

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
ХАРКІВСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ

**FUNDAMENTALS OF STRUCTURE
AND REACTIVITY OF ORGANIC COMPOUNDS**

Methodical instructions for 1st year students' self-work
in Biological and Bioorganic Chemistry
(module 1)

**ОСНОВИ БУДОВИ ТА РЕАКЦІЙНОЇ ЗДАТНОСТІ
ОРГАНІЧНИХ СПОЛУК**

Методичні вказівки для самостійної роботи студентів 1-го курсу
з біологічної та біоорганічної хімії
(модуль 1)

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Основи будови та реакційної здатності органічних сполук: метод. вказ. для самостійної роботи студентів 1-го курсу з біол. та біоорг. хімії /уклад. Г.О. Сирова, Л.Г. Шаповал, В.М. Петюніна та ін. – Харків: ХНМУ, 2014.– 45 с.

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Subject I. CLASSIFICATION, ISOMERISM AND NOMENCLATURE OF ORGANIC COMPOUNDS

Motivational characteristic of subject

During the study of chemical processes in the organism you will meet a lot of different organic compounds. To understand the variety of substances, it is necessary to know their scientific classification and nomenclature.

Objective

To study the structure and isomerism of important classes of mono-, poly- and heterofunctional compounds. To develop the ability to use chemical nomenclature for the naming of biologically active substances.

Training questions

1. To know the classification of organic compounds according to the carbon skeleton and functional groups.
2. To be able to make formulae of structural isomers of main classes of organic compounds.
3. To be able to name simple organic substances according to IUPAC nomenclature and radical-functional nomenclature.
4. To know the structure of the most important classes of poly- and heterofunctional compounds, to be able to write formulae of their isomers.

Methodological questions

1. Regularity of changes of properties in a homologous series is an example of transition from quantitative to qualitative changes.
2. Poly- and heterofunctionality is one of the characteristic signs of substances involved in the processes of vital activity.

Initial level

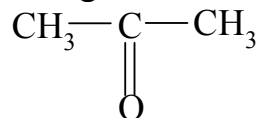
1. Basics of A.M. Butlerov's Theory of chemical structure of organic compounds.
2. General concepts of isomerism.
3. Main classes of organic substances.
4. Basic rules of systematic nomenclature of individual classes of organic compounds.

Practical skills

1. To learn to identify the belonging of compounds to the corresponding class.
2. To be able to name the organic substances.

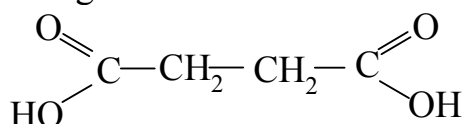
Test questions

1. What class of compounds does acetone belong to? Acetone is found in the urine of patients suffering from diabetes, the structure of acetone is:



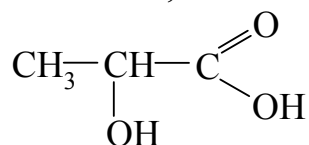
Name it according to IUPAC nomenclature and radical-functional nomenclature.

2. What class of chemical substances does succinic acid which is formed in Krebs cycle belong to?



3. Write a structure of halothane (1,1,1-trifluoro-2-bromo-2-chloro ethane), a substance used for inhalation narcosis.

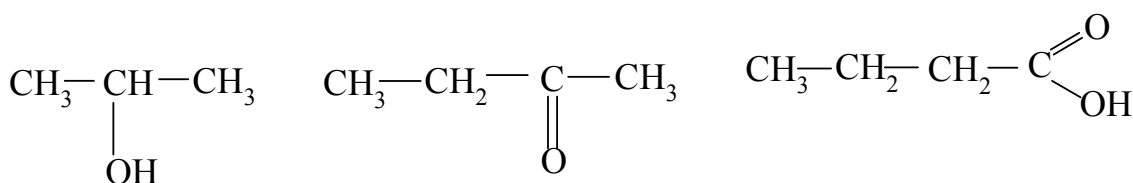
4. What functional groups does lactic acid, the product of decomposition of glycogen (animal starch) in the muscles, contain? Its structure is:



Give IUPAC name.

Teaching tasks

Task №1. What functional groups are in composition of the following molecules?

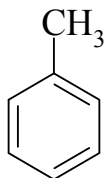


Name the classes to which these compounds belong to.

Solution. Nowadays more than six million of organic compounds are known. The reason of such variety is the ability of carbon atoms to connect together to form open and closed chains. In this case, the carbon atoms can be combined in various combinations to cause isomerism of the carbon skeleton. In order to understand such a huge number of substances precise classification is needed. All organic compounds are usually divided into three major groups:

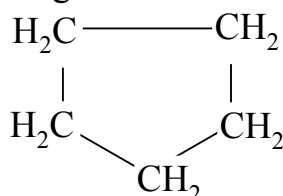
1. Acyclic compounds having an open chain of carbon atoms, for example:

3) aromatic containing aromatic ring, for example:



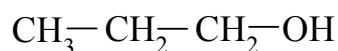
methylbenzene (toluene);

4) alicyclic containing non-aromatic cycles, for example:



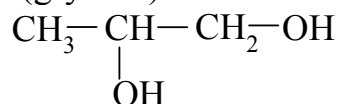
cyclopentane

Alcohols are derivatives of hydrocarbons formed by replacing of one or more hydrogen atoms by hydroxyl groups. Depending upon the number of hydroxyl groups alcohols are classified as: monohydric alcohols with one hydroxyl group:



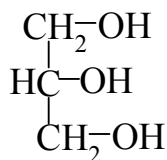
propanol;

dihydric alcohols (glycols) with two hydroxyl groups:



propylene glycol;

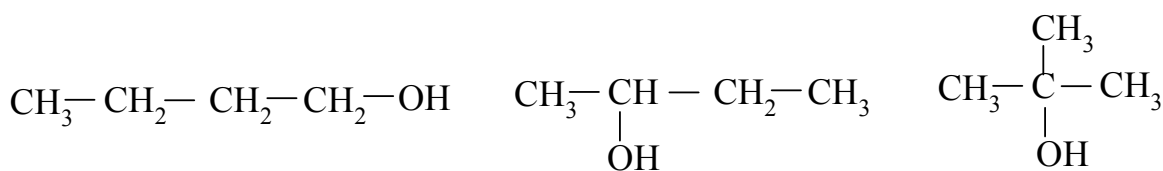
trihydric alcohols (glycerols) with three hydroxyl groups:



glycerin

Tetra-, penta-, and hexahydric alcohols also exist.

Depending upon the position of hydroxyl group monohydric alcohols are classified as primary, secondary, and tertiary ones. In primary alcohols the substituent is connected to the primary carbon atom, i.e. with carbon bonded to only one neighboring carbon; in secondary alcohols – with secondary carbon atom; in tertiary ones – with tertiary carbon:

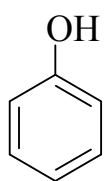


butan-1-ol

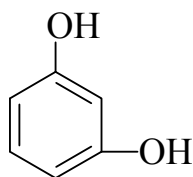
butan-2-ol

2-methylpropan-2-ol

Compounds in which hydroxyl group is directly connected to carbon atom of benzene ring are called phenols. Phenols similarly to alcohols can be mono-, di-, and trihydric:

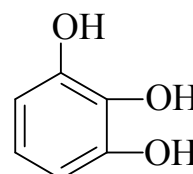


phenol



resorcinol

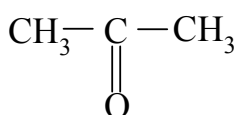
(dihydric phenol, diphenol)



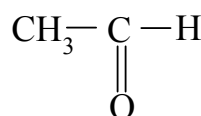
pyrogallol

(trihydric phenol)

Compounds containing carbonyl group >C=O are known as oxo compounds. If carbon atom of carbonyl group is bonded to two hydrocarbon radicals then compound is said to be a ketone, if carbon atom of carbonyl group is bonded to one radical then compound is an aldehyde:



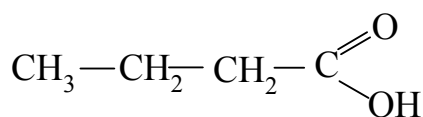
acetone (dimethylketone)



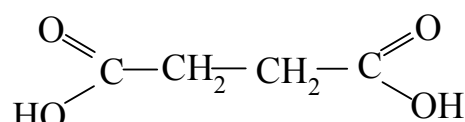
acetaldehyde

Compounds containing carboxyl group -C(=O)OH belong to carboxylic acids.

Monobasic and dibasic acids are distinguished according to the number of carboxyl groups:

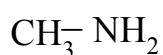


butyric (monobasic)

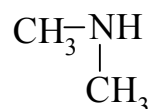


succinic (dibasic)

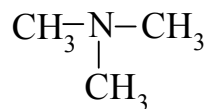
Amines are derivatives of ammonium in which hydrogen atoms are substituted by hydrocarbon radicals. Depending upon number of hydrocarbon radicals primary, secondary and tertiary amines are distinguished:



methylamine



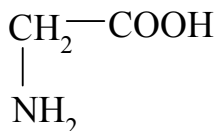
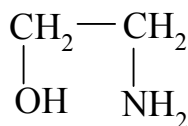
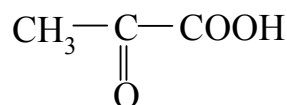
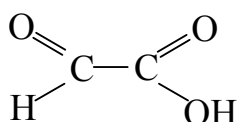
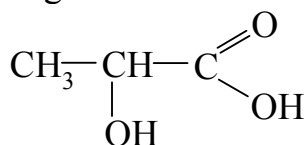
dimethylamine



trimethylamine

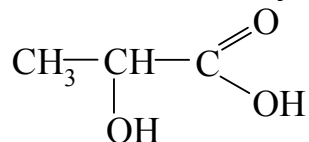
In the given task the first compound is a secondary alcohol, the second one is a ketone, the third one is a carboxylic acid, and the fourth one is a secondary amine.

Task №2. Define classes of heterofunctional compounds which the following substances belong to:



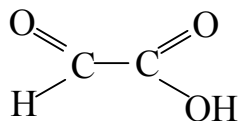
Solution. Organic compounds containing different functional groups are called heterofunctional compounds. Combinations of functional groups make up the following classes of compounds:

1) hydroxy acids which contain hydroxyl and carboxyl groups:

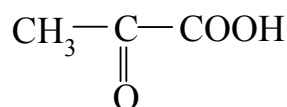


lactic acid;

2) aldo- and keto acids which contain carbonyl and carboxyl groups:

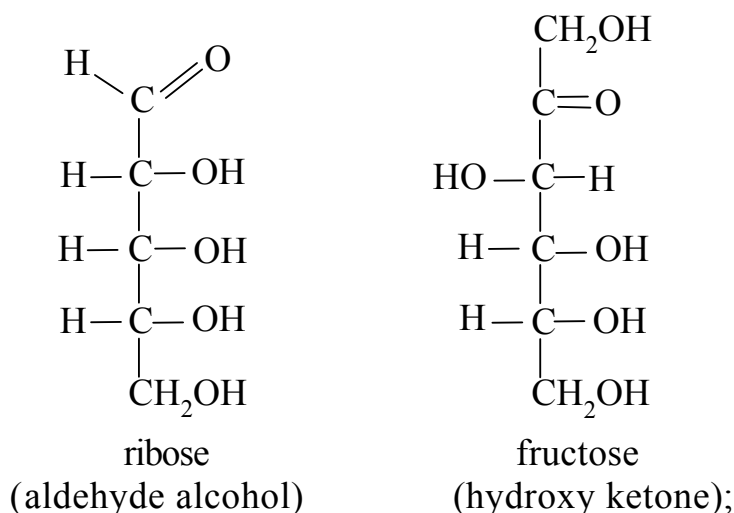


glyoxalic acid

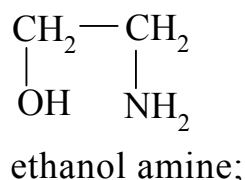


pyruvic acid;

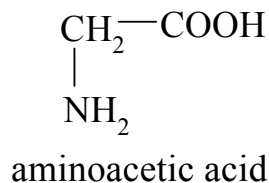
3) aldehyde alcohols and hydroxy ketones which contain hydroxyl and carbonyl groups:



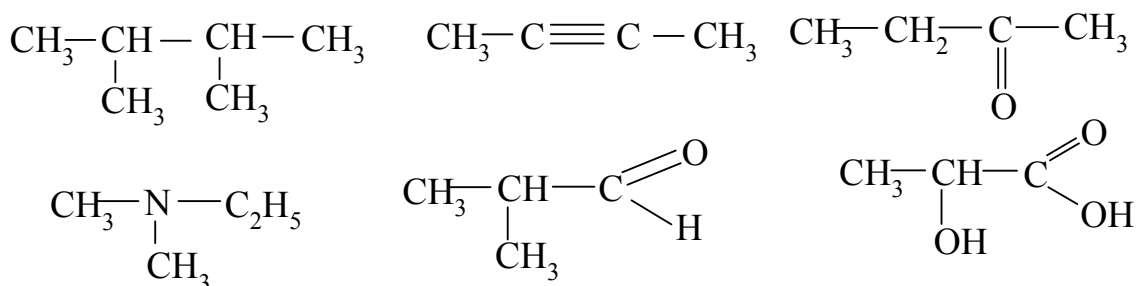
4) amino alcohols which contain hydroxyl and amino groups:



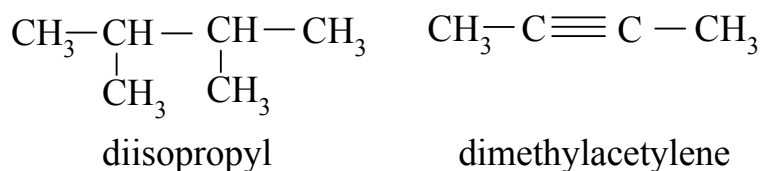
5) amino acids which contain carboxyl and amino groups:



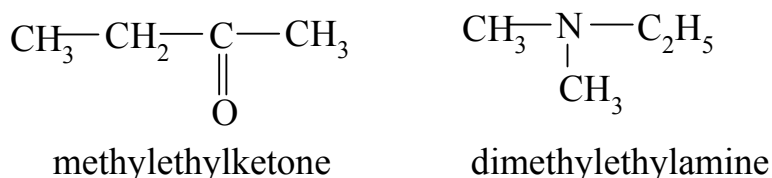
Task № 3. Name according to radical-functional (rational) nomenclature:



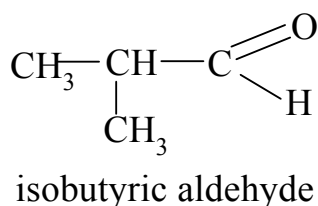
Solution. Organic chemistry, which describes the millions of compounds, requires accurate and precise nomenclature, so that every single formula matches one name. At an early stage of development of chemistry compounds were given names associated primarily with the source of obtaining. Some of such names are still common: acetic acid, lactic acid, acetone, etc (trivial names). New radical-functional nomenclature gives names associated with the structure. The names of hydrocarbons are derived from the name of the first member of the corresponding homologous series with the indication of positions of substituents:



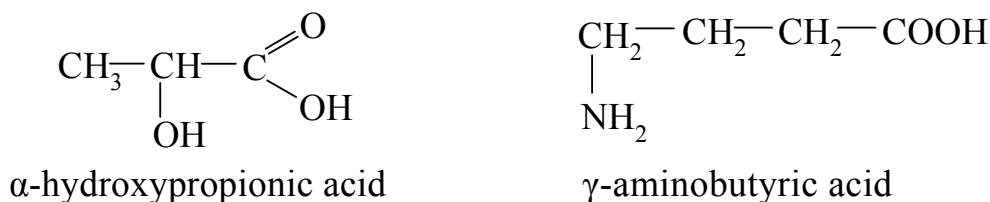
Ketones and amines are named according to the hydrocarbon radicals in their composition:



Names of aldehydes come from the names of corresponding acids:

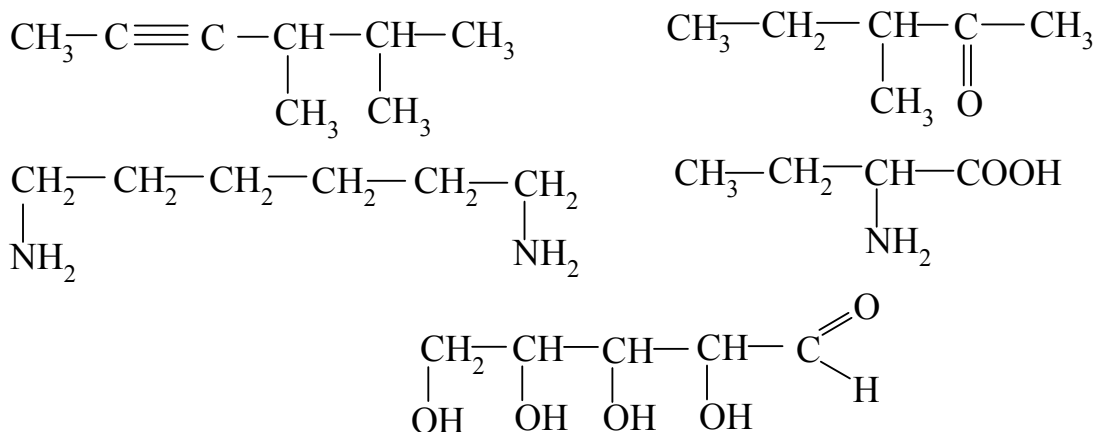


Names of heterofunctional compounds containing carboxyl group are derived from names of corresponding acids with designation of other functional groups. The mutual position of functional groups is indicated by Greek letters:



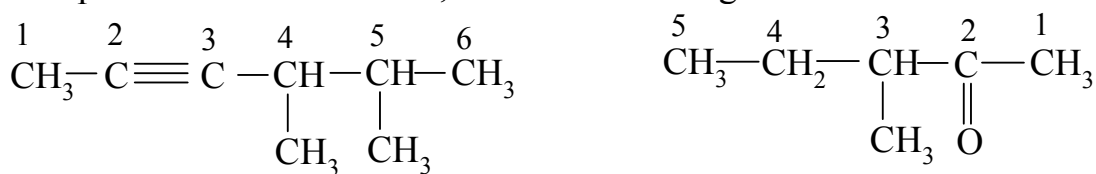
Radical-functional nomenclature is reasonable for comparatively simple compounds. Not all isomers with great number of carbon atoms can be given radical-functional (rational) names.

Task № 4. Name according to IUPAC nomenclature:



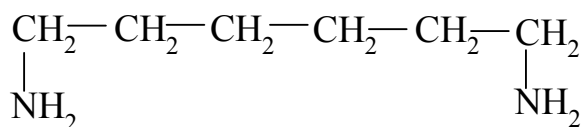
Solution. Modern official scientific nomenclature has been developed and offered by International Union of Pure and Applied Chemistry (IUPAC nomenclature). The basis for the IUPAC name of the compound is the longest carbon chain in the molecule. The names of saturated hydrocarbons have suffix -ane, names of hydrocarbons with double bond have suffix -ene, names of hydrocarbons with a triple bond have suffix -yne. The compounds of other classes differ by secondary suffixes added to the name of the corresponding hydrocarbon. In particular, alcohols have secondary suffix -ol, aldehydes – -al, ketones – -one, carboxylic acids – -oic acid, amines have prefix –amino.

Compounds listed in the task, have the following names:



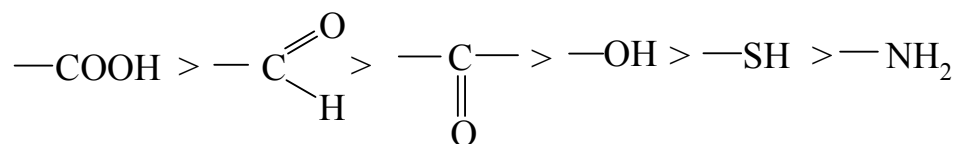
4,5-dimethyl-2-hexene

3-methyl-pentanone-2

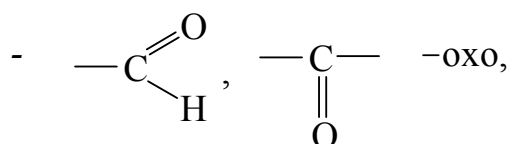


1,6-diaminohexane

In heterofunctional compounds one group is treated as the principal functional group. The other group is regarded as the secondary functional group and may be treated as substituent. The order for the preference of principal functional group is as given below:

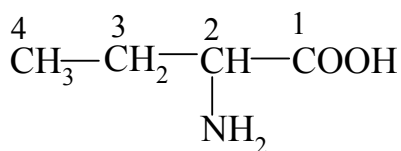


The principal functional group is written as suffix while the secondary functional group is written as prefix:

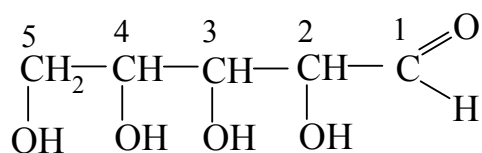


-OH - hydroxy, -SH - mercapto, -NH₂ - amino.

The IUPAC names of heterofunctional compounds are given below:



2-aminobutanoic acid



2,3,4,5-tetrahydroxypentanal

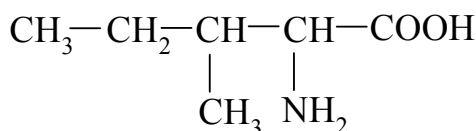
Revision exercises

№ 1

1. Write the structural formulae of isomers of carboxylic acid $\text{C}_4\text{H}_8\text{O}_2$. Name them according to IUPAC.
2. Write the rational and IUPAC names of aminalonn $\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{COOH}$. Aminalonn participates in brain metabolism.
3. Write the structural formula of 1,1,2-trichloroethane which is used for short-term narcosis. What class of compounds does it belong to?

№ 2

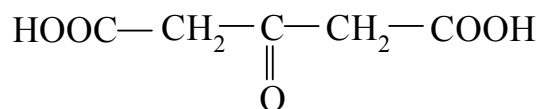
1. Write the structural formulae of isomers of butanol ($\text{C}_4\text{H}_9\text{OH}$). Name them according to IUPAC.
2. Write the IUPAC name of proteinogenous amino acid having the structure:



3. Write the structural formula of 2-oxobutanedioic acid (oxaloacetic acid) which is the intermediate in carbohydrates metabolism.

№ 3

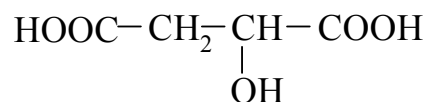
1. Write three structural formulae of isomers of aldehyde $\text{C}_5\text{H}_{10}\text{O}$. Name them according to IUPAC.
2. Write the IUPAC name of acetone-dicarboxylic acid which belongs to ketone bodies detected in urine of patients suffering from diabetes mellitus:



3. Write the structural formula of xylite (pentanepentaol-1,2,3,4,5) which is used as sugar substitute.

№4

1. Write three structural formulae of isomers of alcohol $C_5H_{11}OH$. Name them according to IUPAC.
2. Write the IUPAC name of malic acid which participates in Krebs cycle:

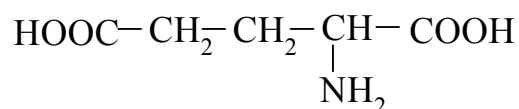


Indicate functional groups in the molecule.

3. Write the structural formula of o-hydroxybenzoic acid (salicylic acid) which is the parent structure of analgesic, antipyretic and anti-inflammatory drugs.

№5

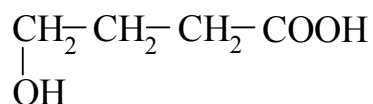
1. Give examples of primary, secondary and tertiary amines. Give their rational names.
2. Write the IUPAC name of glutamic acid which is used for nervous system diseases treatment:



3. Write the structural formula of glycerin (propanetriol-1,2,3) which enters the composition of lipids.

№ 6

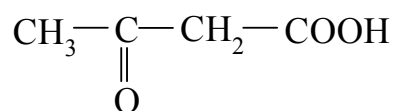
1. Write three structural formulae of isomers of ketone $C_5H_{10}O$. Name them according to IUPAC.
2. Write the IUPAC name of γ -hydroxybutyric acid which is used in anesthesiology:



3. Write the structural formula of penicillamine (2-amino-3-mercapto-3-methylbutanoic acid) which is used in case of poisonings with heavy metals.

