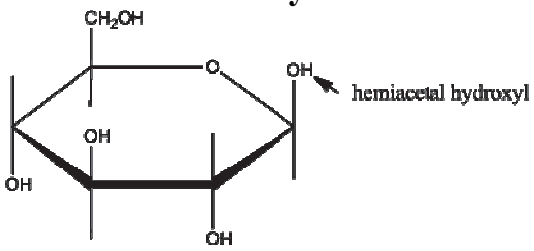
Step 2 - Acetal Formation:



Acetal

The biological significance of hemiacetal and acetal:

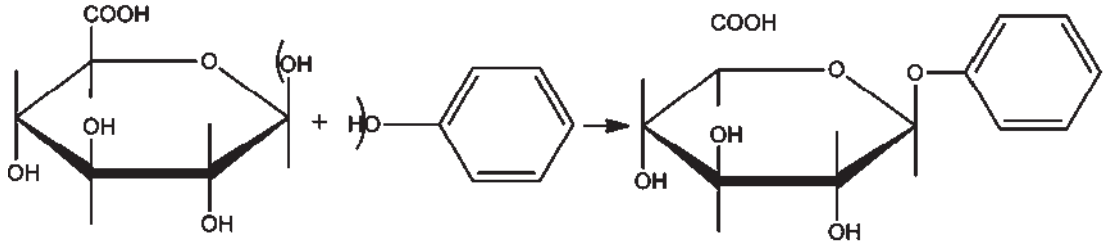
a)In the human body **monosaccharides are cyclic hemiacetal:**



Glucose

b)Disaccharides and polysaccharides are acetals

c)In the form of acetals which are derived from toxins:



Glucuronic Phenol

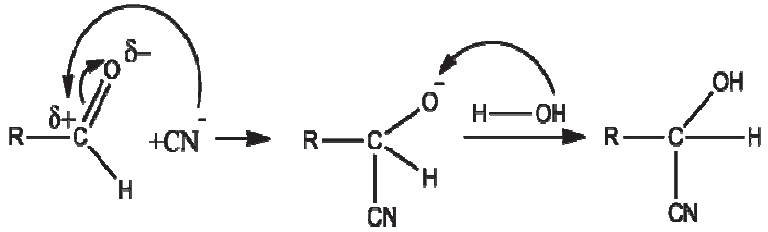
4. Interactions with acid hydrogen cyanide HCN.

Prussic acid– is weak acid, so it is necessary to create the dissociation of the alkaline medium (catalyst):

$$HCN + OH^- \rightarrow HOH + CN^-$$

Cyanide-anion CN^- is the nucleophile.

Graphically, the reaction mechanism can be written as follows:



(2) (3)

Cyanohydrin Oroxinitril

In step (1) cyanide-anion as the nucleophile attacks the carbon of the aldehyde group. As a result, it breaks the double bond carbon-oxygen, and cyanide-ion associates (2), with the formation of an intermediate particle with negative charge on oxygen, which is neutralized by a proton from a water molecule (water easily dissociates under the action of the negative charge of oxygen, that is, **water is the protonation**, which is produced by the final product - **a cyanohydrin**.

Biological significance of cyanohydrins:

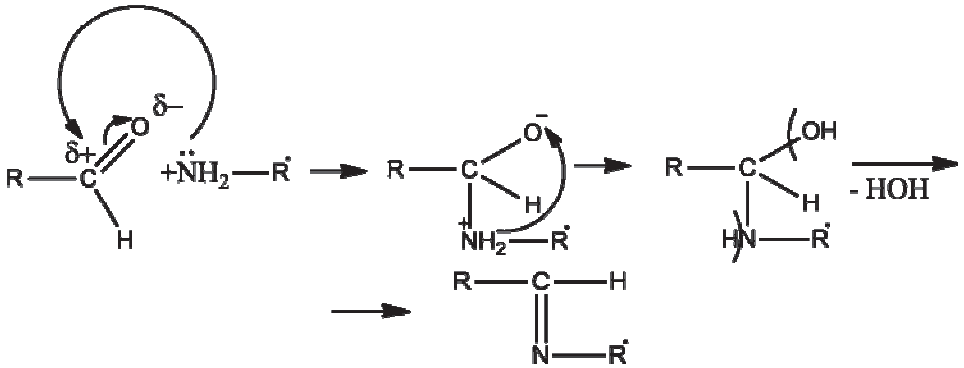
a) They are intermediates in the synthesis of amino acids in vitro;

b) Some cyanohydrins, such as **amygdaline**, located in the nuclei of stone plants (citric, plum, almond). When injected into the human body, they decompose to form hydrogen cyanide (prussic) acid, which can potentially lead to poisoning.

5. Interaction with ammonia and amines (the reaction of accession-cleavage).

Amines are strong nucleophiles, which are due to the unshared electron pair of the nitrogen atom, so they directly attack carbon of the aldehyde group.

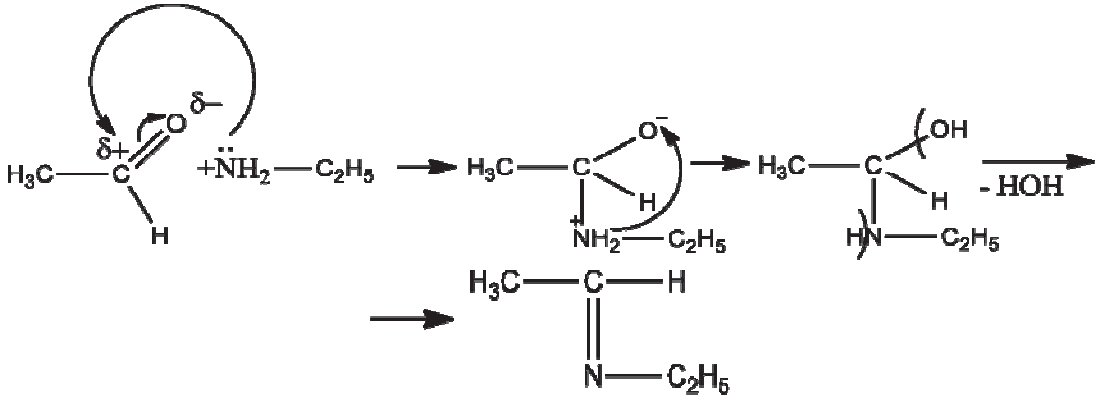
Graphically, the reaction mechanism can be written as:



Amine or Schiff base

At the first stage (1) amine as a strong nucleophile attacks the carbon of the aldehyde group. As a result, breaks the double bond carbon-oxygen, and amine attached. Forms an intermediate particle (2) with a negative charge on oxygen and nitrogen occurs in the positive charge (because it gave undivided electron pair in contact with carbon). From nitrogen cleaved the proton and neutralizes the negative charge on oxygen (particle 3). These carbon particles associated with two electronegative atoms – oxygen and nitrogen, each of which pulls the electron density itself. That is, in the electron density is unevenly distributed, making the system unstable. Therefore, it is cleaved by a water molecule, and the final product is formed as **imine** or **Schiff base** (4).

For example, the interaction of acetaldehyde with ethylamine:



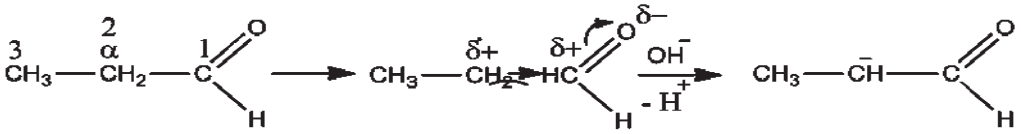
The biological significance of Amines:

a) Amines or Schiff bases are of great biological importance because they are intermediates in the synthesis of proteins in the human body, which is called transamination. **Transamination** - this enzymatic reaction is reversible amino group transfer between the amino and keto acids without releasing ammonia.

b) Amines are intermediates in the synthesis of proteins compound in vitro.

6. Reactions caused by the mobility of α-hydrogen atom.

α-hydrogen is a hydrogen atom at the carbon atom bound to the aldehyde group (1):



(2) (3)

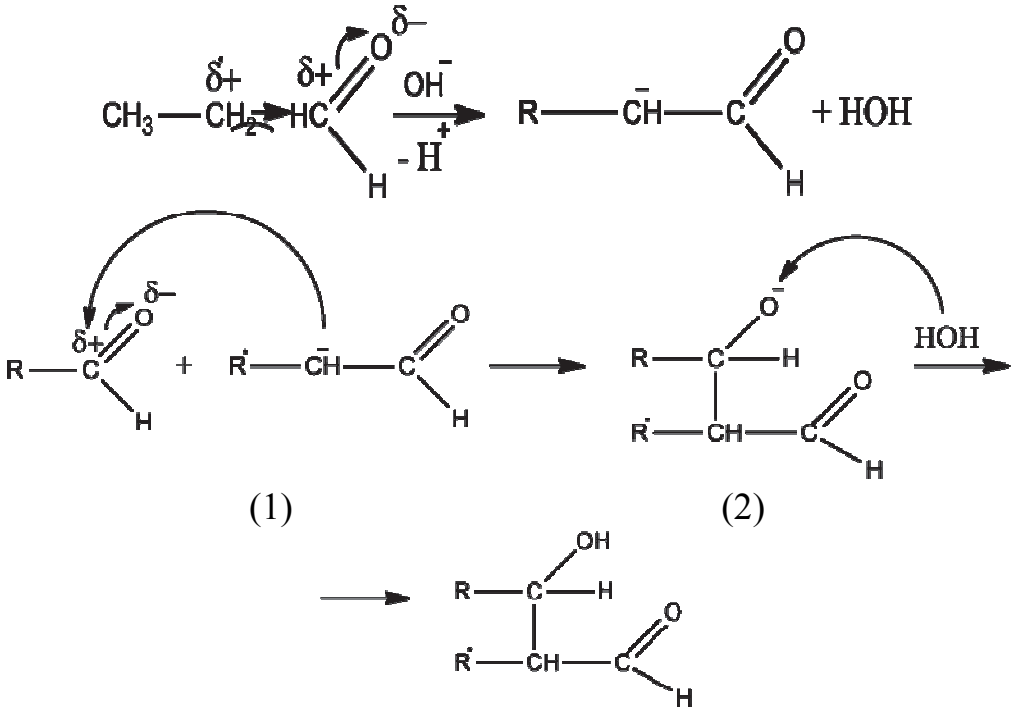
Carb-anion

As result of the polarization due to the aldehyde group on carbon,there occurs a partial positive charge δ+, which from the α-carbon atom, the electron density is shifted to σ-bond (inductive effect). At this carbon occurs a partial positive charge $\delta' +$ (2). In the alkaline environment of the carbon is cleaved from the proton, i.e., from the CH- acid center. In the presence of alkali, which is the catalyst, the proton is split off easily. The end product is a carb-anion (3), which as a nucleophile attacks the carbonyl carbon of a second molecule of aldehyde.

The reactions caused by the mobility of α-hydrogenatom reactions include aldol condensation reaction haloformic.

Aldol condensation is the reaction of a compound of two molecules of aldehyde. Graphically, the mechanism of aldol condensation can be shown as:

$$NaOH \rightarrow Na^{+} + OH^{-};$$



(1) (2)

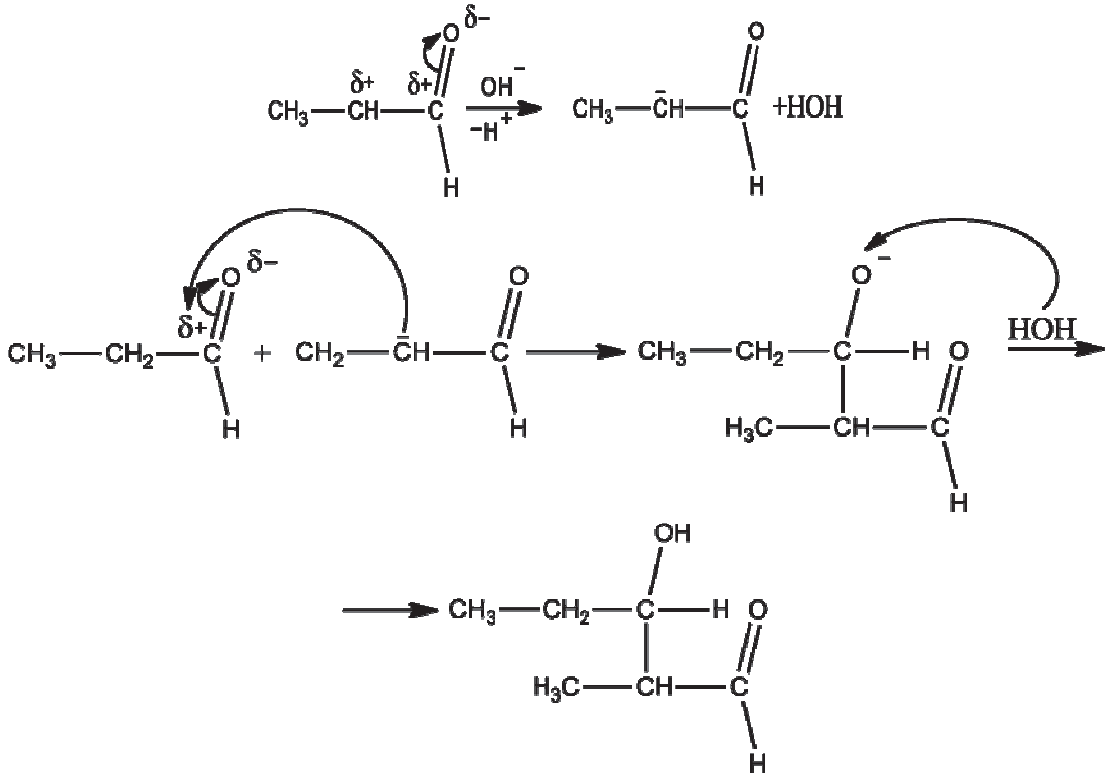
(3) Aldol

In the step (1) carbanion as a nucleophile attacks the carbonyl carbon.

As a result, it breaks the double bond carbon-oxygen and the carbanion, which is attached to carbon and is formed by the intermediate particle, (2) with a negative charge on the oxygen ion. To neutralize this charge is the protonation of water (water under the influence of the negative charge of oxygen dissociates more easily), and the final product is formed aldol(3). It is called this because it contains an aldehyde group, which gives the end of Aldol, and an alcoholic hydroxyl group, which gives ending ol.

Example: aldol condensation may be an interaction of two molecules of propanol.

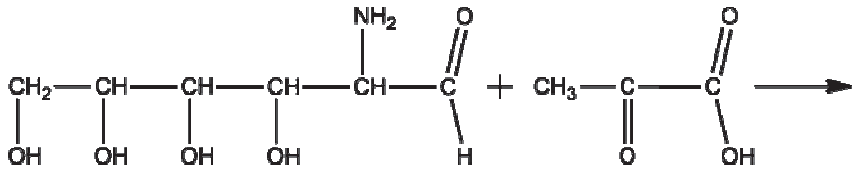
$$NaOH \rightarrow Na^{+} + OH^{-};$$



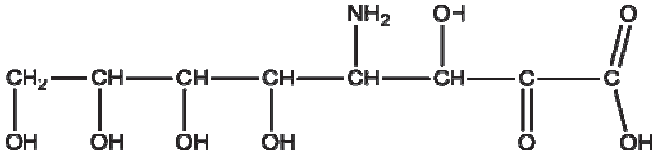
The biological significance of the aldol condensation:

a) The mechanism of aldol condensation in nature is the formation of glucose in the process of photosynthesis;

b) In the human body is synthesized neuraminic acid, a scheme of formation which can be written as:



Mannosamin STC



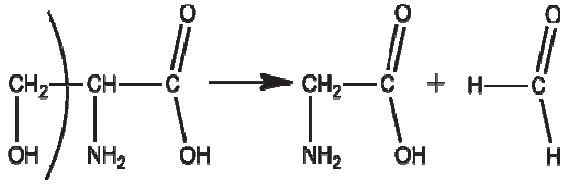
Neuraminic acid

c)Synthesis of citric acid in the Krebs cycle (see "carboxylic acids");

d) The synthesis of steroid hormones.

Reverse aldol condensation reaction is called **aldol cleavage**:

a) In the human body is exposed to such a splitting of the amino acid serine. The scheme of this process is as follows:



Serin Glycine Formaldehyde

b) In animal organisms is the splitting of fructose - 1,6 - phosphate, and in the plant, on the contrary, the synthesis of it;

Aloform reaction– is getting halo form, i.e. chloroform, bromoform and iodoform.

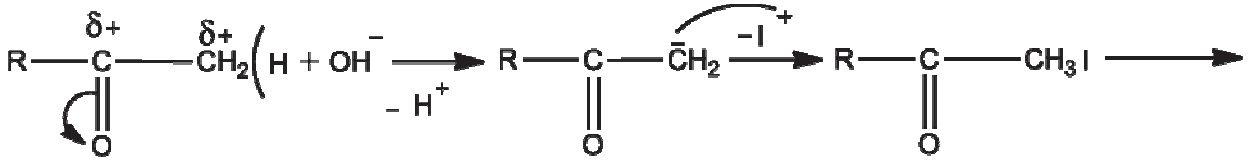
Graphically, the reaction mechanism can be written as:

$$I_2 + NaOH \rightarrow NaI + NaIO; (1)$$

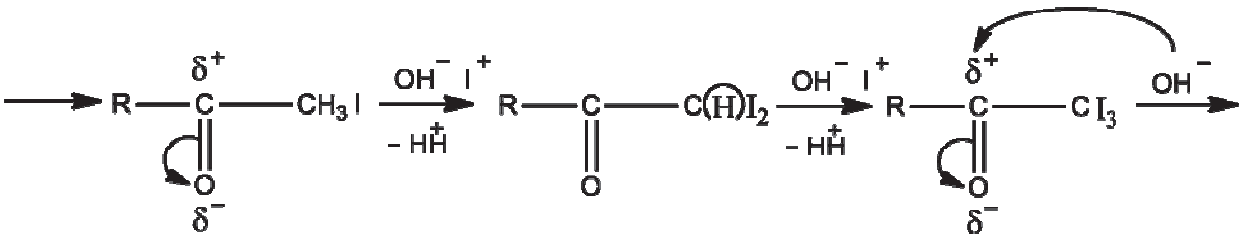
$$NaIO + HOH \rightarrow HOI + NaOH; (2)$$

$$HIO \rightarrow I^+ + OH^-; (OH^- \text{ is a nucleophile}) (3)$$

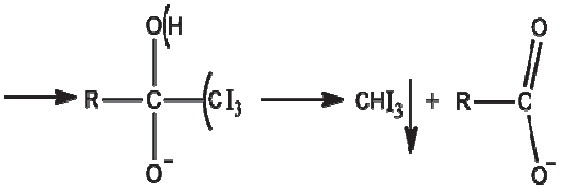
I_2 that is in alkaline solution disproportionate (1). The salt is hydrolyzed by NaIO (2). The acid in these conditions HOI dissociates to form OH^-, which is the nucleophile (3).



(4) (5) (6)



(7) (8) (9)



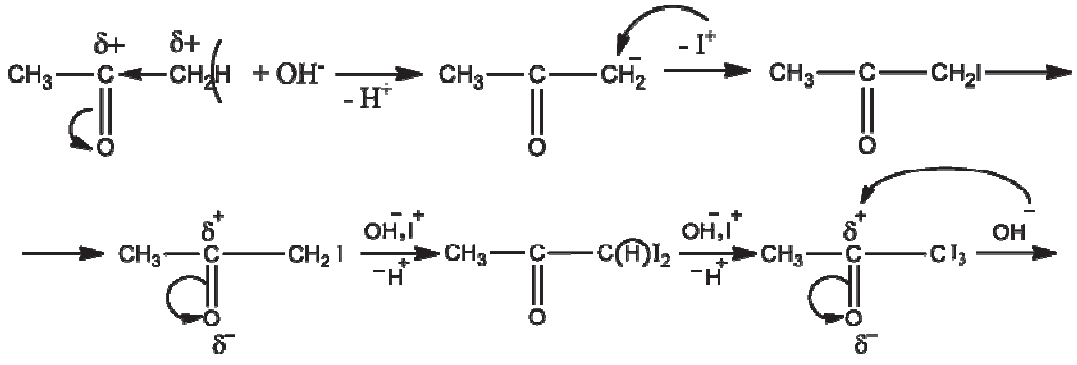
(10) (11)

In step (4) splits off a proton from carbon to δ '+ is formed and the carb-anion (5), which is attacked by an ion I^+. The result is an intermediate (6), in which one hydrogen atom is replaced by an iodine atom. Next comes the gradual detachment of the proton and its replacement by iodine atom (stage 7, 8, 9). At the intermediate (9) is a nucleophile attack of OH^- which joins the carbon atom (10) and pushes the molecule CH_3I (11). This is - **iodoform**, a substance pale - yellow color with a characteristic odor. By-product (12) - is an anion, which gives the sodium cation with the salt.

Haloform,an example of the reaction may be the interaction of acetone with iodine in alkaline medium:

$$I_2 + NaOH \rightarrow NaI + NaIO;$$
$$NaIO + HOH \rightarrow HOI + NaOH;$$
$$HIO \rightarrow I^+ + OH^-;$$

Acetone

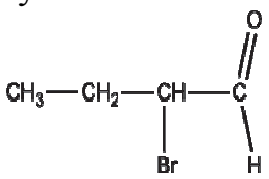


Iodoform

The biological significance of haloform:

a) Chloroform $SNCl_3^-$ Means for anesthesia (not recently used, as in the decomposition yields free radicals).

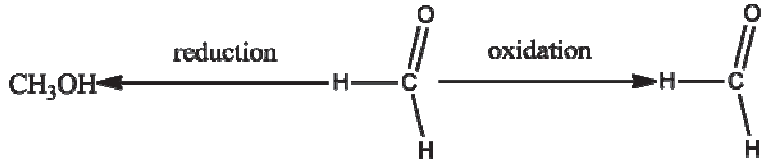
b) If α-hydrogen atom is replaced by Br, is obtained lachrymatory (tear gas), for example, the brom butanoic aldehyde:



c) The formation of iodoform CHI_3 used as a simple test for acetone in the urine of patients with diabetes. In addition, the iodoform is used as an antiseptic.

7. Reactions due to the absence of α-hydrogen atom (reaction disproportionation).

In a series of oxidation - reduction processes aldehydes are intermediate between alcohols and carboxylic acids, i.e. aldehydes reduced to alcohols and oxidized to carboxylic acids.



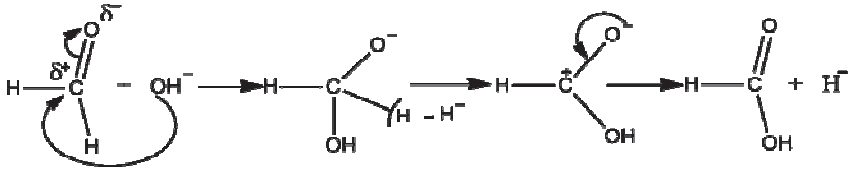
Alcohol Aldehyde Acid

Disproportionation reactions are in the presence of a catalyst - alkali water in the presence and absence of α-hydrogen atom.

Graphically, the reaction mechanism can be written as:

Step 1:

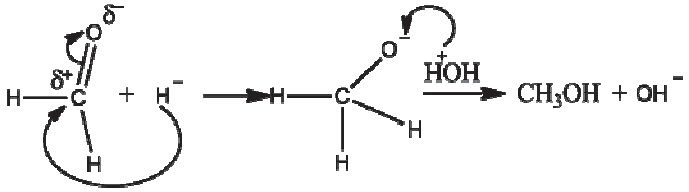
$$NaOH \rightarrow Na^{+} + OH^{-};$$



(2) (3) (4)

As a result of dissociation of sodium hydroxide catalyst is formed, while the nucleophile OH^{-}, which attacks the carbon of the aldehyde group (1). Hydroxyl groups attached to carbon as a result of rupture of the double bond carbon - oxygen, and oxygenoccurs as a negative charge (2). To get rid of the negative charge, the system pushes hydride - anion H^{-} and forms the intermediate particle (3), in which there is a redistribution of electron density, closed the double bond carbon - oxygen, and forms the final product - acid (4).

Step 2:

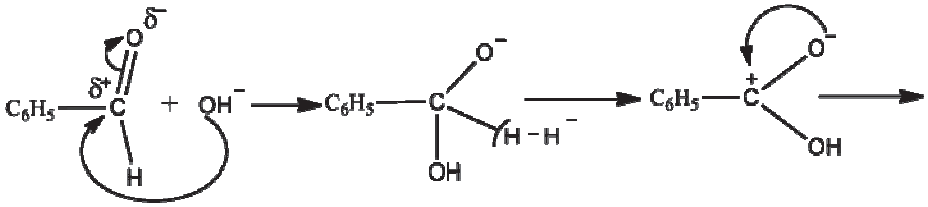


(5) (6) (7)

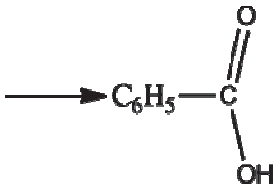
In the second phase hydride-anion attacks the second molecule of aldehyde (5).

As a result of rupture of the double bond carbon-oxygen, hydrogen atom attached to carbon and oxygen, there is a negative charge (6). To neutralize the negative charge is the protonation of water (6). Formed one more final product - alcohol and the catalyst is released - OH^{-} is an example of a disproportionation (oxidation-reduction) benzaldehyde:

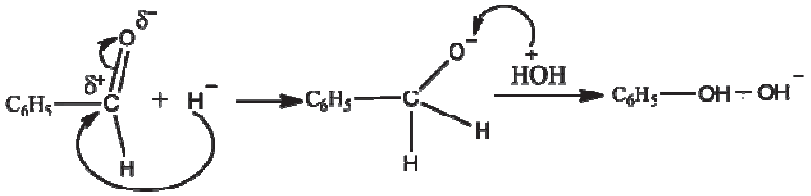
$$NaOH \rightarrow Na^{+}+OH^{-};$$



Benzaldehyde



Benzoic acid



Benzyl Alcohol

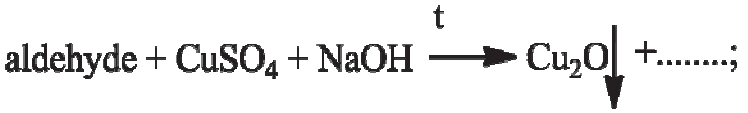
Aldehyde disproportionation occurs during alcoholic fermentation of glucose.

3.9. Oxidation of aldehydes and ketones

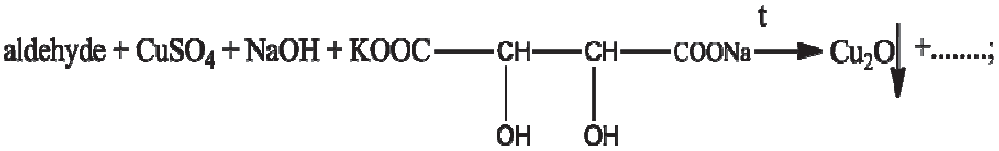
Aldehydes and ketones are oxidized. Aldehydes are oxidized more easily than ketones. They even oxidize atmospheric oxygen. Consider the oxidation of aldehydes, which are of practical importance.

a) The reaction of Tollens (silver mirror reaction) - the interaction of aldehydes with ammonia solution of silver:

b) The reaction of Trommer - the interaction of aldehydes with cuprum (II)hydroxide in alkaline medium:



c) The reaction of Fehling - the interaction of aldehydes with cuprum (II)hydroxide in alkaline medium in the presence of Rochelle salt:



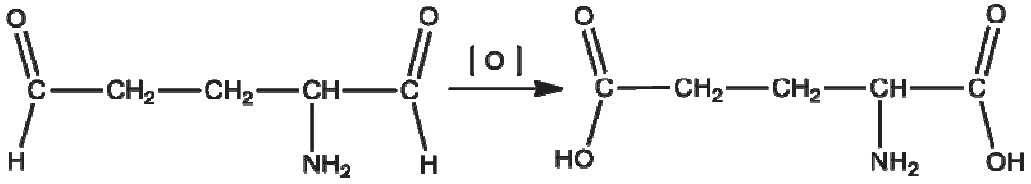
All these reactions are accompanied by an external effect, i.e. precipitation and staining. Therefore used as the aldehyde group on the quality, and clinical analysis - for the determination of monosaccharaides in biological fluids. The most common test that is used is the Trommer test.

Oxidation of ketones is accompanied by rupture of the carbon chain.

The biological significance of the oxidation of aldehydes and ketones:

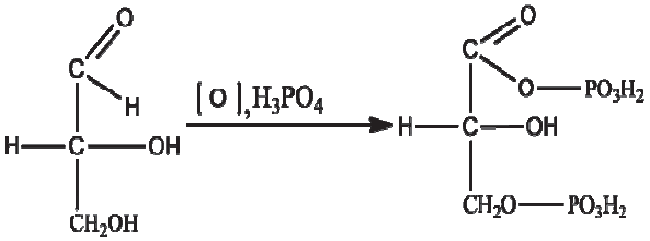
a) Due to its high reactivity, aldehydes are toxic to the human body, so they are oxidized to harmless carboxylic acids. For example:

b)The oxidative deamination of amino acids, glutaraldehyde is oxidized to glutaric acid



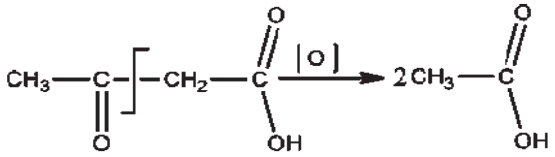
Glutaral Dihydro glutaric acid

c) Glyceraldehyde is oxidized to glyceric acid and phosphorylated at the same time:



Glyceraldehydes 1, 3 - difosfo glyceric acid

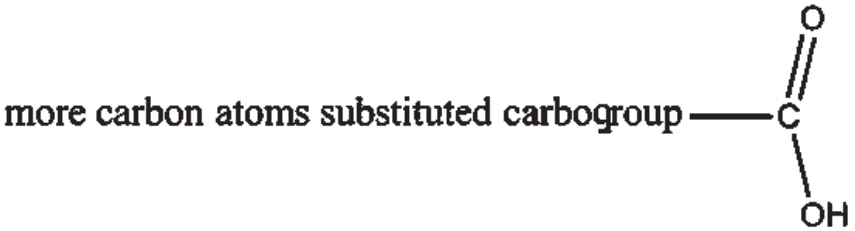
Aceto-acetic acid (acetoacetate) as the keto acid is oxidized with rupture of the carbon skeleton:



Acetoacetate (β-ketobutanoic acid) Acetate

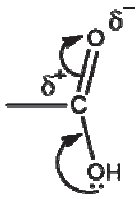
3.10. Nucleophilic substitution in carboxylic acids and their derivatives

Carboxylic acids are derivatives of alkanes, in which one or more carbon atoms substituted carbongroup



Carboxyl consists of oxo- and hydroxyl groups, which mutually influence each other, so these groups change their properties compared with the oxo and the hydroxyl group in aldehydes in alcohols.

Electronic structure of carboxyl:

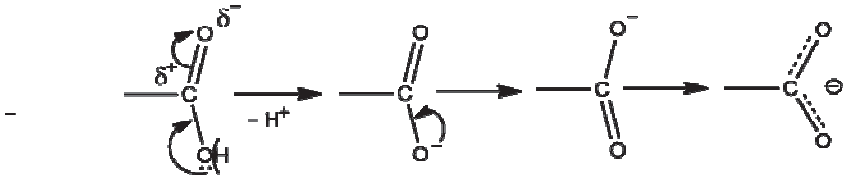


In the oxo oxygen atom, as the more electronegative one pulls over the π-electron density of the double bond, this results in a carbon that occurs as a partial positive charge, as in aldehydes. Hydroxyl oxygen atom as a more electronegative pulls itself from the electron density on the carbon σ-bond, but its lone electron pair is a pairing of π-electron density of the double bond. As a result of decreases in carbon a partial positive charge in comparison with aldehydes, carboxylic acids, so are the substitution reactions (rather than joining in aldehydes). This reflects the influence of the hydroxyl group at the oxo group.

On the other hand the shift in the unshared electron pair of oxygen to carbon with a partial positive charge increases the ease of removal of a proton. That is, acidity of carboxylic acids is higher than that of alcohols. This demonstrates the effect of oxo-hydroxyl group at the - group.

Acidic properties of carboxylic acids:

Carboxylic acids exhibit acidic properties due to removal of a proton (Bronsted). But it is a much stronger acid than alcohols, which also contain a hydroxyl group. Elevated carboxy acid properties are explained as follows:



(1) (2) (3) (4)

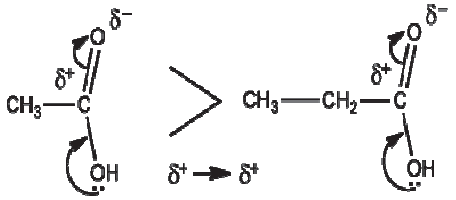
(4) Carboxyl (1) is the redistribution of electron density in such a way that the resulting displacement of the oxygen lone pair to pair it easy to split off from the proton and the anion is formed (2). This anion is a redistribution of electron density and there is an anion (3). Eventually, the electron density is distributed evenly between the two oxygen atoms and the carbon atom and forms a three-center delocalized conjugated system. In this system, the electron density is distributed evenly, which makes its thermodynamic stability and ease of removal of a proton.

Acidity of carboxylic acids depends on the structure of the radical and the presence substituents:

a) Acidity in the homologous series:

H-COOH> CH_3-COOH>CH_3-CH_2-COOH

3, 77 4, 4, 88

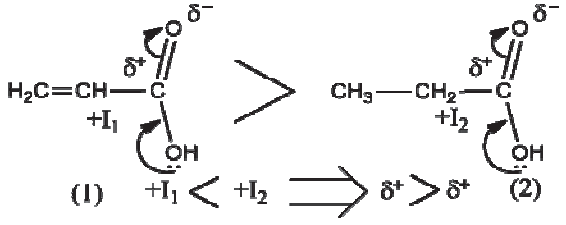


In homologous series the acidity decreases as a result of the positive inductive effect of the long radical decreases the partial positive charge on carbon, there by decreasing the displacement of the unshared electron pair of oxygen to carbon, ie on the oxygen atom remains high electron density, and the proton is split off more difficult.

b) Influence of unsaturated radical:

CH_2= CH-COOH > CH_3-CH_2-COOH

4,25 4,88.



Unsaturated acid is stronger than saturated, as a positive inductive effect sp^2- hybrid carbon atom ($+I_1$) is less than the positive inductive effect sp^3- hybrid of a carbon atom ($+I_2$), so δ+>'δ+; there by increasing the displacement of the unshared electron pair of oxygen to carbon (1), ie on the oxygen atom decreases the electron density and the proton is split off more easily.

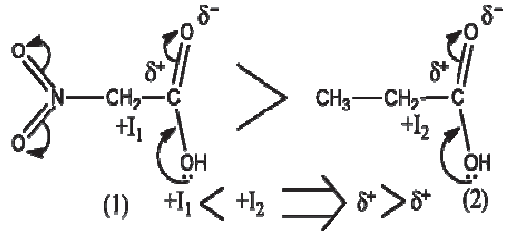
c) Electron impact substituents:

CF_3-COOH>CH_2F-COOH> CH_3-COOH

0,7 2,9 4,76

$O_2NC_6H_4$-COOH>HOOC-C_6H_4-COOH>C_6H_5COOH> CH_3COOH

2,17 2,98 4,2 4,76

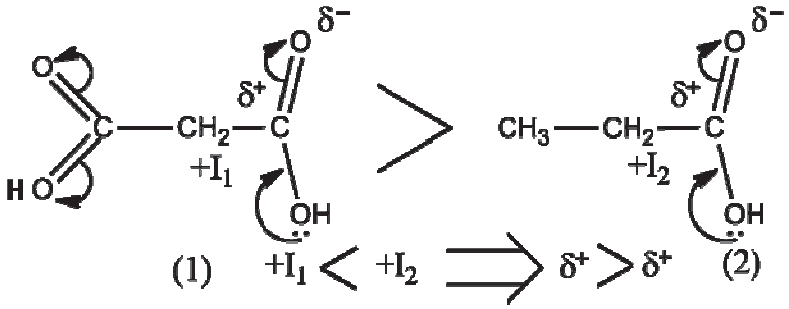


The presence of electron with drawing substituents in the radical, such as F or NO_2 increases the acidity, since F or NO_2 pulls itself from the radical electron density and its inductive effect (I_1) becomes smaller, so why δ+>'δ+; therefore increasing displacement of unshared electron pairs from oxygen to carbon (1), ie on the oxygen atom decreases the electron density and the proton is split off more easily.

d) Impact a lot of atoms:

HOOC-COOH> HOOC-CH_2-COOH>HOOC-CH_2-CH_2-COOH> CH_3-COOH

1, 23 2, 83 4, 19 4.76

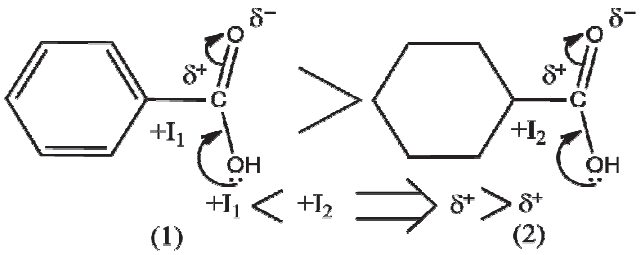


Dibasic acid is stronger than monobasic, since the second carboxyl group pulls itself from the radical electron density and its inductive effect (I_1) becomes smaller, so that δ+>' δ+ thereby increasing the displacement of the unshared electron pair of oxygen to carbon (1), i.e. on the oxygen atom decreases the electron density and the proton is split off more easily.

e) Influence of aromaticity

C_6H_5COOH> $C_6H_{11}COOH$

4,2



Aromatic acids are stronger than acid - derived cycloalkanes, as a positive inductive effect sp^2- hybrid carbon benzene ring ($+I_1$) is less than the positive inductive effect sp^3- hybrid carbon atoms of cyclohexane ($+I_2$), so δ+>'δ+; here fore increases displacement of unshared electron pairs from oxygen to carbon (1), i.e. on the oxygen atom decreases the electron density and the proton is split off more easily.

By being acidic properties of carboxylic acids react with metals, oxides, bases and salts give, for example:

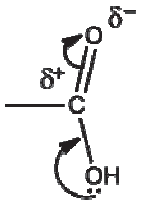
$$CH_3COOH + NaOH \rightarrow CH_3COONa + H_2O$$

In the human body formed of many salts organic acids:

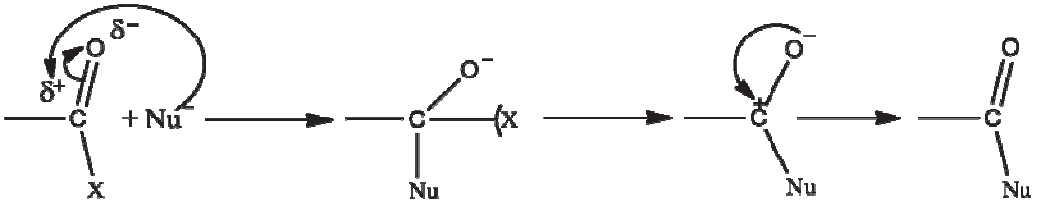
lactic acid	gives salt	Lactates
pyruvic acid	<<	Pyruvate
citric acid	<<	Citrate
oxalate (oxalic acid)	<<	Oxalate
succinate (succinic acid)	<<	Succinate,
malic acid	<<	Malate.

3.11. Nucleophilic substitution in carboxylic acid and its derivatives

In the carboxyl-group shows a positive mesomeric effect (sitar lone electron pair to the carbon atom), which reduces the partial positive charge on carbon in comparison with aldehydes, carboxylic acids, so go for the reaction mechanism of nucleophilic substitution instead of joining in aldehydes. In this case, an effect of the hydroxyl group in the oxo-group.



The scheme of the mechanism of nucleophilic substitution:



(2) (3) (4)

Witre X is -OH, -NH_2,OR-,RCOO-,halogen.

Nucleophile attacks the carbon atom with a partial positive charge (1), followed by a double bond which is broken, and the nucleophile attached (2), and the system pushes the particle X, which carries with it a negative charge (which brought Nu) and the particle is formed (3). As a result of redistribution of electron density of the final product formed by nucleophilic substitution (4).

If the nucleophile is weak, then apply the acid catalysis or base.

Consider the specific reactions that go with carboxylic acids and their derivatives in vitro, as well as in the human body.

