THEME10.
Carbohydrates. Monosaccharides.

I. Training and educational goals:

1. To form knowledge of:
   - Structure, chemical properties and biological importance of the main groups of monosaccharides involved in the processes of life;
   - Modern ideas about the structure of monosaccharides and their reactivity.
2. To form skills:
   - To write Fisher projections and Haworth formulas of biologically important monosaccharides;
   - To characterize stereochemistry of open-chain structures and cyclic forms of monosaccharides;
   - To write and to explain characteristic reactions of monosaccharides;
   - To cary out simple reactions of monosaccharides;
   - To analyze chemical experiment results and execute.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.
- Fostering responsibility, conscientiousness and accuracy when performing a chemical experiment.

Motivational characteristics of the need to study the them:

Carbohydrates are the most abundant organic constituents of plants. They not only serve as an important source of chemical energy for living organisms (sugars and starches are important in this respect), but also in plants and in some animals they serve as important constituents of supporting tissues (this is the primary function of the cellulose found in wood, cotton, and flax, for example).

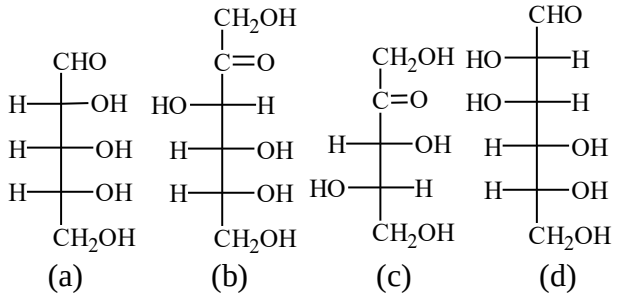
Monosaccharides are polyhydroxy aldehydes and ketones, exists in the equilibrium of open chain and cyclic forms that are hemiacetals. So, monosaccharides have properties of all this families.

Program questions for self-learning and classroom knowledge control:

1. Classification of monosaccharides: aldoses, ketoses; pentoses, hexoses. The structures of the most important representatives of pentoses (D-ribose, 2-deoxy-D-ribose, D-xylose); hexoses (D-glucose, D-mannose, D-galactose, D-fructose). Stereoisomerism of monosaccharides. D- and L-families. Fischer projection formulas.
2. An open-chain structure and cyclic forms. Furanoses and pyranoses; α- and β-anomers. Haworth formulas. A cyclo-oxo tautomerization. Mutarotation. The conformations of pyranose forms of monosaccharides. Physical properties of monosaccharides.
3. The chemical properties. Glycosides. Hydrolysis of glycosides.
4. The biologically important phosphorylation reactions of monosaccharides.
5. Reducing properties of aldoses. Oxidation of monosaccharides: aldonic, aldaricand uronic acids.
6. Reduction of monosaccharides to alditols: xylitol, glucitol (sorbitol), mannitol; their use in medicine.
7. The nucleophilic addition to the carbonyl group of glucose (glycolation reactions of proteins). Ascorbic acid: the structure and the properties. Biological importance of monosaccharides and their derivatives.

Problems.

1. Classify each of the following monosaccharides according to the number of carbon atoms and the type of carbonyl group it contains.

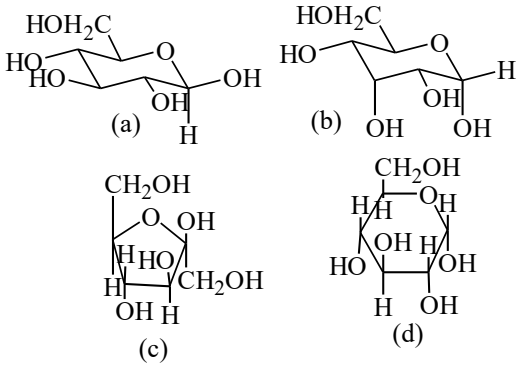


2. Label the stereocenters in each of the monosaccharides in Exercise 1 by an asterisk and determine the maximum number of stereoisomers of each. Assign each of the monosaccharides in Exercise 1 to either the D- or L-family.

3. Write the cyclic forms for each of the monosaccharides in Exercise 1. Indicate which is the α-anomer and which is the β-anomer. Draw conformational formulas for each of the pyranose forms.

4. Write a chair representation of the pyranose form of each of the following monosaccharides in Exrcise 1.

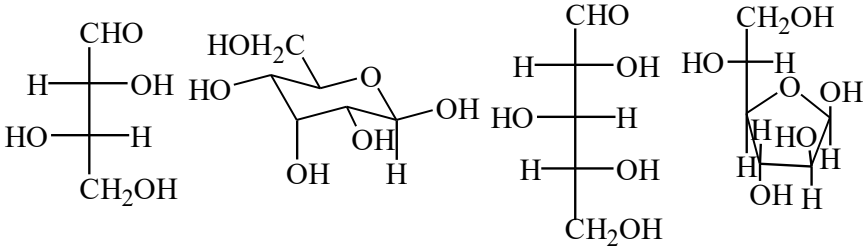
5. Write the Fisher projection formula for each of the following cyclic monosaccharides



6. Write the structure of the products, if any, of the reaction of α-D-galactopyranose with each of the following reagents.

(a) CH_3OH/HCl; (b) Fehling's solution; (c) Br_2/H_2O; (d) HNO_3

7. Write the structure of the aldonic acids and aldaric acids obtained by oxidation of each of the following monosaccharides. Write the structure of alditols obtained by reduction of each of the following monosaccharides:



Which of the products are optically active?

8. Write the reaction of the acid-catalyzed hydrolysis of methyl α-D-glucopyranoside.

9. Direct oxidation of an aldose affects the aldehyde group first, converting it to a carboxylic acid, and most oxidizing agents that will attack 1^o alcohol groups will also attack 2^o alcohol groups. Clearly, then, a laboratory synthesis of an uronic acid from an aldose, requires protecting these groups from oxidation. Keeping this in mind, suggest a method for carrying out a specific oxidation that would convert D-galactose to D-galacturonic acid

10. Fehling's solution and Tollen's reagent are often used to distinguish between simple aldehydes and ketones. In the case of monosaccharides, these two reagents give a positive test with both aldoses and ketoses, because they are carried out in alkaline solutions. Explain this result and write the schemes of corresponding reactions for D-fructose, keeping in mind, that in alkaline solution an enediol rearrangement converts ketoses to aldoses, which are then oxidized.

Salicin can be converted to salicylic acid which, in turn, can be converted into the most widely used modern analgetic, aspirin. Write the scheme of this reaction, show the condition, name the products.

Laboratory work.

Experiment № 1. Glucose has hydroxyl groups.

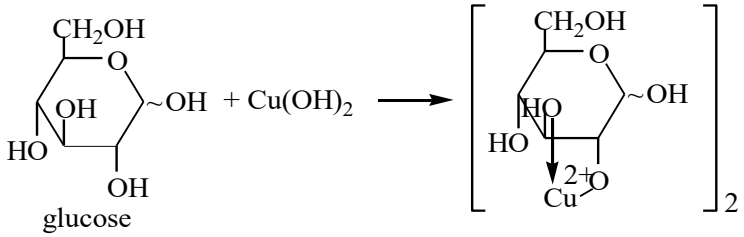
Sequence of operations: Place 1 drop of glucose solution in the test-tube. Add 6 drops of NaOH and 1 drop of $CuSO_4$.

Check the result: blue solution.

Attention: you need this solution for the next experiment.

Write:

$$CuSO_4 + 2NaOH \rightarrow Cu(OH)_2\downarrow + Na_2SO_4$$



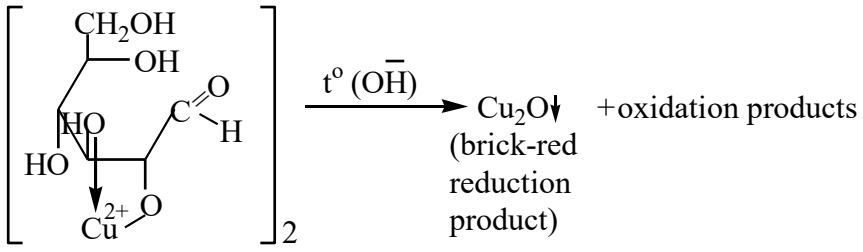
Explain the result and write conclusion.

Experiment № 2. Oxidation of glucose by $Cu(OH)_2$.

Sequence of operations: Take the solution you received in the experiment № 1. Add 8 drops of H_2O. Warm the test-tube.

Check the result: brick-red precipitate.

Write:



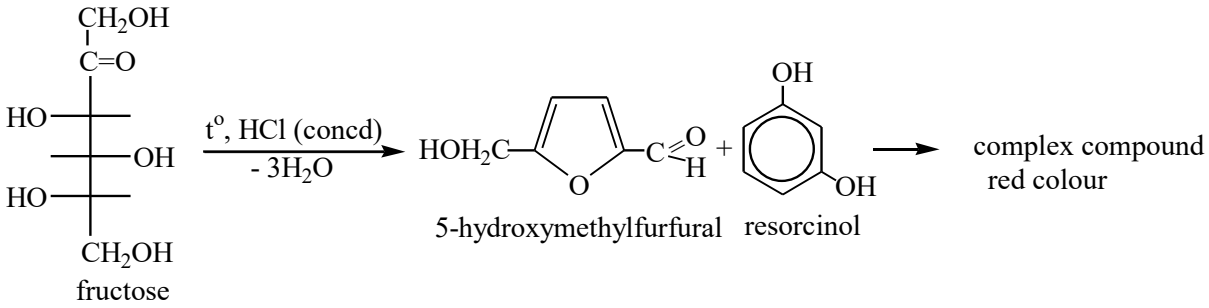
Explain the result and write conclusion.

Experiment № 3. Reaction of fructose with resorcinol.

Sequence of operations: Place 1 crystal of resorcinol and 2 drops of concentrated HCl (Take care!) in the test-tube. Add 2 drops of fructose solution. Warm the test-tube.

Check the result: the change of colour.

