STATE UNIVERSITY OF MEDICINE AND PHARMACY
«NICOLAE TESTEMITANU»

*Department of Biochemistry*

# *BIOORGANIC CHEMISTRY*

## *PRACTICAL GUIDE*

*CHIŞINĂU 2002*

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*Department of Biochemistry*

*Chief of Department –*
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## *PRACTICAL GUIDE*

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# COMPARTMENT ONE.
# STRUCTURE AND CHEMICAL REACTIVITY OF ORGANIC COMPOUNDS – THE BASIS OF THEIR BIOLOGICAL FUNCTIONING

## THEME №1. SPATIAL STRUCTURE OF ORGANIC COMPOUNDS. THEIR CONFORMATION AND STEREOISOMERIA.

The study of the spatial structure of organic compounds has a fundamental importance for biology and medicine because the biochemical processes in the living systems are stereospecific. The stereospecificity of these processes is conditioned by the spatial structure of both organic substrates and enzymes, which catalyze these reactions.

### *INITIAL LEVEL OF KNOWLEDGE*

1. The theory of organic compounds' structure. Structural isomeria. Cis-trans nomenclature.
2. Electronic structure of carbon atom, hybridization types (Sp-3, Sp-2, Sp-1).
3. Covalent bonds. σ- and π- bonds. Donor-acceptor bonds.
4. Classification and nomenclature of organic compounds.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. The spatial structure of organic compounds (configuration). Stereochemical and projection formulas. Molecular models.
2. The conformation of open-chain compounds.
3. The conformation of cyclic compounds.
4. Stereoisomeria. Stereoisomers with one chiralic center. The relative and absolute configuration of enantiomers.
5. Stereoisomers with more than one chiralic center. Enantiomers and diastereomers; the separation of racemic mixtures.

### *QUESTIONS FOR SELF-CONTROL*

1. What is called "structure", "configuration"?
2. Represent the spatial (tetrahedron) structure and stereochemical formulas of methane, ethane and chloroform.

3. Represent the structure and configuration of 1,2-ethanediol.
4. What is called "conformation"? Represent conformation of ethane and n-butane utilizing Newman projection formula.
5. Write the structure, configuration and conformation of cyclohexane. Indicate the axial and equatorial bonds.
6. Write the most stable conformation of menthol (2-isopropyl-5-methylcyclohexanol-1).
7. Which carbon atom is called chiralic (asymmetric)? Chiralic molecules.
8. Which stereoisomers are called enantiomers, diastereomers? Give examples.
9. How can you determine the belonging of enantiomers to D- and L- stereochemical series?
10. Represent the enantiomers of lactic acid using the Fisher formulas.

## *PRACTICAL WORK*

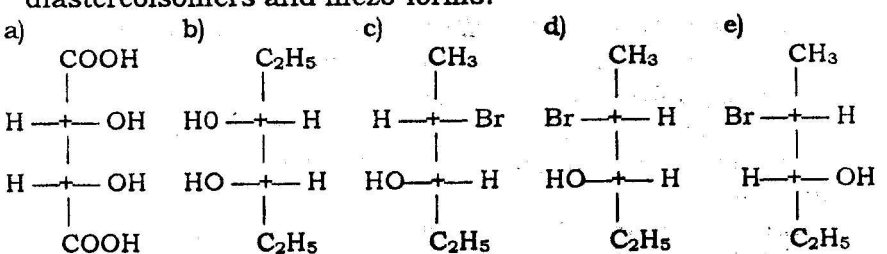
### *Making the molecular models from the plasticine*

Make the models of methane, ethane and cyclohexane (chair conformation) molecules, D- and L- lactic acid enantiomers (tetrahedron and Fisher projection formulas).

## *QUESTIONS AND EXERCISES*

1. What is meant by the notions "structure", "configuration", "conformation"? What kind of formulas are used to represent the configuration and conformation of an organic compound molecule. Represent the structure, configuration and conformations of ethanol, ethylamine, chlorethane and ethanethiol molecules using respective formulas.
2. Represent the structure, configuration and stable conformations of colamine (2-aminoethanol-1), which forms part of cellular membrane phospholipids.
3. Represent the configuration of methanol molecule in space and on the plane.
4. Represent the structure, configuration and stable conformations of n-butane. Which conformation is the most stable? Indicate the energetic state of n-butane conformations.

5. Represent the structure, configuration and conformations of cyclohexane. Indicate the axial and equatorial positions of hydrogen atoms for the chair conformation.
6. Represent the structure and configuration of substituted carbon atoms and the most stable conformation of 1,3-dibrominecyclohexane.
7. Give the definition of notions: asymmetric carbon atom, chiralic center, chiralic molecule, enantiomers, diastereoisomers, racemates, stereoisomers.
8. What substance is used as a configuration standard for determine the enantiomers belonging to D- and L-stereochemical series? Represent the Fisher projection of this substance as D- and L- enantiomers.
9. How can you determine the belonging of enantiomers to D- and L- stereoisomer series? Represent the enantiomers of lactic acid (2-hydroxy-propanoic acid) using Fisher projection formulas.
10. Write Fisher projection formulas of all tartaric acid stereoisomers. Which of these stereoisomers are optic active and which are D- and L-enantiomers?
11. Which of the represented substances are enantiomers, diastereoisomers and mezo-forms?




## THEME №2. THE CONJUGATION AND THE RECIPROCAL INFLUENCE OF ATOMS IN ORGANIC COMPOUNDS' MOLECULES – THE MAIN FACTORS OF CHEMICAL REACTIVITY.

The most important organic substances from the living organisms represent completely or partially conjugated systems. For example, the nucleic acids, proteins, macroergic

compounds, coenzymes, pteridines, porphyrins, carotinoids, quinones etc. are conjugated systems with a different degree of π-electrons delocalization. The majority of medicamentous substances, which have a high action on living cells, are conjugated systems too.

So, we can affirm that the substances, which constitute conjugated sistems, are situated at the origin of life manifestation.

Therefore, the study of electronic structure of conjugated systems is a fundamental theme in the bioorganic chemistry course.

Knowing the particularities of electronic structure and the influence of substitutes in these systems we can explain their thermodynamic stability, chemical reactivity and reaction mechanisms.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Hybridization types of carbon atom.
2. Structure of σ- and π- bonds.
3. Electronegativity of elements.
4. Molecular orbitals.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Open-chain conjugated sistems: diene-1,3 (butadiene-1,3, isoprene); polyenes (β-carotene, retinol (vit.A), retinal).
2. Cyclic conjugated systems. Aromatic state of arenes (benzene), naphthalene, anthracene, phenanthrene, quinones.
3. Aromatic heterocyclic compounds (pyrrole, pyridine, pyrimidine, imidazole, purine, pteridine, porphirine).
4. The polarization of covalent bonds. Electronic effects. Inductive effect.
5. Mezomeric (field) effect. Electron-donor and electron-acceptor substitutes.

### *QUESTIONS FOR SELF-CONTROL*

1. Give the definition of notion: "conjugated system".
2. What is called "conjugation"? What types of conjugation do you now?
3. What does it mean: "electron delocalization"?

4. What is called "conjugation energy" and what correlation exists between its value and the thermodynamic stability of a conjugated system?
5. Give several examples of open-chain conjugated systems, which have a biological importance .
6. Give the definition of "Huekel rule" and of "aromaticity".
7. Explain why benzene is an aromatic system.
8. How can you demonstrate that naphthalene is an aromatic compound?
9. Give examples of aromatic heterocyclic compounds.
10. Why pyrrole is considered an aromatic system with an excess of electronic density?
11. Why pyridine is a $\pi$-deficient system?
12. Show the structure of electronic shell of nitrogen atom (pyrrolic and pyridinic types).
13. Give the definition of inductive electronic effect (I-effect) and show how can it be represented graphic. Which substitutes manifest a negative inductive effect and a positive inductive effect?
14. Which electronic effect is called mezomeric (M-effect). Which substitutes manifest a positive mezomeric effect and negative mezomeric effect?
15. Indicate the type and the sign of substitutes electronic effects in molecules of following substances: p-aminobenzoic acid, benzaldehyde, phenol, aniline.

## *PRACTICAL WORK*
## SOLVING OF SITUATION PROBLEMS.

1. Imidazole forms a part of some important compounds of living organisms (histidine, vitamin $B_{12}$, biotin etc.). Explain why the imidazolic ring is hardly oxidized by the strong oxidants (nitric, chromic acids, solution of $KMnO_4$ in alkaline medium)?
2. The macrocyclic system – porphirin is at the basis of hemoglobin, chlorophyll and other biologic important substances' structure. Write the structural formula of porphirin and explain why porphirin possesses an increased thermodynamic stability?
3. Write the structural formula of pyridoxal phosphate (coenzyme of vitamin $B_6$) and indicate the electronic effects'

type and sign of substitutes from the pyridoxal phosphate molecule.

4. Retinal is the oxidized form of vitamin A. In organism it takes part in the vision process. When combining with opsin it forms rodopsin – an activ receptor of light. Write the structural formula of retinal and indicate the electronic effects of aldehyde group.
5. Well-known heterocyclic system – purine is the chemical basis of many biologic important compounds (some nucleotides, coenzymes, uric acid, medicamentous substances) and represent a condensed heterocyclic system, which consists of pyrimidin and inidazole. Write the structural formula of pyrimidin and explain its increased stability during the oxidation process.

## *QUESTIONS AND EXERCISES*

1. Which of the following substances are conjugated sistems? Name the substances according to systematic nomenclature.
   a) $CH_2=CH-CH=CH_2$; b) $CH_3-CH=CH-CH_2-CH=CH_2$;
   c) $C_6H_5-NH_2$; d) $C_6H_5-CH_2-NH_2$;
   e) $CH_2=\underset{\displaystyle CH_3}{\underset{|}{C}}-CH=CH_2$; f) $CH_2=CH-CH_2-CH=CH_2$.
2. Represent the atomic-orbital models of following substanses' molecules : a) butadiene-1,3; b) benzene; c) toluene; d) hexatriene-1,3,5; e) naphthaline; f) phenanthrene.
3. Give the definition of "conjugation" notion. Indicate the conjugation type in following substances: phenol, toluene, aniline, butadiene-1,3, chlorobenzene.
4. Give the definition of "conjugation energy" notion. Which is the conjugation energy of hexatriene-1,3,5 and benzene? Explain why these values are different?
5. Give the definition of "aromaticity" notion. Write the structural formula of anthracene, phenanthrene, pyrrole, furan, thiophene, pyridine, pyrimidine, imidazole, purine.
6. Show the electronic structure of pyrrolic and pyridinic nitrogen atom. Explain why pyrrole is a heterocyclic system with an excess of electronic density and pyridine is a $\pi$-deficient system?

7. Which is the difference between positive inductive effect and negative inductive effect? Represent graphic inductive effects of substitutes from the following molecules: chlorethane, methanol, thiophene, aniline, p-aminobenzenesulphanilic acid.
8. Give the definition of "mezomeric effect" notion. Represent graphic, indicating the sign of this effect of substitutes in molecules of following substances: salicilic acid, n-nitroaniline, p-aminophenol, benzaldehyde, p-aminobenzoic acid.
9. Which substitutes are called electron-donor (ED) and electron-acceptor (EA)? Determine what kind of substitute is amino-group in ethylamine, aniline and p-aminobenzoic acid; chlorine atom in chlorobenzene molecule, chlorethane.
10. Indicate the electronic effects' type and sign of substitutes in following substances: pyridoxal (vitamin $B_6$), vanillin (p-hydroxy-m-metoxybenzaldehyde) and lactic acid (α-hydroxypropionic acid).

## THEME №3. ACIDITY AND BASICITY OF ORGANIC COMPOUNDS. REACTIONS OF ELECTROPHILIC ADDITION AND ELECTROPHILIC SUBSTITUTION.

The majority of organic compounds from living organisms, participating in metabolic processes, contain functional groups, which are capable to manifest weak acid or alkaline properties.

The study of the regularity, which determined the acido-basic properties of different classes of organic compounds in dependence of their structure, influence of substitutes, etc, has a fundamental importance for understanding the enzymatic acido-basic catalyses, acido-basic character of majority of reactions from living systems.

The study of mechanisms of electrophilic addition and substitution reactions is necessary for prognozing and interpretation of some analogical reaction from living organisms (hydration, ioduration, etc.)

### *INITIAL LEVEL OF KNOWLEDGE*

1. The electronegativity of elements.
2. Electronical effects of substitutes.
3. Electronical structure of pyrrolic and pyridinic nitrogen atom.
4. Sp-3 and Sp-2 hybridization of carbon atom's orbitals.
5. Open-chain and cyclic conjugated systems.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Acid properties of organic compounds, which contain hydrogenous functional groups (alcohols, phenols, thiols, carboxylic acids, amines). Substitutes influence on the acidity.
2. Alkaline properties of organic compounds, which contain heteroatoms with nonbonding (unshared) electrons (alcohols, thiols, ethers, sulfurs, amines, carbonyl compounds). Substitutes influence on the basicity.
3. Acid and basic properties of heterocyclic compounds which contain nitrogen atoms (pyridine, pyrimidine, pirrole, imidazome).
4. Electrophilic addition reactions ($A_E$-reactions). The mechanism of hydrohalogenation and hydration reactions of alkenes (Markovnikov's rule). Hydration of α-, β-unsaturated acids.
5. Electrophilic substitution reactions ($S_E$-reactions). The mechanism of halogenation and alkylation reactions of aromatic compounds (heterocyclic arenes). Substitutes and heteroatoms influence in $S_E$-reactions. Biological importance.

### *QUESTIONS FOR SELF-CONTROL*

1. Give the definition of the notion "acid" according to the Brønsted's theory.
2. Enumerate factors, which influence on the activity of an organic compound. Explain their influence.
3. Compare the acidity of alcohols, thiols, amines. Why these substances have a different acidity?
4. Why carboxylic acids have a more pronounced acidity then phenols, and phenols have a more pronounced acidity then alcohols?

5. Give the definition of the notion "base" accoding to the Brønsted's theory.
6. Which factors determine the basicity of an organic compound. Explain their influence.
7. Compare the basicity of alcohols, thiols, aliphatic and aromatic amines, heterocyclic compounds.
8. Which are the criterions of classification of organic reactions? Which reagents are called electrophilic and which are called nucleophilic?
9. Represent the general mechanism of electrophilic addition reaction.
10. Write the reaction of acrylic acid hydration and explain why it doesn't proceed according to the Markovnikov's rule.
11. Write the general mechanism of electrophilic substitution reaction.
12. Write the reaction of alkylation (methylation) of toluene and benzaldehyde. Describe the mechanism, indicate the role of the catalyst and the influence of substitutes in these reactions.
13. Which are the particularities of electrophilic substitution reaction of aromatic heterocyclic compounds.

