54 CHEMISTRY OLYMPIAD

Final competitions (29.03.2008)

PROBLEM 1

Competing equilibria

Complex formation reactions are often used in chemical analysis to separate components of mixtures of ions. Effective complex formation requires selection of a proper reaction medium – in alkaline solutions hydroxides in case of some metal ions can precipitate, while in solutions of low pH, unwanted protonation of the ligand can hinder formation of the complex.

These effects can be followed on the example of oxalate complexes of iron(III).

Two portions of $1\cdot10^{-4}$ M iron(III) nitrate solutions (**A**) and (**B**), respectively, were prepared. Additionally, the solution **A** contained 0.1 M oxalic acid ($H_2C_2O_4$), while the solution **B** contained 0.1 M sodium oxalate ($Na_2C_2O_4$).

Problems:

a. Calculate the pH and the concentration of free $C_2O_4^{2-}$ ions in solutions **A** and **B**.

b. Performing appropriate calculations, prove that that in one of these solution $Fe(OH)_3$ precipitate is formed.

c. For the solution, in which no precipitate is formed, calculate the molar fraction (related to the total concentration of soluble iron(III) species) of the complex with the maximal number of ligands, i.e. $Fe(C_2O_4)_3^{3-}$.

d. Which solution (containing either oxalic acid or sodium oxalate) is more suitable for separation Fe(III) ions in the form of oxalate complexes. Calculate the %-amount (in relation to total amount of iron(III)) of free Fe^{3+} ions in this solution.

By using simplified dependences, their correctness should be proven.

In calculations use the following equilibrium constants:

cumulative formation constants of Fe^{3+} with $C_2O_4^{2-}$ ions:

$\beta_1 = 1\cdot10^{8}$; $\beta_2 = 2\cdot10^{14}$; $\beta_3 = 3\cdot10^{18}$,

dissociation constants of $H_2C_2O_4$: $K_{a1} = 0.05$, $K_{a2} = 5\cdot10^{-5}$,

solubility product of $Fe(OH)_3$: $K_{s0} = 2.5\cdot10^{-39}$.

PROBLEM 2

Reactions of halogens

A. The sample of potassium iodide of 9,13 g was dissolved in 100 g of hot water. Next, 13,96 g of iodine was added to the resulting solution and stirred vigorously until clear solution was formed. The solution was then concentrated and subsequently cooled down to 2°C, and left for crystallization. The dark brown crystals of salt **A** were formed. Then they were separated from the solution, washed and dried. The sample of 0,950 g of obtained compound **A** was dissolved in water and this solution was titrated with the 21,7 cm^3 amount of 0,2 M $Na_2S_2O_3$ in the presence of starch indicator.

Problem:

a. Provide a chemical formula of compound **A** along with the necessary calculations.

B. Hot, highly concentrated solution of potassium iodide was being saturated with gaseous chlorine until the initially formed brownish precipitate dissolved. At the end, small amount of solid potassium iodide was added to the solution. Orange crystals of hydrated salt **B** crystallized from obtained solution at 0ºC. By the use of X-ray diffraction studies, it was found that anion of salt **B** had the structure analogous to the structure of anion of salt **A**. Moreover it was observed that this compound is unstable in the air, and in the presence of protective atmosphere it decomposes at around 215ºC.

The sample of 15.32 g of salt **B** was heated under nitrogen at temperature of 250°C, and the weight of the reaction product decreased to 4,48 g. The obtained compound was white and water-soluble. Its water solution mixed with $AgNO_3$ solution gives opaque white precipitate soluble among others in ammonia.

Problems:

b1. Provide a chemical formula of compound **B**.
b2. Write the chemical equations for synthesis and decomposition reactions of **B**.

C. On the basis of electric conductivity measurements, the solution of iodine in pyridine was found to conduct electric current. In order to identify the anions present in this solution, the following experiment was done. The solution of iodine in pyridine was placed in a separation funnel, then the chloroform and water solution of silver chlorate (VII) were added. After a few minutes of shaking, water solution containing yellow insoluble precipitate was separated from chloroform. The chloroform solution was moved to crystallizer and left for crystallization. The obtained crystals of salt **C** (chlorate (VII)) were filtered off, washed and dried. The sample of 0,946 g of compound **C** was dissolved in water and a few grams of potassium iodide were added. The formed iodine was titrated with 24,6 cm^3 of 0,2 mol/dm^3 $Na_2S_2O_3$ solution. Crystallographic analysis of salt **C** showed that the structure of cation was analogous to the structure of anions in the case of salts **A** and **B**.

Problems:

c1. Provide appropriate calculations and the chemical formula for compound **C**.

c2. Write the chemical equation for reaction occurring in iodine solution in pyridine.

c3. Write down the chemical equation for synthesis reaction of salt **C**.

c4. Explain the structure of anions in the salts **A** and **B** as well as the structure of cation in the salt **C**.

For calculations use the following molar masses:
K – 39,10 g/mol; I – 126,90 g/mol; Cl – 35,45 g/mol; O – 16,00 g/mol; N – 14,01 g/mol; C – 12,01 g/mol; H – 1,01 g/mol

PROBLEM 3

Hydrogen from methanol and methanol from hydrogen

A. To find a save and economic method of hydrogen storage is now the Holy Grail of investigations carried out in numerous laboratories all over the world. Portable hydrogen stores may supply hydrogen to power, for example, hydrogen fuel cells used in environment-friendly electric cars.

One of the solutions under consideration is 'storing' hydrogen converted to methanol, which can undergo the following catalytic reaction:

$$CH_3OH + H_2O \leftrightarrows 3H_2 + CO_2$$

When 1.00 mole of methanol reacts with 1.00 mole of water, the reaction enthalpy and free enthalpy are $\Delta H^0_r(374K) = +53$ kJ mol^{-1} and $\Delta G^0_r(374K) = -17$ kJ mol^{-1}, respectively.

