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Кафедра органической и медицинской химии

TASKS AND EXERCISES OF ORGANIC CHEMISTRY FOR STUDENTS OF MEDICAL AND PHARMACEUTICAL SPECIALTIES OF KFU

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The textbook is intended for students of medical and pharmaceutical profile, studying the discipline of organic chemistry in the framework of a bachelor's, master's or specialist's degree. The textbook consists of typical tasks and exercises in organic chemistry, including exercises aimed at establishing the structure-property relationship of physiologically active compounds or primary, secondary and intermediate metabolites obtained in the process of biosynthesis.

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Preface

This manual is a collection of typical tasks for medical and pharmaceutical students studying organic chemistry as part of a bachelor's, master's or specialist's degree and contains tasks classified according to the main sections of the program of the discipline "organic chemistry".

It should be noted that this manual is an accompanying material for an improved lecture course in organic chemistry, developed at the Department of Organic and Medicinal Chemistry of the Alexander Butlerov Institute of Chemistry especially for medical and pharmaceutical students. Maintaining continuity in the classical development of the course of organic chemistry, the authors tried to take into account the specifics of these profiles as much as possible. This training course precedes to a certain extent for an interested audience further training sessions in specialized disciplines such as biochemistry, pharmacology, cell and molecular biology, microbiology, virology, etc.

The manual is divided into sections, each of which corresponds to the classes of bioorganic compounds included in the lecture course. A special place in the textbook is given to the problems of systematization and nomenclature of bioorganic compounds, since most of them, in addition to the name according to the systematic nomenclature (IUPAC nomenclature), have trivial names used in medical practice. The collection presents a large series of problems of the biosynthetic and biochemical plan, in solving which it is necessary to use modern methods of both organic synthesis and the latest achievements in the field of biosynthesis.

Many problems are complex, and their exhaustive competent solution supposes not only good knowledge by students of the basics of organic chemistry, chemical properties and basic methods of transformation of organic molecules, but also their understanding of the relationship between the main classes of bioorganic compounds, as well as the laws of "structure of a compound – its bioproperty". In other words, having mastered the course of organic chemistry, the student must know the based properties (both chemical and physical) of classes of bioorganic compounds, be able to analyze the structure of an organic compound and possess the skills of conducting a retrosynthetic analysis, on the basis of which conclusions can be drawn about the toxicity, biodegradation and biotransformation of organic compounds *in vivo* or *in vitro*.

1. Introduction to organic chemistry

- What is the organic chemistry?
- Classification of organic compounds by the R-X formula.
- Valence state of carbon atom.
- Isomers and homologues.
- Geometrical parameters of organic molecules.
- Methods for drawing chemical structures.

Tasks:

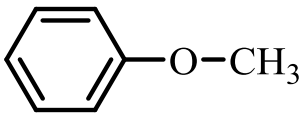
1. Give the definition to following concepts: chemical bond, electronegativity, isomers, chirality, σ- and π-bonds, radical, functional group, molecular formula, structural formula, boiling point, melting point, solubility.

2. Which of the statements are true which are false?

a) Isomers differ in qualitative and quantitative composition;
b) Hexene-1 and cyclohexane are stereoisomers;
c) A substance with formula $\mathbf{C_8H_{16}}$ can be either saturated or unsaturated;
d) Homologues have the same qualitative and quantitative composition;
e) Butin-2, like butene-2, exists in two geometric isomers;
f) In the combustion of any organic substance is released water and carbon dioxide;
g) The boiling point of a substance depends only on the molecular weight of the substance.

3. Indicate the type of valence state (sp-C_{di}, sp^2-C_{tr}, sp^3-C_{te}) of carbon and oxygen atoms in molecules below. Indicate the number of σ- and π-bonds. What is the direction of the σ-bonds of carbon and oxygen atoms (tetragonal, trigonal, diagonal)?

a. $H_2C{=}CH{-}CH_3$ b. $H_2C{=}CH{-}C{\equiv}CH$ c. $H_2C{=}C{=}CH_2$

d. $HC{\equiv}C{-}CH_2{-}OH$ e. $H_3C{-}\overset{\overset{O}{\|}}{C}{-}OH$ f. 

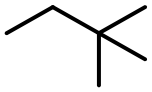
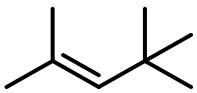
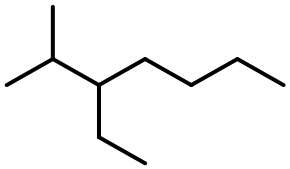
4. From modern organic chemistry perspectives, the formulas presented in task № 3 are redundant. Nowadays, the formulas of organic compounds are presented without displaying carbon atoms and C–H bonds. Draw the structures of the given compounds using "linear formulas":

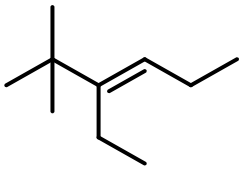
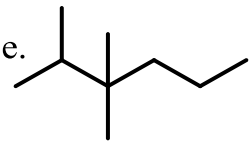
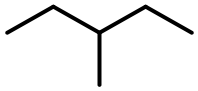
a) 5-Methylhexanol-2; b) 3-Ethylhexene-1; c) 4-Chloropentene-2;
d) Phenylcyclohexane; e) 3-Methyl-5-ethylheptane; f) 3,5-Dimethylhexadiene-1,3;

g) Dimethyldiethyl-methane; h) 4-Methyl-2-isopropyl-1-hexene-4-ol; i) 5-Chloro-2-ethylhexanole;

j) 2,6-dimethylaniline; k) *trans*-1,2-Diaminocyclohexane; l) 1,2-Diaminobutane.

5. Name these compounds according to rational nomenclature and according to IUPAC, calculate the molecular weight:

a.  b.  c. 

d.  e.  f. 

6. Draw the structural formulas of hexane isomers with at least 1 secondary carbon atom.

7. Draw the structural formulas of all hydrocarbons, with a molecular weight of no more than 100, containing a quaternary carbon atom.

8. Draw the structural formulas of all hydrocarbons, with a molecular weight of no more than 90, capable of *cis-trans* isomerism.

9. Draw the formulas of all structural isomers of the compound with the formula **$C_5H_{10}O$** that don't contain unsaturated fragments.

10. Describe the polarity of the bond and the shift of the electron density in these compounds. Which mechanism (homolysis, heterolysis) will the bond breaking predominantly proceed?

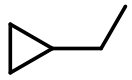
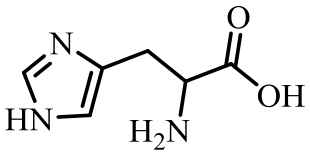
a) **CH_3–H**; b) **CH_3–CH_3**; c**) C_2H_5–OH**; d**) C_2H_5O–H**; e) **C_4H_9–Li**

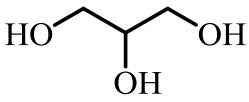
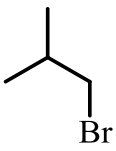
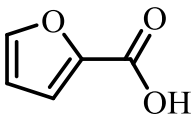
11. Draw Lewis structures (according to the octet rule) for the following substances:

a) **CH_3Br**; b) **C_2H_6**; c) **$C(O)Cl_2$**; d) **NH_2–NH_2**; e) **NH=NH**; f) **N≡N**; g) **H–C≡N**

12. Bond energy is the minimum energy required for the homolytic breaking of a chemical bond. A lower bond energy is characteristic for less strong bonds. The energy of the C–C simple bond is 83 kcal/mol, and the C=C double bond is 148 kcal/mol. Why do the addition reactions in alkenes proceed through double bonds, and not through single bonds?

13. Indicate the character of the hydrocarbon chain in the compounds below (cyclic, acyclic, aliphatic, aromatic, heterocyclic). What compounds are mono- and polyfunctional?

a.  b.  c. 

d.  e.  f. 

14. From the structures listed below, select substances that:

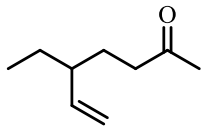
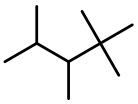
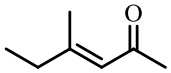
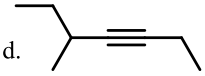
a) can exist as *cis*- and *trans*- isomers (draw these isomers);

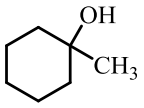
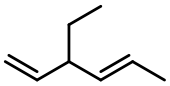
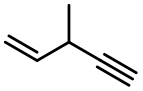
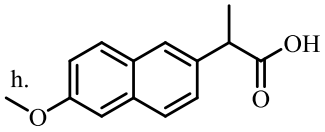
b) can exist as optical isomers (draw these isomers);

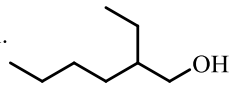
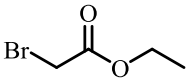
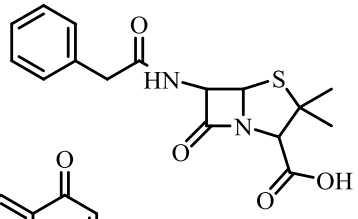
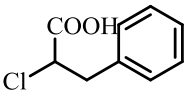
c) are structural isomers;

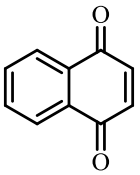
d) contain a system of conjugate multiple bonds.

Indicate the functional groups that are part of these substances.

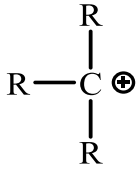
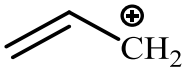
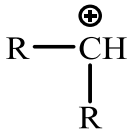
a.  b.  c.  d. 

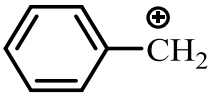
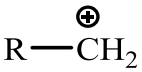
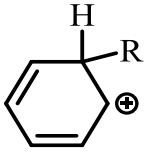
e.  f.  g.  h. 

i.  j.  k.  l. 

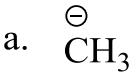
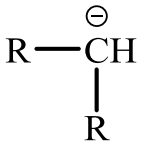
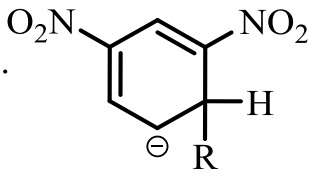
m. 

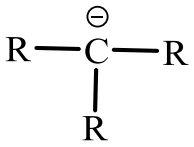
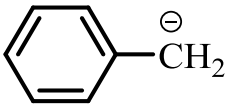
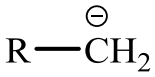
15. Arrange the following carbocations in order of increasing stability. What caused your choice? Use icons: > , < , ≈ .

a.  b.  c.  d. 

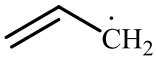
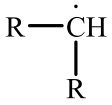
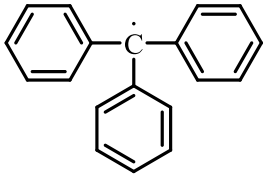
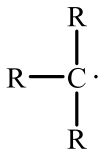
e.  f.  g. 

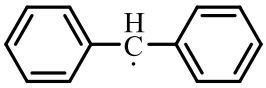
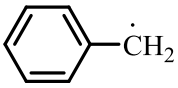
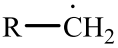
16. Arrange the presented carbanions in order of increasing stability. What caused your choice? Use icons: > , < , ≈ .

a.  b.  c. 

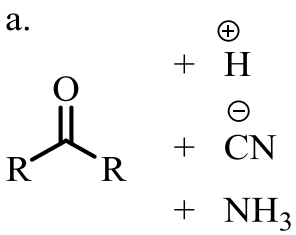
d.  e.  f. 

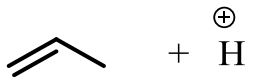
17. Arrange the following radicals in order of increasing stability. What caused your choice? Use icons: > , < , ≈ .

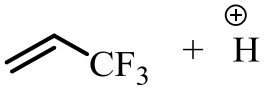
a.  b.  c.  d. 

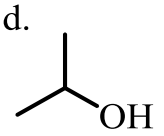
e.  f.  g.  h. 

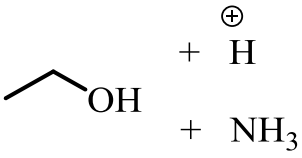
18. What particles are called electrophiles and nucleophiles? Which fragment of the reacting molecule an attack of the electrophile or nucleophile will be directed in the schemes listed below?

a. 

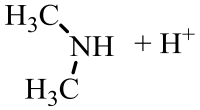
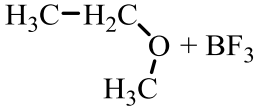
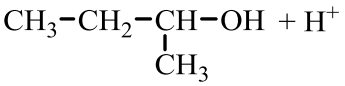
b. 

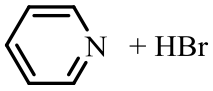
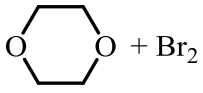
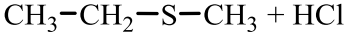
c. 

d. 

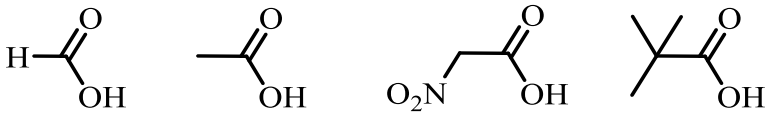
e. 

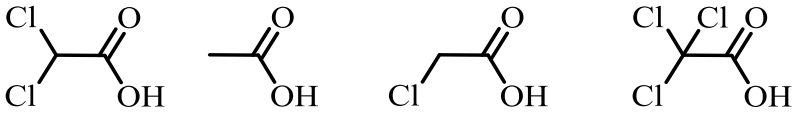
19. Give the definition of Lewis acid, Lewis base. What is the difference between Lewis's theory of acids and bases and the protolytic Bronsted-Lowry theory? Complete the schemes of chemical transformations given below, what types of chemical bonds are formed in the products of the given reactions

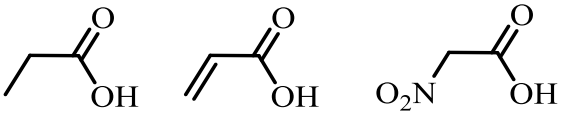
a.  b.  c. 

d.  e.  f. 

20. Give a definition of the concept of acid in the Bronsted-Lowry theory. Arrange the compounds below in order of increasing acidic properties.

I. 

II. 

III. 

2. Hydrocarbons

- Classification of hydrocarbon radicals (R).
- Saturated, unsaturated, aromatic hydrocarbons.
- General concepts of cyclic and heterocyclic compounds.

Tasks:

1. How does the structure of hydrocarbons affect such physical properties as boiling point, melting point, viscosity? How do these characteristics depend on the degree of branching of the molecule?

2. In the photochlorination of methane, in addition to the products of various degrees of methane substitution ($CHCl_3$, CH_2Cl_2, $CHCl_3$, CCl_4), the reaction mixture also contains small amounts of chlorinated derivatives of ethane. How can you explain their appearance?