Write:



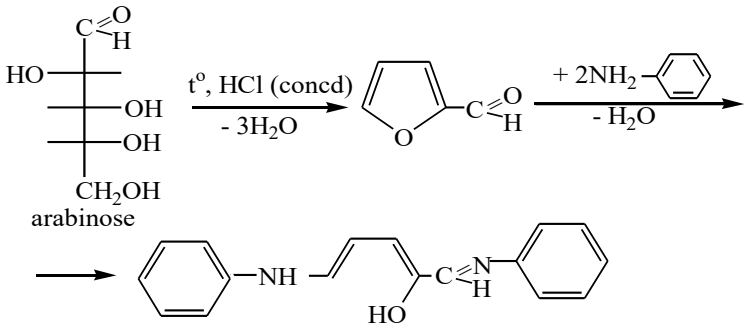
Explain the result and write conclusion.

Experiment № 4. Qualitative test for pentoses.

Sequence of operations: Place some arabinose in the test-tube № 1. Make the mixture of 3 drops of concentrated HCl (Take care!) and 3 drops of H_2O in the test-tube № 2. Add this mixture in the test-tube № 1. Place 1 drop of aniline and 1 drop of CH_3COOH on the filter paper. Place this filter paper on the inner border of the test-tube № 1.Warm the test-tube.

Check the result: the filter paper becomes red coloured.

Write:



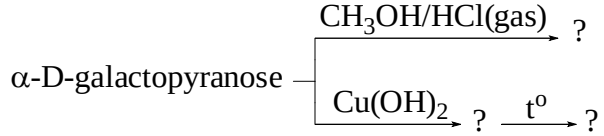
Explain the result and write conclusion.

Test to check knowledge level of current control:

1. Choice-test questions. [3] – p. 104-121

2. Example of written control test:

Write the schemes of the following reactions. Indicate the reaction centers, the type and the mechanism of the reactions.



The list of literature

Main:

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6. Daley, Richard F. Organic chemistry / Richard F. Daley, Sally J. Dalley Wm. C. – Brown Publishers, 1996. p. 1227 – 1237, 1240 – 1245

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THEME11.
Carbohydrates. Oligosaccharides and polysaccharides.

I. Training and educational goals:

1. To form knowledge of:

- Structure, spatial organization, the basic chemical properties of disaccharides, homo- and heteropolysaccharides in relation to their biological functions.

2. To form skills:

- To write formulas of reducing and nonreducing disaccharides, to indicate configuration of their glicosidic linkages;
- To write formulas of homo- and heteropolysaccharides, to explain their spatual structure;
- To write schemes of most important reactions of disaccharides, homo- and heteropolysaccharides;
- To carry out the reaction of oligo-and polysaccharides.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.
- Fostering responsibility, conscientiousness and accuracy when performing a chemical experiment.

Motivational characteristics of the need to study the them:

Disaccharides are the dimers made up of two monosaccharide molecules. The monosaccharides may be either the same or different. The monosaccharides are joined by a glycoside linkage between the anomeric carbon of one monosaccharide and an –OH group of the other.

Polysaccharides, also known as glycans, consist of monosaccharides joined together by glycosidic linkages. Polysaccharides that are polymers of a single monosaccharide are called homopolysaccharides; those made up of more than one type of monosaccharide are called heteropolysaccharides.

Program questions for self-learning and classroom knowledge control:

1. Oligosaccharides. The disaccharides: maltose, lactose, lactulose, sucrose, cellobiose. The structures, the cyclo-oxo tautomerization. The reducing properties. Hydrolysis.
2. Common characteristic and classification of polysaccharides.
3. Homo- and heteropolysaccharides. The homopolysaccharides: starch, glycogen, dextrans, cellulose. Primary structure, hydrolysis. The concept of a secondary structure (amylose, cellulose). Pectins (polygalacturonic acid).
3. The heteropolysaccharides: hyaluronic acid, chondroitin sulfates.
4. Use alginic acid to make dental alginate impression materials.
5. The concept of the mixed biopolymers: proteoglycans, glycoproteins, glycolipids.

Problems.

1. Write the structure of the product of the reaction of β-maltose with each of the following reagents:

a) HOH/H^+ c) Tollen's reagent

b) Br_2/HOH

2. Write the structure of the product of the reaction of α-cellobiose with each of the following reagents:

a) HOH/H^+ c) Fehling's solution

b) Br_2/H_2O

3. Direct oxidation of an aldose affects the aldehyde group first, converting in to a carboxylic acid, and most oxidazing agents that will attack 2^o alcohol groups. Cleary, then, a laboratory synthesis of a uronic acid from an aldose requires protecting these groups from oxidation. Keeping this in mind, suggest a method for carrying out a specific oxidation that would convert D-galactose to D-galacturonic acid.

4. Show how the following experimental evidence can be used to deduce the structure of lactose.

a) Acid hydrolysis of lactose ($C_{12}H_{22}O_{11}$) gives equimolar quantities of D-glucose and D-galactose. Lactose undergoes a similar hydrolysis in the presence of a *β-galactosidase,*

b) Lactose is a reducing sugar.

c) Oxidation of lactose with bromine water followed by hydrolysis with dilute acid gives D-galactose and D-gluconic acid.

Laboratory work.

Experiment № 1. Lactose and sucrose have hydroxyl groups.

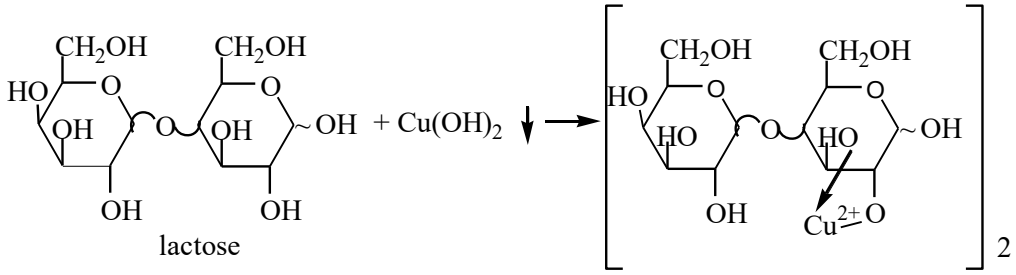
Sequence of operations: Place 1 drop of lactose solution in the test-tube № 1 and 1 drop of sucrose solution in the test-tube № 2. Add 6 drops of NaOH and 1 drop of $CuSO_4$ solutions in two test-tubes.

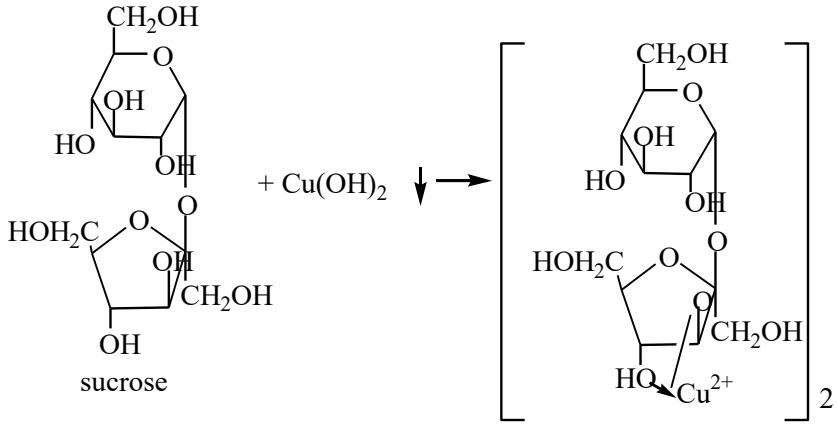
Check the result: blue solution.

Attention: you need these solutions for the next experiment.

Write:

$$CuSO_4 + 2NaOH \longrightarrow Cu(OH)_2 + Na_2SO_4$$





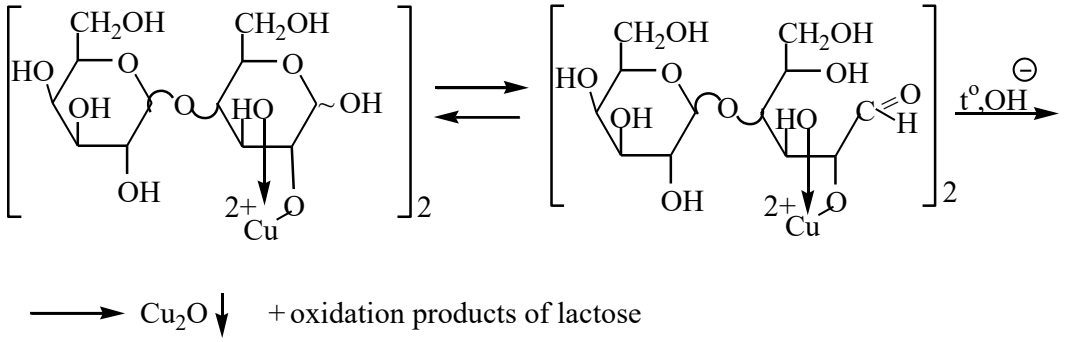
Explain the result and write conclusion.

Experiment № 2. Reducing power of lactose and sucrose.

Sequence of operations: Warm the test-tubes with solutions you received in the experiment № 1.

Check the result: brick-red precipitate in the test-tube №1.

Write:



Explain the result and write conclusion.

Experiment № 3. Proof of sucrose hydrolysis.

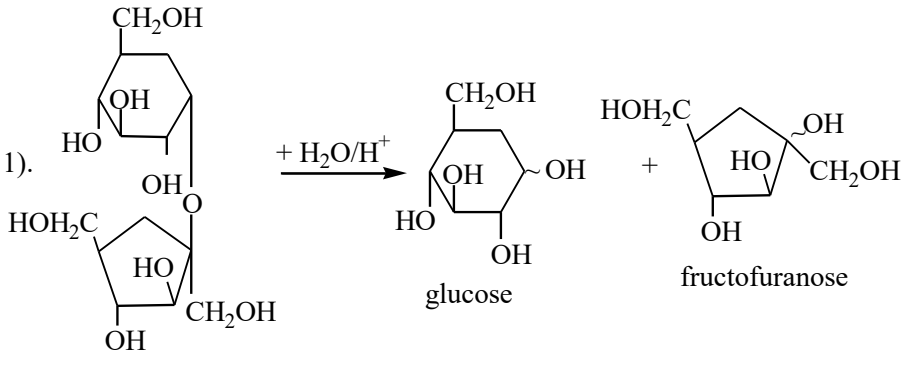
Sequence of operations: Take 2 test-tubes. Place 1 drop of sucrose solution in the test-tube № 1. Add 1 drop of HCl and 6 drops of H_2O. Warm the test-tube № 1 during 0,5-1 minute. Pour half of the solution, received in the test-tube № 1 in the test-tube № 2. Add 6 drops of NaOH, 4 drops of H_2O and 1 drop of $CuSO_4$ in the test-tube № 2. Warm the test-tube № 2.