A reactor maintained at the constant temperature 374 K and supplied with a suitable catalyst is filled with 1.00 mole of methanol and 1.00 mole of water. The construction of the reactor allows for a mixture to be kept under the constant pressure of 1000 hPa.

Problems:

a1. Calculate the equilibrium constant of the reaction of methanol with water vapour at the temperature of 374 K.

a2. Calculate the percentage of methanol that will be converted to hydrogen when the reaction reaches equilibrium.

a3. In another experiment (in the same temperature and pressure) 1.00 mole of methanol, 1.00 mole of water and 20.00 moles of nitrogen are introduced to the reactor. Calculate the percentage of methanol decomposed to hydrogen when the reaction reaches equilibrium.

a4. Reaction of methanol and water is endothermic. Calculate the percentage of methanol to be oxidized to water for the thermal effect of the reaction to be zero, knowing that when 1.00 mole of oxygen reacts with 2.00 moles of hydrogen ($2H_2 + O_2 \leftrightarrows 2H_2O$) the reaction enthalpy and free enthalpy are $\Delta H^0_r(374K) = -485$ kJ mol^{-1} and $\Delta G^0_r(374K) = -450$ kJ mol^{-1}, respectively.

B. In some measurements isotope substituted compounds are used. A mixture of CO_2 and hydrogen enriched with a heavier isotope (deuterium) has been used to synthesize a sample of methanol. Measurements carried out by means of a mass spectrometer have shown that in the sample the amount of methanol molecules containing 3 atoms of deuterium and 1 atom of light hydrogen is 1.55 times larger than the amount of methanol molecules containing 2 atoms of deuterium and 2 atoms of light hydrogen.

Problem:

b. Calculate the percentage of deuterium (in atomic percent) in the hydrogen sample.

In the calculations the gas constant should be assumed to be equal $R = 8.314$ J/(mol·K)

PROBLEM 4

Drug synthesis

Many compounds used as medicines, for example ephedrine and hydroxyzine, contain aromatic rings. Often, convenient substrate for their synthesis is benzaldehyde and its derivatives.

A. Ephedrine, a natural product with molecular weight of 165.2 g mol^{-1}, has been used for thousands of years in traditional Chinese medicines. At present, it is commonly used as a stimulant, appetite suppressant, concentration aid, decongestant, and to treat hypotension. Howbeit, its use is controversial because its structure is similar to some synthetic narcotics.

It can be prepared from compound **A1** according to following scheme:

$$\mathbf{A1} \xrightarrow{CH_3NH_2} \mathbf{A2} \xrightarrow{H_2/\text{catalyst}} \text{ephedrine} + \text{pseudoephedrine}$$

An efficient way to synthesize **A1** is the biochemical method, which involve the fermentation of sucrose in the presence of benzaldehyde. Intermediate of the process, acetaldehyde, condenses with benzaldehyde according to an acyloin reaction giving **A1** (*R* enantiomer). **A1** is quite different in structure than the usual product of aldol condensation of acetaldehyde and benzaldehyde (compound **A0**).

Molecules of ephedrine and pseudoephedrine both contain two asymmetric (stereogenic) carbon atoms and they are diastereoisomers, while pseudoephedrine has the same (*R, R*) configurations of that carbons. The reaction **A1**→**A2** and the reduction of **A2** do not change configurations of the asymmetric carbons.

Spectroscopic data for **A1** are as follows:

IR (film, cm^{-1}): 3454, ~3000, ~2900, 1713 (chosen bands);

^1H NMR (in $CDCl_3$, δ in p.p.m. from TMS): 2.08 (singlet, 3H), 3.88 (broad, 1H), 5.09 (singlet, 1H), 7.34 (multiplet, 5H);

^{13}C NMR (in $CDCl_3$, δ in p.p.m. from TMS): 25.3; 80.1; 127.2; 128.6; 128.9; 137.8; 206.8.

Problems:

a1. Draw the structure of **A0** (main product of the typical aldol condensation of acetaldehyde and benzaldehyde).

a2. Find the structure of **A1** using the spectral data and give the explanation of your results.

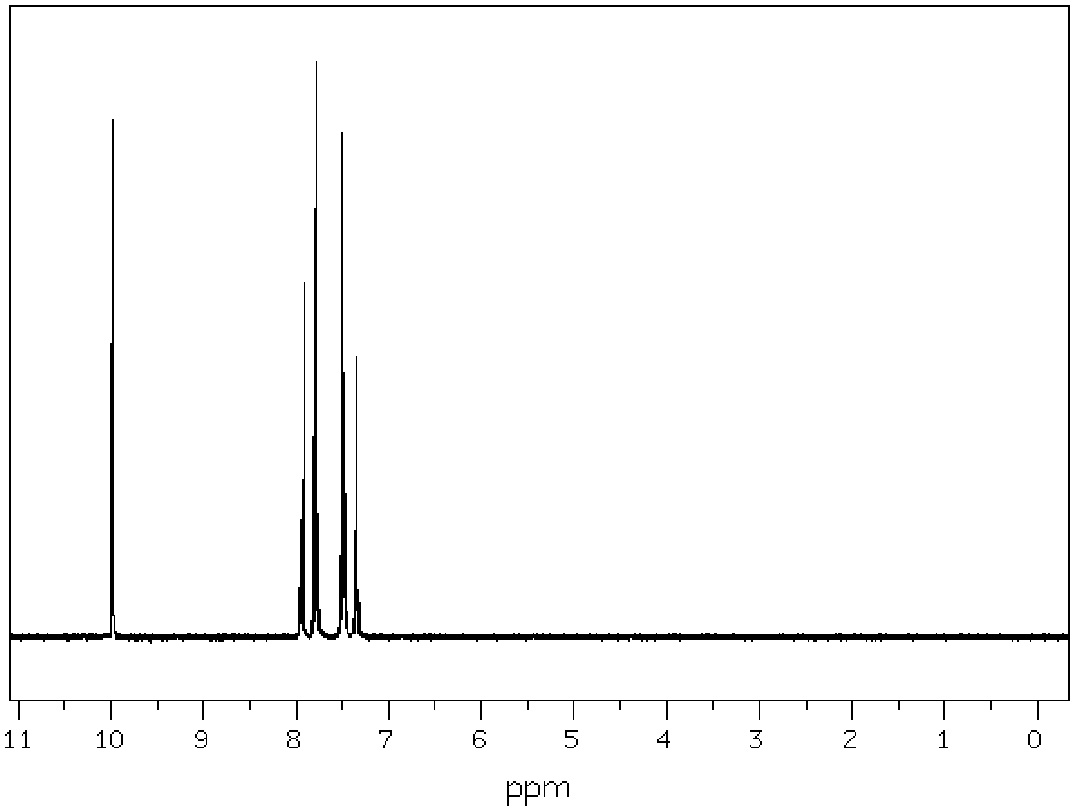
a3. Draw stereochemical structures of **A1, A2,** ephedrine and pseudoephedrine.

