47th

International Chemistry Olympiad

PREPARATORY PROBLEMS

Edited by Anton Sirota

26 theoretical problems
8 practical problems

2015

THE PREPARATORY PROBLEMS FROM THE INTERNATIONAL CHEMISTRY OLYMPIADS, Series 1
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Preparatory problems

47th International Chemistry Olympiad

(IChO-2015)

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P r e f a c e

written by members of the IChO-2015 Science Committee in Baku
(a shortened version)

We are happy to present the preparatory problems for the 47th International Chemistry Olympiad. The members of the Science Committee really did their best to prepare interesting tasks. The set covers all major parts of modern chemistry. All the tasks can be solved by applying a basic knowledge of chemistry, even in case a problem refers to a topic of advanced difficulty.

A great attention is paid to safety. At the registration in Baku the head mentors will be asked to sign a form stating that their students are aware of the safety rules and adequately trained to follow them. Prior to the Practical Examination all students will have to read and sign safety instructions translated into their languages of choice.

Members of the IChO-2015 Science Committee

Topics of advanced difficulty

Theoretical

1. The First Law of thermodynamics: thermodynamic cycles, adiabatic processes, work of adiabatic processes.
2. The Second Law of thermodynamics: spontaneous chemical reactions. Dependence of Gibbs energy of reaction on concentrations. Relation between equilibrium constant, electromotive force and standard Gibbs energy. Latimer diagrams.
3. Integrated rate law for first order reactions, half-life, mean life time. Analysis of complex reactions using steady-state and quasi-equilibrium approximations, mechanisms of catalytic reactions, determination of reaction order for complex reactions.
4. Inorganic complexes: structure and isomerism. Crystal field theory. Trans-effect.
5. Preparation and chemical properties of carbonyl compounds.
6. Oxidoreductase- and transferase-catalyzed reactions in metabolism of nucleotides and xenobiotics.

Practical

1. Advanced procedures in organic synthesis: heating under reflux, vacuum filtration, vacuum distillation, determination of refraction index, use of a nomogram.

2. Kinetics of chemical reactions: photometric studies and analysis of experimental data with the English version of Microsoft Excel software.

Note. The hereunder topics met in the Preparatory problems:

- Clapeyron equation for phase transition
- Rate of heterogeneous reactions
- Claisen rearrangement
- Determination of a melting point
- Calculation of solubility in the presence of complexing agents
- Rotary evaporation
- Liquid-liquid extraction
- Deciphering a compound structure using NMR and mass spectrum data are inalienable parts of the proposed tasks. We do not expect students to get an advanced training in the above skills and concepts, since these will not appear neither in the Practical, nor in the Theoretical Exam set.

THE FORTY-SEVENTH
INTERNATIONAL CHEMISTRY OLYMPIAD

20–29 JULY 2015, BAKU, AZERBAIJAN

PREPARATORY PROBLEMS

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Theoretical problems and their solutions

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PREPARATORY THEORETICAL PROBLEMS

THEORETICAL PROBLEM 1

Brayton cycle

Students have made a device capable to operate in a mode that is close to the ideal Brayton cycle. This thermodynamic cycle has once been proposed for development of internal combustion engines. The device consists of a cylinder with 1 mole of helium fitted with a computer-controlled movable piston. A Peltier element which can heat or cool the gas is mounted in the cylinder wall. The device can operate in the following modes: 1) reversible adiabatic expansion or compression, 2) reversible isobaric cooling or heating.

Through a number of cooling and compression steps, helium is going from the initial state with the pressure of 1 bar and the temperature of 298 K into the final state with the pressure of 8 bar and the temperature of 298 K. (The total number of cooling and compression stages can be from two up to infinity).

1.1 What is the minimum work that should be done on the gas for this? Compare this value to the work during a reversible isothermal compression.

1.2 What is the maximum work that can be done on the gas in this process?

1.3 Let the process be accomplished in three steps. At each step helium is first cooled and then compressed. At the end of each step the pressure increases twice and the temperature returns to the value of 298 K. What is the total heat removed from the gas by a Peltier element?

Once the gas is compressed, it is returned to the initial state (1 bar and 298 K) in two stages (heating and expansion).

1.4 What is the range of possible values of the formal efficiency η for the resulting cycle? η is the ratio of the useful work done by the gas to the amount of heat given to the gas during the heating stage.

1.5 In one of the experiments, the gas has been compressed from 1 bar and 298 K to 8 bar and 298 K in several steps (like in question 3). At the end of each step the

pressure is increased by *x* times and the temperature returns to 298 K. Then helium has been returned to the initial state in two stages – heating and expansion. Theoretical value of η for this cycle is 0.379. How many steps were used?

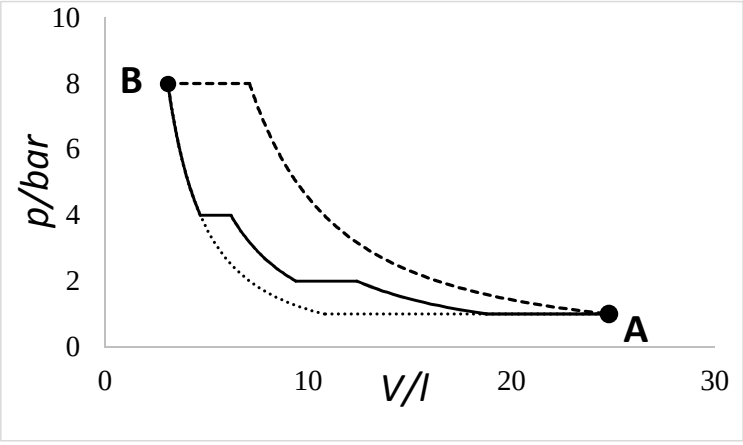
In fact, Peltier elements also consume electric energy during the cooling stage. Assume that they consume as much energy as is removed from the gas.

1.6 What is the maximum possible efficiency of the considered cycle, taking into account energy consumption during cooling?

Hint: In reversible adiabatic process for helium $pV^{5/3} = const$. Isochoric molar heat capacity of helium is 3/2*R*.

SOLUTION OF PREPARATORY PROBLEM 1

1.1 As can be seen from the figure, there are many possible ways to go from point A (1 bar, 298 K) to point B (8 bar, 298 K) using only adiabatic and isobaric segments. The work *W* is equal to the area under the path. It is clear that *W* is minimal if we complete the process in two stages: isobaric cooling and then adiabatic compression.



We will derive a general formula to calculate the work of transformation from (p_1, T_1) to (p_2, T_2) in two stages. If for the reversible adiabatic process $pV^{5/3} = p\left(\frac{RT}{p}\right)^{5/3} = \text{const}$, then $\frac{T^{5/3}}{p^{2/3}} = const$, or $\frac{T}{p^{2/5}} = const$. After the isobaric

stage, the pressure is still p_1 and the temperature is $T = T_2\left(\frac{p_1}{p_2}\right)^{2/5}$. The work at the adiabatic stage is $W_2 = \Delta U = \frac{3}{2}RT_2\left(1-\left(\frac{p_1}{p_2}\right)^{2/5}\right)$, and at the first stage $W_1 = p_1(V_1 - V) = R\left(T_1 - T_2\left(\frac{p_1}{p_2}\right)^{2/5}\right)$.

In total, $W = W_1 + W_2 = RT_1 + \frac{3}{2}RT_2 - \frac{5}{2}RT_2\left(\frac{p_1}{p_2}\right)^{2/5}$. If $T_1 = T_2$,then $W = \frac{5}{2}RT_2\left(1-\left(\frac{p_1}{p_2}\right)^{2/5}\right)$. Thus, $W = \frac{5}{2}\times 8.314\times 298\times\left(1-\left(\frac{1}{8}\right)^{2/5}\right) = 3500$ J.

In a reversible isothermal compression, $W = RT\ln\frac{p_2}{p_1} = 5150$ J.

1.1.1 The maximum work is done when the first stage is adiabatic and the second one is isobaric. We can use the same formula for the reverse process and obtain the work with the opposite sign.

$$W = -\frac{5}{2}RT_2\left(1-\left(\frac{p_2}{p_1}\right)^{2/5}\right) = -\frac{5}{2}\times 8.314\times 298\times\left(1-\left(\frac{8}{1}\right)^{2/5}\right) = 8040 \text{ J}.$$

1.3 According to the first law of thermodynamics, $Q = W + \Delta U = W$. The total work done on the gas during three steps is: $W = 3\times\frac{5}{2}RT_2\left(1-\left(\frac{1}{2}\right)^{2/5}\right) = 4500$ J.

1.4 The maximum efficiency is achieved when the area of the cycle is the largest, i.e. when we complete the cycle in four steps: cooling, compression, heating, expansion.

Then $\eta = \frac{8040 - 3500}{8040} = 0.565$. All the efficiencies from 0 to 0.565 are possible, if we go in more steps.

1.5 The work *W* done on gas during cooling and compression stages can be found from equation $\eta = \frac{8040 - W}{8040} = 0.379$; *W* = 4993 J.

If the number of steps is *n*, then $x = 8^{1/n}$. Since the work at each step is the same, the total work is: $W = n \times \frac{5}{2} R T_2 \left(1 - \left(\frac{1}{8}\right)^{2/5n}\right)$. After some calculations with different integer *n*, we find that *n* = 13.

1.6 $\eta = \frac{8040 - 3500}{8040 + 3500} = 0.393$.

THEORETICAL PROBLEM 2

Liquefied natural gas

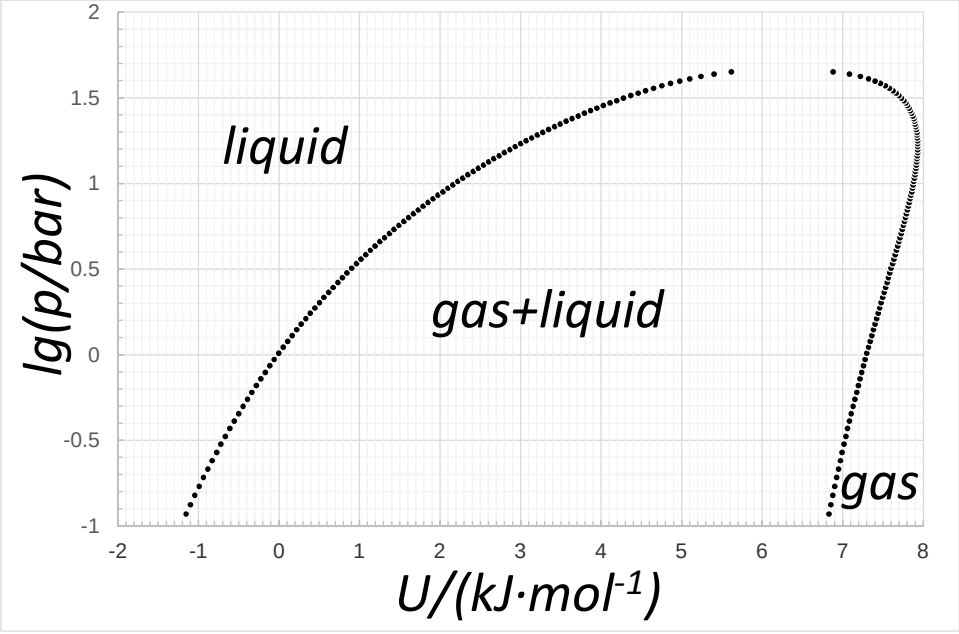
Liquefied natural gas (LNG) is being produced in the world in increasing amounts. It has a high energy density in comparison with the compressed natural gas, so that liquefaction is advantageous for transportation over long distances, especially by sea. The main component of LNG (> 95%) is methane. The dependence of the boiling point of methane on pressure is well described by the empirical equation:

$$\log (p/\text{bar}) = 3.99 - 443 / (T/\text{K} - 0.49)$$

2.1 What is the boiling point of methane at atmospheric pressure?

A typical cryogenic tank for marine transportation of the LNG has a volume of 40 000 m^3, in which it is stored at –159 ℃. This tank has no external cooling, and the pressure inside it is kept constant. Initially the tank is fully loaded with 16 800 tons of liquid methane, but during the sailing time it partially evaporates. The evaporated gas can be used as a fuel in the engine of the marine vessel.

2.2 Estimate how many times larger is the energy density per unit volume of liquefied methane than that of gaseous methane in cylinders under 300 bar pressure at room temperature (298 K). (The compressibility factor of methane at these conditions is close to 1, and thus the ideal gas law can be applied.)



A phase diagram of methane given above is plotted in the coordinates 'logarithm of pressure in bars (log *p*) – internal energy (*U*)'. It is based on the experimental data [Setzmann and Wagner, 1991]. The area encircled by black dots (data points) corresponds to equilibrium coexistence of liquid and gaseous methane, while out of it methane is either completely liquid or completely gaseous. Using the diagram, answer the following questions:

2.3 What is the enthalpy of vaporization of methane under conditions of its transportation?

2.4 What percent of methane will evaporate after 15 days of sailing, given that the total heat leakage through the cryogenic tank is 50 kW?

2.5 For long term storage of LNG, it was suggested not to discharge evaporating methane but to seal the tank. A pilot experiment has been conducted with the same tank initially filled with liquid methane (at temperature –159 ℃) up to exactly a third of its volume. After 9 months of storage, the pressure inside the tank grew up to 16.4 bar. Which part of methane has evaporated inside the tank? Assume that the heat leakage is the same as in the previous question.

2.6 What can be the maximum temperature of the liquefied methane? What would be the pressure in the reservoir containing it?

SOLUTION OF PREPARATORY PROBLEM 2

2.1 $T = 0.49 + 443 / (3.99 - \log p) = 111.5$ K

2.2 Under 300 bar pressure at 298 K, 40000 m^3 have the mass

$m = \frac{pVM}{RT} = \frac{300 \cdot 10^5 \times 40000 \times 0.016}{8.314 \times 298} = 7.75 \cdot 10^6$ kg, or 7750 tons. Thus, LNG has

$\frac{16800}{7750} = 2.17$ times larger energy density.

2.3 The pressure inside the tank is the saturated vapor pressure of methane at the given temperature: $\log p = 3.99 - 443 / (273.15 - 159 - 0.49) = 0.0924$, $p = 1.24$ bar. Using

the diagram, one can calculate the distance between two black points at log p =0.1 to be about $\Delta U = 7.2$ kJ mol^{-1}. Thus, $\Delta H = \Delta U + RT = 8.1$ kJ·mol^{-1}.

2.4 Total heat obtained by methane is $Q = 50000 \times 3600 \times 24 \times 15 = 6.48 \cdot 10^{10}$ J. It will lead to evaporation of $\frac{Q}{\Delta H} \times M = 1.28 \times 10^5$ kg, or 128 tons, or 0.76 % of methane.

2.5 Total heat obtained by methane is $Q = 50000 \times 3600 \times 24 \times 9 \times 30.5 = 1.19 \cdot 10^{12}$ J. It will lead to an increase of the internal energy per mole of methane by $\Delta U = \frac{Q}{m} \times M = \frac{1.19 \cdot 10^{12}}{16800000/3} \times 0.016 = 3.39$ kJ mol^{-1}. From the diagram, the initial internal energy at –159 ℃ is 0.1 kJ·mol^{-1}. The abscise of the point corresponding to the final state on the diagram will thus be approximately 0.1 + 3.4 = 3.5 kJ mol^{-1}. The ordinate is log p = 1.2. The ratio of the lengths of the line segments from this point to the borders of the phase coexistence curve (blue and red line segments in the figure below) is equal to the ratio of the number of moles of methane in vapor and liquid phases. One can find that about 6 / 51 = 12 % of methane is in the gas phase.

2.6 The maximum possible temperature is the critical temperature of methane, corresponding to the maximum of log p vs U curve. From the diagram we find log p_c = 1.65, then p_c= 44.7 bar and T_c = 0.49 + 443 / (3.99 – log p) = 190 K.

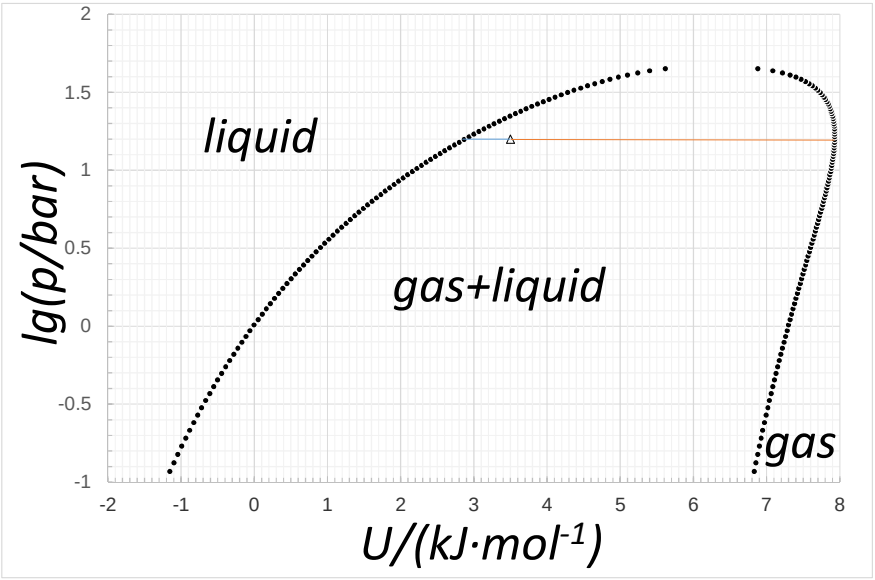
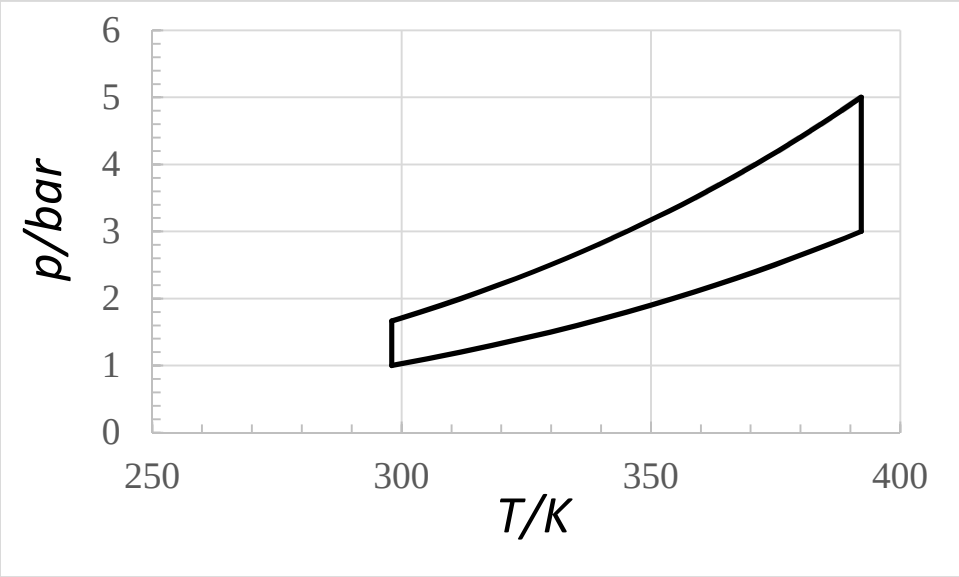


Figure. Graphical answer to question 5

THEORETICAL PROBLEM 3

Carnot cycle

In the following graph, a reversible Carnot cycle for an ideal gas is shown in «pressure-temperature» coordinates. A cycle consists of two isotherms and two adiabates.