3.11.1. Esters and thioesters

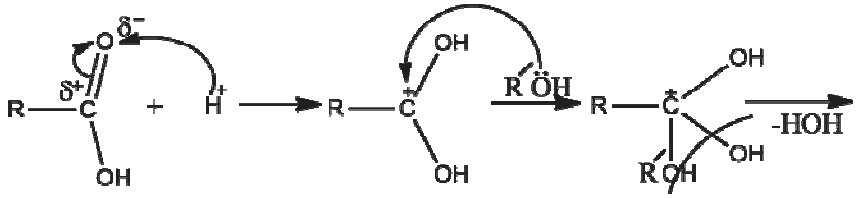
1. The formation of esters.

Most common and most studied derivatives of carboxylic acids include esters (esters). The process of formation of esters is called **esterification reaction.**

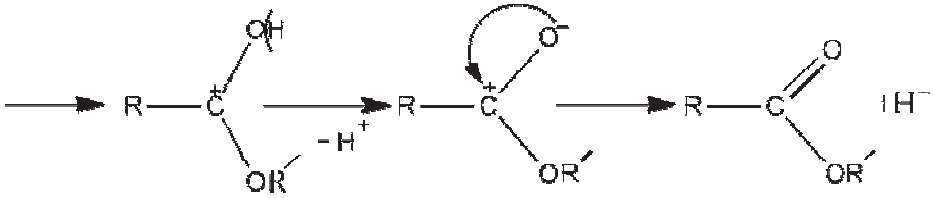
Esterification reaction takes place between carboxylic acids and alcohols on the mechanism of nucleophilic substitution. Since alcohols are weak nucleophiles (see "Aldehydes" - the formation of hemiacetal), then use an acid catalysis.

Graphically, the scheme of the reaction mechanism of esterification can be shown as follows:

$$H_2SO_4 \longrightarrow H^+ + HSO_4^-$$



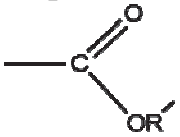
(2) (3)



(4) (5) (6)

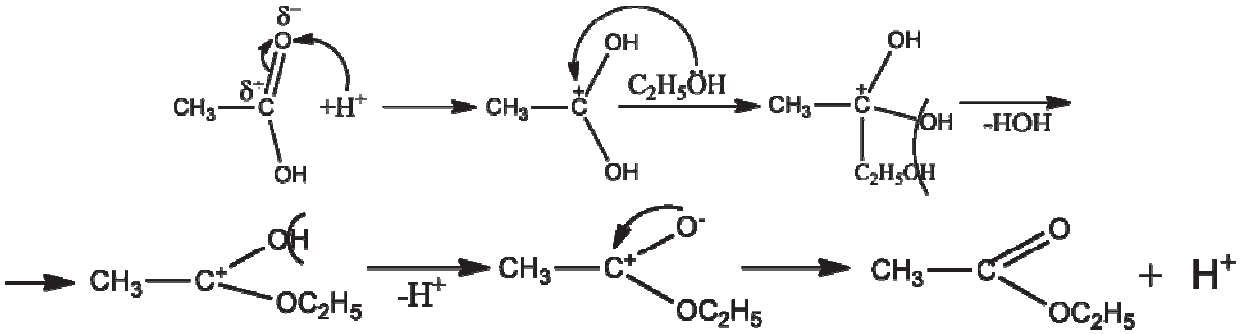
Sulfated acid dissociates and gives catalyst - proton H^+. Proton attacks the (protonated) oxygen oxo (1), which accumulates excess negative charge due to mesomeric effect. Formed carb-cation (2), which is attacked as an alcohol nucleophile. Alcohol is attached at carbon occurs a positive charge, while oxygen is a trivalent alcohol (3). Therefore, the proton is split off from oxygen, and carbon is cleaved from the hydroxyl group (this is confirmed by the method of labeled atoms), which pushes the alcohol, and forms the intermediate carb-cation (4), from which the proton is split off. The result is an intermediate particle (5), in which there is a redistribution of electron density are obtained final product - **ester** (6) and dismissed the catalyst - a proton.

Group of atoms



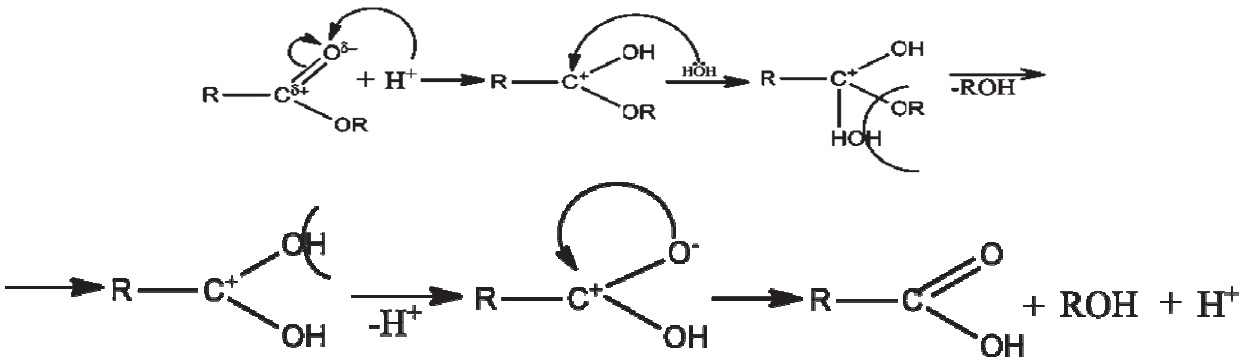
- It is difficult - the ether bond, which is found in many medicinal substances.

An example of the esterification reaction may be the interaction of acetate (acetic acid) with ethanol. Graphically, this can be written as:



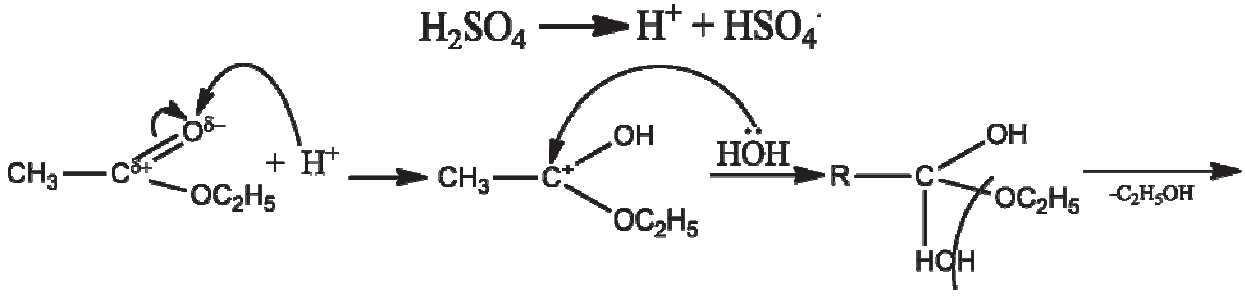
Reverse reaction of esterification is called hydrolysis, which is also on the mechanism of nucleophilic substitution. Hydrolysis can proceed in acidic and alkaline media.

Graphically, the mechanism of **acid hydrolysis** can be shown as follows:

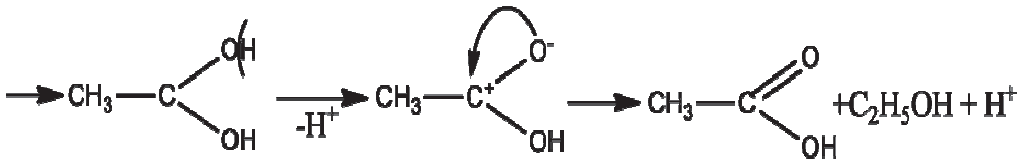


Concentrated sulfuric acid dissociates, gives a proton, which is a catalyst and oxygen attacks the oxo group in the molecule of the ester (1). Formed carb-cation (2), which is attacked by a water molecule as a nucleophile to neutralize the positive charge on carbon. Water is attached to carbon, oxygen, water is trivalent, and the proton is split off from it, and simultaneously cleaved alkoxy group OR 'on carbon (3). Formed back carb - cation, from which the proton is split off (4). In the particle (5) is the redistribution of electron density, and form the final products - acid (6) and alcohol (7), as well as the proton is released as a catalyst. Thus, **the products of hydrolysis of esters in an acidic environment are a carboxylic acid and alcohol**.

Example of hydrolysis of esters in an acidic environment may be the hydrolysis of ethyl acetate:

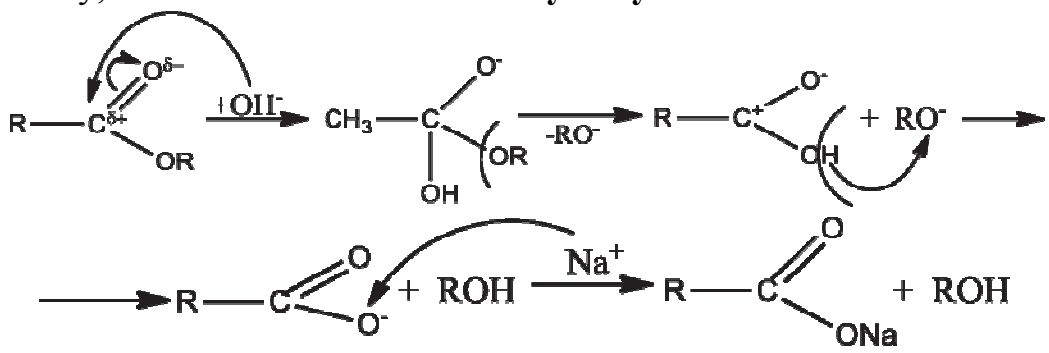


Ethyl acetate



Acetate Ethanol

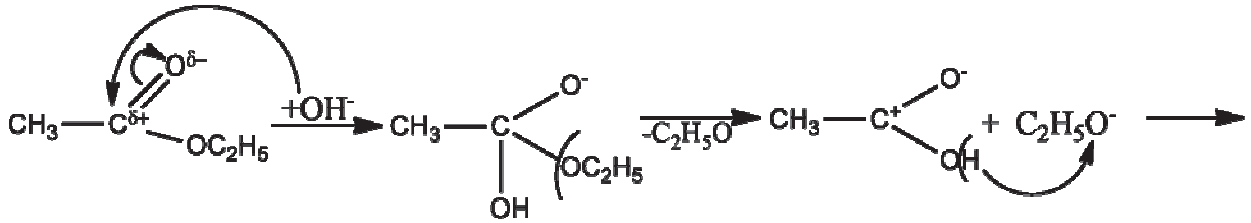
Graphically, the mechanism of **alkaline hydrolysis** can be shown as:



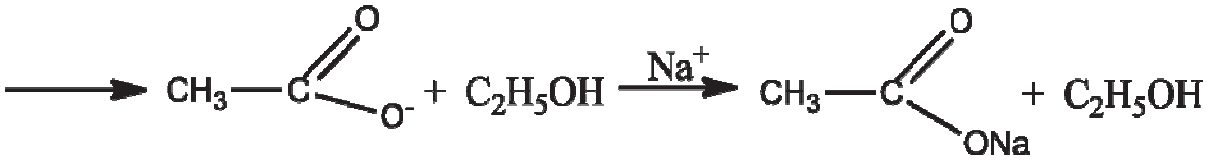
Hydroxide ion, which is the catalyst that attacks the carbon atom of the carboxyl group (1). As a result, the intermediate particle (2), in which the hydroxyl group of associates and pushes alkoxy RO^{-}. Formed particle (3), from which the proton is split off and goes to the alkoxy group. As a result of redistribution of electron density occurs

carboxylate anion (5), which gives a sodium salt of the cation (6). Thus, the products of alkaline hydrolysis of esters are the salt of a carboxylic acid and alcohol.

Example of hydrolysis of esters in alkaline hydrolysis of ethyl acetate can be:



Ethyl acetate



Sodium acetate Ethanol

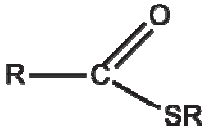
Esters and their hydrolysis in the human body

In humans, esters are **fat**. This is the esters of higher fatty acids and glycerol triatomic. Hydrolysis of fats takes place in the intestine in an alkaline medium under the action of the enzyme **lipase** to glycerol and salts of higher carboxylic acids, i.e. soap.

Ester bond is formed between the amino acids and transfer RNA.

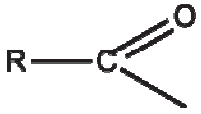
Series of biologically active compounds contains ester bond to the phosphate acid (RNA molecules, DNA, ATP), with sulfuric acid (in the molecules of heparin, chondroitin sulfate).

Many biological importance tyoanalogy complexes efires –**thioethers:**

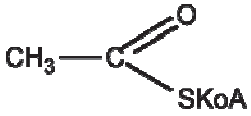


Thioethers are more reactive than the esters, since the group -SR cleaved easier than -OH. The group -SR is more stable due to the low electronegativity of the sulfur atom. In addition, the carbonyl carbon, there is a higher positive charge than the esters.

The human body forms a coenzyme thioesters of **CoA-SH (coenzyme A)**. It is an activator of carboxylic acids, ie carries the remnants of carboxylic acids, which are called acyl (ie, the remnants of carboxylic acids without hydroxyl group):

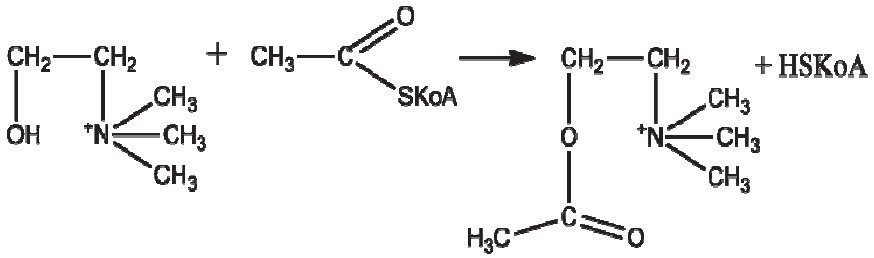


Because of this, it takes part in the reactions, acylation i.e. the introduction of acyl, resulting in synthesized biologically active substances with a long chain. Most importantly, the acetyl-CoA:



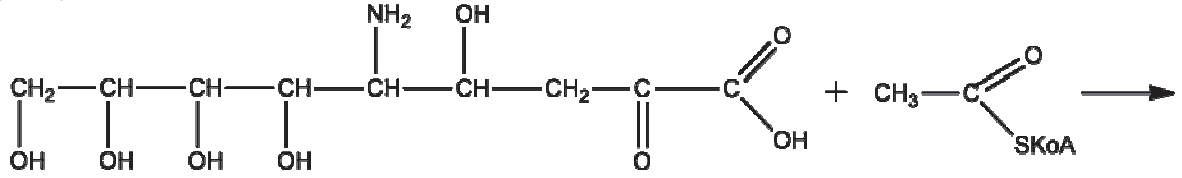
The biological significance of acylation:

a) Synthesis of acetylcholine:

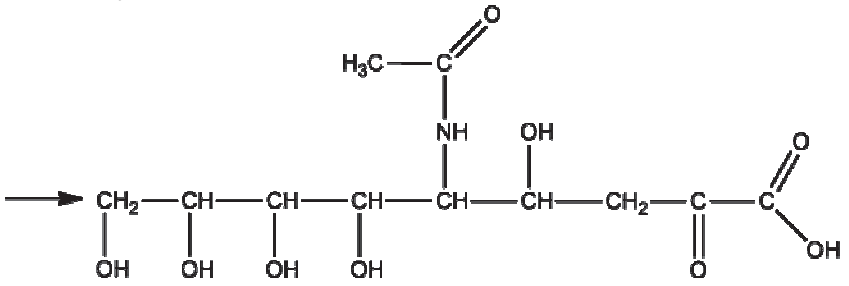


Choline Acetylcholine

b) By acylation of neuraminic acid formed sialic acid:

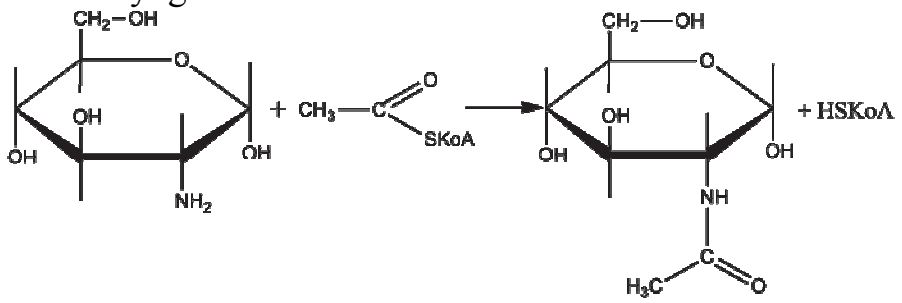


Acetyl-neuraminic acid SKoA



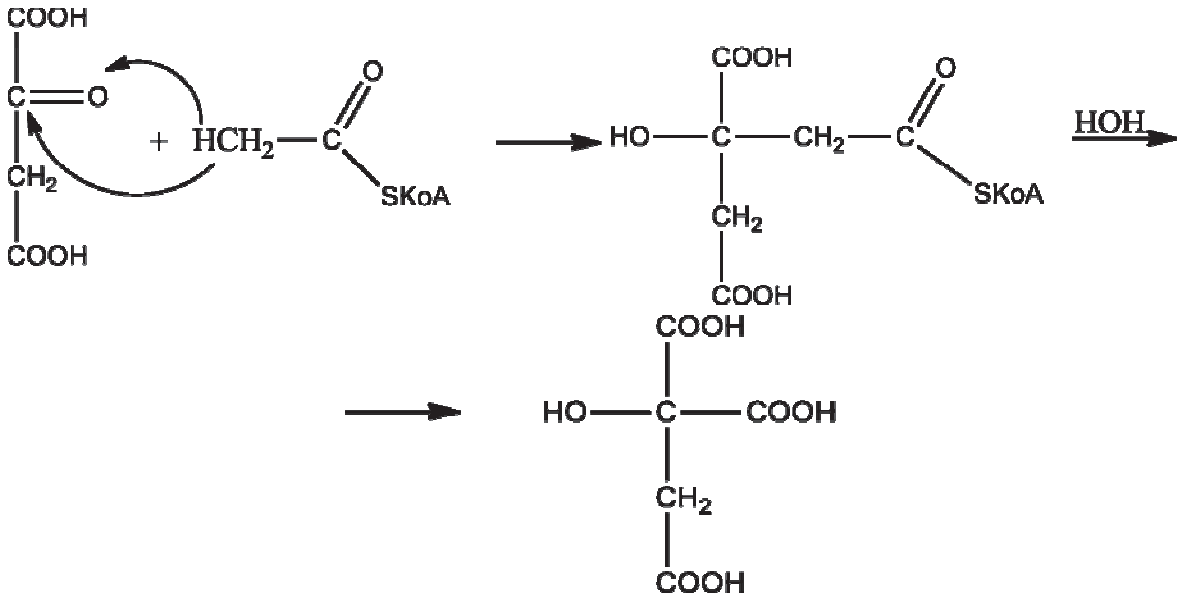
Sialic acid

c)Synthesis of N - acetyl glucosamine

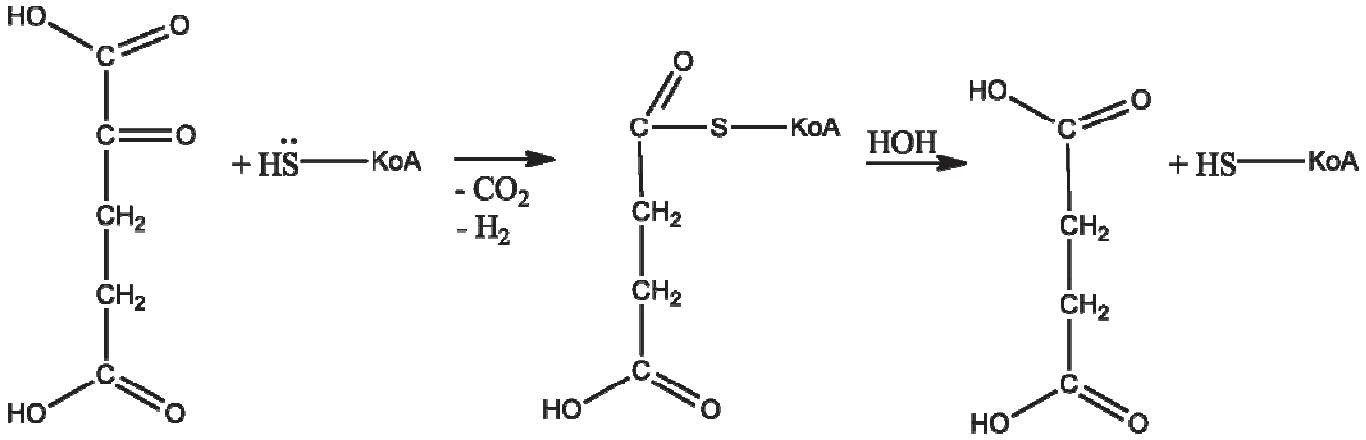


Glucose N-acetylglucosamine

d)Synthesis of citric acid in the Krebs cycle:



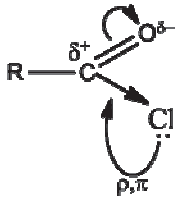
e) The synthesis of succinate (succinic acid) from α-ketoglutaric:



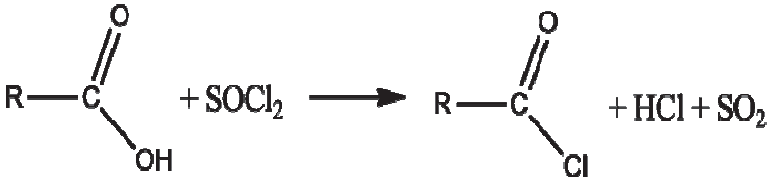
f)Synthesis of the higher carboxylic (fatty) acids, which have an even number of carbon atoms by gradually joining the two carbon atoms.

3.11.2. Halides of carboxylic acids

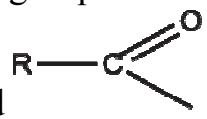
Halides of carboxylic acids - it derived carboxylic acid, hydroxyl group which is substituted by the halogen.



They are formed by the interaction of carboxylic acids with PCl_5, PCl_3 or $SOCl_2$.



Halides more reactive than carboxylic acids. This is explained by the fact that ρ,π - conjugation in the halide is less efficient than in carboxylic acids, as an unshared electron pair of chlorine is to pair with the third energy level to the π-orbital of the carbon second energy level (in acid pair electrons of oxygen and π-orbitals of carbon are on the second energy level). Therefore, bond C-Cl less robust and more easily detached halo than the OH-group. As a result of cleavage of the halogens acyl formed, is, that without a hydroxyl



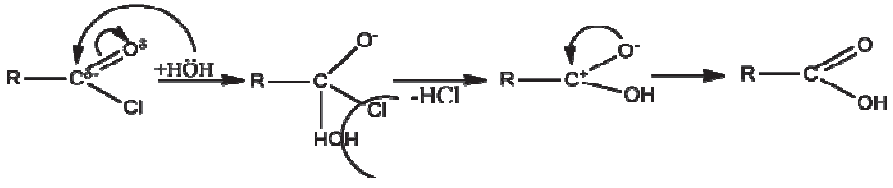
acid residue, so halides used for the acylation reactions.

Chemical properties of halides

Reactions with halides are the mechanism of nucleophilic substitution, and without the catalyst, due to their high reactivity:

1. The hydrolysis of halides.

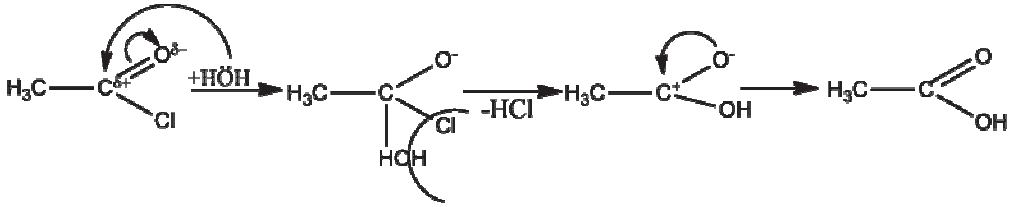
Graphically, the hydrolysis can be show as follows:



(2) (3) (4)

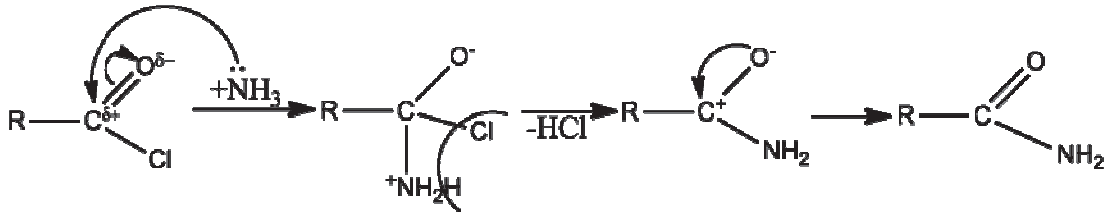
In (1) step attack is a water molecule as a nucleophile on the carbonyl carbon. Dual carbon-oxygen bond is broken and the water joins (2). Water is pushed out of the particle (2) chloride - anion and a proton simultaneously cleaved from the molecule of water, as water becomes trivalent oxygen as a result of accession. Formed an intermediate particle (3), in which there is a redistribution of electron density, and form the final product (4) - carboxylic acid.

An example would be the hydrolysis of acetate acid chloride:



Acetyl chloride

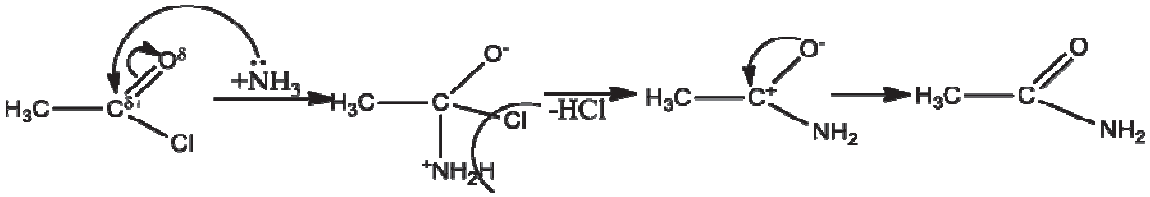
2. The interaction with ammonia.



(1) (2) (3) (4)

In (1) step attack is a molecule of ammonia as a nucleophile on the carbonyl carbon. Dual carbon-oxygen bond is broken and ammonia joins (2). Ammonia is pushed out of the particles (2) chloride-anion and a proton simultaneously cleaved from the molecule of ammonia, as nitrogen is tetravalent with the accession (from the positive nitrogen is easily split off a proton). Formed an intermediate particle (3), in which there is a redistribution of electron density, and form the final product (4) - **amide.**

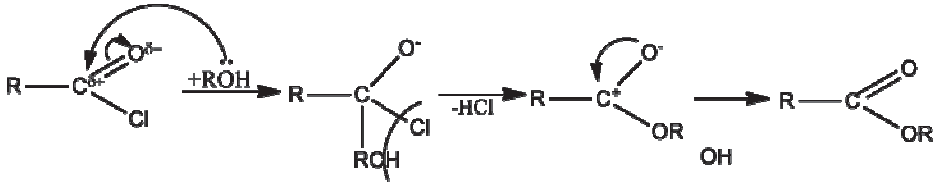
An example might be the interaction of acetyl chloride (chloride acetate acid) with ammonia:



Acetyl chloride

3. Interaction of with alcohols.

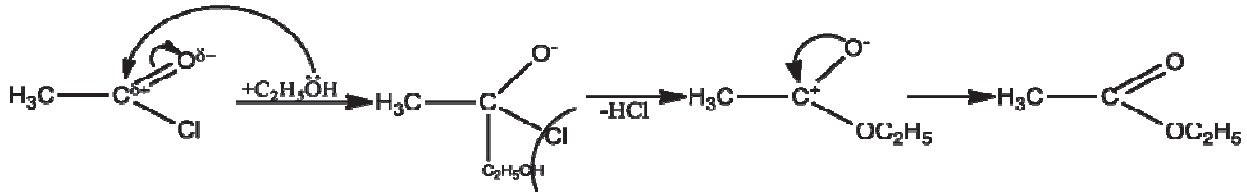
Alcohols - weak nucleophiles. But as a highly halides, reactive the reaction proceeds without a catalyst. Graphically, it can be shown as follows:



(2) (3) (4)

In (1) step attack is a molecule of alcohol as a nucleophile on the carbonyl carbon. Dual carbon-oxygen bond is broken and alcohol joins (2). Alcohol pops out of the particle (2) chloride-anion and a proton simultaneously cleaved from the molecule of alcohol, as oxygen becomes trivalent in the result of a merger. Formed an intermediate particle (3), in which there is a redistribution of electron density, and form the final product (4) - **ester**.

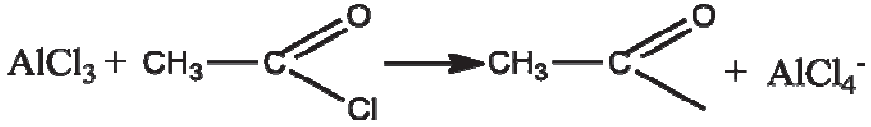
An example might be the interaction of acetyl chloride (chloride acetate acid) with ethanol:



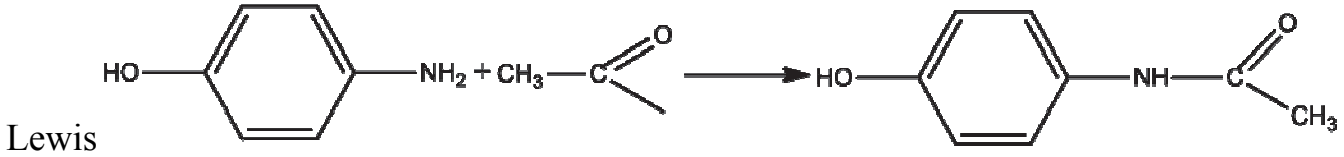
Acetyl chloride

Biological significance of the reactions with halides

As acylating agent halogen anhydride is used for the synthesis of drugs such as **paracetamol**:



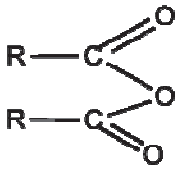
Acid Acyl



Lewis

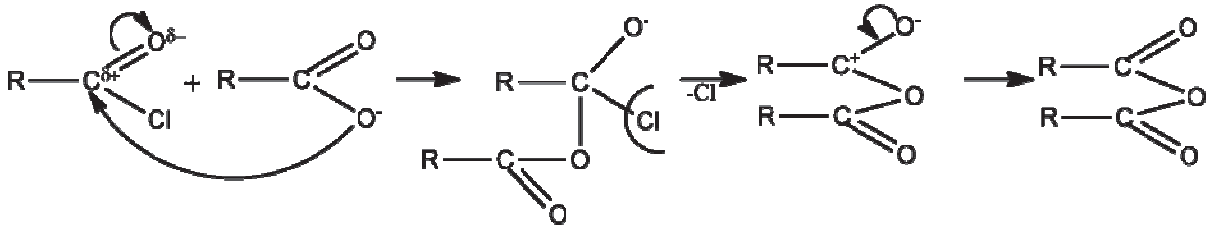
Pair-aminophenol Paracetamol

Anhydrides of carboxylic acids



Anhydrides of carboxylic acids are formed with water molecules are split off from the acid. Since the water molecule split off hard, then easily obtained from the anhydrides halides by the reaction of nucleophilic substitution in which the nucleophile is a carboxylate - anion. Graphically, it can be shown as follows:

(2)

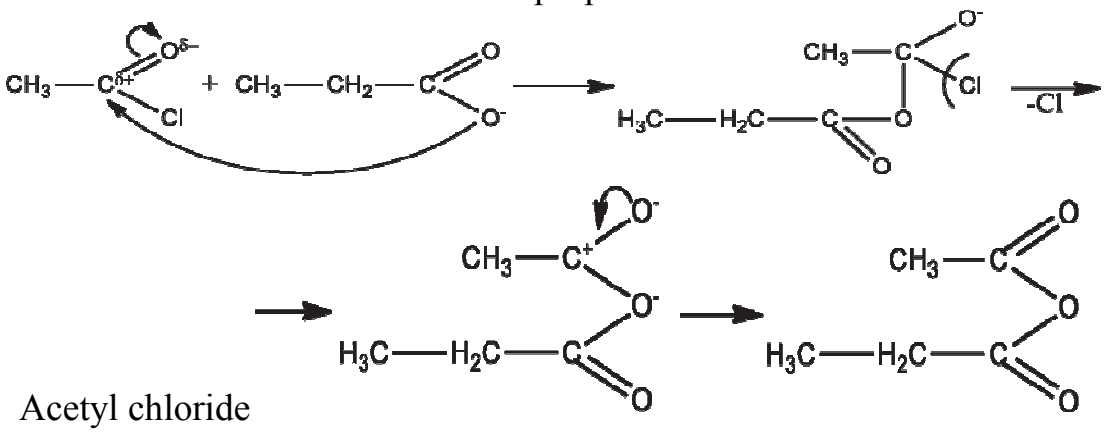


(3) (4) (5) (6)

Salt of the carboxylic acid (1) dissociates and forms carboxylate-anion (2), which is the nucleophile. Further, the carbon halide (3) is attacked by a nucleophile (2). As a result of this attack breaks the double bond C=O, and the nucleophile associates (5). Then cleaved from the carbon chloride-anion formed by the intermediate particle (6), which is the redistribution of electron density, resulting in a final product - **anhydride** (7).

An example might be the interaction of acetyl chloride (chloride acetate acid) and sodium propionate:

Sodium propionate

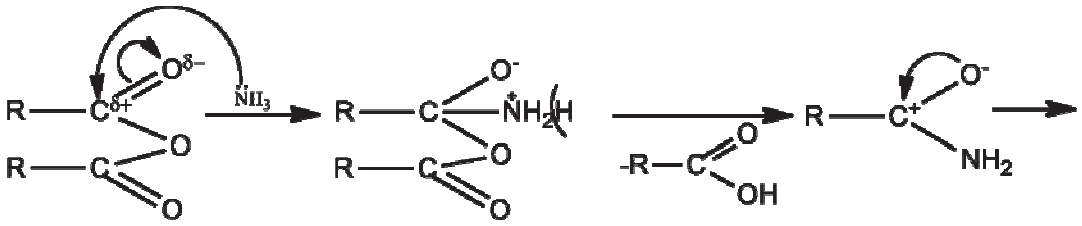


Acetyl chloride

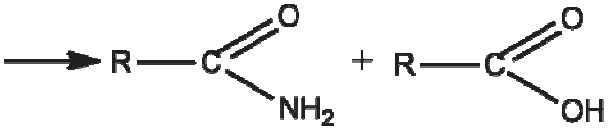
Chemical properties of anhydrides

Reactions with anhydrides are the mechanism of nucleophilic substitution, and without the catalyst, due to their high reactionary ability

1. The interaction with ammonia:



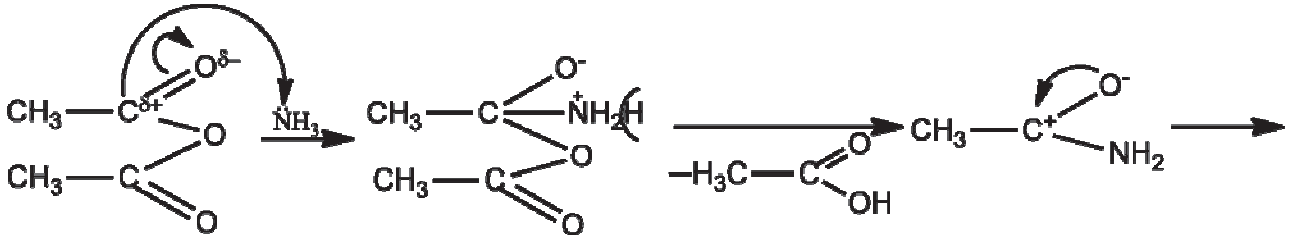
(2) (3)

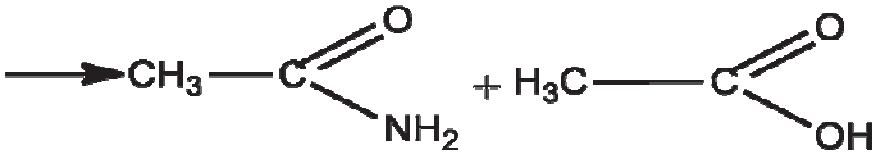


(4) (5)

In (1) step attack is a molecule of ammonia as a nucleophile on the carbonyl carbon - dioxide. Dual carbon-oxygen bond is broken and ammonia joins (2). Ammonia is pushed out of the particle (2) carboxylate-anion and a proton simultaneously cleaved from the molecule of ammonia, as nitrogen is tetravalent with the accession (from the positive nitrogen is easily split off a proton). Formed an intermediate particle (3), in which there is a redistribution of electron density, and form the final product (4) - **amide**, and a by-product - **acid** (5).

An example might be the interaction of acetate acid anhydride with ammonia:

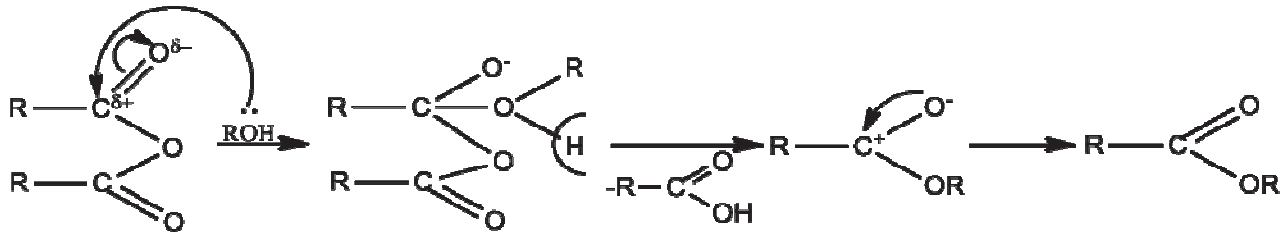




2. Interaction with alcohols.

Alcohols - weak nucleophiles. But as a highly reactive anhydrides, the reaction proceeds without a catalyst.

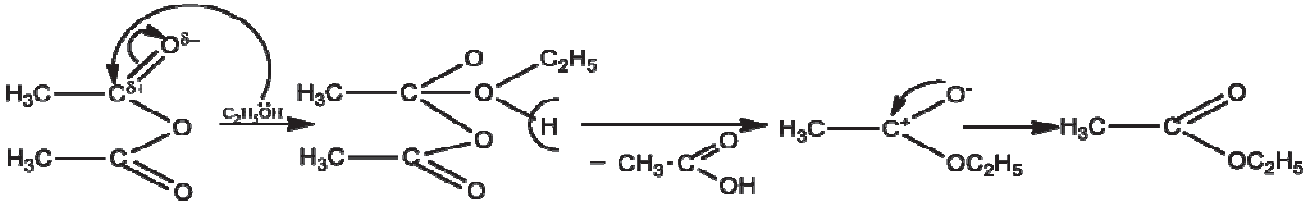
Graphically, it can be shown as follows:



(1) (2) (3)

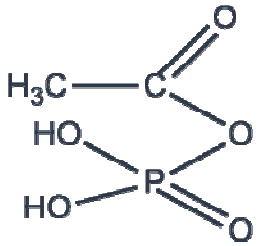
(4) In step (1) attack is a molecule of alcohol as a nucleophile on the carbonyl carbon. Dual carbon-oxygen bond is broken and alcohol joins (2). Alcohol pushes the particles of (2) of the carboxylate anion and a proton simultaneously cleaved from the molecule of alcohol, as oxygen becomes trivalent in the result of a merger. In the intermediate particle (3), is the redistribution of electron density, and form the final product (4) - ester.

An example might be the interaction of acetate acid anhydride with ethanol:

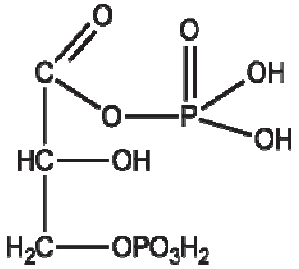


The biological significance of anhydrides

a) In the process of protein synthesis are involved derivatives **Acetylphosphate**. This anhydride acetate and phosphate acid:

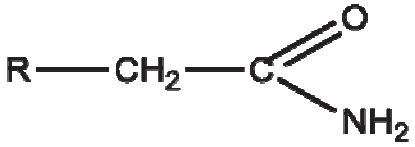


b)Macroergic system in the human body is 1.3-diphosphoglyceric acid, in which anhydrite bond is formed on the first carbon:



3.11.3. Amides of carboxylic acids

Amides of carboxylic acids - are derivatives of carboxylic acids, which the hydroxyl group is substituted with the amino group.