№7

1. Write three structural formulae of isomers of hexanol $C_6H_{13}OH$. Name them according to IUPAC.
2. Write the IUPAC name of acetoacetic acid which forms in the metabolism of higher fatty acids:

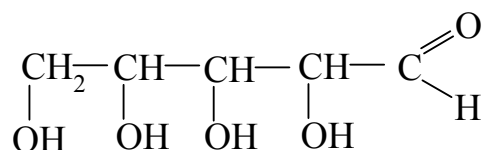


3. Write the structural formula of β -pyridine carboxylic acid (nicotinic acid, vitamin PP).

№ 8

1. Write three structural formulae of isomers of aldehyde $\text{C}_6\text{H}_{12}\text{O}$. Name them according to IUPAC.

2. Write the IUPAC name of monosaccharide ribose which enters the composition of ribonucleic acids:

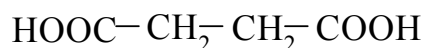


3. Write the structural formula of 2-amino-3-hydroxypropanoic acid (proteinogenous amino acid serine).

№ 9

1. Write three structural formulae of isomers of ketone $\text{C}_6\text{H}_{12}\text{O}$. Name them according to IUPAC.

2. Write the IUPAC name of succinic acid which forms in the metabolism of carbohydrates:

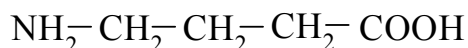


3. Write the structural formula of p-aminobenzoic acid which is the parent structure of anesthetic drugs.

№ 10

1. Write three structural formulae of isomers of carboxylic acid $\text{C}_6\text{H}_{12}\text{O}_2$. Name them according to IUPAC.

2. Write the IUPAC name of γ -aminobutyric acid which participates in brain metabolism:



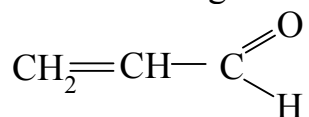
3. Write the structural formula of cadaverine (1,5-diaminopentane) which forms in proteins decay.

№11

1. Write three structural formulae of isomers of octanol $\text{C}_8\text{H}_{17}\text{OH}$ Name them according to IUPAC.

2. Write the IUPAC name of acrolein which is the intermediate in the

synthesis of some organic compounds:

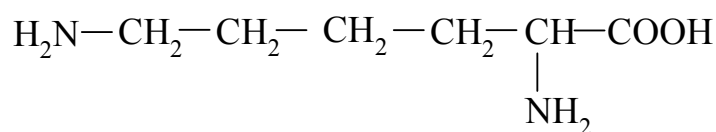


3. Write the structural formula of p-aminophenol (4-amino-1-hydroxybenzene) which is the parent structure of a group of analgesic and antipyretic drugs. Name functional groups.

№ 12

1. Write three structural formulae of isomers of aldehyde $\text{C}_7\text{H}_{14}\text{O}$. Name them according to IUPAC.

2. Write the IUPAC name of proteinogenous amino acid lysine:

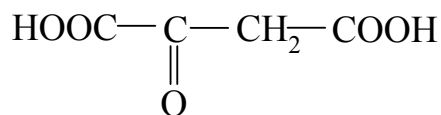


3. Write the structural formula of 5-hydroxypentanal.

№13

1. Write three structural formulae of isomers of ketone $\text{C}_7\text{H}_{14}\text{O}$. Name them according to IUPAC.

2. Write the IUPAC name of the acid which forms in the Krebs cycle:

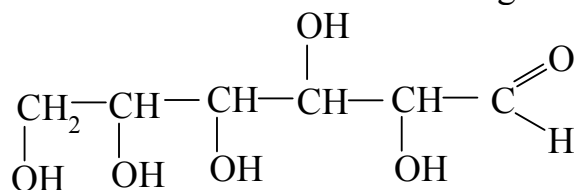


3. Write the structural formula of proteinogenous amino acid cysteine (2-amino-3-mercaptopropanoic acid).

№14

1. Write three structural formulae of isomers of carboxylic acid $\text{C}_8\text{H}_{16}\text{O}_2$. Name them according to IUPAC.

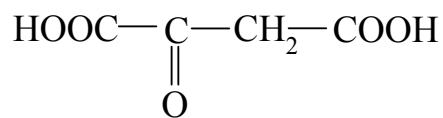
2. Write the IUPAC name of monosaccharide glucose:



3. Write the IUPAC name of 3-oxopentanedioic acid which belongs to ketone bodies detected in urine of patients suffering from diabetes mellitus.

1. Write the structural formulae of isomers of butanal. Name them according to IUPAC.

2. Write the IUPAC name of oxaloacetic acid which is the intermediate in carbohydrates metabolism.



3. Write the structural formula of sorbitol (hexanehexaol-1,2,3,4,5,6) which is used as sugar substitute.

Subject II. SPATIAL STRUCTURE OF ORGANIC MOLECULES. MUTUAL INFLUENCE OF ATOMS.

Motivational characteristic of subject

Chemical and biochemical behavior of substances depends upon their composition, electronic and spatial structure.

Objective

To study the electronic and spatial structure of aliphatic, carbocyclic and heterocyclic compounds as the basis for understanding of the relationship of the structure and biological activity.

Training questions

1. To know the electronic structure and spatial arrangement of bonds formed by carbon atoms in the sp^3 -, sp^2 -, and sp -hybridization states.

2. To know the basic types of conformations of the open-chain compounds (eclipsed, staggered, gauche), and to be able to assess their energy.

3. To understand the features of the electronic structure of conjugated systems with open and closed chains.

4. To know the spatial structure of cycles formed by carbon atoms in the sp^3 -hybridization state (cyclopropane, cyclohexane), the main conformations of cyclohexane and location of axial and equatorial bonds.

5. To know what is the cis-trans-isomerism and what is its reason.

6. To be able to determine the sign and kind of electronic effects of substituents.

Methodological questions

1. Connection between structure and biological activity is the chemical basis of functioning of biologically active substances.
2. Changing in properties at the transition from cyclohexadiene to the benzene is an example of a qualitative leap.

Initial level

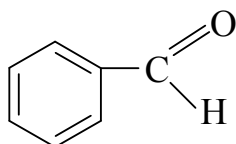
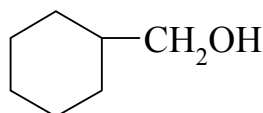
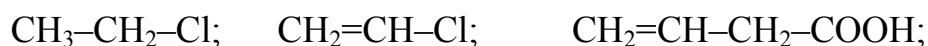
1. Hybridization of atomic orbitals.
2. sp^3 -, sp^2 -, sp -Hybridization.
3. Structure of σ - and π -bonds.

Practical skills

To be able to predict chemical behavior of organic compounds basing on their structure.

Test questions

1. Indicate the type of hybridization of all carbon atoms and electronic effects of substituents in the following compounds:



2. Draw eclipsed and staggered conformations of 1,2-dichloroethane.
3. Draw cyclohexanediol-1,4 in the chair conformation with the most energetically advantageous location of substituents.
4. Give the definition for “conjugation” and explain the reason of increased thermodynamic stability of conjugated systems.

Teaching tasks

Task № 1. Indicate the type of hybridization of all carbon atoms in the molecules of butyric (butanoic) acid and pyridine.

Solution. Organic chemistry is a chemistry of carbon compounds. The properties of organic compounds are determined for the most extent by the electronic structure of the carbon atom and nature of its chemical bonds. In the excited state ($1s^2 2s^1 2p^3$) carbon atom has four unpaired electrons and can therefore form four covalent bonds. In this regard, all the bonds in structures of the type CX_4 are equal.

In order to explain this phenomenon, Linus Pauling introduced the concept of "hybridization" - a kind of interaction of orbitals with similar energy to form so-called hybrid orbitals of lower energy.

For carbon atom three types of hybridization are possible.

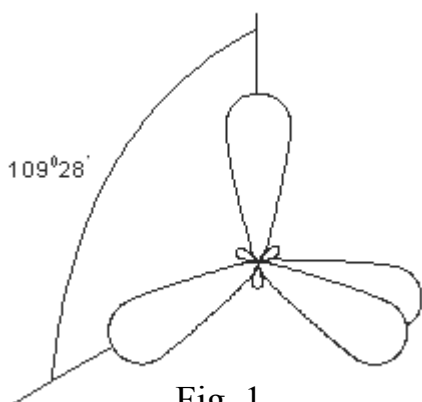


Fig. 1

1. sp^3 -Hybridization is interaction of one s- and three p-orbitals with formation of four energetically equal hybrid orbitals having the form of dumb-bell with uneven lobes (Fig. 1). The highest distance between electrons corresponds to the direction of hybrid orbitals to the vertices of regular tetrahedron at an angle of $109^\circ 28'$. The carbon atoms which are not connected by multiple bonds with other atoms are in the sp^3 - hybridization state and the orbitals have a spatial configuration. Chemical bonds in this case form through an axial overlapping of hybrid orbitals of carbon atoms with the orbitals of neighboring

atoms. As a result σ -bonds forms in which the maximum electronic density is between the nuclei of the atoms on the line joining them. Typical compounds in which carbon atoms are sp^3 -hybridized are saturated hydrocarbons.

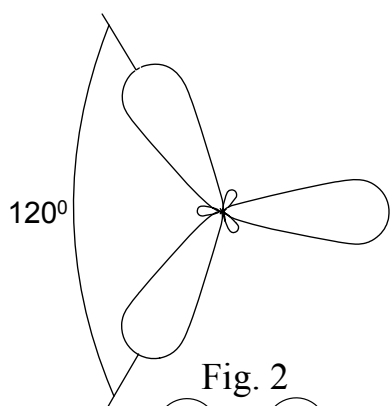


Fig. 2

2. sp^2 -Hybridization is interaction of one s- and two p-orbitals with formation of three hybrid orbitals, the axis of which are located in one plane and directed from the center of the triangle to its vertices at an angle of 120° (Fig. 2). The direction of the unhybridized p-orbital is perpendicular to the plane of hybrid orbitals. During the formation of covalent bonds between sp^2 -hybridized carbon atoms end-on overlapping of hybrid orbitals and side-on overlapping of unhybridized p-orbitals occur (Fig. 3). In the latter case π -bond is formed, the electronic cloud of which is located above and below the plane of σ -bonds. Typical compounds consisting of sp^2 -hybridized carbon atoms are ethylene and its homologues (alkenes).

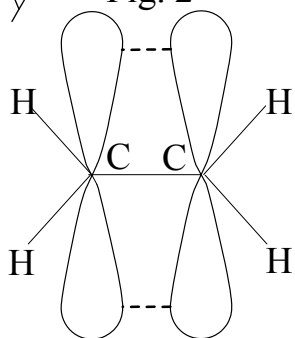


Fig. 3

3. sp -Hybridization is interaction of one s-orbital and one p-orbital with formation of two hybrid orbitals. They are arranged linearly at an angle of 180° . The two remaining unhybridized p-orbitals are located in the mutually perpendicular planes. The two sp -hybridized carbon atoms are bond by one σ -and two π -bonds (Fig. 4). Typical compounds consisting of sp -hybridized carbon atoms are acetylene and its homologues (alkynes).

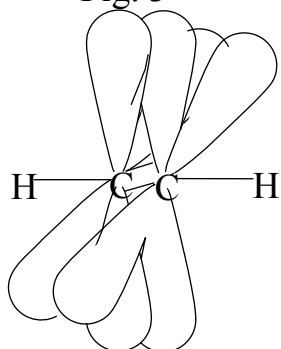
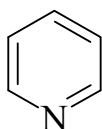


Fig. 4

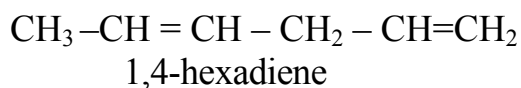
In butyric acid molecule $CH_3-CH_2-CH_2-COOH$, carbon atoms in the radical are linked to other atoms with four σ -bonds, therefore, they are sp^3 -hybridized. The carbon atom of the carboxyl group forms three σ -bonds and one

π -bond, i.e. it is sp^2 -hybridized. In molecule of pyridine all carbon atoms are in sp^2 -hybridization state.



Task №2. Give definition of term “conjugation”. Which atoms are involved in conjugation in the molecules of 1,3-butadiene, benzene and vinyl chloride?

