МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ’Я УКРАЇНИ
ХАРКІВСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ

CLASSIFICATION, NOMENCLATURE AND ISOMERISM OF BIOORGANIC COMPOUNDS. THE NATURE OF THE CHEMICAL BOND. THE SPATIAL STRUCTURE OF ORGANIC COMPOUNDS. MUTUAL INFLUENCE OF THE ATOMS IN THE MOLECULES OF ORGANIC COMPOUNDS

Methodical instructions for 1st year students’ self-work
in Biological and bioorganic chemistry

КЛАСИФІКАЦІЯ, НОМЕНКЛАТУРА ТА ІЗОМЕРІЯ БІООРГАНІЧНИХ СПОЛУК. ПРИРОДА ХІМІЧНОГО ЗВ’ЯЗКУ. ПРОСТОРОВА БУДОВА ОРГАНІЧНИХ МОЛЕКУЛ. ВЗАЄМНИЙ ВПЛИВ АТОМІВ В МОЛЕКУЛАХ БІООРГАНІЧНИХ СПОЛУК

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

Затверджено
Вченою радою ХНМУ
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Класифікація, номенклатура та ізомерія біоорганічних сполук. Природа хімічного зв’язку. Просторова будова органічних молекул. Взаємний вплив атомів в молекулах біоорганічних сполук: метод. вказ. для студентів 1 курсу / уклад. Сирова Г.О., Петюніна В.М., Макаров В.О. та ін. – 2-е вид., переробл., випр., доп. – Харків: ХНМУ, 2018. – 24 с.

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Subject I "Classification, nomenclature and isomerism of bioorganic compounds. The nature of the chemical bond. The spatial structure of organic compounds. Mutual influence of the atoms in the molecules of organic compounds"

1. Number of hours – 4.

2. Material and methodological support.

a) Multimedia support (presentations, scientific films)

b) Tables:

1. Graph structure of the subject.
2. Structures of cycloalkanes
3. Structures of heterocycles
4. Functional groups and corresponding classes of organic compounds
5. Structure of the molecule of methane
6. Structure of the molecule of ethane
7. Structure of the molecule of ethylene
8. Structure of the molecule of benzene

c) Models of molecules.

Educational literature:

1. Biological and Bioorganic chemistry: in two books: Textbook. Textbook 1. Bioorganic chemistry / B.S. Zimenkovsky, V.A.Muzyhenko, I.V. Nizhenkovska, G.O. Syrova; edited by B.S. Zimenkovsky, I.V. Nizhenkovska. – K.: AUP "Medicina", 2017. – 288 p.
2. Fundamentals of bioorganic chemistry: manual / A. O. Syrovaya, E. R. Grabovetskaya, V. N. Petiunina. – Kharkiv : KhNMU, 2016. – 191 p.
3. Fundamentals of structure and reactivity of organic compounds: Methodical instructions for 1st year students / compiled by A.O. Syrovaya, L.G. Shapoval, V.N. Petyunina, E.R. Grabovetskaya, N.M. Tkachuk, V.A. Makarov, S.V. Andreeva, S.A. Nakonechnaya, L.V. Lukyanova, R.O. Bachinsky, S.N. Kozub, T.S. Tishakova, O.L. Levashova, N.V. Vakulenko, N.N. Chalenko. – Kharkov: KhNMU, 2013. – 46 p.
4. Classification, nomenclature and isomerism of bioorganic compounds. The nature

of the chemical bond. The spatial structure of organic compounds. Mutual influence of the atoms in the molecules of organic compounds: methodical instructions for 1st year students' self-work / compiled by A.O. Syrovaya, V.N. Petyunina, V.O. Makarov et al. – 2nd edition, revised, corrected and expanded – Kharkiv: KhNMU, 2018. – 24 p.

5. Text of Lectures.

3. Substantiation of the subject.

While studying the chemical processes occurring in the organism, you meet with numerous and a variety of organic compounds. To orientate in this variety of compounds you need to know their scientific classification and nomenclature.

Chemical behavior of these compounds, including biochemical transformations, is determined by their composition, the electronic and spatial structure, the mutual influence of atoms in these compounds.