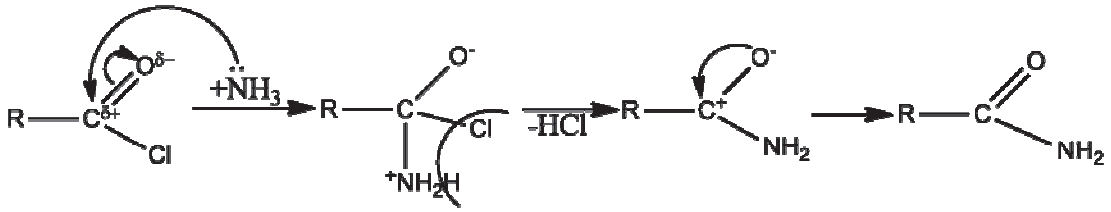


Amides are the mechanism of nucleophilic substitution of halides and anhydrides in the interaction with ammonia.

a) The formation of amides from halides:

Since ammonia is a strong nucleophile, the reaction proceeds without a catalyst.

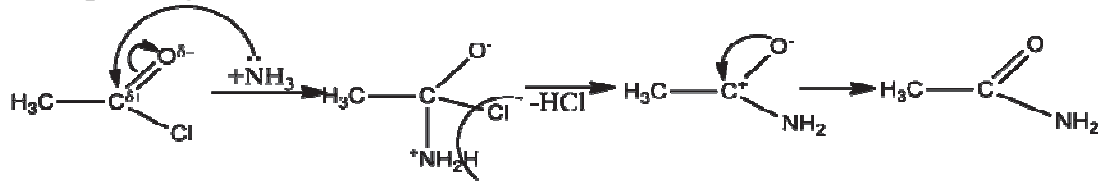
Graphically, it can be shown as follows:



(2) (3) (4)

In (1) step attack is a molecule of ammonia as a nucleophile on the carbonyl carbon. Dual carbon-oxygen bond is broken and ammonia joins (2). Ammonia is pushed out of the particles (2) chloride - anion and a proton simultaneously cleaved from the molecule of ammonia, as nitrogen is tetravalent with the accession (from the positive nitrogen is easily split off a proton). Formed an intermediate particle (3), in which there is a redistribution of electron density, and form the final product (4) - **amide**.

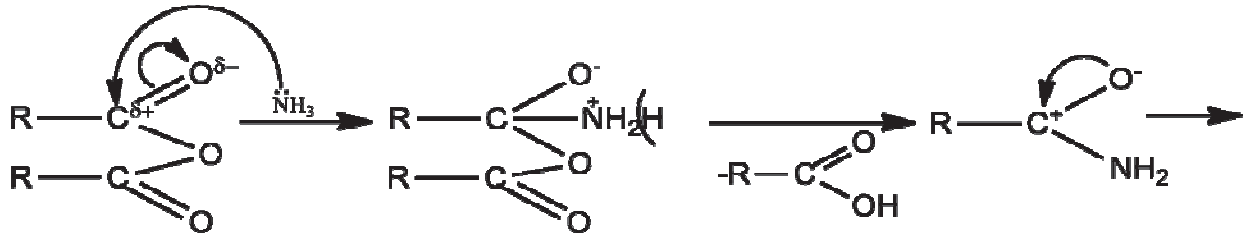
An example might be the interaction of acetate acid chloride with ammonia:



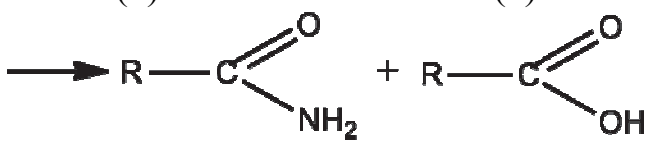
b) The formation of amides from anhydrides:

Since ammonia is a strong nucleophile, the reaction proceeds without catalyst.

Graphically, it can be shown as follows:



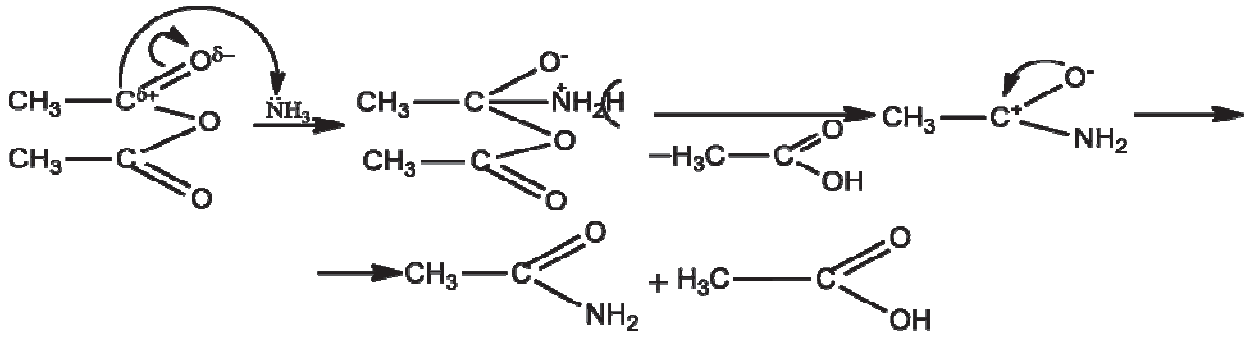
(2) (3)



(4) (5)

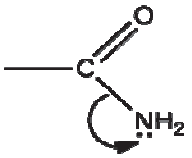
In (1) step attack is a molecule of ammonia as a nucleophile on the carbonyl carbon dioxide. Dual carbon-oxygen bond is broken and ammonia joins (2). Ammonia is pushed out of the particle (2) carboxylate - anion and a proton simultaneously cleaved from the molecule of ammonia, as nitrogen is tetravalent with the accession (from the positive

nitrogen is easily split off a proton). Formed an intermediate particle (3), in which there is a redistribution of electron density, and form the final product (4) - amide, and a by-product - acid. An example might be the interaction of acetate acid anhydride with ammonia:



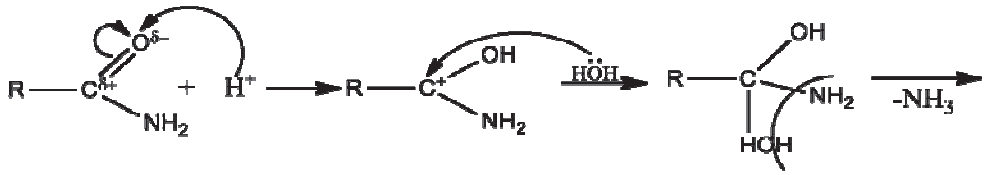
The chemical properties of amides

a) Base properties of amides are mild, as the lone electron pair of nitrogen is in the pairing and less available to the proton:

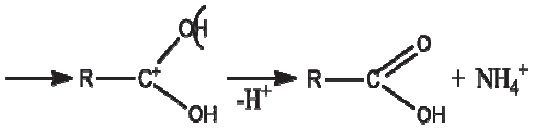


b) Hydrolysis in acidic medium is the mechanism of nucleophilic substitution:

$$H_2SO_4 \rightarrow H^+ + HSO_4^-$$



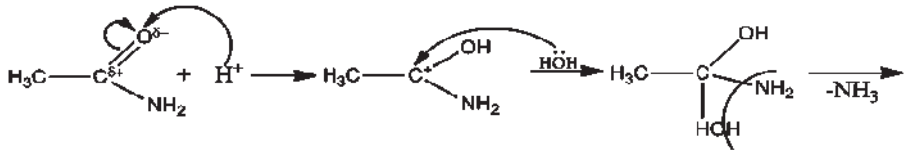
(2) (3)



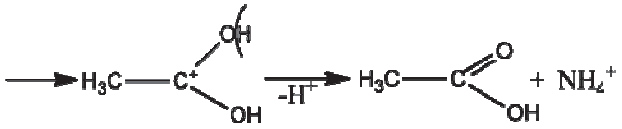
(4) (5) (6)

In (1) step is an attack by a proton as a catalyst for oxygen oxo-group. Dual carbon-oxygen bond is broken and formed carb-cation (2), which is attacked by water as the nucleophile. Formed an intermediate particle (3), which split off from both the amino group and a proton, forming a molecule of ammonia. From carb-cation (4) the proton is split off and formed the final products - acid (5) and the ammonium ion (6).

An example would be the hydrolysis of acetamide:

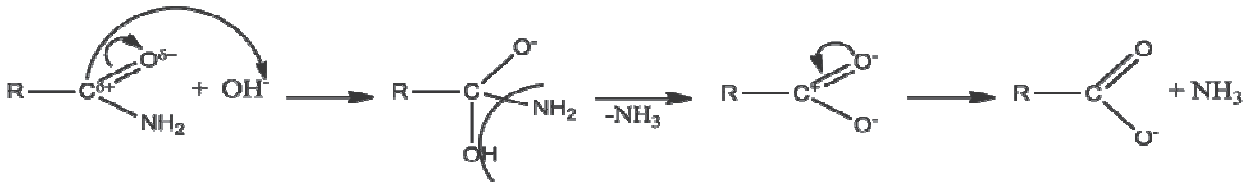


Acetamide



c) Hydrolysis in alkaline medium is also on the mechanism of nucleophilic substitution.

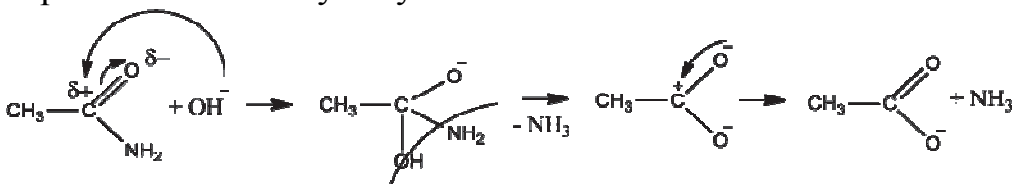
$$NaOH \rightarrow Na^+ + OH^-$$



(2) (3) (4) (5)

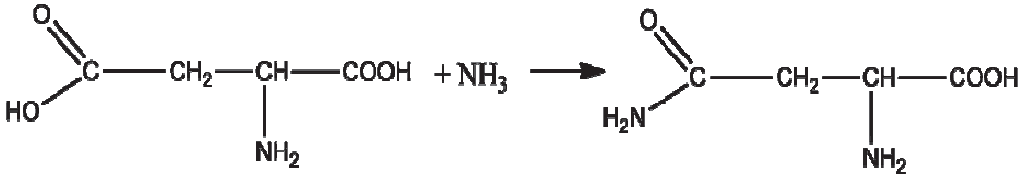
In (1) step is an attack OH - anion as the nucleophile on carbon oxo - group. Dual carbon-oxygen bond is broken and formed anion (2), which split off from both the amino group and a proton, forming a molecule of ammonia. In the intermediate particle (3) are the redistribution of electron density and the formation of end products - the carboxylate anion (4) and the ammonia molecule (5).

An example would be the hydrolysis of acetamide:



The biological significance of amide

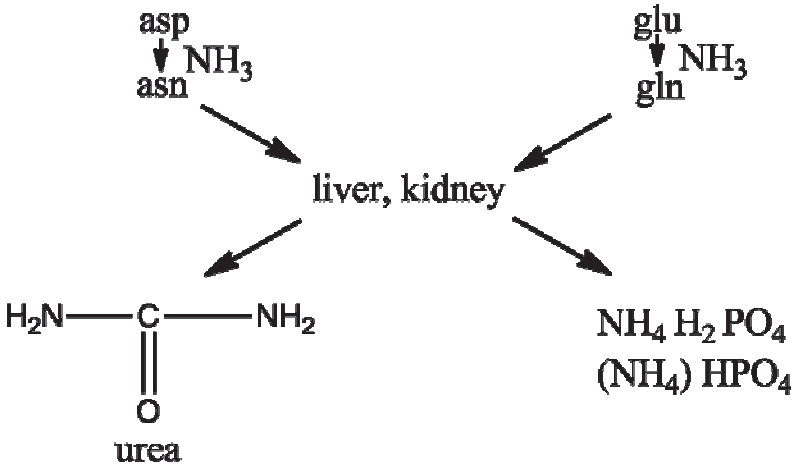
Formation of amides in the human body - a way of neutralizing the ammonia, which is a product of metabolism of amino acids and proteins. Ammonia has a negative effect on the central nervous system. Therefore, it binds to the amino acids - aspartic acid and glutamic with the formation of amides. For example:



Aspartic acid (asp) or asparagine (ASN)

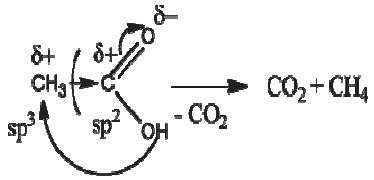
Amide of aspartic acid

Scheme of the binding and excretion of ammonia as follows:



3.11.4. Decarboxylation of carboxylic acids

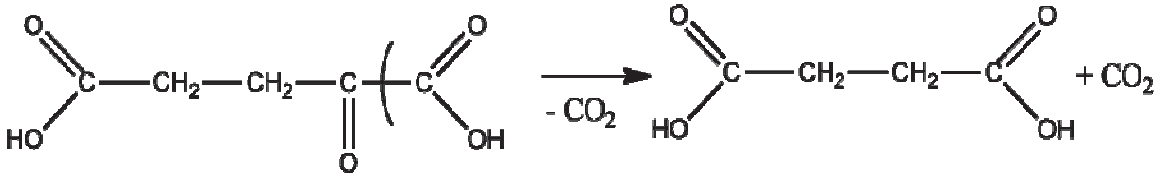
Carboxylic acids feature is decarboxilation reaction. ie cleavage of carbon dioxide. This can be exlain as follows:



As a result of displacement of the electron density to the oxygen atom on carbon-carboxyl group occurs a partial positive charge δ+. This carbon in sp^2-hybridisation of the radical, in which the carbon in sp^3 hybridisation shifts the electron density and the carbon radical occurs a partial positive δ'^{+}charge. So close are two carbon a partial positive charge, so they repel each other and split off carbon dioxide and hydrogen from the carboxyl group is connected to the carbon radical and the alkane is formed

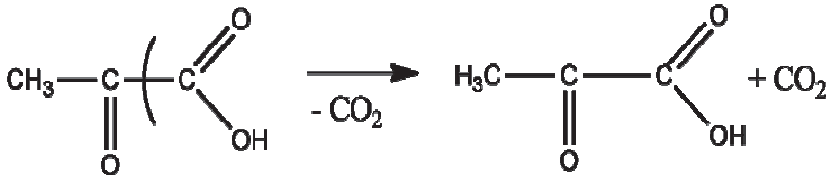
The biological significance of the decarboxylation reaction:

a) As a result of decarboxylation of α-ketoglutaric acid, succinic acid is formed (the reaction proceeds in the presence of CoA-SH).



α-ketoglutaric acid Succinic acid

b) The decarboxylation of β-ketobutyric acid forms acetone.



β-ketobutyric acid Acetone

Acetone, β-ketobutyric acid and β-hydroxybutyric acid are a group of **ketone bodies**, which are found in the urine of patients with diabetes.

The above mechanisms are used to explain the reactivity of heterocyclic and heterofunctional, and biologically active compounds of different classes of organic compounds.

RULES AND SAFETY PRECAUTIONS IN THE LABORATORY FOR ORGANIC CHEMISTRY

General Rules

1. Laboratory course is permitted only with students who are closely acquainted with the subject to be studied. They will learn theoretical material with the help of textbooks, manuals, lecture notes, and will record the equations of respective reactions in the laboratory report accomplish.

2. Duty of students is to receive the necessary work for the group equipment and reagents and place them in the workplace.

3. In the chemical laboratory, it is permitted to work, only with wearing a white coat and a cap. Each student is given a permanent job, which it should get done. Do not litter up foreign objects that are not related to the topic. Disorder and carelessness in carrying out experiments often lead to a necessary repetition of the experiment.

4. With irritating and boiling solutions, tube must be closed by using a pinchcock or a stopper and the tube must be kept in a way that its opening is directed in the opposite direction, that is away from those who are working around.

5. Do not lean over a test tube which is irritated or being used to avoid the fluid from spraying onto your face.

6. In cases where there is a need to clean the smell of substances in the tubes, there should be a slight movement of the palm of hand to direct the flow of air from the tube and gently sniff it off.

7. Reagents, distilled water and electrical energy should be used sparingly.

8. All the work with substances which are obtained during the interaction are harmful to the mechanism of organic gases or substances with an unpleasant smell, should be carried out in a specially reserved room for this purpose i.e. rooms with forced ventilation, or under the hood. Works with substances of this category are prohibited at the work place.

9. Solutions of hydrogen sulphide, acids, alkalis, etc. should be poured into a special MSRP-control to prevent the destruction of sewage systems in the laboratory. Solutions, with compounds containing silver, mercury, lead and iodide ions should be poured into a separate bowl for further regeneration.

10. It is forbidden to perform experiments that are not related to the laboratory work.

11. After completion of work, show your work, clean the tubes, clean your desk, turn off, electric lights, taps and your wash your hands.

Rules for Handling Reagents

- For experiements, solutions and solids are taken in amounts required by the experimental method;
- Reagents remain in closed beakers with lids to prevent contamination;
- Solid reagents are selected carefully with a spatula;
- Liquid reagents are taken with droppers and measured by drops;
- Do not spill and pour excess reagent into the stock, from which it was taken to prevent contamination of reagents
- Concentrated solutions of acids and alkalis and toxic substances should be in a reserved close, whether they are worked with or not

Working With Acids and Bases

1. While working with concentrated acids and alkalis, one needs to be cautious and make sure that they do not get on skin and clothes.

2. At the dilution of concentrated sulphuric acid it should be cautious and gradual that acids are added to water, and not vice versa. This is due to the fact that the dilution of sulphuric acid causes a large amount of heat or exoplotion. Therefore, when water is added to the acid of the solution it can be sprayed, and can get on skin and clothing.

Working With Harmful and Poisonous Substances

When working with harmful and toxic substances (cyanide, salts of barium, mercury, lead, arsenic, mercury metal, sulfide, etc.) it is necessary to ensure that hazardous or toxic substances are not assimilated in the body through the gastrointestinal tract. Consumption of food in the laboratory is strictly prohibited. After working in the laboratory one must wash his or her hands. Cylinders filled with mercury or other devices, must be put on a special stands that in case of damage to the device, the main mass of mercury gets on the stand, rather than on a desktop or floor. If the mercury is still dense mass, it must be very quickly assembled with copper wire or plates, and then a gray-rattling. Works with mercury is allowed only in special rooms.

Working with Flammable Substances

1. While working with diethyl ether, alcohols, benzene and other combustible matter or properties, their reaction is carried out in water baths, or in a flask with a reverse refrigerator.

2. In the laboratory, these substances should be stored in tightly sealed jars with small capacity.

3. Test tubes and beakers with combustible substances should be kept at a sufficient distance from the burners. After working with them replace the burner, and only then, you wash the dish in which these substances were contained.

4. Combustible, flammable and volatile substances can not be stored close to flame or very hot electric devices (thermostats, electronic, etc.).

5. Alkali metals should always be kept in a layer of inert against water and moisture kerosene. Alkali metals and crystalline alkali should be taken only with tweezers or a special forceps. One must wear goggles or a mask. After the end of the remark the remnants of these metals should be moved to a special dish.

Working With Substances Which Form Explosive Mixture

1. It must be remembered that some gases (hydrogen, carbon disulfide, acetylene, carbon oxide etc.), as well as volatile compounds (benzene, alcohols, hexane, etc.), vapourize into air to form explosive mixtures with oxygen. To ensure that, these substances do not accumulate in dangerous quantheies in the laboratory, it is necessary to ensure strong extractor ventilation.

2. Do not liter, and do not put in shock substances which form explosive mixtures (chlorates, perchlorates, per-sulfate, etc.) without permission and relevant instructions of the teacher

Rules of Conduct in case of Fire in Laboratory

1. In case of fire, all electric appliances and gas must be shut down or closed. The fire in the laboratory should be filled up with sand or on-cover fire blanket and a fire extinguisher should be used.

2. Water must be carefully used to fire extinguisher.

The table given below is helpful in an accidental situation. Read and remember them.

Situation	Safe Response
Burns	Flush with ethanol solution or diluted solution of $KMnO_4$.
Cuts and Bruises	Treat as directed by instructions included in first aid kit.
Fainting or collapse	Provide person with fresh air; have it recline in a position so that his head is lower than his body.
Foreign Matter in Eyes	Flush about 15 min with plenty of water, then go to the doctor.
Severe bleeding	Apply pressure or a compress directly to the wound and get medical attention immediately
1. Spills, general ***2. Acid burns*** ***3. Base burns***	1. Wash the damaged area with plenty of water, use the shower if necessary. 2.Use sodium hydrogen carbonate (baking soda) 3. Use 3 % of boric acid or acetic acid

Short methodical directions for practical lesson:
Practical lesson is started from the general questions (5 min).
Explanation of unclear questions (25 min)
Writing of control test (15 min)
Carrying out a laboratory work, filling a laboratory notebook, signing the laboratory notebook by a teacher, announcing of student marks (45 min).

Technological map of practical lesson:

№	***Steps***	***Time (min)***	***Educational handout***	***Residence***
1	General questions	5		Faculty
2	Correction of theoretical student knowledge	20	Tables, task	
3	Control test	15	Test, questions	
4	Performing of laboratory work	40	Chemicals, chemical disits, equipments.	
5	Analysis and conclusion of a practical lesson	10		

TOPIC 1

MAIN TERMS AND CONCEPTS IN ORGANIC CHEMISTRY NOMENCLATURE OF ORGANIC COMPOUNDS

1. ***Actuality of the topic:***

The basic concepts used in organic chemistry are needed to explain the reactivity of substances, including biologically active compounds in normal and pathological processes, as well as understanding the chemistry of drugs in humans.

2. ***General aim:***

General aim is to learn how to name organic compounds, be able to classify organic compounds and be able to identify primary, secondary, tertiary and quaternary carbon atoms.

3. ***The main questions of the seminar:***

Classification of organic compounds:

- The structure of the carbon skeleton;
- The nature of the functional groups (examples of functional groups and classes of compounds).

Polyfunctional compounds (definitions, examples).

Radicals (definition). The radicals of alkanes, alkenes, arenes. Remains of alcohols, carboxylic acids.

Primary, secondary, tertiary and quaternary carbon atoms.

Principles of international nomenclature (IN) of organic compounds.

4. ***Literature:***

Lecture.

Tyukavkina N.A., Bauke Y.I. Bioorganic Chemistry, 1985, pp. 11-34, 1991, pp. 16-39.

Guide to laboratory studies of Bioorganic Chemistry, ed. N.A. Tyukavkina, 1985, pp. 24-27.

5. ***The questions for individual learning:***

5.1. Nomenclature:

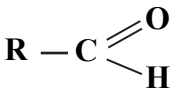
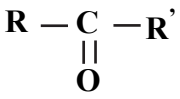
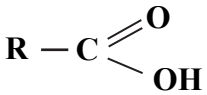
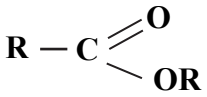
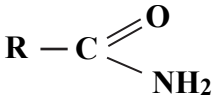
- Trivial;
- Rational;
- Radical-functional.

6. ***The theoretical material:***

Organic compounds are involved in all biochemical processes occurring in organisms. Given that organic matter - a carbon compounds that today there are about 10 million; it is relevant to the issue of classification and nomenclature. The classification of all organic compounds assigned two classification features:

6.1.1. Structure of the carbon skeleton: acyclic and cyclic (carbocyclic and heterocyclic);

6.1.2. The nature of functional groups:

Class name	*The general formula of class*
Halogen derivatives of hydrocarbons	**R – Hal**
Alcohols, phenols	**R – OH**
Ethers	**R – O – R**
Aldehydes	
Ketones	
Carboxylic acids	
Sulphonic	**R – SO_3H**
Esters	
Amides	
Nitriles	**R – C ≡ N**
Nitro compounds	**R – NO_2**
Amine	**R – NH_2**

Nomenclature of organic compounds - a set of rules under which the unique name of building individual organic compounds. There are trivial and rational international nomenclatures.

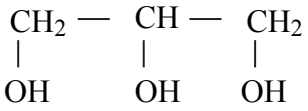
7. ***Examples of task:***

Name the fumaric acid HOOC – CH = CH – COOH according to IUPAC:

Answers: butanedioic acid.

Write the formula of propanetriol:

Answers:

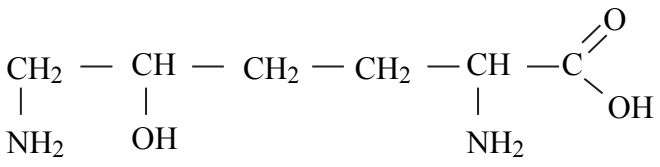


Aminalone – takes part in metabolic processes of the brain, has the structure $H_2N–CH_2–CH_2–CH_2–COOH$. Name it for IN.

Answers: 4-aminobutanoic acid.

Integral part of collagen– oxy lysine – is 2,6-diamino-5-oxoitxanoic acid. Write its structure.

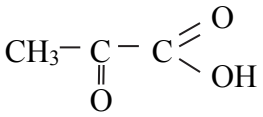
Answers:

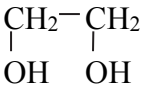


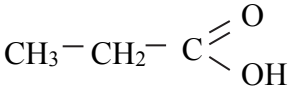
8. ***Homework (must be performed in the laboratory notebook):***

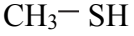
8.1. Write the formulas of these compounds: amino–3–-mercaptopropionic acid; 2–oxobutanedioic acid.

8.2. Which class of organic compounds includes the following compounds?

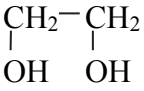


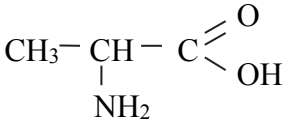






8.3. How are these compounds called in the international nomenclature?





9. ***Tests:***

9.1. Which of the following compounds can be classified as organic?

a) SiH_6;
b) C_2H_6;
c) C_2H_5SH.

9.2. An atom of carbon in organic compounds is:

a) Always tetravalent;
b) It can be trivalent;
c) It can be divalent.

10. ***The algorithm of lab work:***

Construction of molecular models of bioactive compounds.
Safety precautions when working in the chemical laboratory.
Introduction to laboratory equipment and chemical instruments.

TOPIC 2

THE ELECTRONIC STRUCTURE OF CARBON AND ITS CHEMICAL BONDS CONJUGATION AND AROMATICITY ELECTRONIC EFFECTS IN BIOLOGICALLY-ACTIVE COMPOUNDS

1. ***Actuality of the topic:***

The reactivity of compounds is determined by the electronic effect and by the type of chemical communication in the molecules including the mutual influence of atoms. Conjugation and aromaticity – energetically are favorable processes. One of the factors, which determine the reactivity of compounds, is the redistribution of electron density.

2. ***General aim:***

You must know the essence of the phenomenon of conjugation and aromaticity to explain the biological activity of compounds in health and disease.

3. ***The main questions of the seminar:***

3.1. Types of hybridisation of carbon atoms. Electronic structure of σ- and π-bonds.

The principle and the main conclusion of the method of molecular orbitals.

Conjugation in organic compounds:

3.3.1. Pairing open-chain systems (butadiene), the definition of the terms "coupled system" and "pair", types of interface, examples, conjugation energy (delocalization).

3.3.2. Conjugation and aromaticity in systems with closed loop (thearene, heterocycles) aromaticity (definition), the signs of aromaticity, pyrrole and pyridine nitrogen atoms.

Inductive effect, the reasons for its manifestation, graphic.

Mesomeric effect causes its manifestation, graphic.

Pairing and thermodynamic stability.

Importance of conjugation and aromaticity in biological systems.

4. ***Literature:***

4.1. Lecture.

4.2. Tyukavkina N.A., Bauke Y.I. Bioorganic Chemistry, 1985, pp. 29-33, 35-45, 1991, pp. 33-36, 37-50.

4.3. Guide to laboratory studies of Bioorganic Chemistry, ed. N.A. Tyukavkina, 1985, pp. 34-42.

5. ***The questions for individual learning (must be performed in the laboratory notebook):***

5.1. Show aromaticity of imidazole.

5.2. Specify the type of hybridisation of carbon atoms in the molecules of acetic acid and pirole.

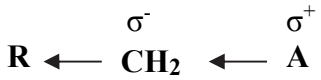
5.3. Indicate graphically electronic effects in molecules and propane, ethanol and vinyl alcohol.

6. *The theoretical material:*

6.1. Reactivity of organic compounds depends on the mutual influence of atoms, which manifests itself in the electronic effects (inductive and mesomeric):

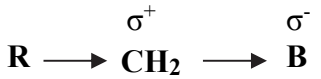
6.1.1. Inductive Effect – the process of transfer of electronic substituent effects on the chain of single bonds (σ-bonds):

6.1.1.1. The positive inductive effect (+I) – substituent pushes electron density of a system of σ-bonds.



A: **- N^-R; - O^-; - CR_3; - CHR_2; - CH_2R; - CH_3**

6.1.1.2. The negative inductive effect (-I) – substitute delayed the electron density itself.



B: **- O^+R_2; - N^+R_3; - NO_2; - CN; - COOH; - COOR;**

- F; - Cl; - Br; - I; - OR; - COR; - OH; - NH_2; - SR

6.1.2. Mesomeric Effect – the process of transmission of electronic substituent effects on the conjugate system of π-bonds. Mesomeric effect appears only when the substituent is included in conjugation by undivided electron pairs or multiple connection:

6.1.2.1. The positive mesomeric effect (+M) – substituent increases electron density in the conjugate system.

Ä: **- Ö; - Ñ$(CH_3)_2$; - ÑHCH_3; - ÑH_2; - ÖCH_3; - ÖH;**

- F; - Cl; - Br

6.1.2.2. The negative mesomeric effect (-M) – substituent decreases the electron density in the conjugate system.

B: **- O^+R_2; - N^+H_3; - NO_2; - CN; - COOH; - COOR;**

6.2. Conjugation system – a system that consists of simple and multiple bonds to alternate (π,π-conjugation) or π-electrons overlap multiple bonds with p-electrons of neighboring atoms (p,π-conjugation).

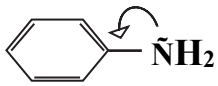
7. *Examples of task:*

7.1. What is pairing? What is the type of conjugation in the molecule of aniline? (Graphically):

Answers:

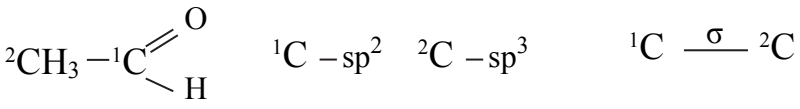
Pair – a redistribution of electron density in the π-bonds, leading to stabilization of the system.

In a molecule of aniline – p,π–conjugation:



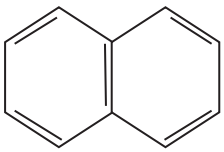
Specify the type of hybridisation of carbon atoms and the structure of the carbon-carbon bond in a molecule of acetaldehyde:

Answers:



Provide evidence of aromaticity of naphthalene:

Answers:



a) Planar skeleton of the molecule as a result of sp^2-hybridisation of the carbon atom;
b) Continuity of the chain of conjugation – π,π;
c) Huckel's rule: 4n+2=10, n=2.

8. *Homework (must be performed in the laboratory notebook):*

Identify the type and symbol of electronic effect in molecules:

Specify the type of hybridisation of carbon atoms and the structure of the carbon-carbon bond in a molecule:

9. ***Tests:***

9.1. An atom of carbon in organic compounds can be in the state of:

a) sp^3, sp^2d, sp–hybridisation;
b) sp^3, sp^2, sp–hybridisation;
c) spd^2, sd^3, sp–hybridisation.

9.2. sp^3–hybrid orbitals are directed under a corner:

a) 109°28′;
b) 120°;
c) 180°.

9.3. sp^3–hybrid orbitals stipulate:

a) There is a location of molecule in plane;
b) Spatial configuration;
c) Linear configuration.

9.4. sp^2–hybrid orbitals are directed under a corner:

a) 109°28′;
b) 120°;
c) 180°.

9.5. sp^2–hybrid orbitals stipulate:

a) There is a location of molecule in plane;
b) Spatial configuration;
c) Linear configuration.

9.6. sp–hybrid orbitals are directed under a corner:

a) 109°28′;
b) 120°;
c) 180°.

9.7. sp–hybrid orbitals stipulate:

a) There is a location of molecule in plane;
b) Spatial configuration;
c) Linear configuration.

9.8. An electronic effect is the displacement of electronic proximity to:

a) Strongly electronegative atom;
b) Less electronegative atom;
c) Electronegative group.

9.9. An inductive electronic effect is the displacement of electronic proximity to more electronegative atom:

a) For π–bond;
b) For σ–bond;
c) For ρ–bond.

9.10. Displacement of electronic proximity to the strongly electronegative atom for σ–bond is called bonding:

a) By a mesomeric effect;
b) By an osmotic effect;
c) By an inductive effect.

9.11. A mesomeric electronic effect is displacement of electronic proximity to more electronegative atom:

a) On the connected system;
b) For σ–bond;

c) For ρ–bond.

9.12. Electrondonors sub-groups:

a) Diminish an electronic proximity in the system;
b) Does not change the electronic proximity in the system;
c) Increases the electronic proximity in the system.

9.13. sub-groups which increase an electronic proximity in the system are named:

a) Electrosimilar;
b) Electron acceptor;
c) Proton donors.

9.14. Electron acceptor sub-groups:

a) Diminish an electronic proximity in the system;
b) Does not change an electronic proximity in the system;
c) Increase an electronic proximity in the system.

9.15. sub-groups which diminish an electronic proximity in the system are named:

a) Electrosimilar;
b) Electron acceptor;
c) Proton donors.

10. *The Control Test:*

Sample 1

1. Point the type and sign of electronic effects in molecules:

Sample 2

1. Point the type and sign of electronic effects in molecules:

Sample 3

1. Point the type and sign of electronic effects in molecules:

Sample 4

1. Point the type and sign of electronic effects in molecules:

TOPIC 3

THE SPATIAL STRUCTURE OF ORGANIC COMPOUNDS ENANTIOMERS THE CONFORMATIONAL ISOMERISM

1. ***Actuality of the topic:***

Most natural compounds exist in certain forms of spatial and biochemical reactions that take place taking spatial factors into account. Only certain isomers exhibit biological activity that may be lost in the isomerization process, and this can cause pathological changes in the body.

2. ***General aim:***

Determine the type of isomerism, understand the difference between conformation and configuration and set the communication of spatial structure with biological activity.

3. ***The main questions of the seminar:***

3.1. Definition of isomerism. Types of isomerism.

3.2. Structural isomerism carbon skeleton and position of functional groups.

3.3. Stereoisomers, the configuration of the molecule.

3.4. Enantiomers. Definition polarized light, optical activity, optical isomers, Fiscitr projection, chirality, the chiral center, the relative and absolute configuration, enantiomers, diasteromery, racemic glyceraldehyde, lactic and tartaric acid, enantiomers bond with biological activity

3.5. Conformational isomerism: definition, cause, conformation, and eclipsed inhibited, torsional strain, the projection of Newman.

3.6. Conformations of cycloalkanes (bath suite): angular strain, axial and equatorial direction alternates, conformational isomerism bond with biological activity, examples.

4. ***Literature:***

4.1. Lecture.

4.2. Tyukavkina N.A., Bauke Y.I. Bioorganic Chemistry, 1985, pp. 47, 50-86, 1991, pp. 54-87.

4.3. Guide to laboratory studies of Bioorganic Chemistry, ed. N.A. Tyukavkina, 1985, pp. 27-34, 138-148, and 243-245.

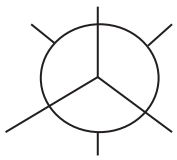
5. ***The questions for individual learning (must be performed in the laboratory notebook):***

5.1. Write the structure, configuration and conformation of ethanolamine.

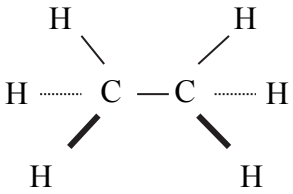
5.2. Write the Fischer projection of enantiomers of alanine CH_3-CH (NH_2)-COOH and indicate the relative configuration.

6. ***Examples of task:***

6.1. Write the structure and configuration of compounds, which stalled the conformation:



Answers:



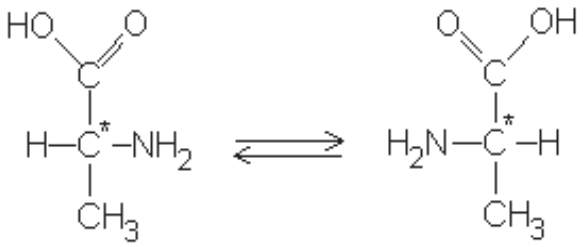
What are enantiomers?

Answers:

Isomers are related to one another as an object and its mirror reflection.

Write the formulas of enantiomers of alanine and show their relative configuration.

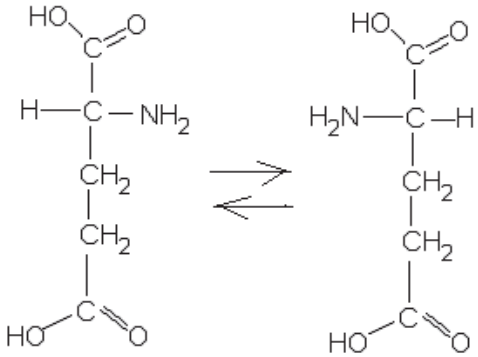
Answers:



D- *L-*

Write formulas of enantiomers of glutamic acid and show their relative configuration: $HOOC–CH_2–CH_2–CH(NH_2)–COOH$.

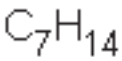
Answers:

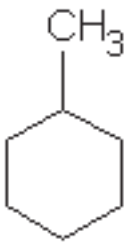


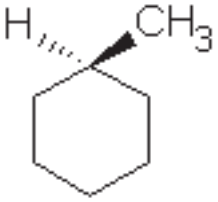
D– L–

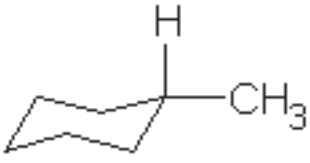
Write the molecular formula, structure, configuration**,** braked conformation of methylcyclohexane.

Answers:









Molecular *Structure* *Configuration* *Conformation*

7. *Homework (must be performed in the laboratory notebook):*

7.1. Write the structure, configuration, staggered, conformation of: chlorocyclohexane ($C_6H_{11}Cl$); mercaptoethanol (C_2H_5SH); amino cyclohexane (H_2N-C_6H_{11}).

7.2. Write the enantiomers in Fischer projection:

Serine CH_2 (OH)-CH (NH_2)-COOH;

Cysteine CH_2 (SH)-CH (NH_2)-COOH;

Isoleucine $(CH_3)_2CHCH_2CH(NH_2)$ COOH.

Write the structure and configuration of Newman conformation:

8. *Tests:*

8.1. Isomers are matters which have identical high-quality and quantitative composition, but different properties as a result of:

a) Different structure;
b) Different molar mass;
c) Different concentration.

8.2. Cis–trans isomerism conditions the different location of atomic groups relatively by:

a) Double bond;
b) Triple bond;
c) Simple bond.

8.3. A classic example of cis-trans–isomerism is:

a) Malic – succinic acids;
b) Methylsuccinic (pyruvic) – milk acids;
c) Fumarovic – maleinic acids.

8.4. Such configuration of vitamin A takes part in the process of vision:

a) Cis-;
b) D-;
c) Trans-.

8.5. Enantiomers is the type of isomerism, conditioned by the ability of matters to revolve:

a) Light ray;
b) Plane of polarization;
c) Plane of symmetry.

8.6. the ability to revolve a matters' plane of polarization is called:

a) electric activity;
b) osmotic activity;
c) optical activity.

8.7. Chiral center is an atom of carbon, which is bonded by:

a) Four different sub-groups;
b) Three different sub-groups;
c) Two different sub-groups.

8.8. Chiral is the ability of matters to exist in a kind of:

a) Symmetric molecules;
b) Two incompatible mirror reflections;
c) Two compatible mirror reflections.

8.9. Enantiomers are isomers which behave with each other as:

a) An object and trans is an isomer;
b) Object and cis in a reflection;
c) Object and the mirror.

8.10. The formulas of enantiomers is written down in a projection:

a) By Fischer;
b) By N'yuman;
c) By Tollens.

8.11. Optical isomers are enantiomers which revolve:

a) Plane of molecule in different sides;
b) Plane of polarization on a different side, but on an identical corner;
c) Plane of polarization on a different corner.