Solution. Electronic structure of molecules containing several multiple bonds depends on their mutual position. If there is at least one sp^3 -hybridized carbon atom between multiple bonds, the bonds are said to be isolated:



The properties of such compounds are similar to ethylene ones. If the carbon atoms bound by multiple bonds with other atoms are separated by a single bond, then such systems are called conjugated, and multiple bonds are called conjugated bonds. A typical example of the conjugated system is 1,3-butadiene. In this compound all four carbon atoms are sp^2 -hybridized, and hence each carbon forms three σ -bonds lying in the same plane at an angle 120° and has one p-orbital which is perpendicular to the plane of σ -bonds (Fig. 5).

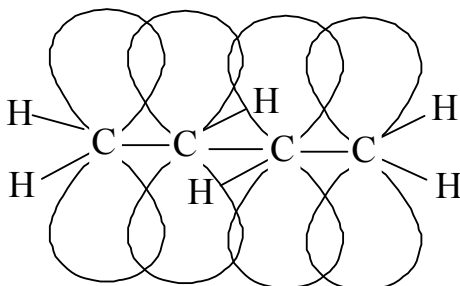


Fig. 5

Side-on overlapping of the four p-orbitals leads to the formation of the π -electronic cloud which is common for the whole molecule. The above is confirmed by electron-graphic studies, which shows that the bond length between the first and second, and between the third and fourth carbon atoms is 0.136 nm, i.e. it is slightly longer than the length of the double bond. The distance between the second and third carbon atoms is 0.148 nm which is shorter than a length of single bond.

In the conjugated system p-electrons are not attached in pairs in certain bonds, they are delocalized, i.e. arranged throughout the system. The delocalization of p-electrons is accompanied by the decrease in energy. Thus, the conjugated system of 1,3-butadiene possesses lesser energy than a system with two isolated double bonds. The energy gain that results from the delocalization of the electrons in the conjugated system and leads to the stabilization of the molecule is called the conjugation energy. Many biologically active substances contain conjugated systems: heme – non-protein

part of the blood hemoglobin, vitamin A, nucleic bases (adenine, guanine, cytosine, thymine, uracil), etc.

Examples of closed conjugated systems are aromatic and many heterocyclic compounds. All carbon atoms in benzene are sp^2 -hybridized. Each carbon forms three σ -bonds which lie in the same plane at an angle of 120° and six unhybridized p-electrons form a common electronic cloud making annular conjugation (Fig. 6).

In the benzene molecule lengths of all carbon – carbon bonds are the same and equal to 0.139 nm. The energy of conjugation in benzene is comparatively high, it equals 227.8 kJ / mol. This explains great stability of the benzene molecule.

In the above cases, the conjugated system is formed by the overlap of orbitals of the π -bonds. This type of conjugation is called π,π -conjugation. For organic compounds p, π -conjugated systems are also possible. In this case, π -orbital of the double bond conjugates with p-orbital of the substituent. For example, in the molecule of vinyl chloride $H_2C=CH-Cl$ p-orbital of chlorine, which carries a lone pair of electrons, enters the conjugation.

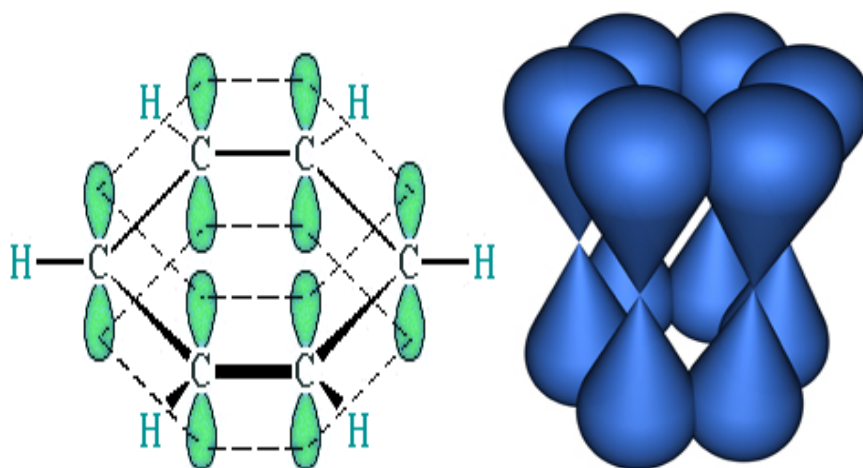


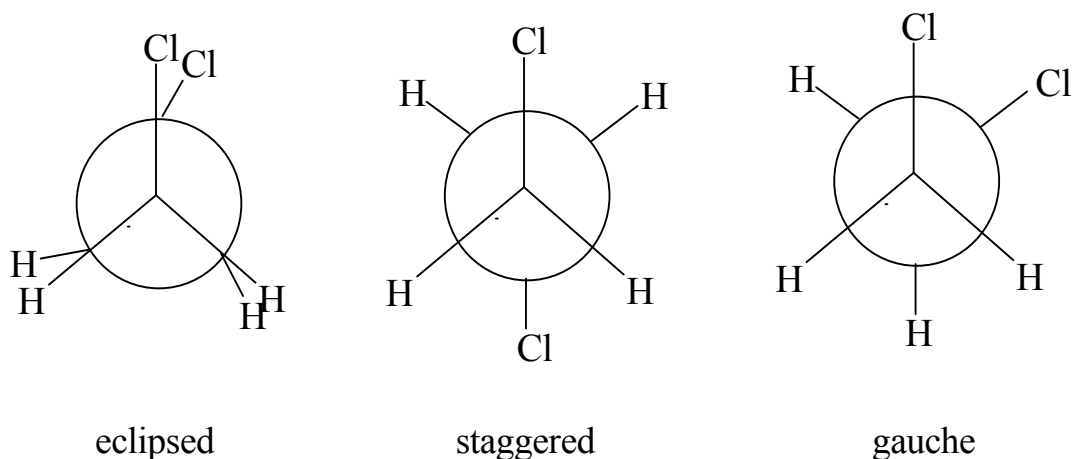
Fig. 6

Task № 3. Draw eclipsed and staggered conformations of 1,2-dichloroethane. Which one possesses lesser energy?

Solution. The mutual arrangement of atoms bonded only by σ -bond is not rigid as atoms can rotate around the axis connecting them. Structures formed due to this rotation are called conformations. These are different forms of molecules of the same substance. Any specific conformation is only a temporary state of molecules which continuously change from one conformation to another. The majority of molecules exist in the form of a more energetically favorable conformation, i.e. in which unbound atoms are at a maximal distance.

Conformations of 1,2-dichloroethane can be depicted by the Newman projection formulas. Newman projections are obtained by transferring of the molecule to the plane along the C-C bond.

Conformation in which the substituents (chlorine atoms) are located at a minimal distance and eclipse each other is called eclipsed conformation. Maximal distance between substituents corresponds to the staggered conformation. The other conformations are called gauche.



Task № 4. Draw the most favorable conformation of methylcyclohexane.

Solution. Cycles formed by sp^3 -hybridized carbon atoms can not be flat (except for cyclopropane), since tetrahedral configuration will be disturbed. Due to the fact that in molecules of first two members of saturated cyclic hydrocarbons – cyclopropane and cyclobutane – the angle formed by lines connecting the nuclei of atoms is less than normal tetrahedral, respectively, 60° and 90° , the region of maximum overlap of atomic orbitals of carbon atoms is not on these lines but above them (Fig. 7). Such σ -bonds (the so-called "banana" bonds) in respect with location of maximal electronic density are similar to π -bonds. The least deviation from the tetrahedral angle is observed in cyclopentane – $0,44^\circ$.

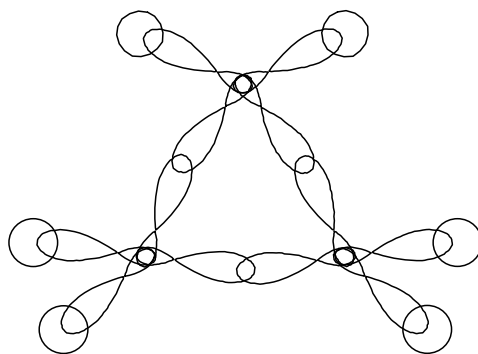


Fig. 7

Cyclohexane molecule can not exist in the form of a regular hexagon as in this case the angle between the bonds would be equal to 120° . The main conformations of cyclohexane deprived of angular strain are chair and boat conformations (Fig. 8). A large portion of the molecules exists in the more energetically favorable chair conformation. Twelve C-H bonds in a molecule of cyclohexane are divided into two groups. Six axial bonds (symbol "a" Fig. 8) are directed perpendicular to the cycle alternately up and down.

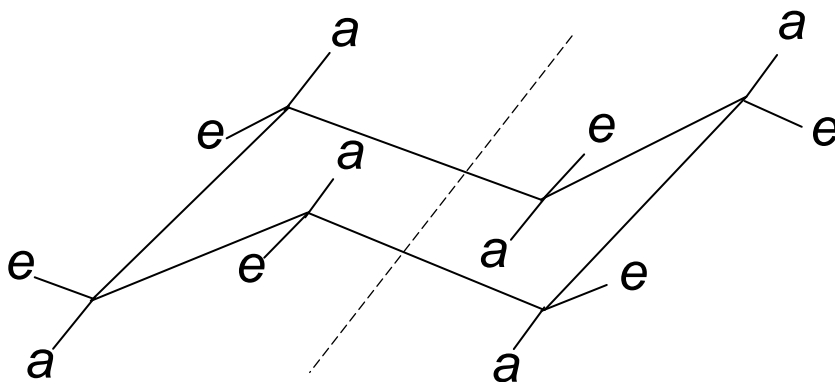


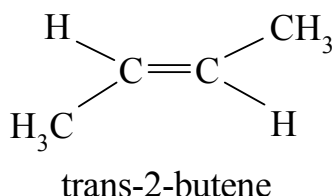
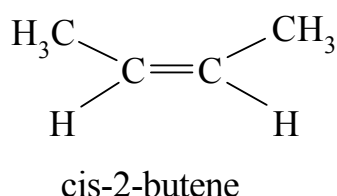
Fig. 8

Remaining six bonds are located peripherally (around the cycle) at an angle to the axis of symmetry $109^{\circ}28'$, they are called equatorial (symbol "e"). The substituent in a molecule of cyclohexane can possess either axial or equatorial location. These forms are the conformers. The equatorial position of the substituent is energetically more favorable and therefore its existence is more likely.

The most favorable conformation of methylcyclohexane is the chair conformation with equatorial location of the methyl group.

Task №5. What is the difference between cis- and trans-isomers of 2-butene?

Solution. In contrast to the single bond, free rotation of the atoms around the double bond is restricted. Substitution of hydrogen atoms at the sp^2 -hybridized carbon atoms may occur in two ways: on the same or different sides of the double bond:



This type of isomerism is called geometric or cis-trans-isomerism. Isomers in which the substituents are located on the same side of the double bond are called cis-isomers, those with substituents at different side are trans-isomers. Cis- and trans-isomers are not only different in spatial structure, but they also have different certain physical, chemical and physiological properties.

Cis-trans isomerism is quite common for biologically active compounds, e.g. higher unsaturated fatty acids (lipids structural components) are all cis-isomers. This favors more compact arrangement of the cell membranes.

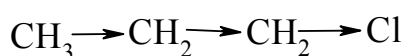
Task №6. Determine electronic effects in molecules of chloroacetic acid and benzoic aldehyde.

Solution. In studying the properties of organic compounds it is important not only to know their electronic structure, but also to take into account the mutual

influence of the atoms in the molecule. A.M. Butlerov was the first to suggest the ideas of the mutual influence of atoms. Then these ideas were developed by his pupil V.V. Markovnikov. Nowadays the relationships between the structure and reactivity of compounds are defined. They are called effects. The most important are the electronic and spatial (steric) effects.

The presence of atoms in the molecule which are significantly different in electronegativity leads to polarization of bond between them, which in turn causes the polarization of adjacent C-C and C-H bonds. This polarization gradually decays as the distance from the atoms causing polarization increases.

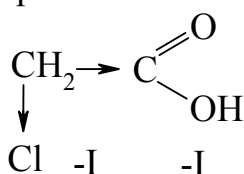
Shifting of the electronic density of σ -bond to one of the bonded atoms transmitted through the chain of σ -bonds in the molecule is called inductive effect (I-effect). The direction of shifting of the electronic density is indicated by the arrow which coincides with the valence dash and directed towards the more electronegative atom:



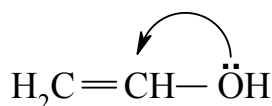
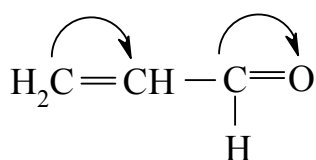
If the electronic density is shifted from the carbon atom to the substituent, the inductive effect of substituent is negative (-I effect). If, on the contrary, the electronic density is shifted from the substituent, the inductive effect of substituent is positive (+I-effect).