3. Write the possible reaction products of isopentane with chlorine in the light. Which product will dominate and why? Which product will be predominantly formed during the sulfochlorination of isopentane in the light? ($R–H + SO_2 + Cl_2 \rightarrow R–SO_2Cl + HCl$)?

4. A hydrocarbon with the molecular formula $\mathbf{C_5H_{12}}$ forms only one product in the reaction with 1 mol of chlorine. What is the structural formula of isomeric pentane?

5. What reaction products can be obtained during the electrolysis of a solution of sodium salt of: a) butyric acid; b) isobutyric acid; c) isovaleric acid; d) cyclohexanecarboxylic acid?

What products can be obtained by heating these same solid salts with alkali?

6. The electrolysis of an aqueous solution of the RCOOH gave the compound $\mathbf{C_6H_{14}}$, which is also can be formed during the catalytic hydrogenation of 2,3-dimethylbutene-2. Establish the structure of the acid and write the reaction schemes.

7. The reaction of an unknown bromoalkane with sodium leads to the formation of a single product with a molecular weight of 114; the ratio of primary, secondary and tertiary carbon atoms in this product is 2:1:1. What structure is corresponding to the reaction product and the initial bromoalkane?

8. What cyclic alkanes are called strained? Compare the chemical properties of cyclopropane, cyclobutane, cyclopentane and cyclohexane in the reaction with hydrogen bromide, bromine, oxidizing agents.

9. Bromination of a cycloalkane with the formula $\mathbf{C_6H_{12}}$ leads to the formation a single product containing 65.5% bromine by weight. Determine the formula of the initial hydrocarbon, as well as the formulas of the reaction products.

10. Chlorination of a cycloalkane with the formula $\mathbf{C_6H_{12}}$ leads to the formation of three products containing 45.7% chlorine by weight. Determine the formula of the starting hydrocarbon, as well as the formulas of possible reaction products.

11. What alcohol is obtained by hydration of 2,4-dimethylpentene-2? What product will be obtained when this alkene is hydrated in the presence of an acid? In the presence of alkali? In the presence of peroxides?

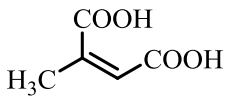
12. Determine the seniority of the deputies in the following ranks according to the *E,Z* -nomenclature:

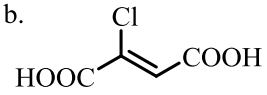
a) CH_3, Cl, Br, CF_3;

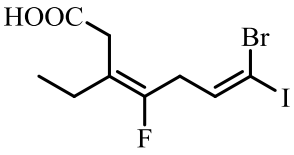
b) CN, COOH, I, F;

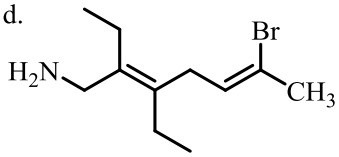
c) NH_2, F, COH, CH_3.

13. Determine the geometric configuration of double bonds according to the *E,Z*-nomenclature:

a. 

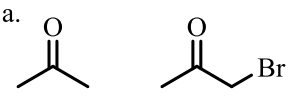
b. 

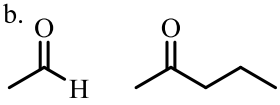
c. 

d. 

14. The alkene obtained by dehydration of isopropanol was involved in the Prilezhaev reaction. The resulting compound interacts with hydrogen chloride. Write the reactions, name the obtained compounds according to the IUPAC nomenclature.

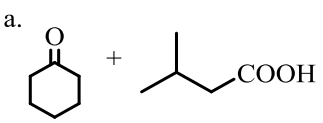
15. Write an alkene, the ozonolysis of which leads to the production of the following products:

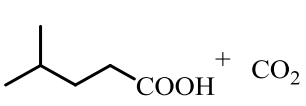
a. 

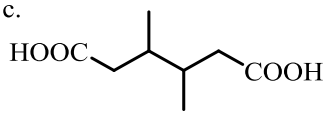
b. 

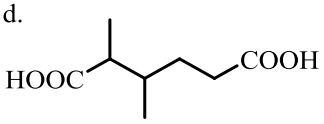
16. What isomers of pentene can be used to produce secondary alcohols? Tertiary alcohols?

17. Which alkenes need to be oxidized to get the following compounds?

a. 

b. 

c. 

d. 

18. 2,5,5-trimethylhexadiene-1,3 reacted with one equivalent of hydrogen bromide. The analysis of the obtained compound was carried out using ozonolysis. What

bromine derivative was obtained if trimethylacetic acid aldehyde is present among the ozonolysis products?

19. Suggest a method for obtaining rubber products from potatoes. Calculate the maximum mass of rubber that can be obtained from 1000 kg of potatoes if the starch content in the tubers is not more than 22%, and the reaction yield at each stage is not more than 90%.

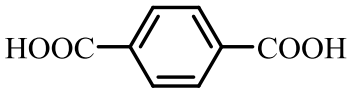
20. Draw diene synthesis products between: a) isoprene and butadiene; b) isoprene and acrylonitrile; c) cyclohexadiene-1,3 and crotonaldehyde; d) maleic anhydride and cyclopentadiene; e) cyclopentadiene and acetylene dicarboxylic acid diethyl ester.

21. What reactions can be used to distinguish between butin-1 and butin-2?

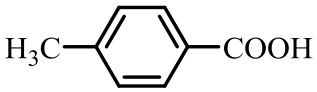
22. Compare the molecular structures of 2-butene and 2-butyne. How can you explain the presence of geometric isomers in the first case and the absence of them in the second?

23. What products are obtained by the interaction of isopropylacetylene with: a) water in the presence of $HgSO_4$; b) hydrogen bromide; c) ammonia solution of Ag_2O; d) Grignard reagent; e) acetaldehyde in the presence of alkali; f) metallic sodium?

24. What structure correspond to aromatic hydrocarbon with the formula $\mathbf{C_9H_{12}}$ if terephthalic acid was obtained during its exhaustive oxidation, and *p*-toluic acid is present among the products during oxidation under mild conditions?



terephthalic acid



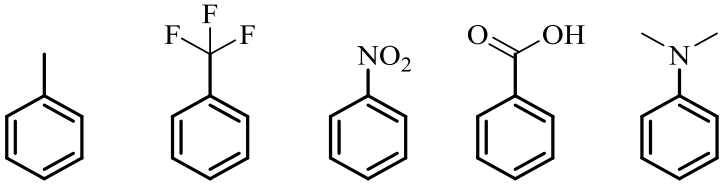
***p*-toluic acid**

25. What compound should be taken for the reaction with benzyl bromide to obtain isobutylbenzene by the Wurtz reaction? What co-products can be formed in this case?

26. What substances do you need to start from in order to obtain by the Friedel-Crafts reaction: a) methylbenzene; b) 4-isobutyl toluene; c) *p*-xylene.

Write the reaction equations and indicate the conditions for their implementation.

27. Name these compounds by the IUPAC nomenclature. Which ones are easier to nitrate than benzene? Why? Which position is preferred for nitration?



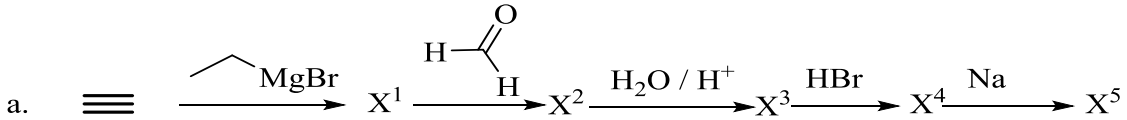
a. b. c. d. e.

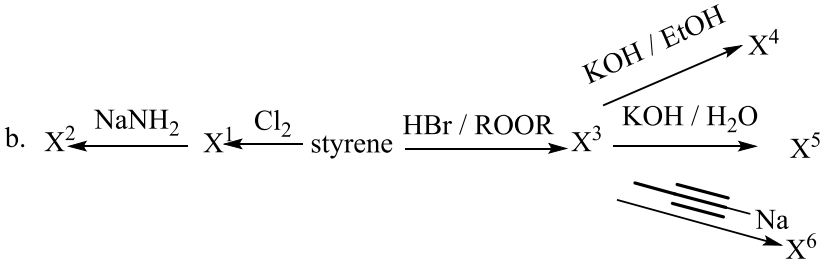
28. What substances are predominantly formed during alkylation: a) *p*-nitrotoluene; b) *o*-nitrotoluene; c) *o*-methoxybromobenzene; d) *o*-dichlorobenzene;

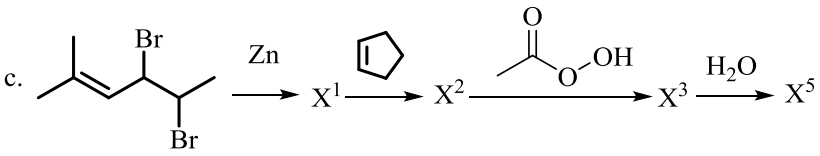
e) *p*-toluenesulfonic acid; f) *m*-dimethoxybenzene; g) *p*-phenolsulfonic acid; h) *m*-chlorobenzenesulfonic acid.

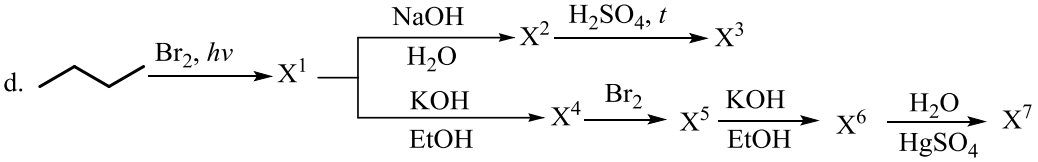
29. Write the sequence of reactions required to obtain *p*-bromobenzoic and *m*-bromobenzoic acids from benzene.

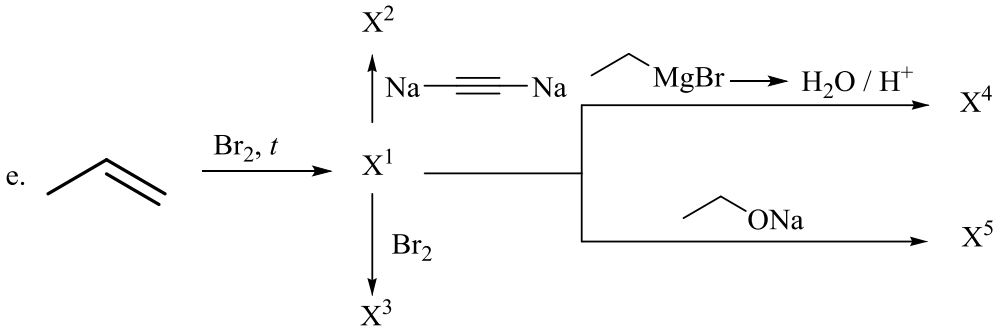
30. Decode chain reactions:

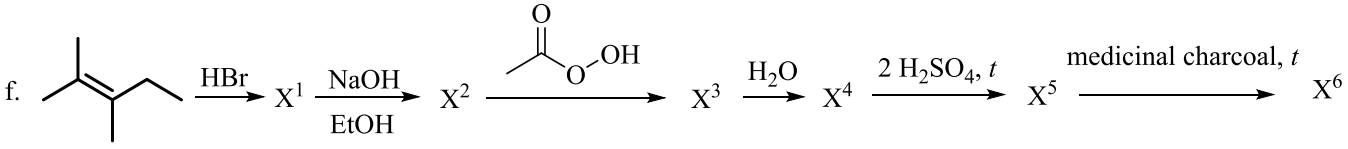




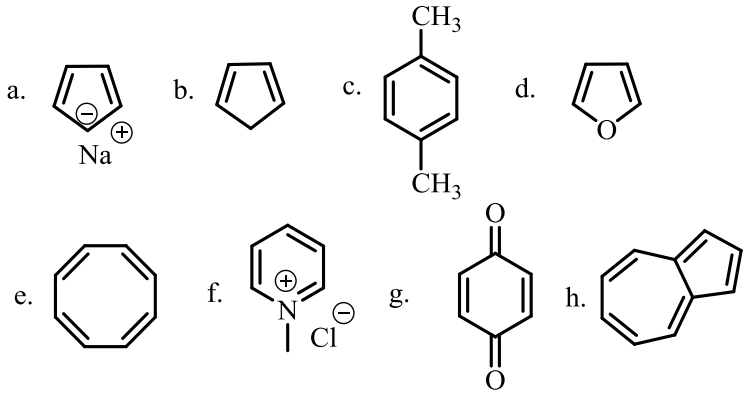




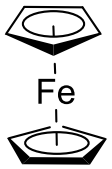




31. What are the criteria for aromaticity? Formulate the Hückel rule. Which of the following compounds are aromatic:



32. The reaction between potassium cyclopentadienide with $FeCl_2$ forms a compound $(C_5H_5)_2Fe$ called ferrocene (**A**). Write a reaction scheme and explain the high resistance of this compound to heat, the action of acids and bases, and its ability to enter into substitution reactions. Write the reaction of ferrocene bromination.



A

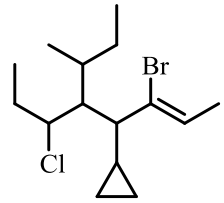
33. Polycyclic aromatic hydrocarbons are hazardous to the environment due to their potential toxicity, mutagenicity and carcinogenicity. However, in 1988 it was discovered that the enzyme, PYR-1 dioxygenase isolated from *Mycobacterium vanbaalenii*, degrades the 4-ring pyrene. Further, the NJS-P gene was isolated from *Mycobacterium sp*., it's encoding the synthesis of an enzyme, dioxygenase, capable of oxidizing various polyaromatic compounds to the corresponding quinones and phenols. Anthracene, phenanthrene, pyrene and benzo[a]pyrene are enzymatically oxidized. Using anthracene as an example, write the reaction of its oxidation to quinone. What products can be formed during the oxidation of phenanthrene, pyrene and benzo[a]pyrene?

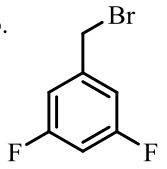
3. Haloalkanes, alcohols, phenols

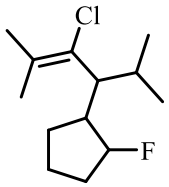
- Classification of functional groups (X).
- Natural alcohols and phenols. Anesthetics.
- Polyatomic alcohols, inositol.

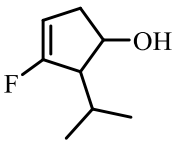
Tasks:

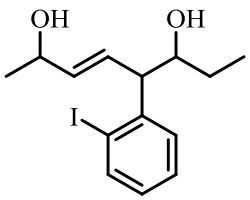
1. Name the compounds according to IUPAC nomenclature:

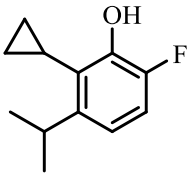
a. 

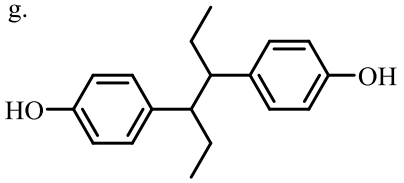
b. 

c. 

d. 