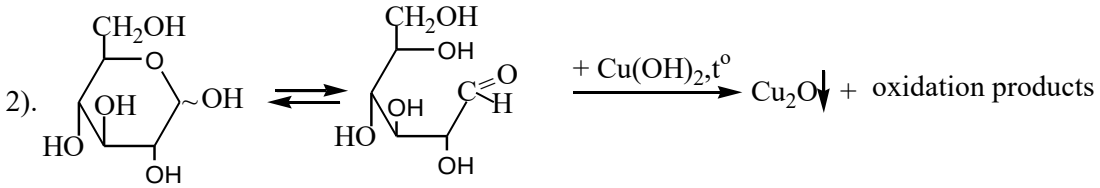
Check the result: brick-red precipitate.

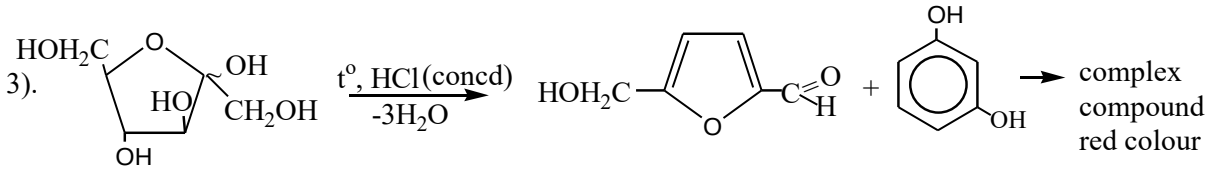
Add 1 crystal of resorcinol and 2 drops of concentrated HCl (Take care!) in the test-tube № 1.

Check the result: the change of colour.

Write:







Explain the result and write conclusion.

Experiment № 4. Discovery of the starch.

Sequence of operations: Place 5 drops of the starch paste solution in the test-tube. Add 1 drop of very diluted I_2 solution.

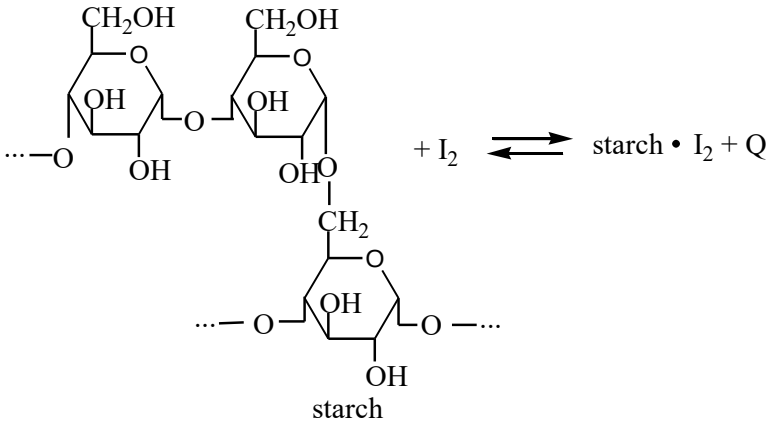
Check the result: blue solution.

Warm the test-tube.

Check the result: colourless solution.

In getting cold the solution become blue again.

Write:



Explain the result and write conclusion.

Experiment № 5. Starch has no reducing power.

Sequence of operations: Place 10 drops of the starch paste in the test-tube. Add 3 drops of NaOH and 1 drop of $CuSO_4$ solution. Shake the test-tube.

Check the result: blue precipitate of $Cu(OH)_2$

Warm the test-tube.

Check the result: black precipitate of CuO.

Write:

$$CuSO_4 + 2NaOH \rightarrow Cu(OH)_2 + Na_2SO_4$$

$$Cu(OH)_2 \xrightarrow{t^o} CuO\downarrow + H_2O$$

Explain the result and write conclusion.

Experiment № 6. Acidic hydrolysis of the starch.

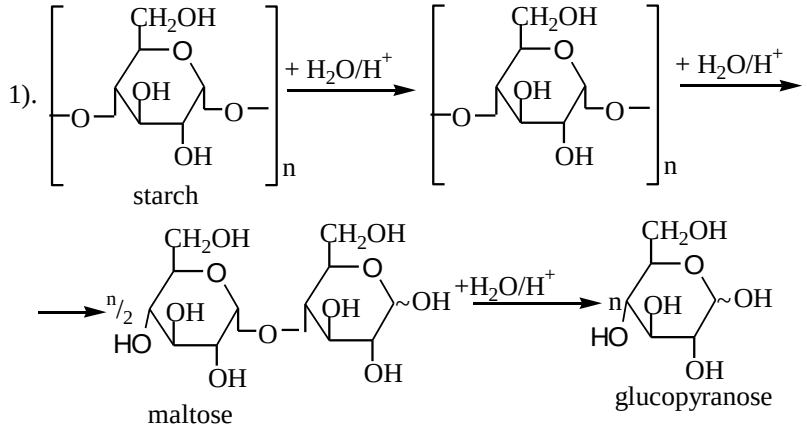
Sequence of operations: Place 1 drop of the starch paste solution in the test-tube. Add 2 drops of H_2SO_4. Warm the test-tube on the water bath during 20 minutes. Place 1 drop of this solution in the glass. Add 1 drop of very diluted I_2 (with KI) solution.

Check the result: solution has no blue colour.

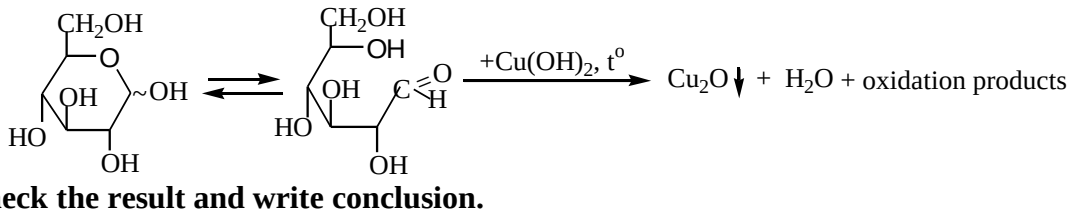
Add 8 drops of NaOH and 1 drop of $CuSO_4$ solutions in the test-tube. Warm the test-tube.

Check the result: brick-red precipitate.

Write:



2). $CuSO_4 + 2NaOH \rightarrow Cu(OH)_2\downarrow + Na_2SO_4$



Check the result and write conclusion.

Test to check knowledge level of current control:

1. Choice-test questions. [3] – p. 104-121
2. Example of written control test:

Disaccharides and Polysaccharides.

Variant 1

1. Draw the structure and indicate type of glycosidic linkages between structural units:

chondroitin-4-sulfate

([D-glucuronic acid-β-1,3-N-acetyl-D-galactosamine-4-sulfate-β-1,4]$_n$

The list of literature

Main:

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8. Schmid, George H. Organic chemistry / George H. Schmid. – Mosby, 1996. p. 1118 – 1130

THEME 12.
Amino acids

I. Training and educational goals:

1. To form knowledge of:
   - The rules of IUPAC nomenclature α-amino acids, which is part of proteins;
   - Structure, chemical properties and biological significance of natural amino acids as heterofunctional compounds;
   - A biologically important reactions α -amino acids;
   - Qualitative reactions α -amino acids.
2. To form skills:
   - To write Fisher projection formulas of D- and L- stereoisomers of natural α-amino acids;
   - To predict a predominant ionic form of natural α-amino acid at given pH of its water solution;
   - To write typical organic and biochemical reactions of natural α-amino acids;
   - To perform qualitative reactions with amino acids and simple reaction underlying their quantitative analysis.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.
- Fostering responsibility, conscientiousness and accuracy when performing a chemical experiment.

Motivational characteristics of the need to study the them:

Natural α-amino acids are monomers of the proteins. Natural α-amino acids are amphoteric compounds – acids and bases, in living organism they exist in different ionic forms at different pH. There are several biochemical processes for natural α-amino acids metabolism (deamination, transamination, hydroxylation and decarboxylation).

Program questions for self-learning and classroom knowledge control:

1 Amino acids obtained from proteins. Classification of proteinogenic amino acids. Structure, nomenclature. Stereoisomerism. Acid and base properties, a dipolar ion structure. Essential amino acids.

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

3. The qualitative tests for of α-amino acids.

4. The 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.

5. Oxidative and not oxidizing deamination reactions, the hydroxylation reactions (phenylalanine → tyrosine, tyrosine → 3,4-dihydroxyphenylalanine, tryptophan → 5-hydroxytryptophan, proline → 4-hydroxyproline), deamination of amino acids.

6. Cysteine oxidation. Disulfide bond.

Problems.

1. Write Fischer projection formulas for each of the following amino acids:
   (a) L-Valine, (b) D-Cysteine (c) L-Glutamine (d) L-Phenylalanine

2. Write the structure of each of the following amino acids in solution at pH=3, pH=8, pH=11
   (a) Leu, (b) Met, (c) Asp, (d) Lys

3. Write the structure of the predominant form of each of the following amino acids at the pH of blood 7,4

(a) Ser (b) Glu (c) His (d) Gly

4. Write the structure of the predominant form of threonine in each solution of the following pH:

(a) pH=0,2 (b) pH=9,8 (c) pH=13 (d) pH=5,0

5. Explain why there is a difference of 2,4 units between the pK_a of carboxyl group of alanine (2,3) and the pK_a of acetic acid (4,7).

6. Which of the side chains of the 20 amino acids are charged at pH=7.

7. Write the structure of the product of the reaction of isoleucine with each of the following reagents:

a. CH_3OH/HCI
b. Basic aqueous solution of bensoyl chloride
c. acetic anhydride

8. Write the structure of the product formed in each of the following reactions:

(a) Asn + NaOH/HOH(Heat) →
(b) Lys + HCI →
(c) Asp + NaOH →
(d) Trp + $NaNO_2/HCI$ →
(e) Phe + $H_2C=O$ →

9. Write the structure of the product of each of the following reactions:

(a) 2-oxopropanoic acid + Glutamic acid $\xrightarrow{\text{aminotransferase}}$

(b) 2-oxobutandioic acid + alanine $\xrightarrow{\text{aminotransferase}}$

(c) Histidine $\xrightarrow{\text{decarboxylase}}$

(d) Write the scheme of the deamination reaction of Glu.