Using this graph, calculate the following magnitudes or show that it is impossible:

3.1 The useful work of the cycle.

3.2 The efficiency η of the cycle.

3.3 The isochoric molar heat capacity of a gas.

3.4 The number of atoms in the molecule of a gas.

Hint: In reversible adiabatic process for an ideal gas, $pV^{(1+R/C_V)} = const$ where C_V is the isochoric molar heat capacity.

Hint: in reversible adiabatic process for an ideal gas, $pV^{(1+R/C_V)} = const$ where C_V is the isochoric molar heat capacity.

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SOLUTION OF PREPARATORY PROBLEM 3

3.1 This is impossible because we do not know the number of moles of a gas.

3.2 $\eta = \frac{T_2 - T_1}{T_2} = \frac{390 - 298}{390} = 0.24$.

3.3 Since $pV^{(1+R/C_V)} = p\left(\frac{RT}{p}\right)^{(1+R/C_V)} = const$, then $\frac{T^{(1+R/C_V)}}{p^{R/C_V}} = const$, or $\frac{T}{p^{R/(C_V+R)}} = const$.

Thus, we can find C_V from the initial and final temperatures and pressures of the adiabate: $\ln\frac{T_2}{T_1} \Big/ \ln\frac{p_2}{p_1} = R/(C_V + R)$

$C_V = R\left(\ln\frac{p_2}{p_1} \Big/ \ln\frac{T_2}{T_1} - 1\right) = 3\,R.$

3.4 It can be any number from 3 and above (the molecule should be non-linear).

THEORETICAL PROBLEM 4

Quasi-equilibrium model

Equilibrium constants are often included into the rate equations for complex chemical reactions. For some rapid reversible steps the ratio of concentration of products to concentration of reactants is assumed to be equal to equilibrium constant, though reaction as a whole still proceeds and chemical equilibrium is not attained. This is *quasi-equilibrium approximation*. The concept of quasi-equilibrium makes rate equations much simpler which is vitally important for complex reactions.

Consider kinetics of a complex reaction

$$A + B \xrightarrow{k_{eff}} C + D$$

The following mechanism was proposed

$$A + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} AB \xrightarrow{k_2} AB^* \xrightarrow{k_3} C + D$$

The rates of the forward and reverse reaction of the first step are almost equal,

$$r_1 \gg r_{-1}$$

i.e., quasi-equilibrium is reached.

4.1 Calculate k_{eff}, if $k_1 / k_{-1} = 10$ mol^{-1} dm^3, $k_2 = 20$ s^{-1}.

Metallic platinum loses its mass interacting with the flow of atomic fluorine at $T = 900$ K. Partial pressure of F in the incident flow near the surface is 10^{-5} bar, see Fig.1.

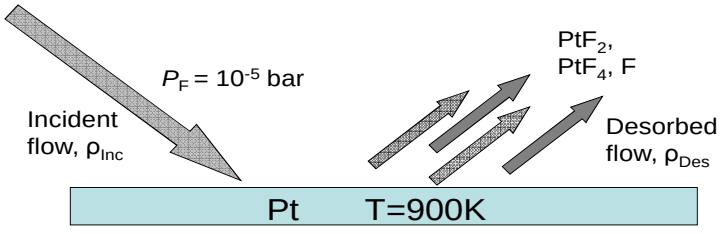


Fig. 1. Gasification of Pt by a flow of atomic fluorine

No solid products of interaction of Pt with F were found on the surface. Gaseous species PtF_4 и PtF_2 were detected in the flow desorbed from the surface. The ratio $p^2_{PtF_2} / p_{PtF_4}$ was equal to $1 \cdot 10^{-4}$ bar and did not vary with the change of the incident atomic fluorine flow.

Use the data in the Table to answer the following questions:

Table

Reaction	K_p (900 K), bar^{-1}	Gaseous species	p(900 K), bar
$2\ F(g) = F_2(g)$	$1.7 \cdot 10^3$	PtF_2	$2 \cdot 10^{-6}$
$Pt(s) + 2F(g) = PtF_2(g)$	$5 \cdot 10^8$	PtF_4	$4 \cdot 10^{-8}$

4.2 Find the maximum partial pressure of molecular fluorine near the platinum surface under the given experimental conditions. Assume first that gasification does not proceed.

4.3 Why is the ratio $\dfrac{p^2_{PtF_2}}{p_{PtF_4}} = 10^{-4}$ bar constant near the surface?

4.4 Make the necessary assumptions and estimate the partial pressure of atomic fluorine in the desorbed flow.

4.5 Put forward the quasi-equilibrium model to account for the rate of gasification of Pt with atomic fluorine,

$$r_{Pt} = \frac{dn_{Pt}}{dt} \ \{\text{mol of Pt / Pt surface area / time}\}$$

Make use of the dimensionless *equilibration probability,* α, which is equal to the fraction of incident fluorine flow involved in gasification. Consider other steps of gasification as quasi-equilibrium. The flow ρ_i of each gaseous species i is related to its partial pressure p_i as

$$\rho_i = c \frac{p_i}{(m_i)^{1/2}}$$

where m_i is a molecular mass, c is constant.

4.6 Estimate the *equilibration probability* α under the experimental conditions, described in the Table.

4.7 How many grams of Pt will be gasified from 1 cm^2 of the Pt surface in 15 minutes, if the incident flow of atomic fluorine is $2 \cdot 10^{18}$ atoms/cm^2/s?

_____

SOLUTION OF PREPARATORY PROBLEM 4

4.1 In this case, the quasi-equilibrium step precedes the rate-limiting one,

$r_1 \approx r_{-1}$,

$k_1[A][B] >> k_{-1}[AB]$

and $[AB] >> \frac{k_1}{k_{-1}}[A][B]$.

Using the stationary state condition $\frac{d[AB^*]}{dt} >> 0$ one gets

$$r = k_{eff}[A][B] = k_3[AB^*] = k_2[AB] = \frac{k_1 k_2}{k_{-1}}[A][B]$$

$$k_{eff} = \frac{k_1 k_2}{k_{-1}} = 200 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$$

4.2 Maximum partial pressure of F_2 will be attained if the equilibrium is reached in the reaction

$$2 F \rightleftarrows F_2 \qquad (2 a).$$

$$K_p = 1.7 \cdot 10^3 \text{ bar}^{-1} = \frac{p_{F_2}}{p_F^2}; \quad p_F = 10^{-5} \text{ bar}$$

$$p_{F_2} = 1.7 \cdot 10^{-7} \text{ bar}$$

Partial pressure of molecular fluorine near the surface is negligible.

4.3 It is safe to assume that quasi-equilibrium is achieved in the reaction

$$Pt(s) + PtF_4(g) = 2\ PtF_2(g) \qquad (2 b)$$

The measured ratio $\frac{p_{PtF_2}^2}{p_{PtF_4}}$ is equal to the equilibrium constant of this reaction.

4.4 One may assume that quasi-equilibrium is also achieved in the reaction

$$Pt(s) + 2\ F(g) = PtF_2(g) \qquad (2\ c)$$

within the desorbed flow. Then

$$p_{F_{Des}} = \left(\frac{p_{PtF_2}}{K_p(\text{eq. 2c})} \right)^{1/2} = \left(\frac{2 \cdot 10^{-6}}{5 \cdot 10^{8}} \right)^{1/2} = \left(4 \cdot 10^{-15} \right)^{1/2} = 6.3 \cdot 10^{-8}\ \text{bar}$$

4.5 For the gasification of platinum, the following mechanism could be proposed:

$$F_{(Inc)} \xrightarrow{\alpha} F_{(Des)} + Pt_{(s)} \rightleftarrows PtF_2, PtF_4$$

Here the rate-limiting step is "equilibration" of atomic fluorine on the surface. It precedes the quasi-equilibrium steps. "Equilibrated" fluorine takes part in the quasi-equilibrium gasification of Pt. Interaction products do not accumulate on Pt surface. Hence

$$\alpha\, \rho_{F_{Inc}} = \rho_{F_{Des}} + 2\, \rho_{PtF_2} + 4\, \rho_{PtF_4},$$

or

$$\alpha \frac{p_{F_{Inc}}}{(m_F)^{1/2}} = \frac{p_{F_{Des}}}{(m_F)^{1/2}} + 2\frac{p_{PtF_2}}{(m_{PtF_2})^{1/2}} + 4\frac{p_{PtF_4}}{(m_{PtF_4})^{1/2}}.$$

Under the experimental conditions (see the Table and question 2.2)

$$\alpha \frac{p_{F_{Inc}}}{(m_F)^{1/2}} >> 2\frac{p_{PtF_2}}{(m_{PtF_2})^{1/2}}$$

The rate of gasification is

$$r_{Pt} = \frac{dn_{Pt}}{dt} = \rho_{PtF_2} + \rho_{PtF_4} >> \rho_{PtF_2} >> \frac{\alpha}{2}\rho_{F_{Inc}}$$

4.6 As it was shown in 2.4,

$$\alpha \frac{p_{F_{Inc}}}{(m_F)^{1/2}} >> 2\ \frac{p_{PtF_2}}{(m_{PtF_2})^{1/2}}$$

$$p_{F_{Inc}} = 10^{-5}\ \text{bar}, \quad p_{PtF_2} = 2 \cdot 10^{-6}\ \text{bar},$$

$$\alpha = 2\frac{p_{PtF_2}(m_F)^{1/2}}{p_{F_{Inc}}(m_{PtF_2})^{1/2}} = 0.4 \times \frac{4.35}{15.26} = 0.1$$

4.7. $r_{Pt} = \frac{dn_{Pt}}{dt} = \rho_{PtF_2} + \rho_{PtF_4} >> \rho_{PtF_2} >> \frac{\alpha}{2}\rho_{F_{Inc}}$

$$r_{Pt} >> \rho_{PtF_2} >> \frac{0.1}{2}\rho_{F,In} = \frac{0.1}{2} \times \frac{p_{F_{In}}}{(2\pi m_F RT)^{1/2}} N_A = \frac{0.1}{2} \times 2 \cdot 10^{18} = 10^{17} \text{ atoms} / \text{cm}^2 / \text{s}$$

In 15 minutes-,

$$15 \times 60 \cdot 10^{17} = 9 \cdot 10^{19} \text{ atoms cm}^{-2} = 1.5 \cdot 10^{-4} \text{ mol cm}^{-2} = 0.029 \text{ g cm}^{-2}$$

will be gasified.

THEORETICAL PROBLEM 5

The Second Law of thermodynamics applied to a chemical reaction

When does chemical reaction proceed spontaneously? The Second Law gives the answer.

Consider *a system*, a chemical reactor in Fig. 1. Pressure *p* and temperature *T* inside the reactor are kept constant. There is no transfer of matter into or out of the system.

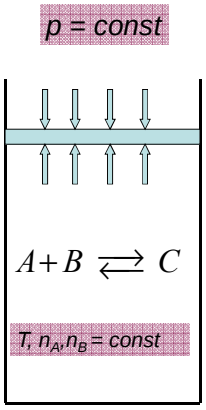


Fig. 1. Chemical reaction inside a reactor

According to the Second Law, every spontaneous process in such a reactor leads to the decrease of the Gibbs free energy, G_{system}, i.e. $\Delta G_{system} < 0$.

If the chemical reaction, e.g. A + B = C (a), is the only process inside the reactor

$$\Delta G_{System} = \Delta G_{Reaction(a)} \quad \Delta\xi(a)$$
$$\Delta\xi(a) = \Delta n_C = -\Delta n_A = -\Delta n \qquad (1)$$

where $\Delta G_{reaction}$ and $\Delta\xi$ are the Gibbs free energy and *the extent of reaction* (a), respectively, Δn_A, Δn_B, Δn_C are changes of the numbers of moles of A, B, C in the reaction (a).

5.1 Relate $\Delta\xi$ to Δn_i of reactants and products of the following reaction

$$\frac{1}{6}\ C_6H_{12}O_6 + O_2 = CO_2 + H_2O \qquad (a)$$

5.2 Prove that, according to the Second Law, $\Delta G_{reaction} < 0$ for any single spontaneous chemical reaction in the reactor (Fig.1).

The Gibbs free energy of the chemical reaction (a) is:

$$\Delta G_{\text{reaction}} = \Delta G^{o}_{\text{reaction}} + RT \ln \frac{[C]}{[A][B]} < 0 \qquad (2)$$

where [C], [A], [B] are time variant concentrations inside the reactor in the course of spontaneous reaction. Using the law of mass action, relate $\Delta G_{\text{reaction}}$ to the ratio of rates of forward r_1 and reverse r_{-1} reaction (a). Consider both reactions as elementary ones.

5.3 Derive the expression (2) for $\Delta G_{\text{reaction}}$ of the following chemical transformations:

(a') $H_2(g) + Br_2(g) = 2\ HBr(g)$

(a'') $H(g) + Br_2(g) = Br(g) + HBr(g)$

(a''') $CaCO_3(s) = CaO(s) + CO_2(g)$

5.4 For which of these reactions the relation between $\Delta G_{\text{reaction}}$ and r_1, r_{-1} derived in Problem 2 is valid?

5.5 The *observed rate* of chemical reaction, r_{obs}, is defined as $r_{\text{obs}} = r_1 - r_{-1}$.

Let reaction (a) proceed spontaneously. At a certain moment

$r_{\text{obs}} / r_1 = 0.5$, [A] = 0.5 mol dm^{-3}, [B] = 1 mol dm^{-3}, [C] = 2 mol dm^{-3}.

Find the equilibrium constant, K, of the reaction (a), T=298K.

5.6 Plot r_{obs} as a function of

a) r_1 at $\Delta G_{\text{Reaction}}$ = const;

b) r_1 at r_{-1} = const;

c) $\Delta G_{\text{Reaction}}$, at r_1 = const.

5.7 Which thermodynamic and kinetic parameters of a chemical reaction are influenced by a catalyst? Put plus (+) into the cell of the Table if a catalyst may cause a change of the corresponding parameter, (–) otherwise.

Table

r_{obs}	r_1	r_1/r_{-1}	$\Delta G_{\text{reaction}}$	r_{obs}/r_1

SOLUTION OF PREPARATORY PROBLEM 5

5.1 $\Delta\xi = \Delta n_{H_2O} = \Delta n_{CO_2} = -6\,\Delta n_{C_6H_{12}O_6} = -\Delta n_{O_2}$

5.2 If spontaneous chemical reaction is the only process in the reactor, $\Delta G_{system} < 0$.

The value of $\Delta\xi$ for spontaneous reaction is positive, Δn_i are positive for the products and are negative for the reactants (minus sign makes them positive!). Thus,

$$\Delta G_{Reaction} = \frac{\Delta G_{System}}{\Delta\xi} < 0\,.$$

Since both forward and reversed reactions are elementary ones, the following equality may be written at equilibrium:

$$r_1 = k_1[A]_{eq}[B]_{eq} = r_{-1} = k_{-1}[C]_{eq}$$

and

$$\frac{k_1}{k_{-1}} = \frac{[C]_{eq}}{[A]_{eq}[B]_{eq}} = K$$

$[C]_{eq}$, $[B]_{eq}$, $[A]_{eq}$ are concentrations at equilibrium, K is the equilibrium constant of the reaction. Making use of the well-known formula

$$\Delta G^0 = -RT\ln K$$

from equation (2) one gets

$$\begin{aligned}\Delta G &= -RT\ln K + RT\ln\frac{[C]}{[A][B]} = \\ &= RT\ln\frac{k_{-1}}{k_1} + RT\ln\frac{[C]}{[A][B]} = \\ &= RT\ln\left(\frac{k_{-1}}{k_1}\frac{[C]}{[A][B]}\right) = RT\ln\frac{r_{-1}}{r_1}\end{aligned} \qquad (3)$$

5.3 (a') $\Delta G_{Reaction} = \Delta G^0_{Reaction} + RT\ln\frac{[HBr]^2}{[H_2][Br_2]}$

(a'') $\Delta G_{reaction} = \Delta G^0_{reaction} + RT\ln\frac{[HBr][Br]}{[H][Br_2]}$

(a''') $\Delta G_{reaction} = \Delta G^0_{reaction} + RT\ln[CO_2]$

5.4 Equation (3) may be used only in case (a''). Other two reactions are not elementary ones.

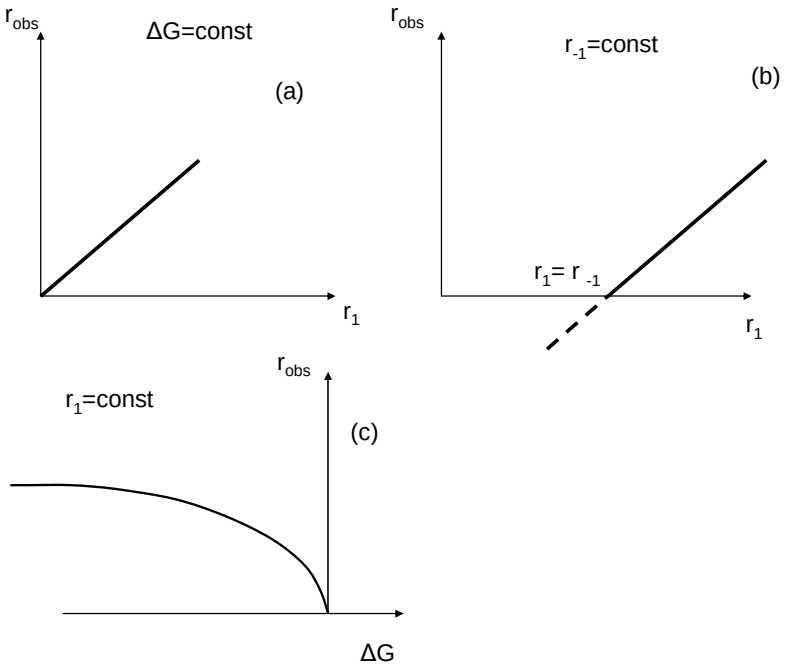
5.5

$$\frac{r_{obs}}{r_1} = \frac{r_1 - r_{-1}}{r_1} = 1 - \frac{r_{-1}}{r_1} = 0.5; \quad \frac{r_{-1}}{r_1} = 0.5$$

$$\frac{r_{-1}}{r_1} = \frac{k_{-1}}{k_1}\frac{[C]}{[A][B]} = \frac{k_{-1}}{k_1}\frac{2}{0.5\times 1} = 0.5; \quad \frac{k_{-1}}{k_1} = 0.125\ \text{mol}\,\text{dm}^{-3}$$

$$\frac{k_1}{k_{-1}} = K = 8\ \text{mol}^{-1}\text{dm}^3$$

5.6



5.7 Table

r	r_1	r_1/r_{-1}	$\Delta G_{reaction}$	r / r_1
+	+	–	–	–

THEORETICAL PROBLEM 6

Catalytic transformation of a single molecule on a single nanoparticle

Use of catalytic nanoparticles opens new ways to study and to understand catalysis. The exiting measurements were performed at Cornell University (NY, USA). The researchers observed the catalytic transformation of single molecules on the surface of a spherical nanoparticle (d = 6 nm) formed by Au atoms.