Electron-donating substituents – metal atoms and alkyl groups $-\text{CH}_3, -\text{C}_2\text{H}_5,$ etc. have positive inductive effect. In the latter case, the +I-effect is due to the slight polarity of C-H bonds (electronegativity of carbon atoms is 2.5, and electronegativity of hydrogen is 2.1 according to Pauling scale). With the increasing number of carbon atoms in the alkyl radical +I-effect increases: $\text{C}_3\text{H}_7- > \text{C}_2\text{H}_5- > -\text{CH}_3.$

Negative inductive effect of electron-withdrawing substituents is shown by the following: $-\text{OH}, > \text{C} = \text{O}, -\text{COOH}, -\text{NH}_2, -\text{OR},$ and halogens. The inductive effect influences the properties of organic compounds. Thus, replacement of hydrogen atom in acetic acid radical with chlorine possessing -I-effect, increases the acidity due to the displacement of electronic density towards halogen atom:

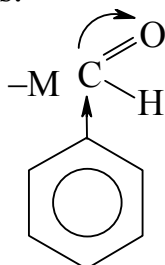


If a molecule has a system of conjugated double bonds or one double bond adjacent to a substituent having a lone pair of electrons, the transfer effect occurs along the system of π -bonds and the effect of substituent is called mesomeric effect or effect of conjugation (M-effect). Mesomeric effect occurs in cases when the substituent has either π -bond ($>\text{C} = \text{O}, -\text{COOH}, -\text{NO}_2$), or a lone pair of electrons ($-\text{OH}, -\text{NH}_2,$ halogens). When such substituents are connected to sp^2 - or sp -hybridized carbon atoms, the electrons of π -bonds or paired electrons of substituents are conjugated with π -electrons of the carbon skeleton. Mesomeric effect is indicated by curved arrows:



Origin of arrow indicates which π - or p-electrons displace, and the arrow end indicates the bond or atoms to which they displace. Electrons of π -bonds are highly mobile, so the M-effect is transmitted from one end of the conjugated system to another practically without decaying.

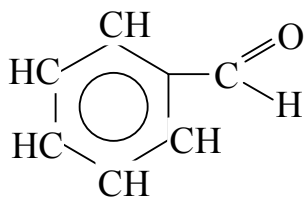
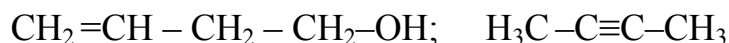
If the substituent attracts the electronic density of the conjugated system, the mesomeric effect is considered as negative (-M-effect). If the substituent donates its electronic pair to the conjugation, mesomeric effect is considered as positive (+M effect). Substituents having π -bond ($>C=O$, $-COOH$, $-NO_2$) possess negative mesomeric effect; substituents having unshared electrons ($-OH$, $-NH_2$, halogen) possess a positive one. In the molecule of benzaldehyde, carboxylic group is in π, π -conjugation with the aromatic system and due to oxygen atoms exhibits negative inductive and negative mesomeric effects.



Revision exercises

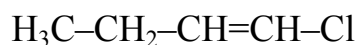
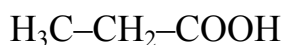
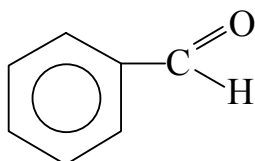
№ 1

1. Determine the type of hybridization of all carbon atoms in the following compounds:



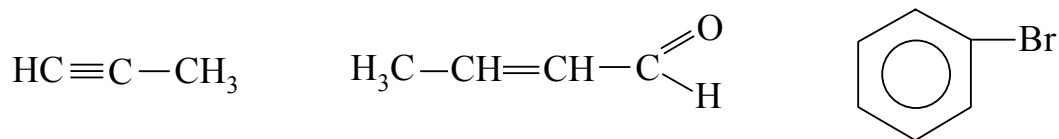
2. Draw cyclohexanediol-1,3 in chair conformation with the most favorable position of substituents.

3. Determine electronic effects of substituents in the following compounds:

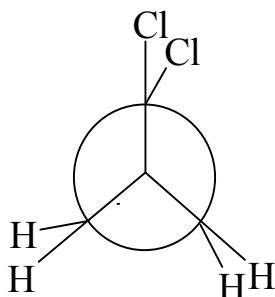


№ 2

1. Determine the type of hybridization of all carbon atoms in the following compounds:



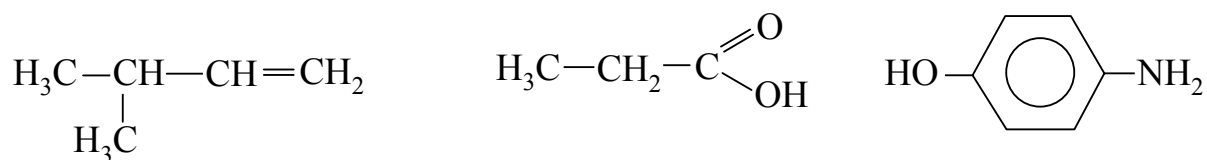
2. Name the conformation given in Newman projection. What is the compound?



3. Give the structure of pyrrole and prove that it is aromatic.

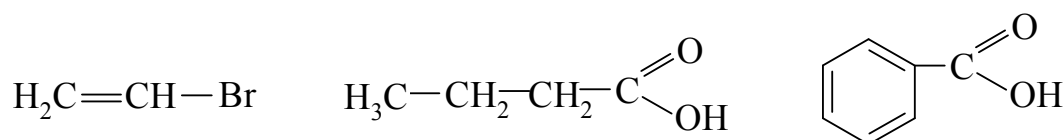
№ 3

1. Determine the type of hybridization of all carbon atoms in the following compounds:



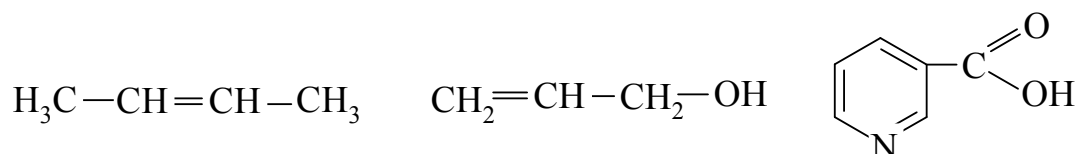
2. Draw 1,2-dimethylcyclohexane in chair conformation with the most favorable position of substituents.

3. Determine electronic effects of substituents in the following compounds:



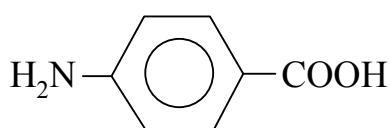
№ 4

1. Determine the type of hybridization of all carbon atoms in the following compounds:



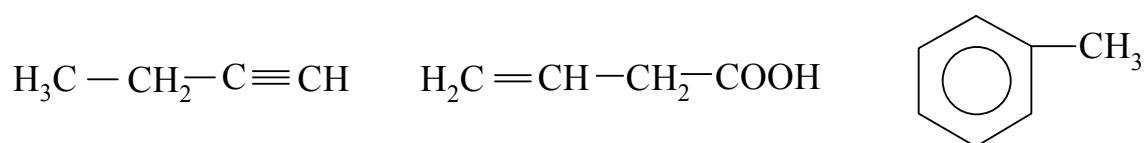
2. Draw Newman projection of staggered conformation of ethanol. Evaluate the energetic state of this conformation.

3. Determine electronic effects in the molecule of p-aminobenzoic acid:



№ 5

1. Determine the type of hybridization of all carbon atoms in the following compounds:

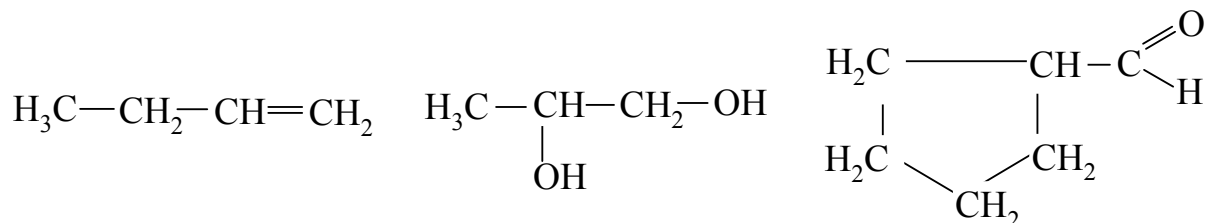


2. Draw the most favorable conformation of cyclohexanol.

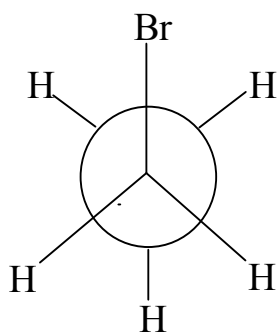
3. Give the structure of pyridine and prove that it is aromatic.

№ 6

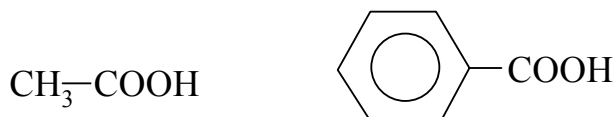
1. Determine the type of hybridization of all carbon atoms in the following compounds:



2. Name the conformation given in Newman projection. What is the compound?

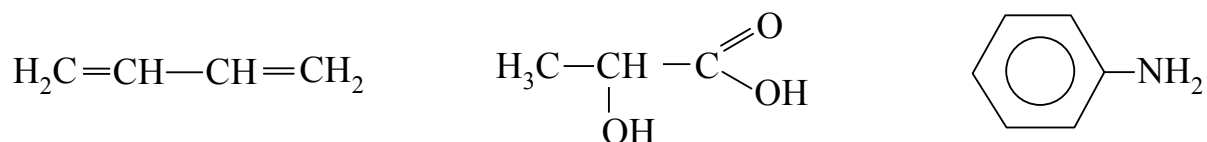


3. Determine electronic effects of carboxyl group in acetic acid and benzoic acid:

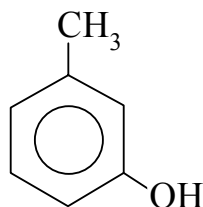


№ 7

1. Determine the type of hybridization of all carbon atoms in the following compounds:

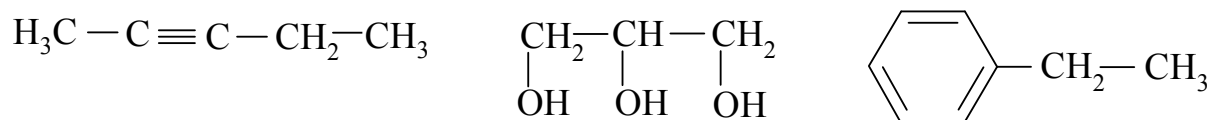


2. Draw the most favorable conformation of bromocyclohexane.
 3. Determine electronic effects of substituents in the m-cresol molecule:

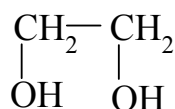


№ 8

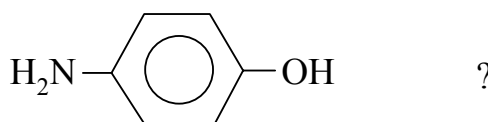
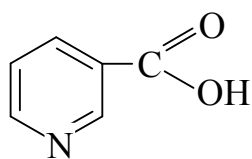
1. Determine the type of hybridization of all carbon atoms in the following compounds:



2. Draw Newman projection of the most favorable conformation of ethylene glycol:



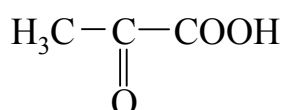
3. Which atoms participate in conjugation in the following molecules:



?

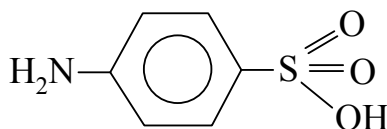
№ 9

1. Determine the type of hybridization of all carbon atoms in the following compounds:



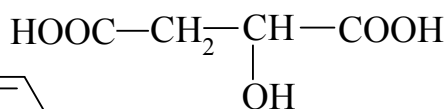
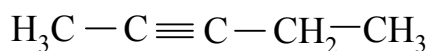
2. Draw the structure and the most favorable conformation of methylcyclohexane.