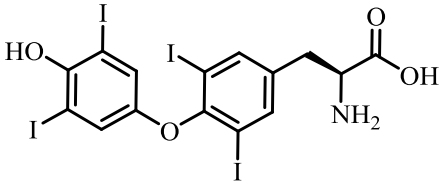
e. 

f. 

g. 

2. List all isomeric secondary and tertiary alcohols of compound $C_6H_{14}O$. Name them by rational nomenclature and by IUPAC nomenclature. How many isomeric alcohols contain an asymmetric center?

3. Thyroxine or T_4 (**A**) is a hormone produced by the thyroid gland. It was first isolated in 1919 by E.K. Kendall from dried biological product of the thyroid glands. Thyroxine affects metabolism, increases body temperature, controls the growth and development of the body, increases protein synthesis and sensitivity to catecholamines, increases heart rate, enhances oxidative processes in the cells of the whole body, in particular in the brain cells. *L*-thyroxine or levothyroxine is a synthetic analogue of thyroxine. It is used to normalize the thyroid gland in hypothyroidism. Indicate what substituents and functional groups are contained in the thyroxine molecule. Write the formation of phenolate anion using the thyroxine molecule as an example.



A

4. Chloroethane is one of the medicines used in anesthesiology. Currently, chloroethane is rarely used for anesthesia. When in contact with the skin, it causes a strong cooling of the skin, ischemia and a decrease in sensitivity, due to rapid

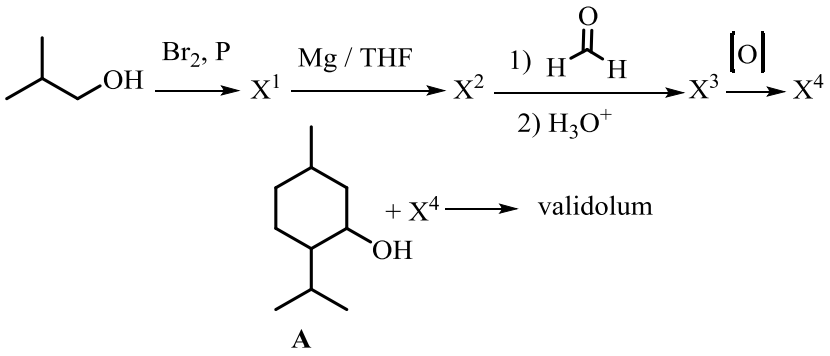
evaporation, which makes it possible to use it for small superficial operations (skin incisions). What are the ways to get this anesthetic?

5. Propyl bromide belongs to the group of organobromine compounds. It is a transparent liquid, very slightly soluble in water, but well soluble in acetone, benzene, ethanol and other organic solvents. It is used for organic synthesis: flavorings, dyes, pharmaceuticals, Grignard reagent, cleaning agents, etc. Write for it the equations of reactions with the following substances: a) potassium cyanide, b) ammonia, c) sodium ethylate, d) sodium, e) sodium hydrosulfide, f) sodium sulfide, g) magnesium (in the presence of diethyl ether), h) aqueous and alcohol solutions of alkali.

6. Isopropanol (propanol-2) is a secondary alcohol widely used in medical practice as an antiseptic, liquids for cars (mainly windshield washers, as well as antifreezes) in glass cleaners, office equipment and as a solvent for industrial organic substances. Write down the possible methods for obtaining isopropanol.

7. Ethanol is widely used in various branches: in medicine as an antiseptic, in pharmacy for the preparation of extracts, tinctures, industry as a feedstock for the production of acetaldehyde (**X^1**), chloroform (**X^2**), diethyl ether (**X^3**), synthetic rubber (**X^4**) and other organic substances. Write the reactions (schemes) for obtaining substances **X^1**, **X^2**, **X^3**, **X^4**.

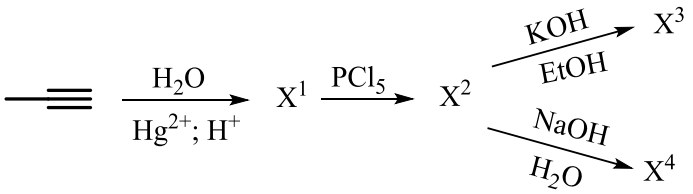
8. The medicine "Validolum" is used in cardialgia and motion sickness syndrome, is an ester of menthol alcohol (**A**) and acid (**X^4**). Solve the chain and determine which acid ester is validol. Name menthol according to the systematic nomenclature.



A

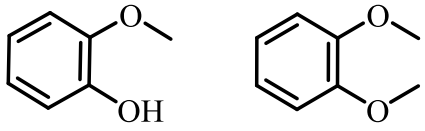
9. Isobutyl alcohol (2-methylpropanol-2) has long been used in various fields. It is used as a solvent, rubber additive, desiccant, printing ink component, varnish, paint remover, perfume, etc. Draw the structure of isobutyl alcohol, give it a name according to the systematic nomenclature. Get it using Gringard synthesis. Dehydrate it. Oxidize the dehydration product with a dilute aqueous solution of $KMnO_4$.

10. In the chain of transformations, substance **X^2** contains a halogen derivative used as a component of insecticides. What kind of substance is it? Name it according to the systematic nomenclature. What is the difference between the interaction of substance **X^2** with an excess of alkali in aqueous and alcoholic solution?



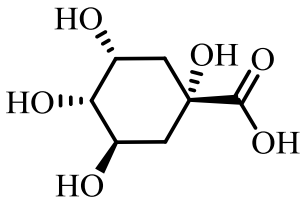
11. Glycerin (propantriol-1,2,3) is the first member of trihydric alcohol series. It is a viscous transparent liquid with a sweet taste. Write the reaction for obtaining glycerin from triolein. What compound is formed as a result of the interaction of glycerin with nitric acid in the presence of concentrated sulfuric acid? Write a reaction, give a name to the product. What is the use of this compound in medical practice?

12. Guaiacol (**A**) and veratrol (**B**) are pyrocatechol derivatives. They are found in nature and can be used in the production of medicinal (**A**) and fragrances (**B**) substances. Name compounds **A** and **B** according to the systematic nomenclature. Suggest a way to obtain them in laboratory conditions from pyrocatechol. How does the oxidation process of pyrocatechol take place?



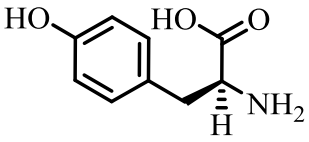
A **B**

13. In 1820, French chemists P.J. Pelletier and J.B. Cavantou isolated hydroquinone (*para*-dihydroxybenzene) during the distillation of quinic acid (**A**). Nowadays it used as a developing agent in the photo industry, in cosmetic medicine for skin whitening; as an antioxidant in food and rubber production, etc. Write the reaction of obtaining hydroquinone from quinic acid (**A**). What compound is formed as a result of hydroquinone oxidation? Write the reaction. React with the resulting product with 1,3-butadiene.

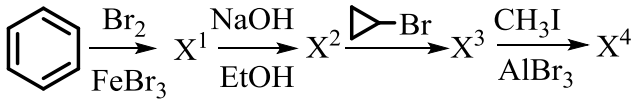


A

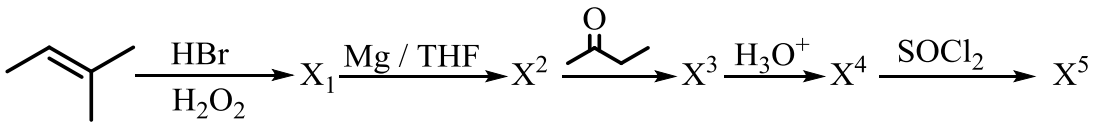
14. The proteinogenic amino acid Tyrosine (**A**) regulates lipid metabolism, promotes the production of melanin and improves the functions of the adrenal, thyroid and pituitary glands. It is a structural derivative of carbolic acid, which has been known since 1834.Carbolic acid is toxic to humans in its pure form. Solve the chain, name the intermediate products, analyze the options for obtaining carbolic acid and its properties.



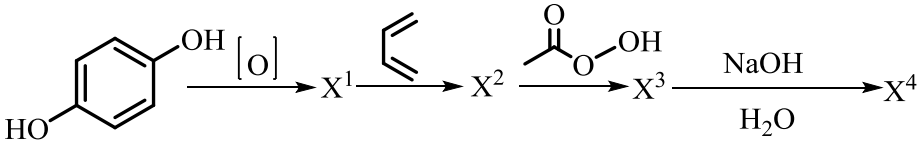
A



15. Solve the chain of transformations, specify the structures of substances $\mathbf{X^1}$-$\mathbf{X^5}$?

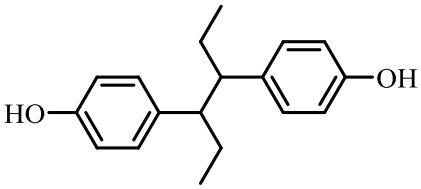


16. Solve the chain of transformations, name the products. What class of organic compounds does the $\mathbf{X^4}$ product belong to?



17. What reactions can be used to convert butanol-2 into: a) 2-fluorobutane, b) butanethiol-2, c) *sec*-butylethyl ether.

18. Sinestrol (**A**) is a hormonal agent that helps to normalize the menstrual cycle of women of childbearing age, to stop the manifestation of climacteric syndrome. It prevents the development of osteoporosis. What class of organic derivatives does (**A**) belong to? Write the reactions (**A**) with: a) sodium hydroxide, b) acetic anhydride, c) bromine.

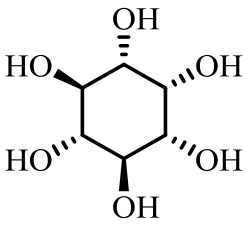


A

19. Get 4,7-dimethyldecene-5 from pentanol-2, acetylene and other necessary reagents. Does this product have optical activity?

20. Determine the structure of the compound of the composition $\mathbf{C_3H_5Br}$ if it is known that this compound does not react with potassium cyanide and the ammonia complex of silver, but turns into 2,2-dibromopropane in the reaction with hydrogen bromide.

21. Inositols are polyols having a six-carbon ring structure where each carbon is hydroxylated. Some of these stereo isomers are biologically active, one of which myo-inositol (**A**) is the most common. It is part of membrane phospholipids and provides osmoregulation. Its phosphorylated derivatives act as secondary messengers in signaling pathways, promote protein phosphorylation, etc. Using example (**A**), get the mono- and diphosphoric esters of myo-inositol. How many steroidal forms does inositol have?



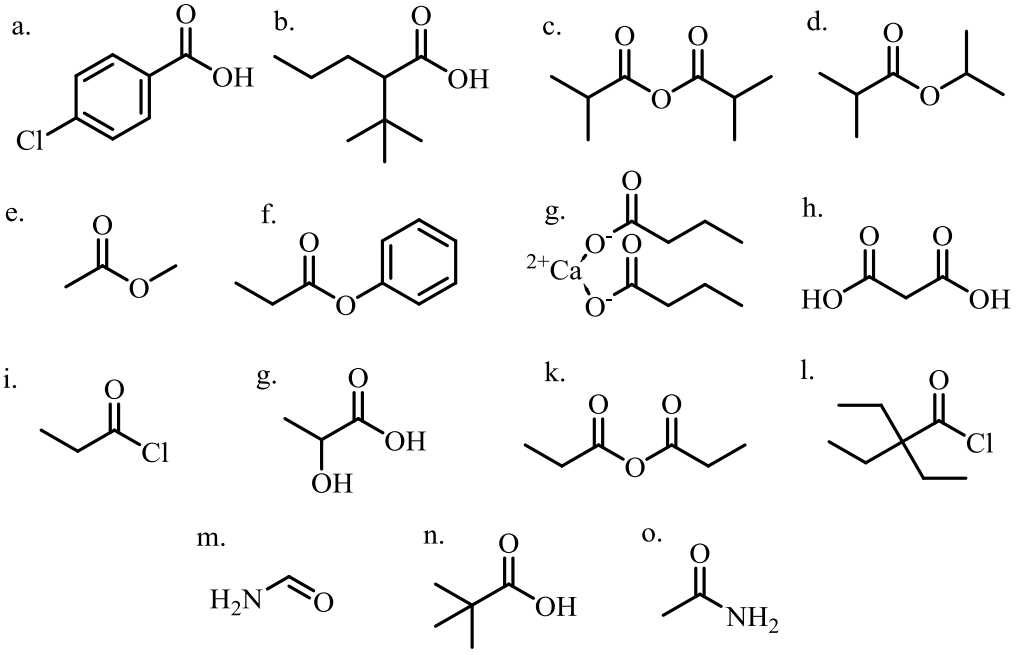
A

4. Carbonyl compounds and derivatives. Carboxylic acids

- Claisen condensation.
- Aromatic acids.
- Hydroxy acids.
- Shikimic acid and shikimate biosynthesis pathway.
- Medicinal compounds obtained by nucleophilic addition to the carbonyl group.

Tasks:

1. Name the compounds according to IUPAC nomenclature:



2. Draw the structural formulas: a) 2-chloro-4-methylhexanone-3, b) 2,3-dimethylbutanal, c) methylethylketone, d) 3-methylbutene-2-al, e) diisopropylketone, f) 4-methylpentanal.

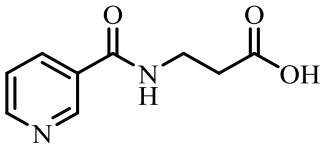
3. Formaldehyde is the first member of the aliphatic aldehydes series. It was synthesized firstly in 1859 by A.M. Butlerov. It is used in medicine for the preservation of biological materials, disinfection, as an antimicrobial reagent. Formaldehyde has a wide range of uses, although it is a carcinogen. Suggest ways to get formaldehyde? Write the reactions of formaldehyde with: a) ammonia solution of silver oxide, b) ethanol, c) hydrogen cyanide.

4. Benzaldehyde is the first member of the aromatic aldehydes series. Benzaldehyde is found in bitter almonds and bird cherry. One of the first studies of bitter almond oil was carried out by N.N. Zinin in 1840. Benzaldehyde has found its application in the perfumery industry as a composition for perfumes, cosmetics and other fragrances. What chemical methods for obtaining benzaldehyde do you know? Write

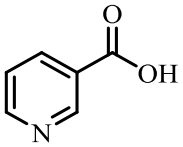
down the reactions of benzaldehyde with: a) hydrocyanic acid, b) isopropylmagnesium bromide, d) $KOH_{conc.}$, E) nitric acid in the presence of sulfuric acid.

5. Write the reaction of aldol-crotonic condensation of isovaleric aldehyde. Name the resulting products.

6. Picamilon (**A**) is a nootropic that improves the functional state of the brain due to the normalization of tissue metabolism and the effect on cerebral circulation, which is involved in many redox reactions, the formation of enzymes and the metabolism of lipids and carbohydrates in living cells. It is a derivative of nicotinic acid (**B**) – niacin, vitamin PP, vitamin B_3. In the 1914s, American physician Joseph Goldberger studied a painful skin disease called pellagra, and he found that it was caused by a lack of vitamin PP. How can you get picamilon from nicotinic acid? Write down your reasoning in the form of chemical reactions.