The experimental design is shown in Fig.1. The dissolved **A** was transformed into dissolved **B** in the presence of Au nanoparticles, adsorbed on the glass slide.

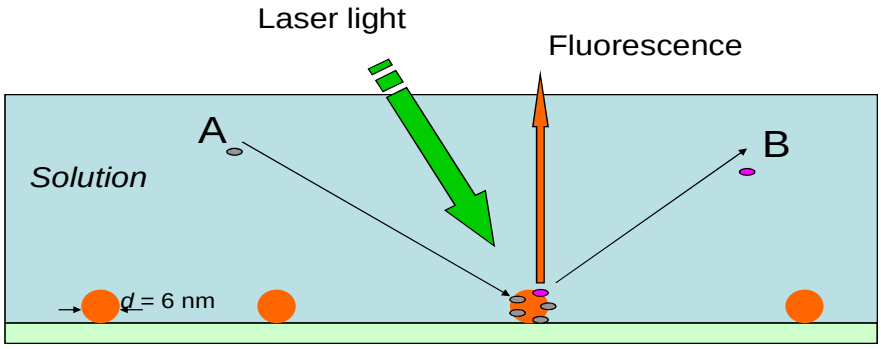


Fig.1. The experimental design

The reaction product **B** is a fluorescent molecule while the reagent **A** is not. Continuous laser light producing fluorescence was focused within a small surface area containing a single Au nano-particle. The time dependence of fluorescence on the wavelength characteristic for **B**, adsorbed on the Au nanoparticle is shown in Fig. 2.

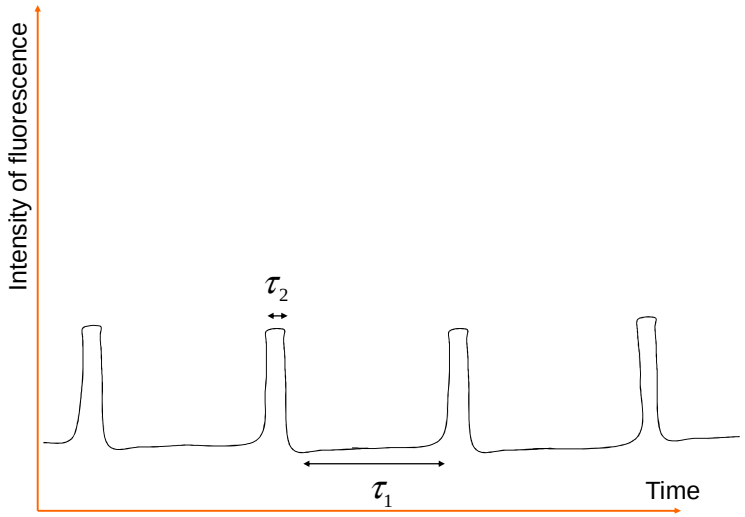


Fig. 2. Time dependence of intensity of fluorescence coming from a single cluster

The fluorescence of **B** in the solution could not be detected under the experimental conditions. The same intensity of fluorescence was observed periodically for the time intervals τ_2. The fluorescence disappeared during the time intervals τ_1 between the peaks (see Fig. 2). The researchers have performed their measurements for long periods of time and for many different single Au nanoparticles. As a result the averaged values of [τ_1] and [τ_2] were obtained.

Answer the following questions about this experiment and the conclusions made by its authors.

6.1 Estimate the number of the Au atoms in a single nanoparticle if its density is equal the bulk density of Au, 19.32 g cm^{-3}. What fraction of Au atoms is involved in the catalysis if catalytically active is the surface layer with the depth equal to two atomic diameters of Au (d_{Au} = 0.350 nm)?

6.2 The resolution of the instruments made it possible to measure the fluorescence emitted from 1 μm^2 area. The number density of Au nanoparticles on the glass slide was 0.035 particle·μm^{-2}. What was the probability (%) of observing fluorescence from a single Au nanoparticle?

6.3 The authors claimed that each peak in Fig. 2 corresponds to the fluorescence of a single molecule B adsorbed on Au nanoparticle. What was the main argument of the authors?

Consider adsorption of **A** on Au nanoparticles to be a fast reversible process. Let *m* catalytic sites exist on the surface of a single nanoparticle. The fraction of catalytic sites occupied by molecules **A**, is equal to

$$\theta_A = \frac{K_{ads}[A]}{1 + K_{ads}[A]}$$

6.4 Relate $[\tau_1]$ and $[\tau_2]$ to the rates of catalytic production/desorption of a single molecule **B** on/from a single Au nanoparticles.

6.5 Plot $[\tau_1]^{-1}$ and $[\tau_2]^{-1}$ as a function of concentration of **A** in the solution.

6.6 How will $[\tau_1]^{-1}$ and $[\tau_2]^{-1}$ change with the increase of nanoparticle diameter from 6 to 12 nm?

SOLUTION OF PREPARATORY PROBLEM 6

6.1 a) $V_{Au\ nano} = 4/3\ \pi R^3 = 1.13 \cdot 10^{-19}$ cm^3,

$m_{Au\ nano} = 1.13 \cdot 10^{-19}$ cm$^3 \times 19.32$ g cm$^{-3} = 2.18 \cdot 10^{-18}$ g,

$N_{Au\ atoms} = 2.18 \cdot 10^{-18}$ g / $196.97 \cdot 6.02 \cdot 10^{23} = 6675$ atoms.

b) $f = V_{surface} / V_{Au\ nano} = (V_{Au\ nano} - V_{core}) / V_{Au\ nano} = 1 - (r^3(\text{core}) / r^3(\text{Au nano})) =$

$= 1 - (3 - 0.7)^3 / 3^3 = 0.55.$

6.2 Suppose you detect a signal from a particular 1μm^2 area. The probability to have one particle within this area is 0.035. For two particles such probability is $(0.035)^2$ and for three it is equal to $(0.035)^3$ etc.

The probability that the detected signal originates from a single Au nanoparticle is:

$$p = \frac{0.035}{0.035 + 0.035^2 + 0.035^3 + ...} = \frac{0.035}{\frac{1}{1 - 0.035} - 1} = 1 - 0.035 = 0.965 = 96.5\,\%$$

B is the only fluorescent molecule in the system. The fluorescence of **B** in the solution could not be detected under the experimental conditions. Thus the signal is

detectable as long as **B** is seating on the Au nanoparticle. The consistent height of the peaks (Fig. 2) indicates that each peak comes from a single molecule. If it were from many molecules, the peaks would have variable heights depending on the number of molecules.

6.4 $[\tau_2]$ is an average time necessary to desorb a single molecule **B** from a single catalytic site on Au nanoparticle. The rate of desorption of **B** molecules from a single catalytic site of Au nanoparticle is

$$r_{des} = [\tau_2]^{-1} = k_{des} \ \{\text{molecules of } \mathbf{B} \text{ desorbed / time}\}$$

where k_{des} is the rate constant for one catalytic site.

$[\tau_1]$ is the average time necessary to form a single molecule **B** on a single Au nanoparticle. The number of catalytic sites occupied by substrate **A** is

$$\theta_A m = \frac{K_{ads}[\mathbf{A}]}{1 + K_{ads}[\mathbf{A}]} m$$

All these sites equally participate in catalytic formation of a single **B** on a single Au nanoparticle,

$$r_{cat} = \frac{k_{cat}\, m\, K_{ads}[\mathbf{A}]}{1 + K_{ads}[\mathbf{A}]} = [\tau_1]^{-1} \ \{\text{molecules of } \mathbf{B} \text{ formed / time}\}$$

where k_{cat} is the rate constant for one catalytic site.

6.5

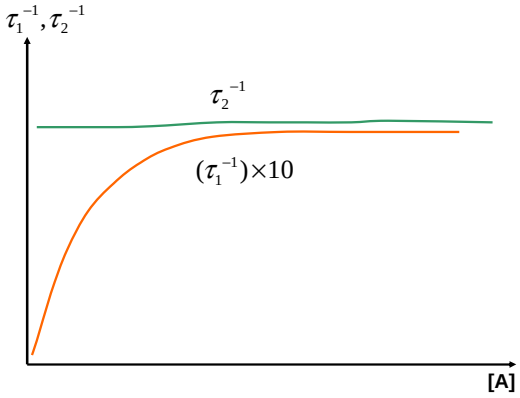


Fig. 3. $[\tau_2]^{-1}, [\tau_1]^{-1}$ vs [**A**]

$[\tau_2]^{-1}$ is independent of [**A**], $[\tau_1]^{-1}$ increases with the increase of [**A**] and approaches constant value when K_{ad}[**A**] >> 1 (see Answer 6.4)

6.6 $[\tau_2]^{-1}$ does not vary. $[\tau_1]^{-1}$ is proportional to the number of catalytic cites, *m*, which is in turn proportional to the area of the surface of Au nanoparticle. $[\tau_1]^{-1}$ varies as the square of diameter i.e. in our case increases by a factor of 4. (See Answer 6.4)

THEORETICAL PROBLEM 7

Esterification of a dicarboxylic acid

Dicarboxylic acid is mixed with ethanol in a molar ratio 1 : x (x > 1) in the presence of a catalyzer. The system reached equilibrium. The equilibrium constants for the formation of monoester from an acid and ethanol and that for the formation of diester from monoester and ethanol are the same: $K_1 = K_2 = 20$.

7.1 At what x the yield of monoester is maximal?

7.2 Find the maximum yield.

7.3 Answer the questions 7.1 and 7.2 at arbitrary k_1 and k_2.

_____

SOLUTION OF PREPARATORY PROBLEM 7

Denote A = acid, E = ethanol, M = monoester, D = diester. Consider two equilibria:

$$A + E \rightleftarrows M + H_2O \qquad K_1 = \frac{[M]\,[H_2O]}{[A]\,[E]} = 20$$

$$M + E \rightleftarrows D + H_2O \qquad K_2 = \frac{[D]\,[H_2O]}{[M]\,[E]} = 20$$

(here water is not a solvent but a product, therefore, it enters the expressions for equilibrium constants).

The equilibrium yield of monoester is:

$$\eta = \frac{[M]}{[A]_0} = \frac{[M]}{[A]+[M]+[D]} = \frac{K_1\dfrac{[A][E]}{[H_2O]}}{[A]+K_1\dfrac{[A]\,[E]}{[H_2O]}+K_1K_2\dfrac{[A]\,[E]^2}{[H_2O]^2}} = \frac{1}{\dfrac{[H_2O]}{K_1[E]}+1+K_2\dfrac{[E]}{[H_2O]}}$$

Denote $[H_2O] / [E] = x$, then $\eta(x) = \dfrac{1}{\dfrac{x}{K_1} + 1 + \dfrac{K_2}{x}}$. By differentiating with respect to x, we find that this function has maximum value at $x = \sqrt{K_1 K_2}$: $\eta_{max} = \dfrac{1}{1 + 2\sqrt{\dfrac{K_2}{K_1}}}$.

At $K_1 = K_2 = 20$, the maximum yield of monoester is: $\eta_{max} = 1/3$.

Substituting the optimal ratio $[H_2O]$ / [E] into the equilibrium constants, we find the relations:

$$[M] = [A]\sqrt{\frac{K_1}{K_2}}, \quad [D] = [A].$$

From the material balance with respect to water we get:

$$[H_2O] = [M] + 2[D] = [A]\left(2 + \sqrt{\frac{K_1}{K_2}}\right),$$

$$[E] = \frac{[H_2O]}{\sqrt{K_1 K_2}} = [A]\left(\frac{2}{\sqrt{K_1 K_2}} + \frac{1}{K_2}\right)$$

The initial concentrations of ethanol and acid are:

$$[E]_0 = [E] + [M] + 2[D] = [A]\left(\frac{2}{\sqrt{K_1 K_2}} + \frac{1}{K_2}\right) + [A]\sqrt{\frac{K_1}{K_2}} + 2[A],$$

$$[A]_0 = [A] + [M] + [D] = [A] + [A]\sqrt{\frac{K_1}{K_2}} + [A].$$

And the optimal ratio is:

$$x = \frac{[E]_0}{[A]_0} = \frac{\frac{2}{\sqrt{K_1 K_2}} + \frac{1}{K_2} + \sqrt{\frac{K_1}{K_2}} + 2}{2 + \sqrt{\frac{K_1}{K_2}}} = 1 + \frac{1}{\sqrt{K_1 K_2}}.$$

At $K_1 = K_2 = 20$, the optimal ratio is $x = 1.05$.

Answers:

7.1 $x = 1.05$.

7.2 $\eta_{max} = 1/3$.

7.3 $x = 1 + \frac{1}{\sqrt{K_1 K_2}}$, $\eta_{max} = \frac{1}{1 + 2\sqrt{\frac{K_2}{K_1}}}$.

THEORETICAL PROBLEM 8

Three elements

Three elements – **A**, **B**, and **C** form three binary compounds. Each element has the same valence in these compounds. The mass fraction of **A** in the compound with **B** is 75 %, and the mass fraction of **B** in the compound with **C** is 7,8 %. Determine the mass fraction of **C** in the compound with **A** and find all the elements.

_____

SOLUTION OF PREPARATORY PROBLEM 8

Let the valences of elements A, B, and C be *a*, *b*, *c*, respectively. (Do not confuse valences and oxidation numbers!) The formulas of three compounds are: A_bB_a, B_cC_b, A_cC_a. From the mass fractions we can determine the ratios of atomic masses to valences:

$$w(\text{A in } A_bB_a) = \frac{b\,M(\text{A})}{b\,M(\text{A}) + a\,M(\text{B})} = 0.75 \qquad \frac{M(\text{A})}{a} = 3\frac{M(\text{B})}{b}$$

$$w(\text{B in } B_cC_b) = \frac{c\,M(\text{B})}{c\,M(\text{B}) + b\,M(\text{C})} = 0.078 \qquad \frac{M(\text{C})}{c} = 11.8\,\frac{M(\text{B})}{b}$$

We see that the ratio $M(\text{B}) / b$ is the smallest one. Considering several elements with small ratios of atomic mass to valence, we easily find, that B is carbon: $M = 12$, $b = 4$, then A is aluminium: $M = 27$, $a = 3$, and C is chlorine: $M = 35.5$, $c = 1$. The compounds are: Al_4C_3, CCl_4, and $AlCl_3$.

The mass fraction of chlorine in aluminum chloride is:

$$w(\text{Cl in } AlCl_3) = \frac{3 \times 35.5}{3 \times 35.5 + 27} = 0.798 = 79.8\%.$$

This result can be obtained without determining the exact formula of A_cC_a. Indeed, from the above relations, we find that $\frac{M(\text{C})}{c} = 3.93\frac{M(\text{A})}{a}$. Therefore,

$$w(\text{C in } A_cC_a) = \frac{a\,M(\text{C})}{c\,M(A) + a\,M(\text{C})} = \frac{\frac{M(\text{C})}{c}}{\frac{M(\text{A})}{a} + \frac{M(\text{C})}{c}} = \frac{3.93}{1 + 3.93} = 0.798.$$

THEORETICAL PROBLEM 9

Simple experiments with copper(II) chloride

Copper(II) chloride forms brown crystals soluble in water.

9.1 The color of the solutions depends on concentration. Explain this fact.

9.2 Draw the structure of at least three copper containing species that can be present in the solution.

9.3 To the aliquots of the copper chloride(II) solution in the test tubes (a) zinc powder and the solutions of (b) sodium iodide, (c) sodium nitrate, (d) sodium sulfide were added dropwise. What changes happen if they are? Provide equations. In what cases copper is completely or partly reduced?