Laboratory work.

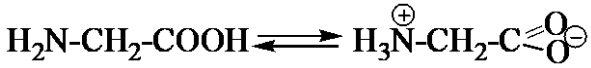
Experiment 1. Glycine solution has neutral pH value.

Sequence of operations: Place 3 drops of glycine solution in the test-tube. Add 1 drop of 0,2% methyl red (indicator) solution.

Check the result: change of colour.

Remember that indicator methyl red colour change zone is at pH 4,4-6,2.

Write:



glycine

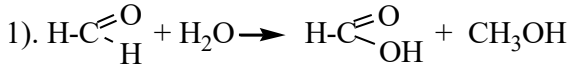
Explain the result and write conclusion.

Experiment 2. Glycine reacts with formaldehyde.

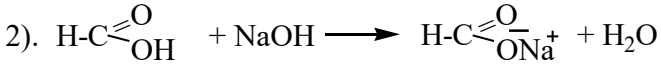
Sequence of operations: Place 3 drops of 40% formadehyde solution in the test-tube. Add 1 drop of 0,2% methyl red (indicator) solution. Note the red colour of solution. Use the thin glass capillary to add only a small amount of 2 M NaOH solution to achieve neutral pH value (the solution will become yellow). Add this solution to glycine solution (obtained in previous experiment).

Check the result: the red colour of solution, that indicated the low pH value of the solution.

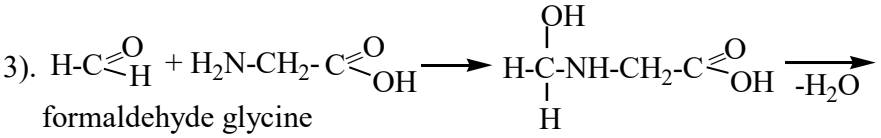
Write:



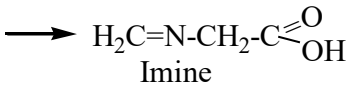
formaldehyde formic acid methanol



formic acid



formaldehyde glycine



Imine

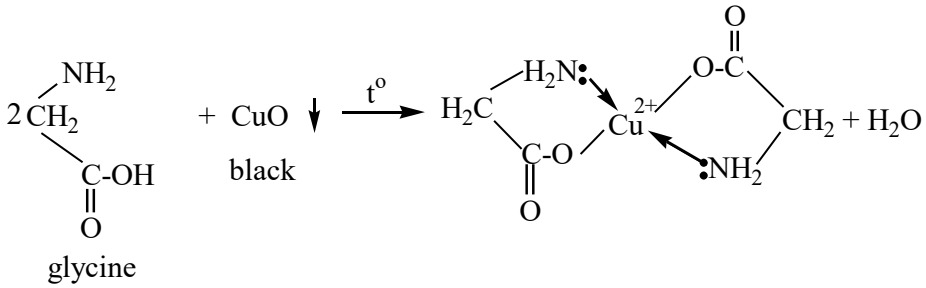
Explain the result (why the solution became acidic?) and write conclusion.

Experiment 3. Formation of copper and glycine complex compound.

Sequense of operations: Place CuO on tip spade in the test-tube. Add 3 drops of 0,2 M glycine solution and warm the test-tube

Check the result: dark-blue copper salt glycine solution.

Write:



glycine

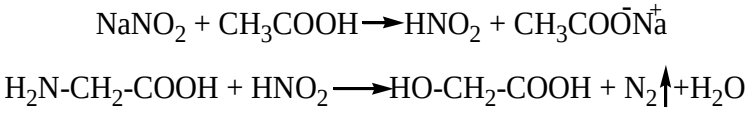
Explain the result and write conclusion.

Experiment 4. Glycine reacts with nitrous acid.

Sequence of operations: Place 5 drops of 0,2 M glycine solution in the test-tube. Add 5 drops of 5% sodium nitrite ($NaNO_2$) solution and 2 drops of concentrated acetic acid. Shake mixture carefully.

Check the result: bubbles of gas.

Write:



glycine

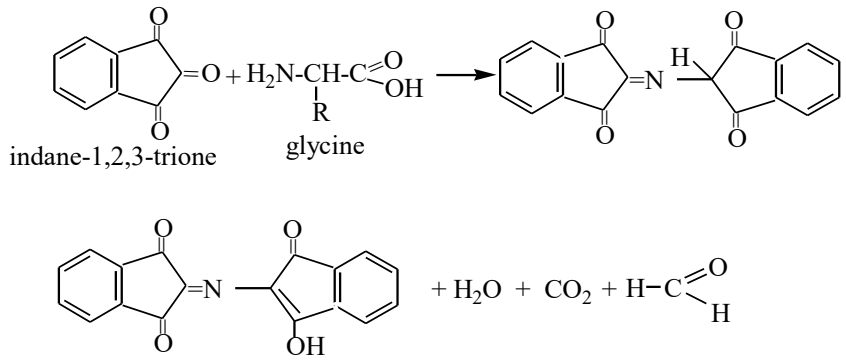
Explain the result and write conclusion.

Experiment 5. Glycine reacts with ningidrin.

Sequence of operations: Place 4 drops of 0,2 M glycine solution in the test-tube. Add 2 drops of ningidrin solution. Warm the test-tube carefully.

Check the result: blue-red colour.

Write:



Explain the result and write conclusion.

Test to check knowledge level of current control:

1. Choice-test questions. [3] – p. 121-127

2. Example of written control test:

Amino acids

Variant 1

1. Write the structure of the predominant form of cysteine at the pH of blood 7,4.

2. Write the scheme of the following reaction. Indicate the reaction centers, the type and the mechanism of the reaction.

$$\text{Glutamic acid} + C_2H_5OH \xrightarrow{H^+,\ t^0}$$

$$+ NaNO_2 + HCl \longrightarrow$$

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. 136-144

2. Bioorganic chemistry: Lecture course for foreign student of the 1st year / Assembled by L.G. Hidranovich. – Vitebsk: VSMU Press, 2004. p. 205 - 217

3. Hidranovich, L. G. Laboratory classes in bioorganic chemistry: учеб. – метод. пособие /L.G. Hidranovich, O.A. Khodos. – Витебск: ВГМУ, 2017. p. 48-51

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6. Daley, Richard F. Organic chemistry / Richard F. Daley, Sally J. Dalley Wm. C. – Brown Publishers, 1996. p. 1166 – 1173

8. Schmid, George H. Organic chemistry / George H. Schmid. – Mosby, 1996. p. 1144 – 1151

THEME 13.
Peptides and proteins.

I. Training and educational goals:

1. To form knowledge of:

- Structural structure of peptides and proteins, the spatial organization of their molecules;
- Chemical behavior of molecules of peptides and proteins in the body.

1. To form skills:

- To write the formula of primary structure of peptide in accordance with its name;
- To show electronic and spatial structure of peptide bond and to write the schemes of reactions of protein hydrolysis in acidic and bacic solutions;
- To perform simple and qualitative reaction with amino acids in the protein;
- To determine experimentally the influence of some factors on the stability of the protein in solution.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.
- Fostering responsibility, conscientiousness and accuracy when performing a chemical experiment.

Motivational characteristics of the need to study the them:

Proteins are natural polymers made up of α-amino acid monomers. Proteins are the major components of muscles, skin, and bones; they transport small molecules and ions within systems; and other proteins known as antibodies recognize and neutralize invading foreign substances such as viruses and bacteria. As enzymes and hormones, proteins catalyze and regulate the reactions that occur in the body; as muscles and tendons they provide the body with the means for movement; as skin and hair they give it an outer covering; as hemoglobins they transfer all-important oxygen to its most remote corners; as antibodies they provide it with a means of protection against disease; and in combination with other substances in bone they provide it with structural support.

Protein has a primary structure - the sequense of amino acids bonded by peptide (amide) bond. This polyamide chain folds in certain particular ways to give it the shape it needs for its particular task. This folding of the polyamide chain gives rise to higher levels of complexity called the secondary and tertiary structure of the protein.

Program questions for self-lerning and classroom knowledge control:

1. Polypeptides. Primary structure of proteins. The individual representatives of polypeptides: aspartame, glutathione, neuropeptides, insulin.
2. The electronic and the three-dimensional structure of a peptide bond.
3. The hydrolysis of polypeptides.
4. The concept of secondary, tertiary and quaternary protein structures. Hemoglobin, heme.

Problems.

1.Write the sructure of tripeptide Ala-Met-Glu in solution at: (a) pH= 1; (b) pH=3; (c) pH=11

2. Aspartame, a widely used nonnutritive sweetener, is the methyl ester of the dipeptide Asp-Phe. Draw the full structure of aspartame. The isoelectric point of aspartame is 5.9. Draw the structure present in aqueous solution at this Ph.

3. Write a reaction showing how 2,4-dinitrofluorobenzene could be used to identify the N-terminal amino acid of Val-Ala-Gly.

4. What products would you expect (after hydrolysis) when Val-Lys-Gly is treated whith 2,4-dinitrofluorobenzene?

5. Write the reaction involved in a sequential Edman degradation of Met-Ile-Arg.

6. Give the amino acid sequence of the following polypeptides using only the data given by partial acidic hydrolysis

(a) Ser, Hys, Pro, Thr → Ser-Thr + Thr-Hys + Pro-Ser

(b) Ala, Arg, Cys, Val, Leu → Ala-Cys + Cys-Arg + Arg-Val + Leu-Ala

Laboratory work.

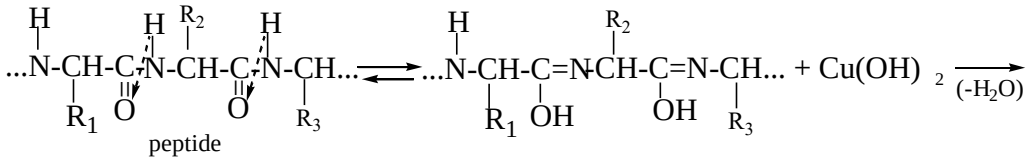
Experiment 1. Biuret test on peptide linkage.