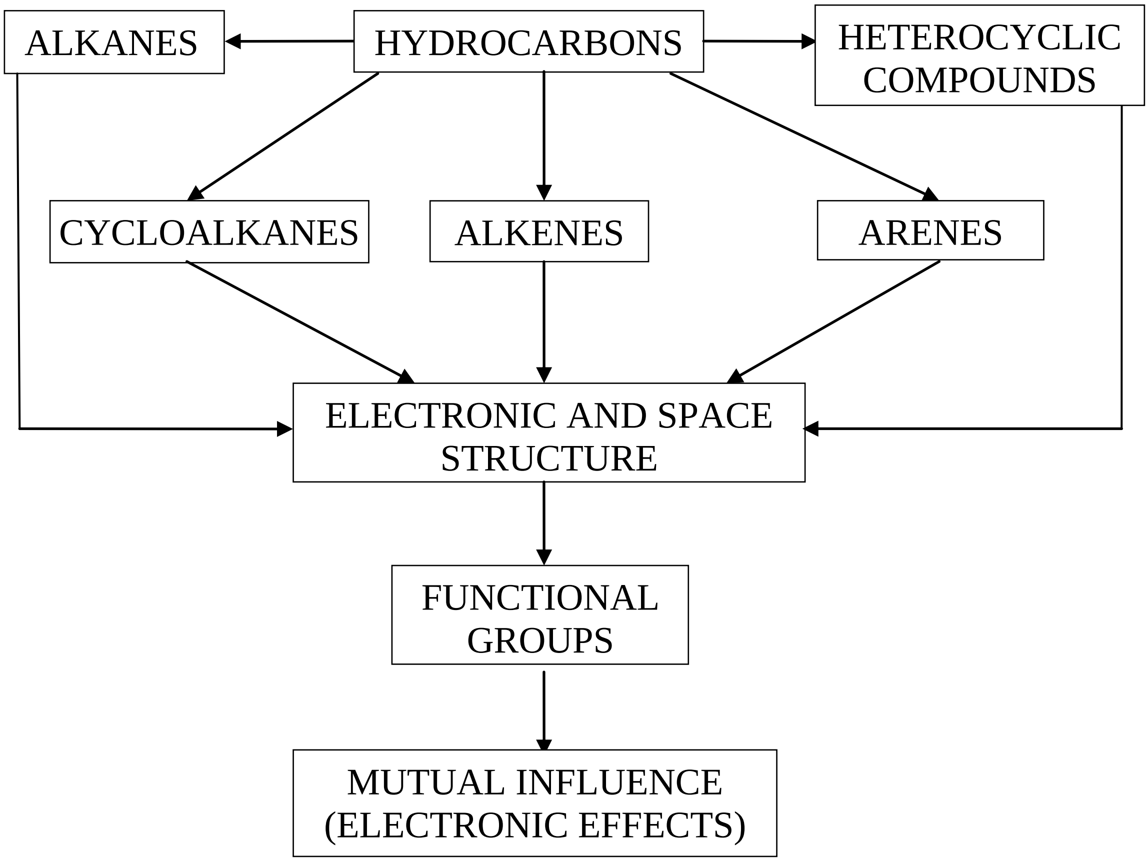
4. The purpose of the subject:

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

5. Practical skills:

1. To be able to classify organic and bioorganic compounds.
2. To be able to name bioorganic compounds according to IUPAC nomenclature and radico-functional nomenclature.
3. To be able to give formulas of bioorganic compounds according their name.
4. To be able to characterize spatial structure of bioorganic compounds.
5. To be able to determine the sign and kind of electron effects of substituents in the molecules of bioorganic compounds.

6. Graph structure of the subject.



6. Plan of students' work.

№	Stages	Time	Training and visual aids	Location
1.	Motivational characteristics and plan of the subject. Answers to the students' questions	25 min		Class room
2.	Control of students' knowledge baseline	20 min	Tests for initial control	
3.	Students' knowledge correction by solving of educational tasks (individual work)	95 min	Methodical instruction for students, lecture notes, reference data, posters. Manuals, reference materials, tables.	
4.	Control of knowledge	25 min	Tests for control	
5.	Analysis and conclusions. Home work	15 min		

7. **Tasks for self-work:**

- list of questions to be study:

1. Classification of organic substances according to the carbon skeleton and functional groups.

2. Nomenclature of bioorganic compounds: trivial, radico-functional (rational), international (substitutive, IUPAC nomenclature).

3. Isomerism of organic compounds. A.M. Butlerov’s contribution to the development of fundamental principles of isomerism.

4. Electronic structure of carbon atom. The nature of the chemical bond in organic compounds.

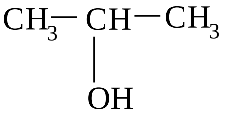
5. Spatial structure of organic and bioorganic compounds:

   a) conformations of compounds with sp^3-hybridized carbon atom;
   b) structure of cycloalkanes. Bent (“banana”) bonds;
   c) open and closed conjugated systems. Aromaticity. Huckel's rule.

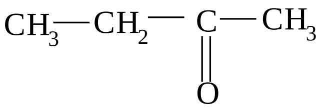
6. Mutual influence of atoms in the molecules of organic and bioorganic compounds. Inductive and mesomeric effects.

Teaching tasks and examples of their solution

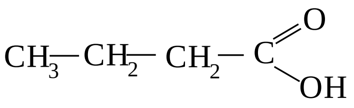
Task №1. What functional groups are in composition of the following molecules?



$CH_3-CH(OH)-CH_3$



$CH_3-CH_2-C(=O)-CH_3$

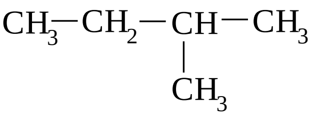


$CH_3-NH-C_2H_5$

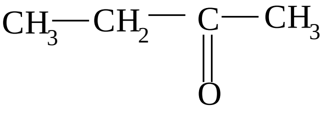
Name the classes to which these compounds belong to.

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:

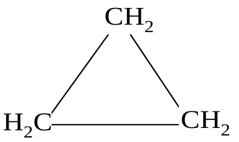


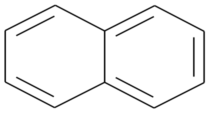
$CH_3-CH_2-CH(CH_3)-CH_3$



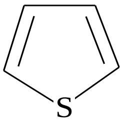
$CH_3-CH_2-C(=O)-CH_3$

2. Carbocyclic compounds containing cycles of carbon atoms, for example:



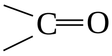


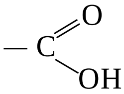
3. Heterocycles containing cycles consisting not only from carbon atoms but also from atoms of other elements, for example:



Each group is divided into classes which properties are due to the definite groups of atoms called functional groups:

$-OH$





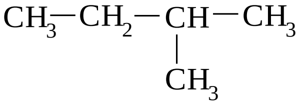
$-NH_2$

–hydroxyl –carbonyl –carboxyl –amino

Let’s consider composition and structure of main classes of organic compounds.