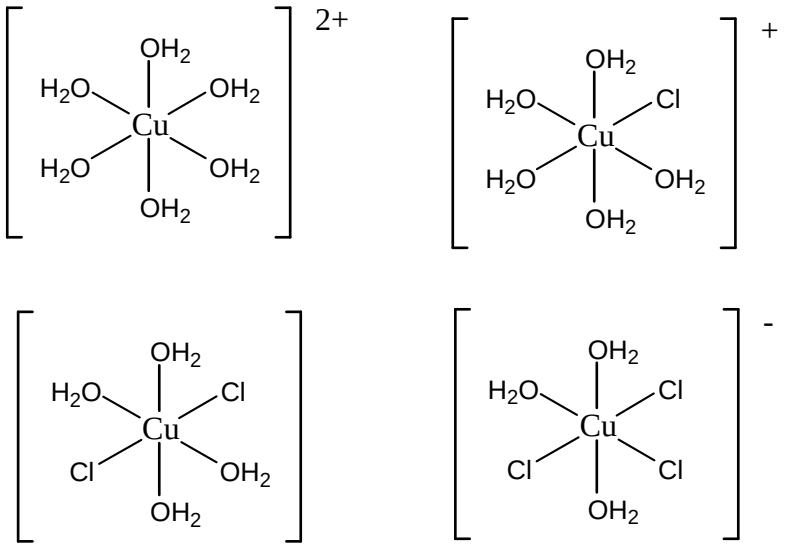
9.4 Suggest a synthetic route to copper chloride(II) starting from copper(II) sulfate aqueous solution.

SOLUTION OF PREPARATORY PROBLEM 9

9.1 A diluted solution of copper chloride is blue due to $[Cu(H_2O)_6]^{2+}$ ions. Upon the concentration of the solution its color changes to green, as the substitution of coordinated water molecules by chloride-ions occurs:

$$[Cu(H_2O)_6]^{2+} + 4\ Cl^- \rightleftarrows [CuCl_4]^{2-} + 6\ H_2O.$$

9.2



See: Bernd M. Rode and Saiful M. Islam. Structure of aqueous copper chloride solutions: results from Monte Carlo simulations at various concentrations // J. Chem. Soc. Faraday Trans., 1992, 88(3), 417-422.

9.3 (a) $CuCl_2 + Zn \rightarrow Cu\downarrow + ZnCl_2$ (red precipitate – copper),

(b) $2\ CuCl_2 + 4\ NaI \rightarrow 2\ CuI\downarrow + I_2\downarrow + 4\ NaCl$ (grey precipitate – mixture of copper iodide and iodine),

(c) No noticeable changes,

(d) $CuCl_2 + Na_2S \rightarrow CuS\downarrow + 2\ NaCl$ (black precipitate).

Copper is completely reduced in (a), and partly reduced in (b) and (d). Surprisingly, copper sulfide CuS is a mixed sulfide-disulfide of copper(I) and copper(II).

9.4 A possible synthetic route is the reduction of copper by zinc followed by chlorination.

$CuSO_4 + Zn \rightarrow ZnSO_4 + Cu$

$Cu + Cl_2 \rightarrow CuCl_2$.

Another way is metathesis reaction with barium chloride with crystallization of hydrated copper chloride. The dehydration can be achieved by heating with thionyl chloride:

$CuSO_4 + BaCl_2 \rightarrow BaSO_4 + CuCl_2$ (from solution $CuCl_2 \cdot 2\ H_2O$ forms).

$CuCl_2 \cdot 2\ H_2O + 2\ SOCl_2 \rightarrow CuCl_2 + 2\ SO_2 + 4\ HCl$

THEORETICAL PROBLEM 10

An element typical for Azerbaijan mud volcanoes expelled water

Azerbaijan is famous for mud volcanoes. About 400 active mud volcanoes are present in this region, both onshore and offshore - more than half the total throughout the world. Mud volcanoes come in a variety of shapes and sizes, but those most common in Azerbaijan have several small cones, or vents, up to about four meters in height. Mud volcanic eruptions in Azerbaijan normally last for less than a few hours, and are characterized by vigorous extrusion of mud breccias, hydrocarbon gases, and waters. Bakhar is a mud volcano with a high seep activity in the dormant period. The reservoirs formed by the volcanoes' activity contain the expelled waters. Those of Bakhar volcano have a composition with Na and Cl as dominant ions. The analyzed waters are enriched in metals and in an element **X** that causes flame coloration. Its' concentration in seeping water of 250 ppm represents a 55-fold enrichment in comparison to seawater. Being concentrated, the expelled water gives the white crystals, among them the compound **Y**, one of the main sources of **X**. The common oxide of **X** contains 31.0 % of the element, whereas the compound **Y** – 11.3 % only.

10.1 What are the element **X** and the compound **Y**?

10.2 Calculate the mass of **Y** that can be obtained from 1 L of expelled water.

10.3 The mass loss under gentle heating of **Y** is 37.8 %. Draw a possible structure of anion in **Y**, knowing that it contains two different types of **X** atoms (three- and four-coordinated).

SOLUTION OF PREPARATORY PROBLEM 10

10.1 The general formula of an oxide is XO_n. The molar ratio of X to O is:

$$\frac{31.0}{M(\mathrm{X})} : \frac{69.0}{16} = 1 : n$$

n = 0.5; 1; 1.5; 2 etc.

n = 0.5 gives M(X) = 3.6 $\Rightarrow$ no element.

n = 1 gives M(X) = 7.2 ⇒ Li, but it doesn't exist in oxidation state II.

n = 1.5 gives M(X) = 10.8 ⇒ B. It's true as boron generally exists in oxidation state. III. X is B.

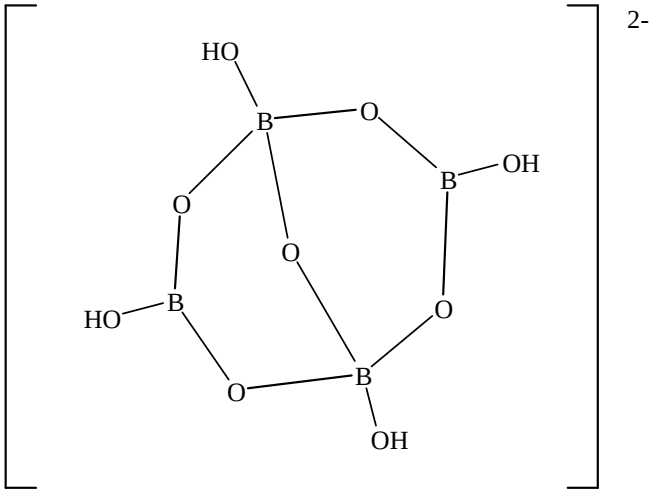
In water solution boron forms anionic oxo-species, the counter ion could be sodium as one of dominant ions in expelled water. The common boron mineral that contains sodium is borax $Na_2B_4O_7{\cdot}10\ H_2O$, it contains 11.3 mass % of boron.

X – B, **Y** – $Na_2B_4O_7 \cdot 10\ H_2O$.

10.2 The density of the diluted solution is 1 kg/L, then 1 ppm is 1 mg/L, 250 ppm is 250 mg of boron. The mass of borax is: $m(Na_2B_4O_7{\cdot}10\ H_2O)$ = 250 / 0.113 = 2212 mg = 2.2 g.

10.3 The mass loss under gentle heating of borax is 37.8 % that corresponds to the loss of 8 water molecules.

The anion $(H_4B_4O_9)^{2-}$ in **Y** contains two three-coordinated and two four-coordinated boron atoms:



THEORETICAL PROBLEM 11

The Prussian blue

The Prussian blue is a component of black and bluish inks for printing. The precipitate formed upon the dropwise addition of potassium ferrocyanide to the ferric chloride solution contains 34.9 % (mass) of iron.

11.1 Give a formulae of the precipitate and write the chemical equation. (Use 55.8 for atomic mass of iron).

11.2 Using the crystal field theory show the *d*-orbital splitting pattern for all Fe atoms in the Prussian blue.

11.3 What causes the intense color of the pigment?

11.4 What product initially forms from potassium ferrocyanide and ferric chloride solution in the inverse-mixing-order route? Give the equation.

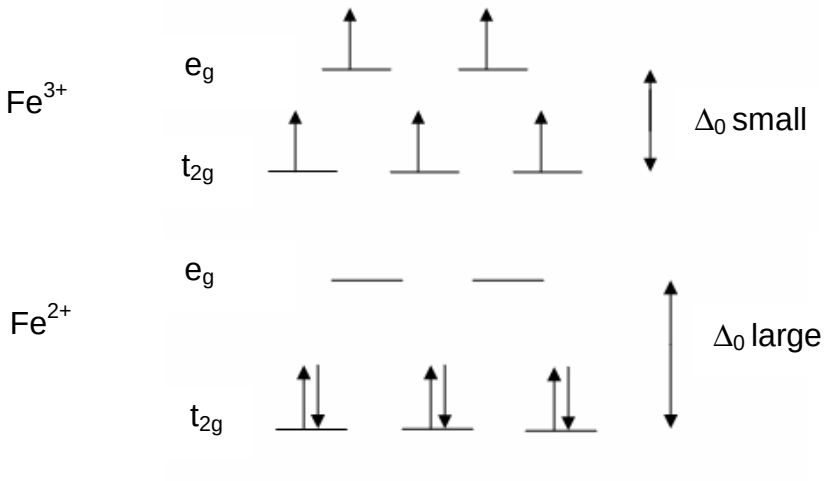
_____

SOLUTION OF PREPARATORY PROBLEM 11

11.1 The precipitate is $Fe_7(CN)_{18} \cdot 14.5\ H_2O$.

$4\ Fe^{3+} + 3\ [Fe(CN)_6]^{4-} \rightarrow Fe^{III}[Fe^{III}Fe^{II}(CN)_6]_3$

11.2



11.3 Most inorganic pigments contain ions that produce colors by selective absorption of specific wavelengths of electromagnetic radiation due to the electron transitions. The intense blue color of Prussian blue is associated with the energy of the transfer of electrons from Fe(II) to Fe(III) via the bridging cyanide group.

11.4 In the inverse-mixing-order route a "soluble" colloidal Prussian blue forms:

$K^+ + Fe^{3+} + [Fe(CN)_6]^{4-} \rightarrow K[Fe^{III}Fe^{II}(CN)_6]$

Soluble Prussian blue contains interstitial K^+ ions instead of interstitial water, that is present in the insoluble form.

THEORETICAL PROBLEM 12

Substitution in square planar complexes

For platinum (II) and (IV) a large number of complexes is known. For most of them the isomers were isolated.

12.1 Explain what is the reason for the existence of different isomers and draw the structures for all $Pt(NH_3)_2Cl_2Br_2$ species.

12.2 The reaction of thiourea with $[Pt(amine)_2Cl_2]$ isomers results in different products. Explain this fact and give the reaction scheme.

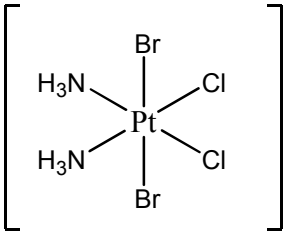
12.3 Give an example of $PtX(amine)Cl_2$ isomeric complexes reacting with thiourea with the formation of one and the same product.

12.4 Explain why do the reactions of $[PtCl_4]^{2-}$ and $[AuCl_4]^-$ with iodide result in different products.

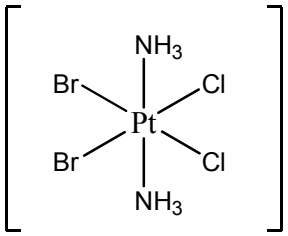
———————

SOLUTION OF PREPARATORY PROBLEM 12

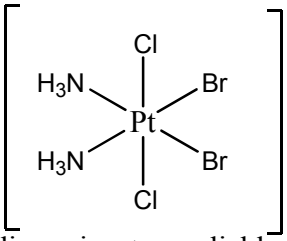
12.1 The isomers can be easily isolated for inert complexes only. An octahedral composition $MA_2B_2C_2$ has five geometric isomers.



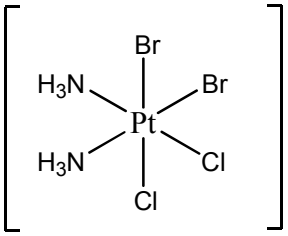
cis-diammine-*cis*-dichloro-*trans*-dibromo-platinum(IV)



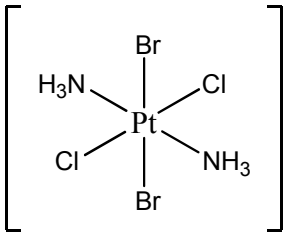
trans-diammine-*cis*-dichloro-*cis*-dibromo-platinum(IV)



cis-diammine-*trans*-dichloro-*cis*-dibromo-platinum(IV)

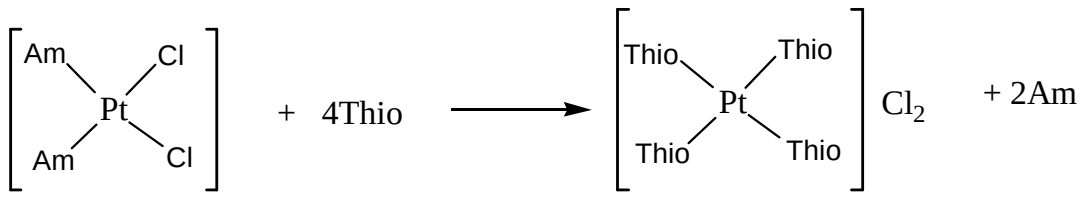


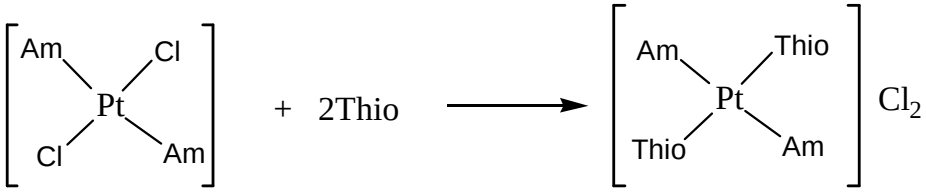
cis-diammine-*cis*-dichloro-*cis*-dibromo-platinum(IV)



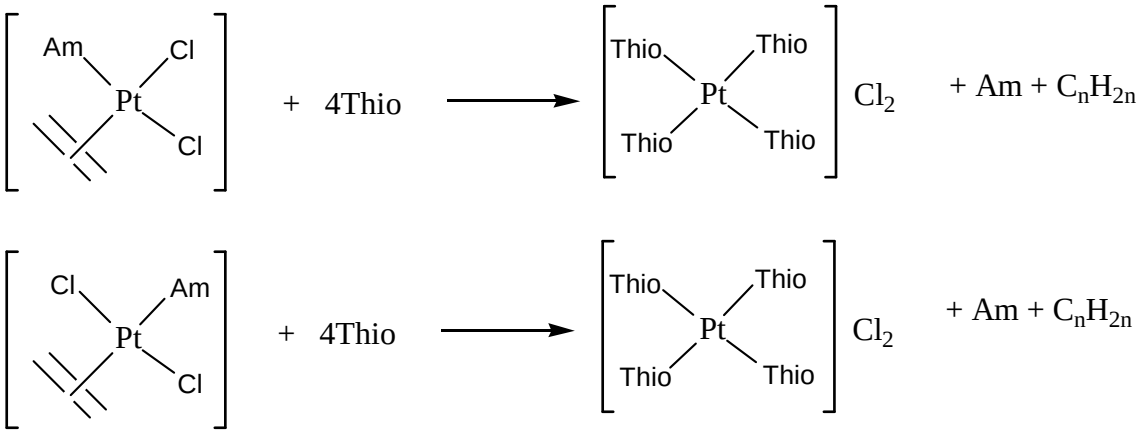
trans-diammine-*trans*-dichloro-*trans*-dibromo-platinum(IV)

12.2 In the *cis*-isomer, all the ligands are substituted by thiourea due to a high trans-activity of the entering ligand. In the *trans*-isomer the amine ligands remain intact.





12.3 The complexes containing groups with high trans-effect (such as alkenes) react with thiourea giving tetrathioureates:



12.4 Platinum(+2) is a weak oxidizer, hence in the case of platinum only the substitution of chloride by iodide ligands occurs. In the case of tetrachloroaurate(+3), the rate of electron transfer exceeds the rate of substitution, so the redox process occurs:

$2\ [AuCl_4]^- + 6\ I^- \rightarrow 2\ AuI + 2\ I_2 + 8\ Cl^-$.

THEORETICAL PROBLEM 13

Using the Latimer diagrams (pH = 0):

$$[Au(H_2O)_6]^{3+} \xrightarrow{1.401\ V} [Au(H_2O)_6]^{+} \xrightarrow{1.692\ V} Au$$

$$[AuCl_4]^{-} \xrightarrow{0.926\ V} [AuCl_2]^{-} \xrightarrow{1.154\ V} Au$$

$$[AuBr_4]^{-} \xrightarrow{0.810\ V} [AuBr_2]^{-} \xrightarrow{0.960\ V} Au$$

answer the following questions:

13.1 Is Au(I) stable to disproportionation in aqueous solutions in the absence and in the presence of chloride and bromide ions? Support your answer by calculations.

13.2 Is it possible to oxidize gold powder by pure oxygen in the aqueous solution in the presence of chloride ions if ($p(O_2)$ = 1 atm and $E^0_{O_2, H^+/H_2O}$ = 1.229 V?

13.3 At what pH interval is it possible to oxidize gold powder by hydrogen peroxide ($E^0_{H_2O_2, H^+/H_2O}$ = 1.763 V) in the presence of chloride-ions? Assume that the activities of all ions in the solution except H^+ are 1.

SOLUTION OF PREPARATORY PROBLEM 13

13.1 Ion $[Au(H_2O)_6]^+$ is unstable towards disproportionation, because

$E°$ ($[Au(H_2O)_6]^+$ / Au) > $E°$ ($[Au(H_2O)_6]^{3+}$ / $[Au(H_2O)_6]^+$).

