CONTROL-TEST.

" Theoretical bases of structure and general patterns of reactivity of organic compounds. Biopolymers and their structural units"

Control test checks and monitors the students` knowledge in accordance to following issues of the curriculum:

1. The theoretical bases of the structure and general principles of reactivity of organic compounds

1.1. Introduction. Classification and nomenclature of organic compounds

The brief historical essay of bioorganic chemistry development. The place of bioorganic chemistry in medical education as one of medico-biological cycle discipline. The goals of bioorganic chemistry as educational discipline in medical establishments of higher education. Contribution of Belarussian chemists to the development of bioorganic chemistry. Chemistry and ethical problems of medicine and pharmacy. The objects studied by bioorganic chemistry.

Classification of organic compounds according to the structure of a carbon chain and the nature of functional group. Main families of organic compounds.

The principal rules of IUPAC nomenclature of organic compounds: substitutive and radical-functional nomenclatures.

1.2. Chemical bonds and mutual influence of atoms in an organic molecule

The electron configuration of carbon atom and atoms organogens. Hybridization of atomic orbitals. Hybridization types. Types of chemical bonds in organic compounds. Main characteristics of σ - and π -bonds. Hydrogen bonds.

Conjugation. The kind of conjugation: π, π- and p, π-. Conjugated systems with an opened chain. Conjugated systems with a closed chain. Aromaticity. The Hückel aromatic criteria. Aromaticity of benzenoid and heterocyclic compounds. Conjugation energy. Thermodynamic stability of biologically important molecules with opened and closed conjugated systems.

Mutual influence of atoms in a molecule: inductive and mesomeric electronic effects of substituents. Electron-donating and electron-withdrawing substituents. The electron density distribution in a molecule. The reaction centers.

1.3. Stereochemistry of organic molecules and stereoisomerism

Configuration and conformation as the way of description of the three-dimensional structure of the molecule. The relationship of a spatial structure and hybridization type of a carbon atom. Molecular models, three-dimensional (stereo-chemical) formulas, Fisher projection formulas, Newman projection formulas.

Chirality. Chiral molecules. A stereocenter. Enantiomerism. Optical activity. The relative D-, L-system of a stereochemical designation. The concept of the R-, S –system of a stereochemical designation. Stereoisomerism of molecules with one, two and more than two stereocenters: enantiomerism and σ-diastereomerism. Meso compounds. Racemate, racemic mixtures. The concept of racemic mixtures separation methods. π-diastereomers of unsaturated compounds.

The relationship between the three-dimensional structure of a compound and its biological activity. The Fisher theory, the D.E. Koshland theory. The complementary interaction.

Conformations of open chain compounds. The kinds of strain in a molecule: torsional strain and Van der Waals strain. Energy characteristics of conformations of alkanes. Angle strain and conformations of six-member cyclic compounds, their energy characteristics. Axial and equatorial bonds. 1,3-Diaxial interaction, inversion of the cycle.

2. Reactivity of hydrocarbons, alcohols, phenols, thiols, amines, aldehydes and ketones, carboxylic acids and their functional derivatives. Biologically important heterofunctional compounds

2.1. Reactivity of hydrocarbons

The concept of reaction mechanism. A substrate, a reagent, a reaction center. Classification of organic reactions according to the result (substitution, addition, elimination reactions;

rearrangements; oxidation-reduction and acid-base reactions). The radical reactions, the ionic reactions, the coordinated reactions. The types of reagents: radicals, electrophiles, nucleophiles, acids, bases. The homolytic cleavage of a covalent bond and the concept of free radicals and chain reactions. The heterolytic cleavage of a covalent bond; carbocations and carbanions.

Reactivity of saturated hydrocarbons. Free–radical substitution reactions, a mechanism, region selectivity. The ways of free radicals' formation: a light promoted, a heat promoted fragmentation (photolysis, thermolysis), oxidation–reductions reactions with participation of metal ions with a changeable valency. The concept of chain processes. The role of free radical oxidation-reductions in biological processes.

Use of paraffin wax and ozokerite in orthopedic stomatology.

Electrophilic addition reactions to alkenes. The mechanism of hydration reaction, an acidic catalysis. The effect of static and kinetic factors on the region selectivity of addition reactions. Markovnikov's rule. The peculiarities of electrophilic addition to the conjugated dienes.

The qualitative tests for discovery of multiple bonds in examined object.

The polymerization reactions of unsaturated compounds. Application of polymers on base acrylic and methacrylic acids, gutta percha in stomatology.