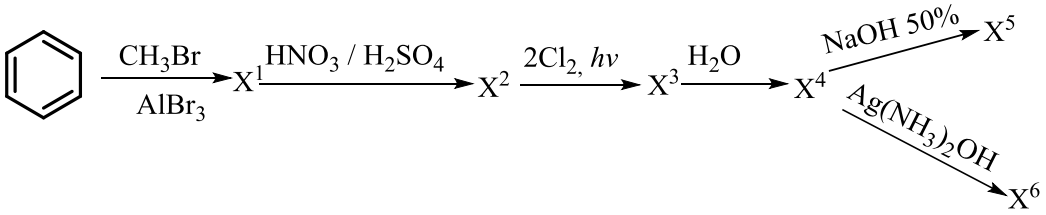


A

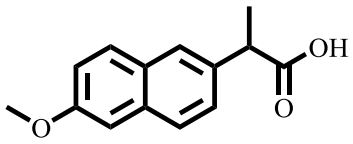


B

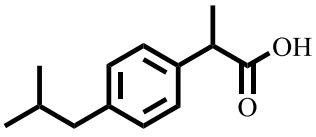
7. Solve the chain of transformations, name the products $\mathbf{X^5}$ и $\mathbf{X^6}$.



8. Naproxen (**A**) and Ibuprofen (**B**) are non-steroidal anti-inflammatory medicines that have anti-inflammatory, analgesic and antipyretic effects. They are used in their pure form and are part of many combination medicines. Which functional groups are contained in naproxen and ibuprofen molecules? Name the compounds according to IUPAC. Write for their reactions: a) with ethanol, b) with thionyl chloride, c) with ammonia, d) with NaOH.



A



B

9. Butyric acid is one of the most important low molecular weight acids that are synthesized naturally in the intestines. It is the main energetic material for epithelial cells and maintains intestinal homeostasis. How to get butyric acid from propyl bromide using Gringard synthesis?

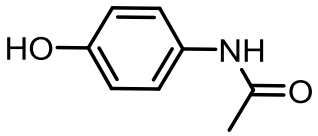
10. Write the reaction products of isobutyric acid with: a) isopropyl alcohol (acid catalyst), b) with PCl_3, c) P_2O_5, heat, d) with methylamine.

11. Methyl propionate is a substance used in various industries as a flavoring agent, as a solvent for oils and cellulose. Write a Claisen ester condensation for it.

12. Solve the chain of transformations, name the product **X**^{5}:

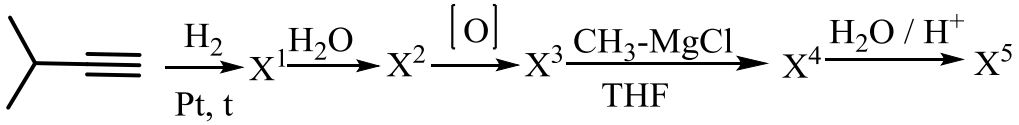
$$CaC_2 \xrightarrow{2\ H_2O} X^1 \xrightarrow[Hg^{2+};\ H^+]{H_2O} X^2 \xrightarrow{LiAlH_4} X^3 \xrightarrow{Br_2,\ P} X^4 \xrightarrow{Mg\ /\ THF} X^5$$

13. Paracetamol (**A**) is a non-steroidal anti-inflammatory agent, has an analgesic, an antipyretic and weak anti-inflammatory effect. Paracetamol has been known since 1886, but its first retail sale began only in 1953, due to insufficient research. What functional groups are contained in the paracetamol molecule? Propose a method for obtaining paracetamol from *p*-aminophenol.



A

14. Solve the chain of transformations, name the products:

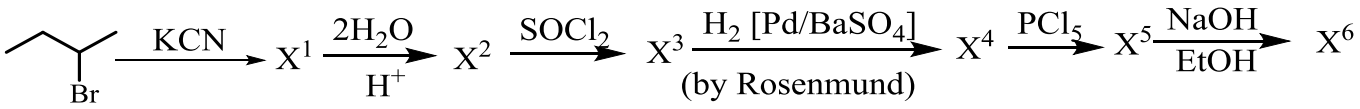


15. Write the equations with which you can carry out the following transformations:

Heptane → methylcyclohexane → toluene → benzoic acid

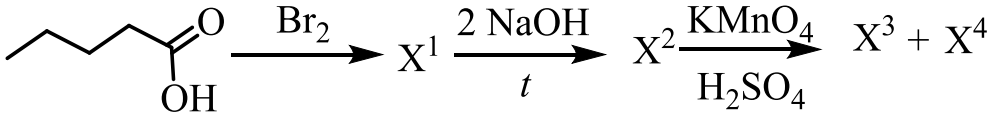
16. A substance having formula $(CH_3CH_2CO)_2O$ interacts with an aqueous solution of sodium carbonate with the gas evolution of carbon dioxide upon heating. Name this substance and explain how it is formed.

17. Solve the chain of transformations, name the products:

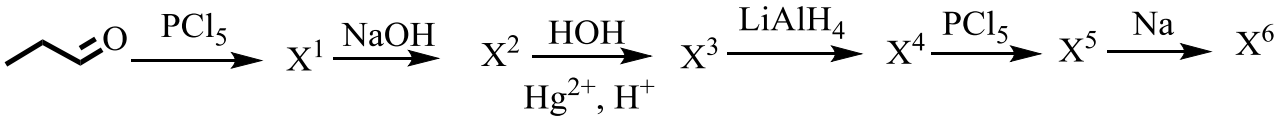


18. Suggest a way for the synthesis of 5-hydroxypentanoic acid lactone from cyclohexanone.

19. Solve the chain of transformations, name the products **X**^{3} и **X**^{4}:



20. Solve the chain of transformations, name the product **X**^{6}:

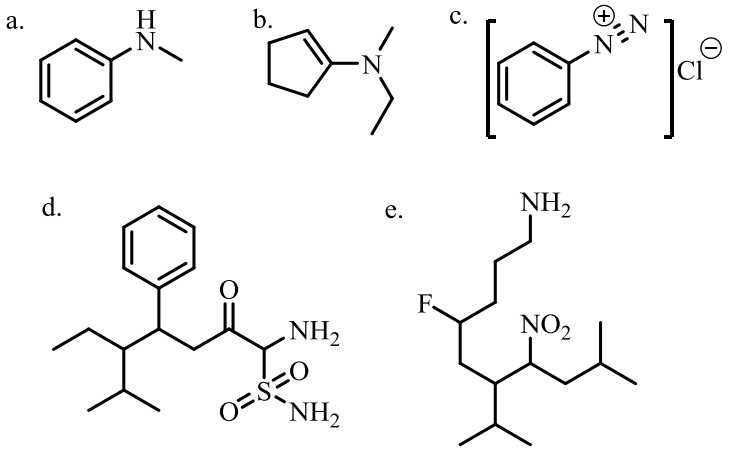


5. Nitrogen containing functional groups

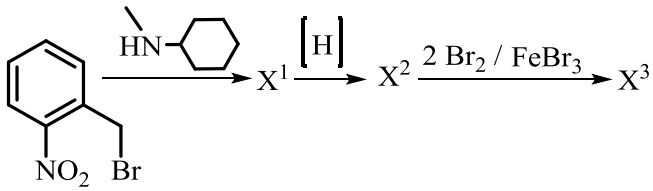
- Reactions of azo coupling.
- Amines, diazo-, azo compounds.
- Nitro compounds used in medicine.
- Nitrogen-containing medicines: main representatives.

Tasks:

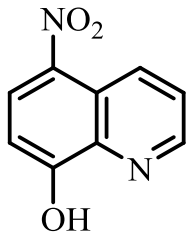
1. Name the compounds according to IUPAC nomenclature:



2. Bromhexine (**X^3**) is a non-narcotic medicine that has an expectorant and antitussive effect. It is used for bronchitis, bronchial asthma, tuberculosis and other diseases. Solve the chain and get Bromhexine. Name the intermediate products:



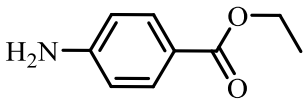
3. Nitroxoline (**A**) is an antimicrobial agent used for infectious and inflammatory diseases, mainly of the urinary tract. What functional groups are contained in the nitroxoline molecule? Write the reaction of nitroxoline with a mixture of Fe + HCl, then, with the resulting compound, carry out a reaction with a mixture of $NaNO_2$ + HCl.



A

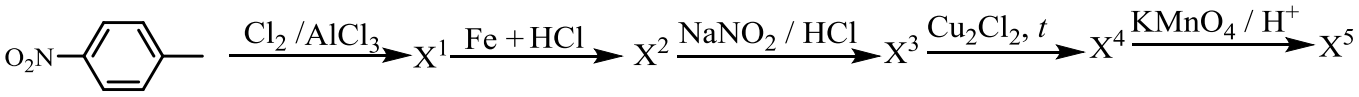
4. Anestezin (benzocaine) is a local anesthetic known since 1898. It is used in dentistry for surface anesthesia, for ear inflammation, for gynecological interventions,

etc. Propose a way for the synthesis of benzocaine (**A**) from *p*-nitrobenzoic acid. Give the names to intermediates.



A

5. Solve the chain of transformations, name the product $\mathbf{X^5}$:

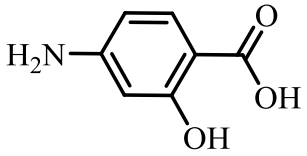


6. Consider the scheme of interaction of bromopropane with ammonia. Give the name of the resulting salt. Carry out sequential reactions of the resulting product with sodium hydroxide, bromomethane, then again with sodium hydroxide and chloroethane. Write down the reaction equations and name the products.

7. What compound is formed if the amide of isovaleric acid is interreacted with bromine and alkali, and the resulting product is acted upon with acetyl chloride? Write the reaction equations.

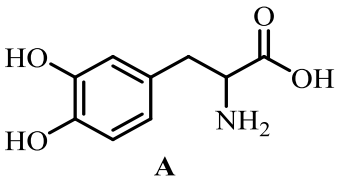
8. It was found that saponification gives the same amine that forms during the reduction of isobutyric acid nitrile when studying the structure of isonitrile. What is the structure of nitrile?

9. *p*-Aminosalicylic acid (**A**) is a medicine used in medical practice in the form of sodium salt in combination therapy for the treatment of tuberculosis and has a bacteriostatic effect. What functional groups are in the molecule? What can you obtain when *p*-aminosalicylic acid acts on a molecule: a) C_2H_5OH + Na, b) $KMnO_4$, H_2O, c) C_2H_5OH, d) CH_3CH_2COOH?



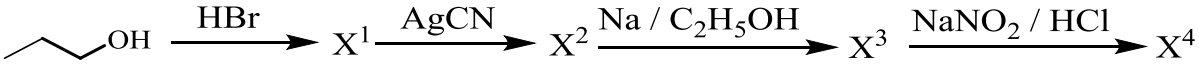
A

10. Levodopa (**A**) is an antiparkinsonian medicine. Parkinson's disease (or "tremor palsy") is characterized by reduced production of dopamine in the human brain. Nowadays, it is almost impossible to completely cure the disease, but it is possible to alleviate the condition of patients, for example, by regular replenishment of dopamine reserves. Levodopa undergoes decarboxylation and dopamine is released upon entering the human body. Write the decarboxylation reaction, name the starting and resulting product according to IUPAC. What substances are formed by the action on the resulting dopamine: a) $NaNO_2$ + HCl, b) an oxidizing agent, c) acetic acid chloride, d) ethyl bromide.

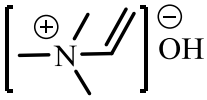


A

11. Solve the chain of transformations, name the products $\mathbf{X^1}$-$\mathbf{X^4}$:

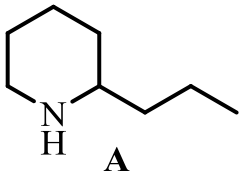


12. Neirin (**A**) is an organic compound, one of the products of putrefaction of protein bodies. It is contained in cadaveric poison. Name the neurin according to the systematic nomenclature. Write down the reaction of hydration of this compound in an acid solution.



A

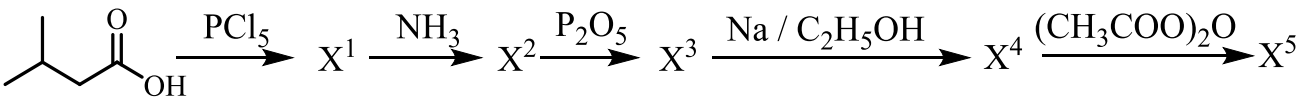
13. Coniine (**A**) is a naturally occurring N-containing organic compound found in Spotted Hemlock (*Conium maculatum*). Coniine is a neuroparalytic poison. Hemlock juice was used for execution in ancient times. Koniin is rapidly absorbed into the bloodstream from the digestive tract. After absorption, it causes paralysis of the endings of the sensory and motor nerves, and also affects the central nervous system, first exciting and then paralyzing it. Therefore, it is currently not used in medical practice. Name the coniin according to the systematic nomenclature. What products are formed during the interaction of koniin with: a) HCl, b) CH_3COCl, c) CH_3CH_2Br.



A

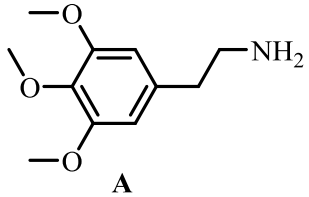
14. Establish the structure of the $\mathbf{C_7H_{10}N_2}$ compound, which under the action of a mixture of sodium nitrite and hydrochloric acid upon subsequent heating with CuCl, gives *p*-chlorobenzyl alcohol.

15. Solve the chain of transformations, name the products $\mathbf{X^1}$-$\mathbf{X^5}$:



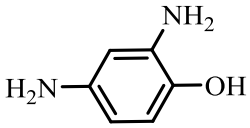
16. Antifebrin (acetanilide) is one of the first synthetic antipyretic agents previously used in veterinary practice. Since the medicine is easily hydrolyzed in the body, it should be used limitedly, in order to avoid the formation of methemoglobin, leading to hemolysis of erythrocytes and suppression of the heart. What products are formed as a result of acetanilide hydrolysis? Write the reaction, name the products.

17. Mescaline (**A**) is a nitrogen-containing organic compound known since the 1897s, which change perception and affects the emotional state and many mental processes. It occurs naturally in cacti (*Lophophora williamsii*). What class of organic compounds does mescaline belong to? Name the compound according to the systematic nomenclature. Write the reaction for the formation of mescaline hydroloride?