B. Antidepressant hydroxyzine has the molecular formula $C_{21}H_{27}ClN_2O_2$ (and $C_{21}H_{29}Cl_3N_2O_2$ for its hydrochloride). It can be synthesized from bromobenzene and compound **B2** according to the following scheme:

$$\text{bromobenzen} \xrightarrow{Mg} \mathbf{B1} \xrightarrow[2.\ H_2O]{1.\ \mathbf{B2}} \mathbf{B3} \xrightarrow{SOCl_2} \mathbf{B4} \xrightarrow{NH_3} \mathbf{B5}$$

$$\mathbf{B5} \xrightarrow[-\ 2\ HCl]{(ClCH_2CH_2)_2NH} \mathbf{B6} \xrightarrow[-\ HCl]{Cl\text{-}CH_2CH_2\text{-}O\text{-}CH_2CH_2\text{-}OH} \text{hydroxyzine}$$

Compound **B2** is a simple derivative of benzaldehyde. Below its ^1H NMR is shown:



Problem:

b. Give structures of **B2 – B6**, hydroxyzine and cation in its hydrochloride.

PROBLEM 5

Analogs of opioid peptides

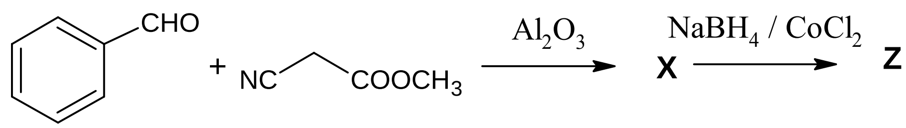
Three compounds **A, B, C -** analogs of endogenous analgesic peptides, were analyzed. It was known, that all compounds were short peptides (all of them contained the same number of amino acids) and were formed with only aromatic amino acids and iminoacid. In the sequence of two peptides proteinogenic amino acid was substituted by unnatural amino acid.

By mass spectrometry it was determined that the molecular mass of peptides **A** and **B** was 14 g/mol higher than the mass of peptide **C**. For all peptides the result of the ninhydrin test was positive.

As a result of chymotrypsin digestion three fragments were obtained from peptides **A** and **C** and only two fragments from peptide **B**. In case of two analyzed peptides the molecular mass of one cleaved fragment was 262 g/mol, additionally the fragment with the molecular mass of 165 g/mol was also obtained from one of those peptides.

Edman degradation (one cycle) of each peptide gave the same derivative with the molecular mass of 298 g/mol. Shortened peptides (resulting from Edman degradation) did not give the purple color in the ninhydrine test.

Unnantural amino acid may be synthesized in the following transformations:



Problems:

a. Give the general scheme of Edman degradation and draw the structural formula of the obtained derivative.

b. Draw the structural formulas of compounds **X** and **Z**. Is the product of the transformations optically active?

c. Give the sequences of peptides **A, B, C** and shortly explain your choice (use the three-letter code; use the letter **U** for the unnatural amino acid).

d. Shortly describe the effect of unnatural amino acid in the sequence of peptides on their stability under physiological conditions.

SOLUTIONS

SOLUTION OF PROBLEM 1

a. Solution **A.** $H_2C_2O_4$ is a diprotic acid. Since the K_{a1} value is quite high and the difference of dissociation constants K_{a1} and K_{a2} is considerable, H^+ ions concentration can be calculated taking into account only the 1st dissociation step; however, a quadratic equation should be solved in this case:

$$K_{a1} = \frac{[H^+][HC_2O_4^-]}{[H_2C_2O_4]} = \frac{[H^+]^2}{c-[H^+]}$$

where c is oxalic acid concentration. After rearrangement:

$$[H^+]^2 + K_{a1}[H^+] - K_{a1}c = 0$$

After solution $[H^+] = 0.05$ M is obtained (degree of dissociation is 50%).
Since $K_{a2} < [H^+]/40$, participation of H^+ ions from the 2nd dissociation step is negligibly small. Thus, pH = -log(0.05) = 1.3.
Since:

$$K_{a2} = \frac{[H^+][C_2O_4^{2-}]}{[HC_2O_4^-]}$$

and approximately $[H^+] = [HC_2O_4^-]$, thus, $[C_2O_4^{2-}] = K_{a2} = 5\cdot10^{-5}$ M.