Electrophilic substitution reactions of aromatic compounds. The mechanism of reaction, the role of catalysts in the electrophile formation. Effect of substituents in an aromatic ring to its reactivity in electrophilic substitution reactions. The alkylation and halogenation reactions *in vivo*.

Aromatic oxidation reactions *in vivo* as the ability to increase hydrophilicity and to remove foreign substances from the human body.

2.2. Acid and base properties of organic compounds

Acidity and basicity according to the Bronsted-Lowry and the Lewis theories. Quantitative and qualitative characteristics of the acids and the bases strength of organic compounds. The general principles of relationship between change of acid and base properties and the nature of an atom of acid or a base center, electron effects of substituents at these centers and solvation effects. Toxic properties of the strong acids and bases. Amphoteric properties. The hydrogen bond as specific manifestation of acid and base properties. The hydrogen bond in the structure of biopolymers.

2.3. Reactivity of alcohols, phenols, thiols and amines

Reaction centers in molecules of alcohols, phenols, thiols and amines. The outline mechanism of nucleophilic substitution reactions at sp^3–hybrid carbon atom. Uni- and bimolecular reactions. Stereochemistry of nucleophilic substitution reactions. The nucleophilic substitution of a hydroxyl group in alcohols. The acid catalysis. The competitive uni- and bimolecular elimination reactions of alcohols. Biologically important dehydration reactions of hydroxyl-containing compounds.

Oxidation reactions of alcohols, thiols, phenols. The biological oxidation with participation of coenzyme NAD^+. A hydride ion transfer in a system NAD^+-NADH. Compounds containing thiol group and phenol hydroxyl group as antioxidants.

2.4. Aldehydes and ketones reactivity

Reaction centers of aldehydes and ketones. Nucleophilic addition reactions. The outline mechanism of a reaction. The addition of the water, alcohols, amines. Formation of cyclic hemiacetals. The aldol addition reactions. Reversibility of nucleophilic addition reactions. The biological significance of acetal formation reactions, retro-aldol reactions, reactions with amines. The toxic properties of aldehydes. Using of aldehydes for disinfection and sterilization.

Oxidation and reduction reactions of carbonyl compounds *in vitro* and *in vivo*.

The qualitative tests for discovery of aldehyde group. The qualitative tests for discovery of acetone.

2.5. Reactivity of carboxylic acids and their functional derivatives

The reaction centers in molecules of carboxylic acids. Acidic properties of mono- and dibasic, saturated, unsaturated and aromatic carboxylic acids. The outline mechanism of nucleophilic substitution reactions at the sp^2–hybrid carbon atom of carboxylic acids and their

functional group derivatives. The reactions of formation and hydrolysis of carboxylic acids functional group derivatives: anhydrides, acid chlorides, esters, amides. The reactivity of carboxylic acid functional group derivatives in acyl transfer reactions. The relative reactivity of esters and thioesters in acyl transfer reactions; their biological significance. Acyl coenzyme A. The biological important acyl transfer reactions with participation of acyl phosphates. The concept of phosphorylation reactions.

Amides of carboxylic acids, their acid and base properties. Functional derivatives of the carbonic acid: complete amide (urea) and *semi* amide (carbamic acid); their acid and base properties and biological significance. Biuret. Urethanes.

2.6. Poly- and heterofunctional compounds participating in the processes of ability to live and being origin of most important medicament groups

Classification of poly- and heterofunctional compounds. Acid and base properties. Typical reactivity of poly- and heterofunctional compounds. The specific properties conditioned by interference of groups: chelates formation of polyhydric alcohols, α-amino alcohols, α-amino acids, and also intramolecular cyclization (of γ- and δ-hydroxyaldehydes, γ- and δ-hydroxy- and amino acids) and intermolecular cyclization (of α-hydroxy- and amino acids). Decarboxylation reactions. The elimination reactions of β-hydroxy- and β-amino acids. Tautomerization: keto–enol and lactim-lactam.

Polyhydric alcohols: ethylene glycol, glycerol, myoinositol, xylitol, sorbitol. The esters of polyhydric alcohols with the inorganic acids and fatty acids. The qualitative test for a diol fragment.

Dihydric phenols: hydroquinone, resorcinol, catechol. Phenols as antioxidants.

Dicarboxylic acids: oxalic acid, malonic acid, succinic acid, glutaric acid, fumaric acid. The dehydrogenation reaction of succinic acid to form fumaric acid.

Amino alcohols: 2-aminoethanol, choline. Formation of choline from L-serine. Acetylcholine. Catecholamines: dopamine, noradrenaline (norepinephrine), adrenaline (epinephrine).

