Problem 1

Salt **X** exists as orange-yellow crystals that are highly soluble in water. To synthesize **X** a charge of 6.360 g of sodium carbonate mixed with 6.414 g of solid simple substance **A** and obtained mixture was left at 280°C during 2 hours. In so doing gas **B** was evolved, total volume of which was equal 1.967 dm^3 (at 128°C and 101.7 kPa). Resulting from synthesis solid residue contains 27.25% of sodium by mass and represents the mixture of two salts **X** and **Y**. One of them is soluble in ethanol, the second one is insoluble essentially. This can be used to isolate the desired product from the resulting solid mixture. Theoretically, in the described synthesis, 6.968 g of salt **X** can be obtained.

1. Define the content of gas **B**. Write down your calculations.

2. Determine the composition and give the formulas for **A**, **X** and **Y**. Write down your calculations.

3. Give the reaction equation carrying out at producing of **X**.

4. Draw the spatial structure of anions of salts **X** and **Y**, indicate valence angles.

5. Suggest two more procedure of synthesis of **X**.

Problem 2

Colloidal quantum dots are semiconductor nanocrystals with a size of 2–10 nm. In this range, the electro physical and optical properties depend on the size of the nanoparticles and differ from the properties of bulk material of a similar chemical composition due to quantum confinement effects. One of the first quantum dots were studied had an **XY** composition from the number of semiconductors of the $A^{II}B^{VI}$ group. Roman numerals indicate the numbers of groups in the periodic table.

1. Determine the composition of **XY**, if it is known that 1) 598 **X** atoms contain in one quantum dot with radius $r = 2.0$ nm; 2) $\rho(\mathbf{XY}) = 5.67$ g/cm^3, the number of formula unit's z in a unit cell is 2; 3) when **XY** is dissolved in hyperchloric acid, a gas with a strong unpleasant odor with a density of 3.31 g/L at 1 atm and 298 K is produced.

There are numerous **XY** synthesis methods, some of which are presented in the scheme (TMS – tetramethylsilane):
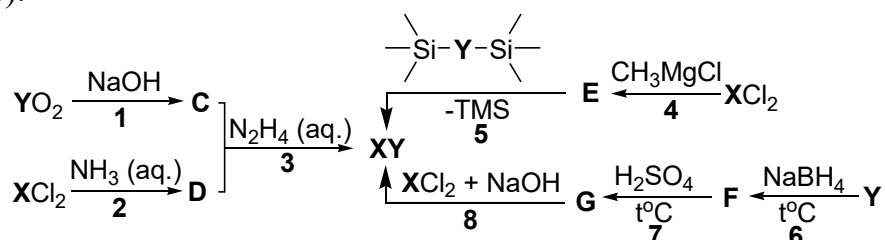
2. a) Identify substances **C** – **G**. b) Write the equations of reaction (1 – 8).

The band gap of quantum dots (E_g^{nano}) is determined as

$$E_g^{nano} = E_g^{bulk} + \frac{h^2}{8r^2\mu} - \frac{1.8e^2}{4\pi\varepsilon\varepsilon_0 r},$$

where E_g^{bulk} – band gap for bulk material, h – Planck constant, r – quantum dot radius, μ – reduced mass of electrons and holes, e – elementary charge, ε_0 – electric constant, ε – dielectric permeability.

3. Determine in which color region quantum dots with radius 3.3 nm will luminesce if the maximum luminescence of nanoparticles with $r = 2.0$ nm are at $\lambda = 446$ nm in the blue region. $\varepsilon(XY) = 10.6$, $1/\mu = 1.37\cdot10^{31}$ kg^{-1}.

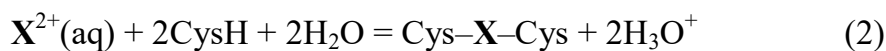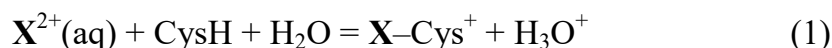| Color:	blue	green	yellow	orange
λ, nm:	435 – 480	500 – 560	580 – 600	600 – 615

XY-based quantum dots have intense narrow bands of luminescence spectra in the visible light region, which almost don't overlap with absorption spectra, which makes it possible to obtain displays with high color rendering quality. However, due to the toxicity of **X** and all its compounds, it usage in electronics is strictly limited in most countries. One of the main causes of $\mathbf{X}^{2+}$ toxicity is the ability to bind to sulfur-containing proteins, inhibiting the activity of enzyme systems. The simplest sulfur containing amino acid is cysteine $C_3H_7NO_2S$:
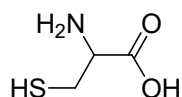
4. a) Calculate the isoelectric point (pI) of cysteine, if $pK_a(-COOH) = 1.9$, $pK_a(-NH_3^+) = 10.4$, $pK_a(-SH) = 8.2$; b) Determine the total charge of the amino acid at pH = 8.5; c) c) To which electrode, anode (+) or cathode (–), moves cysteine during the electrophoresis at pH = 8.5?