Solution **B**. $C_2O_4^{2-}$ ions can be protonated, according to reactions:

$C_2O_4^{2-} + H_2O \leftrightarrows HC_2O_4^- + OH^-$ $\quad K_{b1} = 10^{-14}/K_{a2} = 10^{-14}/5\cdot10^{-5} = 2\cdot10^{-10}$

$HC_2O_4^- + H_2O \leftrightarrows H_2C_2O_4 + OH^-$ $\quad K_{b2} = 10^{-14}/K_{a1} = 10^{-14}/0.05 = 2\cdot10^{-13}$

K_{b1} and K_{b2} constants are very low, but their difference is high. Therefore, OH^- ions concentration can be determined from a simplified equation, taking into account the constant K_{b1} only:

$$[OH^-] = (K_{b1}c)^{1/2} = (2\cdot10^{-10}\cdot 0.1)^{1/2} = 4.5\cdot10^{-6}\text{ M } (c\text{: } Na_2C_2O_4 \text{ concentration})$$

Protonation degree = $[OH^-]/c = 4.5\cdot10^{-5}$ is very low, indicating correctness of the simplified equation. Moreover, $K_{b2} < [OH^-]/40$, i.e. the first protonation step predominates (resulting in $HC_2O_4^-$ ions formation).

Hence, pH = 14 + log(4.5·10^{-6}) = 8.7.
It can be also assumed that $[C_2O_4^{2-}] = c = 0.1$ M.

b. A precipitate of iron(III) hydroxide is probably obtained in solution of higher pH (solution **B**), what can be checked after calculation of free Fe^{3+} ions concentration.
Total concentration of soluble Fe(III) forms, c_{Fe}, is:
$c_{Fe} = [Fe^{3+}] + [FeC_2O_4^{+}] + [Fe(C_2O_4)_2^{-}] + [Fe(C_2O_4)_3^{3-}]$
Using equations defining stability constants of complexes, one can write:
$[FeC_2O_4^{+}] = \beta_1[Fe^{3+}][C_2O_4^{2-}]$, $[Fe(C_2O_4)_2^{-}] = \beta_2[Fe^{3+}][C_2O_4^{2-}]^2$,
$[Fe(C_2O_4)_3^{3-}] = \beta_3[Fe^{3+}][C_2O_4^{2-}]^3$
Therefore: $c_{Fe} = [Fe^{3+}] + \beta_1[Fe^{3+}][C_2O_4^{2-}] + \beta_2[Fe^{3+}][C_2O_4^{2-}]^2 + \beta_3[Fe^{3+}][C_2O_4^{2-}]^3$
and after rearrangement:
$c_{Fe} = [Fe^{3+}](1 + \beta_1[C_2O_4^{2-}] + \beta_2[C_2O_4^{2-}]^2 + \beta_3[C_2O_4^{2-}]^3)$.
Thus: $[Fe^{3+}] = c_{Fe} /(1 + \beta_1[C_2O_4^{2-}] + \beta_2[C_2O_4^{2-}]^2 + \beta_3[C_2O_4^{2-}]^3)$
Free ligand ($C_2O_4^{2-}$ ions) concentration in solution **B** was calculated earlier (problem ***a.***). Inserting this value (0.1 M) and stability constants into the above equation, the concentration: $[Fe^{3+}] = 3·10^{-20}$ M is obtained.
Concentration product $[Fe^{3+}][OH^-]^3 = 3·10^{-20} · (4.5·10^{-6})^3 = 3·10^{-36} > K_{s0}$ – precipitation can occur.

c. If the precipitate is observed only in one solution, it will not be obtained in solution **A**. In this solution the molar fraction of $Fe(C_2O_4)_3^{3-}$, X, in relation to total concentration of soluble iron(III) forms is:
$X = [Fe(C_2O_4)_3^{3-}]/c_{Fe}$
$X = \beta_3[Fe^{3+}][C_2O_4^{2-}]^3/([Fe^{3+}] + \beta_1[Fe^{3+}][C_2O_4^{2-}] + \beta_2[Fe^{3+}][C_2O_4^{2-}]^2 + \beta_3[Fe^{3+}][C_2O_4^{2-}]^3)$,
i.e. $X = \beta_3[C_2O_4^{2-}]^3/(1 + \beta_1[C_2O_4^{2-}] + \beta_2[C_2O_4^{2-}]^2 + \beta_3[C_2O_4^{2-}]^3)$.
After inserting $[C_2O_4^{2-}] = 5·10^{-5}$ M (from problem ***a.***), one obtains: $X = 0.43$.
This denotes that only 43 % of Fe(III) ions present in the solution exist as complexes with the maximal number of oxalate ligands.

d. Sodium oxalate is not suitable for separation Fe(III) as complexes, because $Fe(OH)_3$ precipitate is obtained. Concentration of free Fe^{3+} ions in oxalic acid solution (solution **A**) is calculated identically as that in solution **B** (problem ***b.***), taking $c_{Fe} = 10^{-4}$ M and $[C_2O_4^{2-}] = 5·10^{-5}$ M. After inserting the data into the equation, $[Fe^{3+}] = 1.1·10^{-10}$ M is obtained, equal approximately to 10^{-4} % of total amount of Fe(III) in this solution. Although, the molar fraction of $Fe(C_2O_4)_3^{3-}$ is 0.43 only, the oxalic acid solution is applicable for separation of iron(III) ions in the form of oxalate complexes.