For the reaction

3 $[Au(H_2O)_6]^+ \rightarrow$ 2 Au + $[Au(H_2O)_6]^{3+}$ + 12 H_2O,

$E°$ = 1.692 – 1.401 = 0.291 V.

In the presence of chloride- and bromide-ions Au(I) remains unstable for the same reason:

3 $[AuCl_2]^- \rightarrow$ 2 Au + $[AuCl_4]^-$ + 2 Cl^-, $E°$ = 1.154 – 0.926 = 0.228 V.

3 $[AuBr_2]^- \rightarrow$ 2 Au + $[AuBr_4]^-$ + 2 Br^-, $E°$ = 0.960 – 0.810 = 0.150 V.

13.2 In the presence of chloride ions gold powder can be oxidized by pure oxygen, because $E°(O_2/H_2O)$ exceeds $E°([AuCl_2]^-/Au)$.

$4\ Au + O_2 + 8\ Cl^- + 4\ H^+ \rightarrow 4\ [AuCl_2]^- + 2\ H_2O$, $E° = 1.229 - 1.154 = 0{,}075$ V.

13.3 The redox potential $E(H_2O_2,H^+/H_2O)$ depends on pH (the Nernst equation):

$H_2O_2 + 2\ H^+ + 2\ e^- = 2\ H_2O$

$E(H_2O_2,H^+ / H_2O) = E° - (0.059 / 2) \log(1 / [H^+]^2) = 1.763 - 0.059$ pH.

The potential $E([AuCl_2]^- / Au)$ doesn't change its value in acidic medium:

$E([AuCl_2]^- / Au) = E°([AuCl_2]^-/Au) = 1.154$ V.

So, the reaction

$2\ Au + H_2O_2 + 4\ Cl^- + 2\ H^+ \rightarrow 2\ [AuCl_2]^- + 2\ H_2O$

´ is possible if $E(H_2O_2,H^+ / H_2O) > E([AuCl_2]^- / Au)$:

$1.763 - 0.059$ pH > 1.154,

pH < 10.3. In fact, this pH interval is restricted to acidic medium as in basic solutions dichloroaurate(+1) decomposes to gold(+1) oxide.

THEORETICAL PROBLEM 14

Determination of acetylsalicylic acid purity

Aspirin – acetylsalicylic acid – is used to treat pain and to reduce fever, at low doses, to prevent heart attacks, strokes, and blood clot formation. It is one of the most widely used medications in the world, with an estimated 80 billion of tablets of it being consumed each year. Aspirin tablets can be contaminated with salicylic acid – the reagent for synthesis of acetylsalicylic acid. The content of salicylic acid is controlled in accordance with national pharmacopoeias. It must not exceed 0.1 – 0.3 %. Redox titration using bromine as an oxidation agent is one of the possible techniques to determine salicylic acid in aspirin.

A portion of 4.4035 g of powdered aspirin tablets was dissolved in 250.0 cm^3 volumetric flask. For redox titration, reagent (bromine) was generated *in situ* (in the same titration flask). Bromide-bromate mixture was made of potassium bromide (0.5950 g) and potassium bromate (0.1670 g) in 100 cm^3 of water. 25.00 cm^3 aliquot was transferred to a titration flask, also sulfuric acid and 20.00 cm^3 of the above mixture was added. The volume was made up to 50.0 cm^3 with water. Flask was corked up and stirred for 10 min.

14.1 Write the balanced equations of the reactions described.

14.2 At what maximal pH bromide will react with bromate? The standard redox potentials are: $E^0_{2\,BrO_3^-,H^+/Br_2}$ = 1.52 V, $E^0_{Br_2/2\,Br^-}$ = 1.09 V.

Solution obtained after filtration of the reaction mixture was titrated against a solution of $NaAsO_2$ (c = 0.02015 mol dm^{-3}) and a mean titre of 9.93 cm^3 was obtained.

14.3 Write the balanced equations of the reactions described.

14.4 Calculate the percentage of salicylic acid in tablets by mass.

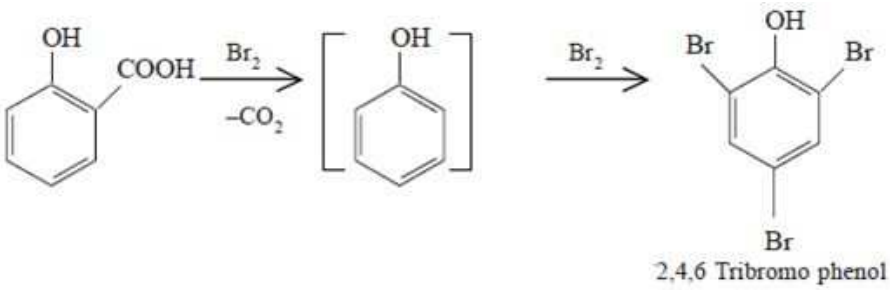
14.5 Do the tablets meet the regulatory requirements?

_____

SOLUTION OF PREPARATORY PROBLEM 14

14.1 $5\ KBr + KBrO_3 + 3\ H_2SO_4 \rightarrow 3\ Br_2 + 3\ H_2O + 3\ K_2SO_4$

Acetylsalicylic acid does not react with bromine, but salicylic acid reacts as follows:



2,4,6 Tribromo phenol

14.2 To predict the direction of a redox reaction, equilibrium constant must be calculated. As the reaction depends on the $[H^+]$ concentration, conditional equilibrium constant must be used. If it is larger than 1, then reaction proceeds and bromine forms.

$\log K' = \frac{\Delta E^{0\prime}}{0.059} \times 10$ where 10 is the number of electrons.

$$= \frac{E^{0'}_{2BrO_2^-/Br_2} - E^{0}_{Br_2/2Br^-}}{0.059} \times 10 = \frac{E^{0'}_{2\,BrO_2^-/Br_2} - 0.059 \times \frac{12}{10} \times pH - E^{0}_{Br_2\,/\,2Br^-}}{0.059} \times 10 = 0$$

$\log K' = 10 \times (1.52 - 0.059 \times 1.2 \times pH - 1.09) / 0.059$; pH = 6.07.

14.3 $Br_2 + NaAsO_2 + 2\ H_2O \rightarrow 2\ HBr + NaH_2AsO_4$

14.4 $n(KBr) = 0.5950\ g / 119.00\ g\ mol^{-1} = 5.00\ mmol$

$n(KBrO_3) = 0.1670\ g / 167.00\ g\ mol^{-1} = 1.00\ mmol \rightarrow n\ (Br_2)_{total} = 3.00\ mmol$ in 100.0 cm^3 and $n(Br_2)_{total} = 0.600\ mmol$ in 20.00 cm^3.

$n(NaAsO_2) = n(Br_2) = 0.02015\ mol\ dm^{-3} \times 9.93\ cm^3 = 0.200\ mmol$ = excess of bromine

$n(Br_2) = 0.600 - 0.200 = 0.400\ mmol$ (bromination of salicylic acid)

n(salicylic acid) = 0.400 / 3 in aliquote (25 cm^3)

n(salicylic acid) = 0.400 mmol × 10 / 3 in 250 cm^3

m(salicylic acid) = 0.400 mmol × 10 ×138.12 g mol^{-1} / 1000 / 3 = 0.1842 g

w(salicylic acid) = 0.1842 g / 4.4035 g = 0.0418 (4.18 %).

14.5 Impurity is present at a level greater than allowed.

THEORETICAL PROBLEM 15

Chemical dosimeter

Chemical dosimeters are widely used for remote determination of high-level doses of radiation. Most common type of dosimeter is a ferrous-ferric sulfate dosimeter. When ionizing radiation passes through the solution, lots of products (radicals, ions, and molecules) are formed. Most of them can oxidize Fe^{2+} into Fe^{3+}.

15.1 Choose the electronic configuration of Fe^{2+} cation:

A) $3d^6 4s^0$ B) $3d^5 4s^0$ C) $3d^4 4s^2$ D) $3d^5 4s^1$

15.2 Write the balanced equations for oxidation of Fe^{2+} with the following particles:

A) H_2O^+ B) OH^- C) H_2O_2

The resulting solution is then titrated and the amounts of Fe(II) and Fe(III) are calculated. For these purpose, permanganatometric and iodometric titrations can be used.

15.3 Write down the balanced redox equation for the reaction between:

a) iron(II) sulfate and potassium permanganate in acidic media;

b) iron(III) sulfate and potassium iodide;

c) sodium thiosulfate and iodine.

15.4 Calculate the concentrations of cations Fe^{2+} and/or Fe^{3+} in each of the following cases:

a) 12.30 cm^3 of potassium permanganate solution (c = 0.1000 mol dm^{-3}) were necessary to titrate 20.00 cm^3 of Fe(II) solution.

b) 1.00 cm^3 of solution containing Fe(III) was diluted up to 20.00 cm^3 and an excess of potassium iodide solution was then added to the prepared solution. The iodine formed was titrated with 4.60 cm^3 sodium thiosulfate solution (c = 0.0888 mol dm^{-3}).

c) An aliquot 5.00 cm^3 was titrated with 0.1000 mol dm^{-3} potassium permanganate solution, the average volume being equal 7.15 cm^3. After that, an excess of potassium iodine solution was added to the flask. Titration of the resulting solution required 13.70 cm^3 of sodium thiosulfate solution with its concentration of 0.4150 mol dm^{-3}.

Frequently, chemical dosimeters are used for measuring doses near nuclear reactors where large amounts of various radionuclides are accumulated.

15.5 Match mother and daughter radionuclide, indicate the type of decay (α or β^-) in each case:

Mother radionuclide:

a) ^{60}Co b) ^{90}Sr c) ^{226}Ra d) ^{137}Cs e) ^{212}Po

Daughter radionuclide:

1) ^{90}Zr 2) ^{137}Xe 3) ^{214}Rn 4) ^{222}Rn 5)^{137}Ba 6) ^{60}Ni 7) ^{60}Fe 8) ^{208}Pb 9) ^{90}Y

Radioactivity *A* is directly proportional to the number of particles *N* of a substance J ($A = \lambda N$), where λ is the decay constant related to half-life by the equation $\lambda = \ln 2 / T_{1/2}$. Radioactivity is measured in becquerel (symbol Bq) units: 1 Bq is one decay per second.

15.6 Using values of half-lives, calculate (in GBq) radioactivity of samples containing:

a) 1.3141 g $^{226}RaCl_2$

b) 1.0 mg $^{90}Sr(NO_3)_2$ and 0.5 mg $^{137}CsNO_3$

$T_{1/2}(^{226}Ra)$ = 1612 years, $T_{1/2}(^{90}Sr)$ = 29 years, $T_{1/2}(^{137}Cs)$ = 30 years.

15.7 Explain why ^{226}Ra is dangerous for humans?

15.8 It is well known that radionuclide ^{64}Cu decays to ^{64}Ni (this is attributed to electron capture, process when nuclei absorb inner electron) and ^{64}Zn (β^- decay). Half-life for electron capture is 20.8 hours, for β^- decay is 32.6 hours.

a) Calculate the average half-life of ^{64}Cu.

b) How much time is required for radioactivity of a ^{64}Cu sample to decrease by 10 times?

SOLUTION OF PREPARATORY PROBLEM 15

15.1 A).

15.2. A) $H_2O^+ + Fe^{2+} \rightarrow H_2O + Fe^{3+}$

B) $OH\cdot + Fe^{2+} \rightarrow OH^- + Fe^{3+}$

C) $H_2O_2 + Fe^{2+} \rightarrow OH^- + OH\cdot + Fe^{3+}$

15.3 a) $10\ FeSO_4 + 2\ KMnO_4 + 8\ H_2SO_4 \rightarrow 5\ Fe_2(SO_4)_3 + 2\ MnSO_4 + K_2SO_4 + 8\ H_2O$.

b) $Fe_2(SO_4)_3 + 6\ KI \rightarrow 2\ FeI_2 + I_2\downarrow + 3\ K_2SO_4$.

c) $I_2 + 2\ Na_2S_2O_3 \rightarrow 2\ NaI + Na_2S_4O_6$.

15.4 a) Concentration of iron(II) can be calculated from equation 15.3(a):

$12.3 \times 0.1000 \times 5 = 20\ x$

$x = 0.3075$ mol dm^{-3}

b) Using equation 15.3(b) one can assume that the amount of iodine occurred after potassium iodide addition is two times smaller than the amount of iron(III). From equation 15.3(c) the amount of thiosulfate spent for iodine titration is two times greater than that of iodine. Therefore, concentration of iron in the initial aliquot is:

$x = 0.0888 \times 4.6$,

$x = 0.4085$ mol dm^{-3}

c) The initial amount of potassium permanganate is 7.15 cm^3 $\times$ 0.1000 mol dm^{-3} = 0.7150 mmol. So, from stoichiometry of 15.3(a) the amount of substance of Fe^{2+} is

$n(Fe^{2+}) = 7.15$ cm^3 $\times$ 0.1000 mol dm^{-3} $\times$ 5 = 3.5750 mmol.

At the endpoint of the redox titration all iron is in the Fe^{3+} form and therefore total iron is determined by titration with sodium thiosulfate.

n(Fe total) = 13.7 cm^3 $\times$ 0.4150 mol dm^{-3} = 5.6855 mmol.

Then, the amount of iron(III) is:

$n(Fe^{3+}) = 5.6855 - 3.5750 = 2.1105$ mmol.

The iron concentrations are:

$c(Fe^{2+}) = 3.5750 / 5 = 0.7150$ mol dm^{-3},

$c(Fe^{3+}) = 2.1105 / 5 = 0.4221$ mol dm^{-3}.

15.5 **a**–6–β^-; **b**–9–β^-; **c**–4–α; **d**–5–$\beta^{-\prime}$; **e**–8–α

15.6 a) First, calculate the number of ^{226}Ra atoms:

$N_{Ra} = N_A \cdot \nu = N_A \cdot m/M = 6.02 \cdot 10^{23} \cdot \times 1.3141 / (226+71) = 2.6636 \cdot 10^{21}$.

Then, the decay constant (half-life in seconds) can be determined:

$$\lambda_{Ra} = \frac{\ln 2}{1612 \times 365 \times 24 \times 3600} = 1.3635 \cdot 10^{-11}\ s^{-1}.$$

The radioactivity is (round to the integer number):

$A_{Ra} = \lambda_{Ra} N_{Ra} = 2.6636 \cdot 10^{21} \times 1.3635 \cdot 10^{-11} = 36.32$ GBq.

b) The same calculations for cesium-137 and strontium-90 give:

$A_{Cs} = 1.5126 \cdot 10^{18} \times 7.3265 \cdot 10^{-10} = 1.108$ GBq

$A_{Sr} = 2.8131 \cdot 10^{18} \times 7.5792 \cdot 10^{-10} = 2.132$ GBq

Total radioactivity is the sum of both values:

$A_{tot} = 3$ GBq.

15.7 The daughter radionuclide of ^{226}Ra is ^{222}Rn – noble gas that is radioactive and can easily penetrate different obstacles.

15.8 a) This process can be described as two competitive reactions of the first order. Then:

$$\lambda_{total} = \lambda_{e\ capture} + \lambda_{\beta}$$

$$\frac{\ln 2}{T_{1/2\,(\text{total})}} = \frac{\ln 2}{T_{1/2\ (e\ capture)}} + \frac{\ln 2}{T_{1/2\ (\beta)}}$$

$$\frac{1}{T_{1/2\,(\text{total})}} = \frac{1}{T_{1/2\ (e\ capture)}} + \frac{1}{T_{1/2\ (\beta)}}$$

$$T_{1/2\,(\text{total})} = \frac{T_{1/2\ (\text{e capture})}\, T_{1/2\ (\beta)}}{T_{1/2\ (\text{e capture})} + T_{1/2\ (\beta)}} = \frac{20.8 \times 32.6}{20.8 + 32.6} = 12.7 \text{ hours}$$

b) The integrated equation of decay is as follows: $A(t) = A_0 e^{-\lambda t}$. Taking into account that radioactivity decreased ten times, time is calculated as follows:

$0.1 = e^{-\lambda t}$,

$\ln 0.1 = -\lambda t$,

$t = \ln 10 / \lambda = 12.7 \times \ln 10 / \ln 2 = 42.2$ h.

THEORETICAL PROBLEM 16

Determination of water in oil

Oil is the most important mineral for Azerbaijan. From chemist's point of view it is a mixture of a great number of substances of different nature – both organic and inorganic. At all stages of petroleum refining, it is important to control the content of inorganic impurities, including water, in oil. One of the popular chemical methods for the determination of water in various organic matrices is named Karl Fischer titration. The method is based on the reaction described by R. Bunsen:

$$I_2 + SO_2 + H_2O \rightarrow HI + H_2SO_4$$

16.1 Indicate the oxidant and reductant in the reaction.

16.2 Put the coefficients in this reaction. Sum of the least integer coefficients is

A) 14 B) 9 C) 7 D) 10

Reagent which was proposed by the German chemist Karl Fischer is a mixture of pyridine, sulfur dioxide, iodine, and methanol. In this case, the following reactions occur during titration:

$$SO_2 + CH_3OH + H_2O + I_2 \rightarrow 2\ HI + CH_3OSO_3H$$

$$Py + HI \rightarrow PyH^+I^-$$

$$Py + CH_3OSO_3H \rightarrow PyH^+\ CH_3OSO_3^-$$

16.3 What is the role of pyridine in the composition of Fischer reagent?

16.4 What substance(s) could be used instead of pyridine?

A) Imidazole B) Pyrrol C) Hydrazine D) Butylamine

16.5 However, the above composition of titrant may lead to various side reactions. Write the possible reactions taking place between the components of the Fischer reagent and the following substances:

a) aldehydes, RC(O)H,

b) ketones, RC(O)R,

c) mercaptans, RSH,

d) organic peroxides, ROOH.

Indicate if an overestimation or underestimation of the water content is observed in each case.