Hydrocarbons are structurally simplest organic compounds consisting only from carbon and hydrogen. Hydrocarbons are classified as follows:

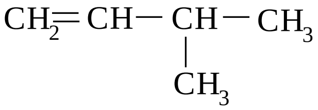
1) saturated (alkanes) with formula C_nH_{2n+2}, for example:



$$CH_3-CH_2-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_3$$

2-methylbutane;

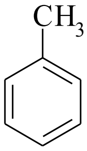
2) unsaturated containing lesser number of hydrogen atoms than saturated and double or triple bonds in the molecules, for example:



$$CH_2=CH-\underset{\displaystyle CH_3}{\underset{|}{CH}}-CH_3$$

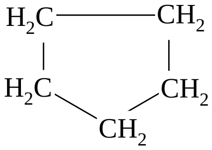
3-methylbut-1-ene;

3) aromatic containing aromatic ring, for example:



methylbenzene (toluene);

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



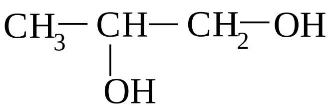
cyclopentane.

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:

$CH_3-CH_2-CH_2-OH$ propanol;

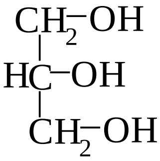
- dihydric alcohols (glycols) with two hydroxyl groups:



$$CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-OH$$

propylene glycol;

- trihydric alcohols (glycerols) with three hydroxyl groups:



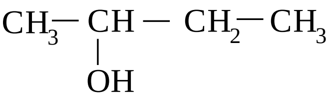
$$\begin{array}{l} CH_2-OH \\ | \\ HC-OH \\ | \\ CH_2-OH \end{array}$$

glycerin

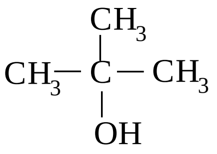
Tetra-, penta-, and hexahydric alcohols also exist.

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:

$CH_3-CH_2-CH_2-CH_2-OH$



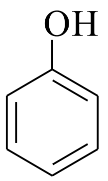
$$CH_3-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-CH_3$$



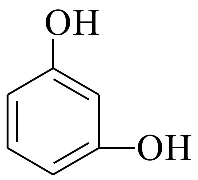
$$CH_3-\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle OH}{\underset{|}{C}}}}-CH_3$$

butan-1-ol butan-2-ol 2-methylpropan-2-ol

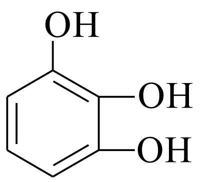
Compounds in which hydroxyl group is directly connected to carbon atom of benzene ring are called phenols. Phenols similarly to alcohols can be mono-, di-, and trihydric:



phenol

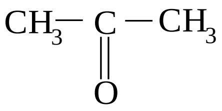


resorcinol (dihydric phenol, diphenol)



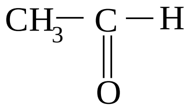
pyrogallol (trihydric phenol)

Compounds containing carbonyl group $>C=O$ are known as oxocompounds. 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:



$$CH_3-\underset{\displaystyle O}{\underset{\|}{C}}-CH_3$$

acetone (dimethylketone)

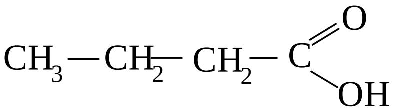


$$CH_3-\underset{\displaystyle O}{\underset{\|}{C}}-H$$

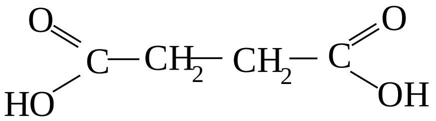
acetaldehyde

Compounds containing carboxyl group $-C\begin{smallmatrix}{=}O\\ -OH\end{smallmatrix}$ belong to carboxylic acids.

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



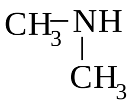
butyric (monobasic)



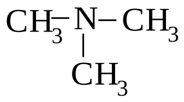
succinic (dibasic)

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:

CH_3-NH_2



$CH_3-NH-CH_3$

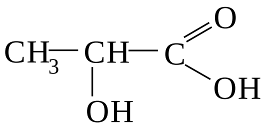


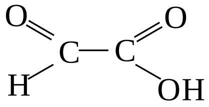
$CH_3-N(CH_3)-CH_3$

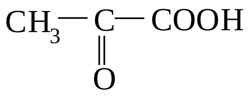
methylamine dimethylamine trimethylamine

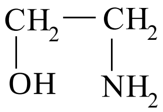
In the given task the first compound is a secondary alcohol, the second one is a ketone, the third one is a carboxylic acid, and the fourth one is a secondary amine.

Task №2. Which classes of heterofunctional compounds do the following substances belong to:

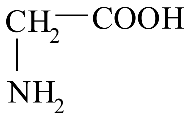








$CH_2(OH)-CH_2(NH_2)$

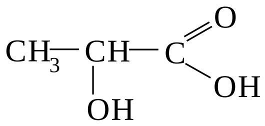


$CH_2(NH_2)-COOH$

?