## LABORATORY WORK

### *1. Sodium ethylate obtaining and hydrolysis.*

Materials: absolute ethanol, sodium metallic, indicator – phenolftaleine, dry test-tubes, rubber corks, water.

Introduce 3 drops of absolute alcohol and a piece of sodium metallic in a dry test-tube. For hydrogen accumulation the test-tube must be closed with a rubber cork. When the reaction is finished approach the test-tube to the flame and take off the cork. It take place an explosion with a whistling sound, which confirm the burning of hydrogen and air mixture. Add 2-3 drops of water and a drop of phenolftalein solution to the white precipitate of sodium ethylate, which was obtained. What do we observe? What is the cause of red colour appearance? Write the reactions, which have been produced in this experience. Compare the ethanol and water acidity.

### 2. *Sodium phenolate obtainind and decomposition with acids.*

Materials: phenol crystals, NaOH 10 %, HCl 10%, water, dry test-tubes.

Introduce several crystals of phenol and 3 drops of water in a dry test-tube and shake well. What do you observe? Add several drops of sodium hydroxide to the obtained emulsion till the solution become transparent. Then acidulate the obtained solution with several drops of hydrochloric acid (HCl) 10%. The solution become turbid (muddy) again. Why? Write the reactions' equations, the observations and the conclusion of this experience. Compare the phenol and ethanol acidity.

### 3. *Basicity of aliphatic and aromatic amines*

Materials: diethylamine, aniline, HCl 10% solution, saturated solution of picric acid, water, universal indicator, test-tubes.

Introduce in twos drops of water in two test-tubes. Add a drop of aniline in the first test-tube, and a drop of diethylamine in the second one. Shake well both test-tubes. What do you observe? Determine the pH of obtained solution in each test-tube using the universal indicator. What do you observe?

Add a drop of hydrochloric acid 10% to the solution of aniline in water. What do you observe? Why the solution becomes transparent? Add 3-4 drops of saturated solution of picric acid to the solution of diethylamine. What do you observe? Why the solution colour changes? Write the reactions' equations of effectuated experience and the conclusion about the aniline and diethylamine basicity.

### 4. *Bromination of unsaturated compounds*

Materials: solution of oleic acid in carbon tetrachloride ($CCl_4$), solution of bromine in carbon tetrachloride, dry test-tubes.

Introduce 1-2 drops of oleic acid in $CCl_4$ and 4-5 drops of bromine in $CCl_4$ in a dry test-tube. What do you observe? Why does the solution decolouration take place? Write the reaction of oleic acid bromination. What is the practical importance of this reaction?

***5. Tribromine aniline obtaining***

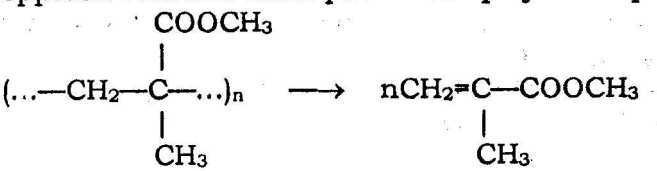
Materials: aniline, bromine water, test tubes.

Introduce a drop of aniline and 5-6 drops of water in a test-tube and shake well. Add several drops of bromine water till a white precipitate of 2,4,6-tribromineaniline will be formed. Write the reaction of 2,4,6-tribromineaniline obtaining. Why does this reaction occur so easy in such soft conditions?

***6. Methyl polymethacrilat depolimerization***

Materials: methyl polymethacrilat, bromine water, test-tube.

Organic glass (plexiglass) is obtained by polymerization of methylic ester of methacrilic acid. During the heating the opposite reaction takes place – the polymer depolymerization.



Methyl polymethacrilat Methyl methacrilat

Introduce a piece of plexiglass in a middle part of a horizontal placed test-tube. Hold the test-tube's bottom inclined a little down. Heat attentively the middle part of the test-tube at the flame till the polymer will melt. When the entire polymer mass melts, stop the heating and observe the appearance of white vapour with a characteristic smell. Little by little the vapour move to the test-tube's bottom and become liquid. After cooling, add several drops of bromine water to the obtained liquid and shake well the test-tube's content. What do you observe? Why did bromine water decolorize? Write the reaction of bromination of the obtained monomer. What conclusion can you do?

## *QUESTIONS AND EXERCISES*

1. Give the definition of notion "acid" according to the Brønsted. Represent in succession of acidity diminution the following substances: methanol, propanol-2, 2-methylpropanol, ethanol, 2-bromoethanol, 2,2,2-tribromoethanol, propanol-

1, glycerol, ethylene glycol, phenol, p-nitrophenol, p-aminophenol.

2. Give the definition of notion "base" according to the Brønsted. Represent in succession of basicity increase the following substances: methylamine; diethylamine, aniline; ethanol, ethantiol, ethylamine; aniline, p-aminophenol, p-nitroaniline; diethyl ether, diethyl sulfate, diethylamine.
3. Write the reaction of hydrohalogenation and hydration of following substance: ethene, propene. Describe the mechanism of the reactions.
4. Compare the reactivity of propene, 2-methylpropene and 2-cloropropene in the reactions of electophilic addition.
5. Write the reaction of acrilic and crotonic acids hydration.
6. Describe the mechanism of electrophilic substitution reaction using the reaction of toluene methylation as example. Indicate the role of electrophilic catalyst.
7. Write the reactions of phenol, aniline and benzoic acid bromination. Describe the mechanism of bromination reaction of benzoic acid and indicate the role of electrophilic catalyst and effect of substitute orientation.
8. Write the reaction of pyrrole nitration, sulfonation and bromination. Indicate the reaction condition and reactants. Explain the increased reactivity of pyrrole.
9. Write the reaction of pyridine nitration, sulfonation and bromination. Indicate the reaction condition and reactants. How can you explain the reduced reactivity of pyridine in these reactions.
10. Write the reactions of benzene, pyrrole and pyridine sulfonation. Explain the mechanism and the conditions for each reaction. How can you explain the different reactivity of benzene, pyrrole and pyridine in these reactions.

## THEME №4. REACTIONS OF NUCLEOPHILIC SUBSTITUTION AND ELIMINATION WITH THE PARTICIPATION OF SATURATED CARBON ATOM ($SP^3$-HYBRID).

Nucleophilic substitution reactions to the saturated carbon atom ($sp^3$-hybrid) are characteristic for the halogen

derivatives (halides), alcohols, thiols, amines and other functional derivatives of saturated compounds.

Nucleophilic substitution and elimination reactions take place in the living organisms too, therefor the knowledge of the factors, which influence them, and their mechanisms permit to prognoses the chemical reactivity of biological substrates and nucleophilic reactants (for example – biological alchylation).

### *INITIAL LEVEL OF KNOWLEDGE*

1. The electronegativity of organogenic elements.
2. The polarization and polarizability of covalent bonds.
3. Electronic effects of substitutes.
4. Conjugated systems.
5. Classification of organic reactions.
6. Reactants' types. Nucleophilic and electrophilic reactants.
7. Acidity and basicity of organic compounds.
8. Electronic structure of the carbonilic group.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Nucleophilic substitution reactions ($S_N$-reactions) with the participation of saturated carbon atom ($sp^3$-hybrid). Hydrolysis reactions of halogen derivatives (halides) ($S_N1$ and $S_N2$ mechanisms).
2. Alkylation reaction of alcohols, thiols, phenols, ammonia and amines. Alkylating agents. Biological role of alkylation reactions.
3. Elimination reactions. Dehydrohalogenation of halogen derivatives (halides) and alcohol dehydration (E1 and E2 mechanisms).

### *QUESTIONS FOR SELF-CONTROL*

1. How do you can explain the capacity of halogen derivatives (halides), alcohols, thiols and other saturated compounds to participle in nucleophilic substitution reactions?
2. Which are the conditions for nucleophilic substitution reaction occurring?
3. Which are the necessary conditions for nucleophilic substitution reaction occurring according to the $S_N1$ mechanism.

4. Write the reaction between the ethylic alcohol and hydrogen bromine, indicate the mechanism of this reaction.
5. Which substrates and reagents are necessary for obtaining during nucleophilic substitution reaction the following substances: diethyl ether, methylphenil ether, diethyl sulphur, ethylamine and diethylamine?
6. What agents of biological alkylation do you now?
7. What factors favor the elimination reaction with participation of saturated carbon atom?
8. Give examples of hydration reactions, which occur in the living organism.
9. Write the reaction of dehydrobromination of propyl bromine.
10. Write the reaction of dehydration of isopropanol. Indicate the conditions of this reaction and explain its mechanism.

## LABORATORY WORK

### *1. The obtaining of ethyl chloride from ethanol*

Materials: sodium chloride, ethanol, sulfuric acid (concentrate), dry test-tubes.

Introduce 2 test-spoons of sodium chloride in a dry test-tube and add 5-6 drops of ethanol. Then add 4 drops of concentrate sulfuric acid to the obtained mixture. Shake well the content of the test-tube and heat it attentively at the flame till the boiling. Avoid the abundant elimination of hydrogen chloride. If hydrogen chloride is eliminated intensively interrupt the heating immediately, then heat anew. Repeat this process 3 times, then heat the content of test-tube more intensive and approach the entrance of the test-tube to the flame. The ethyl chloride, which are eliminated, is catching fire and burns with a green flame as a ring around the entrance of the test-tube. Write the reaction of the ethyl chloride from the ethanol and describe its mechanism.

### *2. Determination of the quality of chloroform*

Materials: chloroform – 1% solution, silver nitrate– 0,5% solution, potassium iodide – 5% solution, 1% solution of starch.

The reactions of the determination of products of the $CHCl_3$ breakdown after action of the light and the oxygen from air are at the base of the method of the chloroform quality

determination. The final products of oxidation are HCl, $CO_2$ and $Cl_2$.

The experiment: for HCl identification introduce in a test-tube 2 drops of chloroform (destined for investigations), 3 drops of distilled water and 1 drop of 0,5% solution of silver nitrate. Shake well the content of the test-tube and observe the processes.

For identification of $Cl_2$ introduce in a test-tube 3 drops of $CHCl_3$ (destined for investigations), 5 drops of distilled water and 1 drop of 5% solution of potassium iodide. Shake well the content of the test-tube and observe the processes.

When chloroform contains $Cl_2$ the inferior stratum of chloroform acquires a pink color. If the pink color is absent add 1 drop of starch solution. What do you observe? What conclusion can you do from this experiment? Write the reactions of HCl and $Cl_2$ identification.

### *3. Obtaining of iodoform from ethanol*

Materials: ethanol, solution of iodine in potassium iodide, 10% solution of sodium hydroxide, test-tubes.

The principle of method consists in oxidation of ethanol in acetaldehyde, which after that interacts with an excess of hypoiodic acid (HOI) and than with the sodium hydroxide.

Experiment. Introduce in a test-tube a drop of ethanol, 3 drops of solution of iodine in potassium iodide and shaking well add 1-2 drops of 10% solution of sodium hydroxide till the solution become colourless. While worming the test-tube in the hands we observe the appearance of a yellow precipitate or the solution become turbid and an intense and persistent smell characteristic for iodoform appears. If the yellow precipitate doesn't appear, add 1-2 drops of iodine in potassium iodide and shake well.

The reaction of transformation of ethanol in iodoform is frequently used for ethanol identification.

### *4. Different properties of halogens from the aromatic ring and from the lateral chain*

Materials: benzyl chloride, chlorobenzene, 1% solution of silver nitrate.

The principle of method is based on the easy of hydrolysis of alkyl halogenats in comparison with chlorobenzene hydrolysis.

Experiment. Introduce in a test-tube a drop of chlorobenzene, and in other a drop of benzyl chloride. Add in test-tubes 5 drops of distilled water each. Warm both test-tubes very attentively up to boiling shaking well all the time, then add in each test-tube 1 drop of silver nitrate. What do you observe? Write the reaction which takes place in the test-tube containing benzyl chloride. Conclude and explain your observations.

### *QUESTIONS AND EXERCISES*

1. Describe the mechanism of reaction between propyl bromide (primary) and sodium hydroxide in aqueous medium. Which factors determine the reaction proceed according this mechanism?
2. Write the reaction between tret-butyl bromide and sodium hydroxide in aqueous solution. Describe the mechanism of this reaction and indicate the factors, which influence its proceeding according this mechanism.
3. Write the reaction between L-2-brominebutan and aqueous solution of potassium hydroxide. Describe the mechanism of this reaction and represent the obtained enantiomer using Fisher projection.
4. Write the reaction of ethyl bromide interaction with ammonia; ethylamine; diethylamine. Name the reaction products and indicate its belonging to the class of organic compound.
5. Obtain ethyl bromide (secondary) from butanol-2. Describe the reaction mechanism.
6. Obtain 2,3-dimercaptopropanol-1 from 2,3-diclorpropanol-1. Indicate the reactant and the medicinal importance of the reaction product.
7. Write the reaction between 1-brompropan and concentrated solution of potassium hydroxide in ethanol. Describe the reaction mechanism and name its product.
8. Which product are obtained at the dehydration of following alcohols: propanol-1, propanol-2, 2-metil-propanol-1. Write this reactions, describe its mechanisms, and explain which of them proceed in more soft conditions and why.

9. Write the reaction of malic acid (2-hydroxibutandioic)dehydration and explain its mechanism. Why malic acid is so easy to dehydrate?

## THEME №5. REACTIONS OF NUCLEOPHILIC ADDITION AND NUCLEOPHILIC SUBSTITUTION WITH THE PARTICIPATION OF CARBONILIC CARBON ATOM ($SP^2$-HYBRID).

Reactions of nucleophilic addition and nucleophilic substitution with the participation of carbonilic carbon atom have an essential biological importance; a lot of such reactions take place in living systems. For example, biosynthesis of proteins, lipids, macroergic compounds, nucleic acids etc.