16.6 Fischer reagent is to be standardized prior to use, i.e. it is necessary to set amount of water corresponding to one volume of a titrant. The reagent was prepared by the following procedure: 49 g of iodine were dissolved in 158 g of pyridine, then 38.5 g of liquid sulfur dioxide was introduced while cooling. Thereafter, mixture was diluted up with methanol to 1 dm^3.

a) Using the above data, calculate the theoretical titre of the Fischer reagent (in mg/mL).

b) Calculate the practical titre (in mg/mL) of Fischer reagent, if to reach the endpoint for the titration of 5 g of a mixture of methanol and water (water content of 1% by volume), 19 cm^3 of titrant was spent.

c) Why do the results obtained differ?

d) Calculate the water content (in %) in the sample of sour oil, if the content of mercaptan in sulfur recalculation is 1 wt.% and titration of 1.00 g sample of sour oil dissolved in methanol required 7.5 cm^3 of titrant.

16.7 The modern version of water determination in different samples is coulometric Karl Fischer titration. During the titration iodine is generated electrochemically and the water content is defined as the total amount of current passing through the coulometer. Titration is stopped when the generation of iodide stops in the system.

a) Using Faraday's law, calculate the mass fraction of water in the oil sample (10.0 g), if 375.3 coulombs passed through a coulometer.

b) 1.000 g portion of sugar was dissolved in 15 cm^3 of methanol and chloroform mixture. Calculate the molar and mass fractions of water and sugar, if for a coulometric titration of sugar a total charge of 567.2 coulombs was required, while 31.1 coulombs were required to titrate solvent.

SOLUTION OF PREPARATORY PROBLEM 16

16.1 Reductant – sulfur dioxide, oxidizer – iodine.

16.2 C)

16.3 As a base, pyridine binds to acids that are formed during the process (HI and H_2SO_4) and neutralize them.

16.4 The substance must have basic properties – A), C), D).

16.5 Reactions of ketones and aldehydes with methanol lead to ketals and acetals. The result is overstated, since water is released:

$RCH{=}O + 2\ CH_3OH \rightarrow RCH(OCH_3)_2 + H_2O$.

Reactions of aldehydes with sulfur dioxide and base give sulfite aldehyde derivative. The result is understated, because water is absorbed.

$RCH{=}O + SO_2 + H_2O + Py \rightarrow [RCH(OH)SO_3^-]PyH^+$.

Iodine reacts with mercaptans. The result is overstated, since iodine is consumed:

$2\ RSH + I_2 \rightarrow RSSR + 2\ HI$.

Reaction of hydrogen iodide with peroxides:

$ROOH + 2HI \rightarrow I_2 + ROH + H_2O$.

Hydroperoxides produce equivalent amounts of iodine and water. The Fischer titration is free from interference. If some other strong oxidizing agents (elemental bromine, chlorine) are present, excess SO_2 is passed through the sample. This reduces these substances to chloride and bromide respectively, which no longer interfere. Other peroxides (percarbonate or diacylperoxide) react according to the following equation at different rates:

$R–CO–O–O–CO–R + 2\ HI \rightarrow 2\ RCOOH + I_2$.

In this case, determination of water is performed at low temperatures (up to –60℃), so that any possible side reactions can be «frozen».

16.6 a) First, calculate the amounts of substance of iodine and sulphur dioxide.
$n(I_2) = 49 / (2 \cdot 127) = 0.193$ mol, $n(SO_2) = 38.5 / 64 = 0.6$ mol.

Iodine is completely consumed. One molecule of iodine reacts with one molecule of sulphur oxide, so the theoretical titre is (in mg/cm^3):
$m(H_2O) = 0.193 / 1000 \cdot 18 = 3.5$ mg / cm^3.

b) The practical titre is (use the density of methanol (0.7918) as the density of mixture):
$m(H_2O) = (5 / 0.7918) \cdot 0.01 / 19 = 3.3$ mg / cm^3.

c) The results obtained differ because of the presence of water in the reactants, but also because of water vapor in the air.

d) The amount of iodine that reacted with mercaptans:
$n(I_2) = 0.01 / 32 / 2$ mol.
Multiplying this value by the molar mass of water, the value of overstatement can be calculated (in milligrams):
$m(H_2O) = n(I_2)\, M(H_2O) = 2.8$ mg.
The total mass of determined water is therefore:
$m(H_2O) = 7.5 \times 3.3 = 24.8$ mg.
The mass of water in the sample is:
$m(H_2O) = 24.8 - 2.8 = 22.0$ mg.
Water content (mass %) in the sample is:
$w(H_2O) = 22.0$ mg / 1.00 g $\cdot$ 100 % = 2.20 %.

16.7 a) In oxidation of iodine two electrons are involved. Then, using the Faraday equation water content (mass %) is calculated:
$m(H_2O) = M\, Q / (nF) = 18 \times 375.3 / (2 \times \cdot 96500) = 0.0035$ g.
$w(H_2O) = 0.035 / 10 \cdot 100\% = 0.35$ %.

b) The charge passed during the titration of the sugar sample is:
$Q = 567.2 - 31.1 = 536.1$ C.

Then, water mass is 0.050 g (from Faraday law), and the content (mass %) is 5.0 %. The mole fraction of water is (sucrose – $C_{12}H_{22}O_{11}$):

$$x(H_2O) = \frac{\frac{0.05}{18}}{\frac{0.05}{18} + \frac{0.95}{342}} \times 100\,\% = 50\,\%.$$

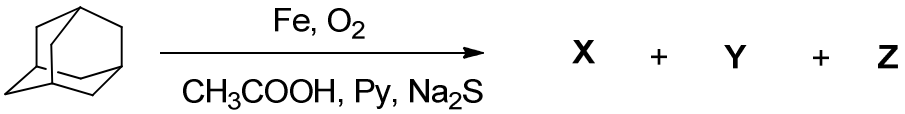
THEORETICAL PROBLEM 17

Oxidation and inspiration

With every breath, I breathe in so much of inspiration.
I feel if there is one thing as free and as important as oxygen, it's inspiration.
(Sharad Sagar)

Oxygen is not only chemical element but also the essential element of life. Its most stable form, dioxygen, O_2, constitutes 20.8% of the volume of the Earth's atmosphere. All forms of oxygen are able to oxidize various compounds, especially organic ones. The type of oxygen-containing functionalities in organic compounds could be efficiently determined by IR spectroscopy. Thus, C=O groups are characterized by intense absorption at 1750 - 1660 cm^{-1} and O–H group is characterized by absorption in the region of 3600-3000 cm^{-1}.

The most typical oxidation of saturated hydrocarbons with O_2 is the burning process. However, some reaction have been developed producing various oxygenated products. For example, Gif reaction (which received this name in honor of Gif-sur-Yvette where Prof. Derek Barton was working when he disclosed this transformation) represents the oxidation of saturated hydrocarbons with air oxygen at room temperature. Thus, the oxidation of adamantane leads to three products:



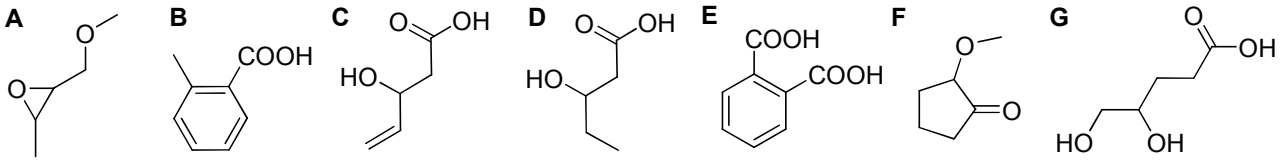
Products **X** and **Y** are isomers. The compound **Y** can be easily transformed to **Z**. IR spectra of the compounds **X** and **Y** contain a band around 3300 cm^{-1}, while IR spectrum of compound **Z** contains band 1720 cm^{-1}.

17.1 Write down the structural formulae of compounds **X**–**Z**.

Without catalysts O_2 has, fortunately, very low reactivity. Otherwise, all living organisms should be oxidized by air. A wide variety of oxidizing reagents have been developed for selective or undiscriminating oxidation of various functional groups in high

yield. Below 7 organic molecules are given. They were synthesized by oxidation with 7 indicated reagents.

Products



Oxidants

a $Me_2SO + (COCl)_2$, then Et_3N (Swern oxidation)

b $CrO_3 + H_2SO_4$; acetone (Jones oxidation)

c SeO_2

d $KMnO_4$, 20 °C, pH 7-7.5

e $KMnO_4$, H_2SO_4, Δ

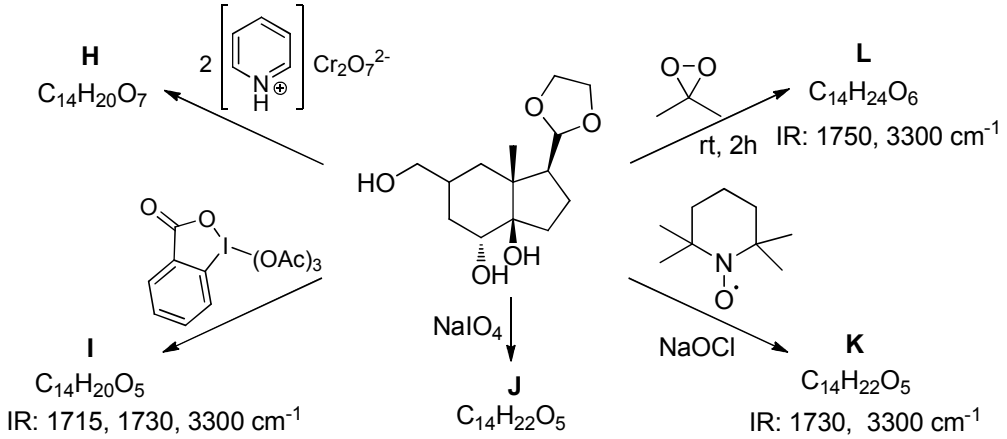
f *meta*-chloroperbenzoic acid (mCPBA)

g $Ag(NH_3)_2OH$, then H^+

These oxidation reactions proceed without C–C cleavage.

17.2 Put the correspondence between the products and the oxidants and determine the starting organic compounds.

Examples of the chemoselective oxidation of the same substrate with different oxidants affording different reaction products are given below.

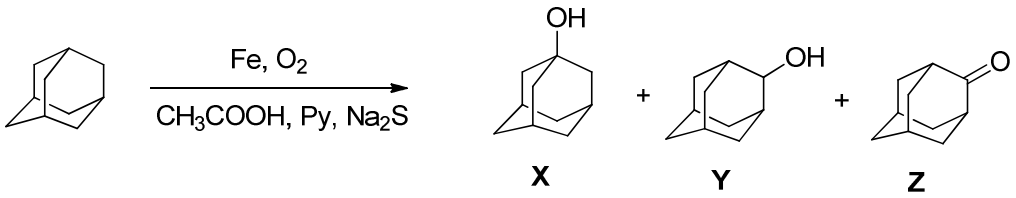


Compounds I, J, and K react with $Ag(NH_3)_2OH$ solution producing the metallic silver precipitation. Compound H could be formed by oxidation of J. The treatment of 1.44 g of L with metallic sodium produces 0.224 L (p = 1 atm, T = 273 K) of hydrogen gas.

17.3 Write down the structural formulae of compounds H–L.

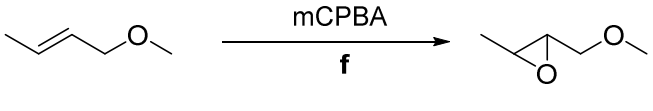
SOLUTION OF PREPARATORY PROBLEM 17

17.1 From the IR spectroscopy data it is possible to conclude that adamantane is oxidized to two alcohols (X, Y) and one ketone (Z). The adamantane molecule has two non-equivalent carbon atoms – secondary one and tertiary one. Thus, we can conclude that one of the products is adamantan-1-ol, the second one is adamantan-2-ol. Only the last compound can be oxidized to ketone, adamantan-2-one (Z).

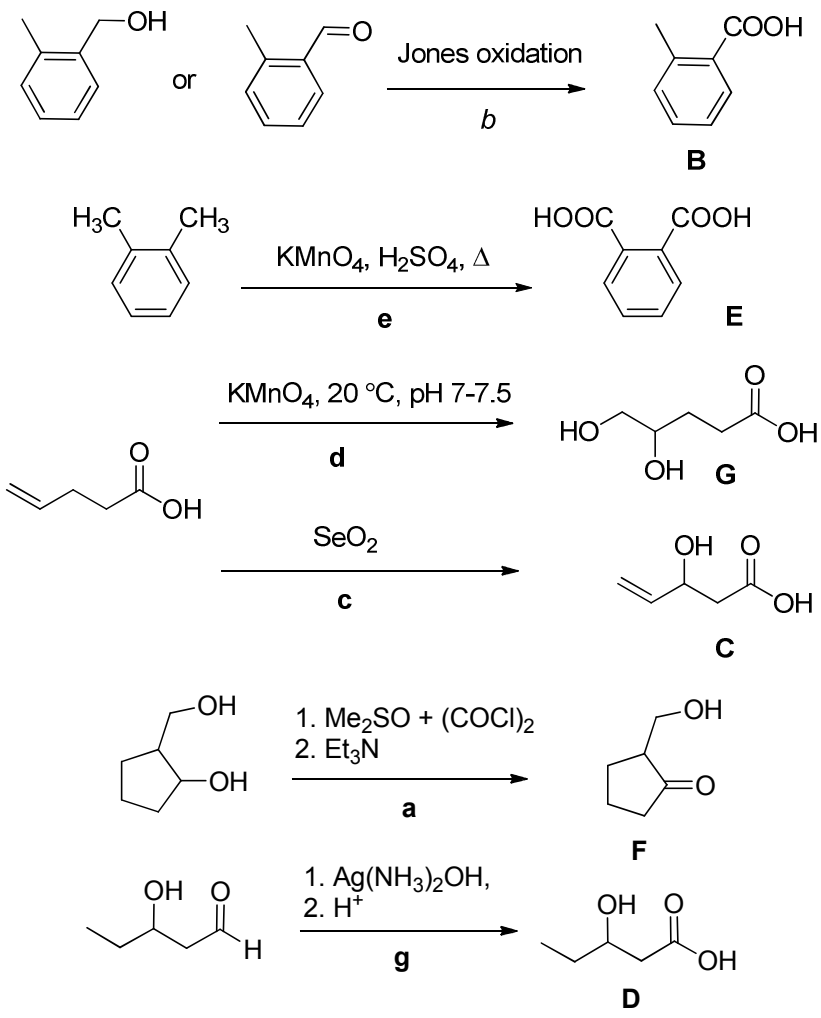


17.2 The oxidation with $KMnO_4$ at room temperature and pH 7-7.5 (system *d*) is the well-known process of the alkene dihydroxylation. The only compound containing 1,2-diol moiety is the compound G. It is the first "reagent-product" pair. System *a* (Swern oxidation) is used for the oxidation of alcohols to aldehydes or ketones. The compound F is the only product containing one of two of these functionalities. It is a second pair. The epoxide A can be formed by epoxidation of the corresponding alkenes with *m*CPBA only (reagent *f*). Other reagents are inappropriate for the preparation of this compound. Compound D contains hydroxyl group. It allows for excluding all oxidants except *c* and *g*. However, SeO_2 is used for allylic oxidation of alkenes and related oxidations of ketones. It is not this case. Therefore, we can conclude that D was synthesized by oxidation of hydroxyaldehyde by $Ag(NH_3)_2OH$ (system *g*). In turn, SeO_2 (reagent *c*) was used for synthesis of allyl alcohol C. Two remaining products are B and E. Two reagents are $KMnO_4/H_2SO_4$ under heating (system *e*) and CrO_3/H_2SO_4 in acetone (system *b*). Even if we do not know about the Jones oxidation, we know that the system *e* should oxidize methyl groups in toluene derivatives. Therefore, phthalic acid (E) was formed by oxidation with system *e* and 2-methylbenzoic acid (B) was obtained from 2-methylbenzaldehyde or 2-methylbenzyl alcohol by Jones oxidation.

Therefore, 7 pairs are: A – *f*; B – *b*; C – *c*; D – *g*; E – *e*; F – *a*; G – *d*.



A



17.3 The molecular formula of the initial compound is $C_{14}H_{24}O_5$. It contains the protected aldehyde group and three different alcohol groups: primary, secondary and tertiary ones; two of them are located in vicinal positions, *i.e.*, form a 1,2-diol system. This system is known to be oxidized with $NaIO_4$ producing compound J ($C_{14}H_{22}O_5$) containing two carbonyl functions. Compound H has two hydrogen atoms less but two oxygen atoms more than compound J and can be obtained by oxidation of this compound. It allows for concluding that H is the corresponding diacid. Compounds I, K, L have both hydroxyl and carbonyl groups. The presence of two bands at 1730 and 1715 cm^{-1} indicates that compound I has two different carbonyl groups. Molecular formula of I differs from that of the initial compound by 4 hydrogen atoms. These data allow to conclude that I is the product of oxidation of primary and secondary alcohols to aldehyde and ketone, respectively. Compound K contains two hydrogen atoms more, than compound I. Therefore, only one alcohol group was

oxidized to the carbonyl moiety. The selection of group is unambiguously determined by the fact that K is oxidized by $Ag(NH_3)_2OH$, *i.e.*, it contains the aldehyde group. Therefore, only primary alcohol is oxidized.

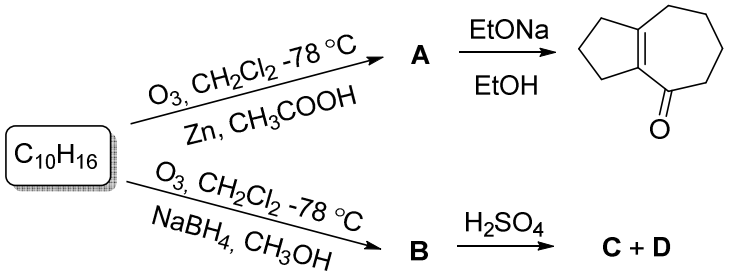
Let us analyze the last product L ($C_{14}H_{24}O_6$). Metallic sodium could react with alcohols and carboxylic groups. This –COOH group could be formed from primary alcohol or by C–C cleavage of the 1,2-diol. In both cases there is a loss of hydrogen atoms, however final product have the same number of hydrogen atoms as the initial substrate. It allows for concluding that there are no carboxylic groups in the molecule. Thus, compound L contains 4 –OH groups according to the quantity of H_2 gas. The 4-th hydroxy group could be only formed by the opening of the ketal ring. Accounting for molecular formula, we can write structure of this compound.