9. *The Control Test:*

Sample 1

1. Write the structure, configuration, staggered, conformation of colamine (H_2N-CH_2-CH_2-OH).

2. Write the enantiomers in Fischer projection malic acid HOOC-CH_2-CH (OH)-COOH.

Sample 2

1. Write the structure, configuration, staggered, conformation of 2-chlorethanol.

2. Write the enantiomers in Fischer projection β-hydroxybutyric acid CH_3-CH (OH)-CH_2-COOH.

Sample 3

1. Write the structure, configuration, staggered, conformation of propyl cycloitxane (C_6H_{11}-C_3H_7).

2. Write the enantiomers in Fischer projection phenylalanine $C_6H_5CH_2CH$ (NH_2) COOH.

Sample 4

1. Write the structure, configuration, staggered, conformation of cyclohexanol C_6H_{11}-OH.

2. Write the enantiomers in Fischer projection as aspartic acid HOOC-CH_2-CH (NH_2)-COOH.

TOPIC 4

REACTIVITY OF ALKANES, ALKENES AND ARENES

1. Actuality of the topic:

The reactions involving alkanes, alkenes and arenes take place in human organs. Studying the mechanisms of chemical reactions gives the possibility to explain the processes (in temper) in normal and pathological states. The knowledge of reaction mechanism is used to produce substances (medications) with knowing properties.

2. ***General aim:***

The general aim is to explain the reactivity of biologically active substances using the mechanism to compare the reactivity of biologically active substances.

3. ***Actual aims and abilities:***

3.1. To explain the dependence of the reactivity on nature of chemical bond and type of functional group.

To apply the knowledge of mechanisms.

To explain the possibility of application for synthesis.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 94-110.

5. ***The main questions of the seminar:***

5.1. The classification of chemical reactions by mechanism.

5.2. The types of chemical bond breakage, free radicals, nucleophilic and electrophilic particulares (definition, examples).

5.3. The mechanism of substitution radical reaction (S_R) beside the carbon atom in alkanes, the mechanism of halogenation reaction, biological meaning of free radicals.

5.4. The mechanism of addition electrophilic reaction in alkenes (A_E); mechanism of halogenation reaction, biological meaning.

5.5. The mechanism of substitution electrophilic reaction in benzene (S_E); mechanism of halogenation reaction, biological meaning. I and II order substituents. The influence of functional group on reactivity of arenes.

5.6. The formulas of ethane, propane, butane, hexane, benzene, methylbenzene, benzoic acid and their isomers.

6. ***The questions for individual learning:***

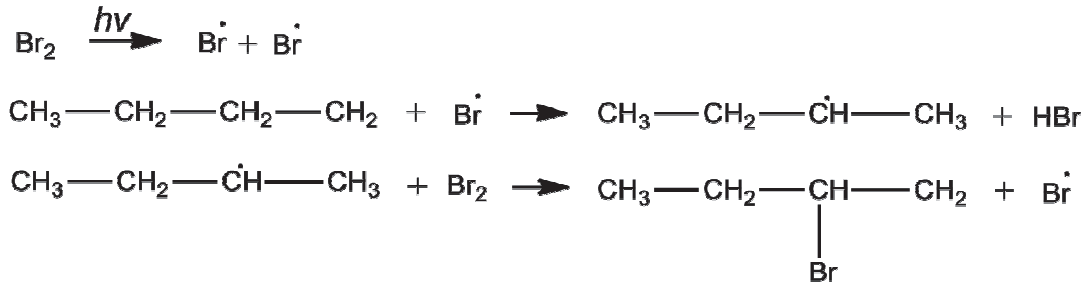
6.1. The substitution, addition and elimination chemical reactions in organic chemistry.

Classification of chemical reaction by mechanism: the hydrogenation, halogenations, hydration, nitration, sulphonation, alkylation, acylation, and dehydrohalogenation chemical reactions in organic chemistry.

7. ***Examples of task:***

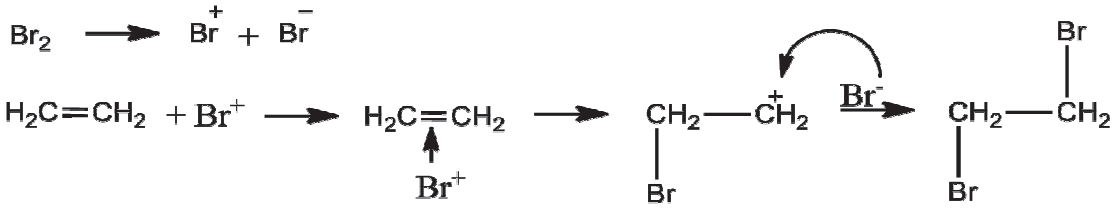
7.1. Describe graphically the reaction mechanism of bromination of butane.

Answer:



Describe graphically the reaction mechanism of ethane bromination.

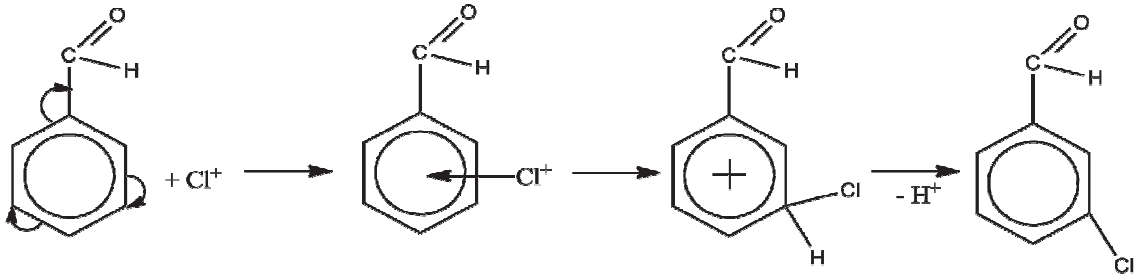
Answer:



π-Complex *σ-complex*

Describe graphically the reaction mechanism of benzaldehyde chlorination.

Answer:



π-Complex *σ-complex*

8. *Homework (must be performed in the laboratory notebook):*

8.1. What are free radicals and electron-seeking reagent (electrophilic) the electrophilic particles. Analyse the reactivity.

8.2. Write the mechanism of butane bromination.

8.3. Write the mechanism of benzoic acid bromination.

9. *Example of control test:*

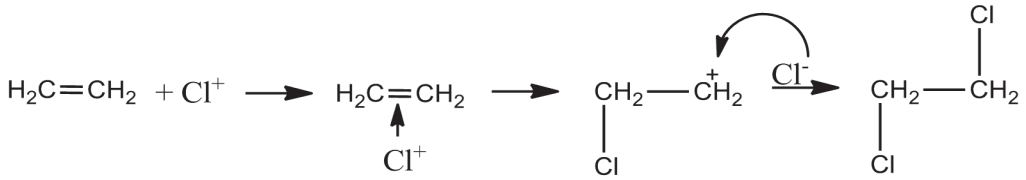
9.1. Why does substitution in alkanes take place by radical mechanism?

Answers:

All carbon atoms in alkanes are in sp^3 state, the type of chemical bond is covalent nonpolar and electrone density does not shift, the formation of active centers (the part of alkane with electron deficiency or with the excess of electrones) is impossible. That is why radical mechanism predominates.

9.2. Write the mechanism of ethene bromination.

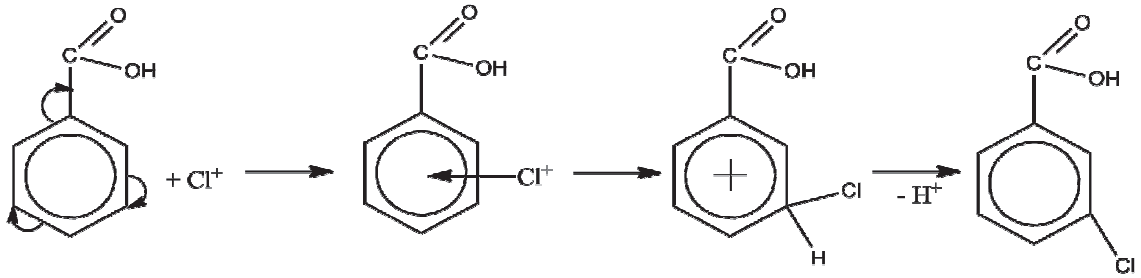
Answers:



π-Complex *σ-Complex*

9.3. Write the mechanism of benzoic acid chlorination.

Answers:



10. ***Tests:***

10.1. What kind of alkane hybridisation is present in a carbon atom:

a) Sp^2;
b) Sp;
c) Sp^3.

In alkene hybridisation of atom of carbon:

a) Sp^3;
b) Sp;
c) Sp^2.

In alkynes hybridisation of carbon atom:

a) Sp^3;
b) Sp;
c) Sp^2.

In alkene reactions mechanism go after:

a) Nucleophilic joining;
b) Electrophilic joining;
c) Radical substitution.

The example of hydrogenation of alkene in a human organism is transformation:

a) Propeonic acid → propanoic acid;
b) Ethane → ethane;
c) Crotonic acid → oil acid.

A reaction of hydrogenation of alkene is joining:

a) To hydrogen;
b) Water;
c) To hydroxyl.

Reaction of hydrogenation of alkene in vitro takes place in the presence of catalysts:

a) Fe, Fe_2O_3, Al;
b) Pt, Ni, Pd;
c) Si, Ni, Cr.

Reaction of hydrogenation of alkene in vitro takes place in the presence of catalyst:

a) Hydroxyl – to the anion;

b) Water;
c) To the proton.

The example of hydrogenation of alkene in the human organism is transformation:

a) Crotonic acid → it is hopantenic acid
b) Propenoic acid → it is oxypropanic acid;
c) Enoic acid → ethanoic acid.

Bromination of alkenes is used as a high-quality reactionon:

a) Of high quality;
b) Unsaturation;
c) Homogeneity.

Hydroxide halogenations and hydration of alkenes takes place by the rule:

a) Markovnikov;
b) Shrouds–Goffa;
c) Edman.

In halogen alkane reactions go after a mechanism:

a) Electrophilic joining;
b) Electrophilic substitution;
c) Nucleophilic substitution.

As a result of elimination of oxycompounds there is such transformation in the organism of man:

a) Butanoic acid → butane acid;
b) Malic acid → fumaric acid;
c) Citric acid → isocitric acid.

11. *The Control Test:*

Sample 1

Types of bond breaking. Show it schematically.
Write the mechanism of iodination of 1-butene.
Write the mechanism of chlorination of aniline C_6H_5-NH_2.

Sample 2

1. Why does electrophile interact with alkenes but not nucleophile?
2. Write the mechanism of chlorination of benzaldehyde C_6H_5-COH.
3. Write the mechanism of bromination of butane.

Sample 3

1. Why do we observe the substitution reaction in alkanes but not the saturation one?
2. Write the mechanism of iodination of propene.
3. Write the mechanism of bromination of phenol.

Sample 4

1. What is the reagent (nucleophile Cl^- or Cl radical) do you use for chlorination of 2-methyl butane?
2. Write the mechanism of chlorination of phenol.
3. Write the mechanism of chlorination of propene.

12. *The algorithm of lab work:*

12.1. Alkane halogenation.

Detailed description:

Into two test-tubes put 1 ml of hexane and 1 ml of bromine water. Wrap the first test tube into a black paper. Both tubes should be exposed to UV-rays for 2 min. Notify the outer effect. Make the conclusion. Describe graphically the reaction mechanism.

12.2. The synthesis of ethylene.

Detailed description:

Put 1 ml of ethanol and sulphuric acid mixture (C_2H_5OH & H_2SO_4 concentrated) and aluminium oxide into the dry test-tube with gas-collecting tube and heat carefully. Put the end of the gas-collecting tube into the test-tube with 5 ml of bromine water. Notify the outer effect. Make the conclusion. Describe graphically the reaction mechanism. Explain the practical importance of these reactions.

12.3. The tribromoaniline synthesis.

Detailed description:

Put 1 drop of aniline into the dry test-tube, then 1 ml of water. Shake the test-tube with mixture and add 2-3 drops of bromine water. Notify the outer effect. Make the conclusion. Describe graphically the titration reaction mechanism. Why the product is 2,4,6- tribromoaniline? Explain the biological importance of bromination reaction.

12.4. Benzene nitration.

Detailed description:

Put 10 drops of benzene into the dry test-tube and then add 10 ml of nitrating acid (mixture of nitric and sulphuric acid). After mixing, put 5 ml of water. Mark the results (smell). Make the conclusion. Describe graphically the titration reaction mechanism. Explain the practical importance of these reactions.

TOPIC 5

REACTIVITY OF ALCOHOLS, PHENOLS, AMINES AND HALOGENATED ORGANIC COMPOUNDS

1. Actuality of the topic:

The study of reactivity of alcohols, phenols, amines and halogenated organic compounds gives the possibility to forecast the transformation in human organism.

2. ***General aim:***

Use electronic mechanism to explain the reactivity of biological active compounds.

3. ***Actual aims and abilities:***

3.1. To explain the dependence of the reactivity on nature of chemical bond and mutual influence of atoms in molecule.

To explain the acidic properties of alcohols, phenols and basic properties of amines. The medical application of reactivity of alcohols, phenols, amines and halogenated organic compounds as pharmaceuticals.

To explain the possibility of uses in pharmaceutical synthesis.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 112-131.

5. ***The main questions of the seminar:***

5.1. Acidity and basicity according to Lowry-Bronsted.

5.2. The dependence of the acidity of alcohols, phenols on carbon chain length and on type of substitute.

5.3. The dependence of the basicity of amines and phenols on carbon chain length and on type of substheute.

5.4. The mechanism of nucleophylic substitution (S_N) beside the nonsaturated carbon atom in halogenated organic compounds. Interaction with a base, ammonia, amines (formation of primary, secondary, tertiary amines and quaternary bases).

5.5. The mechanism of nucleophylic substitution (S_N) in alcohols. The mechanism of elemination reaction of alcohols.

5.6. The formulas to know: propanol, isopropanol, butanol, isobutanol, phenol and its derivative; primary, secondary, tertiary and quaternary bases, colamine, aniline.

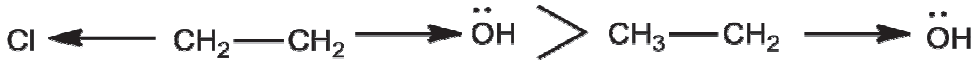
6. ***The questions for individual learning:***

6.1. Write the chemical equation: Novocaine and hydrochloric acid.

7. ***Examples of task:***

7.1. Describe graphically the electronic effects (M and I) and explain which alcohol is more acidic – ethanol or chloroethanol.

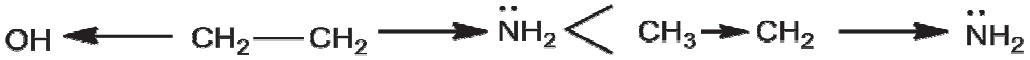
Answer:



Chlorine atom as more electronegative (I^-) shifts the electrone density from alkyl grup (I^+) therefore on oxygen atom the deficiency of electrons arises. In addition to that Oxygen atom as more electronegative (I^-) shifts the electrone density from hydrogen and the atomic mobility increases. Thus the chloroethanol is stronger acid than ethanol.

Describe graphically the electronic effects (M and I) and explain which amine (colamine or ethylamine) is stronger base. Write the chemical equation of interaction ethylamine with hydrochloric acid.

Answer:



In colamine molecular: Oxygen as more electronegative than carbone atom shifts the electrone density from alkyl group therefore the accessibility of electrons on nitrogen atom decreases. Thus the ethylamine is stronger base than colamine.

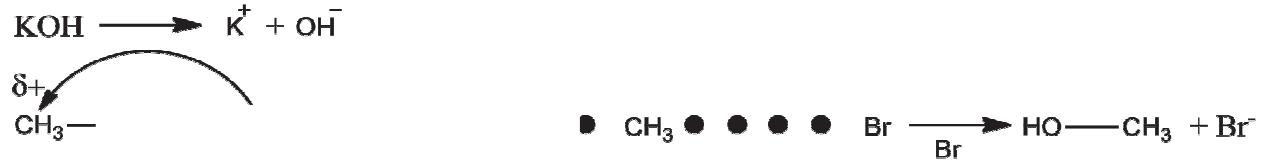
Why do the nucleophile particles attack the halogenated organic compound?

Answer:

In halogenated hydrocarbon (for example in chloroethane $CH_3–CH_2→Cl$) as a result of negative inductive effect on chloride atom, the partial charge appears: on CI is δ- and on C is δ+. Thus only negatively charged nucleophile attach (attack) to positively charged carbon atom that is bonded with negative centre (chloride atom).

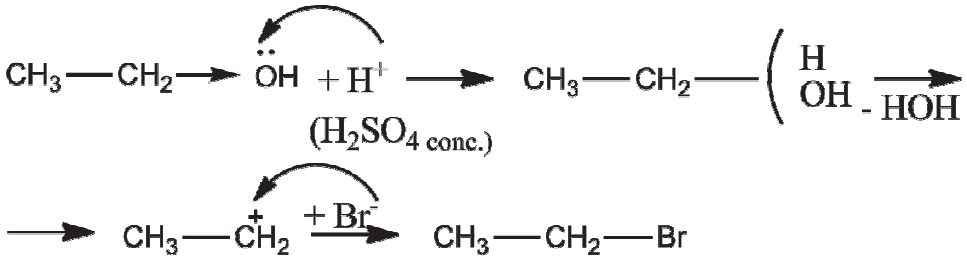
Describe graphically the reaction mechanism of interaction between bromoethane and potassium hydroxide (alkaline hydrolysis).

Answer:



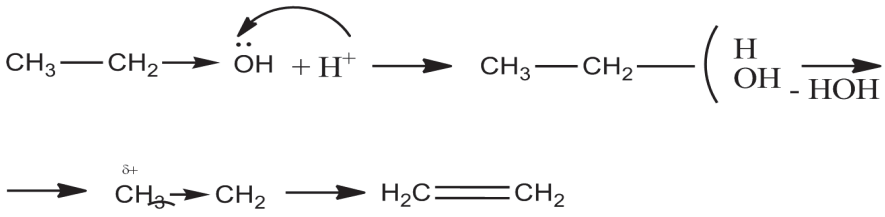
Describe graphically the reaction mechanism of interaction between ethanol and hydrobromide.

Answer:



Describe graphically the reaction mechanism of ethanol elimination (ethanol dehydrogenation).

Answer:



8. ***Homework (must be performed in the laboratory notebook):***

8.1. Describe graphically the reaction mechanism of interaction between isobutanol and hydrogen chloride.

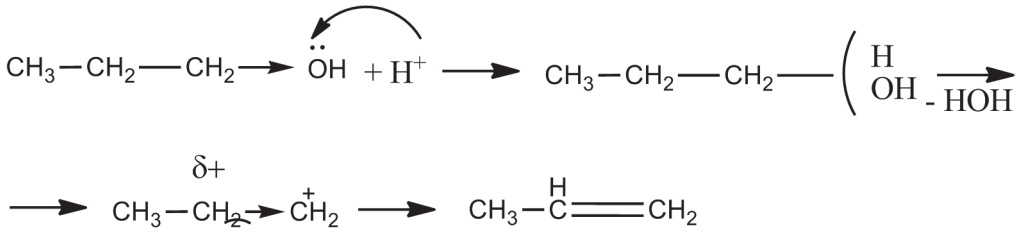
8.2. Describe graphically the reaction mechanism of lactic acid elimination.

8.3. Write the novocaine and hydrochloric acid interaction.

9. ***Example of control test:***

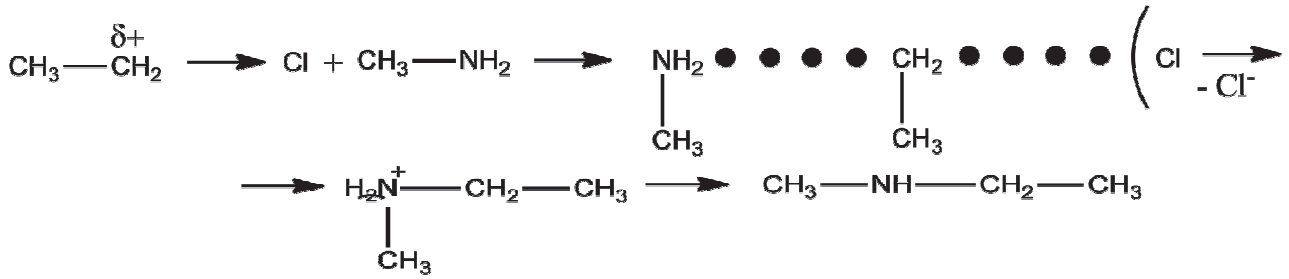
9.1. Describe graphically the reaction mechanism of propanol elimination.

Answers:



9.2. Describe graphically the reaction mechanism of interaction between chloroethane and methylamine.

Answers:



9.3. Why does the nucleophilic substitution need an acidic catalyst?

Answers:

The hydroxyl group (OH) is strong nucleophile and covalently bonded with the alkyl radical that is why the elimination segregation of OH group without catalyst is imposible. The proton attaches to the OH group and water molecule forms.

9.4. Compare the acidity of ethanol and bromoethanol.

Answers:

The bromine atom in 2-bromoethanol molecule Br←CH_2–CH_2→OH which is more electronegative than carbon atom; shifts the electron density from alkyl radical. Therefore on oxygen atom the excess of electron density decreases the polarity of O-H bond decreases too. The presence of electron acceptor (electron-seeking group) decreases acidity of oxy-compound.

10. ***Tests:***

10.1. Salts of phenols are named:

a) Thiols;
b) Phenols;
c) Alcoholates.

Phenol – is:

a) Carbonate acid;
b) Hydrocarboxylic acid;
c) Carbolic acid.

Due to the acid properties a phenol is used as:

a) Antiseptic;
b) Antipyretic;
c) Acesodyne.

Arenes' reactions follow a mechanism:
a) Electrophilic joining;
b) Electrophilic substitution;
c) Radical substitution.

Electron Donor sub-groups in arenes send the second subgroup in:
a) Purpose- or –ortho is position;
b) Para- or –meta is position;
c) Ortho- or –para is position.

Electron-seeking sub-groups in arenes send the second subgroup:
a) Purpose of position;
b) Para- or a purpose is position;
c) Ortho- or a pair is position.

As a result halogenations of arenes such medications appear:
a) Salicylic acid, solution of lughole;
b) Biomicine, elenium, bromitxine;
c) Vitamins A, C.

In the organism of man as a result of iodination of benzoic kernel appears:
a) Oxytocinum;
b) Tiroxine;
c) Tyrosine.

As a result alkylation of benzoic kernel appears such medications:
a) Vitamins of E, K;
b) Acetopitne;
c) Vitamin A.

As a result of nitridation benzoic kernels appear such medications:
a) Novocain;
b) Levomicetin;
c) Vitamin of A.

In alcohols reactions follow a mechanism:
a) Nucleophilic substitution;
b) Electrophilic substitution;
c) Nucleophilic joining.

Elimination is a reaction:
a) Slabbing;
b) Joining;
c) Substitution.

11. *The Control Test:*

Sample 1

1. Compare and explain the acidity of ethanol and propanol.
2. Compare and explain the basicity of methylamine and aniline.
3. Write the mechanism of the interaction between ethyl chloride and ammonia.

Sample 2

1. Compare and explain the acidity of phenol and p-dihydroxy benzene.

2. Compare and explain the basicity of methylamine and ammonia.
3. Write the mechanism of the interaction between propanol and hydrogen chloride.

Sample 3

1. Compare and explain the acidity of propanol and methanol.
2. Compare and explain the basicity of aniline and p-methylaniline.
3. Write the mechanism of the interaction between methyl chloride and ethylamine.

Sample 4

1. Compare and explain the acidity of p-methylphenol and phenol.
2. Compare and explain the basicity of primary and secondary amines.
3. Write the mechanism of elimination of tri hydroxybutanoic acid.

12. ***The algorithm of labwork:***

12.1. The formation of chloroethane.

Detailed description:

Put the 5 mm layer of sodium chloride into test-tube and add 5 drops of ethanol solution, then put 4 drops of concentrated sulphuric acid. Mix the solution in test-tube and heat. Mark the effect. Write the chemical reaction. Make the conclusion.

12.2. The quanitative test on the glycerin.

Detailed description:

Put 2 drops of $CuSO_4$ into test-tube and add 2 drops of NaOH. Mark the effect. Then add 1 drop of glycerin and mix the solution. Write the chemical reaction. Make the conclusion.

12.3. The formation of sodium phenolate.

Detailed description:

Put 3 drops of water into the test-tube and a few crystals of phenol. Estimate the solubility of phenol. Than add drop by drop the sodium hydroxide solution. Mark the effect, after that add the hydrochlocic acid drop by drop. Mark the effect. Write the chemical reactions. Make the conclusion.

12.4. The quanitative test on the phenol.

Detailed description:

Put a few crystals of phenol into the test-tube and 1 drop of iron (III) chloride solution. Mark the effect. Write the chemical reactions. Make the conclusion.

12.5. The quanitative test on the novocaine hydrochloride.

Detailed description:

Put 5 drops of novocaine hydrochloride into the test-tube and 1-2 drops of silver nitrate solution. Write the chemical reaction. Make the conclusion. Explain the biological meaning of basic properties of amines.

TOPIC 6

NUCLEOPHILIC ADDITION IN OXYGEN-CONTAINING COMPOUNDS

1. *Actuality of the topic:*

Studying of the mechanisms of nucleophilic addition in oxo-compounds gives the possibility to forecast the chemical transformations of aldehydes and ketones in human organs.

2. *General aim:*

Use electronic mechanism to explain the reactivity of biological active compounds.

3. *Actual aims and abilities:*

3.1. To explain the dependence of the reactivity on nature of chemical bond and mutual influence of atoms in molecule.

3.2. To explain the possibility of uses in pharmaceutical synthesis.

4. *Literature:*

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 135.

5. *The main questions of the seminar:*

5.1. Electronic structure of the oxo-group. The mechanism of nucleophyllic addition reaction (A_N) to the trigonal carbon atom.

5.2. Interaction with alcohols: mechanism of formation of half-acetalles and acetalles. Their biological meaning.

5.3. Interaction with amines: mechanism of addition-detachment. Biological meaning of imines.

5.4. Aldolic condensation: mechanism of alkaline catalysis; biological meaning (synthesis of the citrate in organism (citrate acid) and neuraminic acid).

5.5. Oxidation and reduction of aldehydes and ketones. The examples of these reactions in human organism.

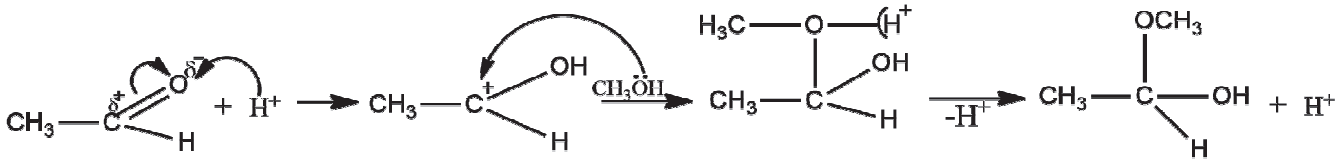
6. *The questions for individual learning:*

6.1. Why do the carbonyl double bond and the carbon-carbon double bond react with different reagents? Give the reasons.

7. *Examples of task:*

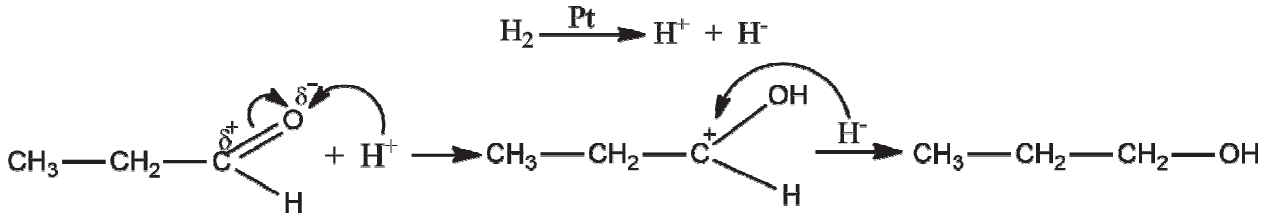
7.1. Describe graphically mechanism of half-acetalle formation in interaction of acetate-aldehyde and methanol.

Answer:



Describe mechanism of reduction of propanalle.

Answer:



8. ***Homework (must be performed in the laboratory notebook):***

8.1. Describe graphically the mechanism of half-acetal and acetal formation in interaction of propanal and ethanol.

8.2. Describe graphically the mechanism of interaction of pyridoxal-phosphate and methyl-amine.

8.3. Describe graphically the mechanism of synthesis of the neuraminic acid.

9. ***Tests:***

9.1. Aldehydes belong to:

a) Oxo-bonds;
b) Oxy– bonds;
c) Carboxyl– bonds.

9.2. Carbon in an aldehydic group is in the state:

a) To sp–hybridisation;
b) To sp^2–hybridisation;
c) To sp^3–hybridisation.

9.3. In an aldehydic group there is displacement of electronic proximity to:

a) Carbon;
b) Hydrogen;
c) Oxygen.

9.4. In the aldehydic group of displacement of electronic proximity to oxygen place is taken for:

a) π–copula;
b) σ–copula;
c) To ionic bond.

9.5. Carbon in an aldehydic group has surplus:

a) Negative charge;
b) Positive charge;
c) Zero charge.

9.6. Reactions in aldehydes follow a mechanism:

a) Nucleophilic substitution;
b) Electrophilic joining;
c) Nucleophilic joining.

9.7. Carbon in an aldehydic group is attacked only:

a) By a nucleophile;
b) By a nelectropile;
c) Radical.

9.8. Reaction of aldehydes with hydrogen follows a mechanism:

a) Nucleophilic substitution;
b) Nucleophilic joining;

c) Electrophilic joining.

9.9. As a result of joining of hydrogen aldehydes:

a) Oxidation;
b) Fall out in sediment;
c) Recommence.

9.10. Aldehydes recommence to:

a) Primary alcohols;
b) Second alcohols;
c) Tertiary alcohols.

9.11. An example of renewal of aldehydes hydrogen in the organism of man is:

a) Proceeding from acetate to ethanol;
b) Proceeding from glyceralaldehyde to glycerin;
c) Proceeding to succinate.

9.12. An example of renewal hydrogen of ketones in the organism of man is::

a) Glycerol aldehydes→glycerin;
b) Tartrate→acetate;
c) Pyruvate→lactate.

9.13. Proceeding in organic compounds in the organism of man takes place for itlp:

a) Coferment of NAD H_2, ubichinon;
b) Albumens;
c) Monosaccharaides

9.14. Reaction of aldehydes with alcohols follow a mechanism:

a) Nucleophilic substitution;
b) Nucleophilic joining;
c) Electrophilic joining.

9.15. A catalyst during reaction of aldehydes with alcohols is:

a) Meadow;
b) Proton;
c) Acid of L'yuis.

9.16. The product of reaction of aldehydes with alcohols is:

a) Acetals;
b) Acetates;
c) Semiacetals.

9.17. Semiacetals in the organism of man – is:

a) Monosaccharaides;
b) Aminoacid;
c) Fats.

9.18. Reaction of aldehydes with amines follows a mechanism:

a) Nucleophilic joining;
b) Nucleophilic substitution;
c) Electrophilic joining.

9.19. The product of reaction of aldehydes with amines is:

a) Amides;
b) Nitrates;
c) Imines.

9.20. In the human organism imine appears in a process of:

a) Transubstitution;

b) Desubstitution;
c) Amination.

9.21. The reaction of aldol condensation takes place between:
a) Alcohols;
b) Aldehydes;
c) Acids.

9.22. As a result of the use of alkaline catalysis in the reaction of aldol condensation intermediate particles appear:
a) Radical;
b) A carb cation;
c) A carb an anion.

9.23. After the reaction of aldol condensation in the human being, is synthesized:
a) Citric acid;
b) Acetic acid;
c) Benzoic acid.

9.24. After the reaction of aldol condensation in the organism of man, is synthesized:
a) Acetic acid;
b) Neuraminic acid;
c) Salicylic acid.

9.25. High-quality reaction of aldehydes is:
a) Reaction of Edman;
b) Reaction of Fisher;
c) Reaction of Trommer.

9.26. Composition of reagent of Trommer:
a) $CuSO_4$+NaOH;
b) $CuSO_4$+Cu $(OH)_2$;
c) $CuSO_4$+H_2SO_4.

9.27. During the reaction of aldehydes with the reagent of Trommer there are aldehydes:
a) Recommence;
b) Oxidize;
c) Exchanged.

9.28. By the product of oxidation of aldehydes the reagent of Trommer is:
a) Alcohol;
b) Ketone;
c) Acid.

9.29. During the reaction of aldehydes with the reagent of Trommer appears as brick red sediment:
a) Cu_2O;
b) CuO;
c) $Cu(OH)_2$.

9.30. High-quality reaction of aldehydes is:
a) Edman's reaction;
b) Fehling's reaction;
c) Fischer's reaction.

9.31. Composition of reagent of Fehling:
a) $CuSO_4$+NaOH+NaOOC-CH (OH)–CH (OH)–COOK;

b) $CuSO_4$+NaOH+HOOC-CH (OH)–CH (OH)–COOH;
c) $CuSO_4$+NaOH+CH_3COOH.

9.32. During the reaction of aldehydes with the reagent of Fehling there are aldehydes:
a) Recommence;
b) Oxidation;
c) Exchange.

9.33. By the product of oxidation of aldehydes the reagent of Fehling is:
a) Acid is an alcohol;
b) Ketone;
c) Alcohol.

9.34. During the reaction of aldehydes with the reagent of Fehling's appears brick. It is red sediment:
a) CuO;
b) Cu_2O;
c) $Cu(OH)_2$.

9.35. High-quality reaction of aldehydes is:
a) Edman's reaction;
b) Fischer's reaction;
c) Tollen's reaction;

9.36. Composition of Tollen's reagent:
a) Ag_2O+NH_4OH;
b) Ag_2O+NaOH;
c) $AgNO_3$+NaOH.

9.37. During the reaction of aldehydes with the Tollen's reagent there are aldehydes:
a) Recommence;
b) Oxidation;
c) Exchange.

9.38. By the product of oxidation of aldehydes in Tollen's reagent:
a) Acid;
b) Ketone;
c) Alcohol.

9.39. During the reaction of aldehydes sediment, with the Tollen's reagent appears:
a) Ammonium of hydroxide;
b) Free silver;
c) Acids.

9.40. The high-quality reaction of Tollen's on aldehydes is called as reaction of:
a) Copper mirror;
b) Silver mirror;
c) Ferrous mirror.

9.41. In a clinical analysis, for the exposure of monosaccarides in biological liquids use:
a) Butlerov's test;
b) Fischer's exact test;
c) Trommer Trommer's test test.

9.42. An example of oxidation of aldehydes in the human being is:
a) Oxidize a amber aldehyde to succinic acid;

b) Oxidize acetal aldehyde to the alcohol;
c) Oxidize an acetone to the acetate.

9.43. An example of oxidation of ketone in human being is:
a) Oxidizeβ-propyl formic acid to two molecules of aldehyde;
b) Oxidizeβ-propyl formic acid to two molecules of acetate;
c) Oxidizeβ-propyl formic acid to two molecules of formiate.

9.44. As a result of galoforms reactions, it is possible to get:
a) Trifluoromethyl, benzoform;
b) Phenol, tetraform;
c) Iodoformium, chloroform.

10. *The Control Test:*

Sample 1

1. Write the reaction mechanism of acetaldehyde reduction.
2. Write the aldol condensation mechanism of acetaldehyde and benzaldehyde.

Sample 2

1. Write the mechanism of the Schiff"s bases formation.
2. Write the reaction mechanism between diethyl ketone and hydrogen.

Sample 3

1. Write the mechanism of the hemiacetal formation after interaction of acetaldehydes and methanol.
2. Write the aldol condensation mechanism of propanal.

Sample 4

1. Write the reaction mechanism between acetaldehyde and propanol.
2. Write the reaction mechanism between pental and hydrogen cyanide (HCN).

11. *The algorithm of labwork:*

11.1. Oxidation of formaldehyde with copper (II) hydroxide.

Detailed description:

Put 5 drops of the sodium hydroxide and water into the test-tube, add 1 drop of the copper (II) sulphate. Note the results. Add 3 drops of formalin solution. Warm the test-tube carefully until boiling. Write the reaction equations, note the effect, and explain the result. What is the meaning of the reaction for clinical analysis?

11.2. Determination of the acetone with iodoformic test.

Detailed description:

Put 1 drop of the solution of iodine in KI into the test-tube and add the sodium hydroxide drop gently until the color disappears. Add 1 drop of acetone. Write the equation of reactions, note the effect and explain the results and biological meaning.

TOPIC 7

NUCLEOPHILIC SUBSTITUTION AND BIOLOGICAL SIGNIFICANCE OF CARBOXYLIC ACIDS AND THEIR DERIVATIVES

1. Actuality of the topic:

Understanding nucleophilic substitution mechanism in carboxylic acids gives us the possibility to predict the chemical conversion of carboxylic acids and their derivatives in human organism.

2. ***General aim:***

The general aim is to interpret the mechanism of nucleophilic substitution in carboxylic acids and their derivatives and predict the consequence of these processes.

3. ***Actual aims and abilities:***

3.1. To know the mechanisms of conversion and specialities of the carboxylic acids and their functional derivatives.

To explain the mechanism of the nucleophilic substitution in carboxylic acids.

To predict the processes connected with conversion of carboxylic acids and their biologically active derivatives.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 149-159.

5. ***The main questions of the seminar:***

5.1. The electronic structure of the carboxyl group and carboxylate anion.

5.2. Acidity of the carboxylic acids. The influence of the different susbtitutes on acidity of carboxylic acids.

5.3. Salts of carboxylic acids, the mechanism of their formation. The formation of salts of carboxylic acids in human organism.

5.4. Mechanism of nucleophilic substitution (S_N) beside the trigonal carbon atom:

- Mechanism of the ester and thioethers formation;
- Mechanism of acidic and alkaline hydrolysis of esters.

5.5. Formation and hydrolysis of esters and thioethers in human organism. Synthesis of biological active substances with acetyl-CoA in human organism.

6. ***The questions for individual learning:***

6.1. Decarboxylation of pyruvic and β-ketobuturic acids.

6.2. Mechanism of acyl chloride formation.

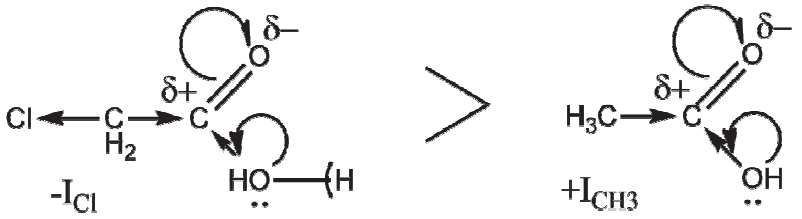
6.3. Mechanism of anhydride formation.

6.4. Mechanism of amide formation. Biological meaning of amides.

7. ***Examples of task:***

7.1. Which acid is stronger and why: acetic acid or monochloroacetic acid.

Answer:

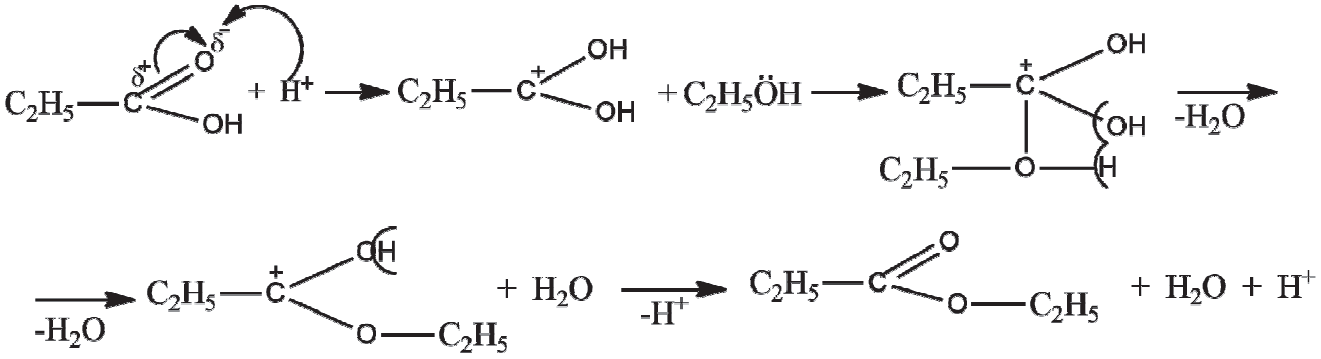


As Cl atom is more electronegative than carbon one in the monochloroacetic acid, the electron density is shifted to Cl atom and the proton in carboxyl group becomes easier to be chipped off.