### *INITIAL LEVEL OF KNOWLEDGE*

1. The electronegativity of organogenic elements.
2. Polarization and polarizability of covalent bonds.
3. Electronic effects of the substitutes.
4. Conjugated systems.
5. Classification of organic reactions.
6. Types of reactants. Nucleophilic and electrophilic reactants.
7. Acidity and basicity of organic compounds.
8. Electronic structure of carboxylic group.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Reactions of nucleophilic addition with the participation of carbonilic carbon atom ($sp^2$-hybrid). The general mechanism. The mechanism of addition of alcohols and primary amines. The role of acid catalysis. The hydrolysis of acetals and imines. The biological role.
2. Reaction of aldol condensation and dissociation. The role of alkaline catalysis. The biological importance.
3. Reaction of nucleophilic substitution at the carbonilic carbon atom (carboxylic acids and its functional derivatives). Acylation reactions (formation of anhydrides, esters, amides and reactions of their hydrolysis). Their mechanism. Acid and basis hydrolysis. Biological role.

4. Condensation of esters. Alkaline catalysis. Biological importance.

### *QUESTIONS FOR SELF-CONTROL*

1. Explain chemical reactivity of aldehydes and ketones in reaction of nucleophilic addition and represent the general mechanism of this reaction.
2. White the scheme of the reactions:
   a) between acetaldehyde and ethanol.
   b) between acetaldehyde and ethylamine.
   Describe the mechanism of this reactions.
3. White the reaction of aldol condensation between two molecules od acetaldehyde. Describe the mechanism and name the reaction product.
4. Represent the general mechanism of nucleophilic substitution reaction with the participation of of carbonilic carbon atom.
5. Write the reactions of anhydride, amide and ethyl ester of acetaldehyde obtaining. What is obtained at the hydrolysis of these substances?
6. Describe the mechanisms of acid and alkaline hydrolysis of methyl acetate.
7. Describe the mechanisms of reactions of propionic acid amide formation and hydrolysis.
8. Effectuate the basic hydrolysis of benzamide and describe the mechanism of this reaction.
9. Write the scheme of ester condensation reaction of ethyl acetate and explain its mechanism.
10. Write the reaction between acetyl coenzyme A and carbon dioxide (IV). Named the reaction product.
11. Represent the scheme of reaction between a α-amino acid and acetyl coenzyme A. What is the biological importance of this reaction?

### LABORATORY WORK

***1. The identification of reducing properties of formic aldehyde***

Materials: 10% solution of sodium hydroxide, 2% solution of copper sulfate, formalin, acetone, test-tubes.

Introduce in two test-tubes: 5 drops of 10% solution of sodium hydroxide, 3 drops of water and 1 drop of 2% solution of copper sulfate in each. In both test-tubes a precipitate of copper (II) hydroxide appears. Add 3 drops of formalin in the first test-tube and 3 drops of water solution of acetone in the second. Heat attentively the both test-tubes until the boiling. What do you observe? Why in the first test-tube the red precipitate appear? Why in the second test-tube the solution become black?

Write the reactions and observations. What conclusion can you do after this experiment?

***2. The identification of acetone by its transforming in iodoform***

Materials: solution of iodine in potassium iodide, 10% solution of sodium hydroxide, acetone, test-tubes.

Introduce in a test-tube a drop of solution of iodine in potassium iodide and add 2 drops of 10% solution of sodium hydroxide until the test-tube's content become colourless. Add to the obtained solution a drop of acetone. What do you observe? Why does a white-yellow precipitate with a characteristic smell appear? Write the scheme of iodoform formation's reaction. What is the clinical importance of this reaction?

***3. The preparation of ethyl acetate***

Materials: sodium acetate (anhydride), ethanol, sulphuric acid (concentrated), dry test-tubes.

Introduce in a dry test-tube 2-3 spatulas of sodium acetate (anhydride), 3-4 drops of ethanol and 2-3 drops of concentrated sulphuric acid. Heat attentively the mixture at the gas flame until the boiling. The eliminated vapors have a smell, which is characteristic for ethyl acetate. The reaction is used for ethanol identification. Write the reaction and describe its mechanism.

## *QUESTIONS AND EXERCISES*

1. Describe the general mechanism of the reaction of nucleophilic addition with the participation of carbonilic carbon atom. Explain the role of acid catalysis and the

substitutes influence on the chemical reactivity of aldehydes and ketones.

2. Write the formation and hydrolysis reactions of the semiacetal and acetal obtained at the interaction of acetaldehyde with ethanol. Describe their mechanism.
3. What is obtained at the interaction of acetaldehyde with ethyl amine? Write the reaction and explain its mechanism. What is the biological importance of imines' formation and hydrolysis reactions?
4. Write the scheme and describe the mechanism of the aldolic condensation reaction of propionic aldehyde. Name the reaction products. What is the biological importance of aldols' formation and hydrolysis reactions?
5. Write the scheme of reaction between acetaldehyde and benzaldehyde in alkaline medium. Describe the mechanism and name the reaction product.
6. Write the reactions of iodoform formation from the acetone and respectively from the ethanol. What is the practical importance of this reaction?
7. For identification of carbonilic combination their interaction with 2,4-dinitrofenilhidrazine is used. Write the reaction between propanal and 2,4-dinitrofenilhidrazine, indicate the mechanism and name the obtained product.
8. Describe the general mechanism of the reaction of nucleophilic substitution with the participation of carboxylic carbon atom. Arrange in order of decrease of chemical reactivity the functional derivatives of carboxylic acids in the reaction of nucleophilic substitution. How can you explain the high reactivity of the anhydrides and chlorine anhydrides in this reaction?
9. Describe the reaction mechanism of formation and hydrolysis in acid medium of ethyl acetate.
10. Write the reactions of formation and acid hydrolysis of the acetamide, describe their mechanisms.
11. What is obtained when condensing ethyl acetate in presence of sodium etoxide in ethanol medium. Write the reaction and describe its mechanism.
12. What is obtained when heating without catalyst the acids: oxalic, malonic, succinic and glutaric. How do you explain the different behavior of these acids when heating?

13. Write the reaction of acid hydrolysis of novocaine and name the reaction products.
14. Nicotine amide (vitamin PP) forms part of coenzyme NAD, which participate in oxidation and reduction reactions in organism. Write the reaction of nicotine amide obtaining from chlorine anhydride.
15. What is obtained at the aldol condensation of two molecules of acetyl coenzyme A. Name the obtained product.
16. Write the reaction of acetyl coenzyme A condensation with pyruvic acid. Name the obtained product.
17. What substance will acetyl coenzyme A interact with to obtain malonil coenzyme A? Write this reaction.

## FINAL WORK № 1.

1. Spatial structure of organic compound. Notions about structure and configuration. Stereochemical and projection formulas.
2. The conformation of open-chain compounds. The conformation of ethane and n-butane. Their energetic characteristic depending on the rotation angle.
3. The conformation of cyclic compounds. The stereochemistry of cyclohexane and its derivatives. The energetic characteristic of cyclohexane conformations.
4. Stereoisomeria of organic compounds. Symmetry and asymmetry of organic compounds. Enantiomers and diastereoisomers. Optical activity of enantiomers.
5. Stereoisomers with one chiralic center. Fisher projection formulas. Relative and absolute configuration of enantiomers. Stereochemical series D- and L- (gliceraldehyde and lactic acid.)
6. Stereoisomers with more than one chiralic center. Tartaric acid. Enantiomers and diastereoisomers of tartaric acid. Racemic mixtures and methods of their separation.
7. Open-chain conjugated systems: diene-1,3 (butadiene-1,3, isoprene); polyenes. Carotinoids: (β-carotene, retinol (vit.A), retinal).
8. Cyclic conjugated systems. Aromaticity. Arenes: benzene, naphthalene, anthracene, phenanthrene. Huekel rule.

9. Aromatic heterocyclic compounds (pyrrole, pyridine, pyrimidine, imidazole, purine, pteridine, porphirine). Biological importance.
10. The reciprocal influence of atoms in organic compounds' molecules. Electronic effects. Electron-donor (ED) and electron-acceptor (EA) substitutes.
11. Acid properties of organic compounds, which contain hydrogenous functional groups (alcohols, phenols, thiols, carboxylic acids, amines). Which factors determine the different acidity of these classes of organic compounds? Substitutes influence on the acidity.
12. Alkaline properties of organic compounds, which contain heteroatoms with nonbonding (unshared) electrons (alcohols, thiols, ethers, sulfurs, amines, carbonyl compounds). Substitutes influence on the basicity. Which factors determine the different basicity of these compounds?
13. Acid and basic properties of heterocyclic compounds which contain nitrogen atoms (pyridine, pyrimidine, pirrole, imidazome).
14. Represent the schemes of hydrohalogenation and hydration reactions of the following substances: propene, 2-methylpropene, 2-chlorinepropene. Describe the mechanism of these reactions. Which of these substances will be the most active in these reactions?
15. Write the reaction of bromination and methylation of toluene and benzoic acid. Describe their mechanism and explain the role of electrophilic catalyst and the influence of substitute in these reactions.
16. Write the nitration, sulfonation and bromination reactions of pyrrole and pyridine. Indicate the reaction conditions and reactants. Explain the different reactivity of pyrrole and pyridine in these reactions.
17. What is the biological importance of reactions of nucleophilic addition. Describe the mechanism of the hydration reactions of the fumaric and cis-aconitic acids. Name the reaction products.
18. What is the biological importance of reactions of electrophilic substitution? Represent the scheme of reactions of triiodtyronine and tyroxine obtaining from the tyrosine.

19. Reactions of nucleophilic substitution with the participation of the saturated carbon atom ($sp^3$) hybrid). Hydrolysis reactions of halides ($S_N1$ and $S_N2$ mechanisms). Which factors determine the reactions' running according the $S_N1$ and $S_N2$ mechanisms?
20. What is the biological importance of alkylation reactions? Represent the methylation reaction of noradrenaline with S-adenosine methionine. Name the reaction products.
21. Elimination reactions (dehydrohalogenation of halides and dehydration of alcohols). E1 and E2 mechanisms. Biological importance of alcohols' dehydration reaction.
22. Nucleophilic addition reactions with the participation of carbonilic carbon atom ($sp^2$-hybrid). General mechanism. Addition reactions of alcohols and primary amines. Their mechanism. The role of acid catalysis. Acetals and imines hydrolysis. The biological role of these reactions.
23. Aldol condensation and dissociation reactions. Role of alkaline catalysis. Biological importance.
24. Reactions of nucleophilic substitution with the participation of carbonilic carbon atom (carboxylic acids and it's functional derivatives). General mechanism. Explain the reactivity of functional derivatives of carboxylic acids in these reactions. Biological importance.
25. Acylation reactions (formation of esters, amides and reactions of their hydrolysis). The mechanisms of these reactions. Role of acid and basic catalysis.
26. Reactions of formation and hydrolysis of anhydrides. The agents of biological acylation – acylphosphate and acylcoenzyme A. Represent the scheme of biological acylation of alcohols, thiols and amines.
27. Esters condensation. Reaction mechanism. Formation and dissociation of β-cetoacids. Biological importance of these reactions.

## COMPARTMENT TWO.

## CLASSES OF BIOLOGIC ACTIV MICROMOLECULAR ORGANIC COMPOUNDS

## THEME №6. HYDROLYSABLE LIPIDS. FOSFOLIPIDS. GLICOLIPIDS. OXIDATION AND REDUCTION OF ORGANIC COMPOUNDS

Lipids are the substances from the living organisms with an heterogen chemical structure, insoluble in water and soluble in organic solvents.

In living organisms the lipids fulfil a lot of important functions. Lipids are the basic structural compounds of cellular membranes, have a protective role, they represent a form of carbon conservation and an important energetic source.

### *INITIAL LEVEL OF KNOWLEDGE*

1. The structure and properties of the double bond. Diastereoisomeria. (E/Z).
2. Electronic structure of free radicals.
3. The conformation of open chains.
4. The mechanism of nucleophilic addition ($A_N$) and nucleophilic substitution ($S_N$) reactions at the carbonilic carbon atom ($sp^2$-hybrid).
5. Ester condensations.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Hydrolysable lipids (neutral). Natural fats as a mixture of triacylglycerides. The structure, nomenclature, synthesis and hydrolysis of triacylglycerides.
2. Superior fatty acids which are found as constituents of lipids. Their structure, nomenclature, conformation. Peroxide oxidation of fatty acids. Arachidonic acid. Biosynthesis of prostaglandins, thromboxans, prostacyclines, leukotrienes. Biological importance of these compounds.
3. β-oxidation of fatty acids. Biological importance.
4. Complex lipids. Phosphatidic acids. Phospholipids: phosphoacylglicerides (phosphatidilcolamines – cephalins,

phosphatidilcolines – lecithins), sphingomyelins. Their structure and hydrolysis. Glycolipids (glycosphingolipids). Cerebrosides and gangliosides. Their structure and biological importance.

5. Reaction of oxidation of alcohols, thiols, sulphurs, carbonilic combinations, amines. Notions of biological oxidation.
6. Reactions of reduction of carbonilic combinations, disulphurs, imines. The principle of action of $NAD^+$ – NADH sistem.

### *QUESTIONS FOR SELF-CONTROL*

1. Represent the conformation structure of palmitic and linoleic acids.
2. Write the scheme of reaction of the dioleostearin obtaining.
3. Write the reaction of oleopalmitostearin hydrolysis in presence of sodium hydroxide. Name the reaction products.
4. Represent the structure of a lecitine, which contain palmitic and linolic acids and effectuated its acid hydrilysis.
5. Write the scheme of reaction of enzymatic oxidation of stearic acid (β-oxidation).
6. Write the scheme of reaction of enzymatic oxidation of propilic alcohol (propanol-1) to the corresponding acid. What product is obtained?
7. Write the reaction of oxidation of ethyl mercaptane (ethanthiol) and indicate the reaction conditions.
8. Write the scheme of process of reciprocal oxido-reduction of cystine.

### LABORATORY WORK

***1. The formation of calcium salt of superior fatty acids***

Materials: soup solution, 5% solution of calcium chloride, test-tubes.

Introduce in a test-tube 1 ml of soup solution and add 1-2 drops of solution of calcium chloride. Shaking well the test-tube content, observe the formation of a white precipitate. Write the reaction of formation of calcium stearate.

### 2. *The dissolution of calcium salt of superior fatty acids in acetic acid.*

Materials: calcium salt of superior fatty acids obtained in the previous experiment, 10% solution of acetic acid, test-tubes.

Add to the white precipitate obtained in the previous experiment 2-3 drops of 10% solution of acetic acid. The precipitate is gradually dissolved at the agitation and the fatty acids are separating and form an oil stratum on the solution. Write the reaction between the calcium stearate and acetic acid. What is the practical importance of this reaction?