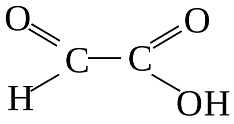
Solution. Organic compounds containing different functional groups are called heterofunctional compounds. Combinations of functional groups make up the following classes of compounds:

1) hydroxy acids which contain hydroxyl and carboxyl groups:

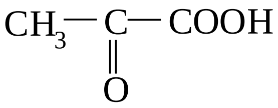


lactic acid;

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

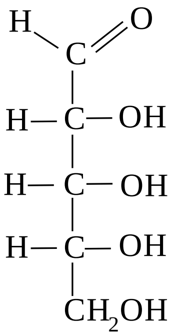


glyoxalic acid

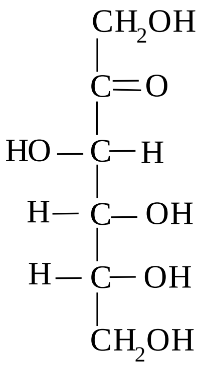


pyruvic acid;

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

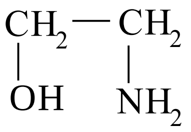


ribose
(aldehyde alcohol)



fructose
(hydroxy ketone);

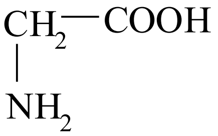
4) amino alcohols which contain hydroxyl and amino groups:



$HO-CH_2-CH_2-NH_2$

ethanol amine;

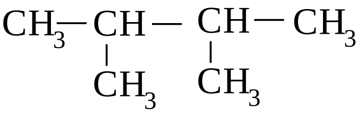
5) amino acids which contain carboxyl and amino groups:



H_2N-CH_2-COOH

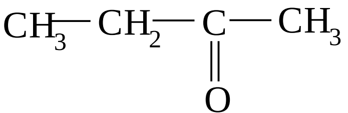
aminoacetic acid

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

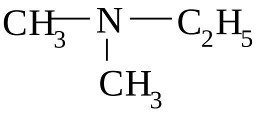


$CH_3-CH(CH_3)-CH(CH_3)-CH_3$

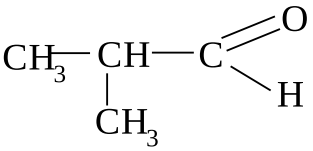
$CH_3-C\equiv C-CH_3$



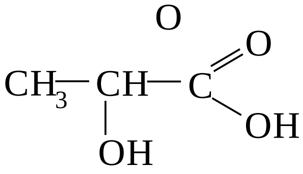
$CH_3-CH_2-C(=O)-CH_3$



$CH_3-N(CH_3)-C_2H_5$

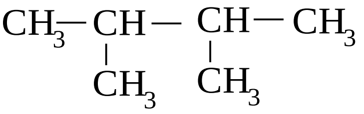


$CH_3-CH(CH_3)-CHO$



$CH_3-CH(OH)-COOH$

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:

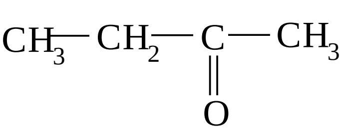


$CH_3-CH(CH_3)-CH(CH_3)-CH_3$

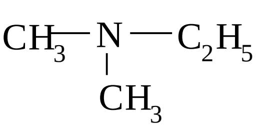
$CH_3-C\equiv C-CH_3$

diisopropyl dimethylacetylene

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



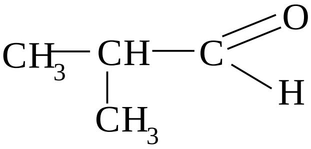
$CH_3-CH_2-C(=O)-CH_3$



$CH_3-N(CH_3)-C_2H_5$

methylethylketone dimethylethylamine

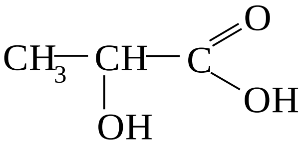
Names of aldehydes come from the names of corresponding acids:



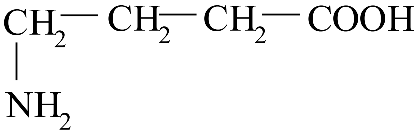
$CH_3-CH(CH_3)-CHO$

isobutyric aldehyde

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:



$CH_3-\underset{OH}{\underset{|}{CH}}-COOH$

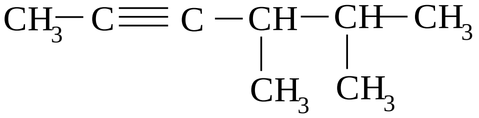


$\underset{NH_2}{\underset{|}{CH_2}}-CH_2-CH_2-COOH$

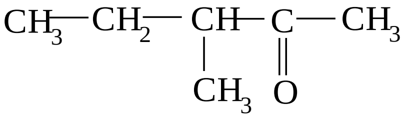
α-hydroxypropionic acid γ-aminobutyric acid

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.