To determine the thermodynamically preferred Cd/Cys ratio during the formation of the organometallic complex, the temperature dependences of the equilibrium constants of the reactions

$$\mathbf{X}^{2+}(aq) + CysH + H_2O = \mathbf{X}\text{–}Cys^+ + H_3O^+ \qquad (1)$$

$$\mathbf{X}^{2+}(aq) + 2CysH + 2H_2O = Cys\text{–}\mathbf{X}\text{–}Cys + 2H_3O^+ \qquad (2)$$

were studied. As a result, the equations for $\ln K$ dependencies on $1/T$ are obtained: $y_1 = -2.93 + 29348/T$ and $y_2 = -3.50 + 37400/T$ for reactions (1) and (2) respectively.

5. Calculate $\Delta_r G°_{298}$ for both reactions based on the presented data.

6. Draw possible structures of the complexes $\mathbf{X}^{2+}$ and cysteine preferably formed in solution at a) pH = 8.5; b) pH = 11.

Physical constants:
$h = 6.63\cdot10^{-34}$ J·s, $N_A = 6.02\cdot10^{23}$ mol^{-1}, $c = 2.998\cdot10^8$ m·s^{-1}, 1 eV = $1.6\cdot10^{-19}$ J, $\varepsilon_0 = 8.85\cdot10^{-12}$ F/m, $e = 1.6\cdot10^{-19}$ C, $R = 8.314$ J/mol·K = 0.082 L·atm/mol·K.

Problem 3

The element X as simple substance exists in the form of several allotropic modifications, including X_1 and X_2, which differ greatly in their reactivity. Compounds of X with most metals and non-metals are known. Consider two similar classes of binary compounds formed by element X.

Substance A_1 ($\omega(X)$ = 56.34%) is formed by comproportionation of substances: elemental X_1 with A_5. Substance A_2 ($\omega(X)$ = 52.54%) is obtained by oxidation of A_1 at 190–210°C with small amounts of colorless gas G. If the same reaction is carried out at elevated temperature – in the range 280–320°C, then the mixture of binary compounds A_2, A_3, A_4 and A_5 is formed. Oxidation state of X increases in the row. Gas G is obtained by decomposition of black-brown binary compound D, the second product of the decomposition reaction is a simple compound D_1. Compound A_6 ($\omega(X)$ = 30.10%) is obtained recently by interaction A_1 with the blue gas G_1 received from G at –78°C in solution CH_2Cl_2.

Substances of series B in most cases can be synthesized by direct interaction of simple substances. Substance B_1 is formed at 180°C in inert atmosphere as a result of interaction of X_2 with the simple substance Y. Molar mass of B_1 and A_1 are the same. Substance B_1 can be oxidized further by substance Y in CS_2 solution with trace amounts I_2, as catalyst, the substance B_2 is formed at these conditions. Molar mass of B_2 is equal to molar mass of A_5. Substances B_5 and B_3 are produced by interaction of simple substances X_1 or X_2, respectively, with Y. Substance B_4 ($\omega(X)$ = 30.10%) is a product of comproportionation B_5 and B_3.

1. Decipher the substances and write the reaction equations.

2. Draw substance structures A_1 and A_6, $B_1 - B_5$. In A_6, the same fragment can be distinguished in the structure of the molecule as in A_1, as well as the same fragments from G atoms can be distinguished similar to G_1. Data for $B_1 - B_5$ series are presented in the table. Substance B_2 has two isomers. B_1 has 3-fold axis.