THEORETICAL PROBLEM 18

Essential ozone

Until NMR became the main method for the determination of structures of organic molecules, the ozonolysis reaction, disclosed by Schönbein in 1840, was intensively used for the ascertainment of the unsaturated bond(s) position(s) in molecules. Imagine that you are in a similar situation (but with modern reagents). You have found that some hydrocarbon $C_{10}H_{16}$ participates in the transformations given in Scheme 1.

Scheme 1

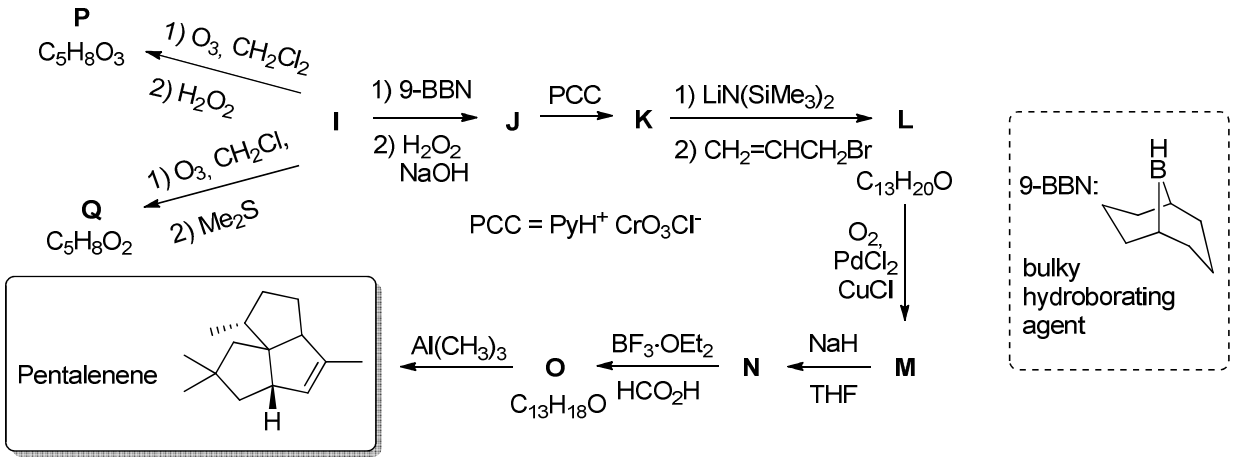


18.1 Determine the structural formulae of the hydrocarbon $C_{10}H_{16}$ and the molecules **A** – **D** accounting for the fact that compounds **C** and **D** are isomers of the initial hydrocarbon; the ozonolysis of **C** followed by the treatment of the reaction mixture with alkaline H_2O_2 produces a single product while the same transformations of **D** afford two compounds.

Some other hydrocarbon **E** (w_C = 90.6 %) under ozonolysis (1. O_3, CH_2Cl_2, –78 ^oC; 2. Me_2S) forms three carbonyl compounds – **F** ($C_2H_2O_2$), **G** ($C_3H_4O_2$), and **H** ($C_4H_6O_2$) in a ratio of 3:2:1. Initial hydrocarbon **E** doesn't decolorize bromine water.

18.2 Write down the structural formulae of hydrocarbon E and products of its ozonolysis **F** – **H**.

Hydrocarbon **I** having center of symmetry was used as an initial material in the total synthesis of *pentalenene* (Scheme 2):

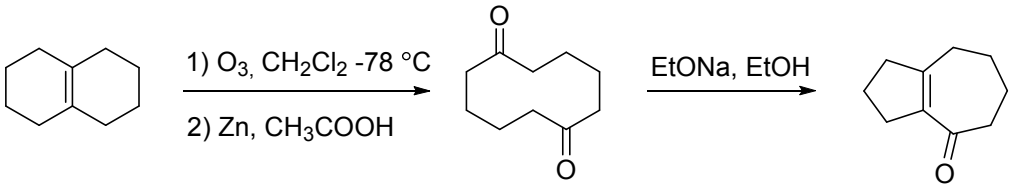


The ozonolysis of hydrocarbon **I** furnishes a single compound **P** or **Q** depending on the treatment of the ozonolysis product. Under treatment with I_2 and NaOH, compound **Q** forms a yellow precipitate containing 96.7% of iodine. Under basic conditions compound **Q** is transformed into compound **R** containing 4 types of hydrogen atoms (4 signals in ^{1}H NMR spectrum with integral intensity of signals 1 : 1 : 2 : 2). Molecular formula of **R** is C_5H_6O. Molecule of compound **N** has bicyclic framework containing **R** as a fragment. Molecule of **O** consists of three rings.

18.3 Descript the scheme of the synthesis of *pentalenene*.

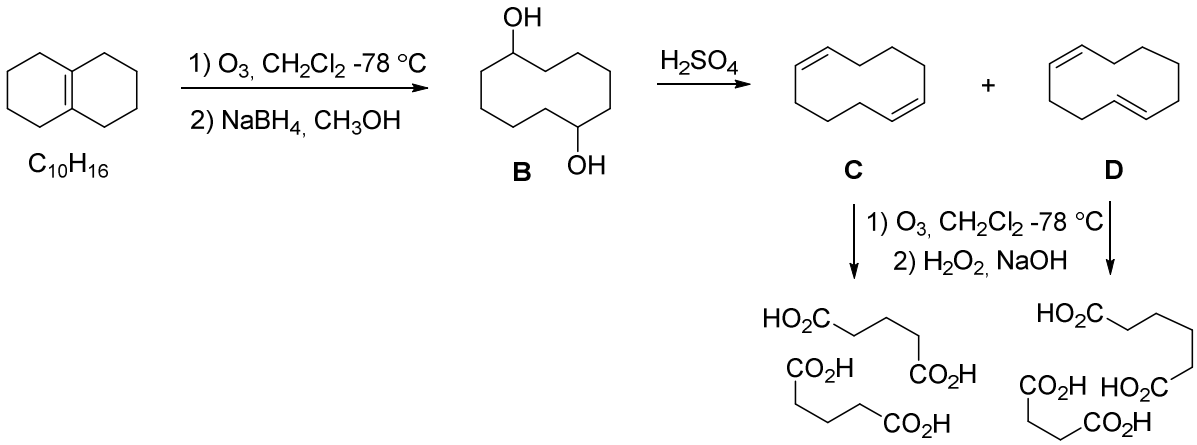
SOLUTION OF PREPARATORY PROBLEM 18

18.1 Treatment of compound **A** with base produces the unsaturated bicyclic ketone ($C_{10}H_{14}O$) which has the same number of carbon atoms as initial hydrocarbon $C_{10}H_{16}$. It allows for concluding that: a) the initial hydrocarbon has endocyclic unsaturated bond; b) compound **A** contains two carbonyls groups and its molecular formula is $C_{10}H_{16}O_2$; c) the unsaturated bicyclic ketone is a product of the intramolecular aldol condensation. Therefore, **A** is cyclodecane-1,6-dione and initial hydrocarbon is octahydronaphthalene:



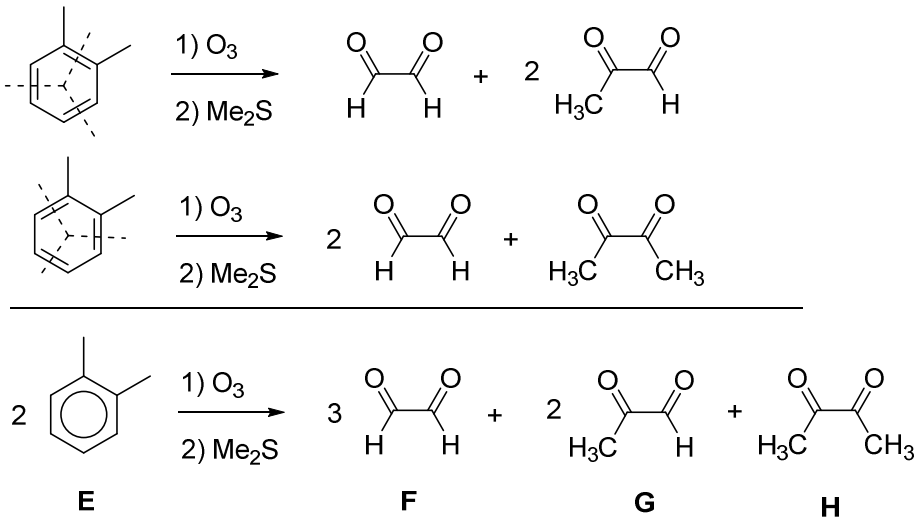
$C_{10}H_{16}$ **A**

The ozonolysis of octahydronaphthalene followed by reduction of ozonide with $NaBH_4$ affords cyclodecane-1,6-diol dehydration of which gives two cyclodecadienes **C** and **D**. Formation of a single product during the ozonolysis of compound **C** demonstrates clearly that **C** is a symmetric product, *i.e.* it is cyclodeca-1,6-diene. So, **D** is cyclodeca-1,5-diene.

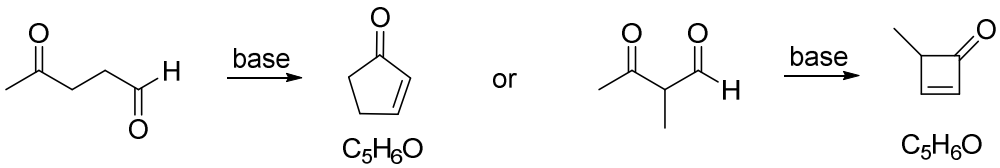


$C_{10}H_{16}$ **B** **C** **D**

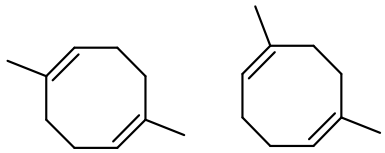
18.2 From the known composition of compound **E** we can determine its molecular formula as $(C_4H_5)_x$. At the same time compound **E** doesn't decolorize bromine water. It allows one to conclude that **E** is an aromatic compound. If x = 2, **E** is C_8H_{10}. The possible alternatives are ethylbenzene and isomeric dimethylbenzenes. The ozonolysis of substituted aromatic compounds leads to two sets of products as there are two Lewis structures for a given aromatic molecule. From molecular formulae of products it is seen that these are glyoxal (**F**) and two its substituted derivatives: monomethyl (2-oxopropanal, **G**) and dimethyl (butan-2,3-dione, or biacetyl, **H**). Therefore, **E** is *o*-xylene (1,2-dimethylbenzene):



18.3 Compound **L** contains 13 carbon atoms. During transformation of **I** to **L** 3 carbon atoms are introduced into molecule. Therefore, hydrocarbon **I** has 10 carbon atoms. The ozonolysis of the hydrocarbon **I** furnishes a single compound **P** (after oxidative treatment of ozonide) or **Q** (after reductive treatment). Accounting for molecular formulae of **P** and **Q**, it is possible to deduce that **P** is ketoacid and **Q** is ketoaldehyde. The positive iodoform test (formation of yellow precipitate of CHI_3 under treatment with I_2 and NaOH) indicates the presence of CH_3CO- fragment in the molecule of **Q**. So, **Q** is 4-oxopentanal and **P** is 4-oxopentanoic acid (levulinic acid). The alternative possibility is 2-methyl-3-oxobutanal (and the corresponding acid), however, this structure can be discarded on the basis of two arguments: a) formation of methylcyclobutenone having high strain energy seems to be low probable; b) NMR data given in the problem are consistent with cyclopentenone but not methylcyclobutenone structure.

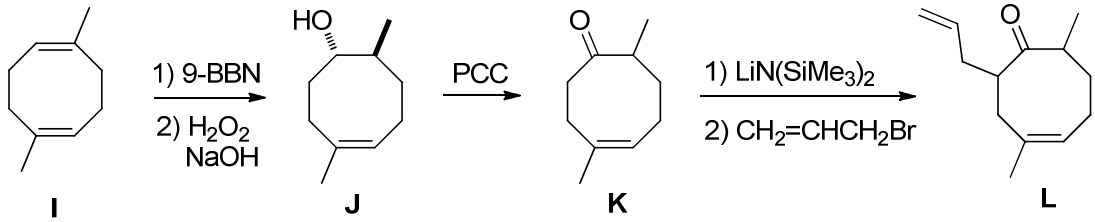


Thus, compound **I** is 1,5-dimethylcycloocta-1,5-diene or 1,6-dimethylcycloocta-1,5-diene. However, only the first compound has a center of symmetry.



I

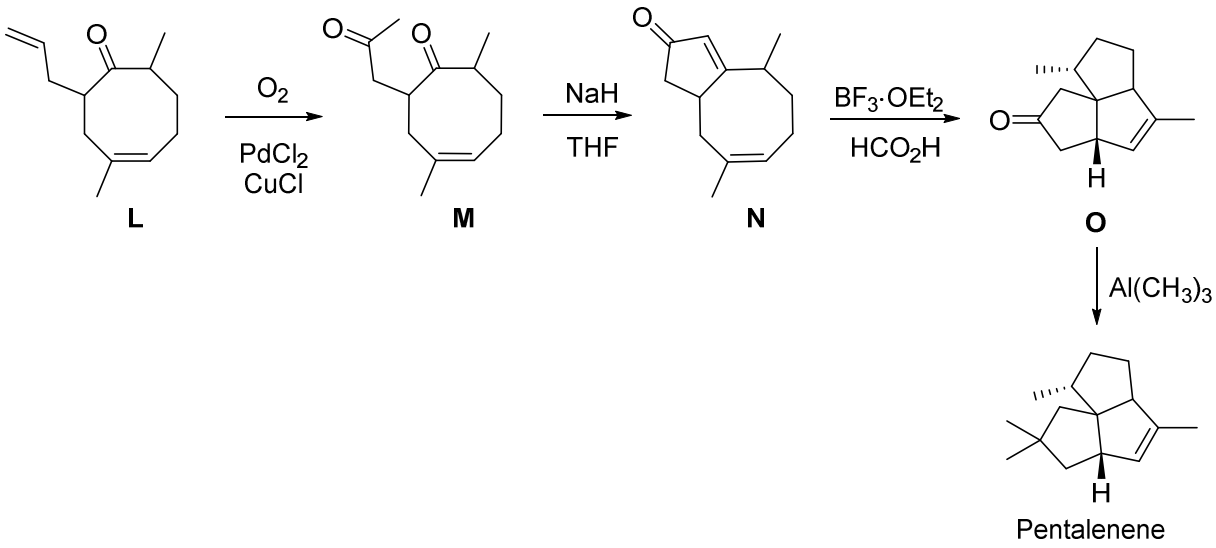
Let's analyze now the synthesis of **L** from **I**. During **K-**to**-L** transformation hydrogen atom is substituted by the allyl fragment CH_2=$CHCH_2$–. Therefore, the molecular formula of **K** is $C_{10}H_{16}O$, *i.e.* formula of **K** differs from formula of **I** by 1 oxygen atom. The **I-**to**-J** is anti-Markovnikov hydration of C=C bond; next step is alcohol-to-ketone oxidation. From formula of **K** it is possible to conclude that only one C=C bond was hydrated during the first step. $LiN(SiMe_3)_2$ is a strong bulky base which selectively deprotonates ketone **K** at the more accessible CH_2 group. Steric effects prevent deprotonation of methane CH-fragment. Alkylation of enolate with allyl bromide accomplishes the synthesis of **L** which is formed as a mixture of *cis*- and *trans*-isomers.



I **J** **K** **L**

Analysis of the final part of synthesis could be simpler if we will start from transformation of **O** ($C_{13}H_{18}O$) into pentalenene ($C_{15}H_{24}$). The comparison of their molecular formulae and information that **O** is tricyclic molecule allow for concluding that **O** has the same tricyclic framework as pentalenene but instead of two methyl groups compound **O** has oxygen atom. So, we can write down structural formulae of **O** even if we don't know this reaction. Molecule **N** is bicyclic and contains cyclopentenone fragment. It is possible to suppose that the second ring in **N** is the 8-membered carbocycle which is present in all previous compounds. The transformation of **N** into **O** is an acid-induced transannular cyclization. The cyclopentenone ring in **N** should be formed by aldol condensation. This leads to the

conclusion that **L**-to-**M** transformation is the oxidation of C=C double bond producing methyl ketone (Waker process). Oxidation of the second C=C bond cannot produce pentalenene. We decipher scheme and can write down structural formulae of all compounds.