Hydroxy acids: lactic acid, malic acid, tartaric acid, citric acid. Oxidation reactions of lactic and malic acids with participation of coenzyme NAD^+. Citric acid, using citrates for conservation of donor blood. Citric acid dehydration *in vivo*.

Aldehyde and keto acids: pyruvic acid, acetoacetic acid, oxaloacetic acid, α-ketoglutaric acid. The condensation reaction of oxaloacetic acid and acetyl coenzyme A. The oxidative decarboxylation reactions of pyruvic acid. Keto–enol tautomerization of and oxaloacetic acid.

β-Hydroxybutyric acid, β-ketobutyric acid, acetone as representatives of «*ketone bodies*», their biological and their diagnostic importance.

Salicylic acid and its derivatives: acetylsalicylic acid, methyl-salicylate, phenyl-salicylate.

p-Aminobenzoic acid and its derivatives possessing anesthetizing action: benzocaine, procaine. Modern anesthetics.

Sulfanilic acid and its amide. Sulfa drugs. Antimetabolite concepts.

3. Biopolymers and their structural components. Low molecular weight bioregulators

3.1. Carbohydrates

Classification of monosaccharides: aldoses, ketoses; pentoses, hexoses. Stereoisomerism of monosaccharides. D- and L-families. An open-chain structure and cyclic forms. Furanoses and pyranoses; α- and β-anomers. Fischer projection and Haworth formulas. A cyclo-oxo tautomerization. Mutarotation. Conformations of pyranose forms of monosaccharides. The structures of most important representatives of pentoses (D-ribose, 2-deoxy-D-ribose, D-xylose); hexoses (D-glucose, D-mannose, D-galactose, D-fructose). Amino sugars (D-glucosamine, D-mannosamine, D-galactosamine), their properties.

Physical properties of monosaccharides.

Chemical properties. Glycosides. Hydrolysis of glycosides. Biologically important phosphorylation reactions of monosaccharides. Reducing properties of aldoses. Oxidation of monosaccharides: aldonic, aldaricand uronic acids. Reduction of monosaccharides to alditols:

xylitol, glucitol (sorbitol), mannitol; their use in medicine. The nucleophilic addition to the carbonyl group of glucose (glycolation reactions of proteins). Ascorbic acid: the structure and properties.

Biological importance of monosaccharides and their derivatives.

Common characteristic and classification of polysaccharides. Oligosaccharides. The disaccharides: maltose, lactose, lactulose, sucrose, cellobiose. Structures, the cyclo-oxo tautomerization. Reducing properties. Hydrolysis.

Polysaccharides. Homo- and heteropolysaccharides. The homopolysaccharides: starch, glycogen, dextrans, cellulose. Primary structure, hydrolysis. The concept of a secondary structure (amylose, cellulose). Pectins (polygalacturonic acid).

The heteropolysaccharides: hyaluronic acid, chondroitin sulfates. Use alginic acid to make dental alginate impression materials. The concept of mixed biopolymers: proteoglycans, glycoproteins, glycolipids.

3.2. Amino acids

Amino acids obtained from proteins. Classification of proteinogenic amino acids taking into account different signs: acid and base properties, chemical nature of a side chain and its substituents (aliphatic, aromatic, heterocyclic, contained the hydroxyl, the amino, the carboxyl or the amide groups, the sulfur contained groups), character of a side chain (hydrophilic and hydrophobic). Structure, nomenclature. Stereoisomerism. Acid and base properties, a dipolar ion structure. Essential amino acids.

The methods of α-amino acids reception: hydrolysis of proteins, synthesis from α-halo carboxylic acids. Reductive amination reactions. Pyridoxal catalysis.

The qualitative tests for of α-amino acids.

Biologically important reactions of α-amino acids. Transamination reactions. Decarboxylation of α-amino acids - the way of formation of biogenic amines and biological regulators: 2-aminoethanol, histamine, tryptamine, serotonin, dopamine, γ-amino butyric acid, their biological role. Oxidative and not oxidizing deamination reactions. The hydroxylation reactions (phenylalanine → tyrosine, tyrosine → 3,4-dihydroxyphenylalanine, tryptophan → 5-hydroxytryptophan, proline → 4-hydroxyproline), participation of ascorbic acid in the amino acid hydroxylation reactions. Deamination of amino acids. Cysteine oxidation. Disulfide bond.

3.3. Polypeptides and proteins

Polypeptides. The electronic and the three-dimensional structure of a peptide bond. The hydrolysis of polypeptides. Individual representatives of polypeptides: aspartame, glutathione, neuropeptides, insulin.