Bond type	B_1	$B_2(1)$	$B_2(2)$	B_3	B_4	B_5
X–X	3	1	2	1	–	–
X–Y	6	10	8	10	12	12
X–Y terminal	–	–	1	2	3	4

Problem 4

The Cope rearrangement is [3,3]-sigmatropic rearrangement of 1,5-dienes, which mechanism for parent hexa-1,5-diene depicted on Figure 1. The reaction goes through a 6-electron concerted transition states and follow rules of orbital symmetry.
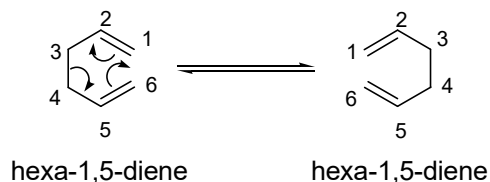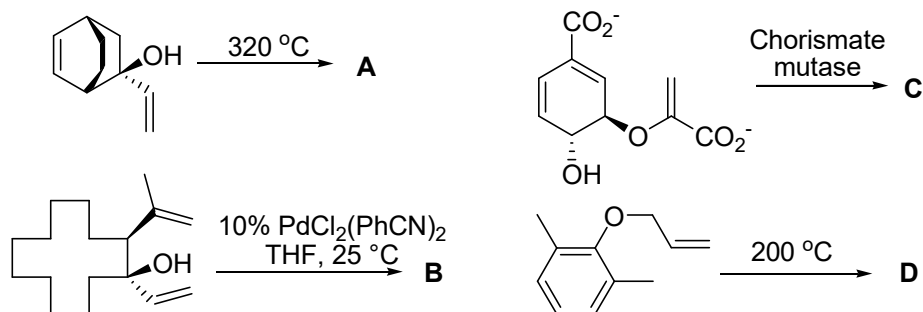

hexa-1,5-diene   hexa-1,5-diene

Fig. 1. Mechanism of Cope rearrangement.

1. **Propose the structure** of two diasteromeric hydrocarbons C_8H_{14}, whose comparable behavior in Cope rearrangement proves the synchronous mechanism of the reaction. Also provide the structure of the rearranged products in each case.

The Cope rearrangement can be extended to hetero-atoms and substituents. In such cases, we have the oxy-Cope and Claisen rearrangement, depending whether the *heteroatom is part of the rearrangement system, or acts as initially a pendant group*, but undergoes a keto-enol tautomerisation afterwards.

2. Determine the products of the following reactions. (Note: **all of the reactions** below fall into the same class determined in **question no. 1.**)

Scheme 1. Examples of oxy-Cope and Claisen rearrangements.

Another interesting feature of the Cope rearrangement is the degenerate variant (the product is structuraly identical to the starting material), as in the parent hexa-1,5-diene. This fact has been subjected to a large number of theoretical studies. In the 60's the hydrocarbon ***barbaralane*** (C_9H_{10}) was designed and synthesized. The compound was named after Professor Barbara M. Ferrier. This compound enters degenerate rearrangement at room temperature and the rearrangement stops only at –110°C. Scheme 2 depicts an optimized synthesis of ***barbaralane*** from 1983.
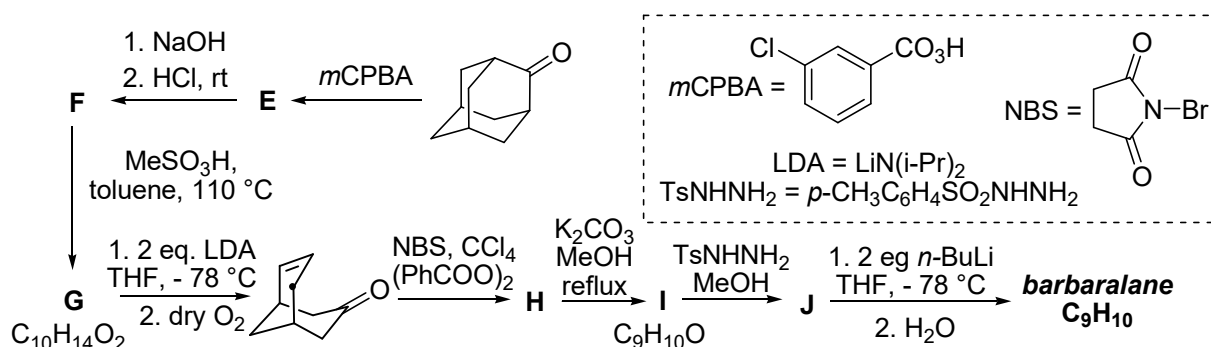
Scheme 2. Synthesis of ***barbaralane***.