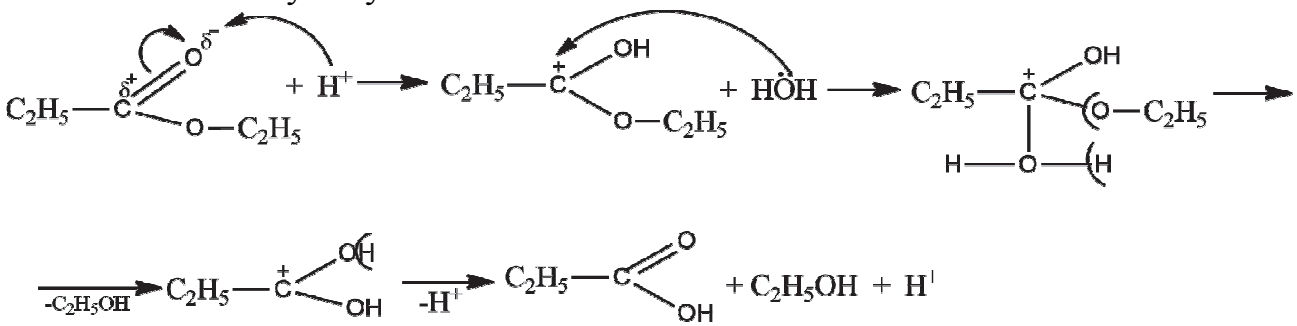
Describe graphically mechanism of formation and hydrolysis of ethyl propionate using acidic catalysis.

Answer:

Esterification mechanism:

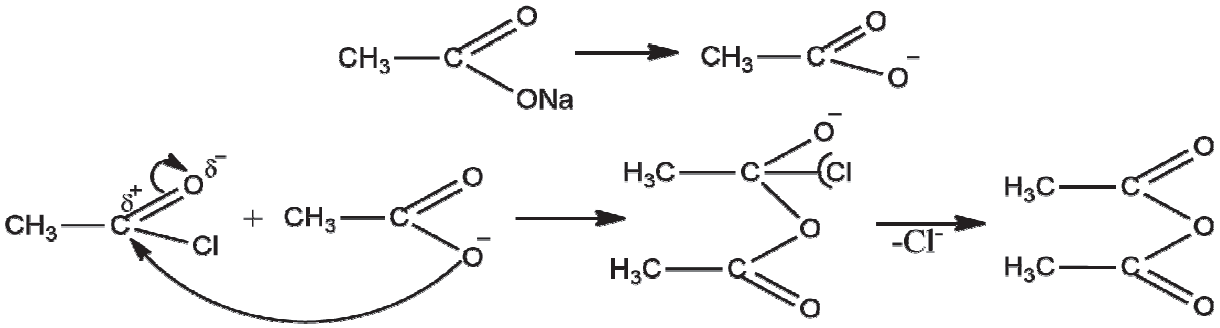


Mechanism of hydrolysis:



Describe the reaction mechanism of anhydride formation of acetic acid.

Answer:



8. ***Homework (must be performed in the laboratory notebook):***

8.1. Write the acids in order of increasing acidity: oxalate (oxalic acid), acetate (acetic acid), monochloroacetate (monochloroacetic acid).

8.2. Describe the reaction mechanism of synthesis and hydrolysis (acidic and alkaline) of methyl acetate.

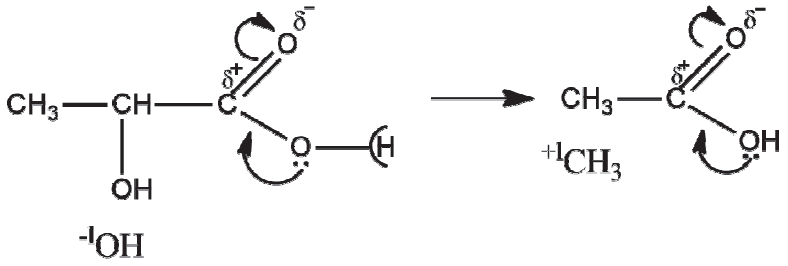
8.3. Write the scheme of synthesis of acetate derivatives: sodium salt, anhydride, chloroanhydride and amide.

8.4. Memorize the structural formulas of formic acid, acetic acid, propionic acid, butyric acid, chloroacetic acid, oxalic acid.

9. ***Exampleofcontroltest:***

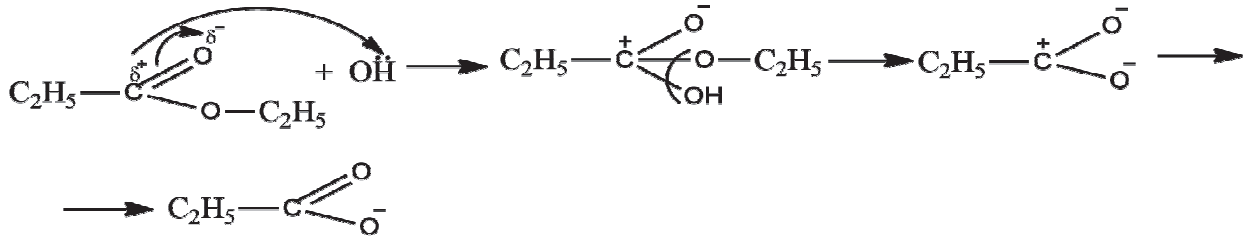
9.1. Which acid is stronger, 2-oxopropanoic or lactic acid? Explain why.

Answers:



9.2. Describe graphically the reaction mechanism of hydrolysis ethyl propionate with alkaline catalyst.

Answers:



10. ***The Control Test:***

Sample 1

1. Choose the acid possessing the higher acidity and explain it: $CH_3–CH_2–COOH$ or $CH_2=CH–COOH$.
2. Write the mechanism of ether formation after interaction of chloroanhydride of acetic acid and methanol.

Sample 2

1. Choose the acid possessing the higher acidity and explain it: $CH_3–COOH$ or HCOOH.
2. Write the mechanism of acidic catalysis between acetic acid and ethanol. Is it possible to use the alkaline catalyst for this reaction?

Sample 3

1. Choose the acid possessing the higher acidity and explain it: $CH_3–COOH$ or $Cl–CH_2–COOH$.
2. Write the mechanism of ethyl propionate formation in the presence of acidic catalyst.

Sample 4

1. What is the acylation reaction? Write the acylating agents.

2. Write the mechanism of alkaline hydrolysis of methyl acetate. What is the medium of fat hydrolysis in human organism?

11. ***The algorithm of labwork:***

11.1. Correlation of the acid strength.

Detailed description:

Put a drop of every acid (hydrochloric acid, formic acid, acetic acid, oxalic acid) and pure water into a piece of indicator paper. Determine pH and make the conclusions.

11.2. Identification of oxalic acid in the form of calcium salt.

Detailed description:

Put 2 drops of sodium oxalate in the test-tube, add 1 drop of calcuim chloride solution. Divide the precipitation into two test-tubes. Into the first test-tube put 1-2 drops of acetic acid and 1-2 drops of chloroacetic acid in the second one. Explain the results, write the reaction equations.

11.3. Decomposition of oxalic acid under itating.

Detailed description:

Put the layer (10-15 mm) of oxalic acid in dry test-tube, close it with cork and gas collecting tube. Heat the mixture passing the formed gas through barium hydroxyde. Write the equations and make the conclusions.

11.4. Synthesis of ethyl acetate.

Detailed description:

Put 0.5 ml of ethanol, 0.5ml of acetic acid, 2-3 drops of 96 % sulfuric acid in dry test-tube and heat carefully. Describe the results of the experiment and write the mechanism of the esterification reaction.

TOPIC 8

FATTY ACIDS. LIPIDS. PHOSPHOGLYCERIDES.

1. Actuality of the topic:

Knowledge of the structure and chemical properties of lipids and their derivatives is necessary to understand the processes of lipids' metabolism in a human organism and the structure of biological membranes.

2. ***General aim:***

Is to interpret the regularity of lipid metabolism in order to predict biochemical reactions, which are accompanied and stimulated by lipids.

3. ***Actual aims and abilities:***

3.1. To know the structure and chemical properties of lipids and their structural components.

To be able to use knowledge for understanding of the biological membrane structure and the regularity of the lipid metabolism as the basis of the metabolic changes in human organism.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundamentals of bioorganic chemistry, Moscow, 2004, pp. 238-249.

5. ***The main questions of the seminar:***

5.1. Lipids, saponification lipids (definition).

5.2. Higher fatty acids: saturated and unsaturated, spatial structure of unsaturated acids, chemical characteristics.

5.3. Fats as triacylglycerol's, their composition, structure, classification, chemical properties (hydrolysis, iodine number, peroxide oxidation).

5.4. Phosphoglycerols: composition, structure of phosphatidylcholine, phosphatidylcolamine, phosphatidylserine and their biological meaning.

6. ***The questions for individual learning:***

6.1. Non-Saponification lipids (definition).

Structure of cholesterine, bile acids.

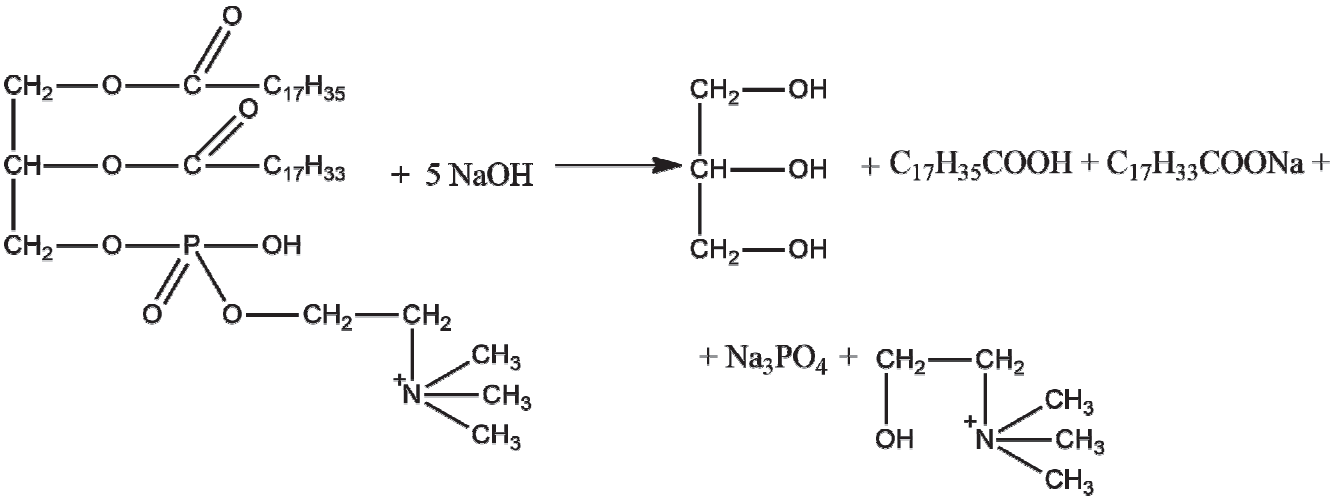
7. ***Examples of task:***

7.1. Write the configuration of oleic acid.

Answer:

Write the scheme of alkaline hydrolysis of 1–stearoyl–2–oleinoyl–3–phosphatidylcholine.

Answer:



8. ***Homework (must be performed in the laboratory notebook):***

8.1. Write the reaction equation of alkaline hydrolysis of dioleoylstearine.

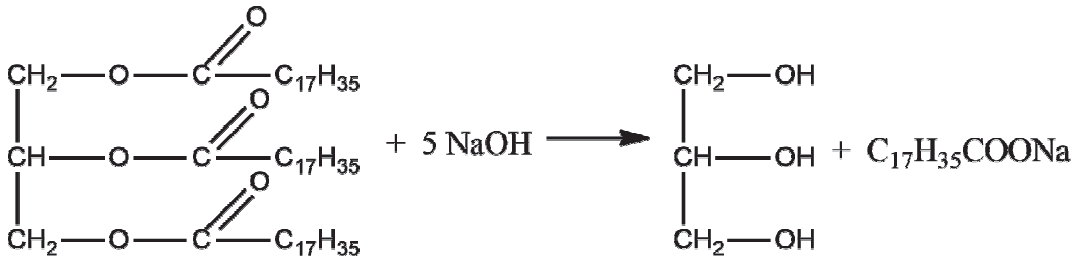
8.2. Write the structure of phosphatidylcholine.

8.3. Write the spatial structure of unsaturated fatty acids: oleic and linoleic.

9. ***Example of control test:***

9.1. Write structure and scheme of alkaline hydrolysis of tristearin.

Answer:



10. ***Tests:***

10.1. Fats–esterys:

a) Tree atom alcohol of glycerol and higher fatty acids;
b) Diatomic alcohol a glycol and higher fatty acids;
c) Tree atom alcohol of glycerol and low of fat acids.

Tailings enter in the complement of fats:

a) Diatomic alcohol a glycol and higher fatty acids;
b) Tree atom alcohol glycerol and higher fatty acids;
c) Tree atom alcohol of glycerol and low of fat acids.

A type of bond in fats:

a) Peptide;
b) Glycoside;
c) Hard fires.

The most widespread are saturated higher fatty acids in composition of fats:

a) Palmitic, stearic;
b) Olein; elaidinoic;
c) Linolic, palmitic.

The most widespread are unsaturated higher fatty acids in composition of fats:

a) Palmitic, stearin;
b) Olein, linolic, linolenic;

c) Linolic, palmitic.

A high-quality reaction is on the unsaturated higher fatty acids in composition of fats:

a) Discolor of copper (II) hydroxide;
b) Discolor of iron (III) chloride;
c) Discolor of bromic water.

Higher fatty acids are unsaturated in composition of fats differ:

a) By the structure of carbon structure;
b) By the number of double bonds;
c) By the type of isometry.

Higher fatty acids are unsaturated in composition of fats have:

a) Trans – configuration;
b) L – configuration;
c) Cis – configuration.

Hard fats are contained by tailings:

a) Unsaturated higher fatty acids;
b) Saturated higher fatty acids;
c) Saturated low fatty acids.

Liquid fats are contained by tailings:

a) Saturated higher fatty acids;
b) Unsaturated higher fatty acids;
c) Saturated low fatty acids.

Fats – it :

a) Alkyl glyceride;
b) Anhydride glyceride;
c) Acyl glyceride.

Fats are better hydrolyzed in:

a) Sour and alkaline environments;
b) Neutral environment;
c) Environment of brome water.

The products of acid hydrolysis of fats is:

a) Ethylene glycol and higher fatty acids;
b) Glycerine and higher fatty acids;
c) Glycerine and salts of higher fatty acids.

The products of alkaline hydrolysis of fats is:

a) Ethylene glycol and higher fatty acids;
b) Glycerine and higher fatty acids;
c) Glycerine and salts of higher fatty acids.

Ion number – is:

a) Amount of grammes of ion, that joins with 100g fat;
b) Amount of ion, that joins in with 100g fat;
c) An amount of grammes of potassium ion, that joins with 100g fat.

Ion number is characterized by a degree:

a) To the saturation of fat;
b) Izomerisation of fat;
c) To the unsaturation of fat.

Than anymore ion number, that:

a) Less biological value of fat;
b) Greater biological value of fat;
c) An ion number does not influence the biological value of fat.

Than greater degree of unsaturation of fat, that:
a) Less biological value of fat;
b) An ion number does not influence the biological value of fat.
c) Greater biological value of fat.

Heating of fats is a result:
a) Peroxide oxidation of fats;
b) Proceeding in fats;
c) Besieging of fats.

Hydrogenation of fats – is:
a) Converting of hard fat into liquid;
b) Converting of liquid fat into hard;
c) Converting of desi fat into butter.

Hydrogenating of fats is a reaction:
a) Hydrogenising;
b) Hydratations;
c) Dehydrogenization.

In the organism of man fats are added as hydrolysis:
a) In a stomach in a sour environment;
b) In an intestine in an alkaline environment;
c) In an oral cavity in an alkaline environment.

The products of hydrolysis of fats in the organism of man is:
a) Glycol and soap;
b) HFA and alcohol;
c) Glycerin and soap.

Medicinal preparations of fats:
a) Linetol, arachidonic;
b) Protargolum, palmitic acid;
c) Soap, stearin acid.

Phospho glicerides are derivatives:
a) Phosphate acid;
b) Phosphate acids;
c) Pyro phosphate acids.

Phosphate acid consists of tailings:
a) Saturated HFA, glycerin, phosphate acid;
b) Unsaturated HFA, glycerin, phosphate acid;
c) Unsaturated HFA, to the glycol, phosphate acid.

A type of bond between the components of phosphate:
a) Glycoside;
b) Peptide;
c) Hard fires.

Phosphate acid has:
a) L – configuration;
b) D –configuration;
c) Cis – configuration.

The remain of choline, which is connected with a remain, enters in the complement of phosphate dilcholine:

a) Phosphate acids;
b) Phosphate acid;
c) To glycerin.

Phosphate glycerides in biological membranes form

a) Lipids bashar;
b) Lipids monolayer;
c) Micelles

11. ***The Control Test:***

Sample 1

1. Write the formation reaction of 1-*O*-palmitol-2,3-di-*O*- stearol glycerol.

Write the configuration of linoleic acid.

Design the chemical method to distinguish between saturated and unsaturated fatty acids.

Sample 2

1. Write the formation reaction of fat containing one residue of linoleic acid and two molecules of palmitic acid.

Write the reaction equation of oxidation of oleic acid by potassium permanganate.

Write the name of products of hydrolysis of oil.

Sample 3

1. Write the reaction equation of interaction between iodine and trioleoylglycerol.

Write the differences between fat, oil and waxes.

What are bile acids? Design the general formula of its.

Sample 4

1. Write the formation reaction of oil.

Write the configuration of linolenic acid.

What is hydrogenation of fats? Write the scheme of the reaction.

12. ***The algorithm of labwork:***

12.1. Formation of the fatty drop and its extraction.

Detailed description:

On the filter paper put 3 separated drops of oil with sizes 1 cm. Touch the center of the first drop with the tube that contains diethyl ether, the second with benzene and the third with water. Describe the results of the experiment and make the conclusions.

12.2. Extraction of free fatty acids from soap.

Detailed description:

In the test tube put 5 drops of saturated soap solution and 1 drop of sulphuric acid. Point the effect, write reaction equation and make the conclusion.

12.3. Formation of unsolutable calciumsalts (unsolutable soap).

Detailed description:

In the test tube put 5 drops of soap solution and 1 drop of calcium chloride solution. Mix the test-tube. Point the effect, write reaction equation, and make the conclusion.

12.4. Unsaturated fatty acids reaction.

Detailed description:

Put 5 drops of oil and 4 drops of bromine water into a test-tube and mix it**.** Point the effect, write reaction equation, and make the conclusion.

TOPIC 9

THE REACTIVITY AND BIOLOGICAL SIGNIFICANCE OF HETEROFUNCTIONAL DERIVATIVES (HYDROXO-ACIDS, OXO-ACIDS, PHENOL-ACIDS).

1. Actuality of the topic:

Itterofunctional derivatives - hydroxo and oxo-acids are the products of metabolism in human organism, phenol-acids are used in medicine as medical products. Reactivity of these compounds is determined by presence of different functional groups in molecule that determines specialties of their chemical conversion in organism.

2. ***General aim:***

To use the knowledge of stereochemistry and reactivity of heterofunctional compounds and interference of the functional groups for the explanation of the specialties of metabolism of carbohydrates, fats and aminoacids and their derivatives in human organism.

3. ***Actual aims and abilities:***

3.1. Explain the dependence of reactivity and biological functions of the heterofunctional compounds on their structure and methods of medicines' synthesis on their basis.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 161-169.

5. ***The main questions of the seminar:***

5.1. Hydroxo-acids (lactic, tartratic, citric, β - oxybutyric, malic acids), properties, specifical reactions: appearance in the organism and biological meaning of these compounds.

5.2. Oxo-acids (pyruvic, aceto-acetic, oxalo-acetic acids). Keto-enol tautomerie. Chemical properties, reaction of decarboxylation.

5.3. Phenol acids and their derivatives. Use of salicylic acid and its derivatives as officinals (Sodium salicylates, methyl salicylate, salol, acetylsalicylic acid).

6. ***The questions for individual learning:***

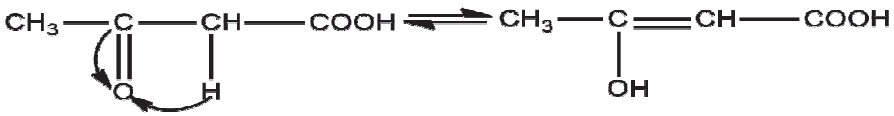
6.1. Classification and isomery of oxoacids. Chirality. Enantiomers, diastereomers. Ketone bodies, their diagnostic significance for identification of pancreatic (insular) diabetes.

7. ***Examples of task:***

7.1. What isomerism is more typical for β-ketoacids (for example, acetoacetic acid)?

Answer:

Due to mutual influence of keton and carboxyllic groups in molecule, the CH-acidic center appears, that cause keto-enol tautomery.



Enol group is more active than keton one.

8. *Homework (must be performed in the laboratory notebook):*

8.1. Write the projectional formulas of lactate enantomers.

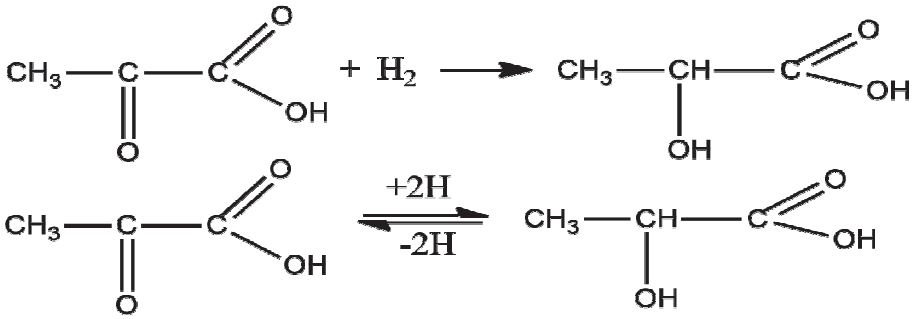
8.2. Write piruvate in keton and enol forms, reduction and interaction with ethanol reactions.

8.3. Write the equation of the specific reactions with α–, β– and γ–oxoacids.

9. *Example of control test:*

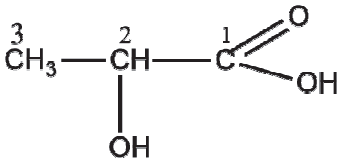
9.1. Write the scheme of lactic acid appearance and make the characteristics of its chemical properties.

Answers:



Pyruvic acid *Lactic acid*

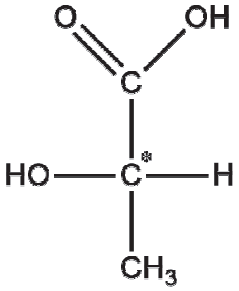
a)



$C_{1,}$–sp^2; $C_{2,3}$–sp^3; C_1–C_2-σ=>sp^2–sp^3; C_2–C_3-σ=>sp^3–sp^3;

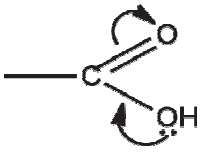
(C_1-C_2) (C_2-C_1)

b) The typical enantomery for lactic acid is:

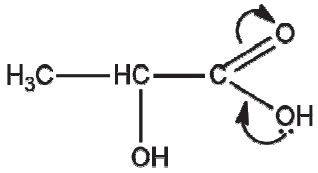


L-configuration

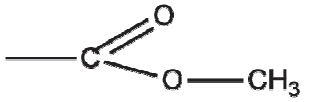
c) p,π -coupling in carboxy-group:

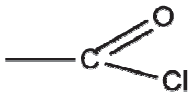


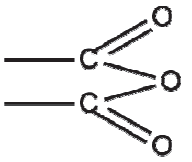
d) Electronic effects:



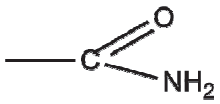
e) Oxy-group shows faint acid properties and forms salt (alcoholates R–OMe), carboxy-group is stronger and makes appropriate salts (R–COOMe – lactates).
f) Due to carboxy-group lactic acid makes derivatives – esters and halogenahydrides:







Anhydrides



Amides

g) Oxy-group can move towards halogen.
h) The reversable conversion of lactate into pyruvate takes place in human organism.

10. ***Tests:***

10.1. A functional group in hydro carboxylic acids is:

a) Hydroxy group;
b) a carboxyl group;
c) Oxo group.

Carboxyl group consists of:

a) Hydroxy- and carboxyl groups;
b) Keto- and oxo groups;
c) Oxo- and oxy groups.

Carbon in a carboxyl – is a group in the state:

a) Sp^2,
b) Sp,
c) Sp^3.

In a carboxyl – there is a displacement of electronic proximity to a group:

a) Oxygen oxi groups;
b) Oxygen with double connection;
c) Carbon.

In a carboxyl – group of displacement of electronic proximity to oxygen oxo groups place is taken for:

a) σ – copula;
b) π - copula;
c) Ionic connection.

As a result of electronic effect on the atom of carbon there is partiality in a carboxyl-group:

a) Negative charge;
b) Zero charge;
c) Positive charge.

Atom of carbon in a carboxyl – attacked a group only:

a) Nucleophile;
b) Electrophile;
c) Radical.

Reactions in hydro carboxylic acids and their derivatives follow after a mechanism of:

a) Nucleophilic joining;
b) Nucleophilic substitution;
c) Electrophilic substitution.

Reaction of acids with alcohols follows after a mechanism of:

a) Nucleophilic joining;
b) Electrophilic substitution;
c) Nucleophilic substitution.

Reaction of acids with alcohols is a reaction:

a) Esterification;
b) To the hydrolysis;
c) Acetylation.

The reaction of esterification is possible in the presence of catalyst:

a) OH^-;
b) H^+;
c) Cl^-.

A type of bond is in esterase:

a) Hard– ether;
b) Glycoside;
c) Peptide.

Formation of water as by-product in the reaction of esterification goes as a result of slabbing:

a) Oxo – group;
b) H^+ from acid and OH^- from an alcohol;
c) H^+ from an alcohol and OH^- from acid.

Reaction of reverse esterification is named:

a) Hydrolysis;
b) Hydration;
c) Hydrogenation.

The hydrolysis of esters goes in environments:

a) Brome water;
b) To sour and alkaline;
c) Chloric water.

The products of acid hydrolysis of esters are:

a) Aldehyde and alcohol;
b) Acid and basis;
c) Acid and alcohol.

The products of alkaline hydrolysis of esters are:

a) Alcohol and salt;
b) Acid and basis;
c) Acid and salt.

In human beings esteres are:

a) Polysaccharides;
b) Protein;
c) Fats.

In human beings difficulty – ether bond appears between:
a) Amino acid;
b) Monosaccharaides;
c) Amino acid and t –RNA.

In human beings difficulty – ether bond appears from H_2SO_4:
a) In a itparin;
b) In amylase;
c) In proteins.

Thioester in the organism of man is:
a) Acetyl coenzyme A;
b) Ethyl coenzyme A;
c) Metal coenzyme A.

Thioester in the body of man carry out a role:
a) Acyclic agent;
b) Alkyl agent;
c) Metallic agent.

A reaction of acetylating is introduction:
a) Alkyl;
b) Acyl;
c) To the methyl.

Acyl is the remain of hydro carboxylic acid without:
a) Oxy are groups;
b) A carboxyl is groups;
c) Oxy -group.

After the reaction of acydylating in the organism of man synthesized:
a) Adrenaline;
b) Acetylcholin;
c) Acetylserine.

Halogen anhydride are the derivatives of hydro carboxylic acids, in which:
a) Oxo – substituted for a group a halogen;
b) Oxy – substituted for a group a halogen;
c) Carboxyl – substituted for a group a halogen.

Halogen anhydride is used in vitro as:
a) Acyl agent;
b) Alkylic agent;
c) Metallic agent.

Halogen anhydride by comparison to hydro carboxylic acids:
a) Less reaction capable;
b) More reaction capable;
c) Same reaction ability.

For halogen anhydrides characteristic reactions:
a) Nucleophilic joining;
b) Electrophilic substitution;
c) Nucleophilic substitution.

Halogen anhydride co-operate with ammonia after a mechanism:

a) Nucleophilic substitution;
b) Nucleophilic joining;
c) Electrophilic substitution.

The products of reaction of halogen anhydride with an ammonia is:

a) Amines;
b) Amides;
c) Imines.

Amides is derivatives of hydro carboxylic acids, in which:

a) Oxo – substituted for a group on NH_2 – group;
b) Carboxyl – substituted for a group on NH_2 – group;
c) OH deputized on NH_2 – group.

Formation of amides in an organism is a way of leading out:

a) Amino acid;
b) To the ammonia;
c) Amines.

Acetopitne – it derivative:

a) Alkane;
b) Alkenes;
c) Benzoyl .

For proof of high quality of acetopitne conduct a reaction from:

a) By a iron (III) chloride;
b) Copper (II) hydroxide;
c) By brom water.

Of high quality preparation of acetophene:

a) Gives the violet color from $FeCl_3$;
b) Does not give violet color from $FeCl_3$;
c) Gives violet color with bromic water.

Of poor quality preparation of acetopitne gives from $FeCl_3$:

a) Red color;
b) Dark blue color;
c) Violet color.

11. *The Control Test:*

Sample 1

1. Write the scheme of pyruvic acid formation in human organism and give the characteristics of its chemical properties.

Sample 2

1. Write the scheme of oxaloacetic acid formation in human organism and give the characteristics of its chemical properties.

Sample 3

1. Write the scheme of β - hydroxy butyric acid formation in human organism and give the characteristics of its chemical properties.

Sample 4

1. Write the scheme of lactic acid formation in human organism and give the characteristics of its chemical properties.

12. ***The algorithm of labwork:***

12.1. Demonstration of the presence of two carboxy-groups in tartratic acid.

Detailed description:

Put 5 drops of solution of tartrate (tartratic acid) into a test-tube, add 2 drops of KOH solution and rub the sides of the test-tube until the sediment appearance. Then add 4-5 drops of KOH solution. Write the reaction equation, describe the results and make conclusions.

The test-tube with solution must be kept for the next experiment.

12.2. Demonstration of presence of hydroxy-groups in tratratic acid.

Detailed description:

Put 2 drops of $CuSO_4$ solution and 2 drops of NaOH solution into a test-tube. The solutions from the previous experiment add to the sediment that appeared. Write the reaction equation, describe the results and make the conclusions. Write do we use this solution and what is its name?

12.3. Decomposition of the citric acid.

Detailed description:

Put the 1cm layer of citric acid and 1 ml of conc. H_2SO_4 into the dry test-tube with gas-collecting tube and heat. The end of the gas-collecting tube is put into the test-tube with 1ml of Barium hydroxyde and then – into the test-tube with Lugol solution that was decolored by NaOH. Write the scheme of the decomposition reaction. Describe the results, make the conclusions.

12.4. Receive and solubility of calcium citrate and calcium tartrate.

Detailed description:

Dissolve several crystals of citrate (citric acid) in one test-tube and several crystals of tartrate (tartratic acid) in another one. Neutralize acids with NH_4OH solution (check with indicator), then add 2-3 drops of $CaCl_2$ solution. The sediment will appear right away, and the other test-tube heat for 2-3 minutes. Write the reaction equations, describe the results and make the conclusions.

12.5. Demonstration of absence of phenol hydroxyle in acetyl salicyllic acid (aspirin) and its hydrolysis (demonstration of acetylsalicyllic acid high quality).

Detailed description:

Put a piece of aspirin tablet into a test-tube. Add 5-6 drops of water, mix and add 1 drop of $FeCl_3$. Explain the visible effect of reaction. If there are no changes, then boil the test-tube for 0,5min and add 1 drop of $FeCl_3$ solution. What do you see? Write the reaction equation, describe the results and make conclusions about the quality of acetysalicyllic acid.

TOPIC 10

THE STRUCTURE AND CHEMICAL PROPERTIES OF α-AMINO ACIDS.

1. Actuality of the topic:

Amino acids are the structural element of peptides and proteins. Understanding the structure and chemical properties of amino acids is necessary for realising of their reactivity, conversions and biological significance in human organism.

2. ***General aim:***

General aim is to explain the structure and function of proteins in the human organs by using the knowledge of amino acid properties.

3. ***Actual aims and abilities:***

3.1. To interpretate speciatilies of α-amino acids structure as the structural basis of proteins which have their function in human organism.

3.2. To make conclusions about α-amino acids' ways of conversion in human organism.

3.3. To predict appearance of proteins and other physiologically active compounds on the basis of reactivity and structure of amino acids, understanding and predict degradation of aminoacids in human organism.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 211-218.

5. ***The main questions of the seminar:***

5.1. Amino acids: definition, composition, structure.

5.2. Acid-base properties of amino acids.

5.3. Chemical reactions of amino acids by carboxy-group: ester and halogenanhydrydes formation. Biological meaning of these reactions.

5.4. Chemical reactions of amino acids by amino-group: N-acyl derivatives formation, interaction with nitrite acid, formaldehyde, phenylisothyocyanate. Biological significance of these reactions.

5.5. Decarboxylation of amino acids and biological meaning of biogen amines' formation.

6. ***The questions for individual learning:***

6.1. Amino acids classification.

Amino acids decarboxylation in human organism.

7. ***Examples of task:***

7.1. What types of isomery are typical for α-amino acids?

Answer:

- Isomery of amino-group location: α-amino acids and β-amino acids;
- Carbon skeleton isomery: leucine-isoleucine;
- Enantiomery: D–methionine – L-methionine.

Explain the amino acids' amphotericity.

Answer:

Amphotericity is explained by the presence of carboxy-group and amonio-group in amino acids. Carboxy-group is the group with acidic properties, it dissociates with appearance of H^+ -ion (or proton); amino-group is the group with basic properties because nitrogen has undivided electron pair. During solution of amino acid in water proton joins to nitrogen, making bipolar ion that has carboxylate-anion and protonned amine group, and has positive charge. Amphoteric character of amino acids is also confirmed by their interaction with alkalines as well as with acids, making salts.

8. ***Homework (must be performed in the laboratory notebook):***

8.1. Write and learn 20 formules of aminoacids, that form proteins; mark irreplaceable aminoacids.

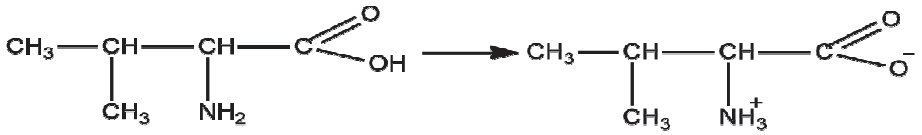
8.2. Write the reaction of interaction between serine and ethanol equation.

8.3. Write the reaction of interaction between asparagine and pitnylisothyocyanate equation.

9. ***Example of control test:***

9.1. Write the scheme of appearance of aminoacid – valine - bipolar ion. What pH does its isoelectrical point located in?

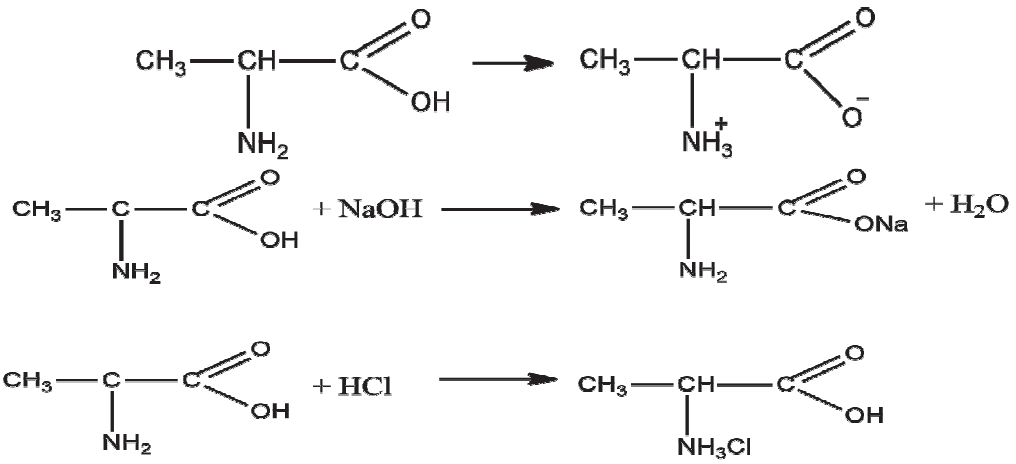
Answers:



IEP is located in subacid medium.

9.2. Write the formulas of three possible alanine salts.

Answers:



10. ***Tests:***

10.1. In the complement of albumens of living organism enter only:

a) β–amino acid;
b) α–amino acid;
c) γ–amino acid.

For amino acid such types of isomers are characteristic:

a) Lactim – lactam;
b) Cis – trans;
c) Structural, enantiomeric excess.

Structural isomers of amino acids is:
a) A leucine – isoleucine;
b) A serine – treonin;
c) A valine – alanine.

The example of structural isomers of amino acid is:
a) α – alanine –γ – aminobutyric acid;
b) α – alanine –β – alanine;
c) β – alanine – β – aminobutyric acid.

The example of enantiomers of aminoacid is:
a) α – alanine –β– alanine;
b) L – alanine –D – valine;
c) L – methionine – D – methionine.

The natural amino acid have only:
a) L – configuration;
b) D – configuration;
c) cis – configuration.

Amino acid show:
a) Only acid properties;
b) Amphoteric properties;
c) Only basic properties.

It exists in water of aminoacid in the form of:
a) To cation;
b) To the anion;
c) Bipolar anion.

The isoelectric state of amino acid exists in the form of:
a) Anion;
b) Bipolar anion;
c) Cation.

Aminoacids are in the isoelectric state at a certain size:
a) Temperatures;
b) Pressure;
c) pH.

Isoelectric point – pH, for which the amino acid is in:
a) Isoelectric state;
b) Kind cation;
c) In a kind an anion.

After the size of isoelectric point the amino acid are classified on:
a) Soluble, insoluble;
b) Neutral, sour, basic;
c) Volatile, non-flying.

Neutral amino acids are:
a) Alanine, valine;
b) Serine, tyrosine;
c) Aspartic.

The example of souramino acid is:

a) Phenylalanine, tryptophane;
b) Cystein, methionine;
c) Aspartic, glutamine amino acid.

The example of basic amino acid is:

a) Leucine, isoleucine;
b) Methionine, valine;
c) Lysine, arginine.

Aminoacid for a carboxy – it is given a group:

a) Esters;
b) Ethers;
c) Amines.

Formation of esters amino acid is used during the synthesis of peptides and albumens for the:

a) Defence of aminogroups;
b) Defence of carboxy – group;
c) Activating of carboxy is groups.

Amino acid for a carboxy – it is given a group:

a) Esters;
b) Ethers;
c) Halogen anhydrides.

Formation of halogen anhydrides amino acid is used during the synthesis of peptides and albumens for:

a) Activating of carboxy is groups;
b) Defence of carboxy – group;
c) defence of aminogroups.

Aminoacid for amino – it is given a group:

a) Amides;
b) N – acylderivatives;
c) N – glycoside derivatives.

Formation of N – acyl of derivative amino acid is used during the synthesis of peptids and albumens for:

a) Activating amino group;
b) Defence of carboxy group;
c) To defence of amino group.

Interaction of amino acid with nitrite acid used for the quantitative analysis of amino acid by:

a) By Van Slyke method;
b) By Boyle Mariotte method;
c) By Shrouds – Goff method.

the method of Van Slyke is used reaction of amino acid from:

a) By nitrate acid;
b) By cyanic acid;
c) By nitrite acid.

The amino acid co-operate for NH_2 – to the group from:

a) By an alcohol;
b) By halogens;

c) By formaldehyde.

Reaction of amino acid with formaldehyde is used for the quantitative analysis of amino acid in a method:

a) By Zensen;
b) By Boyle Mariotte;
c) By Shrouds – Gofa.

Zensen's method use for reaction of amino acid from:

a) Formaldehyde;
b) Metanol;
c) Brome water.

Aminoacid co-operate for amino – to the group from:

a) Phenyl thiocarbodiazon;
b) Phenyl thiocyanate;
c) Phenyl thiocarbocyanine.

Reaction of amino acid from pitnyl thiocyanate is used for determination of amino acid sequence in spiral in a method:

a) By Zensen;
b) By Boyle Mariotte;
c) By Edman.

In the method of Edman cooperation of amino acid is used from:

a) Phenyl thiocarbodiazon;
b) Phenyl thiocyanate;
c) Phenylcarbocyanate.

For quantitative determination of amino acid use methods:

a) By Van Slyke and Zensen;
b) By Kucitrov and Zelinsky;
c) By Edman and Sendzher.

The all amino acid give the violet color from:

a) Brome water;
b) Ninhydrin;
c) A ferum (III) chloride.

Xanta Protein reaction of amino acid is an origin of:

a) Violet color from H_2SO_4;
b) Red color;
c) Yellow color from HNO_3.

The aromatic amino acid gives with the reagent of Million's:

a) Red color;
b) Violet color;
c) cyan color.

Heterocycle amino acid gives with the reagent of Adamkevich:

a) Red color;
b) Violet color;
c) Yellow color.

In the containing of amino acid give with the reagent of Folya:

a) Red color;
b) Violet color;
c) Black color.

The result of decarboxylation serine in the organism of man appears:

a) Colamine;
b) choline;
c) Thiamine.