SOLUTION OF PROBLEM 2

a. As the result of reaction between iodine with iodide, various polyiodides may be formed comprising anions of I_n^- type (n = 3, 5, 7, 9) or I_m^{2-} type (m = 4, 8, 16). They are stable in salts with cations of large ionic radius, e.g. K^+.
For the reaction, the following substances were used: *n(KI)* = 9,13 g / 166,00 g/mol = 0,055 moles of KI and *n(I₂)* = 13,96 g / 253,80 g/mol = 0,055 moles of I_2. It results from the above that the reaction stoichiometry is 1:1 and that the potassium triiodide is formed, $KI + I_2 \rightarrow KI_3$.
The solution of salt **A** reacts with sodium thiosulfate according to the following reaction:
$$I_3^- + 2S_2O_3^{2-} \rightarrow S_4O_6^{2-} + 3I^-,$$

and for the titration of I_3^- $n(Na_2S_2O_3)$ = 0,2 mol/dm^3 × 0,0217 dm^3 = 4,34·10^{-3} mols of thiosulfate were used, thus triiodide in the solution equals: ½ × $n(Na_2S_2O_3)$ = 2,17·10^{-3} moles, which is equal to 2,17·10^{-3} mola × 419,8 g/mol = 0,911 g of KI_3. It was given in the text that 0,950g of salt **A** was used for titration, so the salt **A** is salt hydrate containing 0,950g − 0,911 g = 0,039 g of water which is equal to $n(H_2O)$ = 0,039 g / 18,02 g/mol = 2,17·10^{-3} moles of H_2O. In consequence the chemical formula for salt **A** is $KI_3 \cdot H_2O$.

b1. In the reaction between potassium iodide and chlorine two compounds may be formed, $KICl_2$ or $KICl_4$. The compound **B** is salt hydrate, thus in order to determine its chemical formula it is necessary to make the appropriate calculations from the mass loss during its decomposition reaction (see below).

The chemical formula of compound **B** may be also calculated using the available data.

An example of calculations

- it is obvious that during decomposition reaction of compound **B**, the potassium chloride is formed (it is chloride since in reaction with $AgNO_3$ it gives opaque white precipitate of AgCl soluble in ammonia. It is a potassium salt since K^+ is the only cation occuring in the mentioned compounds used for synthesis, moreover it is stable in water solution). It results from the above that the compound **B** contains both chlorine and potassium, so it must be a potassium salt.
- moreover the compound **B** should contain iodine, since the iodide was used for the reaction and no traces of iodine came out (it appeared only temporarily during synthesis of **B**). Thus, the general formula of compound **B** may be written as $K_xI_yCl_z \cdot nH_2O$.
- in this compound potassium occurs as K^+, whereas in the anion, iodine is a coordination centre (since it has lower electronegativity than chlorine) with Cl^- as ligands. Oxidation states of iodine may be: +1, +3, +5 lub +7, so the chemical formula of **B** may be as follows: $KICl_2 \cdot nH_2O$, $KICl_4 \cdot nH_2O$, $KICl_6 \cdot nH_2O$ or $KICl_8 \cdot nH_2O$, respectively.
- decomposition of compound **B** gives water, iodine, chlorine and one solid product KCl. From the observed mass loss the hydration of salt **B** and its chemical formula may be calculated (an example of calculations for $KICl_2 \cdot nH_2O$ is presented below).
  Observed mass loss: (15,32 g − 4,48 g)/15,32 g = 0,7076 g.
  Decomposition reaction of $KICl_2 \cdot nH_2O$ salt is presented by the following equation:
  $$2KICl_2 \cdot nH_2O \xrightarrow{\Delta T} 2KCl + 2ICl + 2nH_2O$$
  If n = 1 then the theoritical mass loss during the reaction amounts to: (254,92 g − 74,55 g)/254,92 = 0,7076 g, which is in agreement with the observed one.

Thus the compound **B** is **$KICl_2 \cdot H_2O$**.

It is easy to prove, that if the stoichiometry of compound **B** was different and if this salt was more hydrated then the mass loss would be greater.

b2. Synthesis reaction for salt **B**: $KI + Cl_2 + H_2O \rightarrow KICl_2 \cdot H_2O$,

Decomposition reaction for salt **B**: $2KICl_2 \cdot H_2O \xrightarrow{\Delta T} 2KCl + 2ICl + 2H_2O$.

which may be also written as: $2KICl_2 \cdot H_2O \xrightarrow{\Delta T} 2KCl + I_2 + Cl_2 + 2H_2O$

c1. Electric conductivity of iodine solution in pyridine is caused by the presence of anions from autodissociation of iodine: anion I^- and cation I^+ of strong electrophilic properties. This cation forms with pyridine stable complexes of formula $[I(C_5H_5N)_x]^+$ as pyridine is strongly nucleophilic. Consequently, the mixture of iodine in pyridine reacts with silver chlorate (VII) resulting in the formation of AgI and $[I(C_5H_5N)_x]ClO_4$.

It is known from the text, that the reaction of salt **C** with potassium iodide leads to formation of iodine (synproportionation red-ox), which was then titrated with sodium thiosulfate. From this experiment the composition of salt **C** may be determined.