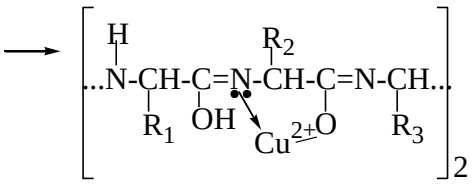
Sequence of operations: Place 5-6 drops of white egg solution (the white protein) in the test-tube. Add 5-6 drops of 2 M NaOH solution and add 1-2 drops of copper (II)-sulphate ($CuSO_4$) solution alongside the test-tube.

Check the result: red-violet colour.

Write:

$$CuSO_4 + 2NaOH \longrightarrow Cu(OH)_2\downarrow + Na_2SO_4$$





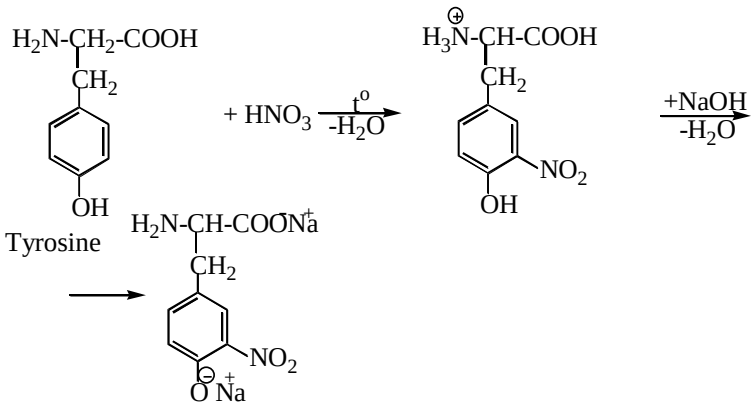
Explain the result and write conclusion.

Experiment 2. Xanthoproteinic test.

Sequence of operations: Place 5 drops of white egg (the white protein) solution in a test-tube. Add 2 drops of concentrated nitric acid. Warm the test-tube carefully, shaking it all the time. Solution and precipitate take in yellow colour. Cool the test-tube. Carefully add 1-3 drops of 2 M NaOH solution.

Check the result: brightly – orange colour.

Write:



Explain the result and write conclusion.

Experiment 3. Three-chlorineacetic acid and sulfosalicylic acid concrets protein.

Sequense of operations: Place 5 drops of white egg (the white protein) solution in test-tube. Add 5 drops of sulfosalicylic acid solution. Repeat this test with three-chlorineacetic acid solution.

Check the result: precipitate of protein.

Explain the result and write conclusion.

Experiment 4. Dehydrating agents concrets protein.

Sequence of operations: Place 5 drops of white egg (the white protein) solution in two test-tubes. Add 10-15 drops of alcohol in the first test-tube, add 10-15 drops of acetone in the second test-tube.

Check the result: precipitate of protein.

Explain the phenomenon, which takes place with protein under the influence of organic solvents **and write conclusions**.

Test to check knowledge level of current control:

1. Choice-test questions. [3] – p. 127-134

2. Example of written control test:

Polypeptides and proteins.

Variant №1

Write the scheme of the following reaction. Indicate reaction centers and the type of the reaction.

$$\text{Ala-Phe-Cys} + H_2O \xrightarrow{H^+ / t^o}$$

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. 145-149

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5. Solomons, T.W. Graham. Fundamentals of organic chemistry / T.W. Graham Solomons. 4th edition – John Willey and sons, inc., 1994. p. 986 - 1005

6. Daley, Richard F. Organic chemistry / Richard F. Daley, Sally J. Dalley Wm. C. – Brown Publishers, 1996. p. 1176 – 1179, 1181 – 1194, 1197 – 1203

8. Schmid, George H. Organic chemistry / George H. Schmid. – Mosby, 1996. p. 1151-1175

THEME 14.
Nucleic acids

I. Training and educational goals:

1. To form knowledge of:
   - Structure and properties of the nucleotides as monomeric units of nucleic acids;
   - Nature of the linkages between monomers in the biopolymer;
   - Primary and secondary structure of nucleic acids;
   - Structure of nucleosidmono-and polyphosphates.
2. To form skills:
   - To write tautomeric forms of nucleic heterocyclic bases and to explain their stability;
   - To write structures of nucleosides and nucleotides in accordance with their names;
   - To write the schemes of hydrolysis reactions of nucleotides in acid and base solutions, to propose conditions for a nucleoside hydrolysis;
   - To write the primary structure of DNA and RNA;
   - To perform qualitative tests for structural units of a nucleotide.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.
- Fostering responsibility, conscientiousness and accuracy when performing a chemical experiment.

Motivational characteristics of the need to study the them:

The essential property of all living systems is the ability to reproduce or replicate themselves. The information required for replication of an organism is contained in molecules called nucleic acids.

The two classes of nucleic acids are **deoxyribonucleic acid (DNA)** and **ribonucleic acid (RNA).** Deoxyribonucleic acid is the master repository of genetic information in cells. **DNA** directs its own replication during cell division. The genetic information in DNA is copied into **RNA** by a process called **transcription.** Subsequent **translation** of the information in **RNA** forms proteins. The genetic information that is stored in DNA, therefore, is passed from **DNA to RNA** to proteins. We begin our study of nucleic acids by examining the chemical composition of nucleic acids.

There are other nucleotides (AMP, ATP, cAMP and cGMP, NAD^+ and $NADP^+$) in living organisms.

The main reactions of nucleic acids, nucleotides and nucleosides are hydrolysis reactions.

Program questions for self-learning and classroom knowledge control:

1. Nucleic (heterocyclic) bases: pyrimidines (uracil, thymine, cytosine) and purines (adenine, guanine). Aromatic properties. A lactim–lactam tautomerization.
2. Nucleosides. Nucleotides. Structure of mononucleotides that can be obtained from nucleic acids. Nomenclature. Nucleotides hydrolysis.
3. Primary structure of nucleic acids. The phosphate diester linkage. Ribonucleic and deoxyribonucleic acids. The nucleotides found in RNA, the nucleotides found in DNA.
4. Hydrolysis of nucleic acids.
5. The concept of the secondary structure of DNA. The role of hydrogen bonds in the formation of the DNA secondary structure. Complementarity of heterocyclic bases.
6. 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.

7. 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.

Problems.

1. Write the sructure of the two tautomeric forms of guanine, cytosine, uracil, and thymine.

2. Write structural formulas showing the hydrogen bonds in complementary base pairs of DNA and RNA.

3. The most stable tautomeric form of guanine is the lactam form. This form is normally present in DNA and it pairs specifically with cytosine. Guanine can tautomeraze to the abnormal lactim form and make the pair with thymine. Write structural formulas showing the hydrogen bonds in these base pairs.

4. Write the structure and give the name of the nucleoside formed by combining each of the following pairs of heterocyclic bases and pentoses.

a) Ribose and guanine
b) Thymine and 2-deoxyribose
c) Cytosine and ribose
d) Adenine and 2-deoxyribose

5. Uridine and 2-deoxyguanosine are stable in dilute base. In dilute acid, however, they undergo rapid hydrolysis yilding a sugar and heterocyclic base. Write the reaction of nucleosides hydrolysis.

6. Write the structures of 5'-guanilic acid, cytidine –5'-phosphate, 2'-deoxyadenosine-5'-phosphate, uridilic acid. Write the reaction of acid and base-catalyzed hydrolylis of nucleotides.

7. ATP is the abbreviation of adenosine triphoshate. Based on the structure of adenosine 5'-monophoshate, propose a structure for ATP.

8. In some cells, biochemists found a cyclic form of AMP in which the phosphate form a cyclic ester between C3' and C5'. Propose structure for cyclic AMP.

9. Write the structure of mRNA portion with following nucleotides sequences:
(a) 5'-end U–A–C 3'-end
(b) 5'-end G–U–A 3'-end

10. Write the structure of DNA portion with following nucleotides sequences:
a. 5'-end A–T–G 3'-end
b. 5'-end T–G–C 3'-end

11. The portion of one chain of DNA molecule has the following nucleotides sequence:
5'-end AGGCTATTCGT 3'-end. Write the sequence of nucleotides in the complementary chain of the DNA molecule.

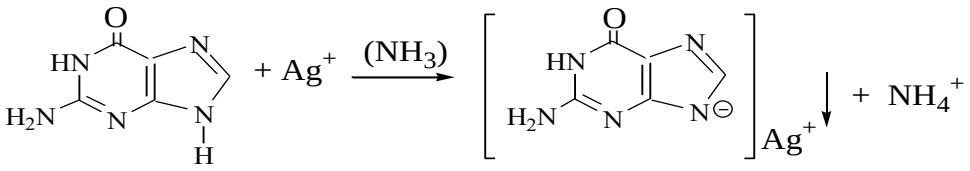
Laboratory work.

Experiment 1. Discovering of purine bases ("silver test").

Sequence of operations: Place 5 drops of yeast hydrolysate in a test-tube. Add one by one some drops of concentrated ammonia solution (unti the universal indicator paper will show basic reaction). Then add 5 drops of 2% ammoniacal silver-nitrate solution. Don't mix contents of the test-tube. Leave the test-tube for 3-5 minutes.

Check the result: bright-brown precipitate.

Write:



guanine

Explain the result and write conclusion.

Experiment 2. Discovering of five-carbon monosaccacharide in products of nucleotides hydrolysis.

a) Quantitative reaction for aldopentoses (Molish test).

Seguence of operations: Place 5 drops of yeast hydrolyzate in a test-tube. Add 3 drops of 1% thymol alcohol solution. Mix and pour concentrated sulphuric acid along the side the test-tube. Shake the test-tube.

Check the result: there is the test-tube the red coloured product of condensation furfural with thymol on the bottom.