### 3. *The oxidation of oleic acid with the potassium permanganate*

Materials: oleic acid, vegetable oil, 5% solution of sodium carbonate, 1% solution of potassium permanganate, test-tubes.

Introduce in a test-tube 2-3 drops of oleic acid or vegetable oil, 2 drops of 5% solution of $Na_2CO_3$ and 1 drop of 1% solution of $KMnO_4$. Shake well the test-tube content. What do you observe? Why? Write the scheme of reaction. What is the practical importance of this reaction?

### 4. *The reaction of oxidation of ethanol with the potassium dichromate*

Materials: ethanol, potassium dichromate, 10% solution of sulfuric acid.

Introduce in a test-tube 2 drops of ethanol, 1 drop of 10% solution of sulfuric acid and 2 drops of potassium dichromate. Warming gradually the test-tube till the solution colour will change from orange to green-blue, indicating the end of reaction (formation of chrome sulfate $Cr_2(SO_4)_3$ ). At the same time the ethanol is transformed in acetaldehyde, which can be recognized by the characteristic smell of ripe apples. Write the reaction of ethanol oxidation.

### 5. *Determination of the quality of diethyl ether*

Diethyl ether, which is used for the narcosis, at the storage under influence of solar light and at the presence of oxygen of air is oxidized forming peroxide compounds and other products, for example, acetaldehyde.

**a) Identification of peroxides.**

Materials: diethyl ether, 10% solution of potassium iodide, 10% solution of hydrochloric acid, 1% solution of starch, test-tubes.

Introduce in a test-tube 4-5 drops of diethyl ether, add 2-3 drops of 10% solution of potassium iodide and 2 drops of 10% solution of hydrochloric acid. At presence of peroxides the ether will be staining in yellow colour because of elimination of free iodine. If colouring is difficult to distinguish, add in the test-tube 1-2 drops of 1% solution of starch. A dark-blue solution will be obtained.

**b) Identification of acetaldehyde.**

Materials: diethyl ether, fuxine sulphurous acid, test-tubes.

Introduce in a test-tube 3-4 drops of diethyl ether and add 3-4 drops of fuxine sulphurous acid solution. Shake the test-tube content. At presence of acetaldehyde a pink staining appears gradually. Write the scheme of reaction of diethyl ether oxidation. Which conclusions can you do about the quality of diethyl ether used in the reaction?

## *QUESTIONS AND EXERCISES*

1. Represent the conformational structure of superior fatty acids, which are constituents of lipids. Write the structure of $\pi$-diastereomers of oleic acid.
2. Represent and characterize the structure of triacylglycerins: 1-oleoil-2-palmitoil-3-stearine-glycerin; 1-linoleoil-2-miristoil-3-arahidono-glycerin. What do we obtain after their alkaline hydrolysis?
3. Write the scheme of reaction of esterification of glycerin for obtaining dioleoil-linoleoil-glycerin. Indicate the mechanism of this reaction, which is catalyzed by acids.
4. Write the scheme of acid catalysis reaction of triacylglycerins: dioleo-stearin, linoleo-dioleine, palmito-linoleo-oleine. Indicate the mechanism of the reaction in acid medium.
5. Represent and characterize the structure of phospholipids: palmito-oleo-phosphatidil-colamine, stearo-linoleo-phosphatidil-coline. What is obtained at their alkaline hydrolysis?

6. Write the scheme of reaction of esterification of glycerin with corresponding acids for obtaining stearoil-oleoil-phosphatidil-coline. Indicate the type of ester bond in molecule.
7. Represent the structure of cephaline, which contain stearic and arachidonic acids. Indicate the hydrophobe and hydrophile parts of molecule. Effectuated the alkaline hydrolysis of this cephaline and indicate the reaction products.
8. What products are obtained at the alkaline and acid hydrolysis of the cephaline and lecithine containing palmito-oleic and stearic acids? Write the scheme of reactions.
9. Represent and characterize the structure of sfingolipids (ceramides and sfingomielines) and of glycolipids (cerebrosides and gangliosides) which contain stearic, arachidonic, linolenic acids.
10. Write the scheme of reaction of peroxide oxidation of oleic acid.
11. Write the scheme and mechanism of β-oxidation of stearic and palmitic acids. Indicate the biological role of this reaction.
12. Give the definition of notions "oxidation" and "reduction" Demonstrate the oxidative capacity of primary, secondary and tertiary alcohols, of phenols, aldehydes, ketones and thiols. Give some examples.
13. Represent the scheme of redox-reactions, which are at the basis of reciprocal transformations: cysteine-cystine and chinone-hydrochinone. Explain the biological role of these processes.

## THEME №7. HETEROFUNCTIONAL COMPOUNDS – METABOLITES AND BIOREGULATORS

The metabolic processes in living organism represent a totality of chemical transformations which are catalyzed by enzymes and coenzymes. The understanding of the chemical reactivity and stereoisomeria of poly- and heterofunctional aliphatic compounds can explain a lot of their metabolic transformations. Among the natural compound with two

functional groups amino-alcohols, hydroxy-, amino- and oxo-acids are prevalent. In addition to the individual activity of functional groups, these compounds show some specific properties, which are determined by the reciprocal influence of the groups present in molecule.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Electronic effects of substitutes.
2. Acidity and basicity of organic compounds.
3. Nucleophilic addition and nucleophilic substitution reactions to carboxylic compounds.
4. Nucleophilic substitution and elimination reactions to the saturated carbon atom ($sp^3$-hybrid).

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Amino-alcohols. Colamine, coline, acetylcoline. Notion about biogene amines: dofamine, noradrenaline, triptamine, serotonine, histamine. Their biological importance.
2. α-, β-, γ- hydroxy and aminoacids. Specific reactions of cyclization and elimination. Lactones and lactams hydrolysis. Biological importance.
3. Monobasic, bibasic and tribasic hydroxyacids. Stereoisomeria (enantiomeria and diastereomeria) of lactic, malic and tartaric acids. Their characterization and biological importance.
4. Oxo-acids (aldehydic and keto- acids): their structure and properties. Keto-enol tautomerism. Chemical reactions of hydroxy- and oxo- acids transformation in Krebs cycle.

### *QUESTIONS FOR SELF-CONTROL*

1. Write the reactions of following transformations: serine → colamine → coline → acethylcoline.
2. Represent the scheme of cateholamines biosynthesis. Their biological importance.
3. Which products are formed when warming the lactic acid with sulfuric acid?
4. Write the specific reactions which take place when warming the α-aminopropanoic, β-hydroxybutiric, γ-hidroxyvaleric acids.

5. Write the rections of hydrolysis of γ-valerolactone and of δ-caprolactam.
6. Write the structural formulas and describe the properties of lactic, malic and citric acids.
7. Represent the projective formulas of stereoisomers of tartaric acid. Indicate the enantiomers and diastereomers. Determine the D- and L- series.
8. Write the decarboxylation reactions of pyruvic, oxalil acetic acids. Which compounds is named "ketone bodies"?
9. Explain the phenomena of tautomerism. Write the scheme of keto-enol equilibrium for oxalil acetic acid and acetyl acetic ester.

## LABORATORY WORK

***1. The demonstration of two carboxylic groups presence in tartaric acid***

Materials: 15% solution of tartaric acid, 5% solution of potassium hydroxide, test-tubes.

Introduce in a test-tube 1 drop of solution of tartaric acid, 2 drops of solution of potassium hydroxide and shake well. Gradually a white crystals slightly soluble in water of acidic potassium salt of tartaric acid (potassium hydrotartrate) are formed. Then add in the test-tube 4-5 drops of solution of potassium hydroxide. Thus the crystalline precipitate gradually solves, as potassium tartrate is formed – a salt which is well soluble in water. Keep solution for the following experience. Write the equations of reactions.

***2. Demonstration of hydroxil groups presence in tartaric acid.***

Materials: potassium tartrate, 2% solution copper (II) sulphate, 10% solution sodium hydroxide, test-tubes.

Introduce in a test-tube 5 drops of solution of copper sulfate and 2 drops of 10% solution of sodium hydroxide. A light-blue precipitate of copper hydroxide immediately drops out. Add to it the solution of potassium salt of tartaric acid (from the previous experience). It take place a dissolution of a light-blue precipitate and formation of a transparent blue solution known under the name of Felling reactive, which does not decompose at warming and is used for detection of glucose.

### *4. Decomposition of citric acid*

Materials: citric acid (crystalline), concentrated sulphuric acid, solution of barium hydroxide, solution of iodine in potassium iodide, 10% solution of sodium hydroxide, test-tubes.

In the dry test-tube, supplied with a gas elimination tube, place a spatula of citric acid and 10 drops of concentrated sulfuric acid and heat up. Approach a burning match to the end of the gas elimination tube; the eliminating gas burns with a blue flame, which is characteristic for carbon (II) oxide. Then the end of the gas elimination tube lower in other test-tube which contain 5 drops of solution of barium hydroxide. A white precipitate immediately appears. Why? Move the gas elimination tube to another test-tube, which contain 2 drops of solution of iodine in potassium iodide, previously decolorized by addition of 1-2 drops of 10% solution of sodium hydroxide; the pale yellow precipitate of iodoform drops out.

Write the reaction of decomposition of citric acid and the reactions for detection of products formed at its decomposition (acetone and carbon dioxide).

### *4. Ketone decomposition of acetoacetic ester*

Materials: acetyl acetic ester, 10% solution of sulphuric acid, solution of barium hydroxide, solution of iodine in potassium iodide, 10% solution of sodium hydroxide, test-tubes.

In a test-tube with a gas elimination tube place 5 drops of acetoacetic ether and 5 drops of 10% solution of sulfuric acid. Heat up cautiously the test-tube and the end of gas elimination tube lower in the second test-tube with 5 drops of barium hydroxide solution. After solution grows turbid, move the gas elimination tube in the third test-tube which contain 2 drops of iodine solution in potassium iodide, previously decolorized by addition of several drops of 10% solution sodium hydroxide. In the second test-tube the pale yellow precipitate with a characteristic smelt of iodoform drops out. Write the equations of reactions.

### *QUESTIONS AND EXERCISES*

1. Write the structural formulas of biogene amines – colamine, coline, noradrenaline, adrenaline. Represent the scheme of their biosyntheses.

2. Write the reactions: a)of colamine and noradrenaline methylation; b)coline acetylation; c) acetylcoline hydrolysis; d) noradrenaline and adrenaline interaction with hydrochloric acid.
3. Write the specific reactions which take place at the warming of α-, β-, γ- and δ-amino and hydroxy acids. Why is contra-indicated the thermic sterilization of antibiotics solutions?
4. Lactones and lactams hydrolysis; write the scheme of acid hydrolysis reactions of γ-valerolactone, γ-butirolactam, δ-valerolactone, δ-valerolactam.
5. Write the reactions of interaction of α-hydroxypropanoic, α-aminopropanoic, α-hydroxysuccinic acids with following reagents: a)NaOH; b)$C_2H_5OH$; c)$CH_3COCl$.
6. What is the behavior of α-hydroxy acids at the warming with concentrated sulfuric acid? Write the reactions, which take place at the warming of lactic and citric acids with sulfuric acid. How can we identify the products of citric acid decomposition?
7. Give the definition of notion "enantiomers". Represent the projective formulas of enantiomers of lactic and malic acids, of α-alanine. How can we determine the belonging to D- or L-steric series?
8. Represent the projective formulas of stereoisomers of tartaric acid. Indicate the enantiomers and diastereomers. Which carbon atom determine the belonging of hydroxy acids to the steric series.
9. Write the structural formulas of the main oxo-acids, which participate at the vital processes: glyoxalic, pyruvic, acetyl acetic, oxalil acetic, α-ketoglutaric and name them according to the systematic nomenclature.
10. Explain the phenomena of tautomerism. Represent the keto-enol tautomerism, which is characteristic for acetyl acetic and oxalil acetic acids. Demonstrate the existence of two tautomeric forms of acetyl acetic ester (using chemical equations).
11. Write the schemes of decarboxylation reactions of acetyl acetic and oxalil acetic acids. Which compounds is named "ketone bodies" and why?
12. Write the reactions of interaction of pyruvic and α-ketoglutaric acids with ethanol and with cyanhydric acid.

## THEME №8. BIOLOGIC ACTIVE HETEROCYCLIC COMPOUNDS.

The enormous importance of heterocyclic compounds is explain by the fact, that they constitute the structural basis of a lot of natural substances and of a number of pharmaceutical preparations. For example, the pyrrolic cycle, both aromatic and hydrogenated, is a structural component of a number of important biologic active compounds – amino acids (proline, triptophan), hemoglobin, chlorophyll, alkaloids, coenzymes, etc.

Pyridine cycle is the basis of nicotine amides structure, which form part of the coenzymes NAD and NADP, of the vitamins $B_6$, PP and other medicinal preparations.

Pyrimidine and purine cycles form part of the nucleic acids, which determine the process of protein synthesis in cells etc.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Effect of conjugation and aromaticity.
2. Electronic structure of pyridine and pyrrole nitrogen atom.
3. Reactions of electrophilic and nucleophilic substitution.
4. Acidity and basicity of organic compounds.
5. Chemical properties of hydroxyl-, amino- and carboxyl-groups.
6. Lactim-lactam tautomerism.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Heterocyclic systems. The five-member aromatic heterocycle with one heteroatom: furan, thiophen, pyrrole, indole and their biologic active derivatives. Their structure and biological importance.
2. The five-member aromatic heterocycles with two heteroatoms: imidazole, pyrazole, thiazole and their biologic active derivatives. Structure, biological and medical importance.
3. The six-members aromatic heterocycles: pyridine, pyrimidine, quinoline and their biologic active derivatives. Their structure and biological importance.
4. Condensed ring aromatic heterocycles: purine, pteridine and their biologic active derivatives. Their structure and biological importance.