3. Determine electronic effects and types of conjugation of substituents with benzene ring in the molecule of sulfanilic acid (parent structure for sulfanilamides):



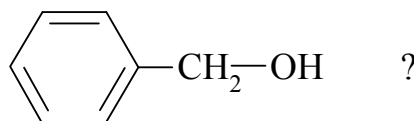
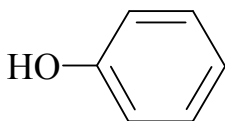
№ 10

1. Determine the type of hybridization of all carbon atoms in the following compounds:



2. Draw the structure and chair conformation of cyclohexanehexaol-1,2,3,4,5,6 (myoinositol contained in muscles) if five OH groups are in equatorial location.

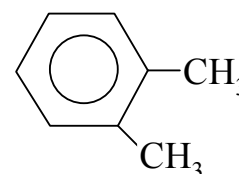
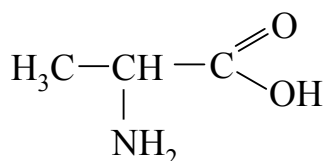
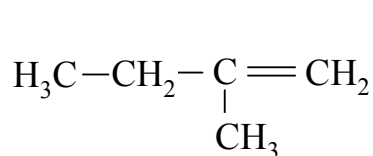
3. What is the effect of hydroxyl group on the electronic density of benzene ring in the following compounds:



?

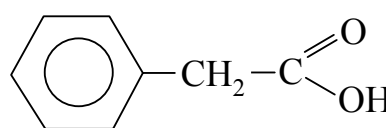
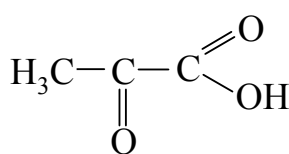
№ 11

1. Determine the type of hybridization of all carbon atoms in the following compounds:



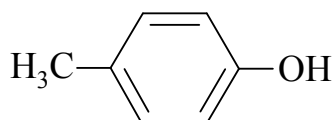
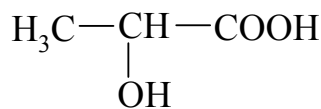
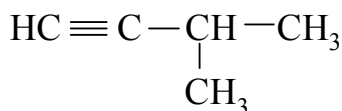
2. Draw Newman projection of staggered conformation of 2-aminoethanol-1. Evaluate the energetic state of this conformation.

3. Determine electronic effects of substituents in the following compounds:



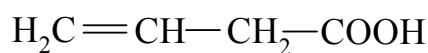
№ 12

1. Determine the type of hybridization of all carbon atoms in the following compounds:



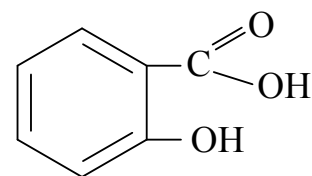
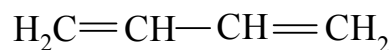
2. Draw the structure and the most favorable conformation of aminocyclohexane.

3. Determine electronic effects of substituents in the following compounds:



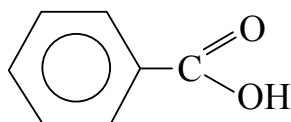
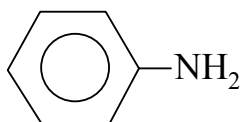
№ 13

1. Determine the type of hybridization of all carbon atoms in the following compounds:



2. Draw the most favorable conformation of 1,2-dibromocyclohexane.

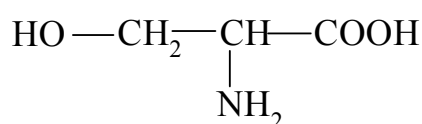
3. What are the effects of substituents on the electronic density of benzene ring in the following compounds:



?

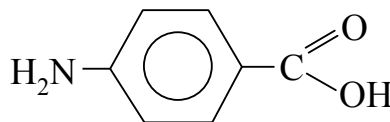
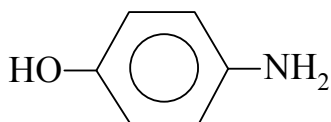
№ 14

1. Determine the type of hybridization of all carbon atoms in the following compounds:



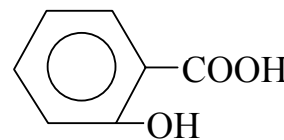
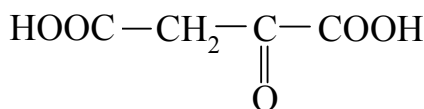
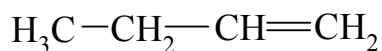
2. Draw Newman projections of eclipsed and staggered conformations of 1,2-dichloroethane. Which one possesses lesser energy?

3. Determine electronic effects of substituents in the following compounds:



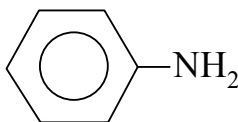
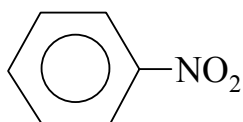
№ 15

1. Determine the type of hybridization of all carbon atoms in the following compounds:



2. Draw the structure and the most favorable conformation of hexachlorocyclohexane (hexachloran).

3. What are the effects of substituents on the electronic density of benzene ring in the following compounds:



?

Subject III. ACID-BASE PROPERTIES OF ORGANIC COMPOUNDS

Motivational characteristic of subject

Acidity and basicity are among the most important properties of substances that often define their activity in the organism.

Objective

To study the acidity and basicity of organic compounds as the most important characteristics which define many of the chemical processes in living organisms.

Training questions

1. To be able to explain the acidic properties of alcohols, phenols and carboxylic acids and their dependence on the number of functional groups and the presence of substituents in the radicals according to the electronic structure of functional groups.
2. To know the mechanism of decarboxylation reaction.
3. To understand what is the C-H acidity and how it affects the properties of the compounds.
4. To be able to explain the basic properties of aliphatic amines, aromatic amines and nitrogen containing heterocycles basing on electronic structure of nitrogen atom.
5. To know classes of organic compounds having amphoteric properties. To be able to illustrate such properties.

Methodological questions

Acidity and basicity are an example of the dialectical unity and struggle of opposites.

Initial level

1. The main propositions of protolytic theory of acids and bases.
2. Electronic effects of the substituents. The electron-donating and the electron-withdrawing substituents.

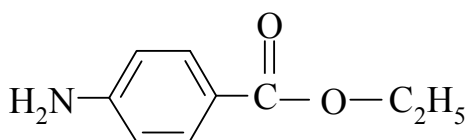
Practical skills

To be able to predict the properties of the acidic and basic compounds depending on their structure.

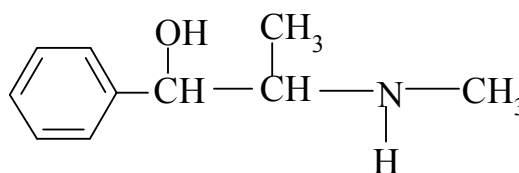
Test questions

1. Write the reaction of glycerol with copper hydroxide (II).
2. Arrange the following acids in order of decreasing of acidity:
 - a) propionic acid, lactic acid, pyruvic acid;
 - b) acetic acid, trichloroacetic acid, dichloroacetic acid.
3. Which of the two compounds – anesthesin or ephedrine is a stronger base?

Why?

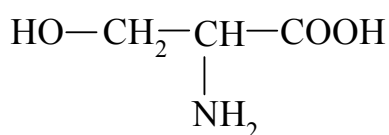


anesthesin

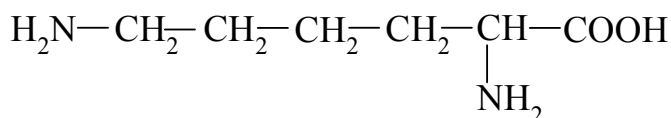


ephedrine

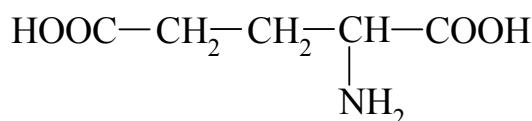
4. What is the pH in water solutions of the following amino acids?



serine



lysine



glutamic acid

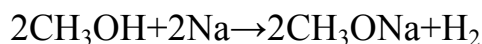
Teaching tasks

Task №1. What is the change in acidic properties in the following series: methanol – glycerol – phenol – acetic acid – oxalic acid?

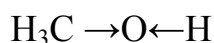
Solution. It is known that acids are donors of hydrogen proton. The following organic compounds can serve as acids: 1) compounds containing hydrogen atoms connected to an electronegative atom (oxygen, sulfur, etc.), 2) compounds having hydrogen atoms at the carbon atom connected to the electron-withdrawing

substituents. From the first group let us consider acidic properties of alcohols, phenols and carboxylic acids.

The polarity of the O - H bond in the alcoholic hydroxyl group is the reason of its ability to heterolytic cleavage. This type of bond cleavage occurs in reactions with active metals with formation of solid, alcohol-soluble products – alcoholates (alcoxides) with ionic bond between oxygen and metal:

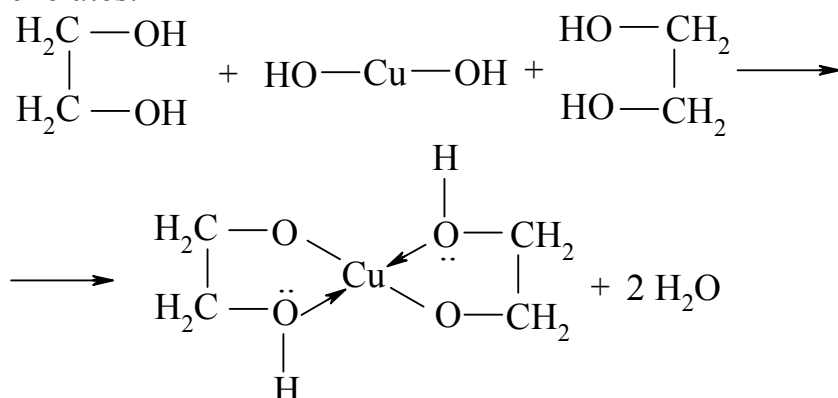


Positive inductive effect (+ I) of a carbon radical decreases the polarity of the O - H bond and therefore reduces the acidic properties of alcohols.



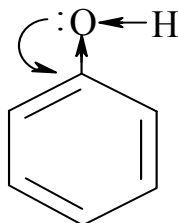
So, alcohols are even weaker acids than water ($\text{pK}_a(\text{water})=15.7$, $\text{pK}_a(\text{methanol})=16$, $\text{pK}_a(\text{ethanol})=18$). For the same reason, the acidity of alcohols decreases with increasing of the number of carbon atoms in the radical.

Acidity of polyhydric alcohols is higher than that of monohydric ones, due to negative inductive effect (-I) of hydroxyl groups ($\text{pK}_a(\text{ethylene glycol})=15.8$). Hydrogen atoms of polyhydric alcohols are easily replaced by some heavy metals with formation of chelates.

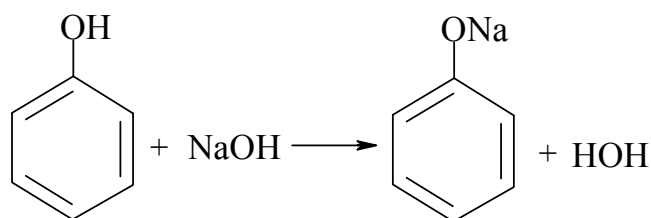


Chelates have bright coloration and their formation is used for the qualitative determination of polyhydric alcohols.

The acidity of **phenols** is stronger than that of alcohols ($\text{pK}_a(\text{phenol})=10$, that is 6 units less than pK_a of aliphatic alcohols). This is because the electron pair of the oxygen atom is shifted to the aromatic ring (+ M effect), which leads to increasing of polarization of O-H bond.

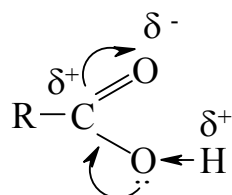


Unlike aliphatic alcohols phenol easily reacts with alkalis forming salts – phenolates:

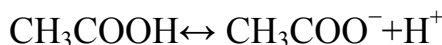


Phenols also react with metals and salts, showing all chemical properties of acids.

