MINISTRY OF HEALTH OF UKRAINE
ZAPORIZHZHIA STATE MEDICAL UNIVERSITY
DEPARTMENT OF ORGANIC AND BIOORGANIC CHEMISTRY

GUIDELINES AND LABORATORY PROTOCOLS OF ORGANIC CHEMISTRY

SEMESTER 2

Heterocyclic and natural compounds

For self-training for practical classes in organic chemistry of students of the International Faculty,
specialty 226 «Pharmacy, industrial pharmacy»

Student ___ group 2 course ______________________ faculty

____
full name

Zaporizhzhia

2021

UDC 547(076.5)
G 94

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of Zaporizhzhia State Medical University as a study guide
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G94 **Guidelines and Laboratory protocols of Organic chemistry**. Semester 2 : Heterocyclic and natural compounds : for self-training for practical classes in organic chemistry of students of the International Faculty, specialty 226 «Pharmacy, industrial pharmacy» : / S. I. Kovalenko et al. – Zaporizhzhia : ZSMU, 2021. – 86 p.

UDC 547(076.5)

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Total		64

CRITERIA FOR EVALUATION OF STUDENT EFFICIENCY

The grade for the discipline is determined by the average score of the student's current performance, which is converted into a 200-point system by the formula:

Score by a 200-point scale = (Average score by a 5-point scale *200)/5

and the results of the final control.

Criteria for assessing of the student's current success.

The current success of students is assessed by a four-point scale by making the following grades:

"5" - the student fully knows, understands and can use in practice the program material, also has extracurricular material related to this topic. The student consistently, logically, reasonably, unmistakably expounds the material, skillfully and correctly formulates conclusions and generalizations.

"4" - the student knows, understands and can use in practice the program material, the student consistently, logically, reasonably expounds the material making minor mistakes, formulates conclusions and generalizations.

"3" - the student knows and can use in practice the main part of the program material. The student inconsistently learns the material, making significant mistakes, vaguely formulates conclusions and generalizations.

"2" - the student does not possess the program material and therefore is not able to use it in practice, to generalize it and draw conclusions.

CHEMISTRY LABORATORY SAFETY RULES

One often forgets that chemical experiment is a potentially dangerous; a careless attitude often results in disastrous consequences. Therefore, extreme caution should be exercised at all time, especially when one handles chemical reactions that are exothermic or when dealing with toxic, reactive chemicals, carcinogens using any glassware.

You are expected to learn and adhere to the following general safety guidelines to ensure a safe laboratory environment both for yourself and people you are working with. Additional safety precautions will be announced in class prior to experiments if there is potential danger. Students who are failed to follow all the safety rules must leave the laboratory and obtain 0 points for the lesson.

PERSONAL PROTECTION

- Laboratory coats and caps provide an important barrier for your clothes and, more important, your skin from chemicals. The laboratory coat should fit comfortably, have long sleeves, and should be clean.
- Laboratory gloves are an essential part of safe laboratory practice and must be worn while handling chemicals.
- Closed toe shoes and long pants must be worn in the lab. Sandals and shorts are not allowed.
- The coats, backpacks, etc., should not be left on the lab benches and table. Beware that lab chemicals can destroy personal possessions.
- Eating, drinking, and smoking are strictly prohibited in the laboratory.
- The most common forms of eye protection include safety glasses (with side shields), goggles, and face shields. Prescription eyeglasses are acceptable provided that the lenses are impact resistant and they are equipped with side shields. Contact lenses are not allowed. Even when worn under the safety goggles, various fumes may accumulate under the lens and cause serious injuries or blindness.
- Long hair must be tied back when using open flames.
- Learn where the safety and first-aid equipment are located. This includes

fire extinguishers, fire blankets, and eye-wash stations.

- Always wash your hands before leaving the lab.
- Inform the teacher immediately in case of an accident.

PROPER HANDLING OF CHEMICALS AND EQUIPMENT

- Consider all chemicals to be hazardous unless you are instructed otherwise. Material Safety Data Sheets (MSDS) are available in lab for all chemicals in use. These will inform you of any hazards and precautions of which you should be aware.
- Know what chemicals you are use. Carefully read the label twice before taking anything from a bottle. Learn how to interpret hazardous materials labels.
- Never taste chemicals.
- No unauthorized experiments are to be performed. Every experimental procedure must be consulted with your teacher.
- Never directly smell the source of any vapor or gas. You should waft a small sample of scent air to your nose with cupped hand. Do not inhale these vapors but detect if the odor is observed.
- The excess of reagents is never to be returned to their bottles. If you take too much, dispose of the excess.
- Many common reagents, for example, alcohols and acetone, are highly flammable. Do not use them near working burner.
- Never leave the burners unattended. Turn them off whenever you leave your workstation. Be sure that the gas is shut off at the bench rack when you leave the lab.
- Never point a test tube or any vessel that you are heating at yourself or your neighbor - it may erupt like a geyser.
- Always pour acids into water. If you pour water into acid, the appearing exothermic reaction causes water transformation into steam with powerful acid splattering.
- Clean up all broken glassware immediately and dispose of it properly.

- Contact the stockroom for special bottle for mercury spills.

FIRST AID IN THE LABORATORY

THE OCCURRENCE OF AN ACCIDENT OF ANY KIND IN THE LABORATORY SHOULD BE REPORTED IMMEDIATELY TO YOUR TEACHER, EVEN IF IT SEEMS RELATIVELY MINOR!

Thermal burns. In the case of a burn, apply cold water and/or ice immediately to the burned area until the pain subsides. Wrap the burned area to protect from infection. It is best to avoid oils and ointments in first aid treatment since these frequently complicate the physician's job.

Chemical burns. Areas of the skin with which corrosive chemicals have come in contact should be immediately and thoroughly washed with soap and warm water. Acid or minor bromine burns may then be treated with 5% sodium carbonate solution. Alkali burns can be washed with 5% acetic acid solution or saturated boric acid solution. If the burns are minor, apply burn ointment; for treatment of more serious burns, see a physician. If chemicals, in particular corrosive or hot reagents, come in contact with the eyes, immediately flood the eyes with water from the nearest outlet. A specially designed eyewash fountain is useful if available in the laboratory. Do not touch the eye. The eyelid as well as the eyeball should be washed with water for several minutes. In all instances where sensitive eye tissue is involved in such an accident, consult an ophthalmologist as soon as possible.

Fire. Your first consideration is to remove yourself from any danger, not to extinguish the fire. If *it is possible to do so without endangering yourself*, turn off any burners and remove containers of flammable solvents from the immediate area to prevent the fire from spreading. For the most effective use of a fire extinguisher, direct its nozzle toward the base of the flames. If your clothing is on fire, DO NOT RUN; rapid movement will only fan the flames. Roll on the floor to smother the fire and to help keep the flames away from your head. Your neighbors can help to extinguish the flames by using fire blankets, laboratory coats, or other items that are immediately available. Do not hesitate to aid your neighbor if he or she is involved in such an emergency; a few seconds delay may result in serious injury. If burns are minor, apply a burn ointment. In the case of serious burns, do not apply any ointment; seek professional medical treatment at once.

Minor bleeding. Allow the blood to flow a few moments. Flush the wound thoroughly with water. Apply an antiseptic and bandage to the wound to prevent contamination. Minor cuts may be treated by ordinary first-aid procedures; seek professional medical attention for serious cuts. If severe bleeding indicates that an artery has been severed, attempt to stop the bleeding with compresses and pressure; a tourniquet should be applied only by those who have received first-aid training. Arrange for emergency room treatment at once. A person who is injured severely enough to require a physician's treatment should be accompanied to the doctor's office, or infirmary, even if he or she claims to be all right. Persons in shock, particularly after suffering burns, are often more seriously injured than they appear to be.

Toxic fumes. If there are complaints of a headache or dizziness in the laboratory in which the odors of such toxic gases are, you should go immediately to a fresh air outside.

Read and Agree with the Safety Rules

__________________________________ _________
Surname, first name Signature

Video materials for practical classes can be found at:
https://www.youtube.com/playlist?list=PL5MKnWeEf-HMCaGpFxdicRH4Ytf617mr0

LESSON 1

TOPIC: HETEROCYCLIC COMPOUNDS. THREE-, FOUR-MEMBERED HETEROCYCLIC COMPOUNDS WITH ONE HETEROATOM.

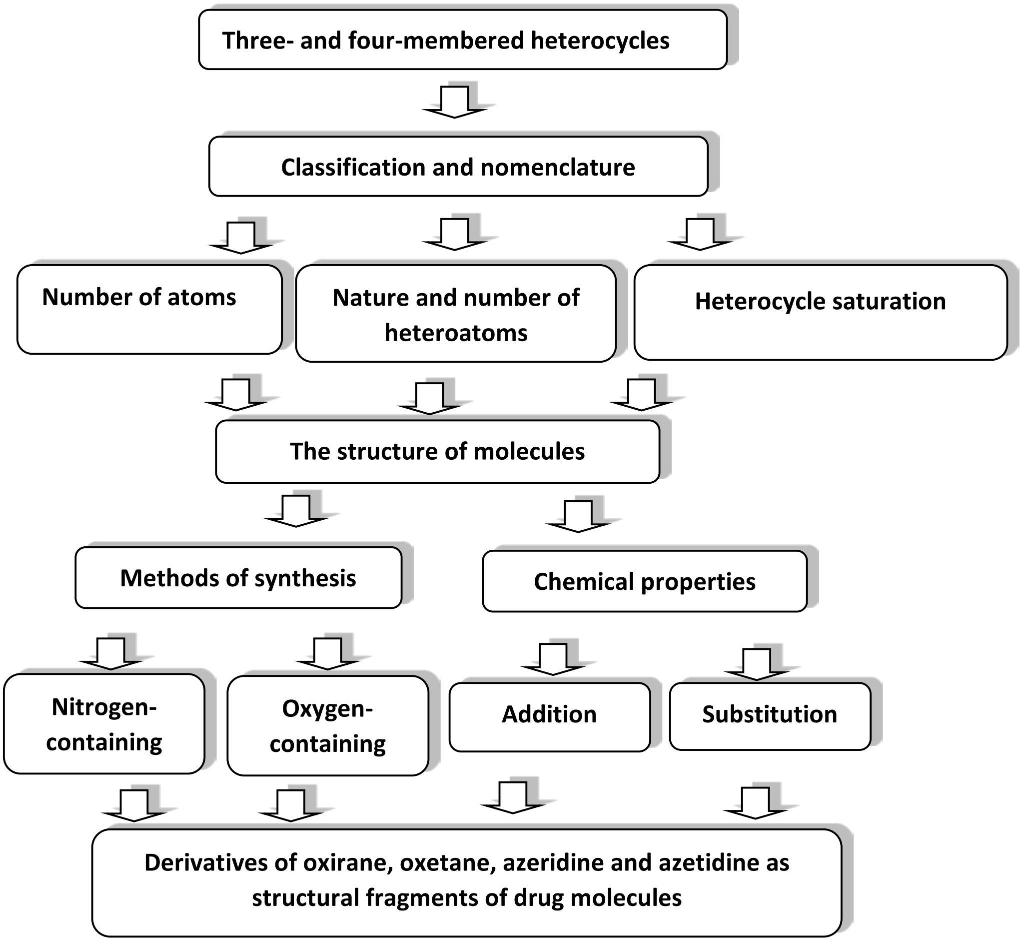
SUBJECT MOTIVATION*:* Heterocyclic compounds are one of the most important classes of organic compounds, which are both widespread in living objects and have been successfully used as medicines for more than a hundred years. Thus, heterocyclic compounds include nitrogenous nucleotide bases (adenine, guanine, cytosine, uracil, thymine), vitamins (thiamine, riboflavin, nicotinic acid and its derivatives, pyridoxine, tocopherols), a range of drugs (pyrazolone-5 derivatives, *β*-lactam antibiotics). Heterocyclic compounds also include most alkaloids - nitrogen-containing heterocyclic compounds of natural, mostly vegetable origin, which often have expressed biological activity (morphine, codeine, cocaine, caffeine). Features of the structure of heterocyclic compounds cause a significant variety of their structures and chemical properties.

OBJECTIVE: to study the basic principles of chemistry of heterocyclic compounds. To form practical skills in the synthesis, modification and identification of heterocyclic compounds.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Classification of heterocycles by cycle size, nature of the heteroatom, number of heteroatoms and degree of saturation.
2. Basic principles of nomenclature of heterocyclic compounds.
3. Acid-base properties.
4. Oxirane, aziridine, oxetane, azetidine. Structure, methods of synthesis and chemical properties.
5. Nucleophilic addition reactions (A_N) at the place of the cycle cleavage.
6. Reactions of aziridine and azetidine as a secondary amines.

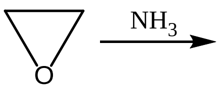
7. Epichlorohydrin. *β*-Propiolactone. Thiophosphamide. Benzotef. Azetidinone-2.



Tasks for self-control

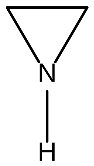
Sample of the answer:

The interaction of oxirane with ammonia yielded:



A. $CH_3-CH_2-O-NH_2$

B.



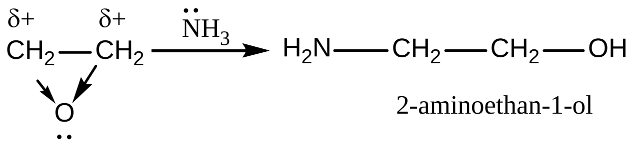
C. $CH_3-NH-CH_2-OH$

D. $H_2N-CH_2-O-CH_3$

E. $H_2N-CH_2-CH_2-OH$

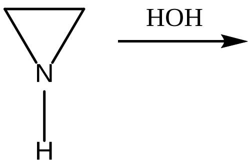
Explanation:

Chemically, oxirane is a very reactive compound. This is due to the angular and torsional tensions of the cycle, as well as the presence of polar bonds C – O. Under the action of nucleophilic reagents (:NH_3) cleavage of C – O bonds occures and attachment of the reagent molecule at the place of the cycle cleavage:



Correct answer is E.

Which compound is formed in the following reaction?

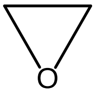


A. $CH_3—CH_2—NHOH$

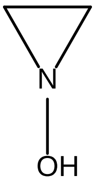
B. $H_2N—CH_2—CH_2—OH$

C. $CH_3—NH—CH_2—OH$

D.

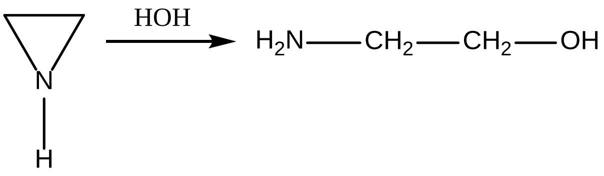


E.



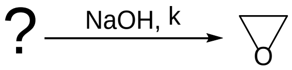
Explanation:

Besides properties of secondary amines, aziridine is characterized by possibility of the addition reactions that occur with the cycle opening. The aziridine cycle cleavage easily undergoes under the action of hydrogen halides, amines, ammonia, water, etc.



Correct answer is B.

№1 To obtain the heterocyclic compound in the laboratory, the organic compound was treated with a concentrated alkali solution to give oxirane.



Select the starting material.

A) $HOCH_2–CH_2–Cl$

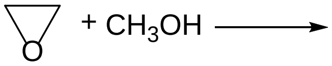
B) $HOCH_2–CH_2–CH_2–Cl$

C) $CH_2=CH_2$

D) $HOCH_2–CH_2–OH$

E) $CH_3–CH_3$

№ 2. By which of the following mechanisms does the reaction occur?