3. Decode Scheme 2 and draw the structure of compounds **E – H** and ***barbaralane.***

4. How many signals are observed in the ^{13}C NMR spectra of ***barbaralane*** at room temperature and at –110°C?

Problem 5

In 1884 A. E. Favorsky discovered that the heating of hydrocarbon **I** ($w_C = 88.89\%$) with alcoholic solution of KOH at 170°C leads to its isomerization to product **Ia**. When **Ia** is shaken with a mixture of water and sulfuric acid (1:3) in a sealed tube, crystals of hydrocarbon **A** ($C_{12}H_{18}$, $T_{melt} = 164°C$) are formed, and compound **A** possess only one singlet in the ^{1}H NMR spectrum ($\delta = 2.2$ м.д.).

1. *Decode structure* **I**, **Ia** *and* **A**, *if* **I** *and* **Ia** – *position isomers of multiple bond.* The mechanism of the isomerization was investigated in 1951 using the hydrocarbon **II**, which is homologue of **I**. It was found that the treatment of **II** by KOH solution in alcohol (175°C, 3 h) leads to isomer **IIa** formation. The isomerization process is reversible and proceeds through isomeric compound **IIb**.

2. Decipher the structure of **II**, **IIa** and **Iib**. Take into account, that **II** and **IIa** contain the equal number of sp-hybridized carbon atoms, but its amount in **IIb** two times less. Upon oxidation of the equilibrium mixture by $KMnO_4/H^+$, only CO_2, CH_3COOH, CH_3CH_2COOH and $CH_3CH_2CH_2CHOOH$ are formed as carbon-containing products.

3. *Write reaction equation of oxidation* **II**, **IIa** *and* **IIb** *by* $KMnO_4$ *in acidic media*.

The reverse conversion of **IIa** to **II** can also be carried out in practice. For this purpose **IIa** is treated by base **X** with further hydrolysis of the reaction mixture. Compound **X** could be obtained by the reaction of equimolar amount of KH with liquid compound $C_3H_{10}N_2$.

4. *Indicate the structural formulas of* $C_3H_{10}N_2$ *and* **X**. The ^1H NMR spectra of $C_3H_{10}N_2$ has a quintet, singlet and triplet with the integral ratio 1:2:2, and the singlet could exchange with D_2O. In the answer sheet indicate the role of the bases KOH and **X** in the transformations **II → IIa** and **IIa → II**.

A rearrangement **IIa → II** can multiply occur inside the molecule in the presence of **X**. Such transformation called zipper-reaction. The reaction was used as a key step of the synthesis of natural Elenic acid:
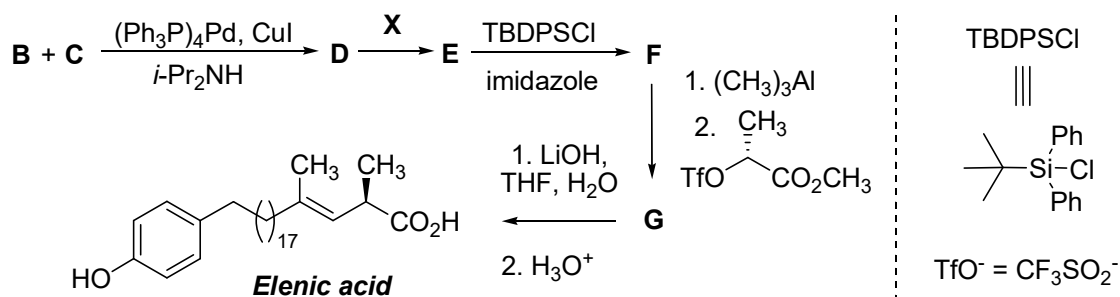
5. *Decipher structures* **B – G**. The ^1H NMR spectrum of **B** ($w_C = 32.73\%$, $w_H = 2.27\%$) showed a singlet at 4.9 ppm (1H) and two doublets at 6.6 ppm (2H) and 7.5 ppm (2H). Compound **C** is the unbranched homologue of **I** ($w_C = 86.33\%$).

Problem 6

The lead battery was invented by the French chemist Louis Gaston Plante in 1859. In the charged state, the left electrode of the battery (with a more negative potential) consists of metallic lead, and the right one of lead oxide PbO_2. The electrolyte is a solution of sulfuric acid (20–30 weight %). When two lead plates are immersed in acid (uncharged state), a thin layer of $PbSO_4$ is formed on the electrodes and the solution is saturated with the same salt. When the battery is charged at its electrode connected to the positive pole of the source, lead is oxidized to PbO_2, and the second electrode turns into pure lead. The concentration of sulfuric acid increases.