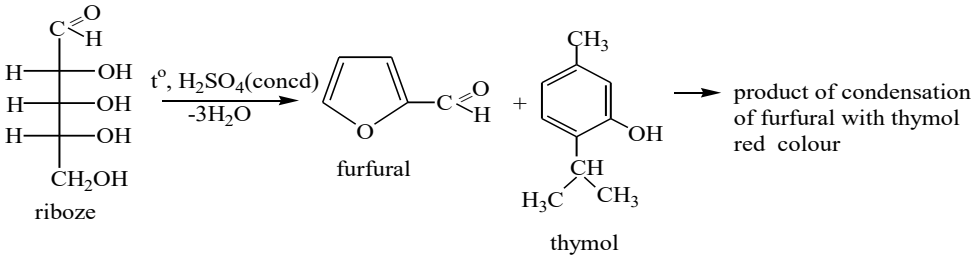
b) Discovering of ribose and deoxyribose.

Seguence of operations: Place 5 drops of yeast hydrolyzate in a test-tube. Add 2 drops of 1% diphenylamine solution. Warm the test-tube on water bath during 15 minutes.

Check the result: blue-green colour.

Remember: 1) concentrated sulphuric acid with five carbon monosaccacharide lead to their dehydration and formation of furfural, which gives red coloured product of condensation with thymol; 2) diphenylamine gives blue colour with deoxyribose, but green colour with ribose.

Write:



riboze — furfural — thymol — product of condensation of furfural with thymol red colour

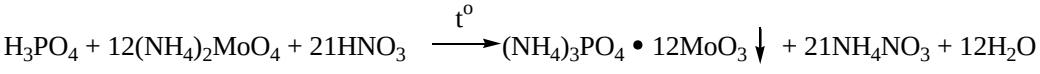
Explain the result and write conclusion.

Experiment 3. Discovering phosphoric acid in product of nucleotides hydrolysis.

Sequence of operations: Place 5 drops of yeast hydrolysate in the test-tube. Add 10 drops of molibdenic reagent. Warm the test-tube. The liquid becomes lemon-yellow. Cool the test-tube.

Check the result: lemon-yellow precipitate.

Write:



ammonium phoshomolibdic

Explain the result and write conclusion.

Test to check knowledge level of current control:

1. Choice-test questions. [3] – p. 135-145

2. Example of written control test:

Nucleosides. Nucleotides. Nucleic acids. Nucleoside mono- and polyphosphates.

Variant №1

Write the scheme of the following reaction. Indicate reaction centers and the type of the reaction.

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. 150-156

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Supplementary:

5. Solomons, T.W. Graham. Fundamentals of organic chemistry / T.W. Graham Solomons. 4th edition – John Willey and sons, inc., 1994. p. 1017 - 1039

6. Daley, Richard F. Organic chemistry / Richard F. Daley, Sally J. Dalley Wm. C. – Brown Publishers, 1996. p. 1283 – 1287, 1294 – 1298, 1302-1309

8. Schmid, George H. Organic chemistry / George H. Schmid. – Mosby, 1996. p. 1188 - 1205.

THEME 15

Control-Test. ” Theoretical bases of structure and general patterns of reactivity of organic compounds. Biopolymers and their structural units”

I. Educational and training goals.

A student must possess knowledge of:

1. Program material from the theme № 1 to № 14.

A student must gain the following skills:

- to show basic knowledge of main principles of structural, electronic and spatual structure of organic molecules and main reactivity of mono, poly and heterofunctional organic compounds;
- to make analysis of 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

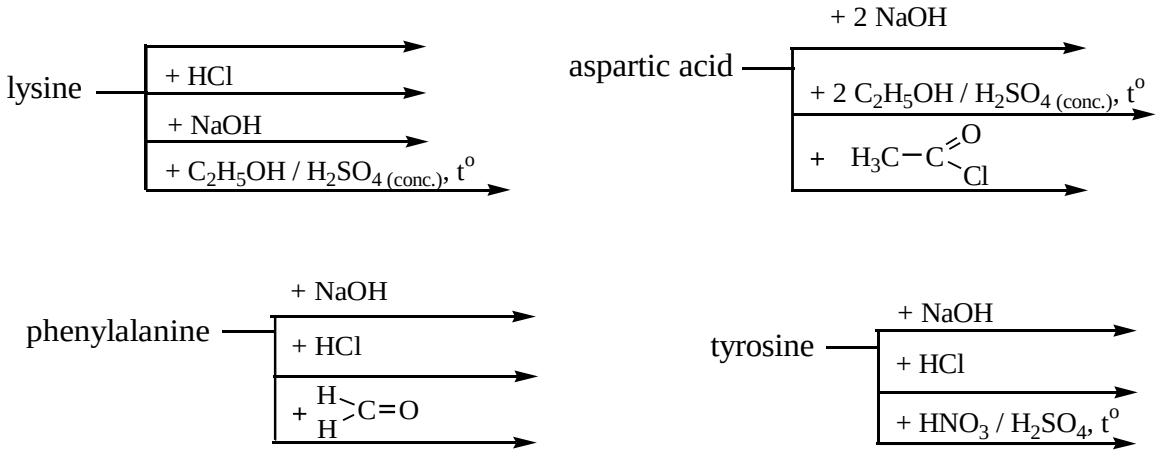
Summary multiple-choice test questions are questions №1-201 located on pages 67-104 of the educational manual [3].

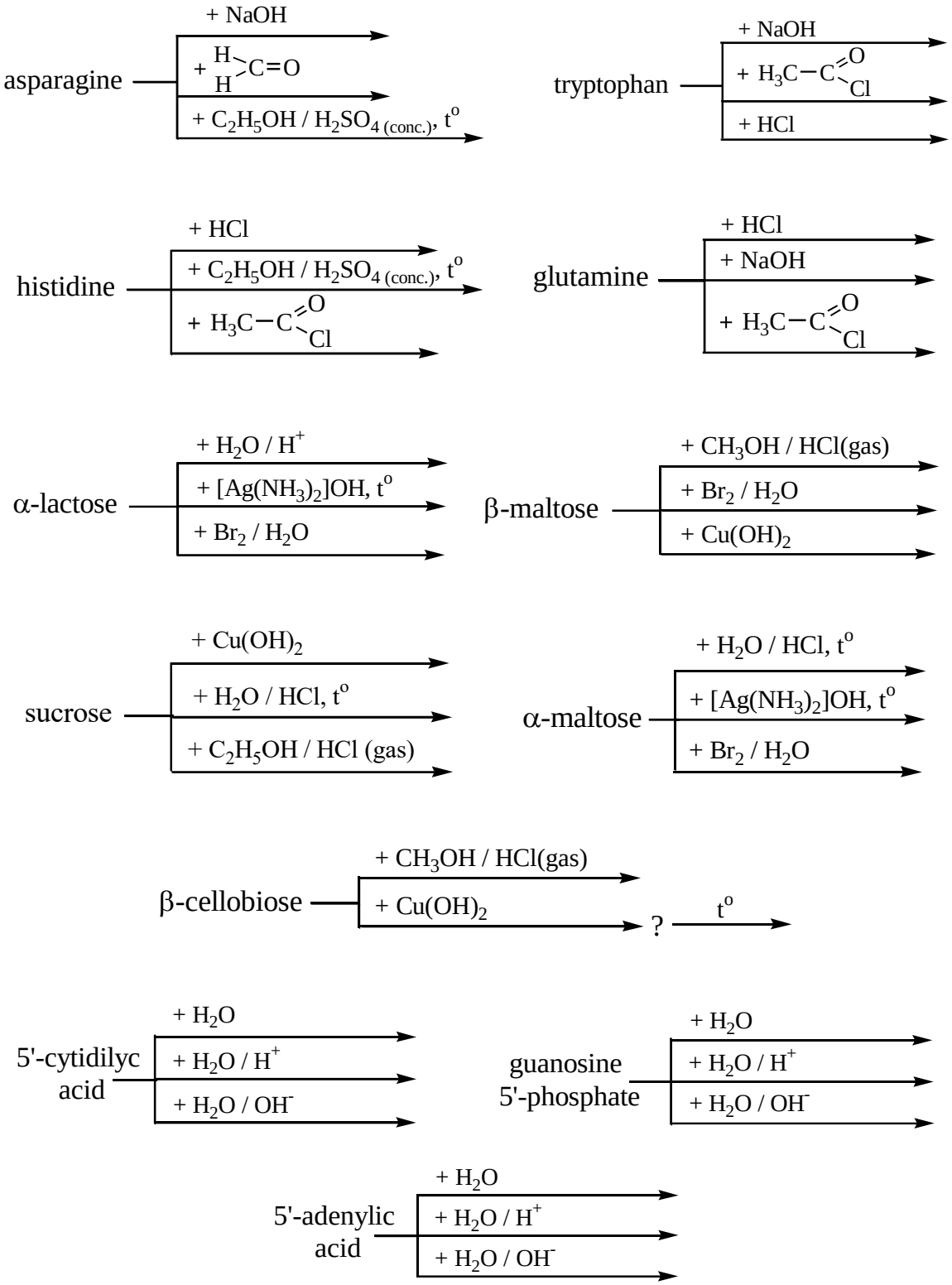
Summary questions for written control:

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, taking part in each reaction, indicate the mechanism of the following reactions:



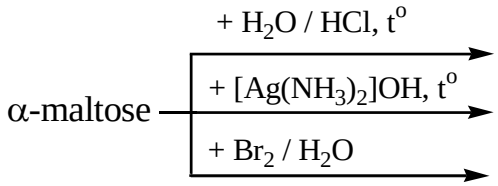

asparagine
+ NaOH
+ H2C=O
+ C2H5OH / H2SO4 (conc.), t°
tryptophan
+ NaOH
+ H3C−C(=O)Cl
+ HCl
histidine
+ HCl
+ C2H5OH / H2SO4 (conc.), t°
+ H3C−C(=O)Cl
glutamine
+ HCl
+ NaOH
+ H3C−C(=O)Cl
α-lactose
+ H2O / H+
+ [Ag(NH3)2]OH, t°
+ Br2 / H2O
β-maltose
+ CH3OH / HCl(gas)
+ Br2 / H2O
+ Cu(OH)2
sucrose
+ Cu(OH)2
+ H2O / HCl, t°
+ C2H5OH / HCl (gas)
α-maltose
+ H2O / HCl, t°
+ [Ag(NH3)2]OH, t°
+ Br2 / H2O
β-cellobiose
+ CH3OH / HCl(gas)
+ Cu(OH)2
?
t°
5'-cytidilyc acid
+ H2O
+ H2O / H+
+ H2O / OH-
guanosine 5'-phosphate
+ H2O
+ H2O / H+
+ H2O / OH-
5'-adenylic acid
+ H2O
+ H2O / H+
+ H2O / OH-

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.