A) S_N;

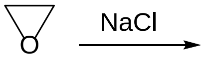
B) A_N;

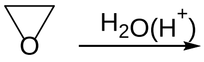
C) A_R;

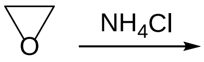
D) S_R;

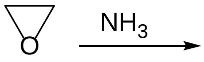
E) S_E.

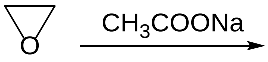
№ 3. Determine which of the following reactions are possible for oxirane: (more than one correct answer are possible)

A) 

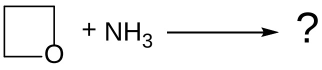
B) 

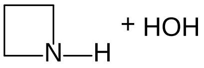
C) 

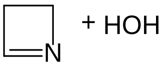
D) 

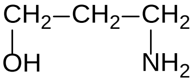
E) 

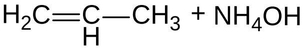
№ 4. Choose the correct option to continue the reaction:

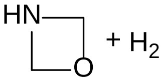


A) 

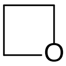
B) 

C) 
$\underset{OH}{CH_2}-CH_2-\underset{NH_2}{CH_2}$

D) 
$H_2C=\underset{H}{C}-CH_3 + NH_4OH$

E) 

№ 5. Which of the following reactions are characteristic for oxetane?



A) nucleophilic addition;

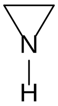
B) radical substitution;

C) nucleophilic substitution;

D) electrophilic addition;

E) electrophilic substitution.

№ 6. With which of these reagents does aziridine react with the opening of the cycle? (more than one correct answer are possiple)

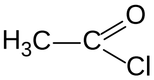


A) NH_3

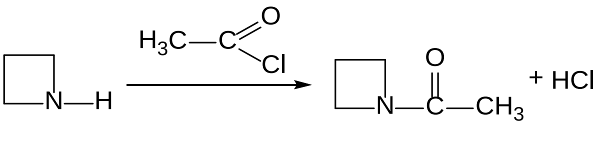
B) CH_3NH_2

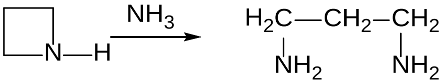
C) CH_3Cl

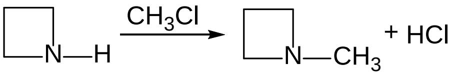
D) HCl(gas)

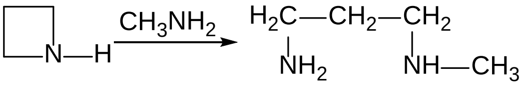
E) 

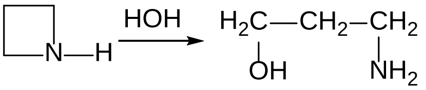
№ 7. Which of the following reactions indicate that azetidine is a secondary cyclic amine?

A) 

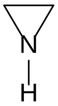
B) 

C) 

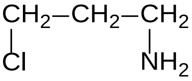
D) 

E) 

№ 8. Which of the following compounds forms aziridine as a result of the cyclization reaction?

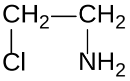


A) $CH_2{=}CH{-}CH_3$

B) 
$CH_2{-}CH_2{-}CH_2$ (Cl on the first CH_2, NH_2 on the last CH_2): $ClCH_2{-}CH_2{-}CH_2NH_2$

C) $CH_3{-}CHCl_2$

D) $CH_3{-}CH_2{-}CH_3$

E) 
$ClCH_2{-}CH_2NH_2$

№9. Oxetane, aziridine, azetidine are an example of three- and four-membered heterocycles and they belong to:

A) saturated heterocyclic compound;

B) unsaturated heterocyclic compound;

C) aromatic heterocyclic compound;

D) compound containing one heteroatom;

E) compound containing two heteroatoms.

LESSON 2

TOPIC: FIVE-MEMBERED HETEROCYCLIC COMPOUNDS WITH ONE HETEROATOM, FEATURES OF THEIR STRUCTURE AND CHEMICAL PROPERTIES.

SUBJECT MOTIVATION: Five-membered heterocyclic compounds with one heteroatom are widespread in nature. They are a part of biologically active compounds, some amino acids, that are involved in the protein's construction. Chlorophyll and heme molecules are based on a system of five-membered nitrogen-containing heterocycle.

OBJECTIVE: to consolidate knowledge of the laws of chemical behavior of aromatic five-membered heterocyclic compounds and their derivatives accordingly to their electronic structure.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Pyrrole, furan, thiophene. Nomenclature. Structure, methods of synthesis. Chemical properties.
2. Aromatic nature of the most important heterocyclic compounds.
3. Acidophobicity of pyrrole and furan.
4. Electrophilic substitution reactions (S_E). Features of nitration, sulfonation and halogenation reactions of acidophobic heterocycles.
5. Reduction and oxidation.
6. Mutual transformations of five-membered heterocycles (Yurie`s cycle reactions).
7. Specific chemical properties of pyrrole and furan.
8. *N*-acidity of pyrrole. Pyrrole salts.
9. Methods of identification of pyrrole, furan and thiophene.

PRACTICAL WORKS PERFORMED IN THE CLASS.

Protocol № 2

Date________________

Experiment 1. Detection of pyrrole vapors.

Put a few drops of pyrrole in a test tube and shake it. Take a piece of pine wood (for example toothpick) and moisten it with concentrated hydrochloric acid. Place the piece of pine wood in a test tube. Describe the observations.

Observation:

Conclusions:

LESSON 3

TOPIC: DERIVATIVES OF FIVE-MEMBERED HETEROCYCLES WITH ONE HETEROATOM (FURFURAL, INDOLE, INDOXYL, ISATIN, ETC.).

SUBJECT MOTIVATION: Five-membered heterocyclic compounds with one heteroatom are widespread in nature. They are a part of biologically active compounds, some amino acids are involved in the protein’s construction. The basis of chlorophyll and hemoglobin molecules is a system of five-membered nitrogen-containing heterocycle.

OBJECTIVE: to consolidate knowledge of the laws of chemical behavior of aromatic five-membered heterocyclic compounds and their derivatives in connection with the electronic structure. To develop skills and abilities to work with periodicals, to conduct organic syntheses and to identify the obtained compounds.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. The synthesis of furfural, chemical properties of furfural as an aromatic aldehyde; nitration of furfural; group of drugs based on 5-nitrofurfural.

2. Indole (benzo[*b*]pyrrole): structure, methods of synthesis, physical and chemical properties (acidic properties, acidophobicity, reduction, electrophilic substitution reactions (S_E)).

3. The most important derivatives of indole: polyvinylpyrrolidone, porphine (as a stable tetrapyrrole aromatic system), metalloporphins, heme, chlorophyll, vitamin B_{12}, indoxyl, indigo, isatin, tryptophan, serotonin, indigo carmine, *β*-indoleacetic acid. Extraction, chemical properties, identification, application.

PRACTICAL WORKS PERFORMED IN THE CLASS.

Protocol № 3

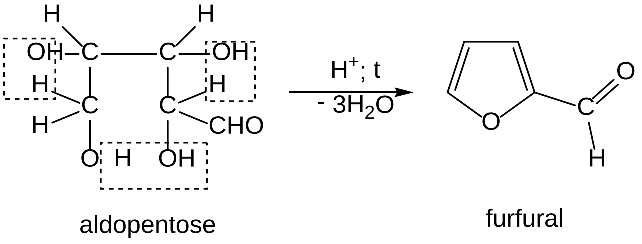
Date_______________

Experiment 1. **The method of furfural synthesis and its detection**

A. Placed in a test tube about 1 g of vegetable raw materials (sawdust, bran, sunflower husk, cherry gum or crushed corn cobs), add 2 ml of concentrated hydrochloric acid, 2 ml of water, 2-3 drops of 1% solution of iron(III) chloride (catalyst) and place the test tube in a water bath.

A strip of filter paper moistened with a mixture of aniline and glacial acetic acid (1:1) is then immersed in a test tube.

Reaction scheme:

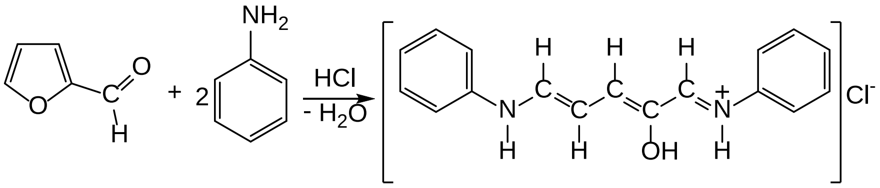


Observation:

Conclusions:

B. Place in a test tube 0.4 ml of freshly distilled aniline, 0.2 ml of concentrated hydrochloric acid, 2 ml of ethanol and 2 ml of freshly distilled furfural (obtained in experiment A) in 2 ml of ethanol. The mixture is heated on a water bath for 5 minutes.

Reaction scheme:

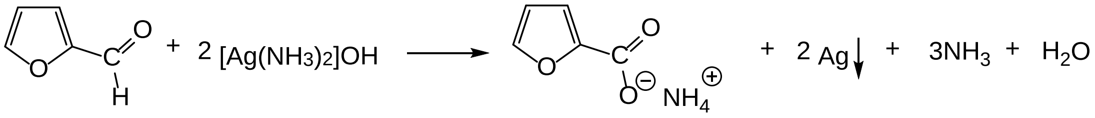


Observation:

Conclusions:

B. Mix 1 drop of furfural solution obtained in experiment A in a test tube, with 1 drop of Tollens reagent.

Reaction scheme:



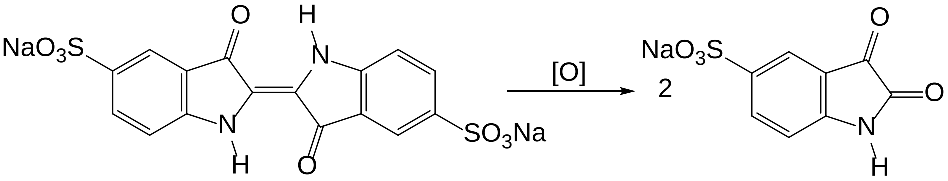
Observation:

Conclusions:

Experiment 2. Reactions with indigo carmine

A. Oxidation. Place in a test tube 0.5 ml of 0.5% solution of indigo carmine and 2-3 drops of concentrated nitric acid.

Reaction scheme:

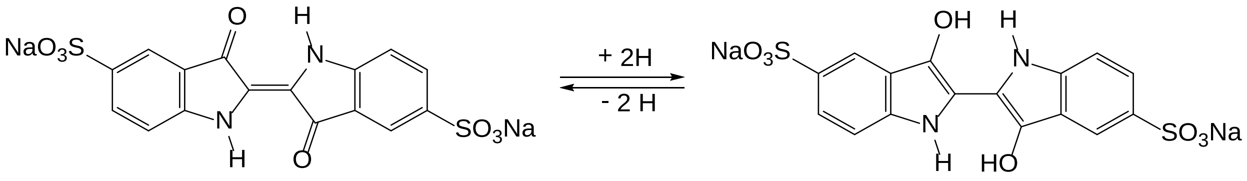


Observation:

Conclusions:

B. Reduction. Place in a test tube 2 drops of 0.5% solutions of indigo carmine and glucose. To the mixture add 1-2 drops of 5% sodium bicarbonate solution until the alkaline reaction medium and dilute with 5 drops of water. The resulting solution is carefully, without shaking, heated in a test tube. After changing the color from blue to light yellow, the tube is shaken vigorously.

Reaction scheme:

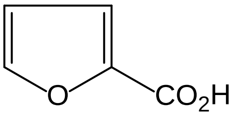


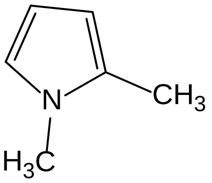
Observation:

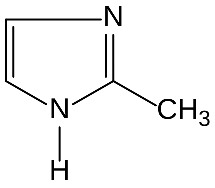
Conclusions:

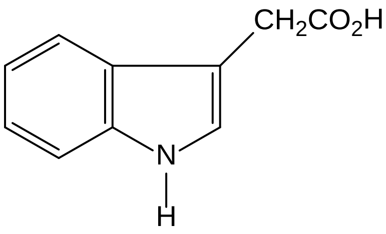
TASKS FOR SELF-CONTROL.

1. Name the following heteroaromatic compounds:









2. Compare the basicity of pyrrole and pyrrolidine. Explain the differences in properties.

3. Indicate at which the position does electrophilic substitution reaction undergo for the following heterocycles: furfural, indole, thiophene. Give the explanation.

LESSON 4

TOPIC: FIVE-MEMBERED HETEROCYCLIC COMPOUNDS WITH TWO HETEROATOMS.

SUBJECT MOTIVATION: Functionally substituted five-membered heterocyclic compounds with two heteroatoms, their hydrogenated analogues: essential amino acids, biogenic amines, alkaloids, are extremely common in nature and play an important role in the metabolism of animals and plants. Knowledge in the field of structure and chemical potential of five-membered heterocycles is necessary for formation of professional skills of the pharmacist, development of scientific creativity.

OBJECTIVE: To generalize and consolidate knowledge of the basic principles of electronic structure and chemistry of five-membered heterocycles with two heteroatoms and to develop student scientific creativity at performance of atypical tasks on the synthesis of functionally substituted heterocycles.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Azoles: pyrazole, imidazole, thiazole, oxazole, isoxazole. Nomenclature. Structure. Methods of synthesis. Chemical properties.
2. Nitrogen atoms of pyrrole and pyridine type.
3. Azole tautomerism of imidazole and pyrazole.
4. Acidic-basic properties. Electrophilic substitution reactions (S_E).
5. S_N reactions for thiazole.
6. Reduction reactions.
7. Pyrazolone-5 and its tautomerism.

8. Drugs based on pyrazolone-5: antipyrine, amidopyrine, analgin. Synthesis of antipyrine.

9. Histidine. Histamine. Benzimidazole. Dibazole. 2-Aminothiazole, methods of synthesis and chemical properties.

10. Thiazolidine - a structural fragment of penicillin antibiotics.

PRACTICAL WORKS PERFORMED IN THE CLASS.

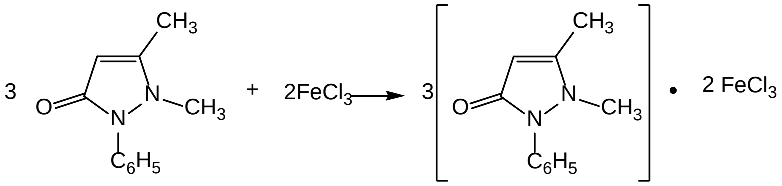
Protocol № 4

Date_______________

Experiment 1. **A qualitative reaction for antipyrine.**

A. Dissolve a few crystals of antipyrine in a test tube in few drops of water. To the resulting solution add 1 drop of 1% solution of iron(III) chloride.

The chemistry of the reaction*:*

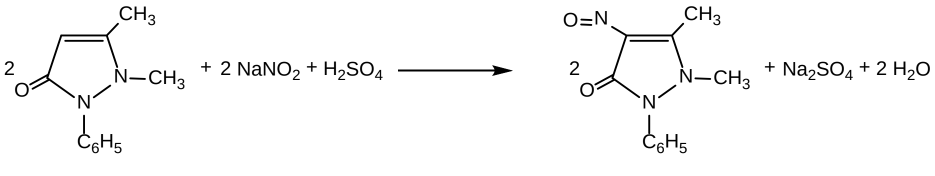


Observation:

Conclusions:

B. Dissolve a few crystals of antipyrine in a test tube in few drops of water. To the resulting solution add 1 drop of 10% sodium nitrite solution and 3 drops of diluted sulfuric acid.