As a result of oxidation of delamination of amino acid in the organism of man takes place the transformation:

a) Valine→ acetic acid;
b) Alanine → pyruvic acid;
c) Aspartic→ oil acid.

As a result of intramolecular delamination of amino acid there is transformation in the organism of man:

a) Amino acid → oxo acid;
b) Amino acid → oxo acid;
c) Amino acid → hydro carboxylic acid is unsaturated.

Glutamate of sodium has a taste:

a) Meat;
b) Milk;
c) Lemon.

From amino acid a serine as a result of chain of transformations to the organism of man appears:

a) Serotonin;
b) Acetylcholine;
c) Histaminum.

Redox – the system in the organism of man are amino acid:

a) α – alanine – β– alanine;
b) Phenylalanine – tyrosine;
c) Cystein of – cystine.

methionine in human beings is a source of:

a) Sulphure and metyl groups;
b) Acetyl group;
c) Aminogroup and alkyl.

From amino acid of tyrosine as a result of chain of transformations in a human being appears:

a) Serotonin;
b) Noradrenalin and adrenalin;
c) Histamine.

In result of decarboxylation tryptophan a toxic biogenic amine appears in a human being:

a) Thiamine;
b) Choline;
c) Tryptophan.

In the result of decarboxilation hystamines of human being's biogenic amine appears:

a) Histamine;
b) Choline;
c) Tryptophan.

11. ***The Control Test:***

Sample 1

1. Write the structural formulas of aromatic amino acids.
2. Write the reaction equation between cysteine and methanol.
3. Write the scheme of decarboxylation of valine.

Sample 2

1. Write the structural formulas of itterocyclic amino acids.
2. Write the reaction equation between arginine and ethanol.
3. Write the reaction equation between alanine and phenylisothiocyanate.

Sample 3

1. Write the structural formulas of monoamino-monocarboxylic acids.
2. Write the reaction equation between lysine and formaldehyde.
3. Write the reaction equation between valine and nitrous acids.

Sample 4

1. Write the structural formulas of oxy amino acids.
2. Write the reaction equation between glycine and ethanol.
3. Write the scheme of decarboxylation of leucine

12. ***The algorithm of laboratory work:***

12.1. Compairing of the aminoacids and their appropriate carbon acids power.

Detailed description:

Put into three test-tubes: into the first - 1ml of distilate water, the second -1ml of acetic acid, the third – 1ml of glycine. Add 2 drops of indicator methyl-red into each test-tube. Describe results, male conclusions.

12.2. Aminoacid and ninhydride interaction.

Detailed description:

Put 4 drops of glycine solution and 2 drops of ninhydrine solution into a test-tube and heat. Describe results and make conclusions.

12.3. Glycin and formaldehyde interaction.

Detailed description:

Put 5 drops of glycin solution and add 1 drop of methyl-red indicator. Note the color. Then add 6 drops of formaline. Describe results, write the reaction equation and make the conclusion.

12.4. Glycin and nitrite acid interaction.

Detailed description:

Put 5 drops of glycine solution, 5 drops of $NaNO_2$ solution and 2 drops of CH_3COOH (conc.) into a test-tube. Write the reaction equation, describe the results, and make the conclusion.

TOPIC 11

PHYSICAL AND CHEMICAL PROPERTIES OF PROTEINS. PROTEINS STRUCTURAL ORGANIZATION.

1. ***Actuality of the topic:***

Knowledge of composition, structure and chemical properties of peptides is necessary for understanding of their functions in human organism in normal condition and in pathology, as well as for using in clinics for diagnostics and curing, and for the synthesis of proteins and peptides in vitro**.**

2. ***General aim:***

Form general idea about proteins as polymeral structural components of all tissues of organism.

3. ***Actual aims and abilities:***

3.1. To explain dependence of physical and chemical properties of proteins on their amino acid composition.

3.2. To use qualitative reactions for amino acids to identificate proteins and determine their amino acidical composition.

3.3. To use the biuret reaction for quantheative determination of proteins.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 218-222.

5. ***The main questions of the seminar:***

5.1. Proteins, definition, proteins' molar mass.

5.2. Analysis of peptides and proteins: determination of amino acidical composition and amino acidical order. Edman's method.

5.3. Peptide and protein synthesis using protection and activation of functional groups.

5.4. The first decoded and synthesised proteins and peptides: insulin, vasopressin, oxytocin; their composition, structure, biological meaning.

6. ***The questions for individual learning:***

6.1. Appearance and properties of peptide bond.

Physical and chemical properties of peptides (amphotericity, Amphion appearance, salts appearance; isoelectric state (IES), isoelectric point (IEP).

Levels of protein structural organisation: primary, secondary, tertialy, quaternary. Bond types.

Methods of extraction, separation and purification of proteins. Determination methods of protein molar mass.

7. ***Homework (must be performed in the laboratory notebook):***

7.1. Write the reaction equations of dipeptide val-cys synthesis using protection and activation of functional droups (6 stages).

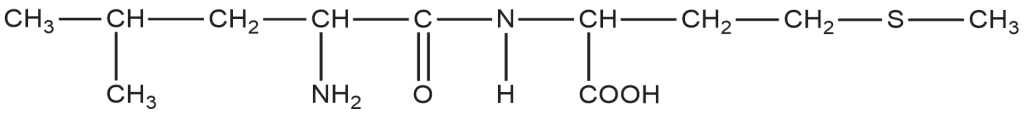
Write tripeptide: ala-lys-leu; what medium is its IEP situated in.

Write the scheme of determination of N-ended amino acid in ser-tri dipeptide using Edman method.

8. ***Example of control test:***

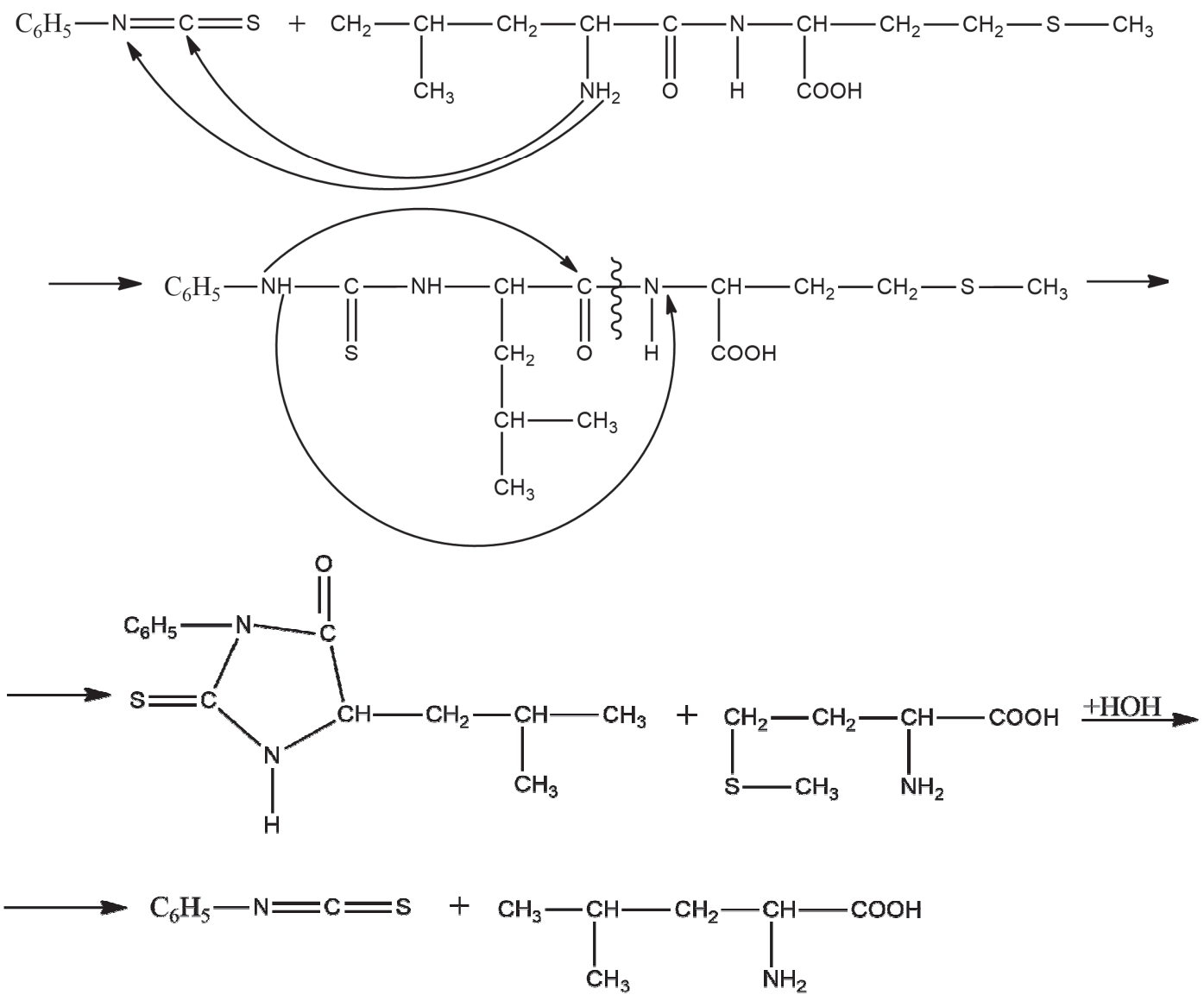
8.1. Write dipeptide leu-meth, what medium is its IEP situated in.

Answer:



8.2. Determine N-ended amino acid in this dipeptide using Edmans method.

Answer:



9. ***Tests:***

9.1. Proteins are high molecular natural bonds which are:

a) Condensated α – amino acid;
b) Biopolymers α – amino acid;
c) Condensates of monosaccharide's.

9.2. Spiral are biopolymers which consist of:

a) β – amino acid;

b) α – amino acid;
c) Monosaccharide's.

9.3. Simple spiral consist of tailings only:
a) α – amino acid and monosaccharide's;
b) β – amino acid;
c) α – amino acid.

9.4. To the simple albumens belong:
a) Albumins, globulins;
b) Glycoprotein's;
c) Glycolipid.

9.5. The products of hydrolysis of difficult albumens can be:
a) β– and α – amino acid;
b) α– amino acid and monosaccarides;
c) Only α – amino acid.

9.6. It belongs to the difficult albumens:
a) Albumins;
b) Globulins;
c) Nucleoproteins.

9.7. After configuration of molecule spiral are classified on:
a) Fibrous and globular;
b) L- and D- of proteins;
c) Cis- proteins of trance.

9.8. To the fibrous albumens belong:
a) Albumen;
b) Myosin, keratin;
c) Hemoglobin.

9.9. It is belonged to the spitre proteins:
a) Keratin;
b) Albumen;
c) Itmoglobin.

9.10. Spiral select from biological material by:
a) Evaporation;
b) Condensations;
c) Extractions or besieging;

9.11. Mixture of albumens is divided for itlp:
a) Gel is filtrations;
b) By extraction;
c) By evaporation.

9.12. In a method of gel filtration for the division of albumens as an adsorbent is used:
a) Starch;
b) Sephadex;
c) Aluminium is an oxide.

9.13. Mixture of albumens is divided for itlp:
a) Extractions;
b) Electrophoresis;
c) Evaporation.

9.14. Mixture of albumens is divided for itlp:
a) Extractions;
b) Evaporation;
c) Affinity chromatography.
9.15. The high-specific method of division of mixture of albumens is:
a) Affine chromatography;
b) There is a paper chromatography;
c) Adsorption chromatography.
9.16. For determination of homogeneity of albumens use:
a) Electrophoresis;
b) Immune phoresis;
c) Cation phoresis.
9.17. To the albumens polymers belong with molar mass:
a) 2000 – 10000;
b) 500 – 1500;
c) Anymore after 6000.
9.18. Specify free properties of solutions of albumens:
a) High viscidity, small speed of diffusion;
b) Pass through a semi-permeable membrane;
c) Does not denaturize.
9.19. Specify free properties of solutions of albumens:
a) High speed of diffusion;
b) Does not pass through a semi-permeable membrane, cut;
c) Does not denaturize.
9.20. Specify free properties of solutions of albumens:
a) High speed of diffusion;
b) Pass through a semi-permeable membrane,not cut;
c) Adsorb other matters, denaturize.
9.21. Denaturizing of albumens is caused by such factors:
a) Radiation, ultraviolet;
b) 0,9% solution of NaCl;
c) Brome water.
9.22. Denaturizing of albumens is caused by such factors:
a) 0,9% solution of NaCl;
b) Concentrated solutions of acids and meadows;
c) Brome water.
9.23. Spiral show :
a) Properties only acids;
b) Properties only bases;
c) Amphoteric properties.
9.24. During dissolution in water of spiral are in form :
a) To the cation;
b) To the zwitterions;
c) To the anion.
9.25. In a sour environment spiral have:
a) Negative charge;
b) Zero charge;

c) Positive charge.

9.26. In an alkaline environment spiral have:

a) Negative charge;
b) Zero charge;
c) Positive charge.

9.27. The isoelectric state of albumens is existence of albumens in a kind:

a) To the cation;
b) To the zwitterions;
c) To the anion.

9.28. Isoelectric point of albumens – is:

a) Pressure of solution, in which spiral are in the isoelectric state;
b) To pH solution in which spiral are in the isoelectric state;
c) Temperature of solution in which spiral are in the isoelectric state.

9.29. The size of isoelectric point of albumens depends on:

a) Amino acid composition;
b) pH albumens;
c) Molar mass of albumens.

9.30. High-quality reactions are on albumens:

a) With brome water;
b) Biuret, xanthoproteic;
c) With a ferum (III) chloride.

9.31. High-quality reactions are on albumens:

a) With brome water;
b) By sulphate acid;
c) Millone, Folya..

9.32. The all amino acid give from ninhydrin:

a) Violet color;
b) Red color;
c) Yellow color.

9.33. A wattle-fence of bond is between amino acid in spiral:

a) Glycoside;
b) Peptide;
c) Hard efires.

9.34. Peptide bond between amino acid appears for an account:

a) Carboxy group of first amino acid and amino group of second amino acid;
b) Amino group of first amino acid and carboxy group of second amino acid;
c) Between carboxy group of two amino acid.

9.35. An atom ofcarbon in peptide bond is in the state of:

a) Sp^2 – to hybridisation;
b) Sp^3 – to hybridisation;
c) Sp – to hybridisation.

9.36. For peptid bondcharacteristic:

a) Cycle is chain tautomerism;
b) Cys – trans – isomeres;
c) Enantiomerism.

9.37. Peptide bond is characterized:

a) Lactic is lantern tautomerism;

b) Cycle is chain tautomerism;
c) Enantiomerism.

9.38. A high-quality reaction is on peptid connection:
a) Xanthoproteic;
b) From $KMnO_4$;
c) Biurette.

9.39. A biurette reaction on albumens is conducted from:
a) $CuSO_4$ + NaOH;
b) $FeCl_{3;}$
c) Cu_2O.

9.40. The result of biuret reaction is:
a) Yellow color;
b) Violet color;
c) Red color.

9.41. Primary structure of albumen – it:
a) Polyglycoside sequence;
b) Polynucleotide sequence;
c) Amino acid sequence.

9.42. Amino acid sequence – it:
a) Primary structure of albumen;
b) Second structure of albumen;
c) Tertiary structure of albumen.

9.43. The primary structure of albumen is supported:
a) By ionic coupling;
b) By peptide coupling;
c) By forces of Van-der-Waal's.

9.44. A polypeptide chain has:
a) N- and S-eventual amino acid;
b) R- and F-eventual amino acid;
c) M- and N-eventual amino acid.

9.45. In to the polypeptide chain of N- the eventual amino acid is numbered:
a) Last;
b) First;
c) Middle.

9.46. In to the polypeptide chain of S - the eventual amino acid is numbered:
a) Last;
b) First;
c) Middle.

9.47. For establishment of primary structure of albumen conduct:
a) A complete hydrolysis of albumen is to separate amino acid;
b) Partial hydrolysis of albumen to the short peptides and set them amino acid sequence;
c) Chromatographic divide spiral into amino acid.

9.48. N - the eventual amino acid in peptides is determined after a method:
a) By Kucherov;
b) By Edman;
c) By Markovnikov.

9.49. First albumen the structure of which was decipitred – was:
a) Insulin;
b) Albumen;
c) Hemoglobin.
9.50. The structure of insulin was decipitred by the American scientist:
a) By Krik;
b) By Sender ;
c) By Watson.
9.51. Insulin is a hormone of the:
a) Thyroid;
b) Liver;
c) Pancreas.
9.52. For the synthesis of peptide defence of NH_2 – groups conduct :
a) Acidylating;
b) Alkylation;
c) Bromation.
9.53. During the synthesis of peptide for activating of COOH – the groupsof it translate :
a) In amid;
b) In halogen anhydride or anhydride;
c) In salt.
9.54. During the synthesis of peptide fordefiance of COON – the groups of it translate:
a) In amid;
b) In halogen anhydride;
c) At esters.
9.55. First synthesized hormones of peptide nature:
a) Oxytocin, vasopressin;
b) Thyroxine, thyrosine;
c) Somatotropin, adrenaline.
9.56. For the acceleration of synthesis of albumens use:
a) A synthesis in solution;
b) A solid phase synthesis by Merifild;
c) A synthesis in a gas phase.
9.57. For the acceleration of synthesis of albumens use:
a) A synthesis in solutions;
b) A synthesis in a gas phase.
c) A liquid synthesis by Shemyakin.
9.58. Second structure of protein – is:
a) A well-organized location is in space of polypeptide chain;
b) A linear location is in space of polypeptide chain;
c) Well-organized location in plane polypeptide chain
9.59. The second structure of albumen is supported mainly:
a) By ionic coupling;
b) By hydrogen bonds;
c) By peptide coupling.
9.60. One of the types of the second structure:

a) β spiral;
b) γ spiral;
c) α spiral.

9.61. A basic type of bonding in the tertiary structure of albumen:
a) Disulphide;
b) Peptide;
c) Glycoside.

9.62. A quaternary structure is supported by:
a) Peptide bond;
b) hydrogen bonds and forces of Van-der-Waal'sa.
c) ionic coupling.

9.63. Substituting in hemoglobin of glutaminic acid by a valine causes a disease:
a) Iron deficiency anemia;
b) Sodium is scarce anemia;
c) Sulphur similar anemia.

10. *The Control Test:*

Sample 1

1. Using the method of the blocking (protection) and activation of carboxyl group, synthesize the dipeptide Ala-Val. What is the pH range of its IEP?

Determine the N-terminal amino acid in dipeptide Ala-Val using Edman degradation method.

Sample 2

1. Using the method of the blocking (protection) and activation of carboxyl group, synthesize the dipeptide Thr-Asp. What is the pH range of its IEP?

Determine the N-terminal amino acid in dipeptide Thr- Asp using Edman degradation method.

Sample 3

1. Using the method of the blocking (protection) and activation of carboxyl group, synthesize the dipeptide Lys-Cys. What is the pH range of its IEP?

Determine the N-terminal amino acid in dipeptide Lys-Cys using Edman degradation method.

Sample 4

1. Using the method of the blocking (protection) and activation of carboxyl group, synthesize the dipeptide Pro-Cer. What is the pH range of its IEP?

Determine the N-terminal amino acid in dipeptide Pro-Cer using Edman degradation method.

11. *The algorithm of lab work:*

11.1. Biuretic reaction.

Detailed description:

Put 5 drops of protein solution, 10 drops of NaOH solution and 1-2 drops $CuSO_4$ solution into the test-tube. Describe the result, make conclusions.

11.2. Xanthoproteic reaction.

Detailed description:

Put 5 drops of protein, 5 drops of HNO_3 (conc.) (carefully!) and itat. Describe the results, write the equation of tyrosine nitrification, and make the conclusion.

11.3. Foll`s reaction.

Detailed description:

Put 5 drops of protein solution, 2 drops of NaOH solution into the test-tube, itat until boiling and add 2 drops of $(CH_3COO)_2$ Pb solution. Describe the results; write the reaction equation of sulphur-containing amino acid with Plumbum acetate.

TOPIC 12

MONOSACCHARIDES STRUCTURE AND CHEMICAL PROPERTIES.

1. *Actuality of the topic:*

Carbohydrates are widely spread in living nature they are contained in the cytomembranes. Carbohydrates are the source of energy for human organism. Becides, carbohydrates are the structural elements of nucleic acids, coenzymes, vitamins. Some of them are used as drugs.

2. *General aim:*

To make the conclusions about reactivity of monosaccharides according to their structure and composition.

3. *Actual aims and abilities:*

3.1. To distinguish the tautomeric forms of monosaccharides.

To know the methods of monosaccharide determination in the biological liquids.

4. *Literature:*

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 189-198.

5. *The main questions of the seminar:*

5.1. What is carbohydrate? The classification of carbohydrates.

5.2. Glucose:

- Non-cyclic form: Fisher projection, D- and L-configuration;
- Cyclic form (pyranose and furanose): Ituorse`s projection, α- and β-anomers;
- Conformation: α - Dand β - D–configuration. Tautorotation (birotation).

5.3. Chemical properties of glucose: formation of itlates, O – and N –glycosides, alkylation, acetylation.

5.4. The formules to know: glucose, fructose, ribose, desoxyribose and their derivatives (glycone, glycarone, glycurone acids, glycosamines, phospho esters).

6. *The questions for individual learning:*

6.1. Ascorbic acid, structure, biological meaning.

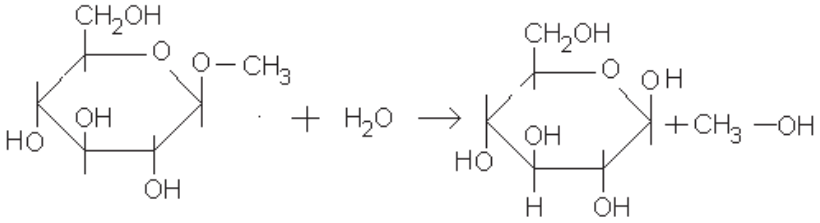
Qualitative reactions on monoatomic alcohols and aldehyde group.

Qualitative reaction on fructose (Selivanov's reaction).

7. *Examples of task:*

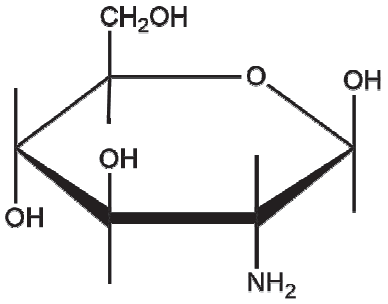
7.1. Write the hydrolysis scheme of O – methyl – β – D – glycopyranoside.

Answer:



Write the formula of glycosamine.

Answer:



8. *Homework (must be performed in the laboratory notebook):*

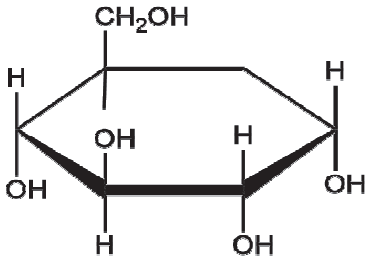
8.1. Write the equation of interaction between glucose and ethanol. Show the bond type and determine the product.

8.2. Write the equation of fructose alkylation with chloromethane. Show the bond type and determine the product.

9. *Example of control test:*

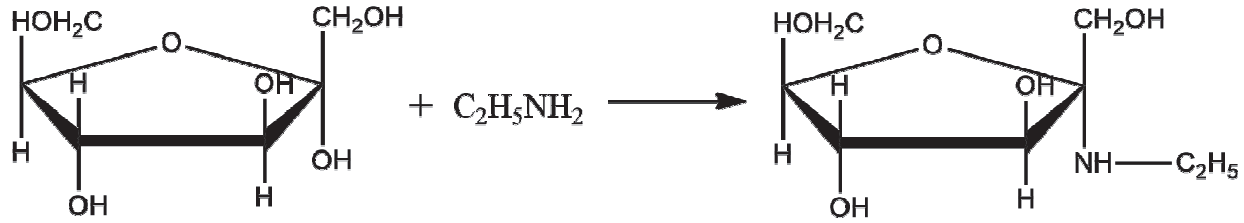
9.1. Write the α - D-glucopyranose formule.

Answer:



9.2. Write the equation of interaction between α,D-fructofuranose and ethylamine. Determine the product and show the bond type.

Answer:



9.3. What is Trommer's reagent and what is it used for?

Answer:

$CuSO_4$+NaOH, is used for monosaccharide determination in bioliquids.

10. *Tests:*

10.1. Monosaccharaides – it polyatomic:

a) Aldehyde – or hydroxyl-ketones;
b) Aldehyde – or acid alcohol;
c) Aldehyde – or alkamines.

10.1. To monosaccharaides belong:

a) Sucrose, lactose;
b) Glucose, fructose;
c) Mannose and maltose.

10.2. Glucose – it:
a) Hydroxyl-ketone;
b) Acid alcohol;
c) Aldehyde alcohol.

10.3. Functional groups in the molecule of glucose – it:
a) Aldehyde and alcoholic oxygroup;
b) Carboxylic- and alcoholic oxigroup;
c) Keto- and alcoholic oxygroup.

10.4. The acyclic form of glucose has:
a) D – configuration;
b) L – configuration;
c) N – configuration.

10.5. The cyclic form of glucose has:
a) λ– and μ – configuration;
b) γ–and δ – configuration;
c) α – and β – configuration.

10.6. The cyclic form of glucose is named:
a) Geptanose;
b) Tetra nose;
c) Piranose.

10.7. Pyranose the cycle of glucose has configuration:
a) Arm-chairs;
b) Baths;
c) Linear.

10.8. The isomer of glucose is:
a) Sucrose;
b) Lactose;
c) Lacto glucose.

10.9. Specify the correct pair of isomers:
a) Glucose is mannose;
b) Glucose is a maltose;
c) Glucose of – sucrose.

10.10. A high-quality reaction on the aldehydic group of glucose is a reaction:
a) By Kucitrov;
b) By Trommer;
c) By Friedel – Crafts.

10.11. A high-quality reaction on polyatomic of glucose is education:
a) Chelates;
b) Red sediment;
c) CO_2.

10.12. Glucose gives citlates from:
a) $FeCl_3$;
b) $Cu(OH)_2$;
c) By brome water.

10.13. Glucose forms O creates are glycosides during reaction from:
a) Aldehydes;
b) Acids;

c) Alcohols.

10.14. Medicinal preparations – cardiac glycosides – get from:

a) Foxgloves;
b) Chamomiles;
c) Tricycles.

10.15. Glucose forms N are glycosides during reaction from:

a) Amides;
b) Amines;
c) Imines.

10.16. N are glycosides of ribose and deoxyribose included in composition:

a) Albumens;
b) Fats;
c) RNA and DNA.

10.17. Alkalization of monosaccharide conduct for itlp:

a) Halogen alkanes;
b) Halogen anhydrides;
c) Free radicals'.

10.18. The product of alkylation glucose has such coupling:

a) O create are glycosides and difficult ether coupling;
b) O create are glycosides and simple ether coupling;
c) O create are glycosides and anhydride coupling.

10.19. As a result of hydrolysis fully alkyles glucose collapses only:

a) OH – glycoside and simple ether coupling;
b) Simple ether coupling;
c) OH – glycoside connection.

10.20. Acidylatings of monosaccharaides conduct for itlp :

a) Halogen alkanes;
b) Halogen acid;
c) Halogen anhydres.

10.21. An acidilate glucose has such coupling:

a) Hard ether;
b) OH – glycoside and simple ether;
c) OH – glycoside and difficult ether.

10.22. As a result of hydrolysis fully acilation glucose collapses only:

a) OH – glycoside and hard efires coupling;
b) Simple ether coupling;
c) All hard efires coupling.

10.23. Glucosein human is a source:

a) Entropies;
b) Energies;
c) Internal energy.

10.24. As a result of non-fermentative glycolization of collagen in the human organism accelerated:

a) Process of trombs formation;
b) Laying of salts;
c) Decline of arteriotony.

10.25. Fructose – it polyatomic:

a) Aldehyde alcohol;
b) Hydroxyl-ketone;
c) Alcohol.

10.26. Functional groups are in the molecule of fructose:
a) Aldehydic;
b) Carboxyl- and oxy-;
c) Oxo- and oxi are groups.

10.27. The cyclic form of fructose is named:
a) Furanozic;
b) Piranozic;
c) Tiazolic.

10.28. The cyclic form of fructose has:
a) λ – and μ– configuration;
b) α– but β – configuration;
c) γ– but δ – configuration.

10.29. Semiacetic hydroxyl in the molecule of fructose is located near:
a) Second atom of carbon;
b) First atom of carbon;
c) Sixth atom of carbon.

10.30. Fructose is distinguisitd from glucose by a reaction:
a) By Kucitrov;
b) By Selivanove;
c) By Fehling.

10.31. In the molecule of desoxyribose oxygroup absents near:
a) Second atom of carbon;
b) First atom of carbon;
c) Fifth atom of carbon.

11. *The Control Test:*

Sample 1

1. Write the structural formula of α-D-glucopyranose.
Write the scheme of β-fructose alkylation. Point the linkage types of the product.

Sample 2

1. Write the structural formula of β-D-mannopyranose.
Write the scheme of α-glucose acylation. Point the linkage types of the product.

Sample 3

1. Write the scheme of galactose reduction.
Write the scheme of the interaction between α-mannose and methyl chloride.

Sample 4

1. Write the structural formula of β-D-fructofuranose.
Write the scheme of N-glucoside formation of α-galactose.

12. *The algorithm of lab work:*

12.1. Demonstration of the presence of hydroxy-groups in D-glucose.

Detailed description:

Put 1 drop of glucose solution, 6 drops of NaOH solution, 1 drop of $CuSO_4$ solution into a test-tube. Note the results, write the reaction equation, and make the conclusions.

12.2. Reduction of copper (II) hydroxyder with glucos ein alkaline medium (Tromer test).

Detailed description:

Add several drops of water to the solution that appeared in the first experiment. Itat the test-tube until boiling. Mark the results, write the reaction equation and make conclusions.

12.3. Selivanov reaction for determination of fructose.

Detailed description:

Put the resorcinol crystal and 2 drops of HCl (conc.) Add 2 drops of fructose solution and itat until boiling. Mark the result, write the scheme of reaction and make conclusions.

TOPIC 13

OLYGO AND POLYSACCHARIDES, STRUCTURE AND THIER CHEMICAL PROPERTIES.

1. *Actuality of the topic:*

Combined hydrocarbones are spread in nature, olygo- and polysacharides are among them. These hydrocarbones are contained in the cyto-membrane, and they are also the source of energy in the organism (starch and glycogen). Some of them are used as blood substheutes (polyglukine), as loading of powders and tablets.

2. *General aim:*

To make conclusions about reactivity of combined hydrocarbons, according to their structure and contains.

3. *Actual aims and abilities:*

3.1. To interptretate the specialities of structure and conversion of olygosaccharides in human organism.

3.2. To interpretate the specialithees of structure and conversion of homopolysaccharides in human organism as of energy source for living processes.

3.3. To explain the mechanism of heteropolysaccharides biological role in human organism.

4. *Literature:*

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 161-169, 200-207.

5. *The main questions of the seminar:*

5.1. What are disaccharides? Disaccharides classification according to their ability to oxidative-reductive reactions.

5.2. Sucrose structure, lactose structure: reductive abilies and oxy-groups (itlates appearance, alkylation, acetylation).

5.3. Homopolysaccharides: starch, glycogen, cellulose, dextranes: composition, structure, primary and secondary structure, chemical properties, biological meaning.

6. *The questions for individual learning:*

6.1. Starch hydrolysis, qualitative reaction for starch determination.

Heteropolysaccharides: hyaluronic acid, heparin, chondroitin sulfate, their composition and the structure of disaccharide fragment, biological meaning.

7. *Examples of task:*

7.1. What are homopolysaccharides (examples)?

Answer:

Homoppolysaccharides are the combined hydrocarbons that consist of units of one polysaccharide. For example: starch, glycogen consist of of α – glucose units; cellulose – β-glucose units.

What products appear as a result of starch hydrolysis?

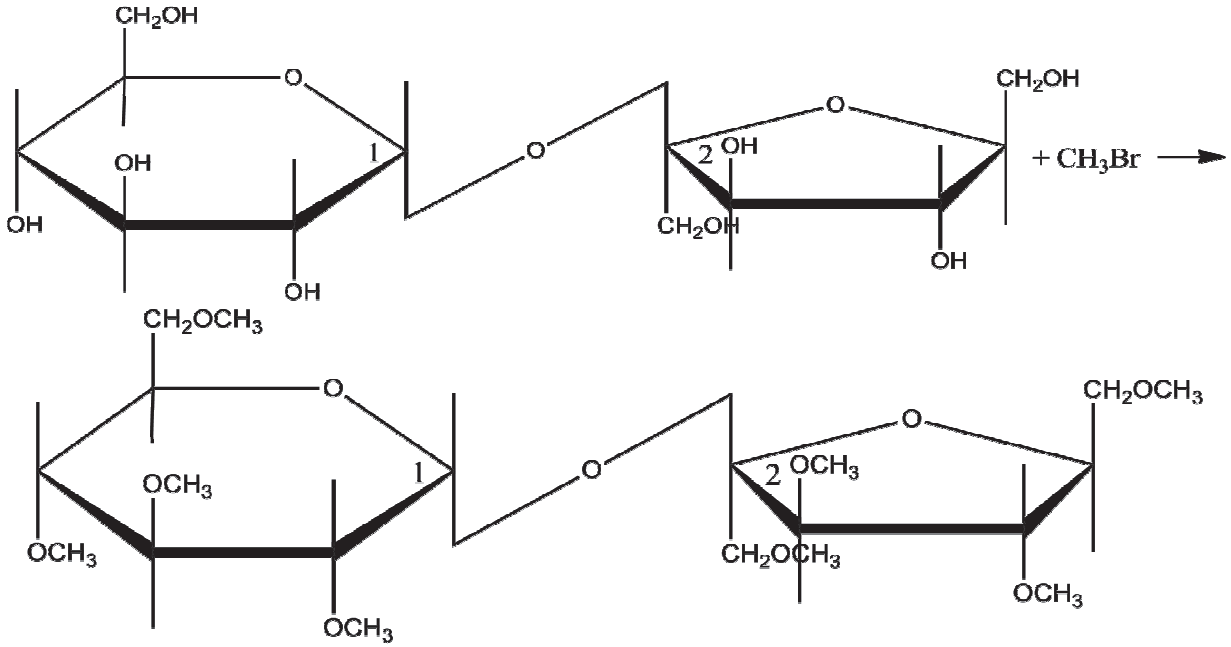
Answer:

$$(C_6H_{10}O_5)n \rightarrow (C_6H_{10}O_5)m \rightarrow (C_{12}H_{22}O_{11}) \rightarrow C_6H_{12}O_6$$

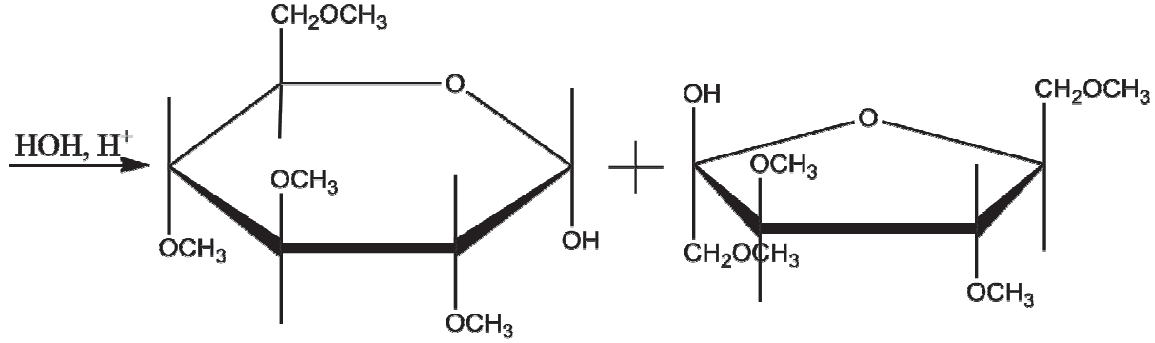
Starch dextrines maltose glucose

Write the scheme of sucrose alkylation, mark the bond types. Write the schema of hydrolysis of received compound and explain which bond is hydrolyzed first.

Answer:



Bonds – α – 1,2-glucoside and simple ether bonds



Only α – 1,2–glucoside bond is under hydrolysis

8. *Homework (must be performed in the laboratory notebook):*

8.1. Write the structural formula of lactose, show the bond type between two monosaccharide units.

8.2. Write the structure of cellulose disaccharide fragment and show the bond type between two monosaccharide units.

9. ***Example of control test:***

9.1. Write the structure of galactose and the scheme of its hydrolysis. What compounds are the reductors in this reaction?

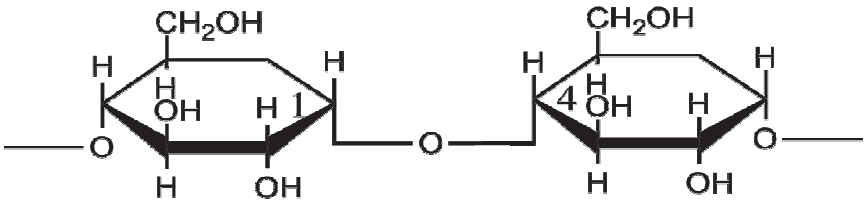
Answer:

lactose *galactose* *glucose*

Lactose, glucose and galactose are the reductors.

9.2. Write the structure of disaccharide fragment of glucose and show the bond type.

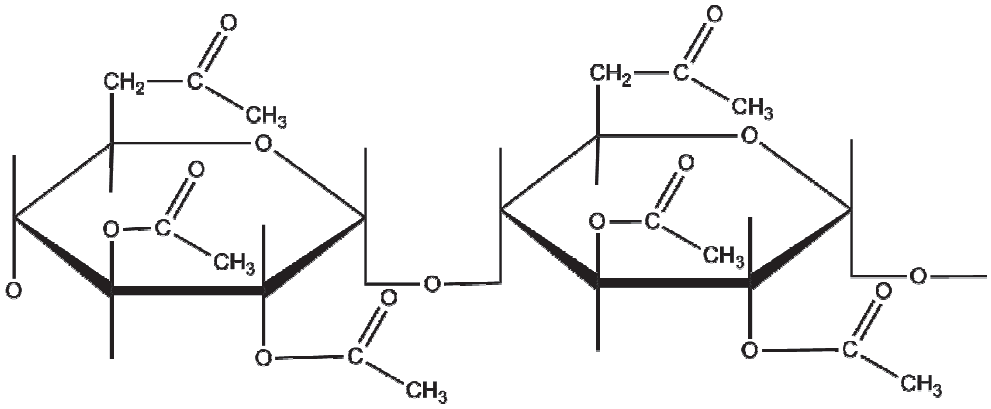
Answer:



α-1,4-glucosidebond

9.3. Write the structure of completely acetylated disaccharide fragment of amilose.

Answer:



10. ***Tests:***

10.1. Oligosaccharides – are hard carbohydrates, which contain:

a) From 2 to 10 monosaccharide tailings;
b) From 5 to 20 monosaccharide tailings;
c) From 1 to 5 monosaccharide tailings.

Disaccharides – it hard carbohydrates, which contain:

a) To 10 monosaccharide tailings;
b) To 2 monosaccharide;
c) To 5 monosaccharide tailings.

To disaccharides belong:

a) Glucose, lactoglucose;
b) Sucrose, lactose;
c) Fructose, mannose.

A sucrose consists of tailings:

a) α– are mannose and β– glucose;

b) α– lactoglucose andβ – fructose;
c) α – glucose and β – fructose.

A type of bond in sucrose between monosaccharide tailings:
a) α – 1, 2 – glycoside;
b) α – 1, 4– glycoside;
c) β – 1, 2 – glycoside.

Sucrose – it:
a) Recuperative sugar;
b) Unrecuperative sugar;
c) Insoluble sugar.

A sucrose is unrecuperative sugar, because absence:
a) Ionic bond;
b) Piranoic cycle;
c) Hemiacetal hydroxyl.

A sucrose can form such derivatives:
a) Citlates;
b) Glycoside;
c) Amides.

Sucrose from Cu $(OH)_2$gives:
a) Esters;
b) Citlates;
c) Salts.

A sucrose and lactose is for oxygroup:
a) Acylation and alkalizations;
b) Forms aldehydes;
c) Forms amides.

During a hydrolysis a sucrose gives:
a) Lactose and lacto glucose;
b) Glucose and fructose;
c) Maltose and fructose.

The products of hydrolysis of sucrose are called:
a) leaden sugar;
b) artificial sugar;
c) inverted sugar.

In the organism of man a sucrose fissions:
a) By the enzyme of sucrose in an intestine;
b) By an enzyme by a lactase in a stomach;
c) By an enzyme by a glucose in an oral cavity.

A lactose is disaccharide which consists of tailings:
a) α– are mannose andβ– glucose;
b) β– lacto glucose andα– glucose;
c) α– glucose and β – fructose.