Primary structure of proteins. The concept of secondary, tertiary and quaternary protein structures. Hemoglobin, heme.

3.4. Nucleic acids

Nucleic (heterocyclic) bases: pyrimidines (uracil, thymine, cytosine) and purines (adenine, guanine). Aromatic properties. A lactim–lactam tautomerization.

Nucleosides. Nucleotides. Structure of mononucleotides that can be obtained from nucleic acids. Nomenclature. Nucleotides hydrolysis.

Primary structure of nucleic acids. The phosphate diester linkage. Ribonucleic and deoxyribonucleic acids. The nucleotides found in RNA, the nucleotides found in DNA. Hydrolysis of nucleic acids. The concept of the DNA secondary structure. The role of hydrogen bonds in formation of the DNA secondary structure. Complementarity of heterocyclic bases.

Nucleoside mono- and polyphosphates. AMP, ADP, ATP. The role of ATP as the accumulator and the carrier of free energy in cell. Macro energy bonds. Nucleoside cyclophosphates (c-AMP, c-GMP) as secondary mediators in the regulation of cell metabolism. Notion about coenzymes. Structures of NAD^+ and its phosphate ($NADPh^+$). NAD^+ - NADH system; hydride transfer as one of the stages of the biological oxidation–reduction reactions with participation of this system.

Control test is composed of:

- multiple-choice questions;
- written questions include writing formulas of bioorganic compounds and their main reactions.

1. ***Multiple-choice questions*** (test) variant contains 15 test questions with one correct answer. Test questions control basic knowledge of the theoretical bases of the structure and general principles of reactivity of organic compounds; reactivity of hydrocarbons, alcohols, phenols, thiols, amines, aldehydes and ketones, carboxylic acids and their functional derivatives, biologically important heterofunctional compounds.

2. *Written control of knowledge contains two questions:*

Question *№* 1 tests students` ability to write the formulas of individual representatives of biopolimers and their structural components:

- oxo- and cyclic forms of biologically important monosaccharides;
- disaccharides, homopolysaccharides and heteropolysaccharides;
- ionic forms of natural α-amino acids at given pH;
- dipeptides;
- nucleosides, nucleotides and dinucleotides.

Question *№* 2 tests students` ability to write the schemes of reactions, represent and name reaction centers involved in each reaction, indicate the mechanism of the specific example of reactions.

SUMMARY QUESTIONS

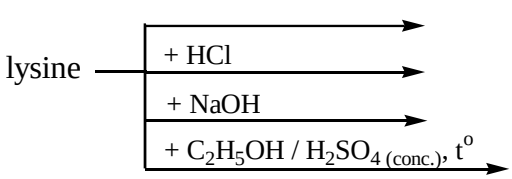
Summary multiple-choice test questions are questions №1-201 located on pages 67-104 of the educational manual [3].

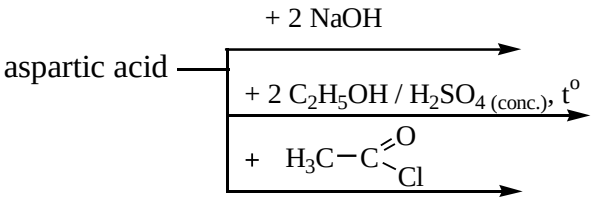
Summary questions for written control:

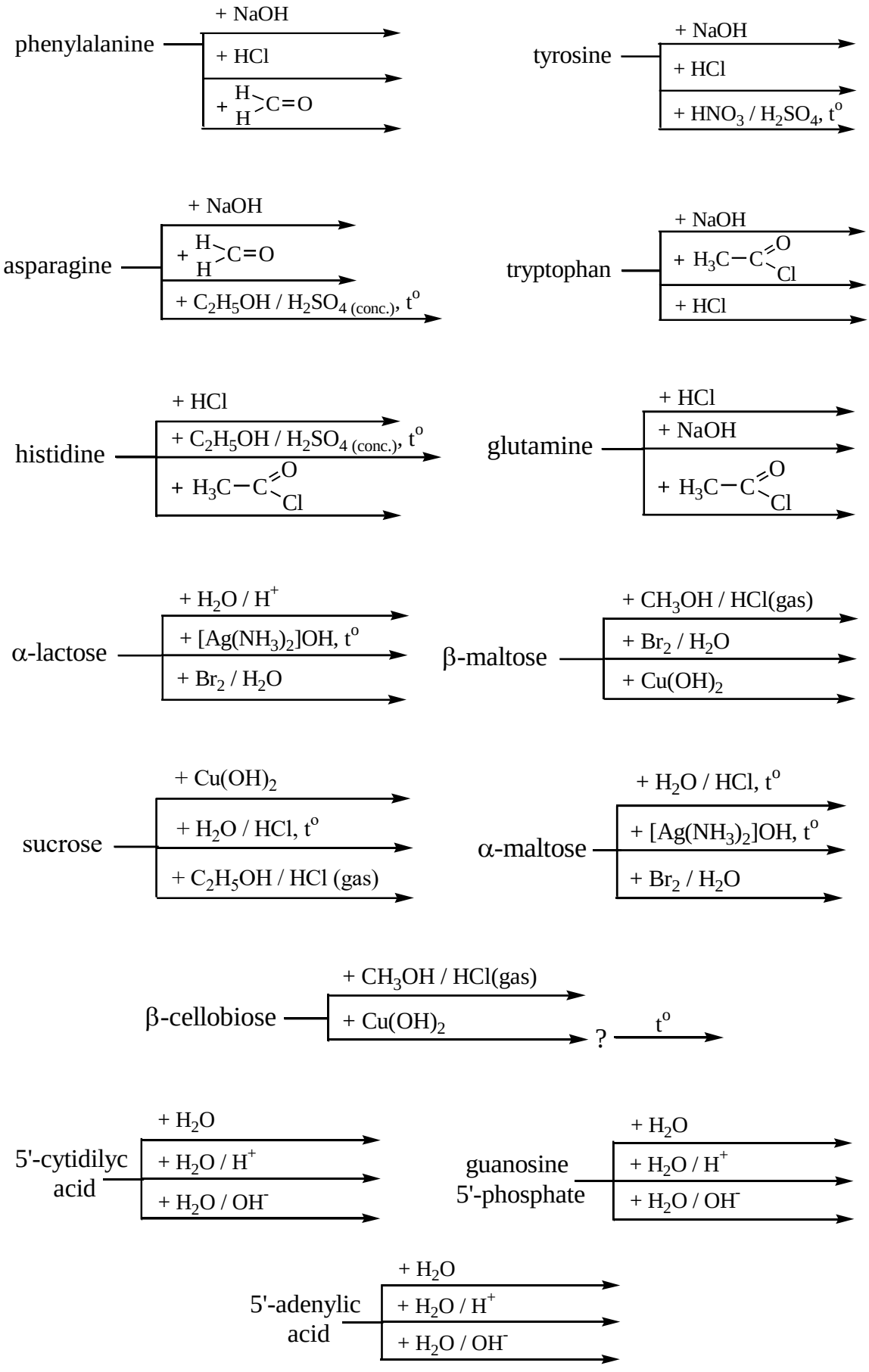
Question *№ 1.* Write the formulas of:

- Oxo- and cyclic forms of biologically important monosaccharides;
- Disaccharides, homopolysaccharides and heteropolysaccharides;
- Ionic forms of natural α-amino acids at given pH;
- Dipeptides;
- Nucleosides, nucleotides and dinucleotides.

Question *№ 2.* Write the schemes of reactions, represent and name reaction centers involved in each reaction, indicate the mechanism of the following reactions:







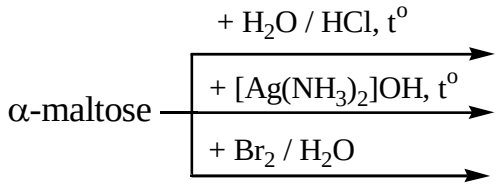
The example of control-test paper (written control):

CONTROL TEST

Theoretical bases of structure and general patterns of reactivity of organic compounds. Biopolymers and their structural units

1. Write the formulas of:
   - D-glucose and its pyranose forms;
   - Arginine at the pH of intestines 6.5;
   - Dipeptide Leu-Asp;
   - Citidine-5`-phosphate.

2. Write the schemes of reactions, represent and name reaction centers involved in each reaction, indicate the mechanism of the following reactions:



The list of literature

Main:

1. Биоорганическая химия = Bioorganic Chemistry: учеб. Пособие для иностранных студентов / О.Н. Ринейская [и др.]. – Минск: Новое знание, 2018. p. 6-156

2. Bioorganic chemistry: Lecture course for foreign student of the 1st year / Assembled by L.G. Hidranovich. – Vitebsk: VSMU Press, 2004. p. 4-256

3. Hidranovich, L. G. Laboratory classes in bioorganic chemistry: учеб. – метод. пособие /L.G. Hidranovich, O.A. Khodos. – Витебск: ВГМУ, 2017.