The chemistry of the reaction:



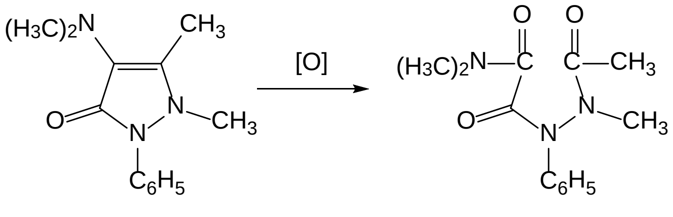
Observation:

Conclusions:

Experiment 2. **A qualitative reaction for amidopyrine**

A. Dissolve a few crystals of amidopyrine in a test tube in few drops of water. To the resulting solution add 1 drop of 1% solution of iron(III) chloride. After the appearance of blue, fast-disappearing color in the test tube add 3 more drops of a solution of iron(III) chloride. To the formed flaky brown precipitate add 2 drops of diluted hydrochloric acid.

The chemistry of the reaction:

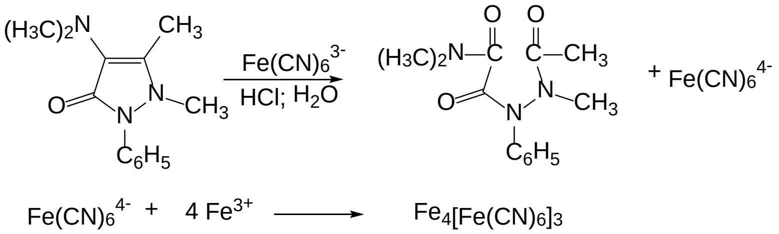


Observation:

Conclusions:

B. Dissolve a few crystals of amidopyrine in a test tube in few drops of water. To the resulting solution add 10 drops of freshly prepared solution of potassium hexacyanoferrate(III) $K_3Fe(CN)_6$ and 1 drop of 1% solution of iron(III) chloride.

Reaction scheme:



Observation:

Conclusions:

TASKS FOR SELF-CONTROL.

1. Write the structural formulas of the following compounds: a) 1,2-diazole; b) 1,3-thiazole; c) 1,2-oxazole; d) 2-amino-4-methylthiazole; e) 2,5-diethyloxazole.

2. Indicate which of the following heterocyclic compounds have aromaticity: a) pyrazole: b) thiazole; c) pyrazolidine; d) thiazoline; e) isoxazole. Determine the type of hybridization of heteroatoms in molecules.

3. Write reaction schemes that confirm the amphoteric nature of pyrazole and imidazole.

4. Write the equation of possible reactions of pyrazole and imidazole with the following reagents: 1) HCl; 2) KOH; 3) CH_3I; 4) CH_3COCl; 5) conc. HNO_3, t°; 6) Br_2 (H_2O); 7) H_2O_2. Name the products.

5. Compare the acidic and basic properties of imidazole and benzimidazole. Explain the answer. Carry out the scheme of tautomeric transformations of imidazole.

LESSON 5

TOPIC: FINAL LESSON ON "THREE-, FOUR- AND FIVE-MEMBERED HETEROCYCLIC COMPOUNDS, THEIR SUBSTITUTED AND CONDENSED DERIVATIVES".

SUBJECT MOTIVATION: Deep knowledge in the field of structure and chemical potential of three, four and five-membered heterocycles, understanding of organic synthesis based on them is a solid foundation for the formation of future knowledge in pharmaceutical chemistry and chemistry of natural compounds necessary for the formation of professional skills.

OBJECTIVE: To generalize and to consolidate knowledge of the basic principles of electronic structure and chemistry of three-, four- and five-membered heterocyclic compounds, their substituted and condensed derivatives.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

To know: the structure, methods of synthesis, reactivity of three-, four- and five-membered heterocycles, the concept of acidophobicity, pyridine and pyrrole nitrogen atoms, azole tautomerism, electrophilic substitution reactions, reduction and oxidation, acid-base properties, acid-base properties qualitative definition of heterocycles, their importance for pharmacy.

1. Three-, four-membered heterocyclic compounds with one heteroatom: oxirane, azeridine, oxatedine, azatedine.

2. Five-membered heterocyclic compounds with one heteroatom: pyrrole, thiophene, furan. Nomenclature.

3. Aromaticity of heterocycles.

4. Acidophobicity of furan and pyrrole.

5. Acid properties of pyrrole.

6. Similarity of furan reactivity with reacrivity of dienes.

7. Functional substituted derivatives of furan, thiophene. Their usage in medicine.

8. Indole: a) structural analysis; b) methods of synthesis; c) the chemistry of indole; d) alkaloids and neuromediators that are derivatives of indole (tryptamine, serotonin), their physiological activity.

10. Five-membered heterocycles with two heteroatoms: pyrazole, imidazole, oxazole, thiazole, benzimidazole. Nomenclature. Methods of synthesis.

11. Aromaticity of heterocycles with two heteroatoms.

12. Tautomerism of pyrazole, 3(5)-oxypyrazole, imidazole.

13. Acidity of pyrazole, imidazole.

14. The basicity of pyrazole, imidazole, thiazole, oxazole.

15. Synthesis of pharmaceuticals.

16. Hydrogenation of heterocycles.

LESSON 6

TOPIC: SIX-MEMBERED HETEROCYCLIC COMPOUNDS WITH ONE HETEROATOM. PYRIDINE, ITS SUBSTITUTED AND CONDENSED DERIVATIVES. NUCLEOPHILIC SUBSTITUTION REACTION IN THE AROMATIC SYSTEM.

SUBJECT MOTIVATION: Six-membered heterocycles with one heteroatom are a part of biologically important natural and synthetic compounds that have a pronounced effect on the living organism and participate in metabolic processes. The main number of organic drugs refers to derivatives of heterocycles.

OBJECTIVE: To form students' knowledge about the structure and chemical properties of six-membered heterocyclic compounds with one heteroatom, to expand students research skills by teaching logical thinking in solving atypical problems of functional analysis of pharmaceuticals.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Nomenclature of six-membered heterocycles.
2. Aromaticity of azines.
3. Chemical properties of pyridine and its derivatives.
4. Methods of synthesis of six-membered heterocycles.
5. The basicity of azines, γ-pyrone.
6. Participation of pyridine and its derivatives in redox reactions.
7. Lactime-lactam tautomerism.
8. Functional analysis of pharmaceuticals (pyridoxine, vitamin B_6). Pyridinecarboxylic acids and their functional derivatives. Nicotinic acid. Nicotinamide (vitamin PP). Cordiamine. Isonicotinic acid. Isoniazid. Ftivazid.

PRACTICAL WORKS PERFORMED IN THE CLASS.

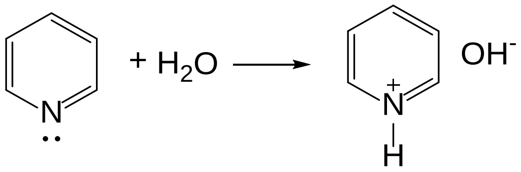
Protocol № 6

Date_______________

Experiment 1 The basic properties of pyridine.

A. Place 2 drops of pyridine and 10 drops of water in a test tube. Using a glass rod apply a drop of the resulting solution on a strip of universal indicator paper.

The chemistry of the reaction:

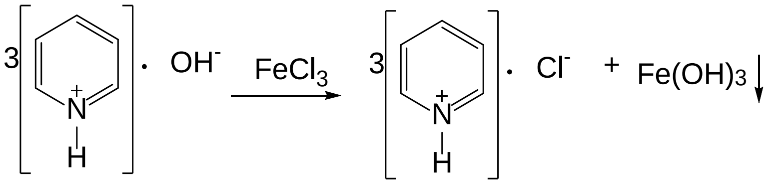


Observation:

Conclusions:

B. Place 2 drops of an aqueous solution of pyridine obtained in experiment A in a test tube, and 1 drop of an iron(III) chloride solution.

Reaction scheme:

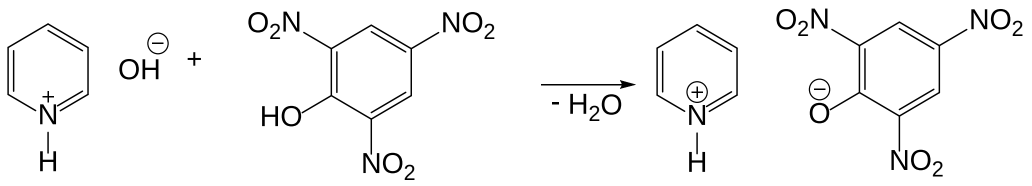


Observation:

Conclusions:

B. Place 1 drop of an aqueous solution of pyridine obtained in experiment A in a test tube and 2 drops of a saturated aqueous solution of picric acid.

Reaction scheme:



Observation:

Conclusions:

TASKS FOR SELF-CONTROL.

1. To which class of organic compounds does pyridoxal belong?

2. Specify reagents that interact with pyridoxal: a) only with the OH group in the side chain b) only with the OH group connected directed with the cycle.

3. Specify the reaction centers of pyridoxal, interacting with: a) $Ag(NH_3)_2OH$ b) CH_3COCl (cat. $AlCl_3$)

4. Specify the type of interaction of pyridoxal with: a) CH_3I cat. b) CH_3I without catalyst.

LESSON 7

TOPIC: OXYGEN-CONTAINING AND SULFUR-CONTAINING SIX-MEMBERED HETEROCYCLIC COMPOUNDS WITH ONE HETEROATOM. SIX-MEMBERED HETEROCYCLIC COMPOUNDS WITH TWO HETEROATOMS: STRUCTURE AND PROPERTIES.

SUBJECT MOTIVATION: Oxygen-containing and sulfur-containing six-membered heterocyclic compounds are a part of biologically important natural and synthetic compounds that have an expressed effect on the living organism and participate in metabolic processes. Six-membered heterocycles with two heteroatoms are a part of biologically important natural and synthetic compounds that have an expressed effect on the living organism and participate in metabolic processes. The main number of organic drugs refers to derivatives of heterocycles.

OBJECTIVE: To form students' knowledge about the structure and chemical properties of oxygen-containing and sulfur-containing six-membered heterocyclic compounds with one heteroatom, as well as six-membered heterocyclic compounds with two heteroatoms. To expand students research skills by teaching logical analysis in solving functional problems.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Features of the α- and γ-pyran structure.
2. Structure and chemical properties of α- and γ-pyrone.
3. Pyrylium salts.
4. Benzopyrones: coumarin, chromone, flavone, isoflavone. Structure, chemical properties.
5. Flavonoids: luteolin, quercetin, rutin. Tocopherol (vitamin E).
6. Features of structure and chemical formula of α- and γ-thiopyran.
7. Diazines: pyrimidine, pyrazine, pyridazine. Nomenclature, structure, methods of synthesis, aromaticity.
8. Chemical properties of diazines. Basicity.
9. Nucleophilic substitution reactions (S_N).
10. Features of electrophilic substitution reactions (S_E).
11. Hydroxy- and amino derivatives of pyrimidine.
12. Barbituric acid. Synthesis, keto-enol and lactam-lactim tautomerism, acidic properties. Barbital. Phenobarbital.
13. Pyrimidine bases: uracil, thymine, cytosine. 5-Fluorouracil, thiamine (vitamin B_1).
14. Piperazine. Basic properties.
15. Oxazine. Phenoxazine. Thiazine. Phenothiazine.

TASKS FOR SELF-CONTROL

1. Write the structural formulas of the following compounds: 1,2-diazine; 2,4,6-trihydroxypyrimidine; pyrazine *N*-oxide; piperazine; uracil; thymine; cytosine; dibenzo[*b,e*]-4*H*-1,4-thiazine.

2. Write schemes of successive chemical transformations that allow to obtain 3,6-dimethylpyridazine from hexadione-2,5 and hydrazine; pyrimidine from malonic ether and urea; pyrazine from ethylenediamine and glyoxal. Name all intermediate products.

3. Describe the electronic structure of diazine. Explain why diazine, despite having two basic centers, forms salts with only one equivalent of acid. Write the reaction equation.

4. Place 1,2-, 1,3- and 1,4 diazines in a descending order, if pK_{BH+} in water (20°C) is: pyridazine - 2.33; pyrimidine - 1.3; pyrazine - 0.6. Explain the answer.

5. Compare the reactivity of pyrimidine and pyridine in electrophilic and nucleophilic substitution reactions. Explain the differences. Write the corresponding reaction equations.

6. Give the scheme of barbituric acid synthesis from malonic ester and urea.

LESSON 8

TOPIC: CONDENSED HETEROCYCLIC SYSTEMS. ALKALOIDS.

SUBJECT MOTIVATION: Purine is one of the most important condensed heterocycle systems. It should be considered the structural basis of many natural compounds. Purine derivatives - adenine and guanine – are a part of nucleic acids. They are carriers of genetic information of living organisms. Alkaloids are organic nitrogen-containing compounds of natural origin, many of which are widely used as medicines due to their high biological activity.

OBJECTIVE: To form knowledge about the peculiarities of the structure and chemical properties of condensed heterocyclic compounds. To develop skills to perform basic reactions to identify a number of derivatives of condensed heterocyclic systems.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Purine: nomenclature, structure, aromaticity. Azole tautomerism. Amphoteric character.

2. Oxopurines: hypoxanthine, xanthine, uric acid. Lactam-lactim tautomerism.

3. Acidic properties of uric acid, its salts (urates). Oxidation (murexide test).

4. Methyl derivatives of xanthine: caffeine, theophylline, theobromine. Acid-base properties. Identification reactions.

5. Aminopurines (purine bases): adenine, guanine.

6. Pteridine: structure, properties, derivatives.

7. Folic acid (vitamin B_9).

8. Alloxazine and isoalloxazine. Structure and attitude to reduction reactions.

9. Riboflavin (vitamin B_2).

10. Describe the concept of "alkaloids". Classify alkaloids by structure. Give the main properties of alkaloids and explain their ability to form salts.

11. Analyze the functions of the following alkaloids: nicotine, quinine, cocaine, papaverine, morphine, codeine, atropine, reserpine, lysergic acid. Indicate their most characteristic chemical properties.

a. perform a functional analysis and give a pharmacological characteristic of drugs that are purine derivatives (mercaptopurine, butylmercaptopurine).

b. perform a functional analysis of riboflavin (vitamin B_2) and folic acid. Indicate their value for biochemical processes.

c. perform a functional analysis of phenazepam. Give the main pharmacological characteristics of diazepines.

PRACTICAL WORKS PERFORMED IN THE CLASS.

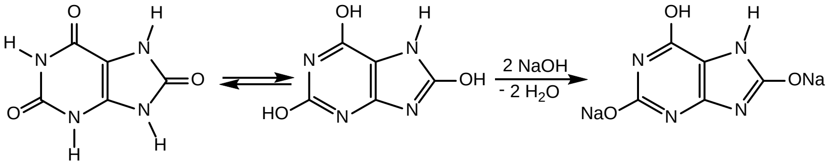
Protocol № 8

Date_______________

1. The solubility of uric acid and its sodium salt in water.

In a test tube place a small spatula of uric acid and shaking add 10 drops of water. To the resulting suspension add 1 drop of 10% sodium hydroxide solution. To the resulting solution add 1 drop of saturated ammonium chloride solution.