A

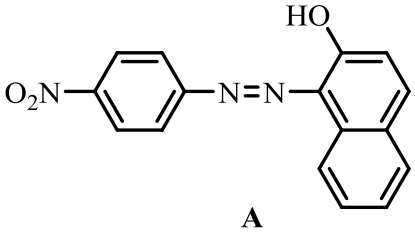
18. Amidol is an organic compound used since 1891 as a photographic developer. Name the amidol according to the systematic nomenclature. Suggest a method for obtaining Amidol from benzene?



A

19. What can happen with a diazonium salt solution if it is left at room temperature for several hours? Write down the reaction using phenyldiazonium hydrogen sulfate as an example.

20. What amines are formed as a result of the reduction of *p*-nitroaniline red (paranitraniline, Para Red) (**A**)? Suggest a method for obtaining (**A**) from *p*-nitroaniline.



A

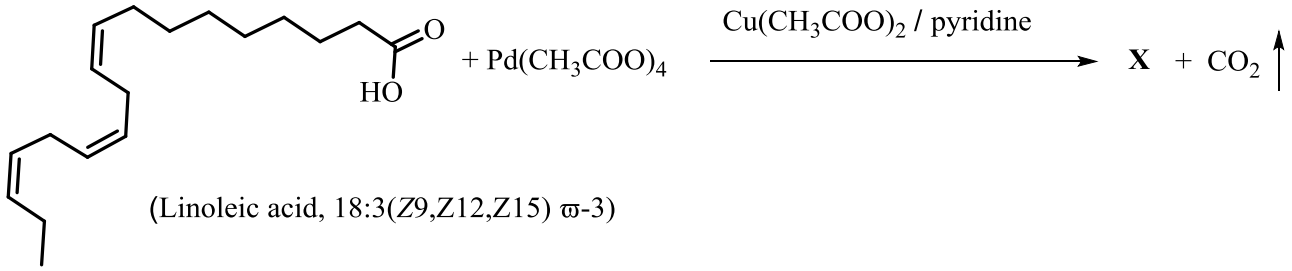
6. Lipids. Fatty acid. Therpene structures

- Nomenclature.
- Esters of glycerin, phospholipids, fatty alcohols.
- Terpene structures: bile acids, hormones.

Tasks:

1. Recent studies of the composition of oils of flowering plants Tladiany Doubtful (the Pumpkin family), growing in the Russian Far East and Northeast China, which is popular in traditional Chinese medicine, showed the presence of punicic acid (9*Z*, 11*E*, 13*Z*-octadeca-9, 11, 13-trienoic acid) 35.6% in its composition. Linoleic acid was up to 40% and oleic acid was compo8%. Draw the structure of punicic acid taking into account geometric isomerism. What is the difference between this acid and common polyunsaturated fatty acids – linoleic and oleic?

2. Vegetable fully *cis*-polyolefins are synthesized by oxidative decarboxylation of the corresponding fatty acids according to the following scheme:



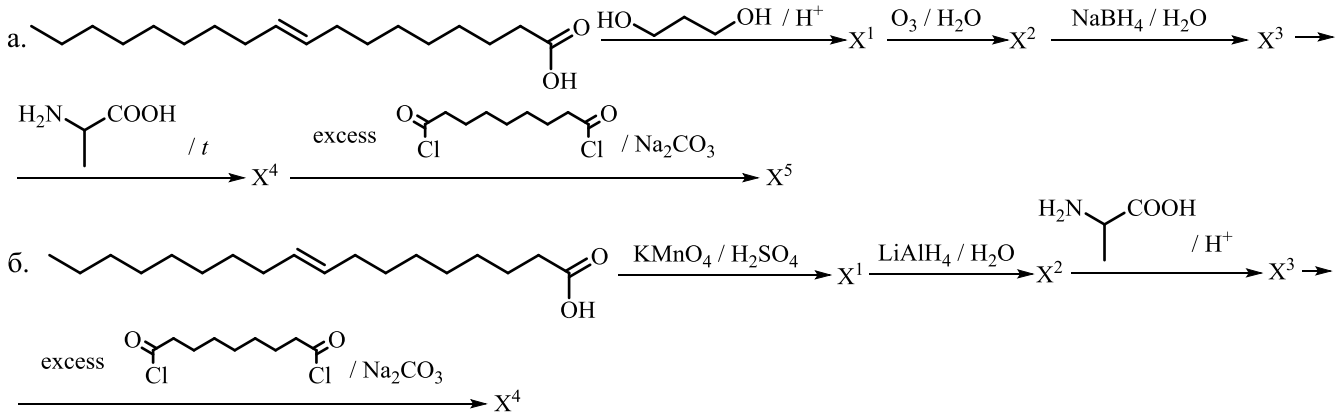
(Linoleic acid, 18:3(*Z*9,Z12,Z15) ϖ-3)

Write the reaction product (**X**) and name it IUPAC nomenclature.

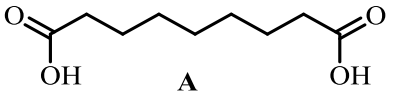
3. Maca or Peruvian ginseng (*Lepidium meyenii*) is a traditional food crop in the Peruvian Andes and now widely advertised as a dietary supplement. Among the various chemical components isolated from the plant is a unique series of non-polar long-chain N-benzyl fatty acid amides known as macamides. These amides are derivatives of oleic, linoleic and linolenic acids and benzylamine or 3-methoxybenzylamine. Give the structures of these macamides and suggest a method for obtaining them in the laboratory.

4. Within the framework of a comprehensive project dedicated to the study of fatty acids contained in blackcurrant oil (*Ribes nigrum*), attention was paid to the synthesis of triacylglycerols obtained from polyunsaturated fatty acids. There is growing evidence of the beneficial effect of γ-linolenic acid ((6*Z*, 9*Z*, 12*Z*) -octadeca-6,9,12-trienoic acid, (18:3(6*Z*,9*Z*,12*Z*), GLA) on the clinical improvement of a number of serious diseases among a number of such fatty acids. γ-Linolenic acid is an important component of black currant oil. Give the structure of glyceryl-1,2-di-γ-linoleate-3-palmiate. What type of ω-acids does γ-linolenic acid belong to?

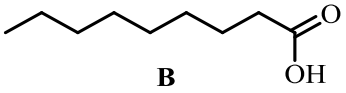
5. Non-toxic components based on lipids, diols, derivatives of oleic acid, amino acids and dicarboxylic acid chlorides were chosen as building blocks of new polymeric materials. The synthesis procedures were simple and carried out under mild conditions. Fill in the scheme of transformations:



6. Azelaic acid (**A**), which occurs naturally in wheat, rye and barley, also finds use as an active ingredient in ointments for the topical treatment of acne and for stimulating hair growth. It works by inhibiting the growth of skin bacteria that cause acne and keeping skin pores clear. Pelargonic acid (**B**), naturally occurring as ester derivatives in pelargonium oil, is used as an herbicide to prevent weed growth both indoors and outdoors. Give the methods of obtaining substances (**A**) and (**B**) starting from oleic acid.

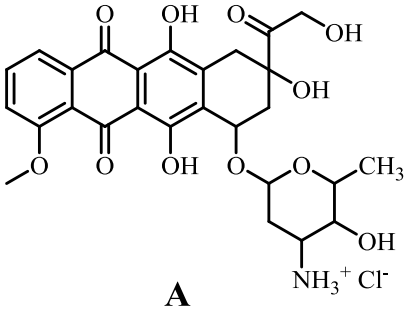


A



B

7. Doxorubicin (**A**) is the leading cytostatic medicine with many side effects. Scientists are still looking for methods that will preserve the therapeutic effect against tumor cells and reduce toxicity to normal cells. One of the approaches to reduce the toxicity of doxorubicin is obtain amide derivatives (**A**) by the reaction of the amino group with ω-3-polyunsaturated fatty acids. Write the reaction of obtaining an amide derivative of doxorubicin (**A**) with clupanodonic acid (*cis*-7,10,13,16,19-docosapentaenoic acid or 22:5(7*Z*, 10*Z*, 13*Z*, 16*Z*, 19*Z*).

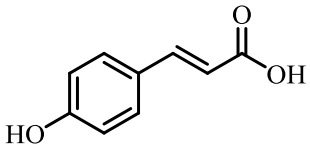


A

8. Suggest at least two chemical reactions that can be used to distinguish which of the two analyzed samples is saturated triacylglycerol, and which is beeswax. Give the

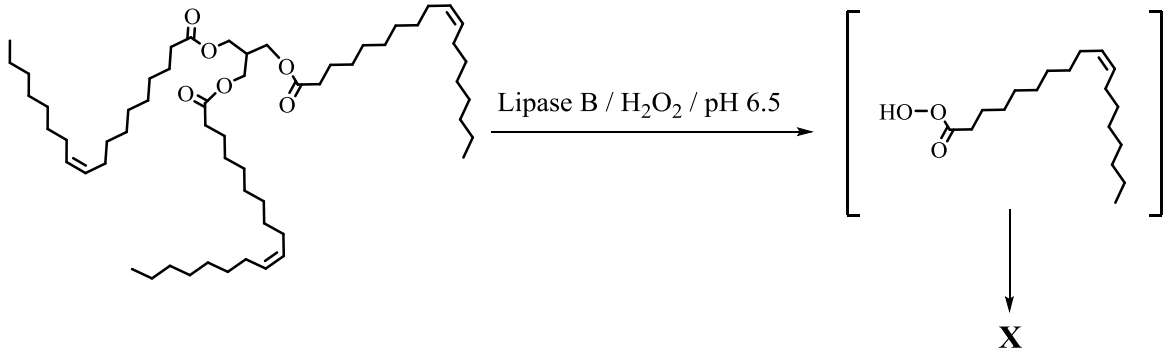
structure of triacontanoyl palmitate – an ester of palmitic acid and triacontanol alcohol (**$C_{30}H_{61}OH$**).

9. Defuscin is a new phenolic ester that has been shown to be a waxy substance, *n*-triaconyl *para*-coumarate, isolated from the herb *Dendrobium fuscescens Griff*, native to the central Himalayas and China. Write the reaction for obtaining defuscin using triacontanol (**$C_{30}H_{61}OH$**) and *para*-coumaric acid (**A**). For defuscin, write the reaction with peracetic acid.



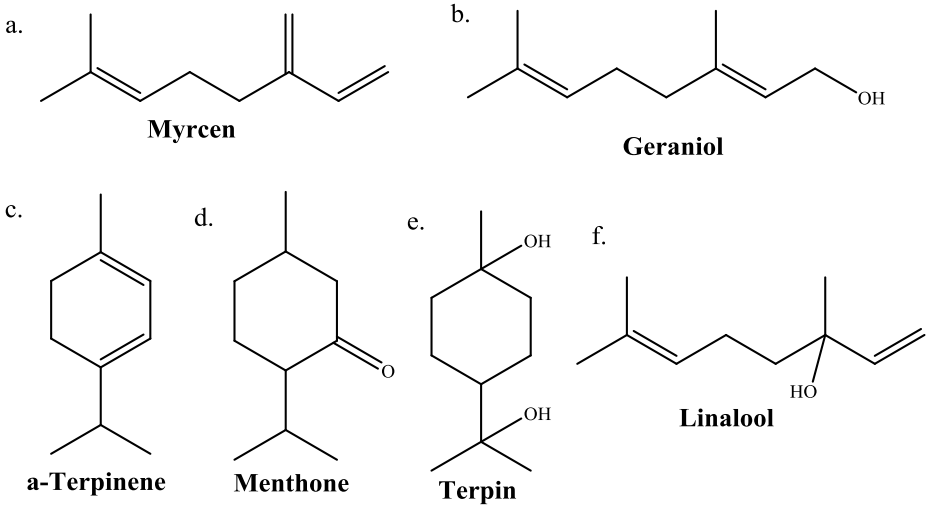
A

10. In 1990, Danish pharmaceutical company Novo Nordisk described the use of lipases for *in situ* production of peracids and subsequent epoxidation of olefins. Nowadays, this method has been applied due to the optimization and commercialization of the immobilized form of lipase *B*. The study of the epoxidation of triolein, it is a triglyceride obtained from glycerol and three units of oleic acid, showed the rapid formation of an intermediate peracid and its subsequent self-oxidation. Based on the above diagram, depict the structure of substance **X**.



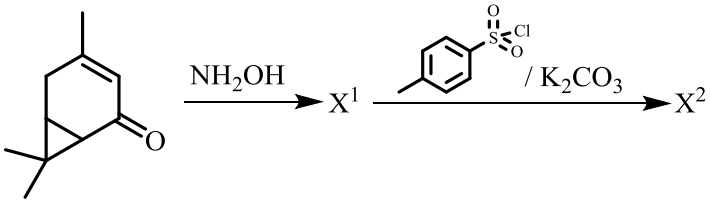
X

11. Name compounds according to IUPAC nomenclature:

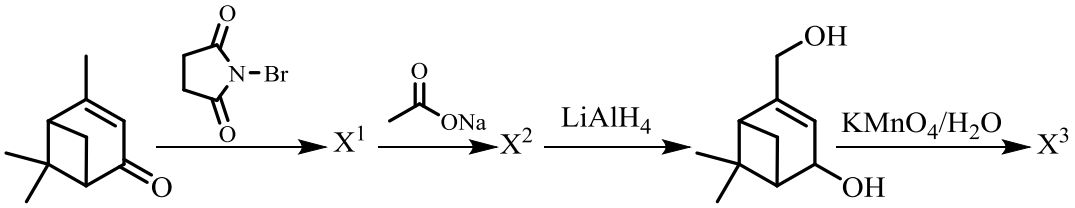


12. 3-Carene-5-one can be obtained by selective allylic oxidation of 3-carene without disturbing its natural carbon skeleton. This functional oxygenated derivative is a

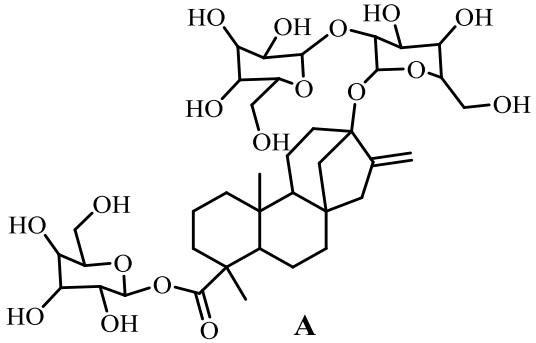
vital intermediate for the production of biologically active chemicals. On the other hand, oxime sulfonates are widely used in medicine and agrochemistry due to their various biological properties such as antiproliferative, insecticidal, antifungal and antibacterial activities. Using 3-carene-5-one as a starting material, decipher the scheme for obtaining sulfonates of 3-carene-5-one oxime.



13. (–)-Verbenone is a monoterpene isolated from the herb verbena. It is a colorless liquid with a woody-coniferous odor, which has antimicrobial action, attractant and repellent activity. Verbenone is obtained by oxidation of α-pinene and is the starting compound in the preparation of various biologically active substances. Solve the chain of transformations by indicating the structures of the substances **X¹-X³**.