THEME 16.
Lipids.

I. Training and educational goals:

1. To form knowledge of:

- Classification, nomenclature of simple and complex saponifield lipids;
- The principle structure and stereoisomerism simple and complex saponifield lipids as the basis for the study of the chemical structure of biological membranes;
- Structural principle of major natural higher fatty acids and the ω-nomenclature;
- Properties of simple and complex saponifield lipids and ideas about their role in lipid and mineral metabolism.
- Notes of lipid peroxidation.

2. To form skills:

- To write structural formulas of simple and complex saponified lipids with elements of stereochemistry, to predict their chemical properties on base electronic structure of reaction centers and to write the cheme of reactions;
- To indicate hydrophobic and hydrophilic fragments in the structure of complex lipids;
- To write the main steps of lipid peroxidation reactions;
- To perform the characteristic reactions for higher fatty acids and saponifield lipids.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.
- Fostering responsibility, conscientiousness and accuracy when performing a chemical experiment.

Motivational characteristics of the need to study the them:

Lipids are compounds of biological origin that dissolve in nonpolar solvents, such as chloroform or diethyl ether. *The* name lipid comes from the *Greek* word *lipos,* for fat. Unlike carbohydrates and proteins, which are defined in terms of their structures. lipids are defined by the physical operation that we use to isolate them.

Lipids are characterized by specific structures, configuration and conformations, reactivity. Simple saponified lipids - waxes, fats and oils, complex saponified lipids – phospholipids of cell membranes in living organisms. Waxes are used to compose inelastic impression materials in dentistry. Lipid peroxidation processes damages cell membranes in vivo and results rancidity of oils in vitro.

Program questions for self-learning and classroom knowledge control:

1. Classification. Biological significance of lipids. Waxes: the structure, properties, use as dental impression materials.
2. Neutral fats. The common natural fatty acids that can be obtained from lipids: palmitic, stearic, oleic, linoleic, linolenic, arachidonic acids. Features of unsaturated fatty acids, ω-nomenclature.
3. Phospholipids. Phosphatidylethanolamines, phosphatidylserines, phosphatidylcholines (lecithines), phosphatidylinositols as the structural components of cellular membranes.
4. Rancidness of fats that is free radical chain process as the model of the peroxidation of polyunsaturated fatty acids in the cell membranes, its mechanism and its biological role.

Problems.

1. How would you convert stearic acid into each of the following?
   (a) Ethyl stearate

(b) Sodium stearate
(c) Stearyl chloride
(d) Stearamide
(e) N,N-Dimethylstearamide

2.Using oleic acid as an example illustrate the following reactions of the double bond.
(a) Addition of bromine
(b) Addition of hydrogen
(c) Hydroxylation
(f) Addition of HCI

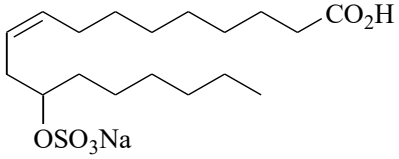
3. Write the structure and name triacylglycerols formed by combining of the following fatty acids with glycerol:
(a) Palmitic acid, oleic acid, stearic acid
(b) Linoleic acid, stearic acid, linolenic acid
(c) Oleic acid, linoleic acid, stearic acid.

4. Both triacylglycerols and phospholipids have fatty acid ester components, but only one group can be considered amphipathic. Indicate wich is amphipathic and explain why. Using 1-0-stearoyl-2-0-oleioyl-3-0-palmitoyl-glycerol and lecithin ullustrate yours answer.

5. Write the structure of phosphatidyl serine and show it's the hydrophilic and hydrophobic portions.

6. Under suitable conditions all of the ester linkages of phosphatide can be hydrolyzed. What organic compounds would you expect to obtain from the complete hydrolysis of (a) lecithin, (b) cephalin, c) choline – containing plasmalogen.

7. Castor oil react with sulfuric acid to give a sulfated castor oil known as "Turkey-red oil" due to its use as a surfactant or wefting agent in "Turkey-red" dyeing using madder root (the active due is alizarin). Turkey-red oil soaps, obtained by hydrolysis of the oil, are not particularly good detergents (i.e. they form micelles not so well). The structure of a typical Turkey-red oil soap is given below. Suggest why these amphipathic compound might not form micelles very well.



Show the hydrophilic and hydrophobic portion of "Turkey-red oil".

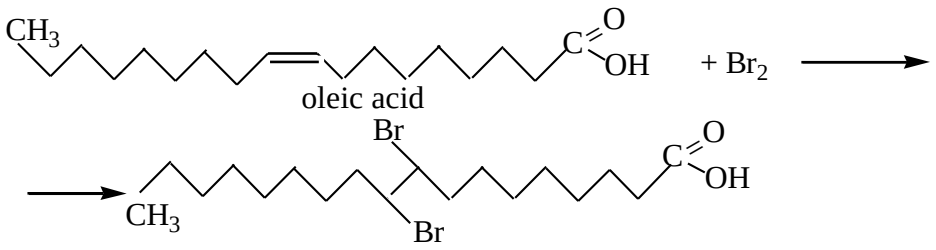
Laboratory work.

Experiment 1. Oleic acid reacts with bromine water.

Sequense of operations: Place 3-4 drops of oleic acid in a test-tube. Add 1-2 drops of KBr solution, 1-2 drops of $KBrO_3$ solution and 2-3 drops of 10% H_2SO_4 in a test-tube. This reaction results yellow solution of bromine water. Shake a test-tube.

Check the result: bleaching of solution.

Write:



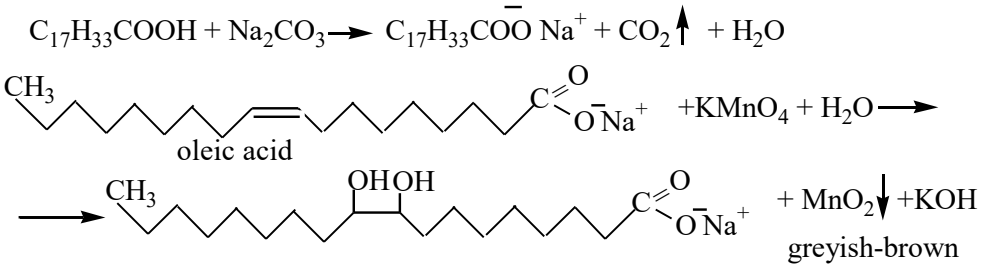
Explain the result and write conclusion.

Experiment 2. Oleic acid reacts with $KMnO_4$ solution.

Sequence of operations: Place 2 drops of oleic acid in a test-tube. Add 2 drops of 5% Na_2CO_3 solution and 2 drops $KMnO_4$ solution. Shake the test-tube.

Check the result: bleaching of solution.

Write:



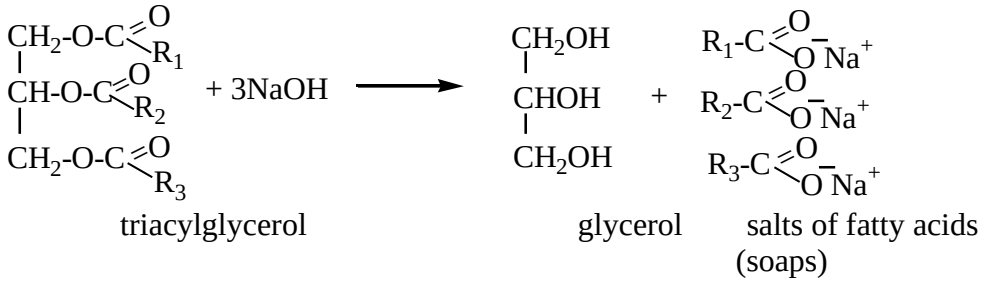
Explain the result and write conclusion.

Experiment 3. Saponification of fats.

Sequense of operations: Place 0,5 ml of castor oil in a test-tube. Add 0,5 ml of alcohol and 0,5 ml of 35% NaOH solution. Mix and warm contents of the test-tube on water bath during 5-7 minutes. Place some drops of solution in a new test-tube, add 2-3 ml of distilled water and warm it. Complete dissolving of the substens in water shows its complete saponification. Add 3-4 ml of saturated hot NaCl solution. (Salting-out soap).

Check the result: layer of soap lift up.

Write:



Explain the result and write conclusion.

Test to check knowledge level of current control:

1. Choice-test questions. [3] – p. 145-151

2. Example of written control test:

Lipids.

Variant №1

Write the structure of the following beeswax, illustrate the conformation of alkyl chains. Write the scheme of the following reaction. Indicate interacted reaction centers of the substrate and the reagent. Indicate the type and mechanism of the 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. 157-166

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4. Hurynava, A.S. Restorative dental polymer materials: Manual./ A.S. Hurynava. – Vitebsk: VSMU, 2016. p. 42-44

Supplementary:

5. Solomons, T.W. Graham. Fundamentals of organic chemistry / T.W. Graham Solomons. 4th edition – John Willey and sons, inc., 1994. p. 938-947, 963-967

6. Daley, Richard F. Organic chemistry / Richard F. Daley, Sally J. Dalley Wm. C. – Brown Publishers, 1996. p. 192-195, 382-383

8. Schmid, George H. Organic chemistry / George H. Schmid. – Mosby, 1996. p. 675-683

THEME 17.
Low-molecular weight bioregulators

1. Training and educational goals

1. To form knowledge of:
- classification, structure and biological role of steroids;
- stereochemical structure of steroids;
- reaction centers and reactivity of steroids.
- classification and physiological influences of alkaloids.

2. To form skills in:
- writing structural formulas of steroids according to their systematic names;
- characterizing the configuration of chiral centers in α, β-stereochemical nomenclature, ring junctions and three-dimensional structures of 5α and 5β series of steroids;
- writing the schemes of the reactions for different reaction centers of steroids.
- writing of acid-base reactions for alkaloids;
- performing qualitative reactions for alkaloids.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.
- Fostering responsibility, conscientiousness and accuracy when performing a chemical experiment.