## QUESTIONS FOR SELF-CONTROL

1. Represent the structure of furacillin, biotin and explain their biological importance.
2. Write the scheme of reactions of decarboxylation of histidine and triptophane. Name the obtained products.
3. Represent the structure of antipyrine, amidopyrine and analgyne, characterize their physiological action.
4. Write the reaction of obtaining of methyl pyridine iodide and of its interaction with hydrogen atom.
5. Write the reactions of obtaining of nicotinic acid, nicotinamide, cordiamine, isonicotinic acid, tubazid (isoniazid), phthivazid. What is their biological importance?
6. Represent the structure of barbituric acid and its derivatives: barbital, phenobarbital, barbamil. Their biological importance.
7. Write the structural formulas of 8-hydroxychinoline, enteroseptol, vitamin B1 and explain their physiological action.
8. Represent the tautomerism of barbituric acid, xantine, and uric acid.
9. Represent the structure of methylated xanthines (theophylline, theobromine, coffeine) and explain their physiological action.
10. Write the structural formulas of pteridine, folic acid and riboflavin. Their biological role.

## LABORATORY WORK

### *1. Reaction of antipyrine and amidopyrine with iron (III) chloride*

Materials: crystalline antipyrine and amidopyrine, 1% solution of iron (III) chloride, test-tubes.

Introduce in a test-tube several crystals of antipyrine, add 5 drops of water and 1 drop of 1% solution of iron (III) chloride ($FeCl_3$). An intensive and stable orange-red staining appears. For comparison place in other test-tube several crystals of amidopyrine. Add 5 drops of water and 1-2 drops of iron (III) chloride. A violet staining appears, but it is evanescent.

The staining of antipyrine in presence of iron chloride is caused by formation of a complex compound - ferropyrine, and of amidopyrine – by formation of oxidation products.

The reaction with iron chloride is qualitative, permitting to distinguish the amidopyrine from antipyrine.

***2. Reaction of antipyrine and amidopyrine with nitrous acid***

Materials: crystalline antipyrine and amidopyrine, 10% solution of sulfuric acid, 5% solution of sodium nitrite, test-tubes.

Introduce in one test-tube several crystals of antipyrine, in another – of amidopyrine. In both test-tubes add 2 drops of water, 2 drops of 10% solution of sulfuric acid and 2 drops of 5% solution of sodium nitrite in each. In the first test-tube a emerald-green staining appears; the reaction product is a nitrozocompound. In the second test-tube an unstable violet staining appears; the violet products is formed as a result of amidopyrine oxidation.

The reaction with nitrous acid is used in pharmaceutical practice for difference antipyrine and amidopyrine from each other.

Write the scheme of nitration of antipyrine.

***3. Solubility of uric acid and its sodium salt in water.***

Materials: uric acid, 10% solution of sodium hydroxide, test-tubes.

Place in a test-tube a small quantity of uric acid (several crystals). Add on drops 8 drops of water, shake well and be convinced, that the uric acid does not solve. Its solubility in water is 1:39 000. However, is worth adding 1-2 drops of 10% solution sodium hydroxide, as the turbid solution is instantly clarified in consequence of formation of the easily soluble sodium salt. Keep solution for the following experience. Write the reaction of uric acid interaction with sodium hydroxide.

***4. Identification of uric acid (murexid reaction)***

Materials: sodium urate (from the previous experiment), concentrated nitric acid, 10% solution of ammonia, test-tubes.

On subject glass with the help of the pipette place 2 drops of solution of sodium salt of uric acid (sodium urate, which was obtained in the previous experiment). Add 1 drop of

the concentrated nitric acid and cautiously evaporate it above the flame of the burner. As soon as the solution will be evaporated and a weak reddening of the stain on the place of the former drop appears, stop warming. When the glass will cool down, near the stain place 1 drop of 10% solution of ammonia. On the place of contact the appearance of a strip of purple-violet colour is observed (murexid reaction)

Murexid reaction is applied at analysis of urinary stones, and also to identifying the coffeine, theobromine and other purine bases, as qualitative reaction to the purine ring.

### *QUESTIONS AND EXERCISES*

1. Write the structural formulas of heterocyclic systems with one heteroatom: furan, thiophen, pyrrole, pyridine, quinoline. Explain the acid-alkaline properties of these compounds. Write the reaction of methyl pyridine iodide formation and its interaction with the hydride-ion. What biological process have this reaction at the basis?
2. How can you explain the tendency of heterocyclic systems (furan, thiophen, pyrrole, pyridine) to participate in the reactions of electrophilic substitution. Write the reactions of halogenation, nitration and sulfonation of these compounds and name the obtained products.
3. Notion of tetrapyrrolic compounds. Represent the structure of porphyrine, protoporphyrine and heme. What is their biological role?
4. Represent the structure of medicinal substances, which have at the basis the pyridinic cycle: nicotinic acid and its amide (vitamin PP), cordiamine, isonicotinic acid, isoniazide, phthivazide, pyridoxale and pyridoxale phosphate, oxine and enteroseptole.
5. The five-member heterocycles with two heteroatoms: imidazole, pyrazole, thiazole. Write the structure of pyrazole derivatives: antipyrine, amidopyrine, analgine, butadione. Explain the importance of reactions of antipyrine and amidopyrine with iron (III) chloride with nitrous acid.
6. Represent the structure and explain the amphoter properties of imidazole. Write the structure of histidine and the reaction of its decarboxylation. Name the obtained product and its biological role.

7. The six members heterocycles with two heteroatoms: pyridine and pyrazine. Represent the tautomerism of barbituric acid. Which type of tautomerism determines its acid properties? Write the formulas of the barbituric preparations: barbital, phenobarbital, barbamil, cyclobarbitol. What is the biological action of these preparations?
8. Represent the structure of vitamin $B_1$ (thiamin), vitamin $B_2$ (riboflavin), vitamin $B_6$ (folic acid). What is their biological role?
9. Write the structural formulas of the purine and of the hydroxipurines, hypoxanthine, xanthine, uric acid and ammonia urate. What illnesses are determined by the formation of insoluble salts of uric acid?
10. Represent the structure of methylated xantines: theophylline, theobromine, coffeine. Explain the essence of murexid reaction and its importance. What is the biological importance of methylated xantines?
11. Write the structural formulas of the indol and triptophane. Represent the scheme of metabolic transformation of triptophane.

## THEME №9. ALKALOIDS. HETEROFUNCTIONAL COMPOUNDS FROM THE BENZENE SERIES – REPRESENTATIVES OF SOME GROUPS OF MEDICINES.

Modern medicine disposes of a large assortment of medicinal substances, destined for treatment, prophylaxis and diagnostics. Creation of some efficient pharmaceutical preparations is a complex problem, which requires the achievements of organic and bioorganic chemistry.

As the initial substances for the production of a number of medicines are used heterofunctional derivatives, which contain different functional groups in the benzene ring (hydroxyl, carboxyl, amino, etc.).

### *INITIAL LEVEL OF KNOWLEDGE*

1. Conjugated and aromatic systems.
2. Chemical properties of hydroxyl, amino and carboxyl groups.

3. N-alkylation and acylation reactions.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Structure and biological role of some alkaloids – derivatives of pyridine, quinoline, indole, tropane. Their importance.
2. p-Aminophenol and its physiologic active derivatives. Analgesic and antipyretic drugs.
3. p-Aminobenzoic acid and its derivatives of medical importance. Local anesthetics and folic acid.
4. Sulfanilic acid and its derivatives. Sulfanilamides. Importance in medicine. Salicylic acid and its derivatives. Analgesic, antipyretic antiseptic and antituberculosis drugs.

### *QUESTIONS FOR SELF-CONTROL*

1. Write the structural formulas of the nicotine, morphine, chinine, cocaine, rezerpine. Their importance in medicine.
2. Write the structural formulas of the fenetedine and paracetamol. Characterize their physiological action.
3. Represent the structure of the local anesthetics - anesthesine and novocaine.
4. Write the reactions of esterification of the salicylic acid with the participation of hydroxyl group. What others pharmaceutical preparations of this series do you know?
5. Write the reactions of esterification of the salicylic acid with the participation of carboxyl group. Characterize the pharmaceutical preparations of this series.
6. Write the structure of p-aminosalicylic acid and characterize its physiological action.
7. Write the reactions of obtaining of the amide of sulphanilic acid (streptocide).
8. Represent the structure of sulphanilamides: ethazol and norsulfazol.
9. Which relation exists between structure and physiological action of sulphanilamides.

### LABORATORY WORK

***1. Reaction of sublimation and decomposition of salicylic acid***

Materials: salicylic acid, dry test-tubes.

Introduce in a test-tube some salicylic acid and warm it till the melting and boiling. The acid is partially sublimated. If you continue the boiling, warming not only the lower part of test-tube, but its walls too, in order to the vapours of boiling acid pass through a warm zone, immediately a characteristic smell of phenol appears, which remain and after the test-tube cooling.

Write the reaction of decarboxylation of salicylic acid. Why the salicylic acid is decarboxylated more easy then the benzoic acid?

***2. Reaction salicylic acid with iron (III) chloride.***

Materials: salicylic acid, 2% solution of iron (III) chloride.

Introduce in a test-tube several crystals of salicylic acid and dissolve them in 1-2 ml of water. Add to the obtained solution 1 drop of 2% solution of iron (III) chloride. What do you observe and how do you explain the experiment's result?

***3. Aspirin hydrolysis.***

Materials: aspirin, 2% solution of iron (III) chloride.

Introduce in one test-tube several crystals of aspirin and dissolve their in 1-2 ml of water. Separate the solution in two parts. Boil the first part of solution several minutes, then cool it. Add several drops of 2% solution of iron (III) chloride in each test-tube. Observe, that a red-violet colour appears only in the test-tube, which was boiled. What conclusion can you do proceeding from the structure of aspirin? Write the reaction of aspirin hydrolysis. What is the practical importance of the reaction of aspirin with iron (III) chloride?

***4. The demonstration of phenol hydroxide presence in phenyl salicylat (salol).***

Materials: salol, ethanol, 2% solution of iron (III) chloride, test-tubes.

Introduce in a test-tube several crystals of phenyl salicylat and dissolve them in 2-3 drops of ethanol. Add to the obtained solution 1 drop of 2% solution of iron (III) chloride. What do you observe? How can you explain the result of experience proceeding from the structure of salol's structure?

### 5. *The reaction of benzoic and salicylic acids with bromine water and potassium permanganate.*

Materials: benzoic acid, salicylic acid, bromine water, 1% solution of potassium permanganate ($KMnO_4$), test-tubes.

Introduce in the first test-tube several crystals of benzoic acid and in the second – some salicylic acid. Dissolve them in 2-3 drops of water and add several drops of saturated bromine water in each. Benzoic acid doesn't decolorize the bromine water, but in the test-tube which contain salicylic acid the colour of bromine water disappears and a precipitate is formed. Why? Write the reaction.

The experiment with potassium permanganate is effectuated in analogical way. Be convinced that benzoic acid doesn't decolorize the solution of potassium permanganate, and salicylic acid decolorize the potassium permanganate. How can you explain the high reactivity of salicylic acid in this reaction.

### 6. *The identification of streptocide by transformation in azo-colouring.*

Materials: White strepticide, 10% solution of hydrochloric acid, 1% solution of $NaNO_2$), β-naphthol, test-tubes.

Introduce in a test-tube several milligrams of streptocide and add 3-4 drops of 10% solution of hydrochloric acid. After cooling the mixture to 5°C, introduce 2-3 drops of sodium nitrite and let it for several minutes. Add to the obtaining mixture several drops of alkaline solution of β-naphthol. A red-orange colour, which is characteristic for nitrogen (azo) colouring is obtained. Write the reaction of diazotization of streptocide and the reaction of formation of the azo-colouring. Which is the importance of this reaction?

### 7. *The reactions of identification of alkaloids.*

Materials: 1% solution of quinine chloride, iodide in potassium iodide, 0,5% solution of tannin, saturated solution of picric acid, test-tubes, pipettes.

Dilute in a test-tube 1 drop of 1% solution of quinine chloride with 5 drops of water. Then put 3 drops of obtained solution on the subject glass at the 2 cm from each other. Near to the first drop put 1 drop of iodide in potassium iodide, near to the second – a drop of 0,5% solution of tannin, and near to the

third - a drop of picric acid. What do you observe at the contraction of the drops? Write the reaction of interaction of quinine with picric acid.

### *QUESTIONS AND EXERCISES*

1. Structure and physiological action of the following alkaloids nicotine, morphine, heroin, papaverine, atropine, cocaine, rezerpine, strychnine. Importance in medicine.
2. Write the reaction of obtaining of phenetedine and paracetamol. Importance of p-aminophenol in medicine.
3. How is the salicylic acid obtained in industry? Why the salicylic acid has a more pronounced acidity then the benzoic acid? Write the reactions of obtaining and hydrolysis of the salicylic acid derivatives: sodium salicylate, methyl salicylate, phenyl salicylate (salol), acetyl salicylic acid (aspirin). What is the importance of these preparations? How the aspirin quality can be determined?
4. Write the reaction of obtaining of p-aminosalicylic acid. What is its utilization in medicine and how can you explain its physiological action?
5. Write the reactions of obtaining of anesthesine and novocaine from p-aminobenzoic acid. What is the medical importance of these preparations?
6. Characterize the importance of folic acid. Explain the physiological action of folic acid.
7. Write the reactions of obtaining of sulphanilamide (streptocide) from aniline.
8. Represent the structure of sulphanilamides: ethazol, sulphapiridazine, sulphadimetoxine and norsulfazol. How can you explain the antibacterial action of the sulphanilamides.
9. Write the structure of the derivatives of phenyl acetic acid – Ibuprofen (Brufen) and ortofen (voltarene). What is the importance of these preparations?

## THEME №10. ISOPRENOIDS. FAT-SOLUBLE VITAMINS. STEROIDS.

Terpenes and steroids constitute an important group of biologic active compounds. A lot of representatives execute functions of regulation of some important physiological processes (hormones, vitamins, bile acids). Among the isoprenoids it can be found substances of a powerful physiological action and of a great therapeutical importance (camphor, menthol, ethereal oils, cardiotonic glycosides). A profound understanding of the structure and properties of these compounds contributes essential to the explication of their physiological action on the organism.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Conformation of cyclohexane, cis- and trans- junction of cyclohexane rings.
2. Chemical properties of hydroxyl, carbonil- and carboxyl groups.
3. Tautomerism of monosaccharides.
4. Structure and properties of O- glycosides.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Isoprenoids. Terpenes. Monocyclic and bicyclic terpenes (limonene, menthol, α-pinene, camphor). Conjugated polyenes. β-Carotene, fat-soluble vitamins (A, E, K). Biological importance.
2. Steroids. Sterane (gonan). Conformational structure of 5α- and 5β-sterane. Hydrocarbons - precursors of steroids.
3. Sterols. Cholesterol. Engosterol. Vitamins D. Biological importance.
4. Steroid hormones. Corticosteroids. Sexual hormones: androgen, estrogen, gestogen hormons. Biological importans.
5. Bile acids: cholic, deoxycholic, glycocholic, taurocholic acids. Biological importance.
6. Cardiac glycosides. Aglicones of cardiotonic glycosides: digitoxigenin and strophanthin. Importance of cardiac glycosides in medicine.