The chemistry of the reaction:



lactam form

uric acid (2,6,8-trioxopurine)

lactim form

disodium salt of uric acid

Observation:

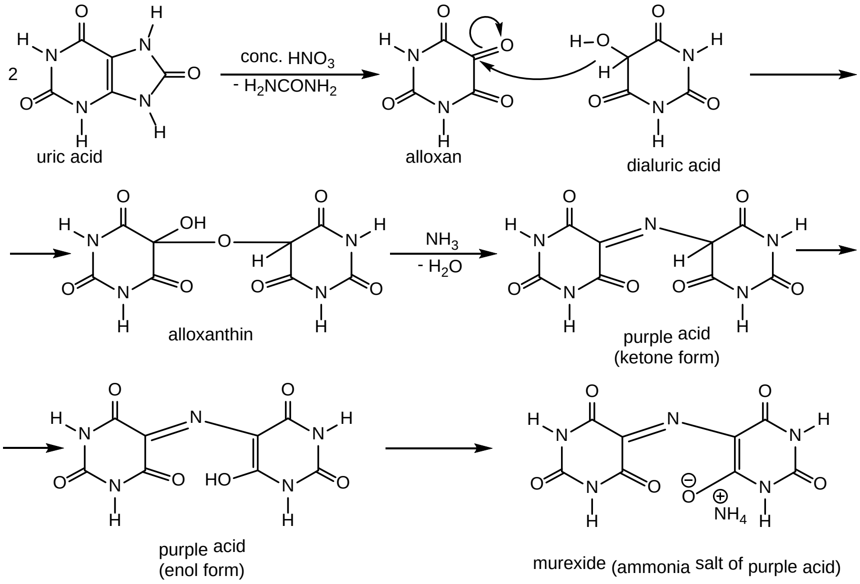
Conclusions:

Experiment 2. **The identification of the uric acid (The murexide test).**

THE EXPERIMENT IS PERFORMED IN THE FUME HOOD!

A few crystals of uric acid and 3-4 drops of concentrated nitric acid are placed in a porcelain cup. The resulting mixture should be carefully evaporated until dryness over a burner flame. After residue cooled and moistened with 1-2 drops of 10% ammonia solution the pink-red colour would appear.

The chemistry of the reaction:



Observation:

Conclusions:

TASKS FOR SELF-CONTROL.

1. Write the structural formulas of the following compounds: benzo[*b*]pyridine; benzo[*c*]pyridine; 8-hydroxyquinoline.

2. Using the Skraup synthesis, write schemes for the synthesis of: 8-hydroxyquinoline; 6-methoxy-8-nitroquinoline; 8-hydroxy-5-nitroquinoline.

3. Place in a row to reduce the basicity of condensed azines, if pK_{BH+} in water (20°C) is: pyridine - 5.25; quinoline - 4.94; isoquinoline - 5.42; acridine - 1.60. Explain what factors affect the basicity of these compounds.

4. Does 8-hydroxyquinoline have an amphoteric character? Write the reaction schemes of 8-hydroxyquinoline with a solution of sulfuric acid, salts of copper(II) and iron(III). Name the products and indicate their usage.

5. Using the example of nitration and sulfonation reactions, explain the rules of orientation in quinoline and isoquinoline cycle.

6. Explain why in the molecule of 9-chlorocridine halogen atom is mobile and can easily be replaced.

7. Write a scheme for the synthesis of phenothiazine from benzene and other necessary reagents. Name intermediates.

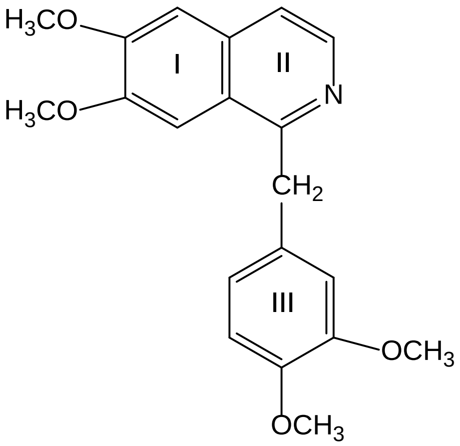
8. Explain why uric acid is dibasic and not tribasic. Write schemes for the synthesis of acidic and medium salts.

9. Describe the structure and properties of azepine and diazepine.

10. Write the structural formulas of the most important alkaloids of the pyridine, piperidine, quinoline, isoquinoline, morphinan (phenanthreneisoquinoline), purine, tropane and indole groups.

11. Write a diagram of the interaction of nicotine with hydrochloric acid. Name the product.

Tasks for self-control



Papaverine is an antispasmodic drug

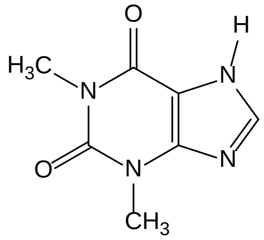
1. Indicate in the papaverine molecule the types of cycles I, II, III (aromatic carbocycle, non-aromatic carbocycle, aromatic heterocycle, non-aromatic heterocycle).

2. What are the electronic effects of the nitrogen and oxygen atoms? (+I, -I, +M, -M).

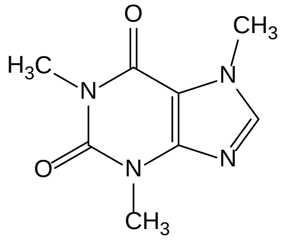
3. To which class of organic compounds does papaverine belong? (primary amine, secondary amine, tertiary amine, ether, ester).

5. Determine the reactivity of each of the cyclic fragments of the papaverine molecule in the reactions of electrophilic and nucleophilic substitution.

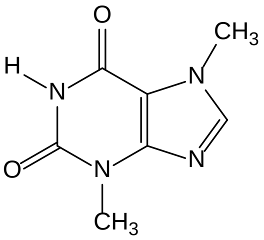
Compounds for functional analysis



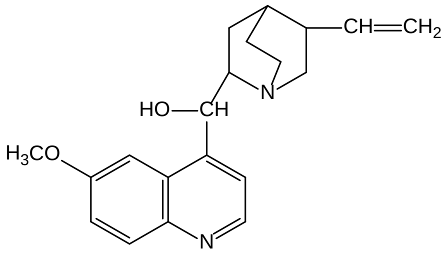
Theophylline



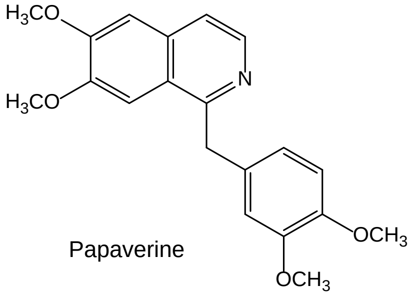
Caffeine



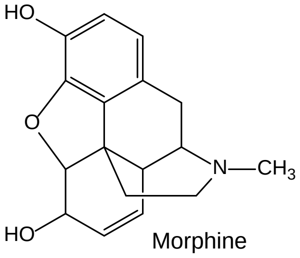
Theobromine



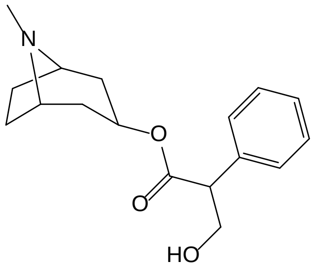
Quinine



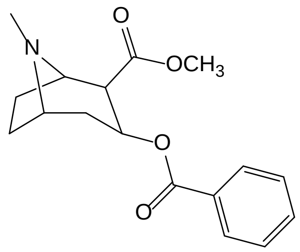
Papaverine



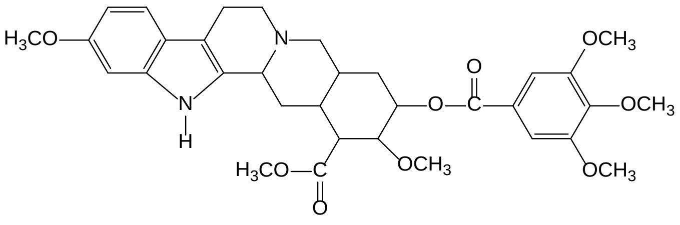
Morphine



Atropine



Cocaine



Reserpine

LESSON 9

TOPIC: FINAL LESSON ON "SIX-MEMBERED HETEROCYCLIC COMPOUNDS, THEIR SUBSTITUTED AND CONDENSED DERIVATIVES".

SUBJECT MOTIVATION: Condensed heterocycle systems, the most important of which is purine, should be considered as the structural basis of many natural compounds. Purine derivatives - adenine and guanine – are a part of nucleic acids - carriers of genetic information of living organisms. Alkaloids are organic nitrogen-containing compounds of plant origin, many of which are widely used as medicines due to their high biological activity.

OBJECTIVE: To generalize and structure knowledge about methods of synthesis, structure and chemical properties of six-membered and condensed heterocyclic systems.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Six-membered heterocycles with a nitrogen atom: pyridine. Nicotinamide (vitamin PP) as a component of redox pyridine coenzymes. Pyridoxine and molecular forms of vitamin B_6.

2. Six-membered heterocycles with two nitrogen atoms. Diazine: pyrimidine, pyrazine, pyridazine. Nitrogen bases are pyrimidine derivatives (uracil, cytosine, thymine).

3. Pyrimidine derivatives as drugs: 5-fluorouracil, potassium orotate. Barbituric acid: barbiturates as hypnotics and antiepileptics (phenobarbital, veronal).

4. Six-membered heterocycles with different heteroatoms. Phenothiazines (aminazine, etc.) as psychotropic (neuroleptic) drugs.

5. Seven-membered heterocycles with two heteroatoms. Diazepine: Benzo-1,4-diazepine as the most common tranquilizer and anxiolytic.

6. Purine and its derivatives. Amino derivatives of purine (adenine, guanine), their tautomeric forms; biochemical significance in the formation of nucleotides and coenzymes.

7. Hydroxy derivatives of purine: hypoxanthine, xanthine, uric acid. Methylated derivatives of xanthine (caffeine, theophylline, theobromine) as physiologically active compounds with activity on the central nervous and cardiovascular systems.

8. Synthesis and chemical properties of drugs derived from pteridine.

9. The biological role of folic acid (vitamin Bc).

10. Alloxazine and isoalloxazine (flavin).

11. Biological role of riboflavin (vitamin B_2).

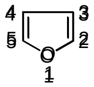
12. Classification of alkaloids.

13. Describe the methods of alkaloids isolating from plant materials.

14. Perform a functional analysis of alkaloids of the pyridine, quinoline, isoquinoline, morphinan and tropane.

TEST TASKS FOR PREPARATION FOR THE FINAL LESSON BY THE TOPIC «SIX-MEMBERED HETEROCYCLIC COMPOUNDS, THEIR SUBSTITUTED AND CONDENSED DERIVATIVE»

1. Furan - a five-membered heterocycle, which is a part of many drugs. It has the following structure:



Indicate the most probable position for the electrophilic attack.

A. 1

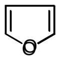
B. 2

C. 3

D. 1,2

E. 1,3

2. Specify the type and sign of the electronic effects of the oxygen atom in the furan molecule:



A. -I

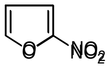
B. + I

C. -M

D. + M

E. -I; + M

3. Specify the most acceptable reagent for the synthesis of 2-nitrofuran:



A. HNO_3 (diluted)

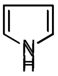
B. HNO_3 (conc.)

C. CH_3COONO_2

D. HNO_3; H_2SO_4

E. HNO_2

4. Indicate the main reason why pyrrole can't be nitrated by conc. HNO_3



A. Cationic polymerization in acidic environment.

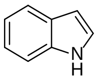
B. Insufficiently high π-electron density on C-atoms.

C. Insufficient electrophilicity of the reagent.

D. Salt formation with HNO_3.

E. Weak basicity of pyrrole.

5. Specify the type and sign of the electronic effects of the nitrogen atom in indole molecule.



A. -I

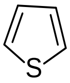
B. +I

C. -I; +M

D. -I; -M

E. +I; +M

6. Choose the most correct name for the product of complete hydrogenation of thiophene.



A. 2,3-Dihydrothiophene

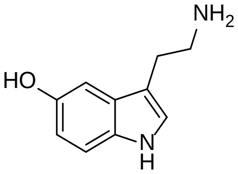
B. 1,2-Dihydrothiophene

C. 3,4-Dihydrothiophene

D. 2,3,4,5-Tetrahydrothiophene

E. 1,2,3,4,5-Pentahydrothiophene

7. Serotonin - a biogenic amine involved in the transmission of nerve impulses, has the following structure:



Select reagents that can be used for qualitative detection of phenolic hydroxyl and amino groups.

A. $FeCl_3$; $NaNO_3$

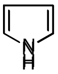
B. $FeCl_3$; HNO_2

C. $AgNO_3$; Br_2

D. $K_2Cr_2O_7$; I_2

E. $FeCl_3$; $AgNO_3$

8. Specify the reagent that can be used for sulfonation of pyrrole:



A. H_2SO_4 (conc.)

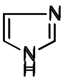
B. H_2SO_4 (diluted)

C. Oleum

D. H_2SO_4; HNO_3

E. Pyridine sulfotrioxide

9. Imidazole - a heterocycle that underlies such drugs as naftizin, metronidazole, etimizole and others.



Specify the electronic effects of the pyrrole atom of Nitrogen.

A. +I; +M

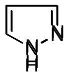
B. -I; -M

C. -I; +M

D. -M

E. +M

10. Pyrazole - a heterocycle that is part of antipyrine, amidopyrine, analgin, butadione, etc.



Specify the electronic effects of the pyridine atom of Nitrogen.

A. +I; -M

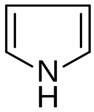
B. -I; +M

C. -I; +M

D. +I; +M

E. -I

11. Pyrrole is a heterocycle that is part of the heme, chlorophyll.



Specify the product of the interaction of pyrrole with HNO_3.

A. 3-Nitropyrole

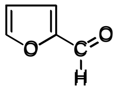
B. Pyrrole nitrate

C. 2-Nitropyrole

D. A mixture of polymerization products

E. 2,5-Dinitropyrrole

12. Furfural is the starting product for the synthesis of furacillin, furazolidone, furadonin.



Choose a reagent that can be used to obtain its semicarbazone.

A. H_2-NH-C(S)-NH

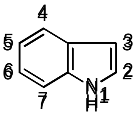
B. H_2 N-OH

C. $H_2NC_6H_5$

D. H_2N-NH-C(O)-NH

E. H_2N-NH_2

13. Indole is an aromatic heterocycle, which is a part of many natural compounds and drugs:



Indicate the most probable position at which the S_E reactions will take place.

A. 2

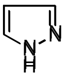
B. 3

C. 4

D. 5

E. 6

14. Pyrazole - an aromatic heterocycle with amphoteric properties



Indicate the most probable product of the interaction of pyrazole with conc. HNO_3 when heated.

A. 3-Nitropyrazole

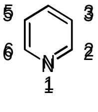
B. Pyrazole nitrate

C. 4-Nitropyrazole

D. 5-Nitropyrazole

E. 3,5-Dinitropyrazole

15. Pyridine - aromatic heterocycle with weak basic properties undergo electrophilic and nucleophilic reactions.



Specify the compounds formed by the interaction of pyridine with SO_3.

A. Pyridine sulfotrioxide

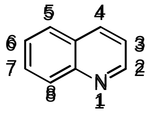
B. 2-Sulfopyridine

C. 3-Sulfopyridine

D. 4-Sulfopyridine

E. 3,5-Disulfopyridine

16. Quinoline is a heterocycle that underlies such drugs as quinine, quinazole, 5-nitrooxyquinoline, enteroseptol and others.



Indicate the most probable product of the interaction of quinoline with $NaNH_2$.