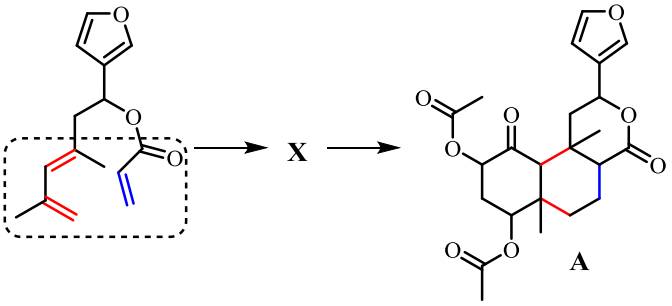
14. The main components isolated from the leaves of *Stevia rebaudiana Bertoni* (family *Asteraceae*) are the structurally similar glycosides stevioside and rebaudioside A. These compounds, known as stevia sweeteners, are glycosides of the isoprenoid, steviol. Stevioside is about 150-250 times sweeter than sucrose, while rebaudioside *A* is about 200-300 times sweeter than sucrose. Both are not high in calories. Using the structure of stevioside (**A**) as an example, carry out the hydrolysis of all ether bonds and get steviol, determine which classification group of isoprenoids steviol belongs to, and also name the number of chiral carbon atoms in its molecule.



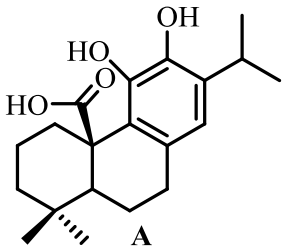
A

15. Salvinorin *A* (**A**) was isolated from the leaves of *Salvia divinorum*, a mexican medicinal plant also used in spiritual practices. Salvinorin *A* is the most potent naturally occurring hallucinogen known to date as a highly selective opioid receptor agonist. It is a promising leader in the treatment of central nervous system disorders, including depression, pain, and drug addiction because of the latter's unusual biological activity.,

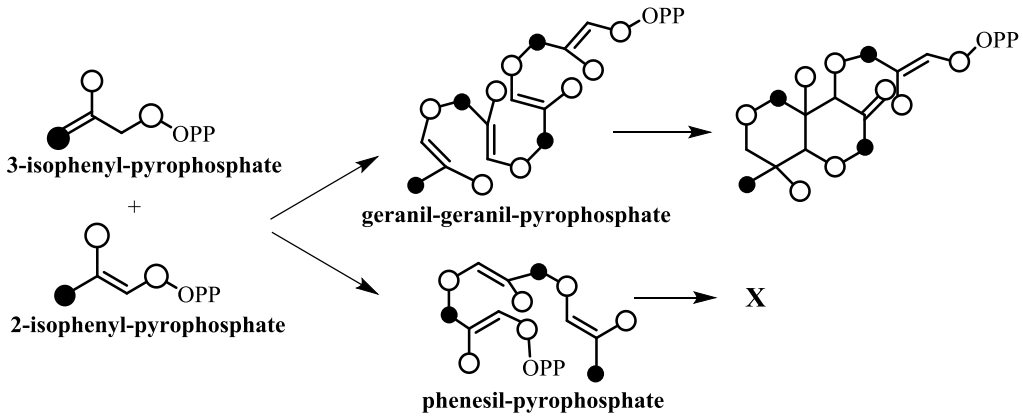
The reaction of [4+2]-cycloaddition (Diels-Alder) is used at one of the stages of synthesis (**A**). Draw the intermediate product (**X**) resulting from this reaction.



16. The main carbon skeleton of all diterpenes isolated from rosemary is carnosic acid (**A**), which was first isolated in 1965. It is now well known that this compound is the main constituent of rosemary, accounting for 1.5-2.5% of dried leaves. Carnosinic acid (**A**) exhibits antioxidant properties and is capable of reversibly oxidizing to the corresponding O-quinones of the abietane type, rosmaquinones. Draw the oxidation product of carnosic acid (**A**) and suggest an oxidizing agent.

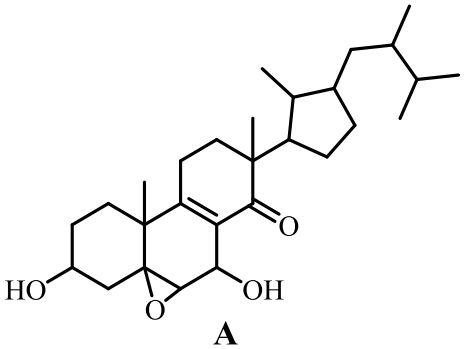


17. 3-Isoprenyl pyrophosphate and 2-isoprenyl pyrophosphate are starting materials for the biosynthesis of terpenoids in the classical mevalonate biosynthesis pathway. Farnesyl pyrophosphate and geranyl-geranyl-pyrophosphate are formed when 3-isoprenyl pyrophosphate interact with 2-isoprenyl pyrophosphate at the stage of biosynthesis, then in the course of various acts of intramolecular interaction, cyclic systems are formed. Using the example of farnesyl pyrophosphate from the above diagram, depict the structure of the bicyclic metabolite **X** (light and dark circles indicate carbon atoms, for convenience and clarity of Ruzicka's rule).



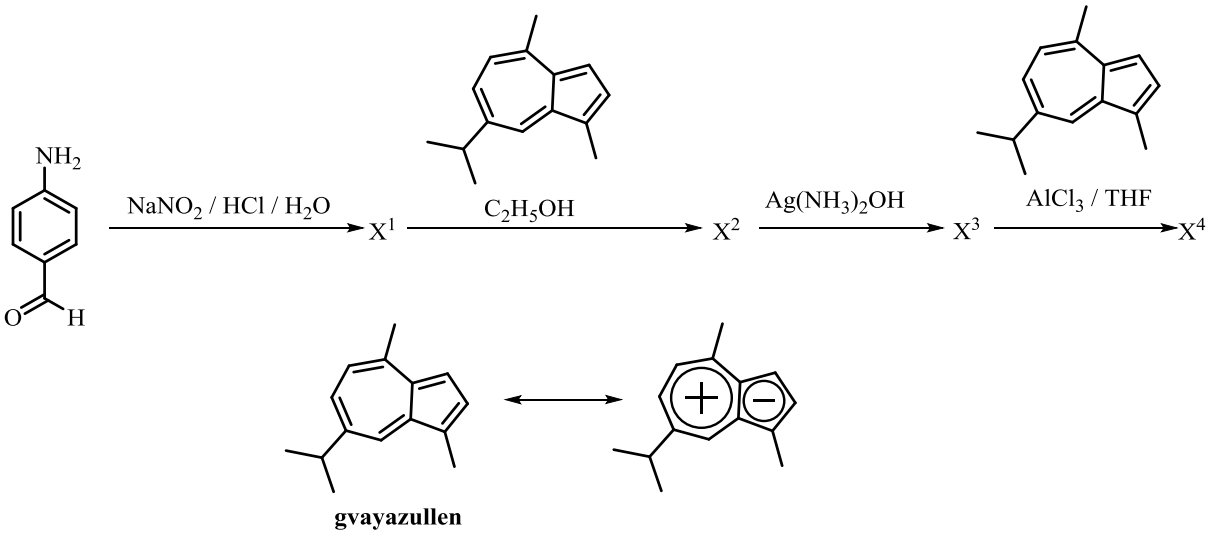
18. Strofasterin *A* (**A**) was recently isolated from the fungus *Stropharia rugosoannulata*, which is widespread in the northern temperate zone. Strofasterin *A* has been shown to reduce oxidative stress in neurons in the brain and thus may provide an

opportunity to treat Alzheimer's disease at the molecular level by stabilizing age-related and disease-related processes that induce oxidative and proteotoxic stress within brain neurons. Determine to which classification group of isoprenoids (**A**) belongs, which functional groups and how many chiral carbon atoms are included in its structure.



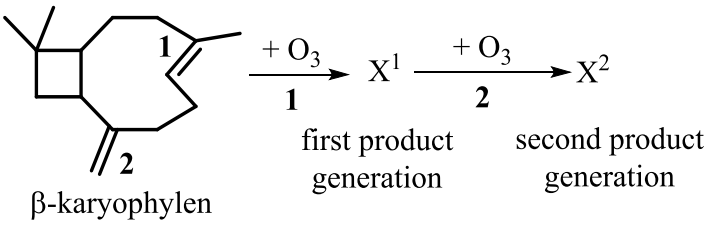
A

19. Fill out a conversion diagram showing an easy way to create new extended (and delocalized) π-electronic systems containing guaiazulene, which is a bicyclic sesquiterpene found in some essential oils such as guaiac and chamomile oils. Take into account that the guaiazulene molecule has a dipole moment, the diagram of which is shown below.



gvayazullen

20. Sesquiterpenes are isolated from flowers and foliage of various conifers and deciduous plants. Among the most common sesquiterpenes, β-caryophyllene is released during the growing season by pines, citrus fruits and various types of agricultural plants. It is assumed that, due to the rapid degradation of β-caryophyllene and the low volatility of some degradation products, β-caryophyllene has a high potential for the formation of suspended particles in the air. The structure of the degradation products of β-caryophyllene under laboratory conditions was determined by ozonolysis due to its high reactivity with respect to ozone and a high potential for the formation of aerosols. Supplement the scheme of β-caryophyllene ozonolysis.



β-karyophylen

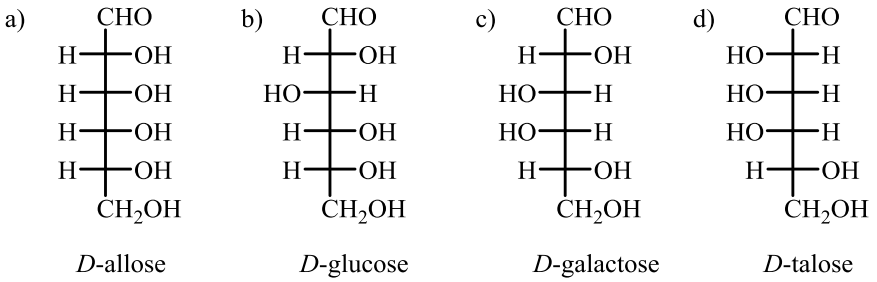
7. Carbohydrates

- Mono, di- and polysaccharides.
- Glycans, cyclodextrins.
- Sialic acids.
- Glycosides: N, O, S.

Tasks:

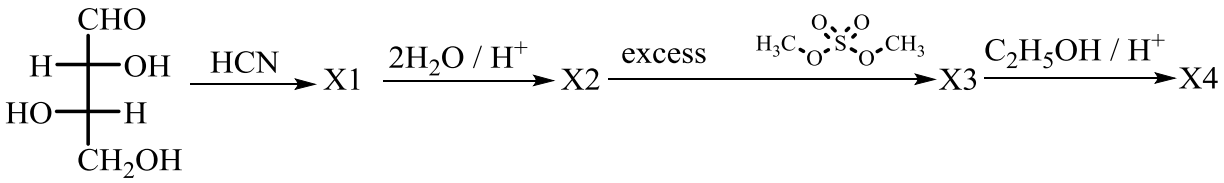
1. Write reactions that prove that in a molecule of *D*-mannose there are five hydroxyl groups and one aldehyde.

2. Write the cyclic forms (Hewors projection) of the following carbohydrates (a-d), determine the number of stereoisomeric forms for these carbohydrates.



3. Give the scheme for the reduction of *D*-altrose to hexahydric alcohol. Will the resulting alcohol have optical activity?

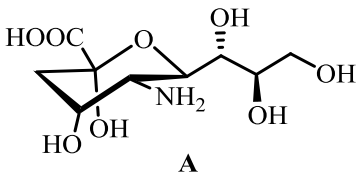
4. Solve the chain of transformations, name the products **X1**-**X4**:



5. Write the acylation schemes with acetic anhydride for the cyclic forms of *D*-ribose, *D*-glucose and *D*-galactose.

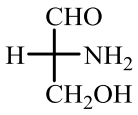
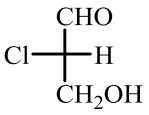
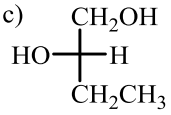
6. Write schemes for the epimerization of *D*-arabinose, *D*-lyxose and *D*-xylose.

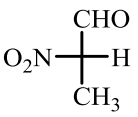
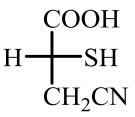
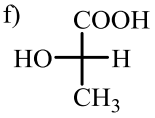
7. What compounds are called sialic acids? Using the example of neuraminic acid (**A**), give the scheme of its acylation with acetic acid chloride to the corresponding N-acetylneuraminic acid.



A

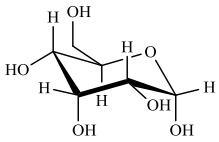
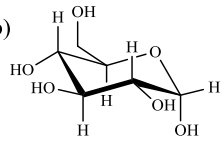
8. Name compounds using *D/L*-nomenclature.

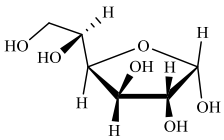
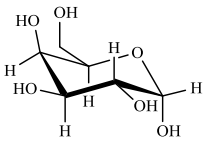
a) 
b) 
c) 

d) 
e) 
f) 

9. Write the reactions of *D*-mannose with the following compounds: a) Br_2 (H_2O); b) HNO_3; c) $NaBH_4$; d) Ag $(NH_3)_2OH$; e) $C_6H_5NHNH_2$; f) CH_3OH (HCl).

10. Using compounds a-d, write the reducing and non-reducing forms of disaccharides: a-d, b-c, c-d, b-d. Name the reducing disaccharides.

a) 
b) 

c) 
d) 

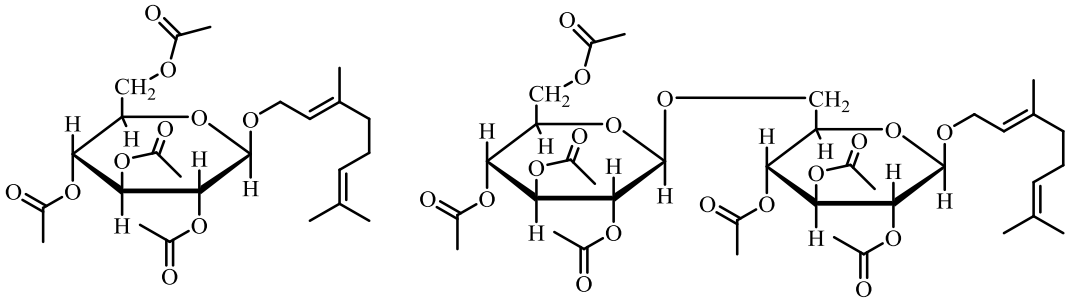
11. Xylitol is a five-carbon sugar alcohol and it widely found in nature but it is also a normal intermediate in human metabolism. It is used as an alternative sweetener, recommended for diabetics and for the prevention of dental caries. Xylitol is currently produced in large quantities chemically and by yeast, using yeast *D*-xyloreductase, enzymes that, using either NADH or NADP, reduce *D*-xylose to xylitol. Draw the structures of the pyranose and furanose forms of *D*-xylose, as well as the reaction of *D*-xylose reduction to xylitol.