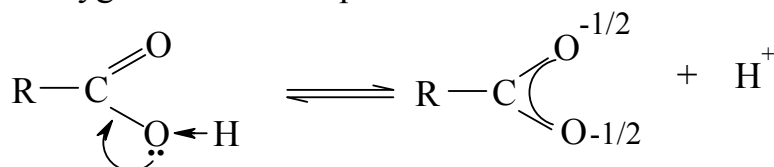
Acidic properties are mostly expressed in the series of carboxylic acids – compounds containing carboxyl group $-\text{COOH}$. The presence of the carbonyl group near to hydroxyl group causes the conjugation of paired electrons of oxygen of the hydroxyl group with electrons of the carbonyl π -bond:



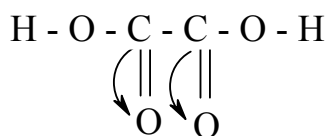
As a result the electronegativity of oxygen atoms increases, which leads to increasing polarization of the O - H bond and facilitates the removal of a proton. In aqueous solution, the lower carboxylic acids significantly dissociate to produce protons:



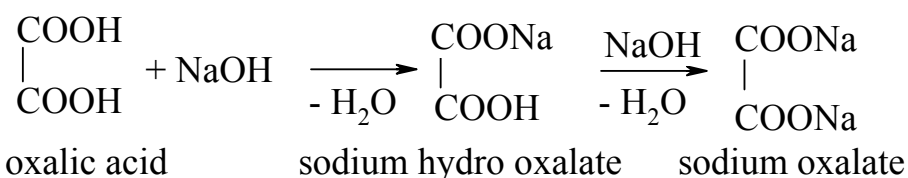
Carboxylate anion is a delocalized three-centered system in which bonds of carbon atom with two oxygen atoms are equalized:



Carboxylic acids are weak electrolytes. The more stable the anion formed by the dissociation, the greater equilibrium of dissociation process is shifted to the right. Therefore, the greater is the stability of the anion, the stronger is the acid. Stability of the anion, in its turn, is determined by the degree delocalization of negative charge. Therefore, the factors facilitating the delocalization of the charge, increase acidity and those factors which inhibit delocalization reduce acidity. This fact is also true for other classes of compounds exhibiting acidic properties. In particular, the dicarboxylic acids are stronger acids than monobasic ones with the same number of carbon atoms due to the $-I$ effect of the second carboxyl group:



Carboxylic acids change the coloration of the indicator and show all properties of acids, interacting with metals, bases, basic oxides, and salts. Let's consider this on example of dibasic acids which play important role in biochemical reactions. All dibasic acids can form acid salts and neutral salts:

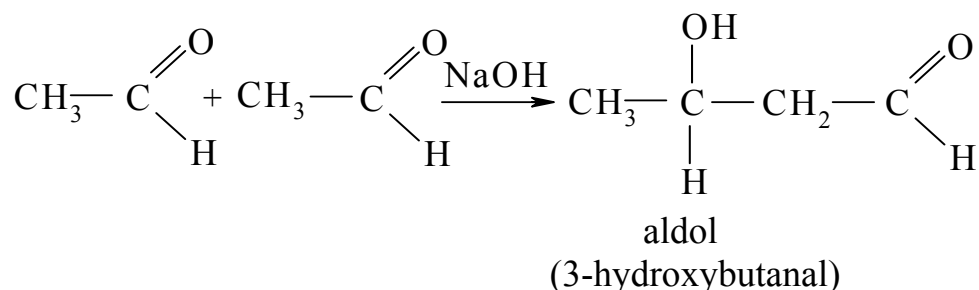


Thus, in a row: methanol – glycerol – phenol – acetic acid – oxalic acid acidity increases.

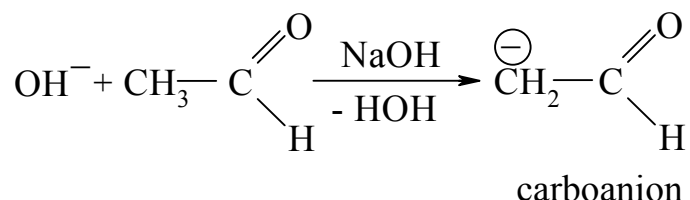
Task №2. What products can be formed from acetic aldehyde and benzoic aldehyde in basic medium?

Solution. Organic compounds having hydrogen atoms in α -position relative to the electron-withdrawing substituents (carbonyl, nitro, etc.) can detach hydrogen proton under appropriate conditions exhibiting acidic properties. This phenomenon is called CH-acidity and the compounds are said to be CH-acids.

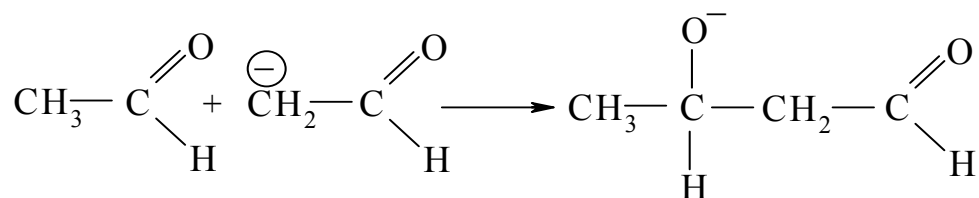
Aldol condensation reaction can serve as example of CH-acidity. Aldol condensation is the reaction between molecules of aldehydes in aqueous alkaline solution.



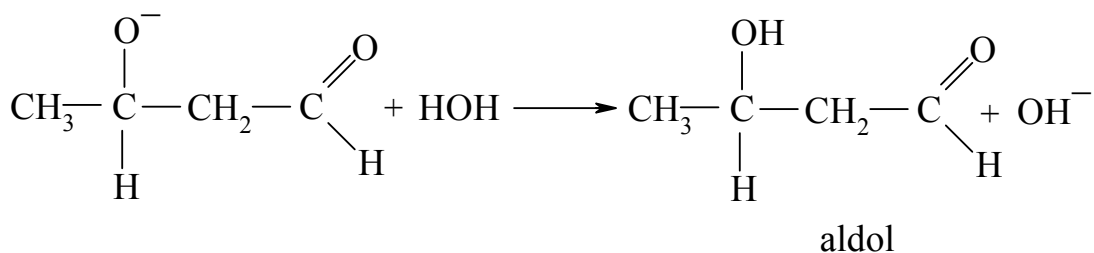
Hydroxyl group of alkali attracts hydrogen proton from α -carbon atom and molecule becomes carboanion:



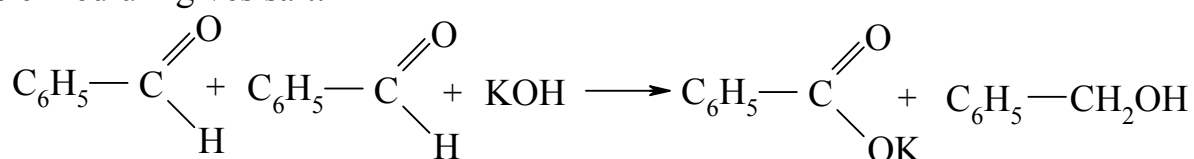
This anion is rather stable because α -carbon atom becomes sp^2 -hybridized and enters into conjugation with π -bond of carbonyl group. Then carboanion combines with the other molecule of carbonyl compound:



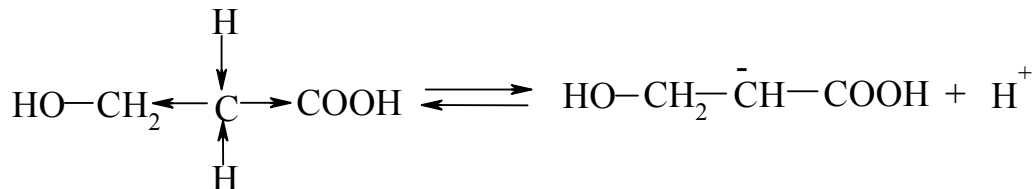
Anion formed is unstable due to the absence of conjugation and stabilizes itself by combination with the proton from water molecule:



CH-acidity can be performed only by substances having hydrogen atoms at α -carbon atom. For example, there are no α -carbons in benzaldehyde molecule, so, under the influence of alkali benzaldehyde does not form aldols. Under the same conditions it enters Cannizzaro reaction in which one molecule of the aldehyde is reduced to benzyl alcohol, and the second is oxidized to benzoic acid. Benzoic acid in basic medium gives salt:



The CH-acidity is manifested strongly in compounds containing methyl group between two electron-accepting substituents: in β -hydroxy acids, β -amino acids, etc. In this case, the hydrogen proton at the carbon atom can be released easily and the molecule is cleaved into a carbanion:

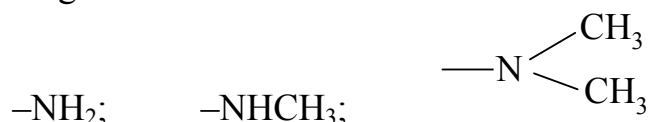


This phenomenon causes specific reactions of these compounds.

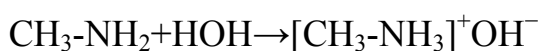
Task № 3. Compare basic properties of methylamine, dimethylamine and aniline.

Solution. According to the Bronsted protolytic theory bases are acceptors of protons. Organic compounds can accept proton either by the unshared electrons or by electrons of π -bond.

Basic properties are mostly expressed in the series of amines - compounds containing substituents:

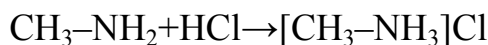


Similar to ammonia the chemical properties of amines are substantially determined by the presence of unshared electrons of nitrogen. So, amines join protons when dissolved in water and accumulation of hydroxyl groups makes solution basic:

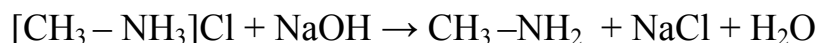


Ion $[\text{CH}_3\text{-NH}_3]^+$ can be considered as a complex ion containing nitrogen as the central atom. Coordination number of nitrogen is 4, and hydrogen atoms or alkyl groups are located in the inner coordination sphere.

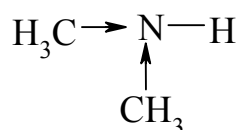
Basic properties of amines are also manifested by their ability to interact with acids to form salts:



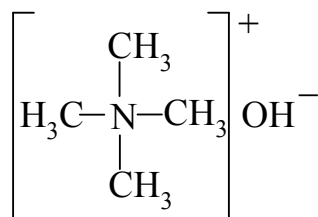
Salts of amines are crystalline solids, readily soluble in water. Alkalies being stronger bases than amines replace amines from their salts:



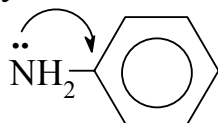
Amines are stronger bases than ammonia due to the +I effect of hydrocarbon radicals.



Introduction of the third alkyl group (in tertiary amines) decreases basicity due to steric hindrance caused by the shielding effect of the three alkyl groups. Quaternary ammonium bases possess strong basic properties which are comparable in strength with alkali.

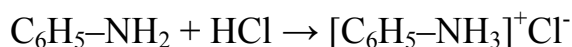


The basic properties of aromatic amines are significantly weaker than that of aliphatic ones. This is due to the conjugation of the lone pair of electrons of the nitrogen atom with the π -electron system of the ring:



As a result, the electronic density of the nitrogen atom is reduced and the ability to combine proton decreases. Addition of hydrogen proton in this case leads to reducing of number of atoms participating in conjugation, and as a result, to less delocalization of electronic density which is not favorable from energetic point of view.

An aqueous solution of aromatic amines does not change color of indicators, they do not form salts with weak acids. They react with strong acids to produce salts:

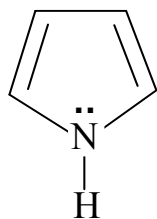


Electron-accepting substituents reduce basicity of aromatic amines and electron-donating substituents increase it.

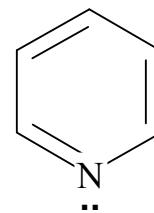
Task №4. Which heterocycle – pyrrole or pyridine is the stronger base?

Solution. Basic properties are also inherent to nitrogen-containing heterocyclic compounds. In these compounds basicity depends on whether unshared electrons of nitrogen enter in conjugation with the electrons of the atoms of carbon cycle or not. In pyrrole basic properties are expressed very weakly, because unshared electrons of nitrogen are involved in conjugation with the ring to form aromatic system. So, hydrogen proton can not be accepted by pyrrolic nitrogen.