Motivational characteristics of the need to study the them:

Steroids are important "biological regulators" that nearly always show dramatic physiological effects when they are administered to living organisms. Among these important compounds are male and female sex hormones, adrenocortical hormones, D vitamins, the bile acids, and certain cardiac poisons.

Program questions for self-learning and classroom knowledge control:

1. The concept of biologically active compounds. The significance of the spatial structure and physical-chemical properties of bioregulators in their interaction with receptors and the implementation of action at the molecular level.

2. Steroids. Gonan (steran, perhydrocyclopentanophenanthrene), stereochemical structure of 5α, 5β series of steroids. Physical properties of steroids. Hydrocarbons that are parent structures of steroid groups: estrane, androstane, pregnane, cholane, cholestane.

3. Steroid hormones. Sex hormones: estrogens, androgens; progestins; adrenocortical hormones. Structure, biological role.

4. Bile acids: cholic, glycocholic and taurocholic acids, their structure. Reactions with taurine and glycine, the biological role.

5. Cholesterol as one of sterols, its conformational structure. Its properties, its role in metabolism and structure of cell membranes, in development of cardiac pathology. 7-Dehydrocholesterol, its transformation to vitamin D_3 (cholecalciferol).

6. Ergosterol, its transformation to vitamin D2 (ergocalciferol). The role of vitamin D in regulation of calcium-phosphorus metabolism.

7. Alkaloids. Botanical and chemical classification of alkaloids. Alkaloids as poisons in medicines.

8. The structure and effect on the human body of nicotine, quinine, papaverine, morphine, atropine.

9. Methylated xanthine derivatives (theobromine, theophylline, caffeine) and their use in medicine

Problems.

1. Draw the two basic ring systems for the 5α and 5β series showing all hydrogen atoms of the cyclohexane rings. Label each hydrogen atom as to whether it is axial or equatorial (using estradiol (1,3,4(10)-estra-triene-3,17β-diol) as an example).

2. Designate with the star the eight stereocenters of cholesterol.

3. The adrenocortical steroids are apparently involved in the regulation of a large number of biological activities including carbohydrate, protein, and lipid metabolism, water and electrolyte balance, and reactions to allergic and in flammatory phenomena. Cortisone and cortisol, two adrenocortical steroids, have the systematic name 17α, 21-dihydroxy-4-pregnene-3,11,20-dione and 11β, 17α, 21-trihydroxy-4-pregnene-3,20-dione. Draw a three-dimensional formula for cortisone and cortisol.

4. Androsterone, a secondary male sex hormone, has the systematic name 3α-hydroxy-5α-androstan-17-one. Give a three-dimensional formula for androsterone.

5. Norethynodrel, a synthetic steroid that has been widely used in oral contraceptives, has the systematic name 17α-ethynyl-17β-hydroxy-5(10)-estren-3-one. Give a three dimensional formula for norethynodrel.

6. Show how you might convert cholesterol into each of the following compounds:

(a)5α,6β-Dibromocholestan-3β-ol

(b)Cholestane - 3β,5α,6β-triol

(d) 5α-Cholestan-3-one

7. The estrogens (estrone and estradiol) are easily separated from the androgens (androsterone and testosterone) on the basis of one of their chemical properties. What is the property and how could such separation be accomplished?

8. Write the photochemical reaction of conversion of ergosterol to vitamin D.

9. Acid hydrolysis is carried out to identify cocaine. Determine the reaction centers for which hydrolysis takes place and write the scheme of the reaction. Indicate the mechanism of the reaction.

10. Nicotinic acid and its amide are known as the two forms of coenzyme NAD^+. Suggest the schemes of the reactions for the synthesis of nicotinamide from nicotinic acid. Indicate the mechanisms of the reactions.

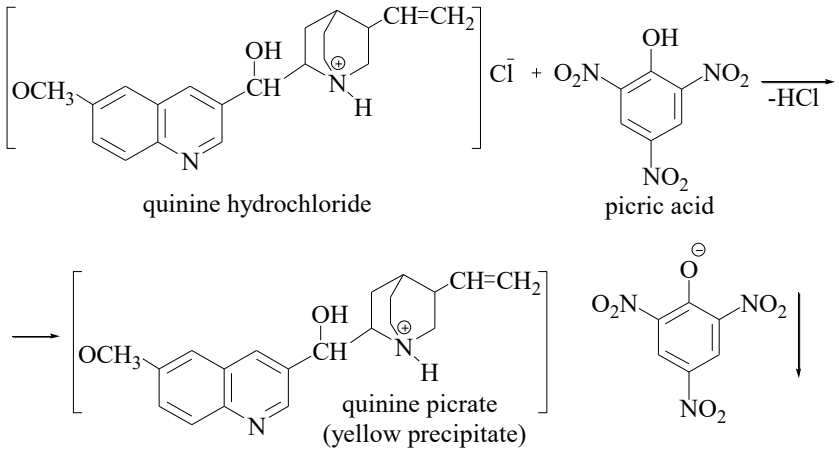
Laboratory work.

Experiment № 1. Common reactions for alkaloids.

Place three drops of quinine hydrochloride solution on a glass slide. Add 1 drop of iodine to the first drop of quinine, 1 drop 0,5% of tannin solution to the second drop of quinine, 1 drop of saturated solution of picric acid to the third drop of quinine.

Check the result: colored precipitates.

Write:



Explain the result and write conclusion.

Test to check knowledge level of current control:

1. Choice-test questions.
2. Example of written control test:

Low-molecular weight bioregulators

Variant №1

Write the schemes of the following reactions. Indicate the types of the reactions; show the electron density distribution in reaction centres.

Quinine + HCl → ?

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. 167-173

2. Bioorganic chemistry: Lecture course for foreign student of the 1st year / Assembled by L.G. Hidranovich. – Vitebsk: VSMU Press, 2004. p. 269-281

THEME 18.
Organic compounds used in dentistry

I. Training and educational goals:

1. To form knowledge of:
   - The structure of macromolecular compounds and classification of polymers;
   - Types of polymerization - radical and ionic polymerization mechanisms and the influence on the structure and properties of polymeric materials;
   - Structures of typical initiators, activators and inhibitors of free-radical polymerization reactions.
   - The structure of macromolecular monomers of modern composite materials.
2. To form skills:
   - To write structural formulas of simple monomer for an addition polymerization;
   - To write the schemes and the outline mechanism of free-radical addition polymerization reactions;
   - To write formulas of different polymers and to classify them;
   - To carry out simple experiments on the reaction of polymerization and depolymerization of polymers.

Upbringing goals:

- Formation of ideological ideas based on establishing cause-and-effect relationship between chemical phenomena.

Motivational characteristics of the need to study the them:

Polymer dental materials are classified by following categories:

1. Dental materials for the orthopedic stomatology:
- Impression materials for casts and models;
- Denture base resins, materials for crowns, a false tooth and bridges.
2. Direct restorative dental materials for the therapeutic stomatology:
- Materials for permanent restorations to repair anatomy shape and functions of tooth;
- Materials for temporary filling of cavity preparation during treatment of high caries activity;
- Materials for liners and bases before placement of permanent restorations;
- Root canal filling materials;
- Preventive materials: pit and fissure sealants to prevent decay and caries.
3. Prosthesis called complete dentures replaced missing teeth; bone and gingiva after the teeth have been lost or extracted.

Monomers of direct restorative dental polymers are based on derivatives of acrylic and methacrylic acids esters. The high-molecular monomers of the modern composite dental materials: Bis-GMA, NTG-GMA, HEMA, PMDM, UDMA are among them. These polymers are synthesized by the radical addition polymerization reaction. Activators, initiators and inhibitors are used for it.

Program questions for self-learning and classroom knowledge control:

1. The general characteristic of high-molecular compounds. The monomer, the simple repeating unit, the degree of polymerization. Polymers, oligomers, copolymers. Classification of polymers.

2. The types of polymerization: radical and ionic. The radical mechanism of the polymerization reaction of acrylic and methacrylic acids esters. Activators, initiators and inhibitors of radical polymerization reactions.

3. Composite tooth restorative dental materials of chemical and light promoted hardening. The high-molecular monomers of the modern composite dental materials: Bis-GMA, NTG-GMA, HEMA, PMDM, UDMA.

4. The chemical compounds used for providing adhesion of a restorative material to the tooth and enamel tissues.

Problems.

1. Write the structural formula of the polymer Etacryl (terpolymer of methyl methacrylate, ethyl methacrylate and methyl acrylate) on the board.

In this example students understand concepts: high molecular weight compounds, monomers, polymers, oligomers, copolymers. Teacher offers students explaining concepts: biopolymers, synthetic and modified macromolecular compounds.

2. Write on a blackboard scheme for the polymerization of ethylene and substituted ethylenes.

In this example students understand the concept of ionic and radical polymerization mechanism, consider using flowcharts, explain the differences in the structure and properties of polymers produced by different mechanisms.

3. Write the scheme of methacrylate polymerization by a radical mechanism using chemical initiator benzoyl peroxide.

The role of activators and inhibitors in the radical polymerization initiation stage is discussed. It explains how the monomers are stabilized. Students use Tables 28, 29, 30, 31. Students explain where these polymers are used in dentistry. Teacher and students discuss laboratory experiments in which unsaturation of methacrylate and methyl methacrylate monomers resulted the process of a polymer depolymerization is proved. The characteristics of these processes are analyzed.

4. Write the formula of example of polymer on base one of macromolecular monomers of modern composite materials using Table 28 and classify this polymer.

5. Write the scheme of reaction provided adhesion the restorative material to the tissues of enamel and dentin.

In this reaction the monomer for restorative polymer is HEMA, the linking residue of enamel or dentin collagen is lysine, the adhesive is glutaraldehyde. For solution students use Tables 28, 32.

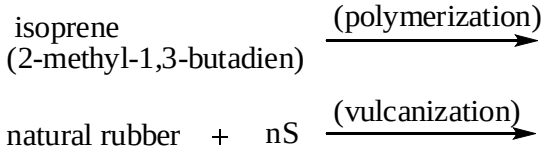
Test to check knowledge level of current control:

1. Choice-test questions. [3] – p. 151-157

2. Example of written control test:

Polymers and dental materials
Variant №1

Write the scheme of the polymerization reaction for synthesis of rubber and vulcanization of rubber.



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