1. Draw the simplest circuit diagram of the electrical circuit of a lead battery with the polarity of the electrodes and interface surfaces (vertical bar).

Below are the half-reactions 1 and 2 occurring on the electrodes:

	Half-reaction	E^0, V
1	$PbSO_4 + 2e^- = Pb + SO_4^{2-}$	−0.359
2	$PbO_2 + SO_4^{2-} + 4H^+ + 2e^- = PbSO_4 + 2H_2O$	+1.682
3	$Pb^{2+} + 2e^- = Pb$	−0.126

2. a) Write the total reaction expressing the final products of chemical transformations in the battery; b) Find the standard EMF of the electrochemical cell; c) Calculate the standard Gibbs energy of the total reaction; d) Calculate the equilibrium constant of this reaction at a temperature of 25°C.

At the interface of the Pb | electrolyte, a chemical interaction should take place with the formation of $PbSO_4$.

3. Write the corresponding chemical reaction.

The $Pb(SO_4)_2$ salt is first formed on the PbO_2 | electrolyte interface, but due to its instability, extremely low solubility and ability to decompose with oxygen evolution, the surface of the PbO_2 electrode is also covered with a thin layer of $PbSO_4$.

4. Write chemical reactions of a) $Pb(SO_4)_2$ formation and b) $Pb(SO_4)_2$ decomposition.

In a fully charged battery at 25°C, the concentration of Pb^{2+} ions in solution is $0.93 \cdot 10^{-6}$ M.

5. Determine the potential of the lead electrode Pb | H_2SO_4 in this state.

In some working condition at 25°C, the electrolyte contains 376 g of H_2SO_4 per 1000 g of water. The acid activity coefficient in such a solution is $\gamma(H_2SO_4) = 0.165$, and the water activity is $a(H_2SO_4) = 0.7$.

6. Calculate the EMF of the electrochemical cell of the battery with this electrolyte.

Additional information:

I. Gas constant $R = 8.314$ j·mol^{-1}K^{-1};
II. Faraday Constant $F = 96485$ C·mol^{-1};
III. The relationship of the Gibbs energy of the reaction with the EMF: $\Delta_r G = -nFE$;
IV. In concentrated solutions, the molality of m_i components (mol/1000 g of solvent) is replaced by a_i activities. The relationship between these quantities is $a_i = \gamma_i m_i$, where γ_i – is the activity coefficient. In extremely dilute solutions, the activity became concentration ($a_i \to \gamma_i m_i$ at $m_i \to 0$)
V. Nernst formula for electrode potential

$$E = E^0 + \frac{RT}{nF} \ln \frac{a(\text{Ox})}{a(\text{Red})},$$

where a is the activity of the oxidized and reduced forms, n is the number of electrons in the half-reaction.