A type of bondis in a lactose between monosaccharide tailings:
a) α –1,2 – glycoside;
b) α – 1,4 – glycoside;
c) β – 1,4 – glycoside.

A lactose has:

a) Linear configuration;
b) Located in a plane;
c) A piranoic cycle has conformation of bath.

Lactose – it:

a) Recuperative sugar;
b) Unrecuperative sugar;
c) Insoluble sugar.

Lactose is a recuperative sugar, because it contains:

a) Ionic connection;
b) Piranoic cycle;
c) Semiacetal hydroxyl.

Lactose can renew:

a) $Cu^{+2}$and Ag^{+1};
b) $Fe^{+3}$and Al^{+3};
c) Cu^{+1} and Cl^{+1}.

During reaction of lactose from $Cu(OH)_2$ appears for temperatures:

a) Dark blue sediment of $Cu(OH)_2$;
b) Brick is red sediment of Cu_2O;
c) Yellow sediment of Cu_2O.

Lactose:

a) O^- and N^- forms glycosides;
b) Forms only N^- glycosides;
c) Forms only O form glycosides.

During a hydrolysis lactose gives:

a) α – mannose and β - glucose;
b) β – lactoglucose andα – glucose;
c) α – glucose and β – fructose.

In human beings lactose is contained in the free and CPLD state:

a) In woman's milk;
b) In a stomach;
c) In a brain.

In human beings lactose fissions in stomach – intestinal pathway, under the action of enzyme

a) Glucose;
b) Sucrose;
c) Lactase.

In the organism of man there is the inherited immunity to:

a) Cellobiose;
b) Lactose;
c) Sucroses.

A maltose is disaccharide which consists of:

a) Two tailings β– glucose;
b) Two tailings β – lactoglucose;
c) Two tailings α – glucose.

A type of bondis in a maltose between monosaccharide tailings:

a) α – 1, 2 – glycoside;

b) α – 1, 4– glycoside;
c) β – 1, 4 – galactoside.

α – 1, 4– glycoside bondhas in a maltose:

a) Linear configuration;
b) Located in a plane;
c) Angular configuration.

Maltose – it:

a) Recuperative sugar;
b) Unrecuperative sugar;
c) Insoluble sugar.

A maltose it recuperative sugar, because present:

a) Ionic connection;
b) Piranoic cycle;
c) Semiacetal hydroxyl.

A maltose can renew:

a) $Cu^{+2}$and Ag^{+1};
b) $Fe^{+3}$and Al^{+3};
c) $Cu^{+1}$and Cl^{+1}.

During reaction of maltose from Cu $(OH)_2$ appears:

a) Dark blue sediment of Cu (OH);
b) Brick is red sediment of Cu_2O;
c) Yellow sediment of Cu_2O.

Maltose:

a) O- and N- forms glycosides;
b) Forms only N- glycosides;
c) Forms only OH are glycosides.

During a hydrolysis a maltose gives:

a) 2 molecules α– mannose;
b) 2 molecules α – glucose;
c) 2 molecules β – fructose.

A maltose is intermediate bondduring a hydrolysis:

a) Hyaluronic acid;
b) Dextranes;
c) Starch.

Polysaccharidess – it:

a) Polyoxycarbonyl bonds with general formula $Cm(H_2O)n$;
b) Polyoxycarbonyl bonds with general formula $Cn(H_2O)n$;
c) Polyoxycarbonyl bonds with general formula CnH_2nOn.

Molecular formula of homo polysaccharidess:

a) $C_6H_{10}O_6$;
b) $C_6H_{10}O_5$;
c) $C_6H_{12}O_6$

Starch – it:

a) Product of photosynthesis;
b) Polymerizations;
c) To catabolism.

Starch – it homo polysaccharidess, which consists of tailings:

a) α – mannose;
b) α – glucose;
c) β – fructose.

Starch consists of two factions:
a) Dextranes and cellulose;
b) Cellulose and glucose;
c) Amylase and to the amylopectin.

A type of bondis between monosaccharide tailings in amylose:
a) α – 1, 2 – forms only N– glycosides;
b) α– 1, 4 – glycosides;
c) β – 1, 4 – galactose.

Primary structure of amylase:
a) Polypeptide sequence;
b) Poly nucleic sequence
c) Poly glycosides sequence.

Second structure of amylase– it:
a) Spiral;
b) Ramified chain;
c) Bunch of polyglycosides chains.

An amylopectin has unlike amylose:
a) Linear polyglycosides chain;
b) Apolyglycosides chain is ramified;
c) A polypeptide chain is ramified.

A type of bondis between monosaccharide tailings in an amylopectin:
a) α –1, 2 – glycosides bondin points a fork;
b) α – 1, 4 – glycosides connectionmainly to the chain;
c) α – 1, 4 –mainly to the chain andα – 1,6 is glycosides connectionin points a fork.

Intermediate bonds of hydrolysis of starch:
a) Dextrin, maltose;
b) Dextranes, lactose;
c) Cellulose, glucose.

The last product of hydrolysis of starch is:
a) β– fructose;
b) α – glucose;
c) β – glucose;

A high-quality reaction is on starch:
a) Discolor of brome water;
b) The violet color is with a iron (III) chloride;
c) The dark blue color is with iodine.

Starch is used in pharmacy for: preparation:
a) Pastes, powders, pills;
b) Suspensions;
c) Emulsions.

Reserve power carbohydrate for animals – it:
a) Cellulose;
b) Dextrin;
c) Glycogen.

Glycogen – it homo polysaccaride, which consists of tailings:

a) α– mannose;
b) α – glucose;
c) β – fructose.

A type of bonding between monosaccharide tailings in a glycogen:

a) α – 1,2 – glycoside connectionin points a fork;
b) α– 1,4– glycoside connectionmainly to the chain;
c) α – 1,4 –mainly to the chain andα – 1,6 is glycoside bondin points a fork.

Cellulose (cellulose)– it homopolysaccaride, which consists of tailings:

a) α – mannose;
b) α – glucose;
c) β – glucose.

A type of bondis between monosaccharide tailings in a cellulose:

a) β – 1,4 – glycosides;
b) α – 1,4 – glycosides;
c) β– 1,4 – galactose.

Primary structure of cellulose – it:

a) Spiral;
b) Linear polyglycoside chain;
c) A polyglycoside chain is ramified .

Second structure of cellulose – it:

a) Linear polyglycoside chain;
b) A polyglycoside chain is ramified
c) Bunch of parallel polyglycoside chains.

A cellulose dissolves:

a) In the reagent of Schweitzer, H_2SO_4 (conc.);
b) In water, benzole;
c) Of Frommer's reagent, HCl (conc.)

Bond which does not destroy in the organism of man:

a) β – 1,4 – glycoside;
b) α – 1,4– glycoside;
c) β– 1,4 – galactoside.

Cellulose, which is contained in bread, grouts, fruit, green-stuffs called:

a) By artificial fibers;
b) By food fibers;
c) By synfiles

The food fibers of fruit and green-stuffs stimulate work:

a) To the brain;
b) Cells of CNS;
c) Intestine.

The food fibers of fruit and green-stuffs adsorb:

a) Toxic matters;
b) Hemoglobin;
c) Phosphates.

For the decline of calorie content of foods use:

a) Acetyl cellulose;
b) Methyl cellulose;

c) Nitro cellulose.

Dextranes consist of tailings:

a) α – glucose;
b) β– lactoglucose;
c) α – fructose.

From dextranes get blood substitutions under the name:

a) Polyglycine:
b) Polyhybrid;
c) Polyglucose.

Dextranes promote in an oral cavity :

a) The fall of teeth;
b) Development of caries;
c) Loosening of gums.

11. ***The Control Test:***

Sample 1

1. Write the reaction equation of sucrose and methyl chloride. Point the linkage types of the product.
2. Write the formula of disaccharide fragment of amilose. Point the linkage type.

Sample 2

1. Write the formula of lactose. Point the linkage type. Write the reaction proving the reducing property of its.
2. Write the scheme of alkylation of cellulose disaccharide fragment. Point the linkage type of the product.

Sample 3

1. Write the reaction equation of sucrose hydrolysis. What do the substabces exhibit the reducing properties.

Write the formula of disaccharide fragment of glycogen. Point the linkage type.

Sample 4

1. Write the reaction equation of lactose and acyl chloride. Point the linkage types of the product.
2. Write the formula of disaccharide fragment of cellulose. Point the linkage type.

12. ***The algorithm of lab work:***

12.1. Demonstration of the presence of hydroxyle groups in sucrose.

Detailed description:

Put 1 drop of sucrose solution and 6 drops of NaOH solution, 5-6 drops of water and 1 drop of copper sulfate solution into the test-tube. Mark the results, write the reaction equation and make conclusions.

12.2. Demonstration of absence of reductive abilities in sucrose.

Detailed description:

The solution that was received in the first experiment must be heated until boiling. Mark the results, make the conclusions.

12.3. Demonstration of sucrose hydrolysis.

Detailed description:

Put 1 drop of sucrose solution and 1 drop of HCl solution, 6 drops of water into a test-tube and boil for 1 min. Hydrolysed solution put into two test-tubes. Add 6 drops of NaOH solution, 4-5 drops of water and 1 drop of $CuSO_4$ solution into the first one and itat until boiling. Put the resorcinol crystal, 2 drops of HCl concontrated into the second one and itat untiol boiling. Mark the results, write the scheme and make the conclusions.

12.4. Presence of reductive abilities in lactose.

Detailed description:

Put 1 drop of lactose solution, 4 drops of NaOH solution, 1 drop of $CuSO_4$ solution and itat until boiling. Mark the results, write the reaction equations and make conclusions.

12.5. Acidic hydrolysis of starch.

Detailed description:

Put 1 drop of starch gleu, 2 drops of sulfuric acid inte the test-tube and put the test-tube into the boiling water. After 20 and 40 min. Make the qualitative reaction on the starch with one drop of hydrolysed solution. Mark the results, write the scheme of starch hydrolysis and make conclusions.

TOPIC 14

HETEROCYCLIC COMPOUNDS, THEIR CLASSIFICATION, STRUCUTURE AND CHEMICAL PROPERTIES.

1. ***Actuality of the topic:***

Structures of heterocycles are the base of such biologically important molecules as vitamines, Coenzymes, nitrogen bases of nucleic acids etc. They are the components of medicines. The knowedge of their properties is neccesary for understanding of biological processes.

2. ***General aim:***

Improve the knowledge of the structure and chemical properties of physiologically active heterocyclic compounds.

3. ***Actual aims and abilities:***

3.1. Make conclusions about biological activity of heterofunctional compounds according to their structure and chemical character.

Make the qualitative reactions for determination of nicotinic acid, antipyrine, and absence of phenol hydroxyde in acetylsalicylic acid.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 39.

5. ***The main questions of the seminar:***

5.1. Pentamerous heterocycles with one heteroatom (pyrrole). Benzopyrene (indole) as a part of tryptophan and its metabolites (tryptamine, serotonin) and toxis compounds (skatole, indole).

5.2. Pentamerous heterocycles with two heteroatoms (pyrazole). Pyrazole derivatives as medical preparations.

5.3. Hexamerous heterocycles with one (pyridine) and two (pyrimidine) heteroatoms, their main properties. Pyrimidine nitrogen bases and their tautomery.

5.4. Heterocyclic compounds (purine) and its derivatives (nitrogen bases of nucleic acids, uric acid). Main properties, tautomerism.

6. ***The questions for individual learning:***

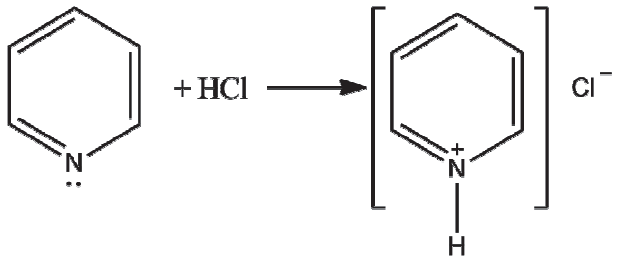
6.1. Heterocycles classification according to the cycle size, quantity and the nature of heteroatoms.

7. ***Examples of task:***

7.1. Explain the main properties of nitrogen atoms in pyridine.

Answer:

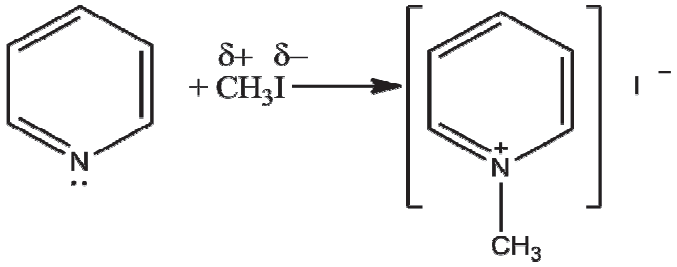
In pyridine the free electron pair of nitrogen atom does not take part in π-electronic density that is why nitrogen has basic properties.



Explain the nucleophyllic character of pyridine.

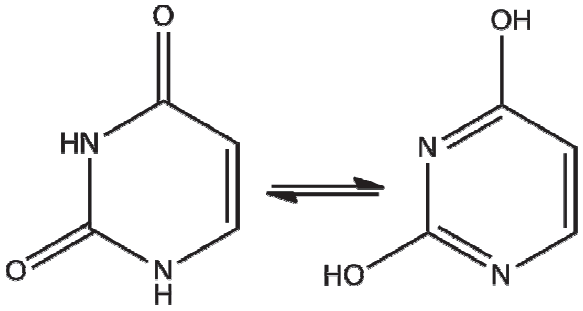
Answer:

Nitrogen atom in pyridine shows nucleophyllic properties because of the presence of free electron pair, for example in reactions with halogenalcanes:



Write the lactim-lactam form of uracil.

Answer:



Lactam *lactim*

8. *Homework (must be performed in the laboratory notebook):*

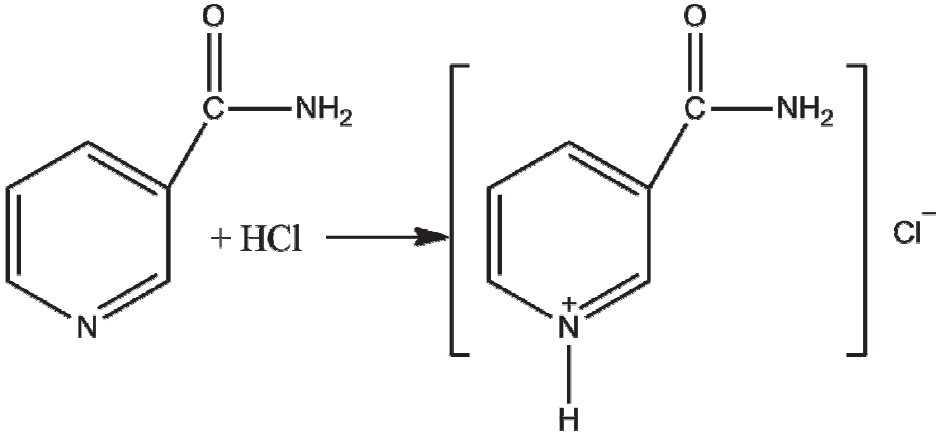
8.1. Write the tautomeric forms of uric acid, what functional group forms salts?

8.2. Write the chemical scheme of NAD action.

9. *Example of control test:*

9.1. Write the equation of pyridinium salt appearance during nicotinamide and hydrochloric acid interaction.

Answer:



9.2. Name purine's biologically active derivative.

Answer:

Uric acid, adenine, guanine, coffeine, toephylline and teobromine.

10. *The Control Test:*

Sample 1

1. Explain the basic property of pyridine. Write the reaction equation between pyridine and HI.
2. Write the structure of uric acids and its salt. What do the imbalances in organism take place due to the formation of insoluble salts of uric acid?

Sample 2

1. Write the scheme of methylpyridinium iodide.
2. Write the reaction equation of pyridine reduction with formation of piperidine.

Sample 3

1. Write the lactam and lactim forms of uracil.
2. Explain acidic and basic properties of purine.

Sample 4

1. Write keto and enol forms of guanine.
2. Explain the difference in the electronic structure of nitrogen atom in pyrrole and nitrogen atom in pyridine.

11. *The algorithm of lab work:*

11.1. Quantheative reaction for nicotinic acid determination (PP vitamine).

Detailed description:

Put 1ml of nicotinic acid solution into the test-tube and heat, add 6-7 drops of $CuSO_4$ solution and 0,5ml NH_4SCN solution. Mark the result of the reaction. Write the formulas of nicotinic acid and nicotinamide.

11.2. Antipyrine and amidopyrine with ferrum (III) chloride.

Detailed description:

Put several crystals of antipyrine in one test-tube, several crystals of amidopyrine in another one, add 2 drops of water and 1 drop of $FeCl_3$ solution into each of them. Mark the result of the reaction. Write the formulas of antipyrine and amidopyrine.

TOPIC 15

NUCLEIC ACIDS, COMPOSITION, STRUCTURE AND BIOLOGICAL SIGNIFICANCE.

1. Actuality of the topic:

Nucleic acids are the main carriers of the genetic information in the organism. The knowledge of the structure and chemical properties of nucleic acids and their monomers (nucleotides) is necessary for understanding of chemical principles of structural organisation of nucleic acid macromolecules and nucleotide coenzymes for next learning of biochemistry and biology**.**

2. ***General aim:***

To fix the knowledge about the principles of the structure and learn about the principles of the biopolymer-cell components of the primary and secondary structures, that is useful for understanding of their biological role.

3. ***Actual aims and abilities:***

3.1. To analyse the meaning of nucleotides for the construction of nucleic acids and the action of nucleotide coenzyme.

To interprete the action of vitamins in the formation of coenzymes catalysing the biochemical reactions in organism.

4. ***Literature:***

4.1. Lecture.

4.2. Zurabyan S.E., Fundumentals of bioorganic chemistry, Moscow, 2004, pp. 225-236.

5. ***The main questions of the seminar:***

5.1. Structural components of nucleic acids, chemical properties. Qualitative reaction.

5.2. Nucleosides: definition, structure, types of linkages, nomenclature, properties.

5.3. Nucleoside phosphate, the meaning of ATP. The role of nucleotides in the formation of coenzymes.

5.4. RNA and DNA: structure, types, types of linkages, complementary pairs. Biological significance of nucleic acids.

5.5. DNA duplex (Double spiral of DRA). Complementary pairs.

6. ***The questions for individual learning:***

6.1. Qualitative reaction on carbohydrate component and phosphoric acid.

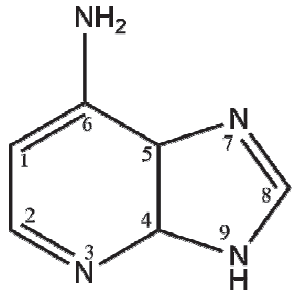
6.2. Formation of N-glicosidic and ester bonds.

6.3. The mechanism action of coenzyme NAD^+.

7. ***Examples of task:***

7.1. Write the structural formula of adenine and point the pyrrol and pyridine nitrogen atoms.

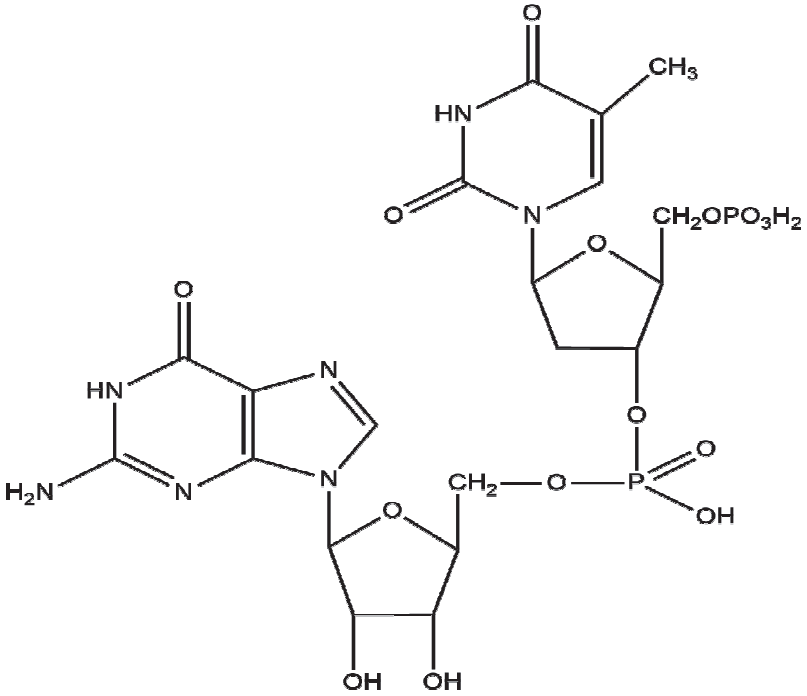
Answer:



1,3,7 – pyridine nitrogen atom
9 – pyrrole nitrogen atom

Write the stracture of DNA-TG fragment.

Answer.



8. *Homework (must be performed in the laboratory notebook):*

8.1. Write the structure of cytidine, deoxyguanosine. Point the lactim-lactam tautomerization.

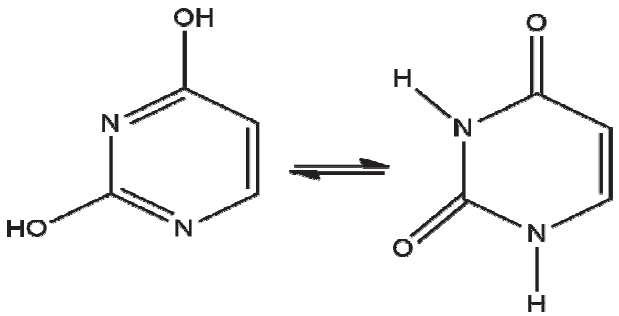
8.2. Write the structure of adenilic and thymidylic acid, point the types of linkages.

8.3. Write the structure of the dinucleotides DNA: T-G.

9. *Example of control test:*

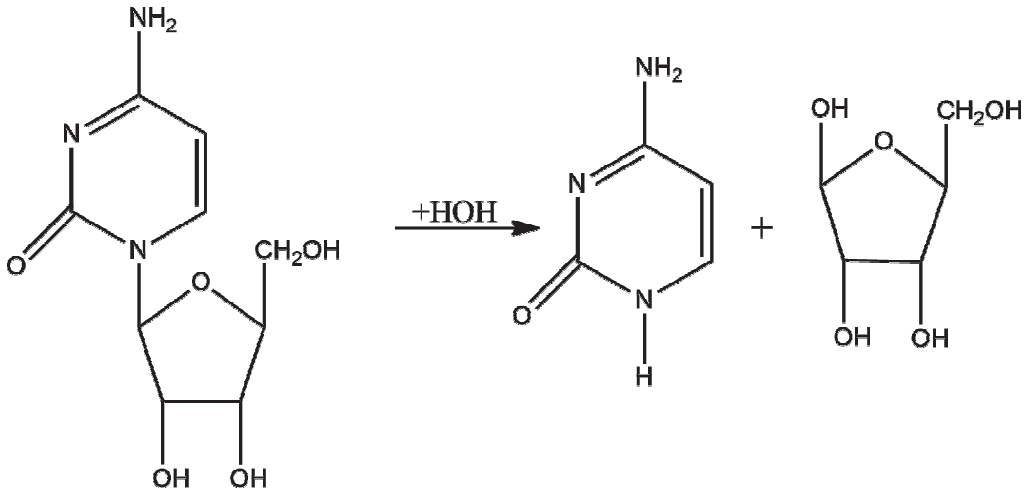
9.1. Write the structural formula of adenine and point the pyrrol and pyridine nitrogen atoms.

Answer:



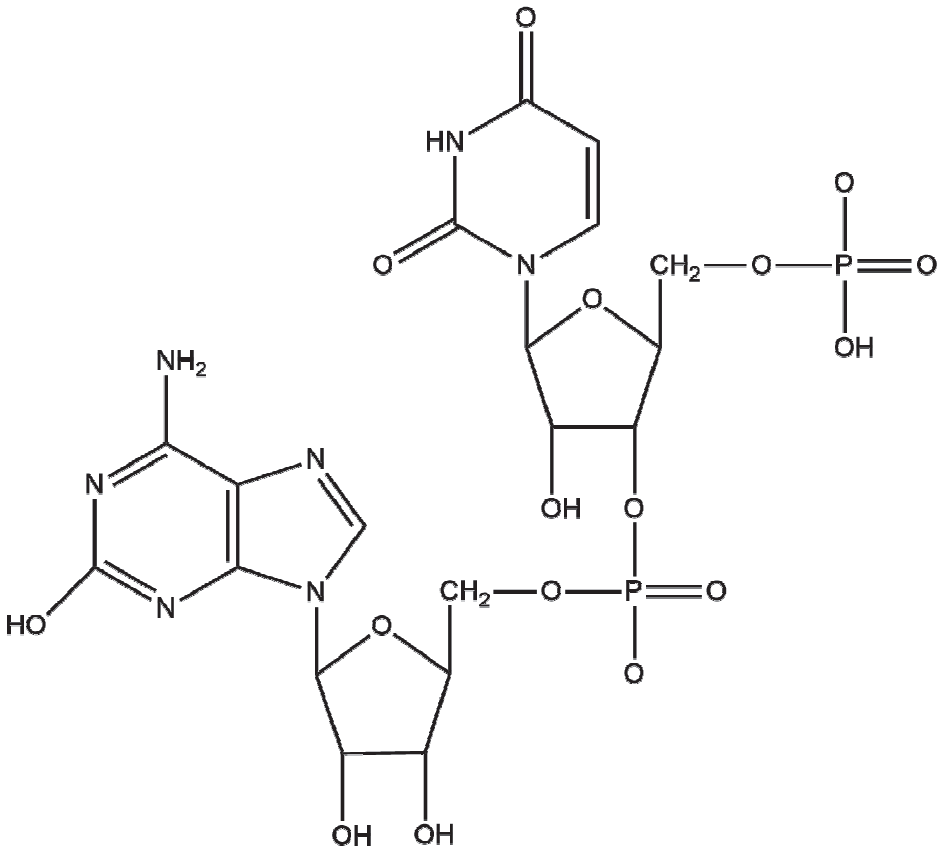
9.2. Write the hydrolysis of cytidine.

Answer:



9.3. Write the structure of the dinucleotides RNA: guanine – cytosine.

Answer:



10. ***Tests:***

10.1. Nucleic acids are calling biopolymers the morphons of which is:

a) Mononucleotides, connected by between itself phosphorus coupling;
b) Mononucleotides, connected by between itself glycoside coupling;
c) Mononucleotides connected by between it anhydride coupling.

Composition of nucleic acids:

a) Glucose, amino acid;
b) Nitrous bases, carbohydrate, phosphate acid;
c) Sulphate acid, phosphate acid, bases.

Nucleic acids are shown by acid properties due to a presence:

a) Carbohydrates;
b) Nitrous basis;
c) Phosphatic acid.

Nitrous bases in rows entering the complement of nucleic acids:

a) To the metadiazine and purine;
b) To imidazole and tiffany;
c) To pyridine and pyrazole

To the metadiazine nitrous bases which enter in the complement of nucleic acids – it:

a) Uracil, thymine, cytosine;
b) Adenine, guanozin;
c) Thymidine, guanine.

To purinoic nitrous bases which enter in the complement of nucleic acids – it:

a) Uracil, thymine, cytosine;
b) Adenine, guanine;
c) Thumidine, uridine.

Nitrous bases in hydrolysis of nucleic acids is possible to discover with the itlp of:

a) Dragendorf's reagent;
b) Fehling's reagent;
c) Million's reagent.

Nitrous bases in nucleic acids are in:

a) To the lactam form;
b) To the lactam form;
c) Cis – to the form.

Such carbonhydrates enter in the complement of nucleic acids:

a) Lacto glucose, mannose;
b) Ribose, deoxyribose;
c) Deoxy glucose, fructose.

Deoxyribose of distinguish from by ribose absence of oxy group near :

a) First carbon;
b) Third carbon;
c) Second carbon.

Ribose and deoxyribose – it polyatomic:

a) Aldehydoalcohol;
b) Hydroxy-ketones;
c) Acid alcohol.

Ribose and deoxyribose in hydrolizate of nucleic acids it is possible to discover for help:

a) Dragendorf's reagent;
b) Fehling's reagent;
c) Millon's reagent.

Phosphatic acid in hydrolysis of nucleic acids is possible to discover with the help of:

a) Tungsten test;
b) Chromic test;
c) Molybdenum test.

Nucleoside – it:

a) OH are glycosides, aglukon which nitrous bases are;

b) N are glycosides, a glucon which nitrous bases are;
c) N are glycosides, a glucon which phosphatic acid is.

In the complement of nucleoside enter:
a) Nitrous basis and phosphatic acid;
b) Nitrous basis and glucose;
c) Nitrous basis and carbohydrate.

In the nucleoside type of bond between nitrous basis and carbohydrate:
a) N – glycoside;
b) OH – glycoside;
c) Hard efires.

The products of hydrolysis of nucleoside is:
a) Phosphate acid;
b) Nitrous basis and carbohydrate;
c) Nitrous basis and phosphate acid.

Nucleoside, which consist uracil and ribose enter, calling:
a) Ureic acid;
b) Uridine.

In the complement of citadines enter:
a) Cytosine and phosphoric acid;
b) Amid and ribose;
c) Cytosine and ribose.

Nucleoside, which consist which adenine and ribose enter, called:
a) Adenosine;
b) Ribose.

In the complement of guano sine enter:
a) Guano sine;
b) Guanylic acid acid;
c) Guanine and ribose.

Nucleoside, which consist which a thymine and deoxyribose enter, called:
a) Deoxyribose;
b) Deoxythymidine;
c) Deoxidized.

Mononucleotides – is:
a) Phosphates of nucleotides;
b) Phosphates of carbohydratess;
c) Phosphates of nucleosides.

Mononucleotides – it:
a) Nucleoside - 5'- phosphates;
b) Nucleoside - 3'- phosphates;
c) Nucleotide - 5'- phosphates.

In the complement of mononucleotides enter:
a) Nitrous basis, carbohydrate, phosphate acid;
b) Amine, glucose, phosphate acid;
c) Nitrous acid, ribose, phosphate acid.

In nucleotides a type of bond is between components:
a) Hard fires;
b) N – glycosides, and hard efires;

c) OH – glycosides and hard fires.

In nucleotides a type of bond is between a carbohydrate and phosphatic acid:

a) OH – glycosides;
b) N – glycoside;
c) Hard efires.

In nucleotides a type of bond is between nitrous bases and carbohydrate:

a) N – glycosides;
b) Hard efires;
c) OH – glycosides.

Tailings enter in the complement of timidile acid:

a) To the thumine, ribose, to the phosphate of sodium;
b) To the thumine, ribose, phosphate acid;
c) Thumine, desoxyribose, phosphatic acid.

Tailings enter in the complement of guanile acid:

a) Guano zine, ribose, phosphate acid;
b) Guanine, ribose, phosphate acid;
c) Guanine, ribose

Deoxy adenosine - 5' – a phosphate is called:

a) Adenine acid;
b) Adenosine acid;
c) Deoxy adenile acid.

Deoxyuridine - 5' – a phosphate is called:

a) Deoxyuridine acid;
b) Uridine acid;
c) Deoxyuridine acid.

The products of hydrolysis of mononucleotides for a hard efires copula is:

a) Nitrous base and phosphoric acid;
b) Nucleoside and phosphoric acid;
c) Nitrous base and carbohydrate.

The products of hydrolysis of adenylic acidfor a hard efires copula is:

a) Ribose and phosphate acid;
b) Adenine and phosphate acid;
c) Adenosine and phosphate acid.

The products of hydrolysis of uridine acid for a hard efires copula is:

a) Ribose and phosphate acid;
b) Uridine and phosphate acid;
c) Uridine and phosphate of sodium.

To composition ATP tailings enter:

a) Adenine, ribose, two molecules of phosphate acid;
b) Adenine, ribose, phosphate acid;
c) Adenine, ribose, three molecules of phosphate acid.

Type of bond between tailings of nitrous bases and carbohydrate in a molecule ATP is:

a) N – glycoside;
b) Hard efires;
c) OH – glycoside.

Type of bond between tailings of phosphate acid in a molecule ATP is:

a) N – glycoside;
b) Hard efires;
c) Anhydride.

In a molecule of ATP energy provided in oneself is:
a) Hard efires bonds;
b) Anhydride coupling;
c) Glycoside coupling.

ATP takes part in activating:
a) Amino acid;
b) Alcohols;
c) Fats.

Aminoacyl adenylate complex appears between:
a) Amino acid and ATP;
b) An alcohol and ATP;
c) Fat and ATP.

Tailings of such nitrous bases enter in the complement of RNA:
a) A, G, C, U;
b) A, G, T, F;
c) A, G, C, F,

A type of connection between mononucleotides in the molecule of RNA is:
a) 1' – 2';
b) 3' - 5';
c) 2' - 5'.

A type of connection between mononucleotides in the molecule of RNA is:
a) Glycoside;
b) Simple ether;
c) Difficultly – ether.

The structural components of DNA tailings are:
a) Nitrous bases, deoxyribose, phosphate acids;
b) Amino acid, nitrous bases;
c) Phosphate acid, nitrous bases.

Tailings of such nitrogenous bases enter in the complement of DNA as:
a) A, G, C, T;
b) A, G, T, F;
c) A, G, C, F,

A type of bond between mononucleotides in the molecule of DNA is:
a) 1' – 2';
b) 3' - 5';
c) 2' - 5'.

A type of bond between mononucleotides in the molecule of DNA is:
a) Glycoside;
b) Simple ether;
c) Hard – ether.

Primary structure of DNA – is:
a) Polynucleotide sequence;
b) Consistentof amino acid;
c) Polyglycoside sequence.

Poly nucleotide sequence – is:

a) Second structure of DNA;
b) Primary structure of DNA;
c) Spiral of DNA.

Second structure of DNA – is:

a) A double spiral is involute on the right;
b) A spiral is involute to the left;
c) Linear chain of mononucleotides

Double spiral of DNA wasset by scientists:

a) Watson and Crick;
b) Boyle-Mariotte;
c) Shrouds – Goff and Paste.

The structure of the DNA duplex is supported:

a) By hard efires coupling between complementary bases;
b) By hydrogen bonds between complementary bases;
c) By glycoside coupling between complementary bases.

Complementary bases in the molecule of DNA are such pairs of bases:

a) A–G;
b) U–C;
c) A–T

Complementary bases in the molecule of DNA are such pair of bases:

a) G–C;
b) U–C;
c) A–G.

The molecules of DNA have:

a) amphoteric structure;
b) liquid – crystalline structure;
c) structure of liquid gas.

11. *The Control Test:*

Sample 1

1. Write the structure of lactim and lactam form of uracil.
2. Write the scheme of hydrolysis of deoxyadenilic acid respectively the ester linkage.
3. Write the structure of dinucleotide fragment of DNA-TG.

Sample 2

1. Write the structure of adenine and point the pyrrole and pyridine nitrogen atom.
2. Write the structure of cytidylic acid, point the linkage types. Write the hydrolysis of it.
3. Write the structure of dinucleotide part of RNA-UG.

Sample 3

1. Write the structure of lactim and lactam form of thymine.
2. Write the structure of deoxyadenilic acid, point the linkage types. Write the hydrolysis of it.
3. Write the structure of dinucleotide part of DNA-CG.

Sample 4

1. Write the structure of deoxyguanosine and point the linkage types.
2. Write the structure of uridine-5'-phosphate, point the linkage types, write the hydrolysis of it.
3. Write the structure of dinucleotide part of DNA-AT.

12. ***The algorithm of lab work:***

12.1. Benedict's reaction of carbohydrate skeleton detection.

Detailed description:

In the test tube add the aquaous solution of yeast, 6 drops of NaOH and 2 drops of copper sulphate.Heat the mixture. Note the result, write the reaction equation, and make a conclution.

12.2. Molybdenic probe for the phosphoric acid residue.

Detailed description:

In the test tube add 5 drops of the aquous solution of yeast and molybdenic probe ($(NH_4)_2MoO_4$ in nitric acid).The mixture must be boiled for 5 min. Note the result, write the reaction equation, and make conclutions.

12.3. Dragendorff probe

Detailed description:

In the test tube add 2 drops of the aqueous solution of yeast and 5-6 drops of Dragendorff`s reagent (BiI_3 + KI). Note the result, write the reaction equation, and make conclusions.

PRACTICAL ABILITIES AND SITUATION TASKS SOLUTION ON THE TOPIC:

«THEORETICAL BASIS OF STRUCTURE AND REACTIVITY OF BIOORGANIC COMPOUNDS »

1. What is the difference between the stearin and paraffin candles?

2. How can we differentiate the mixture of phenol, acetic acid, benzine and ethanol? Write the reaction equations.

3. There are three liquids in the three test-tubes: benzene, toluene, stearene. Identify the substances in each test-tube. Write the reaction equations.

4. There are three liquids in the three test-tubes without labels: acetic acid, formic acid and pentane. Identify the substances in each test-tube. Write the reaction equations.

5. There are three liquids in the three test-tubes without labels: carbon tetrachloride, oktane, brominoethane. Identify the substances in each test-tube. Write the reaction equations.

6. There are different gases in three closed ampules: butene-1, methylamine and acetylamide. Identify the substances in each test-tube. Write the reaction equations.

7. There are five different liquids in the glass amoules: toluene, oleic acid, fomic acid, acetaldehyde and methanol. Identify the substances in each test-tube. Write the reaction equations.

8. How can we separate each gas from the mix of ammonia, methane propene and propine? Write the reaction equations.

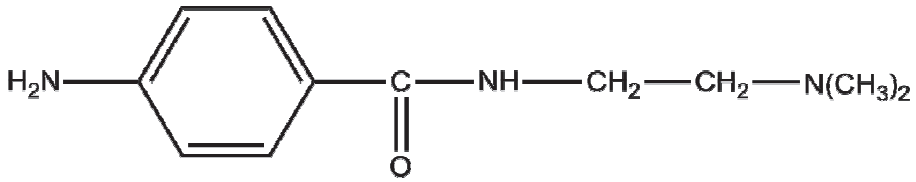
9. How can we differentiate the mixture of aniline, phenol and benzene?

10. Calamine (2 – aminoethanol - 1) takes part in the kefaline biosynthesis. Show the structure, configuration and different conformations of calamine.

11. The bladder cancer is result of aminobenzine action. Explain the mutual action of aminogroup and benzene nucleus in the molecule.

12. Sulphosalicyllic acid is used for determination of protein in boiliquids in clinical laboratory diagnostics. Mark the type and sign of lectron effects in sulfosalicylic acid molecule.

13. Novocainamide as hydrochloride is used for curing of itart arrhythmia. Determine the protonation in novocainamide molecule:



QUESTIONS FOR BIOORGANIC CHEMISTRY MODULE

1. Aldehyde and ketone reactivity.

The electronic structure of Oxo group. The mechanism of nucleophile addition in aldehydes and ketones. Interaction between aldehydes and alcohols, amines, aldol condensation reaction. Biological meaning of these reactions.

2. Reactivity of carbon acids and their derivatives.

The electronic structure of carboxygroup and mechanism of nucleophile substitution. Mechanism of interaction of carbon acids and alcohols, hydrolysis of esters in acidic and basic medium, interaction between halogenanhyride and ammonia. Biological meaning of these reactions. Acetylsalicylic acid, properties, determination of high quality.

3. Hydrocarbons.

Monosaccharaides: glucose, fructose, ribose, desoxyribose. Structure, isomery, properties: O-, N-glycosides formation, alkilation, acetylation of oxygroups, qualitative reactions.

4. Hydrocarbons.

Olygosaccharides: sucrose, lactose. Structure, bond types, spatial structure, chemical properties: alkilation, acetylation of oxygroups, reductive properties, biological meaning.

5. Hydrocarbons.

Polysaccharides: starch (amylose, amylopectin), glycogen, cellulose. Contents, structure, bond types, spacial structure, chemical properties: alkilation, acetylation of oxygroups; qualitative ereaction for starch determination, biological meaning.

6. Aminoacids as structural components of peptides and proteines

The structure of carboxy and aminogroups, isomery, chemical properties of aminoacids: acid base properties, IES, IEP; qualitative and quantheave reactions in aminoacid analysis. Aminoacid transformation in human organism: decarboxylation, oxydesamination, intramolecular desamination. Serine`s methabolism in human organism.

7. Peptides and proteins.

Methods of extraction, separation, purification, determination of homogenety of proteins. The analysis of amino acid order in peptides and proteins by Edman. Main stages of protein synthesis.

8. Nucleic acids.

The structural components of nucleic acids: nitrogen basis, hydrocarbons, phosphoric acid. Chemical properties, qualitative reactions.

Nucleotides: structure, bond type, nomenclature, properties.

Mononucleotides: structure, bond types, nomenclature, properties.