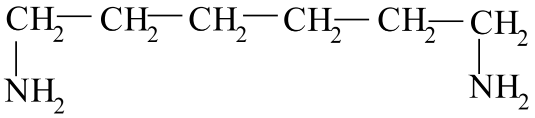
Task № 4. Name according to IUPAC nomenclature:



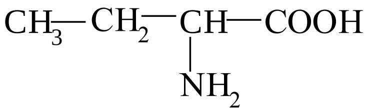
$CH_3-C\equiv C-\underset{CH_3}{\underset{|}{CH}}-\underset{CH_3}{\underset{|}{CH}}-CH_3$



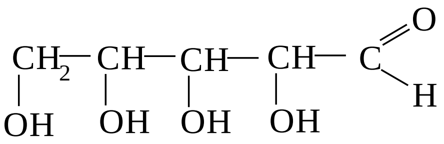
$CH_3-CH_2-\underset{CH_3}{\underset{|}{CH}}-\underset{O}{\underset{\|}{C}}-CH_3$



$\underset{NH_2}{\underset{|}{CH_2}}-CH_2-CH_2-CH_2-CH_2-\underset{NH_2}{\underset{|}{CH_2}}$



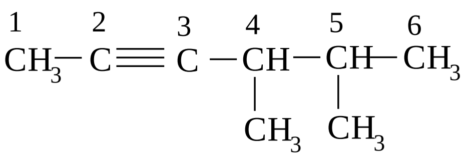
$CH_3-CH_2-\underset{NH_2}{\underset{|}{CH}}-COOH$



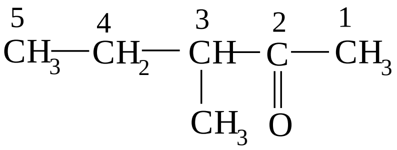
$\underset{OH}{\underset{|}{CH_2}}-\underset{OH}{\underset{|}{CH}}-\underset{OH}{\underset{|}{CH}}-\underset{OH}{\underset{|}{CH}}-CHO$

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:

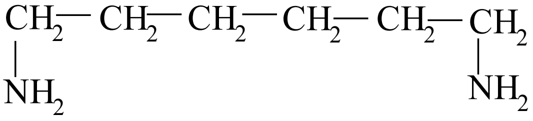


$\overset{1}{C}H_3-\overset{2}{C}\equiv\overset{3}{C}-\underset{CH_3}{\underset{|}{\overset{4}{C}H}}-\underset{CH_3}{\underset{|}{\overset{5}{C}H}}-\overset{6}{C}H_3$



$\overset{5}{C}H_3-\overset{4}{C}H_2-\underset{CH_3}{\underset{|}{\overset{3}{C}H}}-\underset{O}{\underset{\|}{\overset{2}{C}}}-\overset{1}{C}H_3$

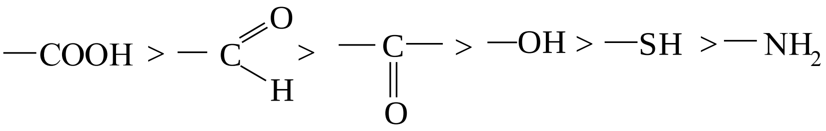
4,5-dimethyl-2-hexene 3-methyl-pentanone-2



$\underset{NH_2}{\underset{|}{CH_2}}-CH_2-CH_2-CH_2-CH_2-\underset{NH_2}{\underset{|}{CH_2}}$

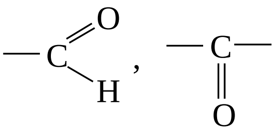
1,6-diaminohexane

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:

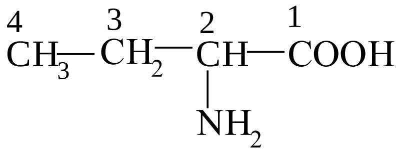


$$-COOH > -C(=O)H > -C(=O)- > -OH > -SH > -NH_2$$

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

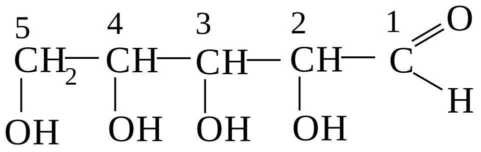
	–OH	–SH	$-NH_2$
−oxo	–hydroxy	–mercapto	−amino

The IUPAC names of heterofunctional compounds are given below:



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

2-aminobutanoic acid



2,3,4,5-tetrahydroxypentanal

Task № 5. 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.

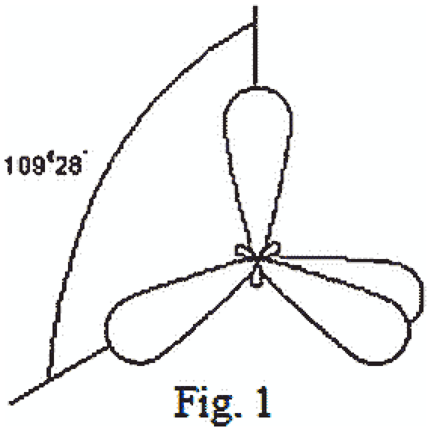


Fig. 1

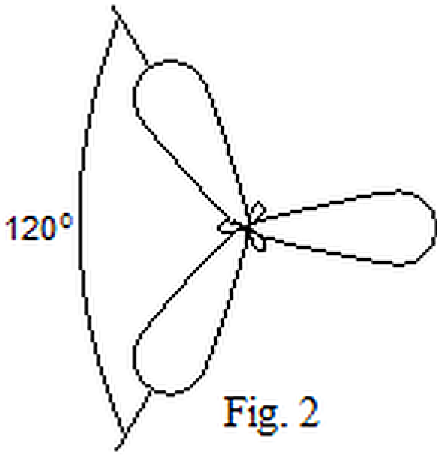


Fig. 2

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°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.