Problem 7

Biosynthesis of an important hormone starts from thyroglobulin, a protein produced in the thyroid body and enriched with the tyrosine (α-amino acid) residues. The peroxide oxidation in the presence of anions X^- leads to the transformation of the aromatic rings of tyrosine into the Y moieties, further oxidation of which is accompanied by intraprotein rearrangement yielding the dehydroalanine and another amino acid units (see the scheme). As required, the formed prohormone is hydrolyzed with elimination of compound A (65.34% of element W), which is further transformed into a more efficient compound B (58.48% of W); the inactive B' isomer is formed as a by-product. Deactivation of A and B occurs via several paths with the formation of metabolites $C – E$. Under certain conditions, deactivation of A affords compound F (67.88% of W) exhibiting anticancer action.
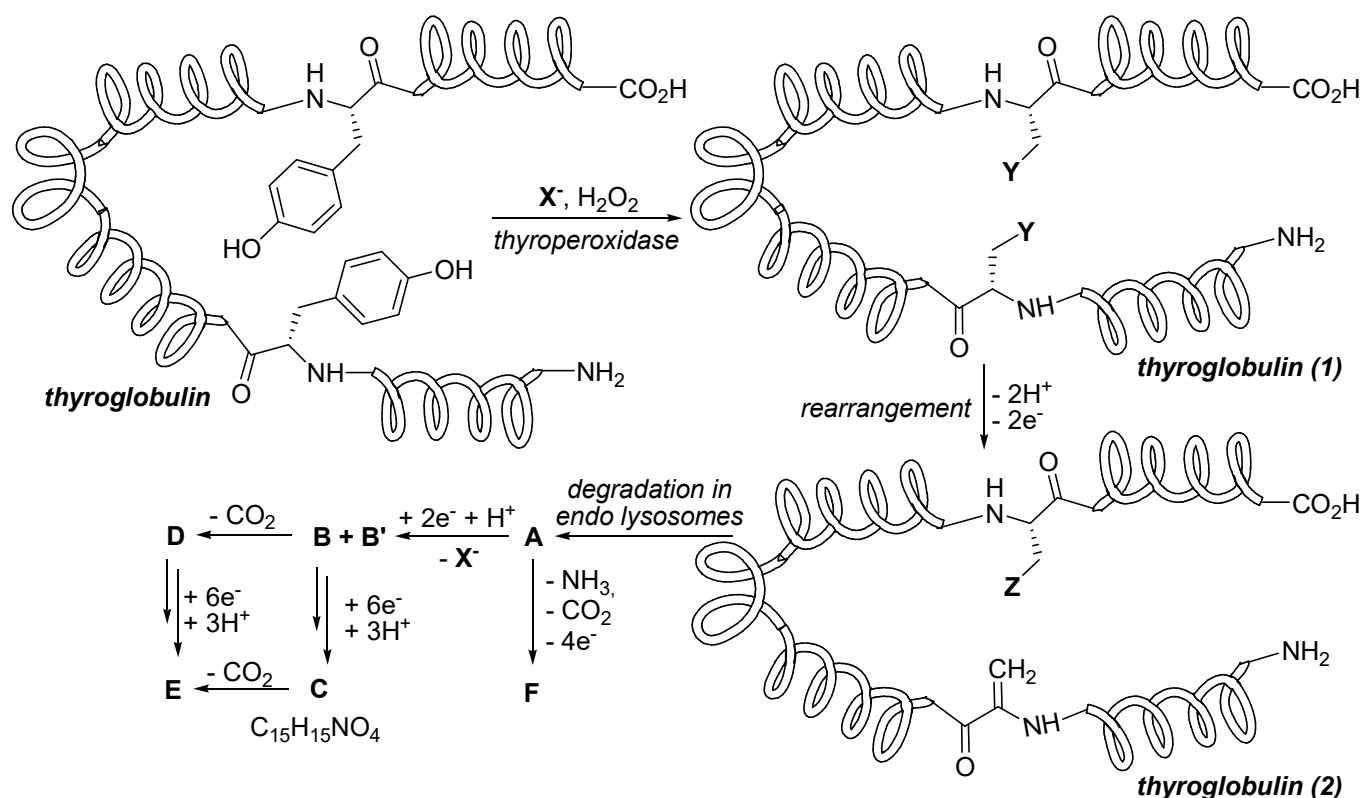
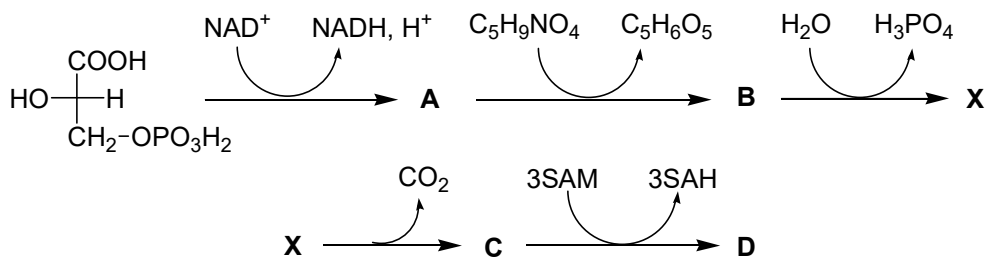1. Determine the anion X^-, fragments Y and Z, and compounds $A – F$. Consider that the compound E shows 10 signals in the ^{13}C NMR spectrum and 8 signals in the ^1H NMR spectrum, two of the latter being exchangeable with D_2O.

Problem 8

Glycerophospholipids are important components of cell membranes. Their biosynthesis starts with the modification of hydroxyl group of glycerol by phosphate group, which results in the chiral product.