12. All aldoses are capable of mutarotation. For example, α-*D*-galactopyranose has $[\alpha]_D$ = +150.7°, β-*D*-galactopyranose has $[\alpha]_D$ = +52.8°. If any of the galactose anomers are dissolved in water and allowed to reach equilibrium, the specific rotation of the solution is +80.2°. What percentage of each anomer is in equilibrium state? Draw the pyranose forms for both galactose anomers.

13. *L*-gulose can be obtained from *D*-glucose by a process that begins with oxidation to *D*-glucaric acid, which cyclizes to form two six-membered ring lactones. Separation of lactones and their reduction with sodium amalgam Na(Hg) reduces the –COOH group to primary alcohol and lactone to aldehyde, giving *D*-glucose and L-gulose. What are the structures of the two lactones, and which one is reduced to *L*-gulose?

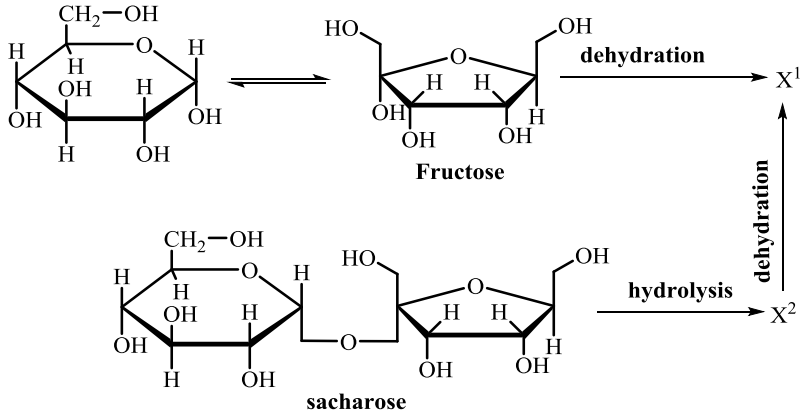
14. A number of terpene glycosides – β-rutinosides were isolated and characterized from the Muscat of Alexandria grape and wine obtained from it. Based on the structure of β-rutinosides (**A**) and (**B**), carry out the complete hydrolysis of these

compounds, give the name of the cyclic form of the main carbohydrate included in their composition.

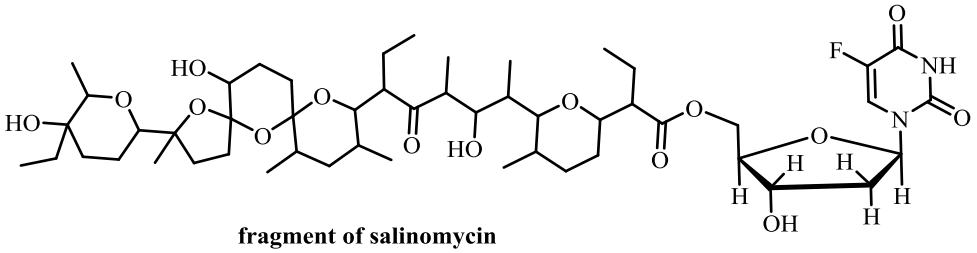


A **B**

15. Nowadays, there is a growing need for valuable chemicals produced from carbohydrate biomass. 5-Hydroxymethylfurfural and its oxidized derivatives are among the most valuable products. 5-Hydroxymethylfurfural can be easily obtained by acid hydrolysis and dehydration of monosaccharides, disaccharides, polysaccharides. The easiest way to synthesize 5-hydroxymethylfurfural is triple dehydration of fructose in the presence of a mineral acid. Get 5-hydroxymethylfurfural (**X^1**) from fructose and sucrose according to the scheme below.



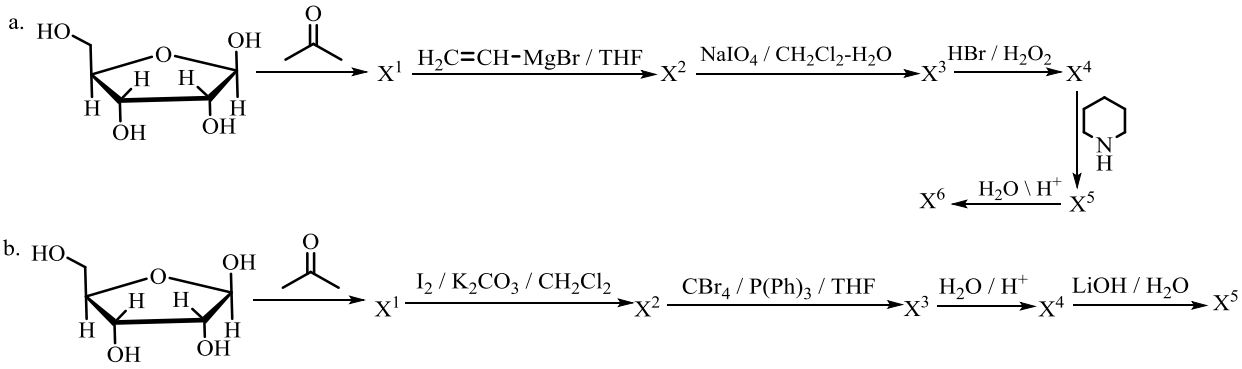
16. The development of nucleoside analogs for use in medicine has a significant impact on clinical chemotherapy used for antiviral and antitumor treatment. One of the best known nucleosides with anti-tumor activity is 5-fluoro-2'-deoxyuridine, which is used in the treatment of several neoplastic diseases such as colon or breast cancer. However, 5-fluoro-2'-deoxyuridine exhibited various side effects in clinical treatment, and its therapeutic effect was limited by the efficiency of cellular uptake and the bioavailability of the medicine. The use of 5-fluoro-2'-deoxyuridine in the bioconjugate (**A**) with salinomycin, an antibiotic belonging to a large group of natural polyesters isolated from *Streptomyces albus*, made it possible to reduce the toxicity of 5-fluoro-2'-deoxyuridine and increase the effectiveness of antitumor therapy. In the structure of the bioconjugate (**A**), select a nucleoside fragment, what type of glycosides this compound belongs to, name the carbohydrate that is part of this glycoside.



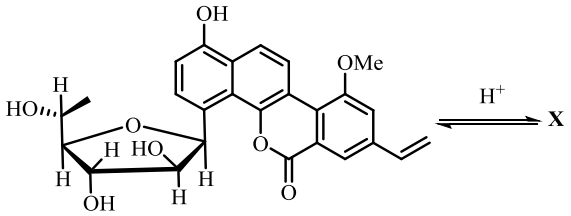
fragment of salinomycin

A

17. Using *D*-ribose as the starting compound solve the chain of transformations, name the products $\mathbf{X^1}$-$\mathbf{X^6}$.



18. Gilvocarcin *V* is an antineoplastic agent produced by the bacterium *Streptomyces griseoflavus Gö 3592* and the most studied member of the special family of benzo[d]-naphtho-[1,2-b]-pyranone-6-aryl-C-glycoside antibiotics, which show excellent anti-tumor action and extremely low toxicity. A feature of aromatic C-glycosides is the formation of a thermodynamically undesirable quinone intermediate. Using gilvocarcin V as an example, depict the structure of the quinone intermediate.

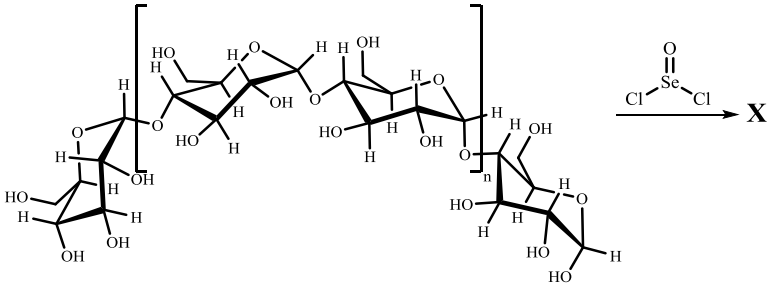


Gilvocarcin V

19. Xanthan gum is a microbial high molecular weight exopolysaccharide produced by the bacteria *Xanthomonas campestris* (a genus of gram-negative bacteria), and it is widely used as an additive in various industrial and biomedical applications. Xanthan gum has good water solubility, excellent biocompatibility. The structure of xanthan gum was established in 1975 and is a linear (1-4)-linked *D*-glucose, similar to the cellulose backbone. Pentasaccharide subunits (1-4) -linked residues of *D*-glucosyl, *D*-mannosyl and *D*-glucuronic acid in a molar ratio of 2: 2: 1 with different ratios of O-acetyl and pyruvyl residues. Draw a monomeric piece of xanthan gum.

20. Se-containing polysaccharides are organic selenium compounds formed by a combination of a polysaccharide and selenium. The biological activity of selenium in the

polysaccharide from the plant hen-of-the-woods (*Grifola frondosa*) is usually higher than that of the microelement selenium and it is more easily absorbed by the human body. Selenium containing polysaccharides can be prepared in the laboratory using a suitable polysaccharide and selenium dichloride oxide ($SeOCl_2$) as a reagent. Currently, the main synthesized selenium polysaccharides are carrageenan polysaccharide selenide, astragalus selenium polysaccharide synthesized by astragalus polysaccharide and $SeOCl_2$. The polysaccharide contains a large number of hydroxyl groups, $SeOCl_2$ can form ester bonds with the terminal glycosidic hydroxyl and hydroxyl groups in the polysaccharide, forming five-membered cyclic selenites. Using the example of the given polysaccharide, write the reaction of the formation of five-membered cyclic selenites.



8. Amino acids. Sulphanylamides

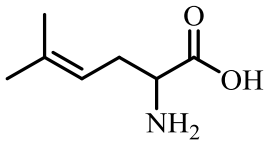
- Classification, structure, nomenclature.
- 22 proteinogenic amino acids.
- Non-proteinogenic amino acids, poisons.
- Sulfanilamides.
- Polypeptide antineoplastic medicines of nature.

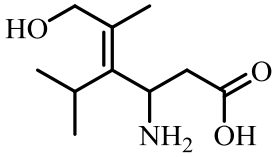
Tasks:

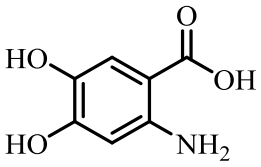
1. Write Fischer's projection formulas for the following optically active compounds: a) α-aminopropionic acid (alanine); b) α-amino-β-methylvaleric acid (isoleucine); c) α-amino-γ-phenylpropanoic acid (phenylalanine); d) α-amino-γ-(1*H*-imidazol-4-yl) propanoic acid (histidine).

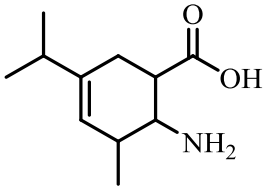
2. Determine in what form (neutral or ionic) the acids listed below will exist in an alkaline (pH = 9) and acidic (pH = 4) buffer solution: a) monobromoacetic acid; b) α-hydroxyacetic acid; c) α-aminopropionic acid.

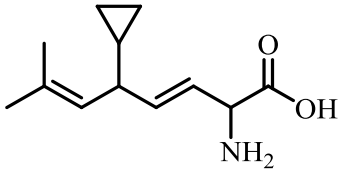
3. Name the compounds according to IUPAC nomenclature:

a. 

b. 

c. 

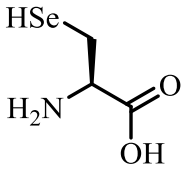
d. 

e. 

4. Draw the structural formulas of amino acids: a) α-aminoacetic acid (glycine); b) 2-amino-3-methylbutanoic acid (valine); c) 2-amino-4-methylpentanoic acid (leucine); d) 2-amino-3-mercaptopropanoic acid (cysteine).

5. What will be the pH of the medium when the following acids are dissolved in water: a) glycine, b) alanine, c) aspartic acid, d) lysine?

6. The big buzz in the biochemistry of selenium was caused in 1986 by parallel discoveries that genes encoding selenoprotein glutathione peroxidase and bacterial format dehydrogenase contain a *TGA* codon in frame in their coding sequence. We now know that this codon governs the incorporation of selenium in the form of selenocysteine into these proteins. Selenocysteine is currently recognized as the 21st amino acid in ribosome-mediated protein synthesis, and its specific incorporation is regulated by the *UGA* codon. Determine the configuration of the chiral center by the *R,S*-system in the selenocysteine molecule. How is selenocysteine different from cysteine?



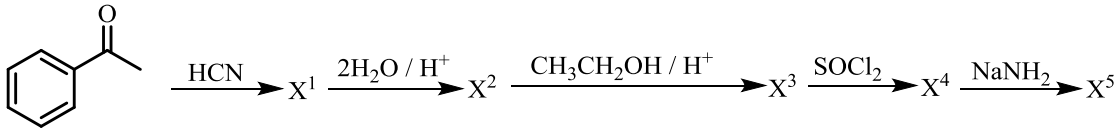
Selenocysteine

7. Proceeding from succinic acid, propose a method for producing aspartic acid through the stage of formation of α-halogenated carboxylic acid. Will the aspartic acid obtained in this way have optical activity?

8. Propose a method for obtaining 2,5-diisopropyl-3,6-diketopiperazine. Does this substance have optical activity?

9. Draw the structure of γ-aminovaleric acid. Write the reaction for obtaining a lactam based on this compound. Does this substance have optical activity?

10. Solve the chain of transformations, name the product **X**^{5} according to IUPAC:



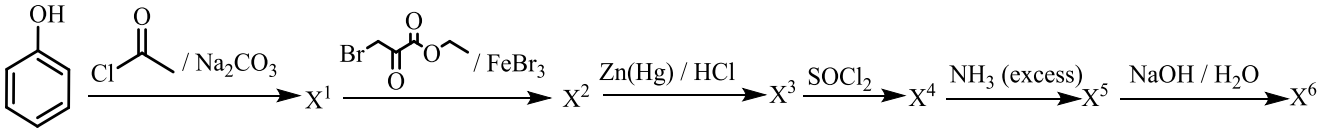
11. α-Amino acids exist in zwitterionic form at neutral pH in aqueous solution. However, with a change in pH, the equilibrium shifts either towards the basic or towards the acidic form of the α-amino acid. What happens if an aqueous solution of alanine, glycine, proline is acted upon with a solution of hydrochloric acid? Write the answer in the form of reaction equations.