## *QUESTIONS FOR SELF-CONTROL*

1. What are isoprenoids? Formulate the isoprene rule.
2. Which substances are named terpenes. Present the classification of terpenes.
3. Write the structural formulas of the following isoprenoids: limonene, menthol, α-pinene, camphor. Their spreading in nature and importance in medicine.
4. Analyse the structure and indicate the isoprene units in β-carotene, vitamin A (retinol) and retinal. Their biological importance.
5. Which organic compound are classified to steroids?
6. Represent the structure of sterane (cyclopentan perhydrophenantren) and number the carbon atoms.
7. Write the configurational and conformational formulas of 5α- and 5β-sterane.
8. Represent the structure of cholesterol, engosterol and vitamin D. Write the structural formula of the colestan and number the carbon atoms. The importance of vitamin D.
9. Classification of steroid hormones. Their biological importance.
10. Write the structural formulas of the hydrocarbons which formed the skeleton of steroid hormones (pregnane, androstane, estrane).
11. Represent the structure of hormones: corticosterane, prednisolone, androsterone, testosterone, estrone, estradiol. Their biological importance.
12. Write the structural formula of the hydrocarbon which formed the skeleton of bile acids – cholane and number the carbon atoms.
13. Represent the structure of acids: 5β-cholanic, deoxycholic, glycholic, taurocholic. The biological importance of bile acids.
14. Write the structural formula of the hydrocarbon which formed the skeleton of the aglicone of cardiotonic glycosides and formulate its name according to the systematic nomenclature. The importance of cardiotonic glycosides in medicine.
15. Represent the structure and configuration of digitoxigenin and strophanthin and name them according to the systematic nomenclature.

## LABORATORY WORK

***1. Demonstration of unsaturated character of terpens.***

Materials: turpentine, bromine water, test-tubes.

Introduce in a test-tube 2-3 drops of bromine water and 1 drop of turpentine. Shake the test-tube and observe the decolorization of the solution. Write the reaction of the interaction of α-pinene with the bromine water. Which is the practical importance of turpentine?

***2. Oxidation of terpens.***

Materials: turpentine, 2% solution of potassium permanganate, test-tubes.

Introduce in a test-tube 1 drop of 2% solution of potassium permanganate, 5 drops water and 1 drop of turpentine. Shake the test-tube. What do you observe? Write the reaction of the interaction between α-pinene and potassium permanganate in neutral medium.

***3. The property of terpens to activate the oxygen.***

Materials: 0,5% solution of starch, 5% solution of potassium iodide, turpentine, test-tubes.

Introduce in a test-tube 1 drop of 0,5% solution of starch, 1 drop of 5% solution of potassium iodide, 1 drop of turbentine and shake well the test-tube. In a few seconds a violet colouring appears, but gradually becomes blue. The fact demonstrates that free iodine is eliminated. Write the reaction of α-pinene oxidation. Which is the importance of terpens oxidation in natural conditions?

## *QUESTIONS AND EXERCISES*

1. Formulate the isoprene rule. Represent the scheme of ocymene obtaining from isoprene according to the isoprene rule. Represent the classification of terpens.
2. Write the structural formula of limonene, α-pinene and camphor. Indicate the isoprene units. What is the practical importance of these substances?
3. In the composition of some ethereal oils the menthol can be found. Menthol (in form of esters) is included in the composition of the preparations with cardio-vascular action.

Write the reaction of obtaining of the ester, which is formed from the menthol and isovaleric (3-methyl butanoic) acid, which enters in the composition of validol. Name the formed ester.

4. Write the structural formula of β-carotene, vitamin A (retinol) and retinal. Indicate the isoprene units. The biological importance of vitamin A.
5. Represent the structure of liposoluble vitamins from K and E groups. Characterize their biological action. Notion about synthetic analogues of these vitamin.
6. Represent the structure of sterane and number the carbon atoms. Configuratin and conformation of 5α- and 5β-sterane. General characteristics and biological role of steroids.
7. Write the structural formula of the hydrocarbons which formed the skeleton of the steroids: estrogen, androgen and corticosteroid hormones, bile acids, sterols, cardiotonic glycosides. Indicate the junction of A and B cycles, characterize these steroids.
8. Represent the scheme of transformation of ergosterine (ergosterol) in vitamin $D_2$ (calciferol). The biological role of vitamins of D group.
9. Represent the structure of cholesterol (colesten-5-ol-3). Which group of steroids it is referred to? Which is the principal hydrocarbon in cholesterol structure? The biological role of cholesterol.
10. Present the classification of the steroid hormones. Write the structural formulas of the following hormones: hydrocortisone (11- α,17-α,21-trihydroxy pregnen-4-dione-3,20), testosterone, estrone, progesterone (pregnen-4-dione-3,20). Indicate what group of steroid their are referred to. Their biological role.
11. Represent the structure and configuration (junction of A, B, C, D cycles) of 5β-cholanic acid, cholic acid (3α-, 7α-, 12α-trihydroxy-5β-cholanic), deoxycholic acid.
12. Represent the structure and configuration junction of A, B, C, D cycles) of genins of cardiotonic glycosides: digitoxigenin and strophanthin. The importance of these glycosides in medicine.

## FINAL WORK № 2.

1. Hydrolysable neutral lipids. Natural fats as a mixture of triacylglycerides. The structure, nomenclature, synthesis and hydrolysis of triacylglycerides. Biological importance.
2. Superior fatty acids which are found as constituents of lipids. Their structure and conformation. Peroxide oxidation and β-oxidation of natural fatty acids. Biological importance.
3. Arachidonic acid. Biosynthesis of prostaglandins, thromboxans, prostacyclines, leukotrienes. Biological importance of these compounds.
4. Phospholipids. Phosphatidic acids. Phosphatidilcolamines (cephalins), phosphatidilcolines (lecithins) – the structural components of cellular membranes. Their structure, synthesis; acid and alkaline hydrolysis.
5. Sphingolipids, ceramides and sphingomyelins. Glycolipids – cerebrosides and gangliosides. Their structure, hydrolysis and biological importance.
6. Reaction of oxidation of alcohols, thiols, sulphurs, carbonilic combinations, amines. Notions of biological oxidation.
7. Reactions of carbonilic combinations reduction, disulphurs, imines. The principle of action of $NAD^+$-NADH sistem.
8. Amino-alcohols. Colamine, coline, acetylcoline. Notion about biogene amines: dofamine, noradrenaline, triptamine, serotonine, histamine. Their structure, obtaining and biological importance.
9. Hydroxy and amino acids. Specific reactions of α-, β-, γ- and δ-hydroxy and amino acids. Lactones and lactams hydrolysis. Biological importance.
10. Monobasic, bibasic and tribasic hydroxyacids. Stereoisomeria (enantiomeria and diastereomeria) of hydroxy acids. Their characterization and biological importance. Citric acid synthesis and its transformation in Krebs cycle.
11. Oxo-acids (aldehydic and keto- acids: glyoxalic, pyruvic, acetyl acetic, oxalil acetic, α-ketoglutaric), their structure and keto-enol tautomerism. Chemical reactions of hydroxy- and oxo- acids transformation in Krebs cycle. The ion of phosphoenol pyruvat - a macroergic compound. Synthesis and transformation of phosphoenol pyruvat ion in glycolysis.
12. The five-member heterocycles pyrrole, indole, pyrazole, thiazole, imidazole and their biologic active derivatives.

Notion about tetrapyrrolic compounds, pyrazolon and its derivatives, histamine. Their structure and biological importance.

13. The six-member heterocycles: pyridine, pyrimidine, quinoline and their derivatives. Barbituric acid, barbiturates, vitamin $B_1$ (thiamin), vitamin PP, tubazid (isoniazid) and phthivazid. Structure, properties and biological importance.
14. Heterocycle compound with condensed rings and their oxo-derivatives: purine (hypoxanthine, xanthine, uric acid). Methylated xanthines. Pteridine, riboflavin (vitamin $B_2$) and folic acid. Structure and biological importance.
15. Structure and physiological action of alkaloids: nicotine, morphine, chinine, heroin, papaverine, atropine, cocaine, rezerpine, strychnine. Importance in medicine.
16. p-Aminophenol and its physiologic active derivatives. Analgesic and antipyretic drugs.
17. p-Aminobenzoic acid and its derivatives. Local anesthetics. Biological importance of p-aminobenzoic acid as a structural part of the folic acid.
18. Sulfanilic acid and sulfanilamide preparations. Antibacterial action of sulfanilamides.
19. Salicylic acid and its derivatives: analgesic, antipyretic antiseptic and antituberculosis drugs.
20. Unhydrolysable lipids. Isoprenoids. Terpenes. Monocyclic and bicyclic terpenes (limonene, menthol, α-pinene, camphor). Conjugated polyenes. β-Carotene, fat-soluble vitamins (A, E, K). Biological importance.
21. Steroids. Sterane (gonan). Conformational structure of 5α- and 5β-sterane. Classification of steroids and the main hydrocarbons of the principal classes of steroids.
22. Sterols. Cholesterol. Engosterol. Vitamins D. Structure and biological importance.
23. Steroid hormones. Corticosteroids. Sexual hormones: androgens, estrogens, gestogen hormons. Structure and biological importance.
24. Bile acids: cholic, deoxycholic, glycocholic, taurocholic acids. Aglicones of cardiotonic glycosides: digitoxigenin and strophanthin. Notion about cardiotonic glycosides. Structure and biological importance of cardiac glycosides.

## COMPARTMENT THREE. BIOPOLYMERS AND THEIR STRUCTURAL COMPONENTS

## THEME №11. PROTEINOGENIC α-AMINO ACIDS. PEPTIDES.

Among the different classes of natural organic compounds amino acids represent ones of the fundamental components of living cells – animal and vegetal. α- amino acids are the structural units of the proteins, which are necessary for existence of living organism. The total number of amino acids, which were found in the proteins, are around 70, but a group of 20 more important amino acids can be marked among the rest because of their presence in all proteins in various proportions.

Peptides are the natural or synthetic substances, which are constituted from a relative little number of amino acids, which are united between them with the peptide bond. Peptides have a great importance not only as a constituent part of proteins, but also have a number of individual biological functions. For example, hormones oxytocin and vasopressin, which are secreted by the hypophysis, are nonapeptides. The insulin also is a polypeptide, which is a regulator of carbohydrate metabolism.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Acidity and basicity of organic compounds.
2. Chemical properties of carboxyl and amino groups.
3. Thiols oxidation and disulphides reduction.
4. Hydrogen bond.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Proteinogenic α-amino acids (components of proteins). Structure, classification and nomenclature. Amino acids' stereoisomeria. Acid and alkaline properties, bipolar structure, isoelectric point.
2. Chemical properties of α-amino acids: reactions of esterification, alchylation, acylation, deamination, condensation, complex salt and phenylthiohidantoines

formation. The importance of these reactions in the analysys of α-amino acids.

3. α-Amino acids reactions of biological importance. Transamination reactions (biosynthesis of α-amino acids), reactions of oxidative deamination, decarboxylation reaction with formation of biogenic amines – colamine, histamine, triptamine, serotonine, cadaverine, β-alanine, γ-amino butyric acid), reaction of hydroxylation (tyrosine, 5-hydroxytryptophan, hydroxyproline formation). Role of coenzymes: pyridoxal phosphate, $NAD^+$, NADP in these reactions.
4. Peptides. Electronical and spatial structure of the peptide bond. Electrochemical properties and hydrolysis of peptides. Composition and primary structure of peptides and proteins. The determination of amino acid sequence in polypeptidic chain. Chemical synthesis and notion about biosynthesis of proteins.

## *QUESTIONS FOR SELF-CONTROL*

1. Present the classification of α-amino acids, their structure and nomenclature.
2. Explain the acid and alkaline properties of α-amino acids. Which is the influence of pH on the amino acids ionization?
3. Write the reactions of valine interaction with hydrochloric acid, sodium hydroxide, copper sulphate in alkaline medium.
4. Write the reactions of phenylalanine interaction with ethanol, acetyl chloride, methyl iodide.
5. Write the reaction between alanine and formaldehyde, leucine and nitric acid. Importance of these reactions.
6. Write the reactions of phenylthiohidantoines, alanine and valine formation.
7. Write the reactions of deamination *in vivo* and *in vitro* of the following amino acids: triptophan, phenylalanine.
8. Write the reactions of decarboxilation *in vivo* and *in vitro* of the following amino acids: histidine, triptophan, serine.
9. Write the reaction of transamination of alanine with oxalilacetic acid. The mechanism of reaction.

10. Represent the structure and determine pH where is the isoelectric point of the following tripeptides: Ser-Ala-Cys; Val-Phe-Asp.
11. Determine the sequence of α-amino acids in tripeptides: Ala-Phe-Val; Val-Ser-Tyr using method Edman.
12. Write the reactions of synthesis of the dipeptides Val-Ser, Thr-Met, Phe-Ala using the method of activation and blockation of groups.

## LABORATORY WORK

### *1. Demonstration of neutral character of solution of glycine.*

Materials: 1% solution of glycine, 0,1% solution of methyl-red indicator, test-tubes.

Introduce in a test-tube 3 drops of 1% solution of glycine and add 1 drop of 0,1% solution of methyl-red indicator. You will be convinced, that the glycine solution isn't acid. The change of indicator colour takes place in the interval of pH 4,4-6,2. Keep the solution for the next experiment.

Explain why glycine hasn't a acid character. Write the reaction scheme, name the product.

### *2. Rection of glycine with formaldehyde.*

Materials: solution of glycine with methyl-red, obtained in the previous experiment, solution of neutral formalin, test-tubes.

Add to the solution, which was obtained in the previous experiment, an equal volume of formalin. It is observed a rapid change of colour from yellow to red, indicating the formation of acid medium. Explain the processes and write the reaction. Which is the importance of this reaction?

### *3. The characteristic reaction of glycine with ions of copper (II).*

Materials: 1% solution of glycine, copper (II) carbonate, test-tubes.