1. The R-isomer of glycerol 3-phosphate is given in the Answer sheet. Draw the Fischer projection of this compound showing free OH-group at the top. Specify its relative configuration (D or L).
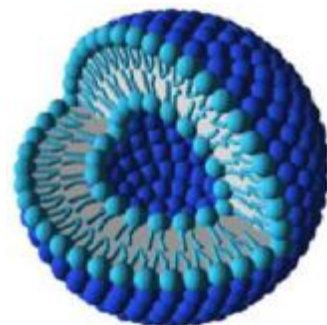
The phosphate group of glycerol 3-phosphate affords esters as a result of the reaction with alcohols, e.g. with compound **D** formed in the organism from the canonical amino acid **X**. Biosynthesis of **X** starts from a glycolysis intermediate, 3-phosphoglycerate. Equations of the reactions are presented in the scheme.

$$
\begin{array}{c}
\text{COOH} \\
\text{HO}-\!\!\!\!\!-\text{H} \\
\text{CH}_2\text{--OPO}_3\text{H}_2
\end{array}
\quad
\xrightarrow[\text{NAD}^+ \quad \text{NADH, H}^+]{}
\quad \textbf{A} \quad
\xrightarrow[\text{C}_5\text{H}_9\text{NO}_4 \quad \text{C}_5\text{H}_6\text{O}_5]{}
\quad \textbf{B} \quad
\xrightarrow[\text{H}_2\text{O} \quad \text{H}_3\text{PO}_4]{}
\quad \textbf{X}
$$

$$
\textbf{X} \xrightarrow[\text{CO}_2]{} \textbf{C} \xrightarrow[\text{3SAM} \quad \text{3SAH}]{} \textbf{D}
$$

SAM is *S*-Adenosyl methionine, SAH is the demethylated product, *S*-Adenosyl homocysteine; NAD^+ and NADH are oxidized and reduced forms of nicotinamide adenine dinucleotide, respectively.

2. Draw the structures of **A** – **D** and **X**, if there is one more (except **X**) canonical amino acid in the above scheme.

Free OH-groups of glycerol 3-phosphate are esterified by fatty acid residues resulting in phospholipids, which contain both hydrophobic and hydrophilic moieties. In aqueous solutions, phospholipids spontaneously form bilayer structures which finally affords spherical liposomes.

3. Estimate the internal cavity volume of a liposome with the external diameter of 100 nm composed of glycerol 3-phosphate-based lipids modified with **D** and two residues of palmitic (hexadecanoic) acid (these lipids further referred to as DPPC). When estimating the length of the lipid molecule, consider the valence angles and the C–C bond length of 0.154 nm; neglect the size of the hydrophilic fragment. Take the carbonyl carbon as the beginning of the hydrophobic fragment.

Liposomes were prepared by solvent evaporation from 0.02 mL of DPPC solution in chloroform (with the concentration of 25 mg/mL), subsequent addition of 5 mL of water and ultrasonic treatment of the resulting system.

4. a) Calculate the concentration of the obtained liposomes (diameter of 100 nm). Take the surface area occupied by a single DPPC molecule on both external and internal sides of the lipid bilayer equal to 0.44 nm^2. Note that all lipid molecules are included in the liposomes, whereas all liposomes consist of the same number of DPPC molecules.

b) Calculate the total internal volume of the liposomes in the resulting system.

Note. If you failed to answer question 3, take the entire volume of a liposome as that of its internal cavity.

Liposomes are widely used for targeted delivery of drugs. A medicine is typically incorporated into the internal cavity, which leads to an enhanced time of the drug circulation in blood и.

5. Calculate the biological half lifetimes of free doxorubicin (*Dox*) and the liposomes with *Dox*, if the process of the drug clearance is described by the first-order kinetics. Both drugs are

administered in the concentration of 75.0 mg/m^2 (referred to the body surface area). After 4 h, the concentration of *Dox* and liposomes were found equal to 66.8 and 67.4 mg/m^2, respectively.

6. Calculate the amount of free *Dox* and *Dox* entrapped into the liposomes that would be found in man 2 h after administration of the drugs. *Dox* concentration inside the liposomes is of 25 mg/mL. The dose of 5 mL of the liposomes described in i. 4 was administrated to a patient. Equal initial masses of *Dox* were introduced with both drugs.

<u>Note</u>. If you failed to answer question 5, use the biological half lifetimes of 1 h for free *Dox* and 2 h for the liposomes with *Dox*.