Amount of sodium thiosulfate used during titration is equal to:

$$n(Na_2S_2O_3) = 0{,}2 \text{ mol/dm}^3 \times 0{,}0246 \text{ dm}^3 = 4{,}92\cdot10^{-3} \text{ moles.}$$

From the stoichiometry of the reaction:

$$I_2 + 2S_2O_3^{2-} \rightarrow S_4O_6^{2-} + 2I^-$$

amounts of I_2 in the solution may be calculated as follows: ½ × $n(Na_2S_2O_3)$ = $2{,}46\cdot10^{-3}$ moles. Since the synproportionation reaction between I^+ and I^- occurs as 1:1, the amount of silver chlorate (VII) is equal to $2{,}46\cdot10^{-3}$ moles. The molar mass as well as the chemical formula of salt **C** may be calculated from the mass of salt **C** used for titration:

$$0{,}946 \text{ g} / 2{,}46\cdot10^{-3} \text{ mol} = 384{,}55 \text{ g/mol.}$$

which corresponds to: **$[I(C_5H_5N)_2]ClO_4$**.

c2. Reaction occurring in iodine solution in pyridine:

$$2I_2 + 2C_5H_5N \leftrightarrows [I(C_5H_5N)_2]^+ + I_3^-$$

which may be also written as: $I_2 + 2C_5H_5N \leftrightarrows [I(C_5H_5N)_2]^+ + I^-$

c3. Synthesis reaction of salt **C:**

$$I_2 + 2C_5H_5N + AgClO_4 \xrightarrow{CHCl_3} [I(C_5H_5N)_2]ClO_4 + AgI$$

c4. In triiodide anion I_3^- (the anion of salt **A**), in ICl_2^- (the anion of salt **B**) and in $[I(C_5H_5N)_2]^+$ (the cation of salt **C**) it may be assumed that I^+ is the coordination center. It means, that in the coordination sphere there are three lone electron pairs and two bonding electron pairs from iodide or chloride ligands. By the use of VSEPR model, the linear arrangement of those ions may be predicted. This structure posses a trigonal bipyramid geometry, in which lone electron pairs are directed towards in the vertices of the base (equatorial plane), whereas electron pairs, originating from ligands located in the remaining two vertices of the bipyramid (axial positions), form the angle of 180°.

SOLUTION OF PROBLEM 3

a1. $\ln K = \dfrac{-\Delta G^0{}_r}{RT} = \dfrac{17\cdot10^3 \text{J}\cdot\text{mol}^{-1}}{8.314\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}\cdot374\text{K}} = 5.47$, hence: $K = 2.37\cdot10^2$

a2. At the equilibrium, the amount of CO_2, H_2, CH_3OH and H_2O in the vessel is x, $3x$, $(1-x)$ and $(1-x)$ moles, respectively. The total amount of gases present in the reactor is $2+2x$. Since the total pressure in the reactor is equal to the standard pressure (1000 hPa), the ratio of the partial pressure of a given compound and the standard pressure is equal to its molar fraction.

First, we write the equation for the equilibrium constant and insert the appropriate expressions for partial pressure.

$$K = \frac{(p_{H_2}/p^0)^3\cdot(p_{CO_2}/p^0)}{(p_{CH_3OH}/p^0)\cdot(p_{H_2O}/p^0)} = \frac{\left(\dfrac{3x}{2+2x}\right)^3\cdot\dfrac{x}{2+2x}}{\dfrac{1-x}{2+2x}\cdot\dfrac{1-x}{2+2x}} = \frac{27x^4}{(2+2x)^2\cdot(1-x)^2}$$

After taking square root from both sides, the equation is:

$$(2+2x)\cdot(1-x) = x^2\cdot\sqrt{27/K}$$

Some more transformations lead to:

$$x^2 = \frac{2}{2+\sqrt{27/K}}$$

Only the positive solution has physical meaning:

$$x = \sqrt{\frac{2}{2+\sqrt{27/K}}}$$

After inserting numerical values we obtain: x=0.925, which means that in the given conditions 92.5% of methanol is decomposed to hydrogen.

a3. The problem is solved analogously to point **a2**, only the total amount of substances in the reactor is now 22+2x moles instead of 2+2x moles. The obtained equation is:

$$(22+2x)\cdot(1-x) = x^2 \cdot \sqrt{27/K}$$

After inserting numerical values the positive solution is calculated (since only it is physically meaningful). It is x = 0.986, which means that in the given conditions 98.6% of methanol is transformed into hydrogen.

a4. In order to obtain 3 moles of hydrogen 53 kJ of heat needs to be consumed by the system. This amount of heat can be produced by oxidation of 53/(0.5·485) = 0.22 moles of hydrogen. Thus (0.22/3)·100%=7.3% of the produced hydrogen needs to oxidized for the total thermal effect to be zero.

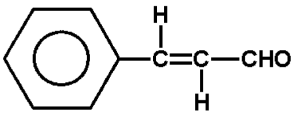
b1. Let x denote the deuterium content (in atomic percent) in the hydrogen sample. The probability that a randomly chosen methanol molecule contains light hydrogen in a selected position (for example in the hydroxyl group) and 3 atoms of deuterium in the remaining positions is $[(100-x)/100]\cdot[x/100]^3$. In the methanol molecule containing 3 atoms of deuterium and 1 atom of light hydrogen the latter can occupy one position out of four. Thus, the percentage of methanol containing three atoms of deuterium and one atom of light hydrogen is : $[(100-x)/100]\cdot[x/100]^3\cdot 4\cdot 100\%$. Two atoms of deuterium (or light hydrogen) can occupy 6 different pairs of positions (1–2, 1–3, 1–4, 2–3, 2–4 and 3–4). The percentage of methanol molecules with two atoms of deuterium and two atoms of light hydrogen is therefore: $[(100-x)/100]^2\cdot[x/100]^2\cdot 6\cdot 100\%$.

Thus the ratio: $$\frac{4\cdot[(100-x)/100]\cdot[x/100]^3}{6\cdot[(100-x)/100]^2\cdot[x/100]^2} = \frac{4\cdot x}{6\cdot(100-x)} = 1.55$$

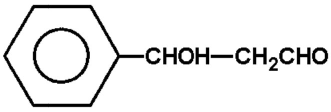
Solving the above equation we obtain x = 69.9, which means that the percentage of deuterium in the hydrogen sample is 69.9% (in atomic percent).