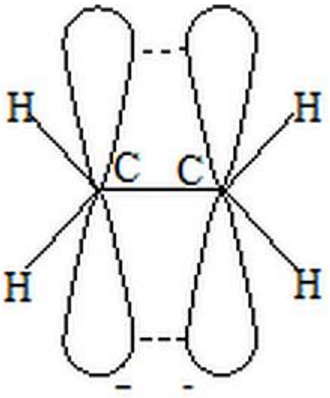


Fig. 3

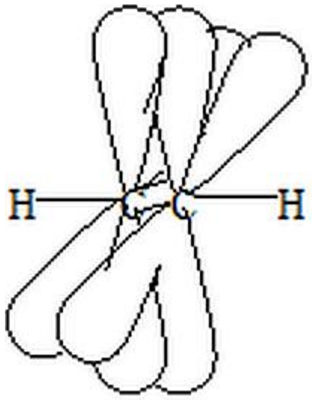


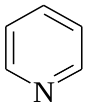
Fig. 4

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-hybridizied 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-hybridizied carbon atoms are ethylene and its homologues (alkenes).

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).

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 №6. 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:

$$CH_3–CH=CH–CH_2–CH=CH_2$$

1,4-hexadiene

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).

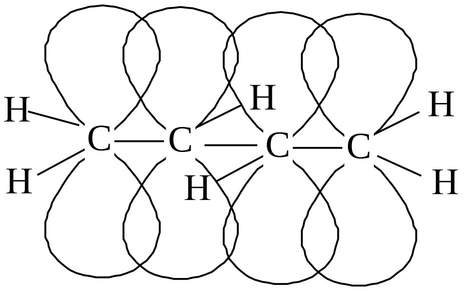


Fig. 5

Side-one 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.

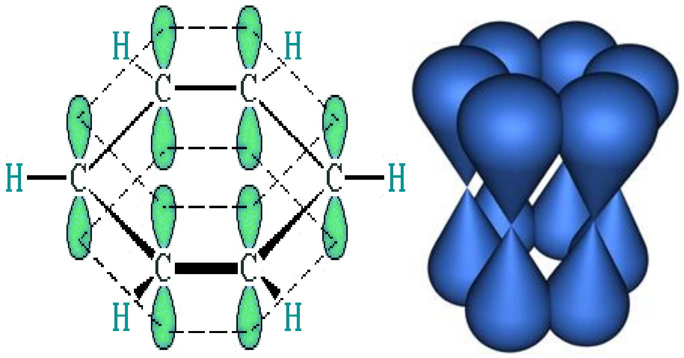


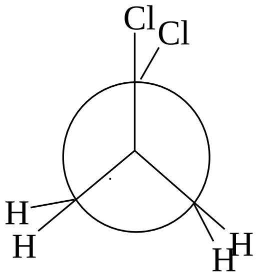
Fig. 6

Task № 7. Draw eclipsed and staggered conformations of 1,2-dichloroethane. Which one possesses lesser energy?

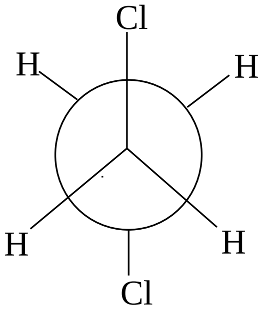
Solution. The mutual arrangement of atoms bonded only by σ-bond is not rigid as atoms can rotate around the axis connecting them. Structures formed due to this rotation are called conformations. These are different forms of molecules of the same substance. Any specific conformation is only a temporary 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.

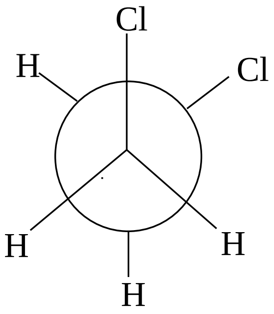
Conformation in which the substituents (chlorine atoms) are located at a minimal distance and eclipse each other is called eclipsed conformation. Maximal distance between substituents corresponds to the staggered conformation. The other conformations are called gauche.



eclipsed



staggered



gauche

Task № 8. 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°.

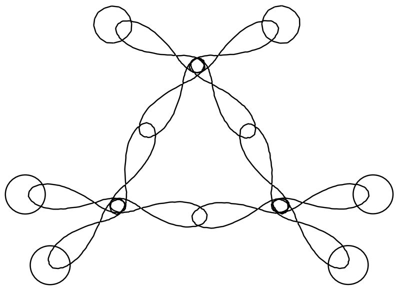


Fig. 7

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.

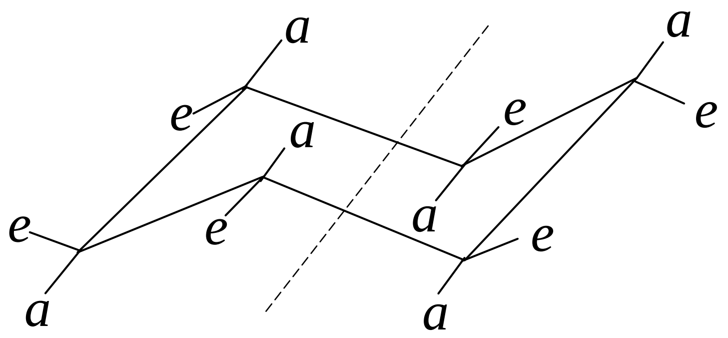


Fig. 8

Remaining six bonds are located peripherally (around the cycle) at an angle to the axis of symmetry 109°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 № 9. 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:

cis-2-butene trans-2-butene

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 № 10. 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.

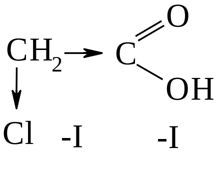
Shifting of the electronic density of σ-bond to one of the bonded atoms transmitted through the chain of σ-bonds in the molecule is called inductive effect (I-effect). The direction of shifting of the electronic density is indicated by the arrow which coincides with the valence dash and directed towards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

$$CH_3 \rightarrow CH_2 \rightarrow CH_2 \rightarrow Cl$$

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).