A. 5-aminoquinoline

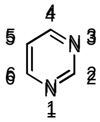
B. 3-aminoquinoline

C. 2-aminoquinoline

D. 6-aminoquinoline

E. 8-aminoquinoline

17. Pyrimidine (1,3-Diazine) is a heterocycle that is part of the nitrogenous bases of DNA, a number of drugs:



Predict the reaction product of pyrimidine with H_2SO_4.

A. Pyrimidinyl dihydrosulfate

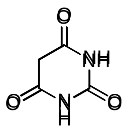
B. Pyrimidinyl sulfate

C. 2-Sulfopyrimidine

D. 4-Sulfopyrimidine

E. 5-Sulfopyrimidine

18. Barbituric acid is the basis of many drugs with hypnotic and anticonvulsant activity:



Specify the types of tautomerism that are characteristic for barbituric acid.

A. lactim-lactam, azole.

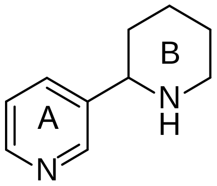
B. lactim-lactam, keto-enol.

C. keto-enol, amino-imine.

D. oxo-oxy, azole.

E. lactim-lactam, thion-thiol.

19. Anabasin is an alkaloid contained in anabasis, tobacco. It used as a strong insecticide.



Specify the heterocycles that contain anabasine.

A. Pyridine and pyrimidine.

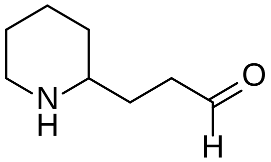
B. Pyridine and piperidine.

C. Pyrazine and pyrrolidine.

D. Pyridine and pyrrole.

E. Pyrimidine and piperidine.

20. Pelletierine is an alkaloid contained in the bark of pomegranate. It is used as an anthelmintic.



Identify the functional groups that are present in pelletierine.

A. Tertiary amino group, ketone group.

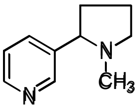
B. Secondary amino group, ketone group.

C. Tertiary amino group, aldehyde group.

D. Secondary amino group, aldehyde group.

E. Primary amino group, aldehyde group.

21. Nicotine is a tobacco alkaloid, a strong poison. It is used as an insecticide.



Indicate which compound is formed during the oxidation of nicotine by $KMnO_4$.

A. α-Pyridinecarboxylic acid.

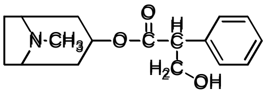
B. β-Pyridinecarboxylic acid.

C. γ-Pyridinecarboxylic acid.

D. Pyrimidinedicarboxylic acid.

E. Benzoic acid.

23. Atropine is an alkaloid of belladonna and datura is used to dilate the pupil in the study of the fundus.



Specify the reagent with which you can prove the presence of the primary alcohol group.

A. HNO_3

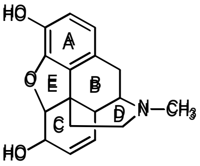
B. H_2SO_4

C. $FeCl_3$

D. $Ag(NH_3)_2OH$

E. $K_2Cr_2O_7\ (H^+)$

24. Morphine is one of the alkaloids of opium. It is used as a narcotic analgesic, causes a morphine addiction – morphinism.



Indicate the presence of which cycles allows you to determine morphine as isoquinoline derivatives.

A. Rings B and D.

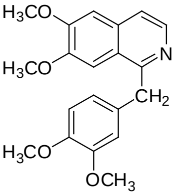
B. Rings A and B.

C. Rings C and D.

D. Rings B and C.

E. Rings C and E.

25. Papaverine is an alkaloid of opium. It is used as an antispasmodic.



Predict the presence of the basic properties of papaverine.

A. The basic properties are missing.

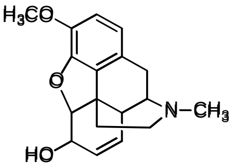
B. Weak basic properties are due to the N-atom.

C. Weak basic properties are due to the O-atoms.

D. Strong basic properties are due to the N-atom.

E. Strong basic properties are due to the O-atoms.

26. Codeine is one of the opium alkaloids. It is used as an antitussive:



Specify a reagent that allows you to distinguish codeine from its closest analogue of morphine.

A. $FeCl_3$

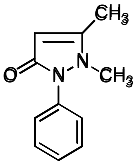
B. Br_2

C. $KMnO_4$

D. $K_2Cr_2O_7$

E. Phenyldiazonium chloride.

27. Antipyrine is an antipyretic and analgesic, having the structure:



Choose the most correct systematic name for antipyrine.

A. 1-Phenyl-2-oxo-4,5-dimethylpyrazole.

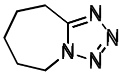
B. 1-Phenyl-2,3-dimethylpyrazolone-5.

C. 1,5-dimethyl-2-phenylpyrazolone-3.

D. 1-Phenyl-2,3-dimethyl-5-hydroxypyrazolone.

E. 1-Phenyl-4,5-dimethylpyrazolone-2.

28. Corazol is a CNS stimulant, that has the structure:



Specify the heterocycle that is present in the corazol.

A. imidazole.

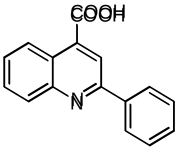
B. tetrazole.

C. triazole.

D. pyrazole.

E. tetrazine.

29. Cinchophen is a drug used in gout, it has the structure:



Specify the heterocycle that is present in the structure.

A. Pyrimidine.

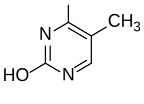
B. Isoquinoline.

C. Indole.

D. Quinoline.

E. Benzindole.

30. Methyluracil is a drug used in case of leukopenia, as well as a wound healing agent:



Specify the heterocycle that is present in the structure.

A. Pyrimidine.

B. Pyrazines.

C. Piperazine.

D. Pyridazine.

E. Piperidine.

31. Mercazolyl is an antithyroid drug of the following structure:

Choose the most accurate systematic name for mercazolyl.

A. 1-methyl-2-mercaptopyrazole.

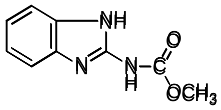
B. 1-methyl-2-mercaptoimidazole.

C. 1-methyl-2-thiopyrrole.

D. 2-mercapto-3-methylimidazole.

E. 1-methyl-2-thiopyrazole.

32. Medamine is an anthelmintic drug that has the following structure:



Select a reagent that with medamine give a product of 2-aminobenzimidazole.

A. $FeCl_3$

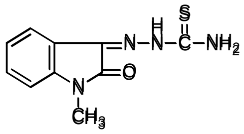
B. bromine water.

C. NaOH

D. $AgNO_3$

E. $CuSO_4$

33. Methisazone is an antitumor drug of the following structure:



Select compounds from which it can be synthesized in one step.

A. *N*-methylizatin and thiosemicarbazide

B. *N*-methylindole and semicarbazide

C. *N*-methylindolone-3 and thiosemicarbazide

D. benzimidazole and semicarbazide

E. 2,3-dioxoindole and thiosemicarbazide

LESSON 10

TOPIC: CARBOHYDRATES. CLASSIFICATION, STRUCTURE, STEREOISOMERISM AND CHEMICAL PROPERTIES OF MONOSACCHARIDES.

SUBJECT MOTIVATION: Carbohydrates are widespread in nature and play an extremely important role in the metabolism of plant and animal organisms. A special place is occupied by carbohydrates that perform in the body reserve (energy depot) and highly specialized functions (nucleotides - carriers of the genetic code; specific polysaccharides - antigens that cause immunity; glycoproteins - specific blood group substances, etc.).

The photosynthetic cycle, which provides the synthesis of organic compounds on the planet, is mainly the conversion of sugar phosphate. Deep knowledge in the field of structure and chemistry of carbohydrates is necessary for the acquisition of professional skills and the study of relevant sections of pharmacognosy, biological, pharmaceutical chemistry, drug technology.

OBJECTIVE: To consolidate knowledge of the principles of stereochemical structure and chemical properties of monosaccharides and the ability to conduct qualitative reactions to identify the most important monosaccharides.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Classification, structure and nomenclature (aldo-, ketopentose and hexose).
2. Stereoisomerism. D- and L-Stereochemical series.
3. Cyclo-oxo (ring-chain) tautomerism; furanose and pyranose. Haworth's formulas; α- and β-anomers.
4. Mutarotation. Conformations of cyclic forms of monosaccharides.
5. Methods of synthesis.
6. Physical properties.

7. Reactions of monosaccharides oxoforms (oxynitrile synthesis, formation of osazone). Reduction in polyols. Oxidation: formation of aldonic, aldaric, uronic acids.

8. Carbonyl-endiol tautomerism. Mutual conversion of monosaccharides under the influence of alkalis (epimerization).

9. Reactions of hemiacetal hydroxyl. Formation of glycosides. O-, N-, S-Glycosides: structure, hydrolysis.

10. Reactions of alcohol hydroxyl groups (acylation, alkylation): formation of esters (acetates, phosphates) and ethers.

11. Reduction properties of monosaccharides.

12. The concept of types of monosaccharides fermentation and their application in industry.

13. Identification of monosaccharides.

14. Amino sugars.

PRACTICAL WORKS PERFORMED IN THE CLASS.

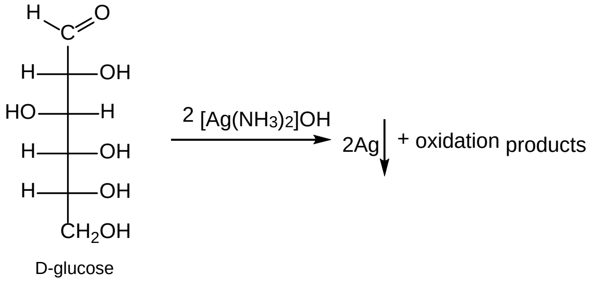
Protocol № 10

Date_______________

Experiment 1. Reduction of the ammonia hydroxide solution of silver by glucose

Place 5 drops of Tollens reagent and a few glucose crystals in a test tube. The content of the test tube is heated in a water bath at 60-70°C for 2-3 minutes. The release of free silver in the form of a mirror or gray sediment is observed.

Reaction scheme:



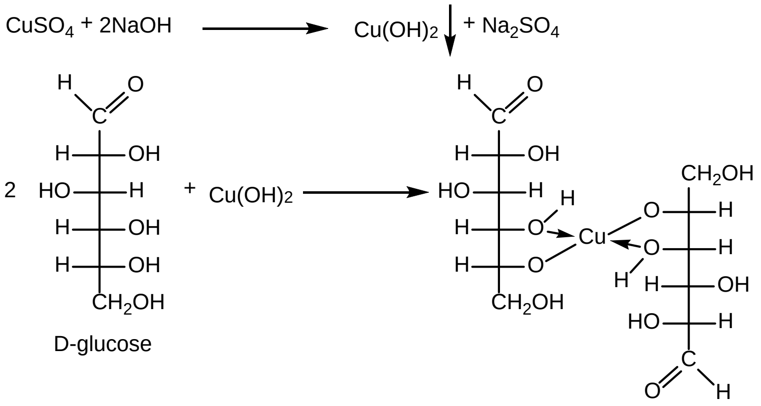
Observation:

Conclusions:

Experiment 2. Evidence of the hydroxyl groups in D-glucose.

Place 1 drop of 0.5% D-glucose solution and 6 drops of 10% NaOH solution in a test tube. To the resulting mixture add 1 drop of 2% solution of copper(II) sulfate $CuSO_4$. The formed precipitate of copper(II) hydroxide $Cu(OH)_2$ dissolves quickly and a clear blue solution is obtained. Save the resulting solution for the next experiment.

Reaction scheme:



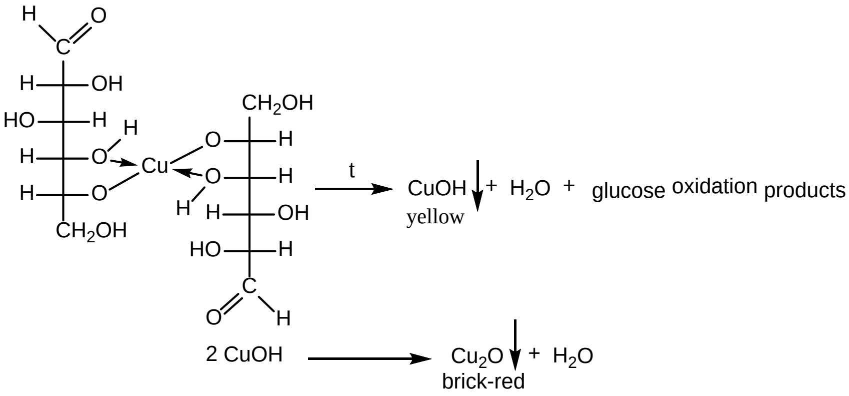
Observation:

Conclusions:

Experiment 3. Reduction of the copper(II) hydroxide by glucose in the alkaline medium (Trommer's test).

To the blue solution obtained in the previous experiment, add a few drops of water to the height of the liquid layer in a test tube about 15-20 mm. Divide in half the content of the test tube. Heat until boiling one of the test tubes, the second one leave without heating for control. When heated, the color of the solution changes from blue to yellow-red. This reaction is called a Trommer test and is used to detect glucose in the urine.

Reaction scheme:



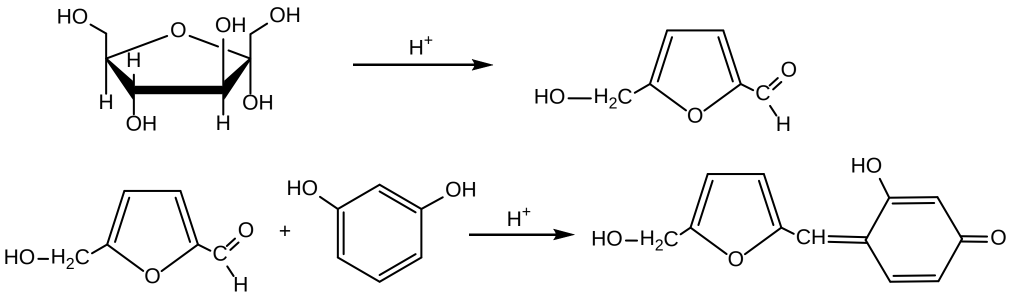
Observation:

Conclusions:

Experiment 4. Selivanov's test for fructose.

Place few crystals of dry resorcinol and 2 drops of concentrated hydrochloric acid in a test tube. Add 2 drops of 0.5% fructose solution and heat until boiling. Gradually the liquid turns red. The reaction occurs due to the formation of an unstable compound - hydroxymethylfurfural. Under the action of concentrated hydrochloric acid, hydroxymethylfurfural condenses with resorcinol to give a colored compound.

Reaction scheme:



Observation:

Conclusions:

TASKS FOR SELF-CONTROL SOLUTION:

1. Write the formula *α*-D-galactopyranose (Haworth projection). Indicate which atom's configuration determines whether it belongs to the D- or L-series?

2. What qualitative reaction is the evidence of the presence of several hydroxyl groups in glucose?

3. Write a diagram of the reaction of reduction of D-glucose, specify the reagent, name the reaction product and explain its significance for pharmacy.

LESSON 11

TOPIC: OLIGOSACCHARIDES AND POLYSACCHARIDES. GLYCOSIDES.

SUBJECT MOTIVATION: Bioses and polysaccharides play an extremely important role in the metabolism of plant and animal organisms. A special place is occupied by specific polysaccharides-antigens that take part in the work of the body's immune system. Deep knowledge of the structure, chemistry of bioses and polysaccharides is necessary to acquire professional skills in the study of the relevant sections of pharmacognosy, pharmaceutical and biological chemistry.