SOLUTION OF PROBLEM 4:

a1. Structure of **A0**:



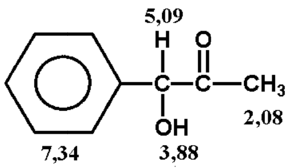
or



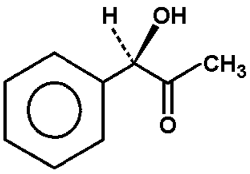
a2. Because compound **A1** is a reaction product of two simple aldehydes it does not contain nitrogen or other heteroatoms (except oxygen). IR spectrum shows the presence of carbonyl (1713 cm^{-1}) and hydroxyl (3454 cm^{-1}) groups. In ^{1}H NMR we have at δ = 7,34 ppm aromatic protons (monosubstituted benzene ring). The signal at 2,08 ppm with relative intensity of 3 goes for methyl group, which is not coupled with any other protons and is not at benzene ring. So it is attached to carbonyl group. The other two signals are for CHOH, whilst the broad one suits for O<u>H</u> and the second at 5.09 p.p.m. is for C<u>H.</u> We can confirm our findings on the basis of ^{13}C NMR. Aromatic carbons are in the range of 127 -140 p.p.m., the signal at 206.8 p.p.m. is for carbonyl carbon, 25.3 p.p.m. – for methyl carbon and that one at 80.1 p.p.m. for <u>C</u>HOH.

Conclusion: compound **A1** is 1-hydroxy-1-phenylpropan-2-on.

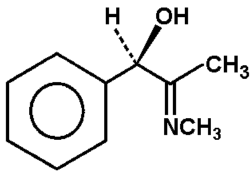
^{1}H MNR interpretation (p.p.m.)



a3.

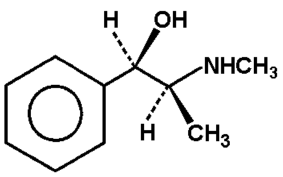


A1

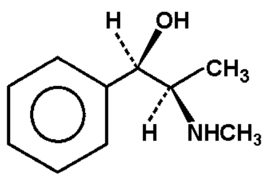


A2

*If we compare molecular weight of **A2** ($C_{10}H_{13}NO$), which is 163.2 with the given molecular weight of ephedrine (165.2), we can see that C=N bond was reduced only (aromatic ring remained intact), so ephedrine is [(-)-2(S)–(methylamine)-1(R)-phenylpropan-1-ol], and the required stereochemical structures are as follows:*



(-)-Ephedrine



(-)-Pseudoephedrine

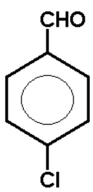
b. *^{1}H NMR spectrum tells us that compound **B2** is para-monosubstituted benzaldehyde (let call it temporarily X-C_6H_5-CHO), where X contains no hydrogen (for example we can include p-bromobenzaldehyde, p-chlorobenzaldehyde, p-nitrobenzaldehyde or p-formylbenzonitrile for **B2).***

***B1** – Grignard compound formed from bromobenzene;*

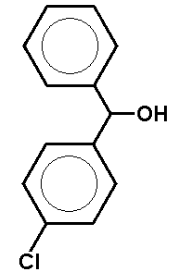
B3* – *benzhydrol derivative: X-C_6H_5-CHOH-C_6H_5;
B4* – *benzhydrol derivative: X-C_6H_5-CHCl-C_6H_5;
B5* – *benzhydrol derivative: X-C_6H_5-$CHNH_2$-C_6H_5 (alkylation product of ammonium by *B4*);
B6* – *product of double alkylation of* B5*, while heterocyclic ring with two nitrogen atoms is formed;

As we can see the chlorine atom present in hydroxizine was not introduced during the course of the synthesis, so it must be originated from the early substrate - ***B2.*** *Indeed we conclude the structure of p-chlorobenzaldehyde for* ***B2****.*

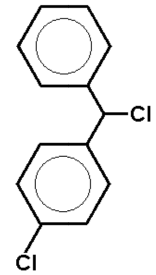
The complete answer to the ***Problem 4b*** is shown below.