Introduce in a test-tube 1 ml of 1% solution of glycine and several crystals of copper (II) carbonate. Warm it carefully. A

blue colour appears, which is characteristic for complex salts of ions of copper (II). Write the reaction.

***4. Xanthoproteic reaction.***

Materials: solution of protein (ovalbumin), concentrated nitric acid, 10% solution of sodium hydroxide, test-tubes.

Introduce in a test-tube 1 ml of the ovalbumin solution and add several drops of concentrated nitric acid. A white precipitate or a yellow turbidity is formed. Warm the mixture up to the boiling and observe the formation of a yellow precipitate. Let the solution to cool, then add some drops of 10% solution of sodium hydroxide. The colour becomes more intense (orange). The presence of which amino acids is characteristic for this reaction? Write the reaction.

***5. Biuretic reaction.***

Materials: solution of protein (ovalbumin), 10% solution of sodium hydroxide, 2% solution of copper (II) sulphate, test-tubes.

Introduce in a test-tube 3-4 drops of the ovalbumin solution and add an equal volume of 10% solution of sodium hydroxide and then 1-2 drops of aqueous solution of copper (II) sulphate. A blue-violet characteristic colour appears. Explain this phenomena. Write the scheme of biuretic reaction.

***QUESTIONS AND EXERCISES***

1. Explain the acid and alkaline properties of monoaminocarboxylic and diaminocarboxylic α-amino acids. Isoelectric point.
2. Write the reactions of interaction of the leucine, lysine, asparaginic acid with the diluted solution of sulphuric acid, with sodium hydroxide, with phenylthiochianat.
3. Write the reactions of interaction of the threonine, valine, phenylalanine with copper sulphate in alkaline medium with formaldehyde and with acetyl chloride. The importance of these reactions.
4. Write the reactions of interaction of the alanine and methionine with nitrous acid and with formaldehyde. Indicate the role of these reactions.

5. Which reactions are used for activation of carboxyl group; for blockade the amino- and carboxyl- groups? Write the respective reactions using as an example the amino acid valine.
6. White the reaction of deamination *in vivo* and *in vitro* of the glutamic acid and histidine. Explaine the role of coenzyme NAD in this reaction. Name the products of reactions.
7. White the reaction of decarboxylation *in vivo* and *in vitro* of the tryptophan, histidine and tyrosine. Indicate the conditions and the role of pyridoxal phosphate in this reaction. Name the products.
8. Represent the scheme of transamination reactions of glutamic and asparaginic acids with the respective oxo-acids. Which is the role of pyridoxal phosphate in these reactions. Name the products.
9. Write the structural formulas of the hydroxy amino acids and their reactions with nitrous acid, with acetyl chloride and with formaldehyde. The importance of these reactions.
10. White the schemes of reactions and conditions of the following transformations: phenylalanine – tyrosine, tryptophan –5-hydroxytryptophan, proline – hydroxyproline.
11. Represent the structure and determine in which medium is the isoelectric point of the following tripeptides: Val-Phe-Leu; His-Thr-Lys; Trp-Met-Gly; Phe-Val-Asp. Demonstrate the spatial and electronical structure of the peptide bond.
12. Write the structure and determine the succession of the N-terminal amino acids in the following tripeptides: Ser-Ala-Cys; Ala-Glu-Tyr; Asp-Phe-Trp; Leu-Ile-Phe; Trp-Phe-Thr, using the Edman method of degradation.
13. Explain the essence of the method of chemical synthesis of peptides using the proceeding of activation and blockage of the functional groups. White the scheme of synthesis reactions of the following dipeptides: Ala-Val; Ile-Met; Phe-His; Asp-Phe.
14. Explain the essence and the practical importance of the biuretic and xanthoproteic reactions. White the scheme of corresponding reactions.

## THEME №12. CARBOHYDRATES. MONOSACCHARIDES.

Carbohydrates together with the proteins and lipids are the most important organic substances in the living organisms. In the human and animal organism carbohydrates fulfil a lot of important functions:

- energetic function – source of energy for the cellular reactions;
- protective and mechanic functions;
- coenzymatic function; etc.

Some monosaccharides form part of nucleotides – structural units of nucleic acids. A lot of representatives of carbohydrates participate in some important processes, for example in the anticoagulation of blood, in the immunologic processes, etc. The most important representative of monosaccharides - D-glucose is determined in blood in a concentration of 0,1% and is a direct source of energy for the cellular reactions.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Relative configuration. The D- and L- steric series.
2. Enantiomers and diastereomers.
3. The conformation of cyclic compounds.
4. Nucleophilic addition to the carbonilic combinations.
5. Structure and properties of semiacetals and acetals.
6. Oxidation and reduction of alcohols and aldehydes.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Classification and structure of carbohydrates. Spreading in nature and biological importance of carbohydrates.
2. Stereoisomeria of monosaccharides. Enantiomeria. The D- and L- steric series. Diastereomers and epimers. The open-chain form and cyclic form of monosaccharides. Oxo-cyclic tautomerism. α- and β-Anomers. Haworth projection formulas. Conformation of monosaccharides.
3. Chemical properties of monosaccharides: formation and hydrolysis of glycosides, ethers and esters. The oxidation and reduction of monosaccharides. Ascorbic acid and its importance.
4. The characteristic of the main representatives of monosaccharides.

## *QUESTIONS FOR SELF-CONTROL*

1. The general characteristics, classification and biological importance of monosaccharides.
2. Write the Fisher projection formulas of D- and L-glyceraldehydes.
3. Represent the structure of D- and L-glucose and indicate how the steric structure of the monosaccharides can be determined.
4. Write the projection formulas of diastereomers and epimers of D-glucose.
5. Explain the phenomena of oxo-cyclic tautomerism. Represent the oxo-cyclic tautomerism of glucose.
6. Write the cyclic (Haworth) formulas of the fructose, ribose, deoxyribose anomers.
7. Which substances are named glycosides and what is the aglycon? Write the reactions of obtaining of α-methyl-glucoside (O-methyl, α-D-glucopyranoside).
8. What product are obtained at the glycosides hydrolysis? Write the reaction of hydrolysis of β-ethylgalactopyranoside.
9. Write the reaction of etherification of glucose with dimethyl sulphate in alkaline medium. Name the reaction's product.
10. Write the reaction of acetylation of α-D-glucose with acetic anhydride. Name the product and indicate what is obtaining at its hydrolysis.
11. What products are obtaining at the monosaccharids oxidation? Write the reaction of obtaining of glucuronic, gluconic and glucaric acids.
12. Write the reactions of reduction of D-glucose and D-xylose with sodium bromide hydride.
13. Characterize the most important representatives of pentoses and hexoses. Write the structure of the principal representatives.

## LABORATORY WORK

### *1. Demonstration of hydroxyl groups presence in D-glucose.*

Materials: 0,5% solution of glucose, 10% solution of sodium hydroxide, 2% solution of copper (II) sulphate, test-tubes.

Mix in a test-tube 1-2 drops of solution of glucose and 6 drops of solution of sodium hydroxide, then add 1 drop of solution of copper (II) sulphate. It is obtained a blue precipitate of copper (II) hydroxide, which immediately is dissolving and the solution becomes transparent and blue. Keep the solution for the next experiment. Write the reaction of the copper (II) gluconate formation.

***2. The reducing properties of glucose.***

**a) The reducing of copper (II) hydroxide in alkaline medium (Trommer test).**

Materials: Solution of copper (II) gluconate, obtained in the previous experiment.

Dilute the blue solution of copper (II) gluconate, obtained in the previous experiment by adding 1-1,5 ml of water and warm attentively at the flame only the superior pert of the solution. The colour changes from blue in yellow-maroon and then a red precipitate of copper (I) oxid is formed. This reaction is name Trommer test and is used for the glucose identification in urine. Write the equation of reaction.

**b) Tollens test.**

Materials: 5% solution of silver nitrite, 10% solution of sodium hydroxide, 10% solution of ammonia, 0,1% solution of glucose.

Introduce in a perfectly clean test-tube 1 drop of solution of silver nitrite and add 2 drops of solution of sodium hydroxide. A precipitate appears. It is dissolved when adding 3-4 drops of ammonia solution. In the obtained solution, which is named Tollens reagent, introduce 1 drop of glucose solution. Shake the test-tube and warm it a little at the flame till the solution becomes turbid.

Then the reaction runs without warming and the metallic silver formed a black precipitate, which is fell on the test-tube walls in form of mirror (reaction of "silver mirror"). Write the reactions, which take place.

**c) Fehlinh test.**

Materials: Fehling solution, 0,5% solution of glucose.

Introduce in a test-tube 2 drops of the glucose solution and several drops of Fehling solution. Shake the test-tube and warm it at the flame till the boiling. The colour chenges from

blue to green and then to yellow-maroon. Finally, a red precipitate of copper (I) oxide is formed.

**d) Selivanov test.**

Materials: 0,5% solution of fructose, Selivanov reactive (a mixture of resorcine and concentrated HCl).

Introduce in a test-tube several crystals of resorcine, 2-3 drops of concentrated hydrochloric acid and 2 drops of fructose. Warm attentively the test-tube at the flame till the appearance of red colour. Write the scheme of reaction.

## *QUESTIONS AND EXERCISES*

1. The general characteristics, classification and biological importance of monosaccharides. White the projection formulas of the most important aldose and ketose.
2. Which stereoisomers are named enantiomers, diastereomers, epimers? Write the projection formulas of the enantiomers, of one diastereomer and of one epimer for D-glucose, D-galactose, D-manose. How can you determine the monosaccharide belonging to the D- and L- steric series?
3. Explain the phenomena of oxo-cyclic tautomerism. What are the anomers? Write the structural formulas of α- and β-anomers of glucopyranose, galactopyranose, fructofuranose, ribofuranose and deoxiribofuranose (using Haworth formulas).
4. Which compounds are named glycosides? What products are obtained at the interaction of ethanol with α-D-glucopyranose and with β-D-ribofuranose in the acid anhydric medium? Represente the scheme of these reactions using Haworth formulas and name the obtained products according to the systematic nomenclature.
5. Write the reactions of obtaining of O-methyl-α-D-fructofuranose and O-ehtyl-β-D-galactopyranose using the Haworth formulas. Which classe of substances the obtained products are referred to? What is getting at their hydrolysis?
6. Write the reaction of interaction of α-D-galactopyranose and β-D-glucopyranose with dimethylsulphate in alkaline medium. Name the getting products.
7. Write the reaction of interaction of α-D-mannopyranose and β-D-ribofuranose with methyl iodide in alkaline medium.

Name the getting products. What is getting at their hydrolysis?

8. Effectuate the hydrolysis of O-methyl-2,3,4,6-tetramethyl-α-D-galactopyranose in acid medium. Name the getting products.
9. Write the reactions of formation of glucoso-6-phosphate and fructoso-1,6-diphosphate in process of glycolysis. What enzymes catalyse these processes. How is fructoso-1,6-diphosphate formed in process of photosynthesis?
10. Write the reactions of obtaining of pentaacetyl-α-D-glucopyranose. Effectuate the hydrolysis of ontained product. Indicate the conditions and reagents.
11. What important products are obtained at the D-glucose hydrolysis: a) with bromine water; b) with nitric acid; c) by protecting the aldehyde group? Write the reactions and name the products. Which monosaccharides are obtained at the decarboxylation of D-glucuronic acid?
12. Which reactions lead to the D-galactonic, D-galactaric, D-galacturonic acids formation from the D-galactose? Write the reactions. Indicate the conditions and reagents.
13. Write the reaction of L-ascorbinic acid (vitamin C) obtaining from the D-glucose. What is the biological importance of vitamin C?
14. What is the essence of Trommer test? What properties of the glucose are at the basis of the methods of its determination in biological liquids? Write the reactions of Trommer, Tollens and Fehling tests. Indicate the reagents.
15. What products are obtained at the D-glucose, D-mannose, D-xylose, D-ribose reducing? Write the reactions. Indicate the conditions and reagents. What is the importance of obtained products.
16. Write the structural formulas od the D-glucosamine, D-galactosamine, N-acethyl-glucosamine, N-acetil-galactosamine. What represent the sialic acids? Represent the structure of neuraminic acid.

## THEME №13. OLIGO- AND POLYSACCHARIDES.

Oligo- and polysaccharides are widely spread in nature and represent natural polymers which are formed in the result of polycondensation of monosaccharides. In living organisms polysaccharides realize a number of important functions: energetic, protective, mechanic and structural, hydroosmotic, coenzymatic, etc. The energetical function is realized by the reserve polysaccharides - starch and glycogen, which constitute the reserve of carbohydrates in cell. The protective, mechanic and structural function is specific for acid heteropolysaccharides. Some polysaccharides (for example heparin and heparansulphate) have a antihemostatic function.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Stereoisomeria of monosaccharides. Enantiomers. Epimers. Diastereomers.
2. The tautomerism and conformation of monosaccharides.
3. The obtaining and properties of glycosides.
4. The reducing properties of monosaccharides.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Oligosaccharides. Disaccharides: maltose, cellobiose, lactose and sucrose. Their structure, oxo-cyclic tautomerism and properties. Conformation of maltose and cellobiose.
2. Polysaccharides. Homopolysaccharides: starch, glycogen, cellulose, dextrans. Pectins: primary structure and hydrolysis. The notion of secondary structure.
3. Heteropolysaccharides (mucopolysaccharides): hyaluronic and hondroitin sulphuric acids, heparin. The notion of mixed macromolecules (proteoglycans).

### *QUESTIONS FOR SELF-CONTROL*

1. Write the structural formulas of maltose, cellobiose, lactose and sucrose. Formulate the complete names and indicate the type of glycosidic bonds.
2. Represent the oxo-cyclic tautomerism of maltose and lactose using Haworth formulas.
3. Write the reaction of hydrolysis of lactose and sucrose, name the getting products.

4. Represent the most stable conformations of maltose and cellobiose.
5. Which polisaccharides are named homopolysaccharides? Characterize the most important representatives.
6. Represent the primary structure of amylose and of glycogen. What products are obtained at their hydrolysis?
7. What are the particularities of dextrans structure? Represent the structure of a dextran's fragment and indicate the type of glycosidic bonds.
8. What substances are obtained at the partial and complete hydrolysis of starch? The biological importance of amidon.
9. Which substances are named heteropolysaccharides? Represent the primary structure of some fragments of chondroitin sulphuric acid, hialuronic acid and heparin. Indicate the type of glycosidic bonds.
10. Name the monosaccharide components of hialuronic acid, chondroitin sulphuric acid and heparin. Represent the structure of these monosaccharides. The biological importance of heteropolysaccharides.