OBJECTIVE: To generalize the knowledge of the principles of structure and chemistry of the most important mono-, di-, homo- and heteropolysaccharides in interrelation with their biological functions.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Nomenclature and structure of disaccharides.
2. Reducing and non-reducing disaccharides: maltose, cellobiose, lactose, sucrose. Structure, nomenclature.
3. Chemical properties.
4. Cyclo-oxo-tautomerism of reducing disaccharides.
5. Hydrolysis.
6. Oxidation (maltobionic, cellobionic, lactobionic acid).
7. The inversion of sucrose.
8. Homopolysaccharides: starch (amylose, amylopectin), glycogen, cellulose, dextrans (blood substitute "Polyglucin"), inulin. Spatial structure of amylose and cellulose.
9. Ethers and esters of polysaccharides. Hydrolysis.
10. Cellulose derivatives (nitrates, acetates, xanthates). Colloidal cotton wool, collodion, cellophane, carboxymethylcellulose; application in medicine. Cellulose as a raw material to produce artificial silk, plastics, hydrolysis alcohol.
11. Pectic substances.

12. Heteropolysaccharides and their use in medical practice: heparin, chitin, hyaluronic acid, natural gums.

PRACTICAL WORKS PERFORMED IN THE CLASS.

Protocol № 11

Date_______________

Experiment 1. The absence of the reducing properties of the sucrose.

Place 1 drop of 1% sucrose solution and 6 drops of 10% sodium hydroxide NaOH in a test tube. Add 5-6 drops of water for dilution (height of the liquid layer is 15-20 mm). Add 1 drop of 2% solution of copper(II) sulfate $CuSO_4$. A clear blue solution of a complex salt of copper(II) with sucrose is formed. Carefully heat the tube over the flame of the burner so that only the upper part of the solution is heated and the lower part remains unheated (for control). Heat only until boiling, but do not boil. The color of the solution doesn't change.

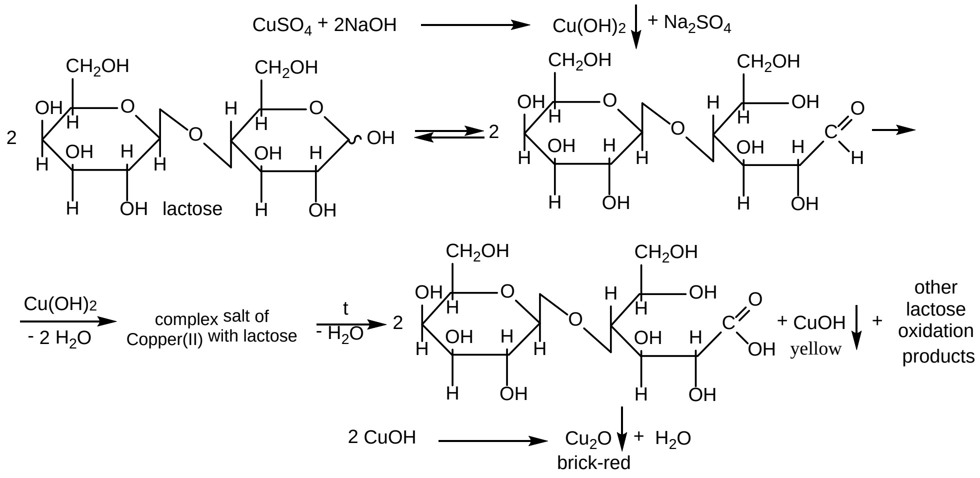
Observation:

Conclusions:

Experiment 2. Reducing properties of lactose.

Place 1 drop of 1% lactose solution and 4 drops of 10% sodium hydroxide NaOH in a test tube. Add 1 drop of 2% copper(II) sulfate $CuSO_4$. The formed blue precipitate of copper(II) hydroxide dissolves when the tube is shaken, forming a blue solution of a complex salt of copper(II) with lactose. Add a few drops of water to dilute the liquid layer to a height of about 15-20 mm. Carefully heat the tube so that only the upper part of the solution is heated, and the lower part remains unheated (for control). Bring to a boil. When heated, the color of the upper part of the solution changes to yellow-red.

Reaction scheme:



Observation:

Conclusions:

Experiment 3. Starch identification reaction.

Place 5 drops of 0.5% starch paste and 1 drop of highly diluted iodine solution in a test tube. The solution turns blue (it is assumed that the starch with iodine forms inclusion compounds (clathrates), colored in characteristic colors - blue (λmax = 620-680 nm) for amylose and red (λmax = 520-555 nm) for amylopectin. Amylose molecules in these complexes form a helix around the iodine molecule, each turn of which contains 6 glucose residues (When heated, the colored starch solution with iodine color disappears and when cooled reappears. Which is probably due to the unwinding of the amylose helix).

Observation:

Conclusions:

Experiment 4. Acid hydrolysis of starch.

Place 1 drop of 0.5% starch paste in a test tube. Add 2 drops of 10% H_2SO_4 sulfuric acid and place the tube in a boiling water bath. The cloudy solution becomes clear after 20 minutes. Place 5 drop of hydrolyzate into a test tube and add 1 drop of a dilute solution of iodine in potassium iodide. If the sample doesn't give a positive iodine-starch reaction (blue color) add 8 drops of 10% sodium hydroxide NaOH to the tube to create an alkaline environment. Then add 1 drop of 2% solution of copper(II) sulfate $CuSO_4$. Will the Trommer test be positive?

Reaction scheme:

Observation:

Conclusions:

TASKS FOR SELF-CONTROL:

1. Write the structural formula of milk sugar (lactose). Give a systematic name. Show the phenomenon of oxo-cyclo-tautomerism.

2. Write the reaction of maltose interaction with the excess of dimethyl sulfate. Name the obtained compound, carry out its hydrolysis. Will the hydrolyzed compound have reducing properties?

3. Write the structural formula of a disaccharide consisting of D-glucuronic acid and *N*-acetylglucosamine linked by a *β*-1,3-glycosidic bond. Which biopolymer contains this fragment?

LESSON 12

TOPIC: AMINO ACIDS, PEPTIDES, PROTEINS.

SUBJECT MOTIVATION: α-Amino acids as structural units of biopolymers - proteins occupy a prominent place in the chemistry of life because life itself, according to one of the historical definitions, is the way of existence of protein bodies. Proteins serve as food, regulate metabolism, promote oxygen uptake, play an important role in the functioning of the nervous system, are the mechanical basis of muscle contraction and the main supporting material of living organisms, participation in the transmission of genetic information, etc. In addition, amino acids have their own significance as effective drugs (gamma-aminobutyric acid, DOPA, methionine, sarcolysin, etc.). An in-depth study of the structure and chemistry of α-amino acids will ensure the assimilation of the biological function of proteins at the molecular level and the ability to successfully solve problems in the analysis of active pharmaceutical ingredients.

OBJECTIVE: To form knowledge of the structure and properties of the most important α-amino acids and chemical bases of the structural organization of proteins for further study of the biological functions of proteins at the molecular level.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Nomenclature, classification and stereoisomerism of α-amino acids.
2. Methods of proteinogenic amino acids synthesis, advantages and disadvantages of isolating amino acids from natural sources and synthetic methods of synthesis of proteinogenic amino acids.
3. Physico-chemical properties of proteinogenic amino acids.
4. Methods of identification of proteinogenic amino acids.
5. Sequencing of peptide and protein molecules. Sanger's reagent. Edman sequencing.
6. Biological role of proteinogenic amino acids.
7. Amino acids as precursors of bioregulators in the body.
8. Fundamentals of the structure of peptide molecules. Peptide bond.
9. Reactions for identification of peptide fragments. The structure of protein molecules. Methods of research of protein molecules.

PRACTICAL WORKS PERFORMED IN THE CLASS.

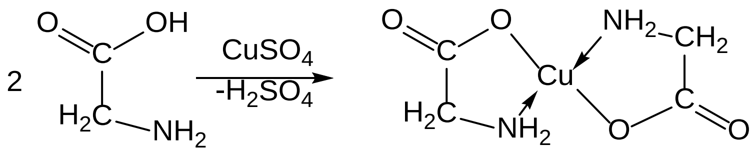
Protocol № 12

Date_______________

Experiment 1. The formation of glycine complex salt with copper(II).

Place in a test tube 0.5 ml of 2% solution of copper(II) sulfate and 1% solution of glycine. The copper salt of glycine easily forms a stable intracomplex compound of blue color.

The chemistry of the reaction:



Observation:

Conclusions:

Experiment 2. Precipitation of proteins with concentrated mineral acids

In a test tube with 1 ml of egg white solution add 1 ml of concentrated nitric acid and mix. A white flaky precipitate falls out.

Observation:

Conclusions:

Experiment 3. Precipitation of proteins by heavy metals salts.

Add dropwise, with shaking a saturated aqueous solution of copper(II) sulfate to 1 ml of egg white solution until the precipitate will be formed. Do that in the first test tube.

In the second test tube, to the same amount of protein, in a similar manner add 20% aqueous solution of lead(II) acetate. Precipitate is formed in both test tubes.

Observation:

Conclusions:

TASKS FOR SELF-CONTROL:

1. Write the structural formulas of essential amino acids. Give systematic names.
2. Write the reaction of glycine with ninhydrin. What is the application of this reaction?
3. What is the meaning of formol titration of amino acids. Give examples, write reaction schemes.

LESSON 13

TOPIC: NUCLEIC ACIDS, NUCLEOTIDES AND NUCLEOSIDES. DRUGS THAT ARE STRUCTURAL ANALOGUES OF NUCLEOSIDES.

SUBJECT MOTIVATION: Adenosine triphosphate, nucleic acids and others are playing significant roles in living organisms and may be used in the complex therapy of various diseases. Knowledge of the chemistry of nucleic acids contributes to a deeper understanding of the mechanism of their pharmacological activity and mastering the course of biochemistry of nucleic acids.

OBJECTIVE: To consolidate knowledge of the chemical structure of biopolymers (nucleic acids) and their role in biological systems. To deepen the idea of the spatial structure and reactivity of structural fragments of biopolymers - amino acids, carbohydrates, nucleic bases.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Nucleotides. Structure and nomenclature of nucleoside phosphates.
2. Hydrolysis of nucleotides and nucleosides.
3. Adenosine triphosphate.
4. Ribonucleic (RNA) and deoxyribonucleic (DNA) acids and their role in protein biosynthesis.
5. Cyclic nucleotides, their role as bioregulators.

TASKS FOR SELF-CONTROL

1. Write the structural formulas of 2'-deoxythymidine-5'-monophosphate, guanosine-3'-phosphate, adenosine-3',5'-monophosphate, describe the types of bonds in their molecules, draw complete hydrolysis and name the products.

2. Draw the structure of the RNA molecule formed by 5'-adenylic acid. What are complementary pairs? Give the formula of a complementary fragment of a DNA molecule.

LESSON 14

TOPIC: CLASSIFICATION, STRUCTURE AND CHEMICAL PROPERTIES OF SAPONIFIED LIPIDS.

SUBJECT MOTIVATION: In pharmaceutical practice, linetol, rose hip oil, sea buckthorn, castor oil, etc. are used as components of drugs. Many saponified lipids are used as bases for ointments, suppositories and as emulsifiers. Phospholipids, being a major component of cell membranes, play an important role in various regulatory processes and cell life.

OBJECTIVE: To summarize students' knowledge of the structure and chemistry of lipids involved in the construction of structural components of the cell.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Lipids: concept and classification.
2. Structure and classification of saponifying lipids.
3. Fats.
4. Fatty acids and features of their structure. The influence of the nature of higher carboxylic acids on the physical state of fats.
5. Indicators of fat quality (iodine number, acid number, saponification number).
6. Hydrogenation of fats.
7. Saponification of fats. Fundamental differences during alkaline and acid saponification of fats.
8. Soaps.
9. The nature of synthetic detergents.
10. Phospholipids. Waxes. Twins.

PRACTICAL WORKS PERFORMED IN THE CLASS.

Protocol № 14

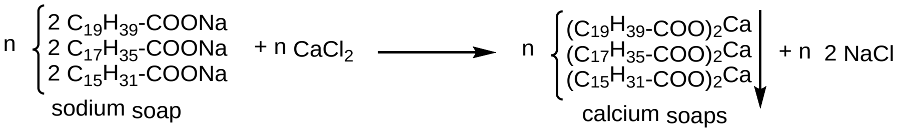
Date________________

Experiment № 1

Formation of insoluble fatty acids calcium salts.

Place 5 drops of soap solution in a test tube and add 1 drop of calcium chloride solution $CaCl_2$. Shake the contents of the test tube. A white precipitate appears.

Reaction scheme:



$$n\left\{\begin{array}{l}2\ C_{19}H_{39}\text{-COONa}\\2\ C_{17}H_{35}\text{-COONa}\\2\ C_{15}H_{31}\text{-COONa}\end{array}\right. + n\ CaCl_2 \longrightarrow n\left\{\begin{array}{l}(C_{19}H_{39}\text{-COO})_2Ca\\(C_{17}H_{35}\text{-COO})_2Ca\\(C_{15}H_{31}\text{-COO})_2Ca\end{array}\right\downarrow + n\ \ 2\ NaCl$$

Observation:

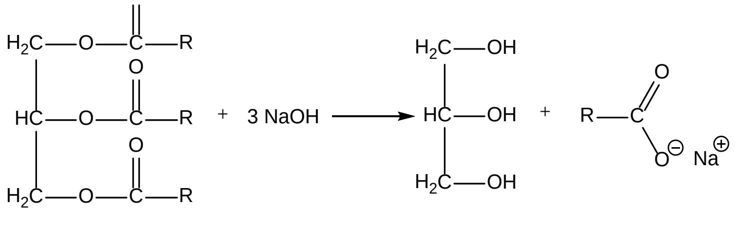
Conclusions:

Experiment № 2

Saponification of fats with water-alcohol solution of alkali.

Place 1 ml of castor oil, 1 ml of ethyl alcohol and 1 ml of 35% sodium hydroxide solution in a test tube. The mixture is thoroughly mixed and heated in a water bath until boiling. The mass quickly becomes homogeneous and then after 3-5 minutes the saponification is completed.

Reaction scheme:



Observation:

Conclusions:

TASKS FOR SELF-CONTROL:

1. Write the schemes of acidic and alkaline hydrolysis of glycerol dipalmitoyl oleate. Name the reaction products.
2. Write the structure of phosphatidylethanolamine, which includes stearic and linoleic acids. Mark the polar and nonpolar parts of the molecule.
3. Explain what is common in the structure of all fats of both vegetable and animal origin. What is the difference between the structure of solid and liquid fats?
4. To which class of compounds does fats and waxes belong? What is beeswax from the chemical point of view?

LESSON 15

TOPIC: CLASSIFICATION, STRUCTURE AND CHEMICAL PROPERTIES OF UNSAPONIFIABLE LIPIDS.

SUBJECT MOTIVATION: Terpenes belong to the group of biogenetically related compounds - isoprenoids. In plant and animal organisms, isoprenoids are the most important low molecular weight bioregulators, which have led to the use of some members of this group as active pharmaceutical ingredients (camphor, menthol, santonin, retinol, α-tocopherol). The release of chemicals into the environment – pheromones, is the way many species communicate. Most pheromones contain isoprene fragments in the structure. Of theoretical importance is the study of stereochemistry of isoprenoids, the diversity of which allows to some extent to deepen students' knowledge in this area.