In the pyridine molecule conjugated system is formed without electrons of nitrogen, so pyridine behaves similar to aliphatic amines.

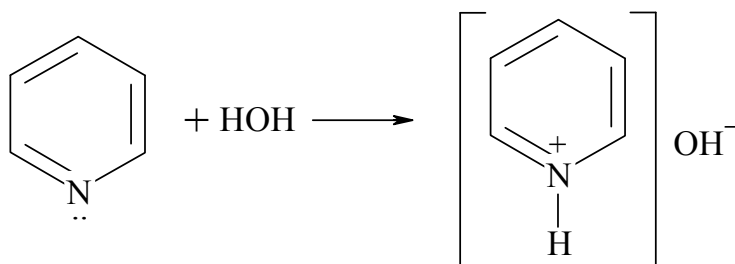


pyrrole

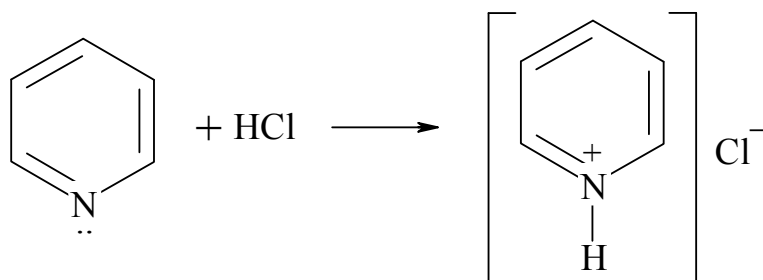


pyridine

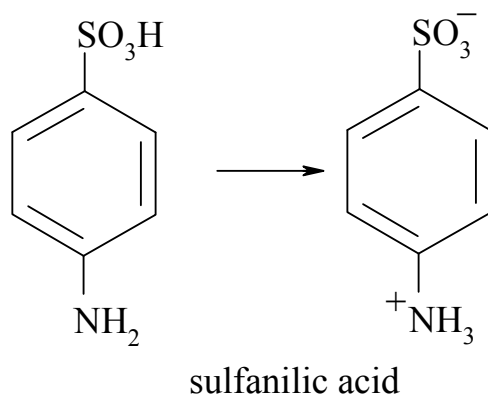
Aqueous solution of pyridine is basic:



Reacting with mineral and organic acids pyridine forms crystalline salts:

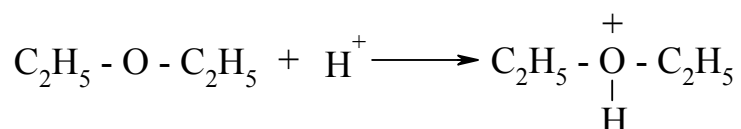


Compounds containing both acidic and basic groups are capable to form internal salts in which proton formed by the dissociation of acidic group is bound by basic group.



Amino acids and some other compounds are also capable to form internal salts.

Proton can also be accepted by unshared electrons of the oxygen atom in alcohols, aldehydes, ethers, etc. In this case oxonium ions – alkyl derivatives of hydronium ion are formed:



Just as the hydronium ion, oxonium bases are unstable – they serve as intermediates in many reactions, especially in case of acidic catalysis, in particular, in etherification and esterification reactions.

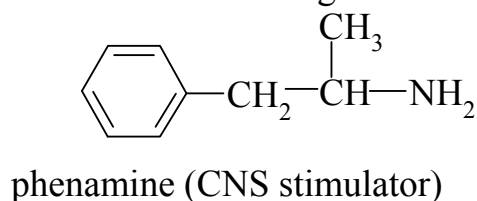
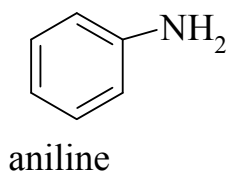
Revision exercises

№ 1

1. Arrange following compounds in order of decreasing of acidity: phenol, p-aminophenol, p-nitrophenol. Explain.
2. What is CH-acidity? Give the mechanism of aldol condensation for propanal.
3. Write the equations for reactions of ethylamine with sulfuric acid and aniline with sulfuric acid. Which amine is the stronger base?

№ 2

1. Which compound – aniline or phenamine is the stronger base? Explain.



2. What is decarboxylation? Write the decarboxylation reaction of pyruvic (2-oxopropanoic) acid.

3. Write the reactions equations of formation of acid salt and neutral salt of succinic acid.

№ 3

1. Which compound – pyrrole or pyridine is a stronger base? Why?

2. Write the reactions equations of formation of acid salt and neutral salt of fumaric (trans-ethylenedicarboxylic) acid.

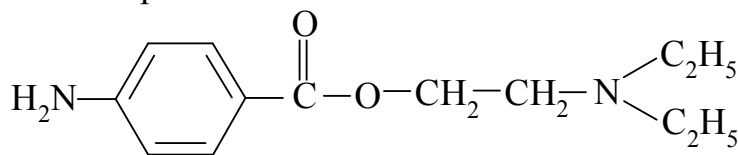
3. Write the equation of reaction of glycerol with copper hydroxide (II).

№ 4

1. Compare acidity of propionic and lactic (α -hydroxy propionic) acids.

2. Give the reactions that characterize the acidic properties of pyruvic acid (2-oxopropanoic) acid.

3. Write the equation for the reaction of the anesthetic novocaine with hydrochloric acid (novocaine is used in medicine in the form of hydrochloric acid salt), and specify the site of protonation in a molecule of novocaine:



novocaine

№ 5

1. Explain the change in acidity in the following series: ethanol, ethylene glycol, phenol.

2. Write the aldol condensation reaction of acetaldehyde in the presence of sodium hydroxide. Give the mechanism for the reaction.

3. Is aromatic character of pyridine kept in acidic medium? Write reaction of pyridine with sulfuric acid.

№ 6

1. Arrange following compounds in order of increasing of acidity: propionic acid, β -hydroxypropionic acid, lactic acid. Explain the answer.

2. What is decarboxylation reaction? Write the reaction of decarboxylation of lactic acid.

3. Write the reactions of 2-aminoethanol with hydrochloric acid and

p-aminophenol with hydrochloric acid. Which compound is the stronger base?

№ 7

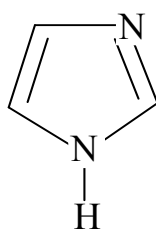
1. Compare the acidic strength of succinic (butanedioic) and tartaric (2,3-dihydroxybutanedioic) acids. What products can be formed in reaction of succinic acid with sodium hydroxide?

2. Write the reaction of adrenaline with hydrochloric acid (epinephrine hydrochloride formation).

3. Give the mechanism of aldol condensation for propanone (acetone) in basic medium.

№ 8

1. Compare the basicity of pyrrole and imidazole. Write the reaction of imidazole with hydrochloric acid.



imidazole

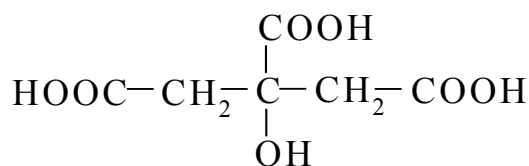
2. Specify acidic centers and place them in order of acidity decreasing in the molecule of α -hydroxypropionic acid.

3. Write the scheme of carboxylation reaction of pyruvic acid (2-oxopropanoic acid). Name the product obtained.

№ 9

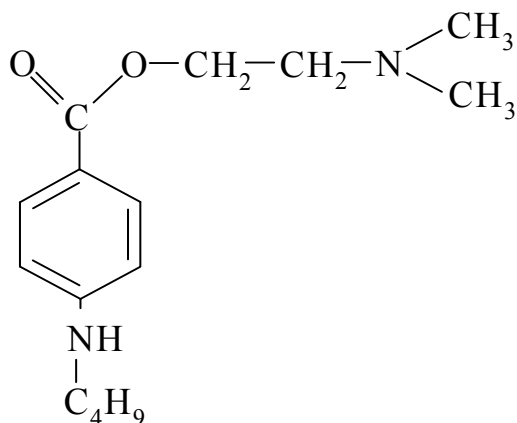
1. Arrange following compounds in order of decreasing of acidity: phenol, p-cresol, p-nitrophenol. Explain.

2. Write the reactions equations of formation of acid salts and neutral salt of citric acid.



citric acid

3. Write the equation for the reaction of the anesthetic drug tetracaine with hydrochloric acid (tetracaine is used in medicine in the form of tetracaine hydrochloride).



tetracaine
№ 10

1. Arrange following compounds in order of increasing of acidity: acetic acid, trimethylacetic acid, trichloroacetic acid.

2. Write the equation of reaction of propanediol-1,2 with copper hydroxide (II). What is the significance of this reaction?

3. Write the reactions equations illustrating amphoteric properties of alanine (α -aminopropionic acid).

№ 11

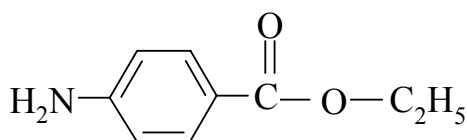
1. Which compound – diphenylamine or dimethylamine is a stronger base? Write salt formation reaction for the stronger base.

2. Write the reactions equations of formation of acid salt and neutral salt of malic acid (2-hydroxybutanedioic acid).

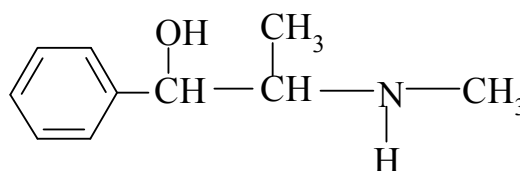
3. Which aldehyde – 2,2-dimethylbutanal or 2-dimethylbutanal enters aldol condensation reaction? Write the reaction equation.

№ 12

1. Compare basic properties of anesthesin and ephedrine:



anesthesin



ephedrine

Write salt formation reaction for the stronger base.

2. Write the decarboxylation reaction for lysine (2,6-diaminohexanoic acid). Name the products.

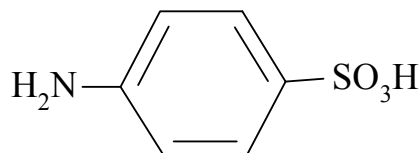
3. Write the reactions equations of formation of acid salt and neutral salt of malonic acid (propanedioic acid).

№13

1. Giving appropriate examples, explain how the presence of electron-donating and electron-accepting substituents in phenol molecule affects the acidic properties?

2. Write the reaction for the formation of hydrochloride of pyridine.

3. Write the formula of internal salt of sulfanilic acid. What is the reason for this compound formation?

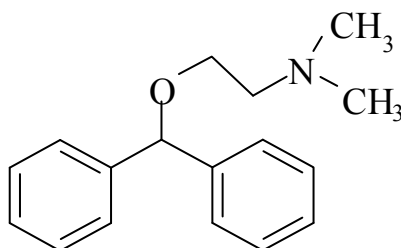


sulfanilic acid

№ 14

1. Arrange following compounds in order of increasing of acidity: benzoic acid, p-nitrobenzoic acid, p-hydroxybenzoic acid. Explain.

2. Write the equation for the reaction of the antiallergic drug dimedrol with hydrochloric acid (dimedrol is used in medicine in the form of diphenhydramine hydrochloride).



dimedrol

3. Write the reactions equations of formation of acid salt and neutral salt of oxaloacetic acid (2-oxobutanedioic acid).

№ 15

1. Which compound – pyrrole or pyridine is a stronger base? Why?

2. Write the reactions equations illustrating amphoteric properties of aspartic acid (2-aminobutanedioic acid).

3. Write the reactions of propylamine with sulfuric acid and aniline with sulfuric acid. Which compound is the stronger base?

SUGGESTED READINGS

1. Biologically important classes of bioorganic compounds. Biopolymers and their structural components: Theoretical course of biological and bioorganic chemistry, Module 1 / A.O. Syrovaya, E.R. Grabovetskaya, N.M. Tkachuk et al. – Kharkov: KhNMU. – 2013.– 183 p.

2. Zurabyan S.E. Fundamentals of bioorganic chemistry / S.E. Zurabyan – M.: Geotar-Med. – 2003. – 320 p.

Навчальне видання

Основи будови та реакційної здатності органічних сполук

**Методичні вказівки для самостійної роботи студентів 1-го курсу з
біологічної та біоорганічної хімії (Модуль 1)**

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Відповідальний за випуск Грабовецька Є.Р.

Комп'ютерний набір та верстка Грабовецька Є.Р.

Ризографія.

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