12. Give a method of obtaining β-aminopropionic acid starting from acrylic acid.

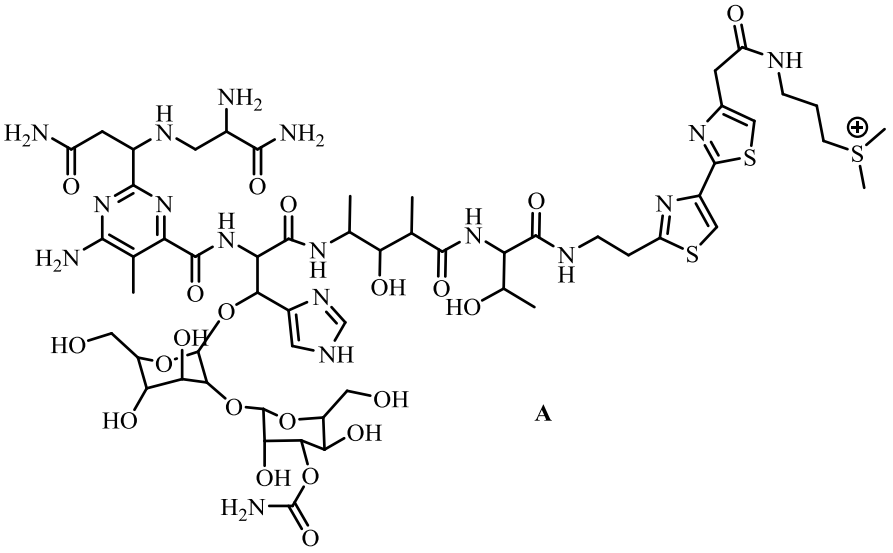
13. Write the structural formulas for the following tripeptides:

a) Gly-Glu-Ala; b) Lys-Trp-Val; c) Ala-Gln-Ser; d) Tyr-Leu-Pro.

14. Solve the chain of transformations, name the products **X**^{1}-**X**^{5} according to IUPAC.



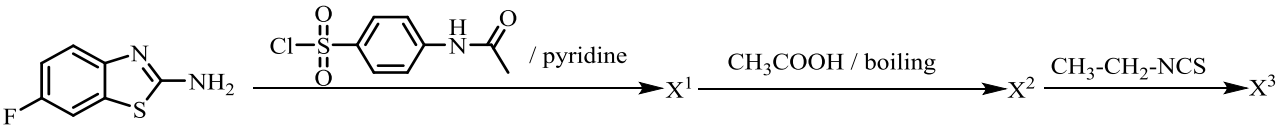
15. Antineoplastic antibiotics of the bleomycin (**A**) group have long been of interest due to their effectiveness in the treatment of certain tumors, not to mention their unique structures and properties in mediating oxygen dioxide activation and selective DNA degradation. At the chemical level, the structure originally assigned to bleomycin was subsequently changed and the new structure (**A**) was confirmed by complete synthesis. In structure (**A**), select the amino acid fragments. How many peptide bonds are in bleomycin? Determine the number of chiral carbon atoms in (**A**) and count the number of optical isomers for bleomycin.



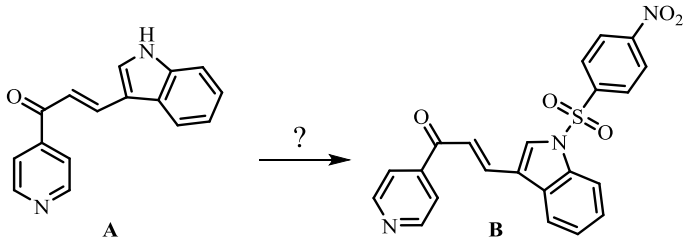
A

16. Compare the two functional groups: amide (-C(O)-NH-) and sulfonamide (-$S(O)_2$-NH-). What are their similarities and differences? Explain your answer using the examples of benzamide and benzenesulfonamide.

17. The sulfonamide derivative **X^3** was synthesized in good yield. The compound was active in the MES and scPTZ tests. The compound was found to be less toxic than the standard drug phenytoin. Solve the chain of transformations and establish the structure **X^3**.

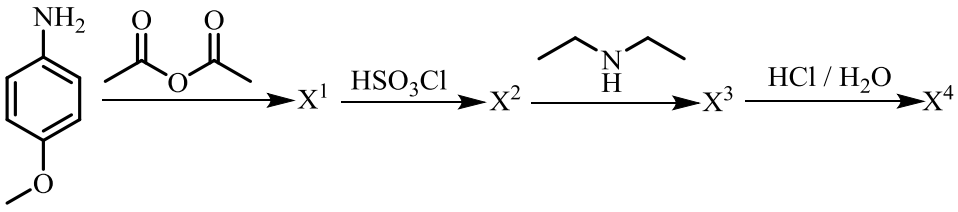


18. In the search for new effective inhibitors of carbonic anhydrase, some sulfonamide derivatives of chalcone based on pyridylindole were synthesized and investigated *in vitro* for inhibitory activity against the isoform of human carbonic anhydrase *IX*. It was found that compound (**B**) has a better binding affinity and selectively inhibits human carbonic anhydrases *IX*, has a significant antiproliferative potential, and also significantly induces apoptosis of cancer cells. Offer a reagent with which (**A**) can be converted to (**B**).

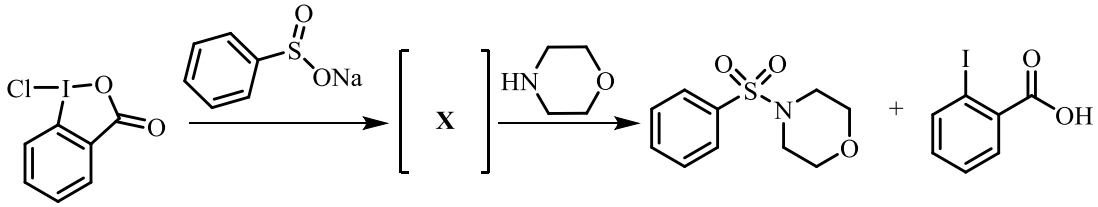


A B

19. Solve the chain of transformations, indicate the products **X^1**-**X^4**:



20. In 2019, a new method was proposed for the formation of a sulfonamide functional group due to group transfer of iodine (III) compounds, combining reagents of hypervalent iodine and sulfinate salts for the gentle transfer of sulfonyl groups to amines and anilines. List the methods which you know for obtaining the sulfonamide group. Proceeding from the scheme, suggest the structure of the transition state (**X**).



9. Review questions

1. What is the reactivity of alkanes? Name the reactions they enter. Give a definition to the following concepts: a) homolytic bond break; b) free radical (R) ; c) the reaction of radical substitution (S_R). In what direction do reactions S_R of alkanes predominantly proceed?

Tasks:

a) When *n*-butane is sulfonated in the light at 25°C, 28% *n*-butyl sulfonyl chloride and 72% *sec*-butyl sulfonyl chloride are formed. What is the mechanism of this reaction? What is the reactivity of the primary and secondary carbon atoms?

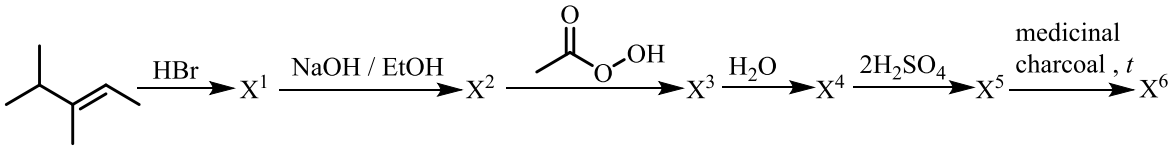
b) The relative rates of substitution of tertiary, secondary, and primary hydrogen atoms in alkane bromination are 1600:82:1. What will be the content of isomeric mono-bromoalkanes in the reaction product of a) propane; b) 2-methylbutane.

2. List the reactions that, in your opinion, are characteristic of alkenes. Give a definition of the concepts: a) heterolytic rupture of the π-bond; b) electrophilic particle; c) carbocation (in terms of molecular orbitals, which means a positive charge); d) the reaction of electrophilic addition (A_E). Compare the ratio of isobutane to bromine in the light and isobutylene in CCl_4. What is the reason for the different course of reactions in your opinion? Bring their mechanisms.

Tasks:

a) The catalytic hydrogenation of 2,3-dimethylbutene-2 gives a compound of the composition C_6H_{14}. The same compound can be obtained by electrolysis of the carboxylic acid salt RCOOH. Determine the structure of the acid, write the reaction schemes.

b) Solve the chain of transformations, name the products according to IUPAC.

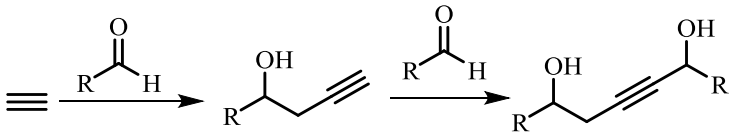


3. Compare the molecular structures of 2-butene and 2-butyne. How, in your opinion, can one explain the presence of geometric isomers in the first case and the absence of them in the second? Explain the change in acidic properties in the following order:

acetylene ($pK_a = 25$)> ethylene ($pK_a = 36$)> ethane ($pK_a > 40$).

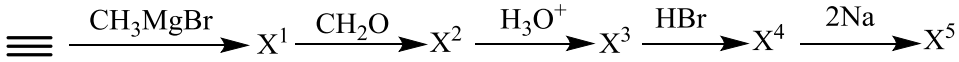
Tasks:

a) A.E. Favorsky found that acetylene reacts with aldehydes and ketones in the presence of alkalis according to the following scheme:



Which compounds can be obtained by the Favorsky reaction from acetylene and: a) HCHO (formaldehyde), b) ethyl methyl ketone; c) trimethylacetal; d) benzophenone?

b) Solve the chain of transformations:



4. Describe the relationship between the chemical properties of alicyclic hydrocarbons and the cycle size. What is the reason for the different reactivity of small and common alicyclic hydrocarbons? Use the example of the reactions of cyclopropane and cyclohexane to illustrate this difference. Compare the chemical properties of propane, propylene and cyclopropane. Note the similarities and differences. Describe the ratio of these compounds to the action of the following reagents: a) Br_2 (*hv*); b) Br_2 (CCl_4); c) HBr; d) $KMnO_4$ (H_2O, 0°C); e) H_2 (Ni); f) H_2SO_4. Write all the relevant reactions.

Tasks:

a) What compounds are formed in the Diels-Alder reaction from 1,3-butadiene and the following dienophiles: a) acrylonitrile; b) crotonic aldehyde; c) acetylenedicarboxylic acid; d) maleic anhydride?

b) Suppose the structural formula and the configuration of functional derivative cyclobutanedicarboxylic acid, which has optical activity, but lost it by acid hydrolysis or by reaction with methyl alcohol in the presence of traces of mineral acid.

5. Compare the molecular structures of *p*-chlorotoluene and benzyl chloride. Describe the C–Cl bonds. In which compound should the heterolytic rupture of this bond with the formation of the chlorine anion occur more easily? Why? Using the example of the reaction of bromobenzene with nitric acid in the presence of sulfuric acid, explain why halogen in aryl halides has a deactivating effect on electrophilic substitution, but at the same time is an *o*-, *p*-orientant.

Tasks:

a) Write the reaction of chlorobenzene with the following reagents: a) H_2SO_4 (conc.); b) HNO_3 (H_2SO_4); c) Br_2 ($FeBr_3$); d) CH_3CH_2Br ($AlBr_3$); e) CH_3COCl ($AlCl_3$). What is the reaction (c) mechanism? What effect does fluorine have on the outcome of the reaction?

b) Get the following compounds from ethylbenzene: a) *p*-bromoethylbenzene; b) 1-bromo-1-phenylethane; c) α, α-dichloroethylbenzene; d) 2,4-dichloroethylbenzene. Give the reaction schemes. Indicate the conditions for their holding.

c) Suggest preparation schemes: a) benzene → *m*-nitrochlorobenzene; b) toluene → *p*-bromobenzyl alcohol; c) chlorobenzene → *p*-nitrofluorobenzene; d) bromobenzene → *p*-chloropropylbenzene.

6. Consider the structure of the phenol molecule. What electronic effects arise between the benzene ring and the hydroxyl group? Vinyl alcohols are characterized by a transition to a more stable tautomeric keto form. Because of what this transition does not take place in phenol?

Tasks:

a) Write the formulas of hydrocarbons: a) cyclopropene; b) 1,3-cyclopentadiene; c) 1,3,5-cycloheptatriene. Which ions corresponding to these compounds should be aromatic and why?

b) The reaction between potassium cyclopentadienide (C_5H_5Na) with $FeCl_2$ forms a compound $(C_5H_5)_2Fe$ called ferrocene (A). Write a reaction scheme and explain the high resistance of this compound to heat, the action of acids and bases, and its ability to enter into substitution reactions. Write the reaction of interaction of ferrocene with propionic acid chloride in the presence of $AlCl_3$.

c) Compare the ratio of isopropylbenzene to bromine a) in the presence of $AlBr_3$; b) in light, reflux. Give the reactions and their mechanisms.

7. What compounds are called Grignard reagents? How are they obtained? Give the electronic structure of any Grignard reagent. Based on the electronic structure, guess the chemical properties of these compounds. What is the role of a hydrocarbon radical in the stability of Grignard reagents?

Tasks:

I) Write the interaction of isobutylmagnesium bromide with: a) water; b) methanol; c) methyl acetylene; d) acetic acid. What gaseous substance is formed in each reaction? Why?

II) Write the schemes for obtaining: a) 1-butanol (two options); b) butanol-2 (two options); c) 2-methylbutanol-2 (two variants); d) isobutyric acid; e) ethylpropyl ketone by reaction with Grignard reagent, name the starting compounds.

III) Get the following compounds from 1-bromobutane and inorganic reagents: a) $CH_3CH_2CH_2CH_2CH_2OH$; b) $CH_3CH_2CH(CH_3)MgBr$; c) $CH_3CH_2C{\equiv}CMgBr$.

8. How do benzene and nitrobenzene interact with electrophilic reagents? Describe the effect of the nitro group on the reactivity using the example of the bromination reaction of nitrobenzene in the presence of $FeBr_3$. What nitrating agents are used to introduce a nitro group into an aromatic nucleus? Which of them, in your opinion, is most expedient to use for nitration of 1,3,5-trimethylbenzene and 2,4-dinitrotoluene.

Tasks:

а) Determine the structure of a compound with the gross formula $C_7H_6BrNO_2$, if you heated this compound with an aqueous solution of potassium hydroxide, it turns into a compound $C_7H_7NO_3$, and when oxidized with $KMnO_4$ in water, it forms *p*-nitrobenzoic acid? Write the reaction for obtaining this compound from toluene.

б) Give the schemes for obtaining the following compounds from benzene: a) *m*-nitrochlorobenzene; b) 1,4-dibromo-2-nitrobenzene; c) 3,5-dinitro-1-bromobenzene; d) *m*-nitrobenzenesulfonic acid.

Suggested readings

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5. Карлов, С.С. Задачи по общему курсу органической химии с решениями для бакалавров: учебное пособие / С.С. Карлов [и др.]. – М.: БИНОМ, Лаборатория знаний, 2016. – 93 с.: ил. ISBN 978-5-9963-1814-8.

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