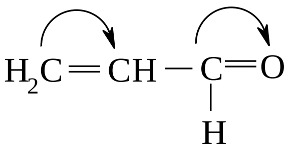
Electron-donating substituents, metal atoms and alkyl groups $-CH_3$,$-C_2H_5$, etc., have positive inductive effect. In the latter case, the +I-effect is due to the slight polarity of C-H bonds (electronegativity of carbon atoms is 2.5, and electronegativity of hydrogen is 2.1 according to Pauling scale). With the increasing number of carbon atoms in the alkyl radical +I-effect increases: $C_3H_7- > C_2H_5-> -CH_3$.

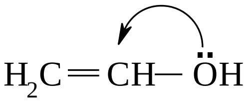
Negative inductive effect of electron-withdrawing substituents is shown by the following: -OH, > C = O, -COOH, $-NH_2$,-OR, and halogens. The inductive effect influences the properties of organic compounds. Thus, replacement of hydrogen atom in acetic acid radical with chlorine possessing -I-effect, 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 (>C = O, -COOH, $-NO_2$), or a lone pair of electrons

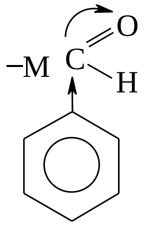
(-OH,-NH_2, halogens). When such substituents are connected to sp^2- or sp-hybridized carbon atoms, the electrons of π-bonds or paired electrons of substituents are conjugated with π-electrons of the carbon skeleton. Mesomeric effect is indicated by curved arrows:





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). Ssubstituents having π-bond (>C = O, -COOH, -NO_2) posses negative mesomeric effect; substituents having unshared electrons (-OH, -NH_2, halogen) posses 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

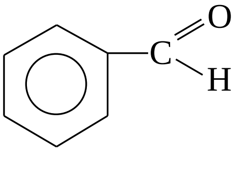
№ 1

1. Write the rational and IUPAC names of aminalon $H_2N-CH_2-CH_2-CH_2-COOH$. Aminalon participates in brain metabolism.

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

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

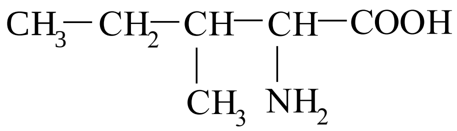
$H_3C–CH_2–COOH$



$H_3C–CH_2–CH=CH–Cl$

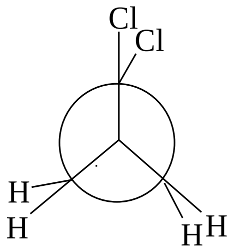
№ 2

1. Write the IUPAC name of proteinogenous amino acid having the structure:



$$CH_3{-}CH_2{-}\underset{\displaystyle CH_3}{\underset{|}{CH}}{-}\underset{\displaystyle NH_2}{\underset{|}{CH}}{-}COOH$$

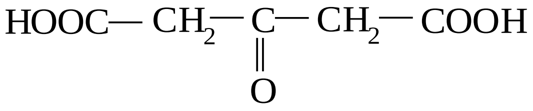
2. Name the conformation given in Newman projection. What is the compound?



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

№ 3

1. Write the IUPAC name of acetone-dicarboxylic acid which belongs to ketone bodies detected in urine of patients suffering from diabetes mellitus:

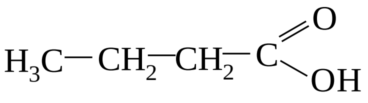


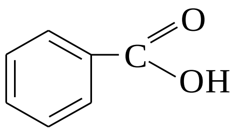
$$HOOC{-}CH_2{-}\underset{\displaystyle O}{\underset{\|}{C}}{-}CH_2{-}COOH$$

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:

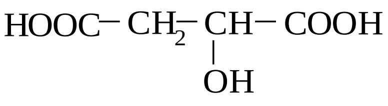
$H_2C{=}CH{-}Br$





№ 4

1. Write the IUPAC name of malic acid which participates in Krebs cycle:



$$HOOC{-}CH_2{-}\underset{\displaystyle OH}{\underset{|}{CH}}{-}COOH$$

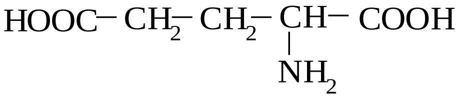
Indicate functional groups in the molecule.

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

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. Write the IUPAC name of glutamic acid which is used for nervous system diseases treatment:

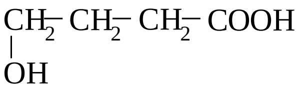


$$HOOC-CH_2-CH_2-\underset{NH_2}{\underset{|}{CH}}-COOH$$

2. Draw the most favorable conformation of cyclohexanol.
3. Give the structure of pyridine and prove that it is aromatic.

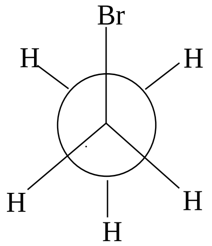
№ 6

1. Write the IUPAC name of γ-hydroxybutyric acid which is used in anesthesiology:



$$\underset{OH}{\underset{|}{CH_2}}-CH_2-CH_2-COOH$$

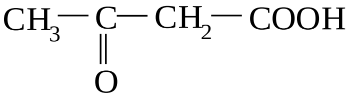
2. Name the conformation given in Newman projection. What is the compound?