Steroids in the animal and plant world are of great biological importance. Steroid hormones control the specific processes of growth, normal development and functioning of the body (sex hormones, vitamin D_2), regulate carbohydrate metabolism, water-salt balance, have anti-inflammatory and anti-allergic effects (corticosteroid hormones), promote stabilization and absorption of acids, show hemolytic activity (sapogenin) and high cardiotonic activity (cardiac glycosides). Knowledge of the structure and properties of steroids is necessary when studying courses in pharmacognosy, pharmaceutical and biological chemistry.

OBJECTIVE: To form knowledge of structural and stereochemical features of the most important biologically active steroids and to develop the ability to use a logical approach to predicting their chemical behavior.

To generalize and deepen knowledge of the principles of structure and chemistry of the most important representatives of terpenoids in relation to their biological functions. Implement a dialectical approach to the knowledge of matter in the study of the properties of isoprenoids.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Features of structure and classification of unsaponifiable lipids.
2. Terpenes. Classification of terpenes by the number of isoprene fragments and the nature of the carbon skeleton.
3. The structure of terpenes. Isoprene rule.
4. Nomenclature of mono- and bicyclic terpenes. Natural sources and synthetic extraction methods.
5. Acyclic terpenes: geraniol, citral.

6. Monocyclic monoterpenes: limonene, menthane, menthol, terpin. Chemical properties.

7. Bicyclic terpenes: α-pinene, borneol, camphor.

8. Synthesis of camphor.

9. Optical activity of α-pinene, borneol and camphor.

10. Diterpenes: retinol (vitamin A), retinal.

11. Tetraterpenes (carotenoids): β-carotene (provitamin A).

12. Prostaglandins. Arachidonic and prostanoic acid as precursors of prostaglandins.

13. Steroids: classification, structural features.

PRACTICAL WORKS PERFORMED IN THE CLASS.

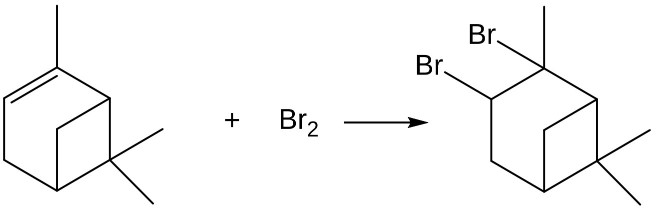
Protocol № 15

Date________________

Experiment 1. The proof of terpenoids unsaturation.

In a test tube put 5 drops of bromine water and 5-10 drops of turpentine. The contents of the test tube are shaken.

Reaction scheme:



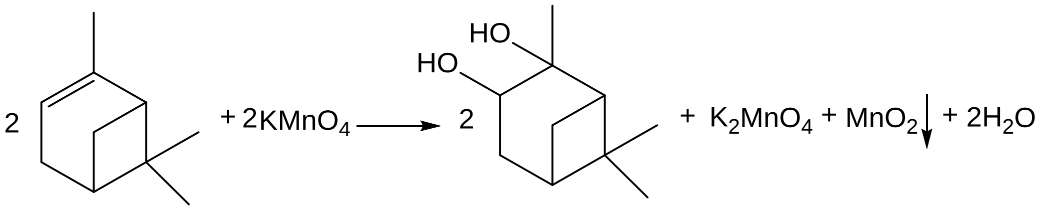
Observation:

Conclusions:

Experiment 2. Oxidation reaction of terpenes.

Mix 1 drop of 1% potassium permanganate solution, 3 ml of water and 3-5 drops of turpentine in a test tube. The mixture is shaken vigorously.

The chemistry of the reaction:



Observation:

Conclusions:

TASKS FOR SELF-CONTROL:

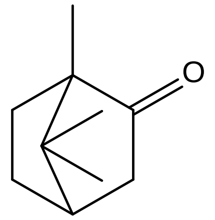
1. Write for limonene schemes of two qualitative reactions that prove the unsaturated nature of this compound.

2. What compounds are formed during storage (under the influence of oxygen) of pinene and what reaction can be observed?

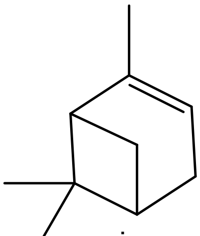
3. Write the reaction schemes of camphor with the following reagents: hydroxylamine, sodium bisulfate, phenylhydrazine, semicarbazide.

4. Write the formulas of two compounds, that could be synthesized in the industry using the pinene (camphor, borneol).

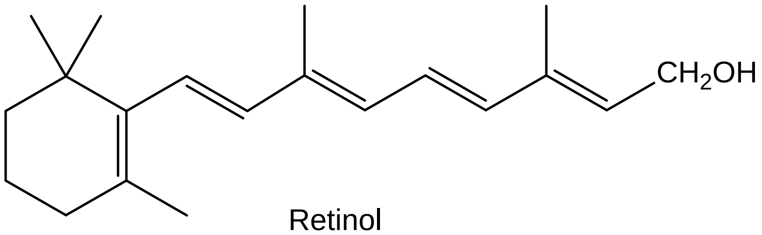
5. Carry out a functional analysis of the following substances:



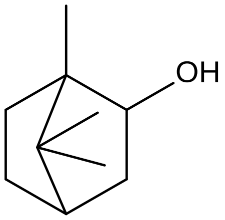
Camphore



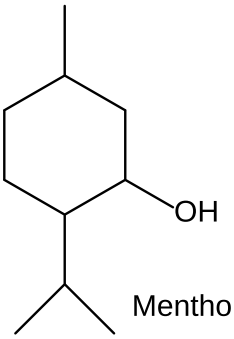
a-pinene



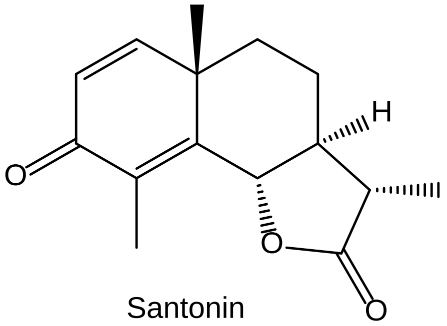
Retinol



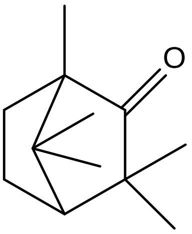
Borneol



Menthol



Santonin



Fenhol

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

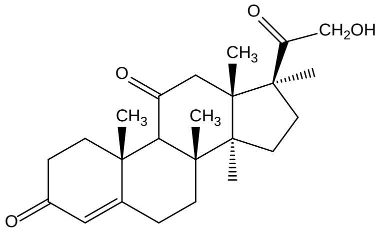
1. Stereochemistry of steran (cyclopentanoperhydrophenanthrene).

2. Classification of steroids: cholestane group, cholan group, pregnane group, estrane group, androstane group.

3. Aglycones of cardiac glycosides, saponins.

4. Bufadienolides.

5. To which group of steroids belongs the substance, the structure of which is given below? List the qualitative reactions to the available functional groups.



6. Give the structure and name of the hydrocarbon that underlies corticosteroids. Number the carbon skeleton.

7. Describe the conformational formula of the female sex hormone - estradiol.

LESSON 16

TOPIC: FINAL LESSON ON "NATURAL COMPOUNDS. CARBOHYDRATES, PEPTIDES, PROTEINS, NUCLEIC ACIDS, NUCLEOTIDES, NUCLEOSIDES AND LIPIDS.

SUBJECT MOTIVATION: Among natural compounds, carbohydrates occupy an important place. They are involved in the construction of vital structures, are material for the biosynthesis of compounds of different classes, they play an important role in cell bioenergy. Carbohydrates are a part of physiologically active glycosides, nucleic acids, polysaccharides, glycolipids and glycoproteins. Some types of carbohydrates are a part of the membranes of plant cells and play a supporting role. Deep knowledge of the structure and chemistry of carbohydrates is necessary to acquire professional skills in the relevant sections of biological chemistry, pharmacology and other disciplines.

OBJECTIVE: To consolidate knowledge of the chemical structure of biologically active compounds and biopolymers, their role in biological systems. To deepen the idea of the spatial structure and reactivity of structural fragments of biopolymers - amino acids, carbohydrates, nitrogenous bases.

To consolidate and to generalize knowledge of structural and stereochemical features of the most important low molecular weight biologically active compounds and creatively develop the ability to use a logical approach to predict their chemical properties.

To consolidate and deepen knowledge of the principles of stereochemical structure, chemical properties of carbohydrates in relation to their biological functions. Be able to perform qualitative reactions to detect carbohydrates and products of their metabolism in biological fluids. To form knowledge of the principles of structure and basic chemical transformations of the most important polysaccharides involved in the processes of life.

THEORETICAL QUESTIONS FOR SELF-TRAINING TO THE CLASSES

1. Write the structural formulas of the following compounds:

1) α-D-glucopyranose; 2) β-D-glucofuranose; 3) α-D-fructopyranose; 4) β-D-galactopyranose; 5) ethyl-α-D-glucopyranoside; 6) methyl-β-D-fructofuranoside.

2. Define the terms: "carbohydrates", "monosaccharides", "aldoses", "ketoses", "aldopentoses" and "ketohexoses". Give examples of compounds and name them.

3. How many chiral centers do molecules of glucose and fructose contain in open and cyclic forms? Mark them. Calculate how many spatial isomers these compounds can have in chain and cyclic forms.

4. What phenomenon is called mutarotation? Give the schemes of cyclo-oxo tautomeric transformations of the following compounds: 1) D-glucose; 2) D-fructose; 3) D-galactose; 4) D-ribose. Name these tautomeric forms.

5. Give the formulas of furanose and pyranose forms of D-mannose. Specify an anomeric carbon atom. What compounds are called anomers? Why aldohexoses do not interact with sodium hydrosulfite and fuchsin sulfuric acid? Write diagrams of qualitative reactions that prove that D-mannose belongs to aldose.

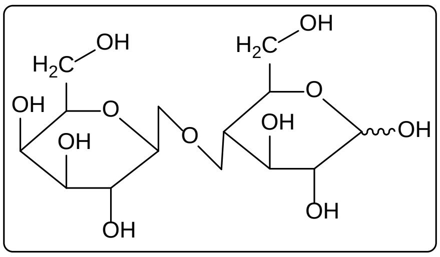
6. Write reaction schemes that can be used to prove that D-glucose is polyoxyaldehyde and D-fructose is polyoxyketone. Give the reaction schemes proving the presence in the molecule of D-glucose and D-fructose: 1) hemiacetal hydroxyl; 2) five alcohol hydroxyls; 3) aldehyde and ketone groups.

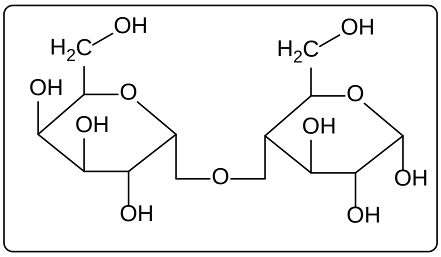
7. Write schemes of D-glucose oxidation in neutral, acidic and alkaline mediums. Name the products. What is epimerization and what compounds are called epimers? Use the example of D-mannose to illustrate the scheme of carbonyl-endiol tautomerism. Are D-fructose and D-glucose epimers? Explain the answer.

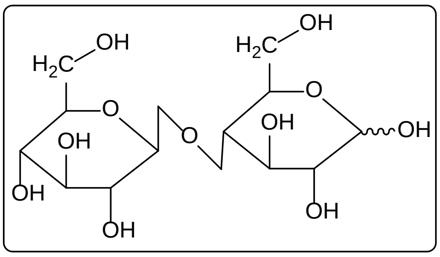
8. Write the structural formulas of the following compounds:

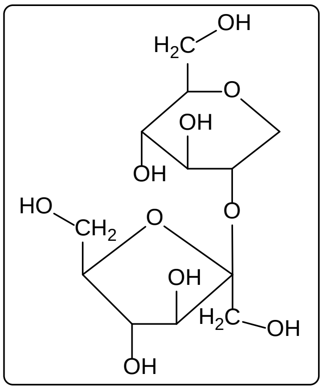
1) α-maltose; 2) methyl α-D-lactoside; 3) cellobionic acid; 4) fragments of amylose, amylopectin and cellulose.

Name the following compounds according to the systematic nomenclature:









9. Define the terms: "oligosaccharides", "reducing disaccharides", "non-reducing disaccharides", "homopolysaccharides", "heteropolysaccharides". Give examples. Explain whether freshly prepared solutions of maltose, cellobiose, lactose and sucrose are capable of mutarotation. Write possible tautomeric transformations.

10. Give the schemes of qualitative reactions that confirm the reducing properties of maltose. Can these reactions be used to distinguish lactose from sucrose? Explain the answer.

11. Why D-glucose in contrast to sucrose gives a positive Trommer test? Write the corresponding reaction equation.

12. Write reactions schemes of lactose with the following reagents:

1) [H]; 2) $[Ag(NH_3)_2]OH$; 3) HCN; 4) H_2NOH; 5) $C_6H_5NHNH_2$; 6) CH_3OH (HCl (gas)); 7) CH_3I; 8) $(CH_3CO)_2O$. Name the products. Is it possible to distinguish with the help of the Trommer test: 1) sucrose from the products of its hydrolysis; 2) lactose from the products of its hydrolysis; 3) lactose from sucrose? Write the corresponding reaction equations.

13. Write a diagram of the conversion of sucrose into invert sugar. What is the name of this phenomenon and what is its essence?

14. From which monosaccharide units are macromolecules are being built, namely amylose, amylopectin, cellulose and glycogen? Show fragments of molecules and indicate the type of glycosidic bond. What are dextrans, inulin and pectin?

15. What types of polysaccharides do chondroitin sulfate, hyaluronic acid, heparin and plant gums include?

16. Describe the influence of the spatial structure of the chain on the properties of compounds, do that on the example of amylose, amylopectin and cellulose.

17. Give schemes of complete hydrolysis of starch and cellulose. Name the products.

18. Write schemes for the synthesis of: 1) cellulose mono- and dinitrate; 2) triacetylcellulose.

19. Explain what happens when starch interacts with iodine.

TASKS FOR SELF-CONTROL:

1. Classification and nomenclature of monosaccharides.
2. Cyclo-oxo (ring-chain) tautomerism of monosaccharides.
3. Conformations of monosaccharides.
4. Chemical properties of monosaccharides.
5. Oxidation and reduction reactions.
6. Amino sugars.
7. Nomenclature and structure of disaccharides.
8. Chemical properties of disaccharides (bioses).
9. Polysaccharides (polyoses). Nomenclature, structure.
10. Chemical properties of polysaccharides: hydrolysis, interaction of free hydroxyls of fiber with nitric acid, acetic anhydride and carbon disulfide.
11. Heteropolysaccharides.
12. Nomenclature of α-amino acids and stereoisomerism.
13. Classification of amino acids.
14. The structure of α-amino acids as bifunctional compounds.
15. Chemical properties of α-amino acids.
16. The structure of peptides and proteins.

17. Structure and chemical properties of nucleotides.
18. Nucleosides.
19. Nucleic acids.
20. The biological role of DNA and RNA.
21. Saponifying lipids.
22. Neutral lipids (triacylglycerides). Classification and nomenclature.
23. Stereoisomerism of unsaturated acids.
24. Chemical properties of lipids.
25. Soaps.
26. Phospholipids.
27. Wax. Spermaceti. Twins.
28. Isoprenoids (terpenes, carotenoids).
29. Classification of terpenes and their structure. Isoprene rule.
30. Stereochemistry of terpenes.
31. Methods of terpenes synthesis.
32. Steroids.
33. Stereochemistry of steran (cyclopentanoperhydrophenanthrene).
34. Classification of steroids.
35. A group of cholestane hormone.
36. A group of holan hormone group.
37. A group of pregnane hormone.
38. A group of estrogen hormone.
39. A group of androstane group.
40. Aglycones of cardiac glycosides, saponins.
41. Bufadienolides.