RNA and DNA. The secondary structure of DNA, complementary bases. Biological meaning of nucleic acids.

ATP, structure, bond types, biological meaning.

9. Saponifiable lipids.

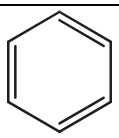
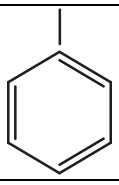
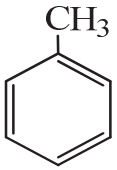
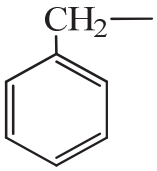
Fats (triacylglycerides). Higher fatty acids: saturated and unsaturated, spacial structure of unsaturated acids, chemical properties (hydrolysis, iodine number, peroxide oxidation).

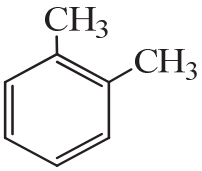
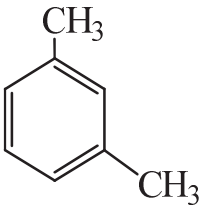
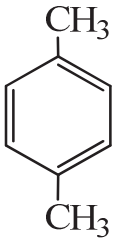
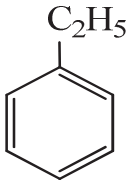
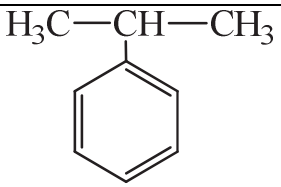
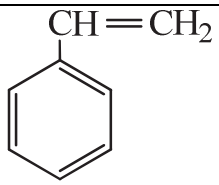
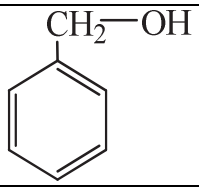
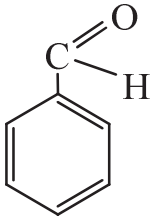
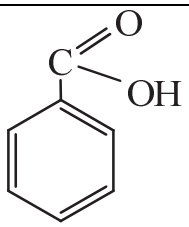
Phosphoglycerols: composition, structure of phosphate dylcholine, phosphate dylcolamine, phosphate dylserine and their biological meaning.

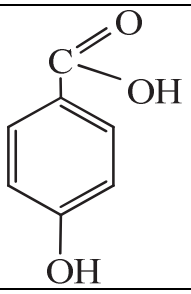
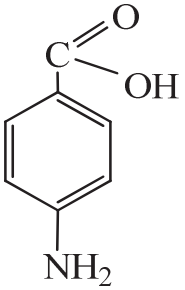
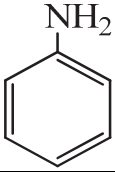
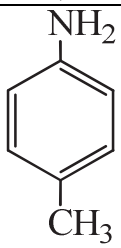
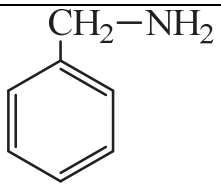
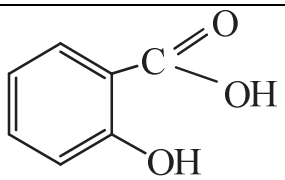
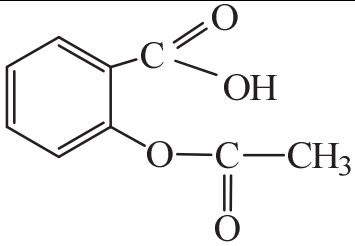
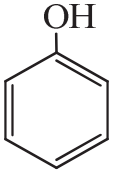
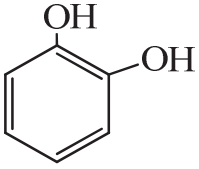
CHEMISTRY DICTIONARY

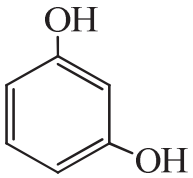
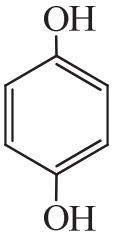
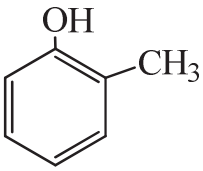
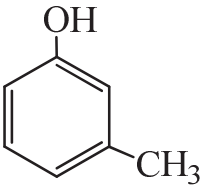
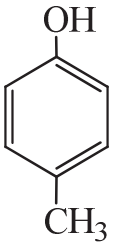
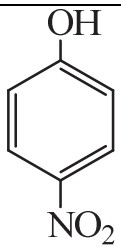
Alkanes		Radicals	
Name	**Formula**	**Name**	**Formula**
Methane	CH_4	Methyl	$CH_3—$
Ethane	$CH_3—CH_3$	Ethyl	$CH_3—CH_2—$
Propane	$CH_3—CH_2—CH_3$	Propyl	$CH_3—CH_2—CH_2—$
		Isopropyl	$CH_3—\underset{\displaystyle\vert}{CH}—CH_3$
Butane	$CH_3—CH_2—CH_2—CH_3$	Butyl	$CH_3—CH_2—CH_2—CH_2—$
		Secondary butyl	$CH_3—CH_2—\underset{\displaystyle\vert}{CH}—CH_3$
Isobutane (2 – Methyl – propane)	$CH_3—\underset{\displaystyle\vert}{\overset{\displaystyle CH_3}{CH}}—CH_3$	Isobutyl	$CH_3—\underset{\displaystyle\vert}{\overset{\displaystyle CH_3}{CH}}—CH_2—$
		Tertiary butyl	$\overset{\displaystyle\vert}{\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{CH_3—C—CH_3}}}$
Pentane	$CH_3—CH_2—CH_2—CH_2—CH_3$	Pentyl	$CH_3—CH_2—CH_2—CH_2—CH_2—$
		Secondary pentyl	$CH_3—CH_2—CH_2—\underset{\displaystyle\vert}{CH}—CH_3$
Isopentane (2– Methylbutane)	$CH_3—CH_2—\underset{\displaystyle\vert}{\overset{\displaystyle CH_3}{CH}}—CH_3$	Isopentyl	$CH_3—CH_2—\underset{\displaystyle\vert}{\overset{\displaystyle CH_3}{CH}}—CH_2—$
		Tertiarypentyl	$\overset{\displaystyle\vert}{\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{CH_3—CH_2—C—CH_3}}}$
2,2 – dimethyl – propane	$\overset{\displaystyle\vert}{\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{CH_3—C—CH_3}}}$		

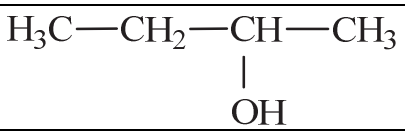
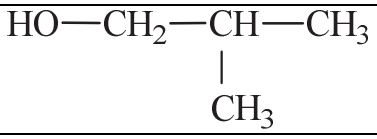
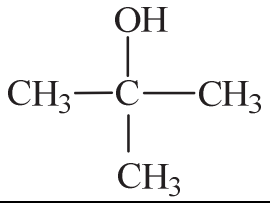
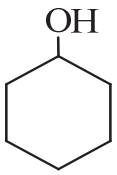
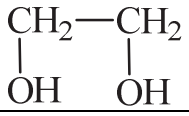
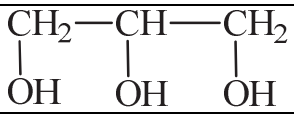
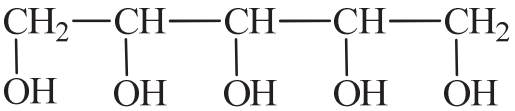
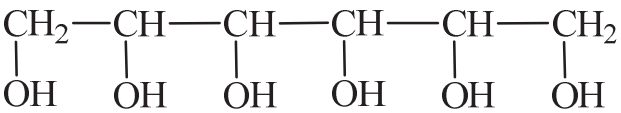
Halogenoalkanes	
Chloromethane	CH_3Cl

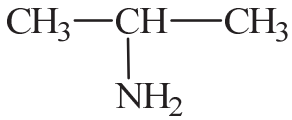
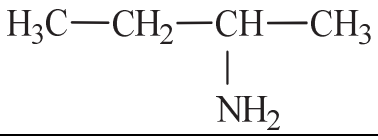
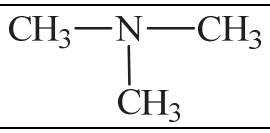
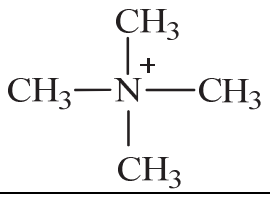
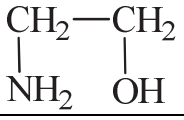
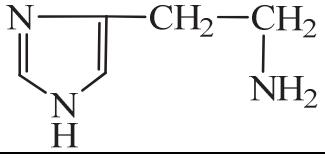
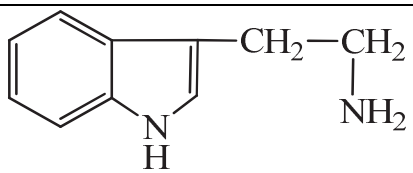
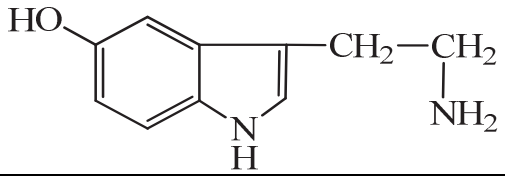
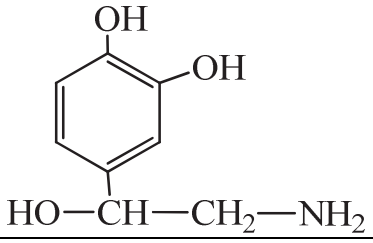
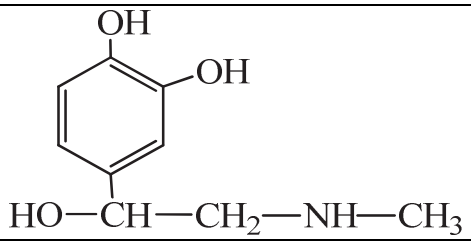
Trichloromethane (chloroform)	$CHCl_3$
Carbon tetrachloride	CCl_4
Triiodide (iodoform)	CHI_3
Chloroethane	$CH_3—CH_2—Cl$
Chloropropane	$CH_3—CH_2—CH_2—Cl$
2 – Chloropropane	$CH_3—\underset{\displaystyle Cl}{\underset{\vert}{CH}}—CH_3$
Chlorobutane	$CH_3—CH_2—CH_2—CH_2—Cl$
2 – Chlorobutane	$CH_3—CH_2—\underset{\displaystyle Cl}{\underset{\vert}{CH}}—CH_3$
Alkenes	
Ethene	$H_2C=CH_2$
Propene	$H_2C=CH—CH_3$
Butene –1	$H_2C=CH—CH_2—CH_3$
Butene – 2	$H_3C—CH=CH—CH_3$
Pentene – 1	$H_2C=CH—CH_2—CH_2—CH_3$
Pentene – 2	$H_3C—CH_2—CH=CH—CH_3$
Arenes (Benzene and its derivatives)	
Benzene	
Phenyl	
Toluene	
Benzyl	

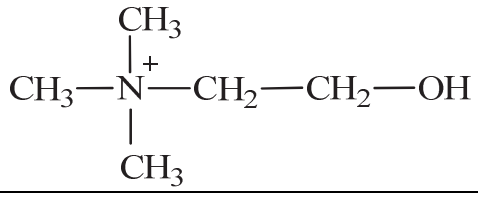
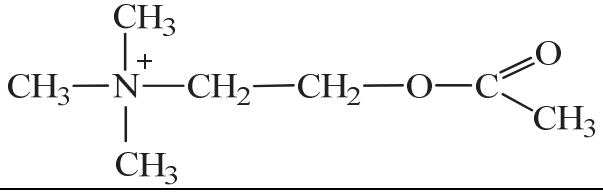
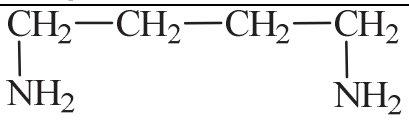
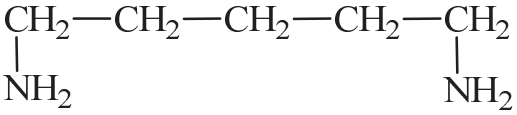
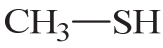
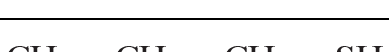
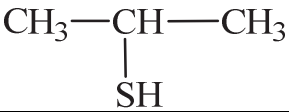
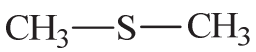
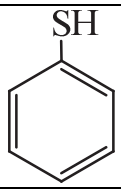
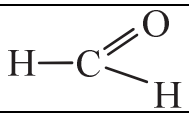
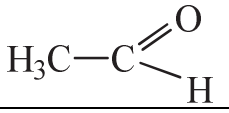
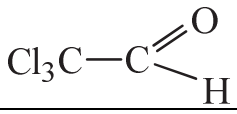
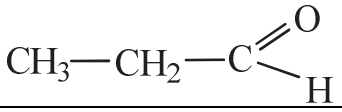
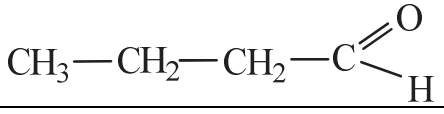
Xylene: o – xylene (o – dimethylbenzene)	
m – xylene (m – dimethylbenzene)	
p – xylene (p – dimethylbenzene)	
Ethylbenzene	
Isopropylbenzene (cumene)	
Sterol (vinyl benzene)	
Benzyl alcohol	
Benzaldehyde	
Benzoic acid	

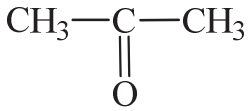
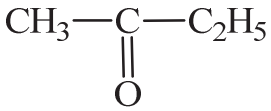
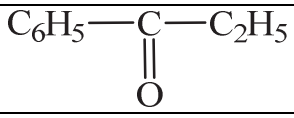
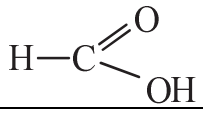
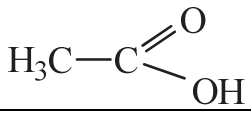
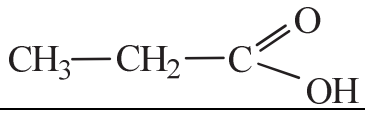
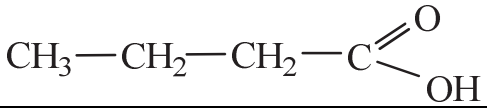
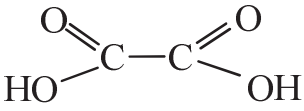
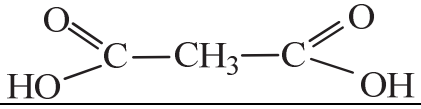
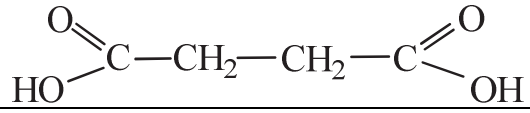
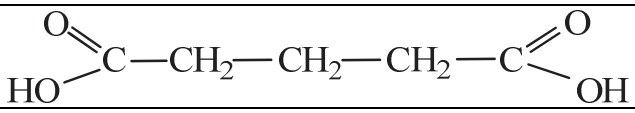
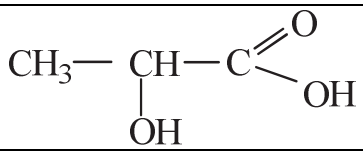
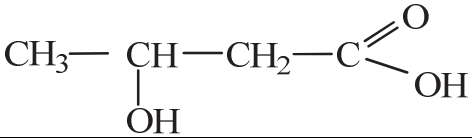
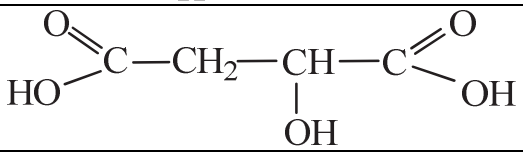
Paraoxybenzoic acid	
Para–aminobenzoic acid	
Aniline (aminobenzene)	
Para–Methylaniline	
Benzylamine	
Salicylic acid	
Acetylsalicylic acid	
Phenol	
Ortho–dioxybenzene (pirokatekhin)	

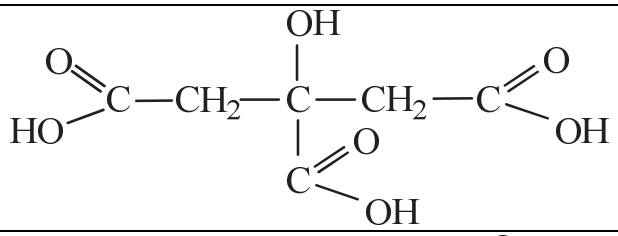
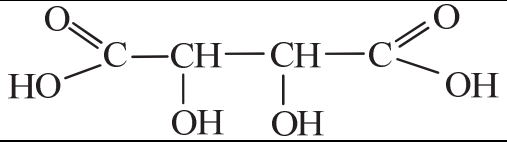
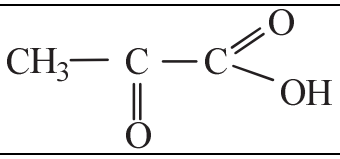
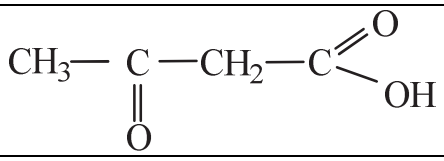
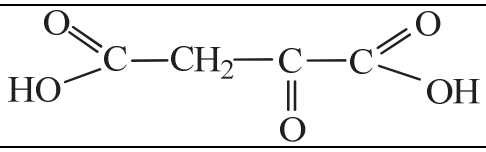
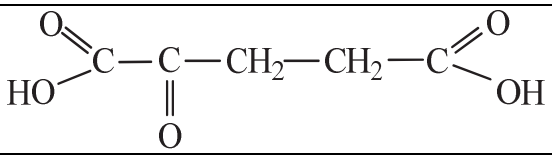
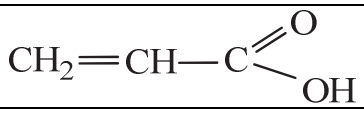
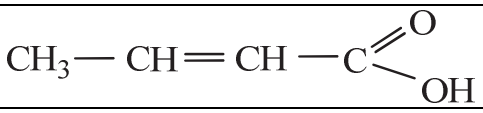
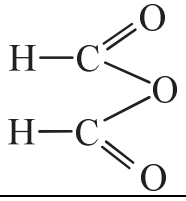
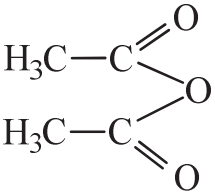
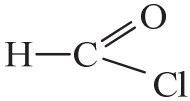
Meta–dioxybenzene (resorcin)	
Para–dioxybenzene (hydroquinone)	
Cresol: ortho – cresol (ortho – methylphenol)	
meta – cresol (meta – methylphenol)	
para – cresol (para – methylphenol)	
Para – nitrophenol	
Alcohols (R–O– alkoxy group)	
Methanol	$CH_3—OH$
Methoxy	$CH_3—O—$
Ethanol	$CH_3—CH_2—OH$
Ethoxy	$CH_3—CH_2—O—$
Propanol	$CH_3—CH_2—CH_2—OH$
Isopropanol	$CH_3—\underset{\displaystyle OH}{\underset{\vert}{CH}}—CH_3$

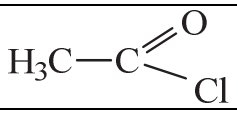
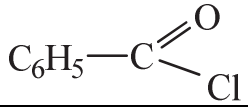
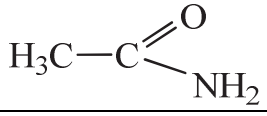
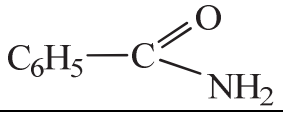
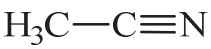
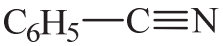
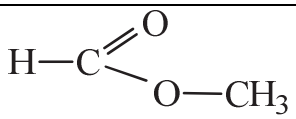
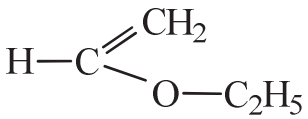
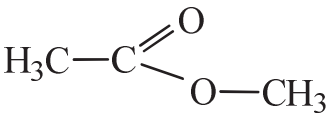
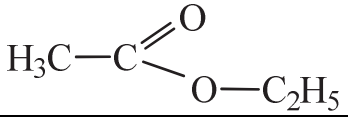
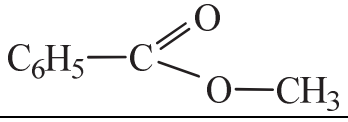
Butanol	$CH_3—CH_2—CH_2—CH_2—OH$
Secondary butanol	
Isobutanol	
Tributanol	
Cyclohexanol	
Vinyl alcohol	$H_2C=CH—OH$
Polyatomic alcohols	
Ethylene glycol (ethandiol)	
Glycerol (propantriol)	
Xylitol	
Sorbitol	
Ester (ethers)	
Dimethyl ether	$CH_3—O—CH_3$
Diethyl ether (medical ether)	$C_2H_5—O—C_2H_5$
Phenyl ethyl ether	$C_6H_5—O—C_2H_5$
Amines	
Metylamine	$CH_3—NH_2$
Ethylamine	$CH_3—CH_2—NH_2$
Propylamine	$CH_3—CH_2—CH_2—NH_2$

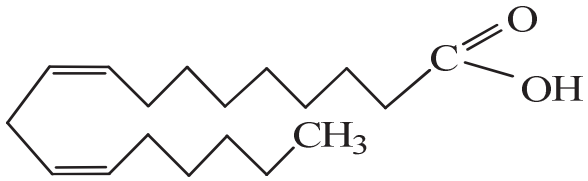
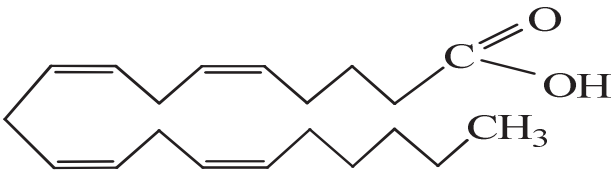
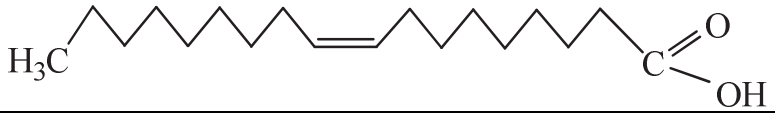
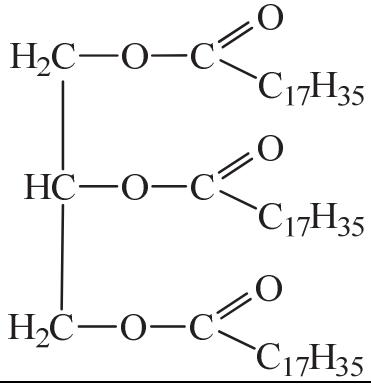
Isopropylamine (2 – aminopropane)	
Butylamine	
Secondary – butylamine	
Primary amine (metylamine)	
Secondary–amine (dimetylamine)	
Tertiary amine (trimetylamine)	
Quaternary basis	
Biogenic amines	
Calamine (ethanolamine)	
Histamine	
Tryptamine	
Serotonin	
Norepinephrine	
Adrenaline	

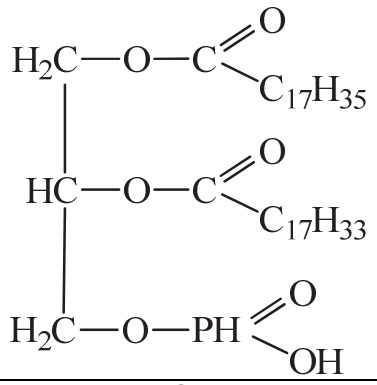
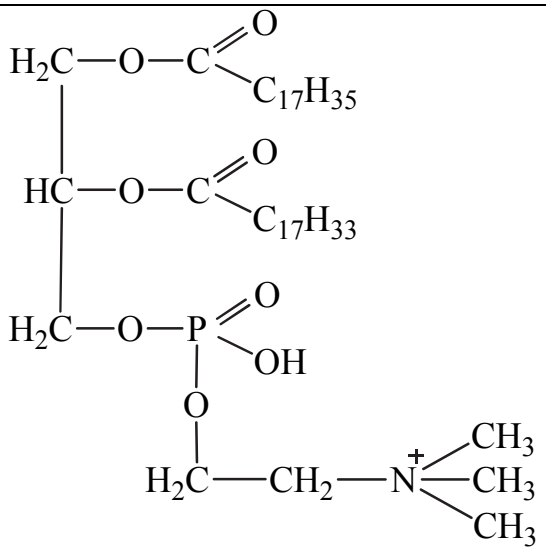
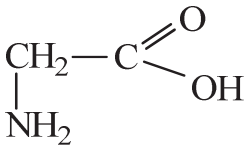
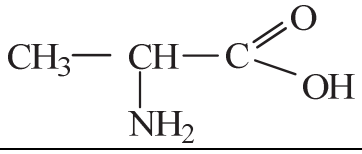
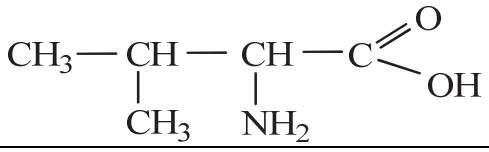
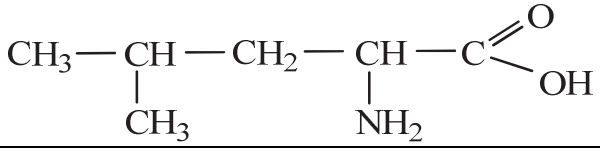
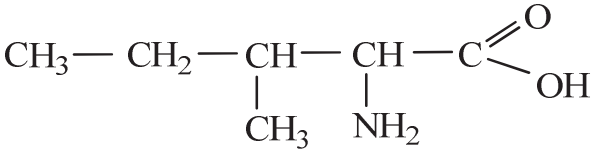
Choline	
Acetylcholine	
Putrescine	
Cadaverine	
Thiols (mercaptans)	
Methanethiol (mercaptomethane)	
Ethanethiol	
Propanethiol	
Isopropanethiol	
Dimethyl sulfide	
Thiophenol	
Aldehydes	
Methanal (formaldehyde, formic)	
Ethanal (acetaldehyde, acetic)	
Trichloracetic aldehyde	
Propanal (propionic)	
Butanal (oil)	
Ketones	

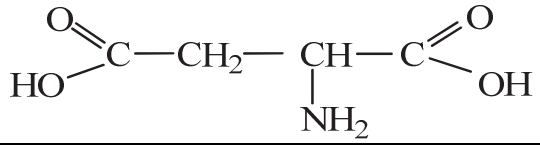
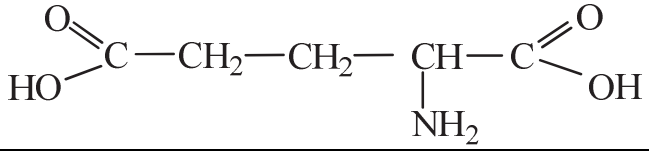
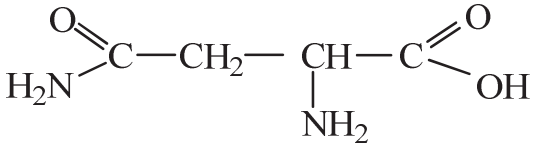
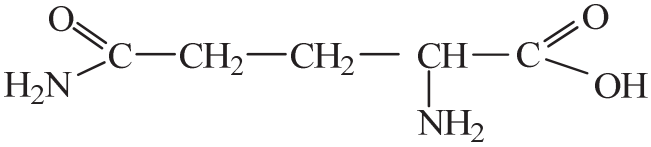
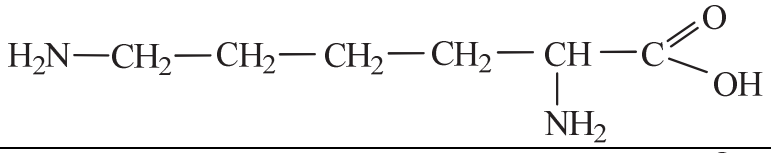
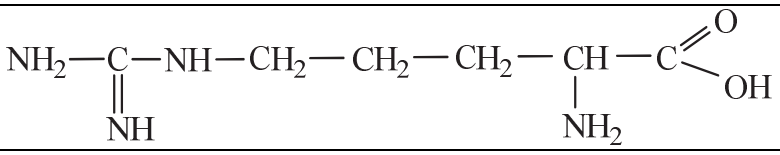
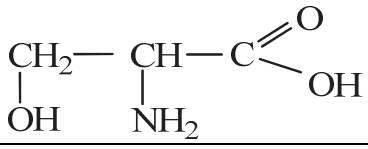
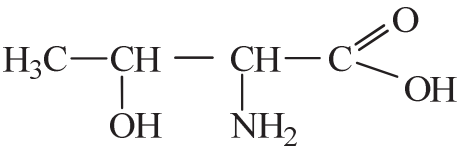
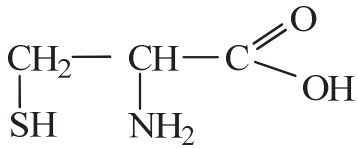
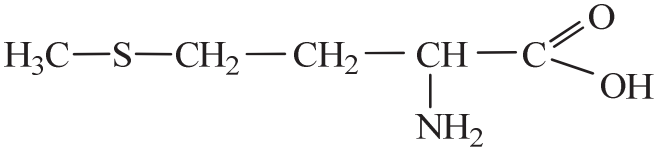
Acetone (dimethylketone)	
Methylethylketone	
Phenylethylketone (propiophenone)	
Carbonic acid	
Formate (methanoic, formic)	
Acetate (ethanoic, acetic)	
Propionate (propanoic)	
Butyrate (butanoic, oil)	
Dicarboxylic acids	
Oxalate (sorrel)	
Malonate (malonic)	
Succinate (amber, butanedioic acid)	
Glucarate (glutaric)	
Oxyacids	
Lactate (milk, 2 – oxypropane)	
β – Oxybutyrate (β – hydroxybutyric, 3 – oxobutanoate)	
Malate (apple, 2 – oxybutanedioic)	

Citrate (lemon acid)	
Tartare (wine acid)	
Oxoacids	
Pyruvate (PA, pyruvic, 2 – oxopropane)	
Acetoacetate (3 – oxobutanoate)	
Oxaloacetate (2 – oxobutandioic)	
α – Ketoglutarate (α – ketoglutaric, 2 – oxopentadioic)	
Unsaturated carboxylic acid	
Acrylate (acrylic, 2 – propenoic)	
Crotonic (2 – butenoic)	
Anhydrides	
Formic	
Acetic	
Halogenanhydrides	
Methyl chloride	

Acetyl chloride	
Benzoyl chloride	
Amides, nitriles	
Acetamide	
Benzamide	
Acetonitrile	
Benzonitrile	
Esther	
Methyl formate (methyl methanoate)	
Ethyl formate	
Methyl acetate	
Ethyl acetate	
Methyl benzoate	

Lipids	
Higher fatty acids	
Palmitic $C_{15}H_{31}COOH$	
Stearic $C_{17}H_{35}COOH$	
Oleic $C_{17}H_{33}COOH$	
Linoleic $C_{17}H_{31}COOH$	
Linolenic $C_{17}H_{29}COOH$	
Arachidonic $C_{19}H_{31}COOH$	
Oleic $C_{17}H_{33}COOH$	
Triacylglycerides (tristearine)	

Phosphatidic acid	
Phosphoglyceride (phosphatidylcholine)	
Amino acids	
Monoaminomonocarboxylic acid	
Glycine (Gly)	
Alanine (Ala)	
Valine* (Val)	
Leucine* (Leu)	
Isoleucine* (ile)	
Monoaminodicarboxylic acid	

Aspartic (Asp) (aspartate)	
Glutamic acid (Glu)	
Asparagine (Asn)	
Glutamine (Gln)	
Diaminomonocarboxylic acid	
Lysine*(Lys)	
Arginine (Arg)	
Oxyamino acid	
Serine*(Ser)	
Threonine (Thr)	
Sulfur-containing amino acids	
Cysteine (Cys)	
Methionine*(Met)	
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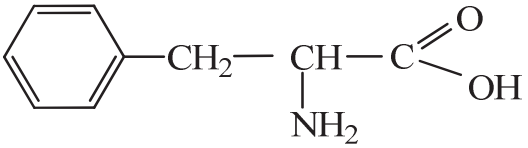
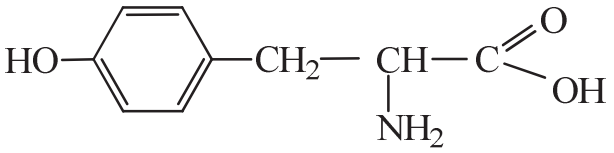
Phenylalanine*(Phe)	

Tyrosine (Tyr)	
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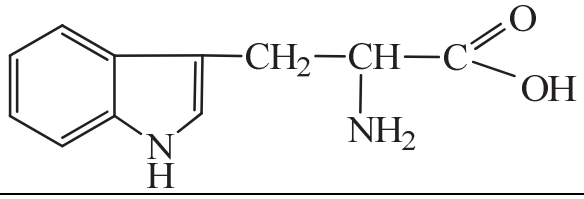
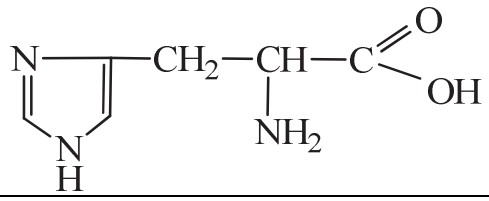
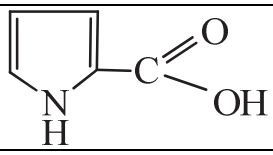
Tryptophan*(Trp)	
Histidine (His)	
Proline (Pro)	
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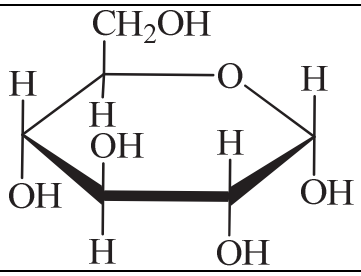
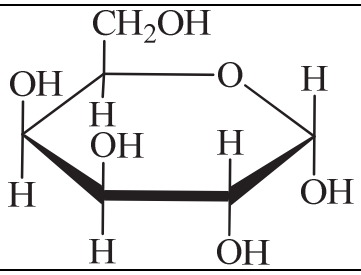
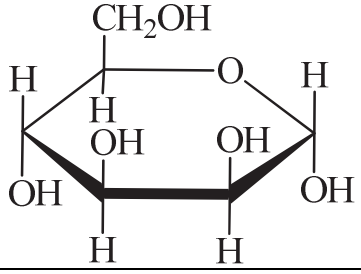
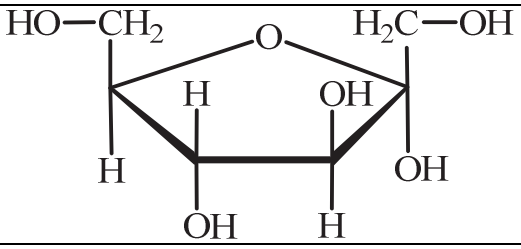
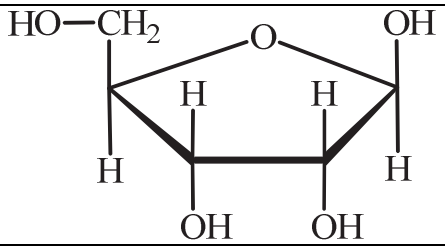
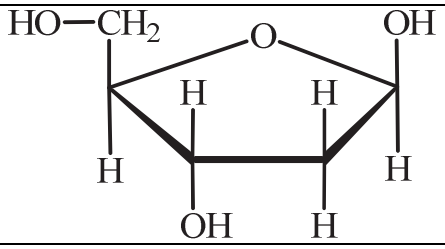
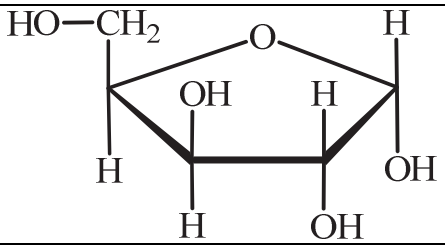
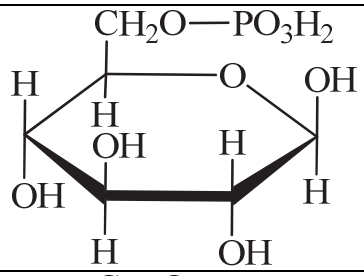
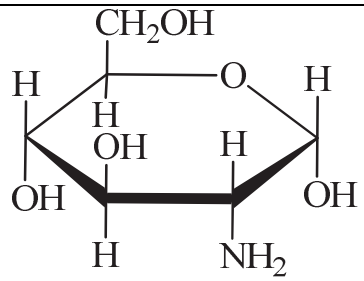
Glucose	
Galactose	
Mannose	
Fructose	

Ribose	
Deoxyribose	
Xylose	
Glucose - 6 phosphate	
Glucosamine	
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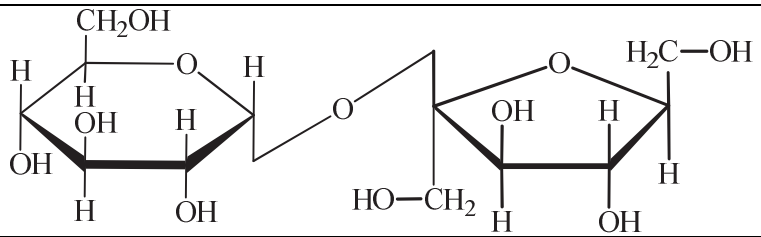
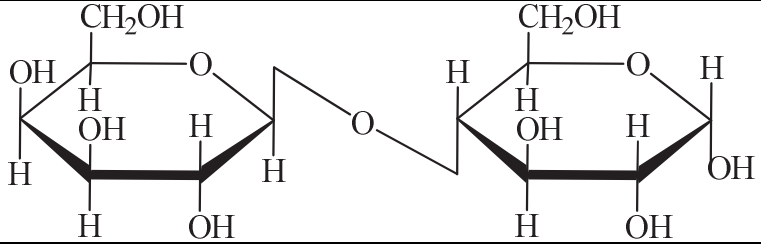
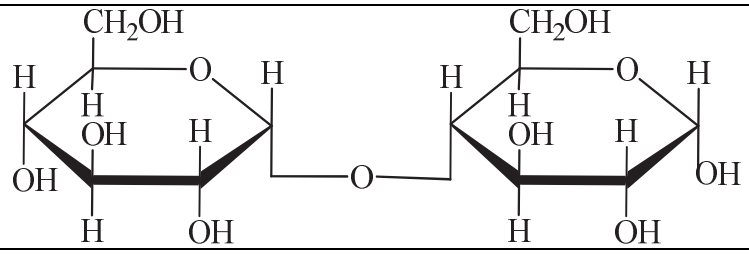
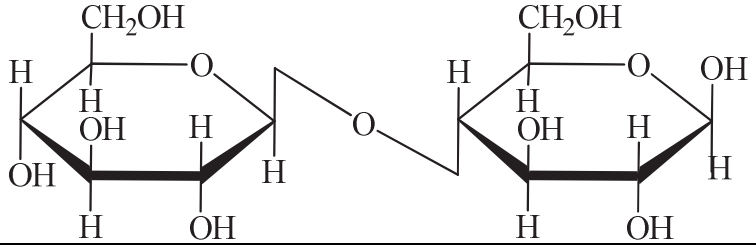
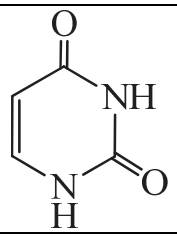
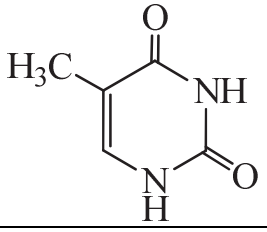
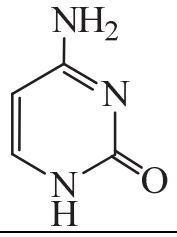
Sucrose	
Lactose	

Maltose	
Cellobiose	
Nitrogenous base	
Pyrimidine line	
Uracil	
Thymine	
Cytosine	
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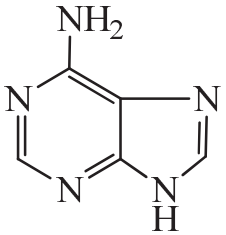
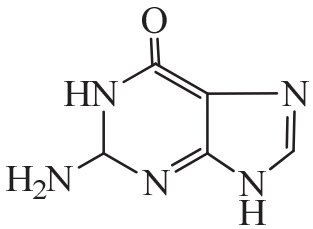
Adenine	
Guanine	

ДЛЯ НОТАТОК

Навчальне видання

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Шунков Василь Сергійович

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Навчальний посібник

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