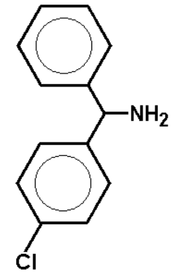
B2



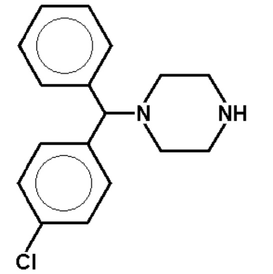
B3



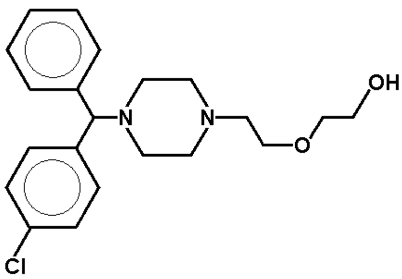
B4



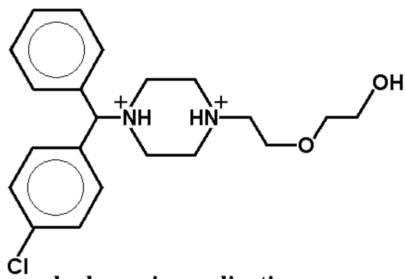
B5



B6



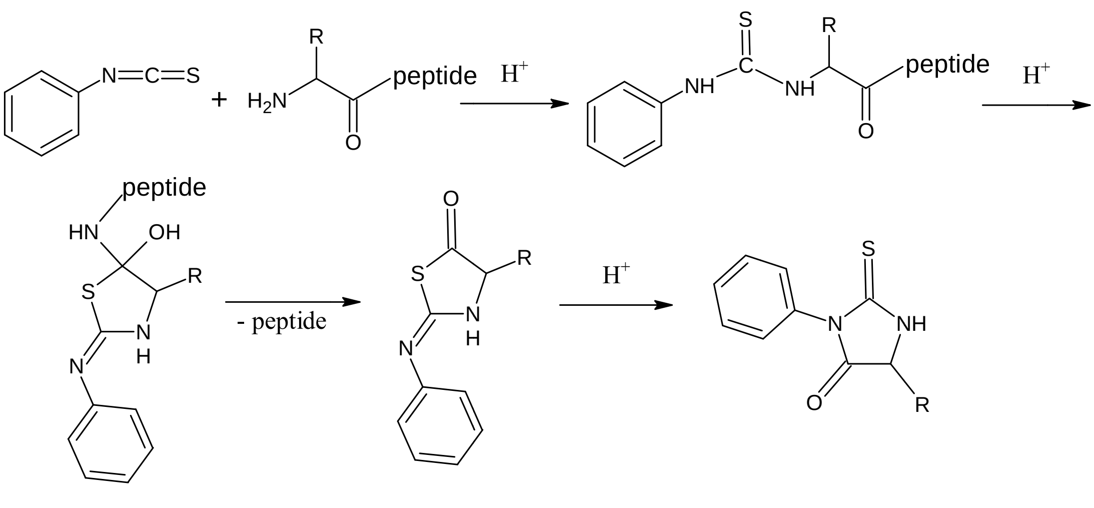
hydroxyzine



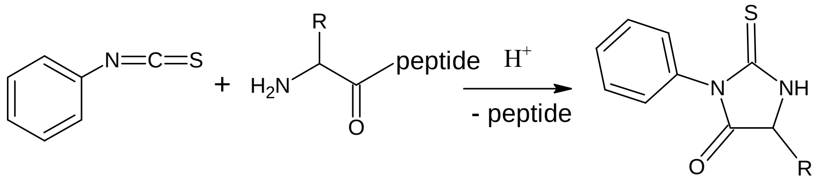
hydroxyzinum dication

<u>SOLUTION OF PROBLEM 5</u>

a. Edman degradation is a method of sequencing amino acids in a peptide. It also allows to identify the N-terminal amino acid. The scheme of reactions is as followed:



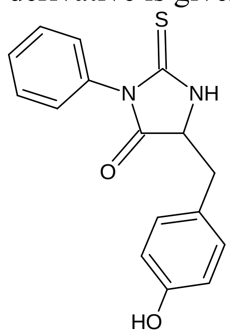
or shorter:



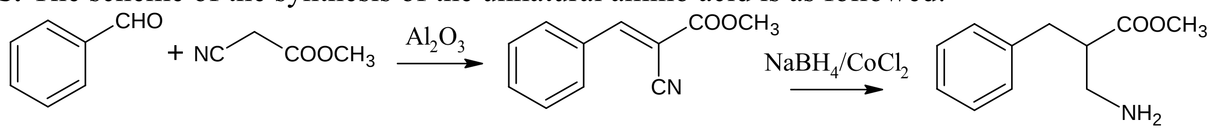
It is known that the molecular mass of obtained derivative is 298 g/mol. The isothiocyanate fragment has the mass of 135 g/mol. It is easy to calculate the molecular mass of the amino acid residue:

298-135= 163, 163+18(H_2O)=181 g/mol – it is the molecular mass of tyrosine (Tyr).

The structural formula of the obtained derivative is given below:



b. The scheme of the synthesis of the unnatural amino acid is as followed:



Compound **X** is the unsaturated nitrile obtained in the Knoevenagel reaction. The reduction with $NaBH_4$ in the presence of $CoCl_2$ of such nitrile leads to the ester of unnatural amino acid (**Z**).

Equimolar mixture of enantiomers is obtained. It means that the product of the synthesis is not optically active.

c. It is known that only aromatic amino acids and iminoacid were found in the sequence of all peptides **A, B, C**. All analyzed peptides give the purple color with ninhydrin, but the shortened peptides obtained in one cycle of Edman degradation do not. It means that the second residue is an iminoacid. Proline (Pro) is the only known natural iminoacid. So the N-terminal part of the peptides is Tyr-Pro.

The molecular mass of peptides **A** and **B** is 14 g/mol higher than the mass of peptide **C**. It suggests the presence of additional CH_2 group. The unnatural amino acid is β-hPhe, so it can be found in the sequence of peptides **A** and **B**.

Chymotrypsin is an enzyme which cleaves peptides at the carboxyl side of aromatic amino acids. After digestion three fragments are obtained from peptides **A** and **C** and only two fragments from peptide **B**. One of the cleaved fragments is N-terminal tyrosine. In case of two analyzed peptides the 262 g/mol fragment is also cleaved. It may contain Pro:

262 – 115(Pro) + 18(H_2O)=165 g/mol – it is the molecular mass of phenylalanine (Phe). 165 g/mol is also the molecular mass of additional fragment obtained in enzymatic digestion of one peptide.

As it was mentioned above, peptide **C** is formed only from proteinogenic aromatic amino acids and iminoacid. The sequence of peptide **C** is:

chymotrypsin

Tyr|Pro-Phe|Phe

In chymotrypsin digestion of peptides **A** and **C** three fragments were obtained, the difference between those two peptides must be in the C-terminal part. So the sequence of the peptide **A** is:

chymotrypsin

Tyr|Pro-Phe|U

The difference between peptide **A** and **B** must be in the third position (enzymatic digestion). So the sequence of the peptide **B** is:

chymotrypsin

Tyr|Pro-U-Phe

d. Peptides with unnatural amino acid in the sequence are more resistant to the enzymatic digestion. The peptide bond on the carboxylic side of the unnatural amino acid is not hydrolyzed.