LESSON 17

TOPIC: CREDIT LESSON

LIST OF CHECKLIST QUESTIONS FOR PREPARATION FOR THE CREDIT CLASS.

1. Three-, four-membered heterocyclic compounds with one heteroatom (oxirane, azeridine, oxatedine, azatedine).

2. Five-membered heterocycles with one heteroatom (pyrrole, furan, thiophene). Biomedical significance of tetrapyrrole compounds: porphyrin, porphyrins, heme.

3. Indole and its derivatives: tryptophan and reactions of the synthesis of tryptamine and serotonin; indoxyl, skatole, skatoxyl - importance in the processes of protein putrefaction in the intestine.

4. Five-membered heterocycles with two nitrogen heteroatoms. Pyrazole, pyrazolone; pyrazolone-5 derivatives as drugs (antipyrine, amidopyrine, analgin). Imidazole and its derivatives: histidine, histamine.

5. Five-membered heterocycles with two different heteroatoms: thiazole, oxazole. Thiazole as a structural component of the thiamine molecule (vitamin B_1).

6. Six-membered heterocycles with a nitrogen atom: pyridine. Nicotinamide (vitamin PP) as a component of redox pyridine coenzymes. Pyridoxine and molecular forms of vitamin B_6.

7. Six-membered heterocycles with two nitrogen atoms. Diazine: pyrimidine, pyrazine, pyridazine. Nitrogen bases are pyrimidine derivatives (uracil, cytosine, thymine).

8. Pyrimidine derivatives as drugs: 5-fluorouracil, potassium orotate. Barbituric acid: barbiturates as hypnotics and antiepileptics (phenobarbital, veronal).

9. Six-membered heterocycles with different heteroatoms. Phenothiazines (aminazine, etc.) as psychotropic (neuroleptic) drugs.

10. Seven-membered heterocycles with two heteroatoms. Diazepines: Benzo-1,4-diazepines as the most common tranquilizers and anxiolytics.

11. Purine and its derivatives. Amino derivatives of purine (adenine, guanine), their tautomeric forms; biochemical significance in the formation of nucleotides and coenzymes.

12. Hydroxy derivatives of purine: hypoxanthine, xanthine, uric acid. Methylation of xanthine derivatives (caffeine, theophylline, theobromine) as physiologically active compounds with action on the central nervous and cardiovascular systems.

13. Carbohydrates: definition, classification. Monosaccharides (aldoses and ketoses; pentose, hexose), biomedical significance of individual representatives.

14. Monosaccharides: pentoses (ribose, 2-deoxyribose, xylose), hexoses (glucose, galactose, mannose, fructose) - structure, properties. Qualitative reactions for glucose.

15. Structure and properties of monosaccharide derivatives. Amino derivatives: glucosamine, galactosamine. Uronic acids. L-ascorbic acid (vitamin C). Reduction products of monosaccharides: sorbitol, mannitol.

16. Oligosaccharides: structure, properties. Disaccharides (sucrose, lactose, maltose), their biomedical value.

17. Polysaccharides. Homopolysaccharides: starch, glycogen, cellulose, dextrans - structure, hydrolysis, biomedical value. Qualitative reaction for starch.

18. Heteropolysaccharides: definition, structure. Structure and biomedical significance of glucosaminoglycans (mucopolysaccharide) - hyaluronic acid, chondroitin sulfates, heparin.

19. Lipids: definition, classification. Higher carboxylic (fatty) acids: palmitic, stearic, oleic, linoleic, linolenic, arachidonic. Simple lipids. Triacylglycerides (neutral fats): structure, physiological significance, hydrolysis.

20. Complex lipids. Phospholipids: phosphatidic acid, phosphatidylethanolamine, phosphatidylcholine, phosphatidylserine. Sphingolipids. Glycolipids. The role of complex lipids in the structure of biomembranes.

21. Steroids as derivatives of cyclopentaneperhydrophenanthrene (steran). The structure of biologically important representatives of steroids: cholesterol, vitamin D, bile acids, corticosteroids, sex hormones.

22. Amino acid composition of proteins and peptides; classification of natural L-α-amino acids. Chemical and physicochemical properties of proteinogenic amino acids. Ninhydrin reaction, its importance in the analysis of amino acids.

23. Proteins and peptides: definition, classification, biological functions. Types of bonds between amino acid residues in protein molecules. Peptide bond: formation, structure: biuret reaction.

24. Levels of structural organization of proteins: primary, secondary, tertiary and quaternary structures. Oligomeric proteins.

25. Physico-chemical properties of proteins, their molecular weight. Deposition methods. Denaturation of proteins.

26. Methods of fractionation and analysis of proteins and peptides (sedimentation, chromatography, electrophoresis). Analysis of the primary structure of proteins and peptides: the methods of Sanger and Edman.

27. Enzymes as biological catalysts of protein nature. Principles of nomenclature and classification of enzymes.

28. Nucleosides, nucleotides. Nitrogen bases of purine and pyrimidine series, which are a part of natural nucleotides. Minor nitrogenous bases.

29. Nucleosides. Nucleotides as phosphorylated derivatives of nucleosides (nucleoside mono-, di- and triphosphates). Nomenclature of nucleosides and nucleotides as components of RNA and DNA.

30. Structure and biochemical functions of free nucleotides: nucleotide enzymes; cyclic nucleotides 3',5'-AMP, 3',5'-GMF.

31. Nucleic acids (deoxyribonucleic, ribonucleic) as polynucleotides. Polarity of polynucleotide chains of DNA and RNA.

32. Structure and properties of DNA; nucleotide composition, complementarity of nitrogen bases. Primary, secondary and tertiary structure of DNA.

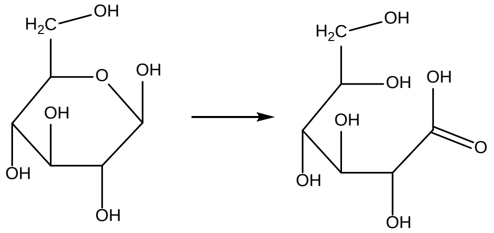
33. RNA: structure, types of RNA and their role in protein biosynthesis.

A list of practical skills that students must possess while studying organic chemistry

1. Conducting iodoform test for acetone.
2. Carrying out the Trommer's reaction with formaldehyde.
3. Carrying out the Wagner's reaction (also known as Baeyer Test) with oleic acid.
4. Proof of fat unsaturation (reaction with $KMnO_4$).
5. Proof of the presence of free phenolic hydroxyl in salicylic acid.
6. Proof of the presence of free phenolic hydroxyl in salol (phenyl salicylate).
7. Obtaining Fehling's reagent.
8. Carrying out Fehling's reaction with glucose, lactose, maltose.
9. Carrying out a qualitative reaction on starch.
10. Obtaining copper gluconate.
11. Carrying out ninhydrin reaction with α-amino acids, peptides, proteins.
12. Carrying out xanthoproteic reaction with aromatic amino acids, peptides, proteins.
13. Carrying out Folin's reaction (Sullivan reaction) with sulfur-containing amino acids, peptides, proteins.
14. Carrying out biuret reaction with peptides and proteins.
15. Precipitation of proteins with trichloroacetic acid.
16. Precipitation of proteins with sulfosalicylic acid.

Approximate list of tests for preparation for classes in the discipline "Organic Chemistry"

1. Indicate which reaction underlies the following transformation:



A. Reduction.

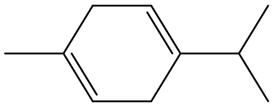
B. Recyclization.

C. Transesterification.

D. Oxidation.

E. Hydrolysis.

2. γ-Terpinene is present in the oil of dill, coriander and pine needles.



What is the maximum number of bromine molecules that can be added to γ-terpinene molecule.

A. 2.

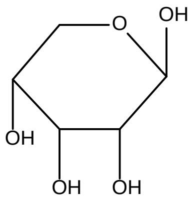
B. 0.

C. 4.

D. 1.

E. 3.

3. Choose the most correct name for the following monosaccharide:



A. *β*-D-Ribopyranose.

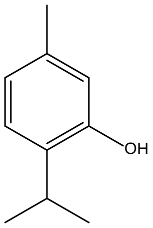
B. *β*-D-Deoxyribopyranose.

C. *α*-D-Ribopyranose.

D. *β*-D-Ribofuranose.

E. *α*-D-Glucopyranose.

4. Thymol is a antiseptic, used in gastrointestinal diseases.



Specify reagents for qualitative detection of thymol.

A. $FeCl_3$; Br_2.

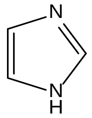
B. $K_2Cr_2O_7$.

C. HCl; Br_2.

D. NaOH; C_2H_5OH.

E. $ZnCl_2$; Cl_2.

5. Imidazole is a heterocycle that underlies in such drugs as naftizin, metronidazole, etimizol, and others.



Specify the electronic effects of the pyrrole atom of Nitrogen.

A. -M.

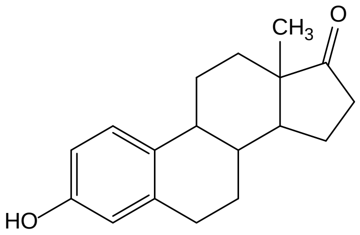
B. -I; +M.

C. +M.

D. +I; +M.

E. -I; -M.

6. Estrone is a female sex hormone.



Specify the reagent for qualitative detection of phenolic estrone hydroxyl:

A. $NaHCO_3$.

B. $ZnCl_2$.

C. $K_2Cr_2O_7$.

D. $AgNO_3$.

E. $FeCl_3$.

7. Choose a compound, that is formed during the rancidity of fats:

A. Glycerin + higher carboxylic (fatty) acids.

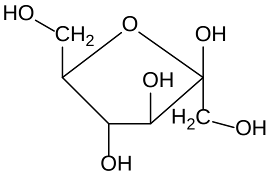
B. A mixture of acids.

C. A mixture of alcohols.

D. A mixture of aldehydes.

E. Acrolein + higher fatty acids.

8. Fructose is a ketohexose, found in fruits, honey.



Indicate the phenomenon that causes a positive reaction of the "silver mirror" to fructose:

A. Epimerization.

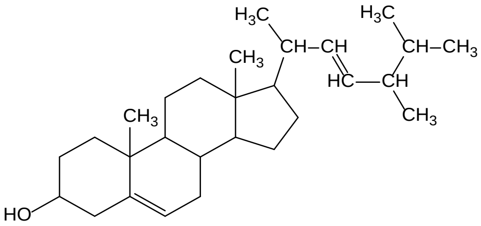
B. Tautomerism.

C. Mutarotation.

D. Structural isomerism.

E. Enantiomerism.

9. Ergosterol is a plant sterol.



Specify the reagent that can be used to prove the presence of alcohol hydroxyl in the ergosterol molecule:

A. $AgNO_3$.

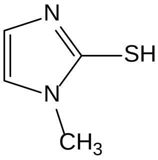
B. $FeCl_3$.

C. $K_2Cr_2O_7$.

D. $Cu(OH)_2$.

E. I_2 (KOH).

10. Mercazolyl is an antithyroid drug of the following structure:



Choose the most correct systematic name for mercazolyl:

A. 2-Mercapto-3-methylimidazole.

B. 1-Methyl-2-mercaptoimidazole.

C. 1-Methyl-2-thiopyrrole.

D. 1-Methyl-2-thiopyrazole.

E. 1-Methyl-2-mercaptopyrazole.

11. Specify the compound that is a cellulose monomer:

A. Fructose.

B. Arabinosis.

C. Ribose.

D. Galactose.

E. Glucose.

12. Choose the strongest acid in the following range:

A. $Cl(CH_2)_4COOH$.

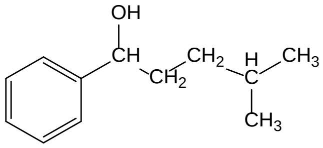
B. $ClCH_2COOH$.

C. $Cl(CH_2)_5COOH$.

D. $Cl(CH_2)_2COOH$.

E. $Cl(CH_2)_3COOH$.

13. 4-Methyl-1-phenylpentanol-1 is one of the 300 components that create the smell of cocoa.



What class of organic compounds does it belong to?

A. Ketone.

B. Tertiary alcohol.

C. Phenol.

D. Secondary alcohol.

E. Primary alcohol.

14. Specify the reagent by which you can distinguish between glucose, glycerin and acetaldehyde:

A. $Cu(OH)_2$.

B. Ag_2O.

C. $KMnO_4$.

D. $FeCl_3$.

E. $K_2Cr_2O_7$.

15. Natural fats have a liquid or solid consistency. Indicate the main reason for the existence of fats in a physical state:

A. The ratio of saturated and unsaturated acids.

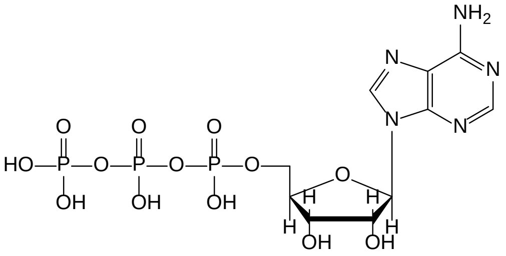
B. The size of molecules.

C. The presence of hydrogen bonds.

D. The method of synthesis.

E. Solvation of molecules.

16. The formula of adenosine triphosphate is the following:



Specify the types of bonds between phosphoric acid residues in the ATP molecule:

A. Amide.

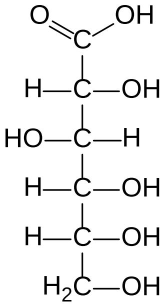
B. O-glycosidic.

C. Ester.

D. Etheric.

E. Anhydride.

17. Specify the most acceptable reagent with which you can obtain gluconic acid from glucose:



A. $KMnO_4$.

B. H_2SO_4.

C. $K_2Cr_2O_7$.

D. HNO_3.

E. Bromine water.

RECOMMENDED LITERATURE

Basic

1. Chernykh, V. P. Organic Chemistry. Basic lecture course : the study quide for students of higher schools / V. P. Chernykh, L. A. Shemchuk ; ed. by V. P. Chernykh ; NUPh. - 5th ed., rev. - Kharkiv : NUph : Golden Pages, 2019. - 440 p.

Additional

1. Bruice P. Y. Organic Chemistry : Hardcover / P. Y. Bruice, 6th ed. Prentice Hall, 2010. - 1440 p.
2. Clayden J. Organic Chemistry : Paperback / J. Clayden, N. Geeves, S. Warren. – 2nd ed. – Oxford University Press, 2012. – 1234 p.
3. Smith M. B. March's Advanced Organic Chemistry. Reactions, Mechanisms, and Structure Hardcover / M. B. Smith, J. March. – 6th ed. – Wiley, 2007. – 2384 p.

Information resources

1. A Publication of Reliable Methods for the Preparation of Organic Compounds // Organic Syntheses. URL : http://www.orgsyn.org
2. Chemical Synthesis Database. URL : http:/www.chemsynthesis.com
3. SynArchive : A total synthesis database // SynArchive. URL : http://synarchive.com
4. Organic chemistry Portal. URL : http://www.organic-chemistry.org
5. Antypenko Oleksii. Playlists. URL : https://www.youtube.com/c/OleksiiAntypenko/playlists
6. Educational E-library // Department of Organic and Bioorganic Chemistry. URL : https://zsmu.sharepoint.com/sites/orgchem/SitePages/NMZ.aspx