## LABORATORY WORK

### *1. Demonstration of hydroxyl groups presence in sucrose.*

Materials: 1% solution of sucrose, 10% solution of sodium hydroxide, 2% solution of copper (II) sulphate, test-tubes.

Mix in a test-tube 1 drop of 1% solution of sucrose, 6 drops of 10% solution of sodium hydroxide, 6 drops of distilled water and 1 drop of 2% solution of copper (II) sulphate. It is obtained a blue precipitate of copper (II) hydroxide, which immediately is dissolving and the solution becomes transparent and blue. Keep the solution for the next experiment. Write the reaction of the copper (II) saccharate formation.

### *2. The non-reducing properties of sucrose.*

Materials: Solution of copper (II) saccharate, obtained in the previous experiment.

Warm attentively the blue solution of copper (II) saccharate, obtained in the previous experiment at the flame till the boiling. The solution colour doesn't changes. Remember,

that in the analogical conditions glucose provokes the colour changing to red. Explain the cause of non-reducing character of sucrose.

***3. The reducing properties of lactose.***

Materials: 1% solution of lactose, 10% solution of sodium hydroxide, 2% solution of copper (II) sulphate, test-tubes.

Mix in a test-tube 1 drop of 1% solution of lactose, 4 drops of 10% solution of sodium hydroxide, 1 drop of 2% solution of copper (II) sulphate. The precipitate of copper (II) sulfate is obtained, which is dissolved at the test-tube shaking. A transparent and blue solution of complex compound of copper (II) and lactose is obtained. Add 5-6 drops of water and warm attentively the solution at the flame. The solution blue colour became yellow-maroon. Remember, that in the analogical conditions sucrose doesn't provokes the colour changing. Represent the oxo-cyclic tautomerism of lactose and explain the cause of the reducing properties.

***4. The characteristic reaction of starch.***

Materials: 0,5% solution of starch, iodine solution in potassium iodide (2g $I_2$ and 5g KI in 100ml water), test-tubes.

Introduse in a test-tube 5 drops of starch solution and 1 drop of iodine solution in potassium iodide. A blue solution is obtained. At the test-tube warming the colour disappears, but at the cooling the colour appears again. The blue colour is due to formation of some inclusion combinations, which result at the iodine deposition into the amylose spiral. Represent the structure of a trisaccharidic fragment of amylose and indicate the glycosidic bonds.

***5. The starch hydrolysis.***

Materials: 0,5% solution of starch, 10% solution of sulphuric acid, iodine solution in potassium iodide, 10% solution of sodium hydroxide, 2% solution of copper (II) sulphate, test-tubes.

Introduce in a test-tube 3 drops of 0,5% solution of starch and 3 drops of 10% solution of sulphuric acid. Warm the test-tube in a water bath for 20 min. To verify if the total

hydrolysis takes place, put 1 drop of hydrolysate on a watch glass and add 1 drop of iodine solution in potassium iodide. If the blue colour doesn't appear, add in the test-tube 8 drops of 10% solution of sodium hydroxide to create the alkaline medium, then add 1 drop of 2% solution of copper (II) sulphate. After a weak warming of the test-tube the blue colour of the solution become yellow-maroon or red. Why? Write the reaction of hydrolysis of maltose. In what conditions it takes place? What is obtained at the total hydrolysis of starch?

### *QUESTIONS AND EXERCISES*

1. Write the structural formulas of disaccharides: maltose, cellobiose, lactose and sucrose. Formulate their complete names accoding to the systematic nomenclature and indicate the type of glycosidic bonds.
2. Represent the oxo-cyclic tautomerism of maltose, lactose and cellobiose. Indicate the reducing fragment in their molecule.
3. What products are obtained at the interaction of maltose, lactose cellobiose with ethanol in acid medium? Write the reaction and name the obtained products.
4. Write the reactions of hydrolysis of maltose, lactose and sucrose; name the getting products accoding to the systematic nomenclature. Which are the natural sources of these disaccharides.
5. Write the reaction of complete methylation of maltose and effectuate the hydrolysis of getting product. Name the substances which was obtained after hydrolysis. What do you can say about their reducing properties?
6. Which polysaccharides are named homolysaccharides? Represent the structure of a fragment of amylose macromolecule, indicate the type of glycosidic bonds in this polysaccharide. What is the biological and practical importance of the starch?
7. Represent the structure of a fragment of amylopectine macromolecule with one point of ramification. Indicate the type of glycosidic bonds in amylopectine.
8. Which polysaccharides are named dextrans? Represent the structure of a fragment of dextran macromolecule, indicate the ramification points and the type of glycosidic bonds. What is the importance of dextrans?

9. Represent the structure of a fragment of glycogen macromolecule with one point of ramification. Indicate the type of glycosidic bonds in this macromolecule. What is the biological importance of glycogen?
10. Explain the bond between the secondary structure of cellulose and the conformation of the macromolecule. Represent the structure of a fragment of cellulose, indicate the glycosidic and hydrogen bonds in the macromolecule. What is the importance of cellulose.
11. Which polysaccharides are named heteropolysaccharides? Write the structure of a disaccharidic fragment. Which are the monosaccharide composition of the hyaluronic acid? Indicate the type of glycosidic bonds.
12. Which are the monosaccharide composition of the chondroitin sulphate? What type of glycosidic bonds are between them? Represent the structure of the disaccharidic fragment of the chondroitin sulphate.
13. Name the monosaccharide composition of the heparine and the type of glycosidic bonds between the monosaccharides. Write the structure of a disaccharidic fragment of heparine. What is the biological role of heparine?

## THEME №13. NUCLEOSIDES. NUCLEOTIDES. NUCLEIC ACIDS.

The principles of structure and chemical properties of nucleic acids and of their structural components are the chemical basis for the interpretation of their biological functions.

Nucleic acids assure the development of different form of life and the stable reproduction of all characteristic properties of the organism, fulfil a number of important functions in biosynthesis of proteins and in the transmission of hereditary information. The structural components of nucleic acids participate in the metabolic processes, in accumulation, transport and transformation of energy.

### *INITIAL LEVEL OF KNOWLEDGE*

1. Oxo-cyclic and lactim-lactam tautomerism.

2. Structure and properties of N-glycosides.
3. Structure and properties of esters.
4. Hydrogen bonds.

### *QUESTIONS FOR INDEPENDENT PREPARATION*

1. Components of nucleic acids. Pyrimidine and purine bases, their structure and lactim-lactam tautomerism.
2. Nucleosides: structure, composition and properties.
3. Nucleotides – monomeric units of nucleic acids. Their structure, nomenclature and properties.
4. Primary and secondary structure of nucleic acids. The notion of protein biosynthesis.
5. Structure and biological importance of the coenzymes – nucleotides: ATP (adenosine triphosphate), HSCo-A, NAD, NADP, FAD-$FADH_2$.

### *QUESTIONS FOR SELF-CONTROL*

1. Write the structural formulas of pyrimidine bases, their nomenclature.
2. Represent the structure of purine bases, formulate their trivial and systematic names.
3. Demonstrate the lactim-lactam tautometism using as example the thymine and guanine.
4. What are nucleosides? Write the structure of adenosine, deoxyguanosine and thymidine.
5. Write the reaction of uridine and adenosine hydrolysis, indicate the conditions.
6. What are nucleotides? Write the general formula of nucleotides and indicate the type of chemical bond in molecule.
7. Represent the structure of mononucleotides AMP, GMP, cAMP and name them.
8. Write the reaction of hydrolysis of nucleotides CMP, AMP; indicate the conditions and name the reaction products.
9. Represent the structure of a fragment of DNA with the succession of bases TGA.
10. Represent the structure of a fragment of RNA with the succession of bases CAG; indicate the phosphodiesteric bonds.

11. Write the structural formulas of the complimentary bases thymine and adenine; indicate the hydrogen bonds.
12. Represent the structure of adenosine triphosphoric acid and its hydrolytic decomposition. What products are obtained?
13. Write the reaction of interaction of valine with ATP. The importance of this reaction.
14. Represent the structure of the coenzymes NAD and FAD.

## *QUESTIONS AND EXERCISES*

1. Characterize the structure of nucleic acids. Pyrimidinic bases: uracil, thymine and cytosine. Write the scheme of lactim-lactam tautomerism and indicate the most stable forms.
2. Purine bases: adenine and guanine. Represent the tautomeria of guanine and indicate the most stable form. Which compound is obtain when acting with nitrous acid on the guanine?
3. Identify among the following heterocyclic compounds the pairs of complimentary bases: purine, cytosine, pyrimidine, adenine, pyridine, guanine. Represent the structure and indicate the hydrogen bond.
4. Which compound is obtain when acting with nitrous acid on the cytosine? Write the scheme of interaction of the obtained compound and the corresponding purinic bases.
5. Represent the general structure, explain the classification and nomenclature of nucleosides. Indicate the type of chemical bond between pyrimidine or purine bases and the rest of the monosaccharide. Write the reaction of hydrolysis of nucleosides and indicate conditions.
6. Represent the structure of the following nucleosides: adenosine, uridine, deoxycytidine, deoxyguanosine. Effectuate their hydrolysis and indicate the conditions.
7. Mononucleotides – the structural units of nucleic acids; characterize the general structure, classification and nomenclature. Indicate the N-glycosidic and hydrogen bonds.
8. Write the structural formulas of the following nucleotides: uridin-5'-monophosphate, adenosine-5'-monophosphate, cytidine-5'-monophosphate, thymidine-5'-monophosphate. Effectuate the reactions of complete hydrolysis in acid medium.

9. Explain the notion of primary structure of nucleic acids DNA and RNA. Represent the structure of some fragments of DNA with the succession of bases TAC and AGT.
10. In the result of hydrolysis of a nucleic acid fragment the following mononucleotides were obtained: UMP, AMP, GMP. Represent the structure of this fragment.
11. Explain the notion of secondary structure of DNA and RNA. What is the difference? Represent the structure of a fragment from the DNA double spiral if the succession of bases in one complimentary chain is ACG.
12. Characterize the structure of nucleoside polyphosphates. Write the structure of adenosine triphosphoric acid. Represent the scheme of the hydrolytical degradation of ATP and explain its biological role.
13. Write the structure of the product of reaction between ATP and a α-amino acid, represent the scheme of interaction of the obtained aminoacyl adenilate with ARN.
14. Represent the structure of coenzyme $NAD^+$ and write the chemical reaction, which is at the basis of the biological action of this coenzyme.
15. Write the scheme of the reversible redox reaction of lactic acid with the participation of coenzyme NAD.

## FINAL WORK № 3.

1. Proteinogenic α-amino acids (components of proteins). Structure, classification and nomenclature. Amino acids' stereoisomeria. Acid and alkaline properties, bipolar structure, isoelectric point.
2. Chemical properties of α-amino acids: reactions of esterification, alchylation, acylation, deamination, condensation, complex salt, anhydrides and phenylthiohidantoines formation. The importance of these reactions in the analyses of α-amino acids.
3. α-Amino acids reactions of biological importance. Transamination reactions (biosynthesis of α-amino acids), reactions of oxidative deamination, decarboxylation reaction with formation of biogenic amines – colamine, histamine, triptamine, serotonine, cadaverine, β-alanine, γ-amino butyric acid), reaction of hydroxylation (tyrosine, 5-hydroxytryptophan, hydroxyproline formation). The mechanism of the reactions of transamination and decarboxylation. Role of coenzymes: pyridoxal phosphate, $NAD^+$, NADP in these reactions.
4. Peptides. Their obtaining, structure, classification and nomenclature. Electronical and spatial structure of the peptide bond. Electro-chemical properties of peptides. The most important representatives of peptides. Their biological role.
5. The analysis of peptides. The acid and alkaline hydrolysis of peptides. The determination of amino acid composition and primary structure of peptides. The determination of amino acid sequence in polypeptidic chain (Edman method). Chemical synthesis and notion about proteins biosynthesis.
6. Classification, spreading in nature and biological importance of carbohydrates. Monosaccharides, classification, structure and characteristics of the most importance representatives of pentose and hexose (ribose, deoxyribose, xylose, ribulose, xylulose, glucose, mannose, galactose, fructose), aminosaccharides (glucosamine, galactosamine. Sialic acids.
7. Stereoisomeria of monosaccharides. Enantiomeria. The D- and L- steric series. Diastereomers and epimers. The open-chain form and cyclic form of monosaccharides. Oxo-cyclic

tautomerism. α- and β-Anomers. Haworth projection formulas. Conformation of monosaccharides.

8. Chemical properties of monosaccharides: formation and hydrolysis of D- and N-glycosides, ethers and esters. The biological importance of phosphoesters. The reduction of monosaccharides (sorbitol, xylitol, mannitol, ribitol).
9. The oxidation of monosaccharides. Gluconic, glucaric and uronic acids. L-Ascorbic acid (vitamin C). The biological importance of glucuronic and ascorbic acids. The qualitative reactions for aldose and ketose identification.
10. Oligosaccharides. Disaccharides: maltose, cellobiose, lactose and sucrose. Their structure, oxo-cyclic tautomerism and properties. Conformation of maltose and cellobiose.
11. Homopolysaccharides: starch (amylose and amylopectine), glycogen, cellulose, dextrans, chitin, pectins. Their primary structure and hydrolysis. The notion of secondary structure (amylose and cellulose).
12. Heteropolysaccharides: hyaluronic and hondroitin sulphuric acids, heparin, muramine. Disaccharide composition, primery structure and biological importance.
13. Components of nucleic acids. Nucleic bases, which enter in the composition of nucleic acids: pyrimidine (uracil, thymine, cytosine) and purine bases (adenine and guanine), their structure and lactim-lactam tautomerism. Deamination reactions.
14. Nucleosides: structure, nomenclature and classification. Configuration of glycosidic center. Hydrolysis of nucleosides. Biological importance.
15. Nucleotides – monomeric units of nucleic acids. Their structure, nomenclature and properties. Biological importance.
16. Primary and secondary structure of nucleic acids. Phosphodiesteric bonds. DNA and RNA, their conposition and hydrolysis. Biological importance. The notion about protein biosynthesis.
17. Nucleoside mono- and polyphosphate: AMP, cAMP, ADP, ATP. Macroergic bonds. Nucleotidic coenzymes: NAD, NADP, FAD-FADH2, HSCoA. Their structure and role in the biological processes.