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

№ 7

1. Write the IUPAC name of acetoacetic acid which forms in the metabolism of higher fatty acids:

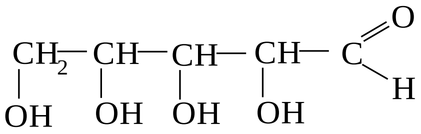


$$CH_3-\underset{O}{\underset{\|}{C}}-CH_2-COOH$$

2. Draw the most favorable conformation of bromocyclohexane.
3. Write the structural formula of β-pyridine carboxylic acid (nicotinic acid, vitamin PP). Determine electronic effects in this molecule.

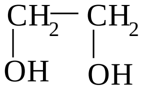
№ 8

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



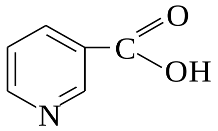
$$\underset{OH}{\underset{|}{CH_2}}-\underset{OH}{\underset{|}{CH}}-\underset{OH}{\underset{|}{CH}}-\underset{OH}{\underset{|}{CH}}-C\overset{\nearrow O}{\searrow H}$$

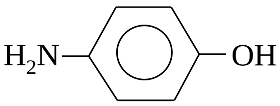
2. Draw Newman projection of the most favorable conformation of ethylene glycol:



$$\underset{OH}{\underset{|}{CH_2}}-\underset{OH}{\underset{|}{CH_2}}$$

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





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№ 9

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

$$HOOC-CH_2-CH_2-COOH$$

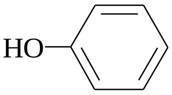
2. Draw the structure and the most favorable conformation of methylcyclohexane.
3. Write the structural formula of p-aminobenzoic acid which is the parent structure of anesthetic drugs. Determine electronic effects in this molecule.

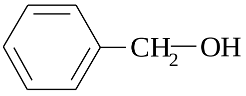
№ 10

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

$$NH_2-CH_2-CH_2-CH_2-COOH$$

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:





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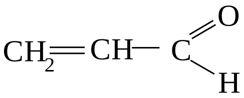
№ 11

1. Write the IUPAC name of acrolein which is the intermediate in the synthesis of some organic compounds:

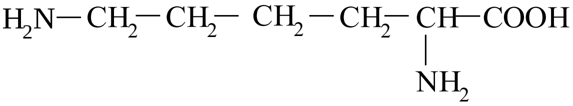


$$CH_2=CH-C\overset{O}{\underset{H}{\lessgtr}}$$

2. Draw Newman projection of staggered conformation of 2-aminoethanol-1. Evaluate the energetic state of this conformation.
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 the IUPAC name of proteinogenous amino acid lysine:



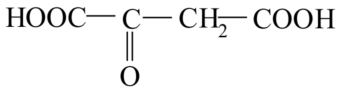
$$H_2N-CH_2-CH_2-CH_2-CH_2-\underset{NH_2}{\underset{|}{CH}}-COOH$$

2. Draw the structure and the most favorable conformation of aminocyclohexane.
3. Determine electronic effects of substituents in the following compounds:

$$H_2C=CH-COOH \qquad H_2C=CH-CH_2-COOH$$

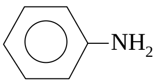
№ 13

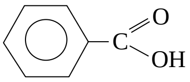
1. Write the IUPAC name of the acid which forms in the Krebs cycle:



$$HOOC-\underset{\overset{\|}{O}}{C}-CH_2-COOH$$

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:





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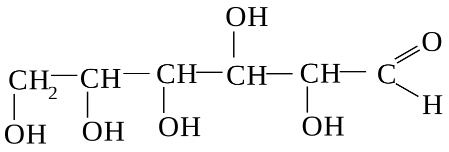
№ 14

1. Write the IUPAC name of monosaccharide glucose:

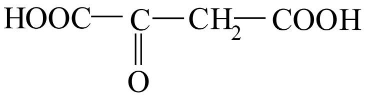


$$\underset{OH}{CH_2}-\underset{OH}{CH}-\underset{OH}{CH}-\overset{OH}{CH}-\underset{OH}{CH}-C\genfrac{}{}{0pt}{}{=O}{-H}$$

2. Draw Newman projections of eclipsed and staggered conformations of 1,2-dichloroethane. Which one possesses lesser energy?
3. Write the IUPAC name of 3-oxopentanedioic acid which belongs to ketone bodies detected in urine of patients suffering from diabetes mellitus.

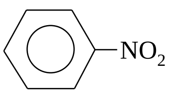
№ 15

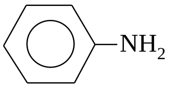
1. Write the IUPAC name of oxaloacetic acid which is the intermediate in carbohydrates metabolism.



$$HOOC-\underset{\overset{\|}{O}}{C}-CH_2-COOH$$

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:





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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.

3. Biological and Bioorganic Chemistry : in two books : Textbook. Textbook 1. Bioorganic Chemistry / B.S.Zimenkovsky, V.A.Muzychenko, I.V.Nizhenkovska, G.O.Syrova; edited by B.S.Zimenkovsky, I.V.Nizhenkovska. —K. :AUP «Medicina», 2017. — 288 p.

Навчальне видання

Класифікація, номенклатура та ізомерія біоорганічних сполук. Природа хімічного зв'язку. Просторова будова органічних молекул. Взаємний вплив атомів в молекулах біоорганічних сполук

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

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