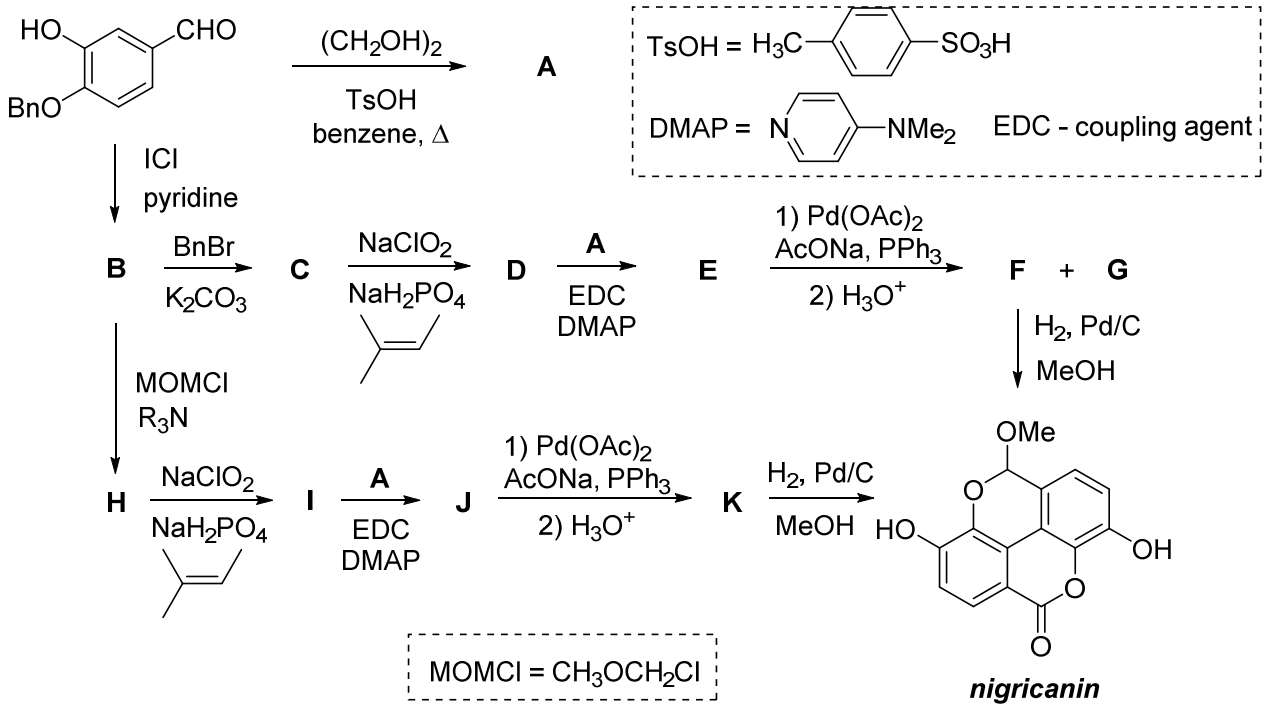
L **M** **N** **O**

Pentalenene

THEORETICAL PROBLEM 19

Two in one

Ellagic acid and its family exhibit antioxidant, anti-cancer, and other types of biological activity. Very recently, the first total synthesis of *nigricanin*, one of the ellagic acid congeners, was described (Scheme 1).

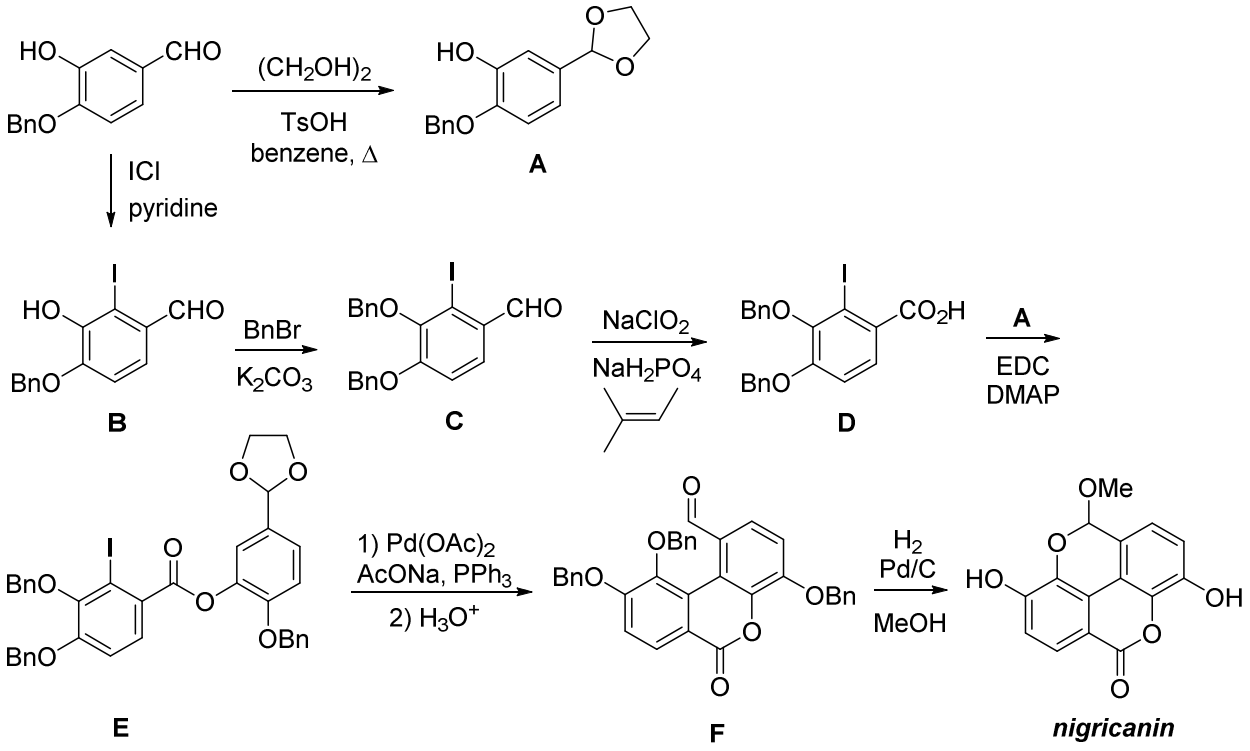


19.1 Decipher this scheme. Write down the structural formulae of compounds **A**–**K** accounting for the facts that **F** and **G** are isomers; molecular formulae of **D** and **E** are $C_{21}H_{17}IO_4$ and $C_{37}H_{31}IO_7$, respectively.

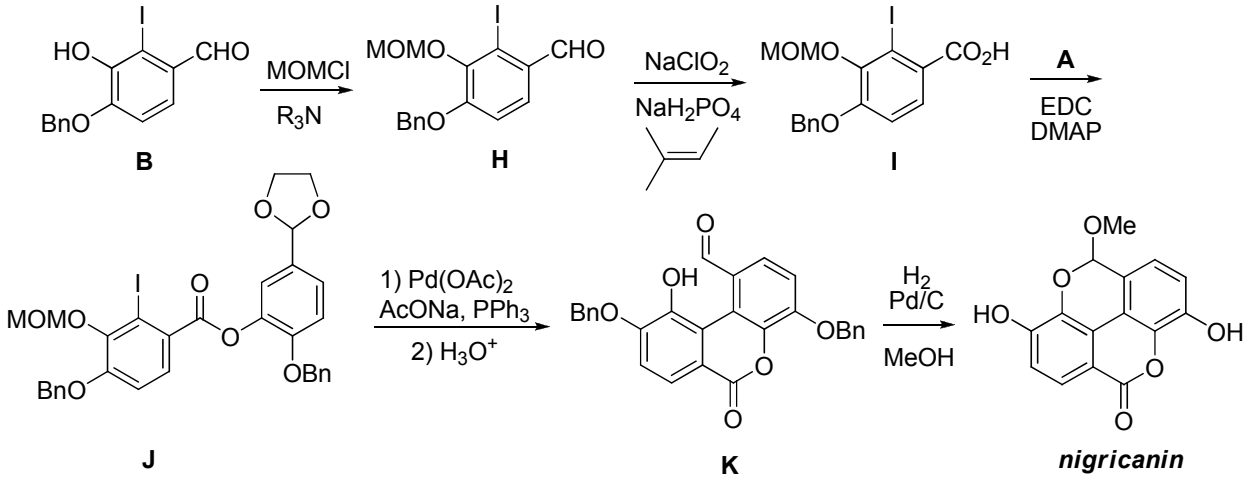
SOLUTION OF PREPARATORY PROBLEM 19

The formation of **A** is the acid-catalyzed aldehyde-to ketal transformation. The formation of **B** is, evidently, iodination of an activated benzene ring. To determine the regiochemistry of this reaction we need to analyze the structure of the target product, nigricanin. From the scheme it is seen that nigricanin is formed from two molecules of the initial 4-benzyloxy-3-hydroxybenzaldehyde. One of them is present in the product as an oxidized form, *i.e.*, an

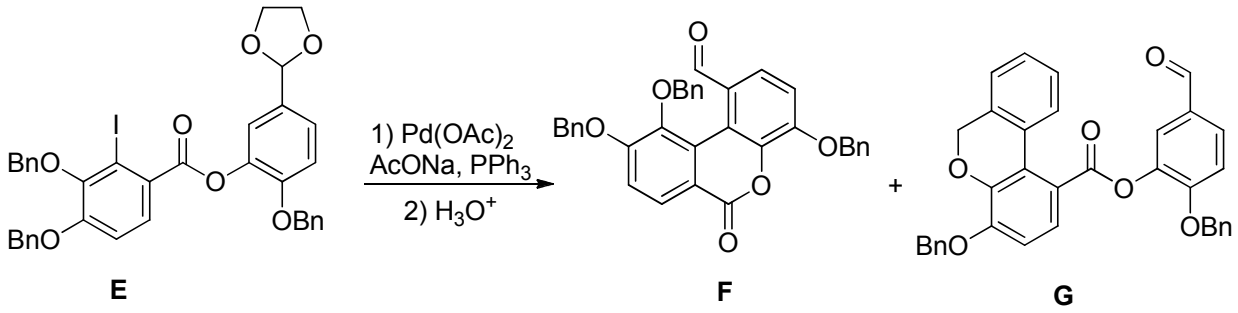
acid derivative, another one is present as an acetal. In the first case, the acid forms ester with 3-hydroxy group of the second molecule. Similarly, in the formation of acetal aldehyde function of the second molecule reacts with 3-hydroxy group of the first molecule. Two molecules are connected by C-C bond between C(2) and C(2') atoms. This bond can be formed only at the Pd-catalyzed transformation of **E** into **F** (and **G**). Therefore, iodine was introduced at the C(2) atom. Reaction of **B** with benzyl bromide is the alkylation of the phenolic group. The reaction of **D** with **A** is, according to the Problem, the condensation process. From the structure of nigricanin it is possible to conclude that it is ester formation. So, **C**-to-**D** transformation is the aldehyde oxidation to the corresponding acid. The second step in the formation of **F** is the acid treatment. This is the hydrolysis of the acetal function. The hydrogenolysis of Bn–O bonds leads to the formation of three hydroxy groups, one of them intramolecularily attacks onto the proximal aldehyde group; methanol participates as the second nucleophile in the formation of the ketal function.



The formation of **H–K** is similar to the formation of **C–F** except for alkylating agent (methoxymethyl chloride instead of benzyl bromide).



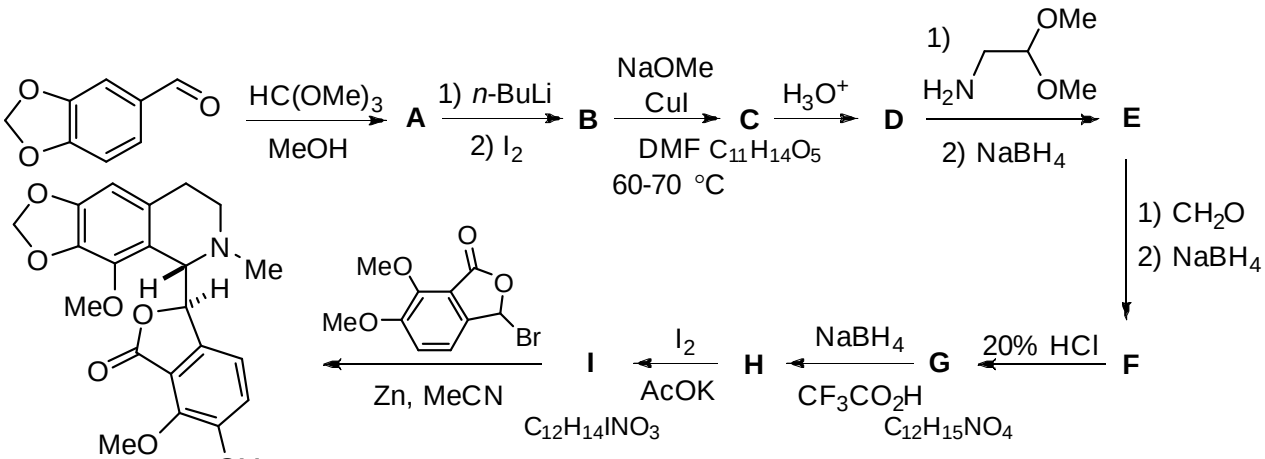
The difference between the utilization of MOM and benzyl groups for the protection of 3-hydroxy group is the formation of the second product **G** during the Pd-catalyzed cross-coupling reaction in the case of the benzyl protecting group on the contrary to the formation of a single product **K** in the case of methoxymethyl protecting group. It allows one to suppose that product **G**, which is an isomer of compound **F**, is formed by cross-coupling of Ar-I moiety with 3-OBn group. Indeed, the six-membered ring can be formed if the *ortho*-carbon atom of this benzyl group participates in the cross-coupling reaction. So, we can write the structural formula of **G**.



THEORETICAL PROBLEM 20

Antitussive "narcotine"

(-)-α-Noscapine is an alkaloid isolated from *Papaver somniferum L.* in 1817 by P. Robiquet which named this compound as "narcotine". This agent demonstrates significant painkilling and antitussive activities. It is also used for treatment of cancer, stroke, anxiety, and so on. Clinically used (-)-α-noscapine is provided through extraction from natural sources or resolution of synthetic racemic compound. There are some syntheses of (±)-α-noscapine. One of them is given in the scheme below.



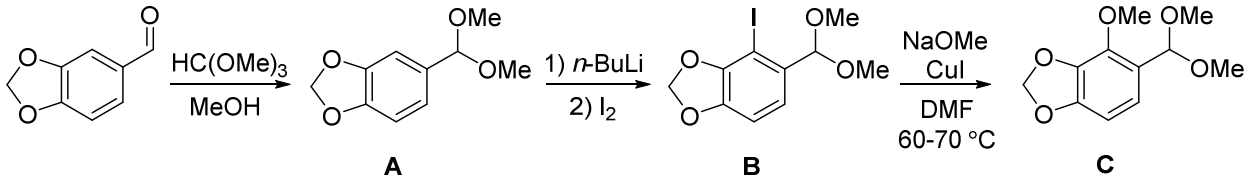
(±)-α-noscapine

20.1 Decipher this scheme. Write down the structural formulae of compounds **A** – **I** if **G** is a tricyclic compound.

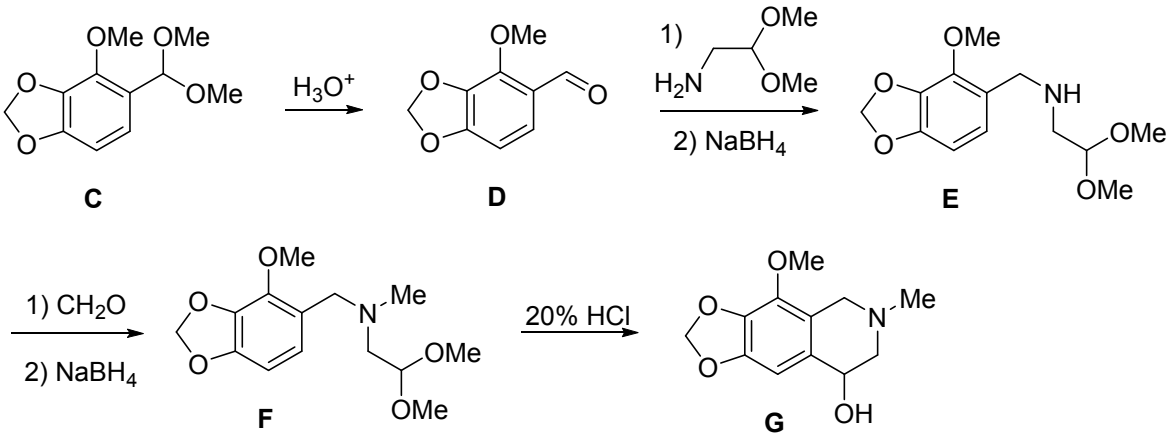
SOLUTION OF PREPARATORY PROBLEM 20

20.1 The analysis of the given scheme allows one to conclude that the **A**-to-**B** transformation is the iodination of **A** and the **B**-to-**C** transformation is the substitution of the iodine atom by methoxy group as compound **C** contains no iodine. The regiochemistry of iodination can be unambiguously deduced from the structure of (±)-α-noscapine (its upper fragment). Comparison of molecular formula of **C** and structure of initial compound leads to conclusion that the first step of the

compound **A** formation is the aldehyde group ketalization. Therefore, we can write the structural formulae of **A-C**.

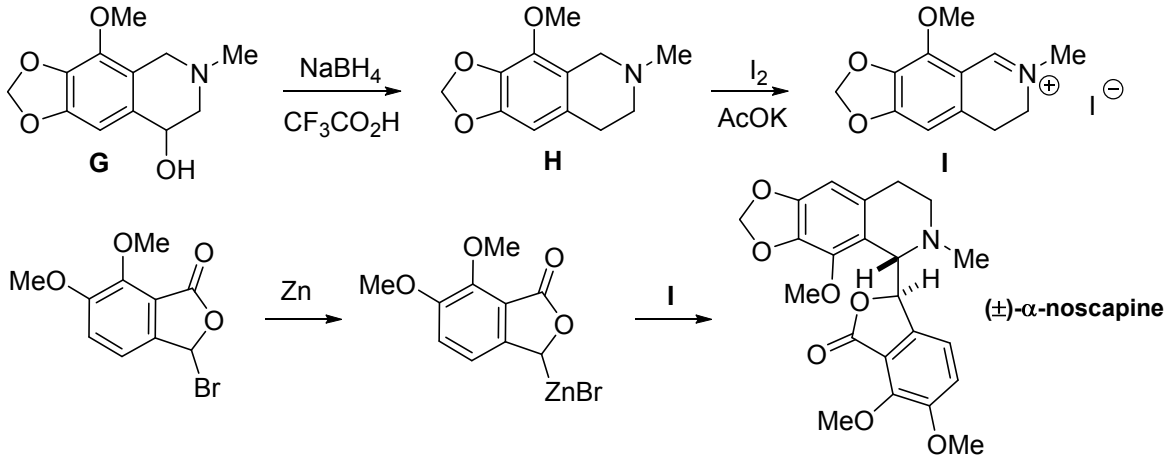


The acid hydrolysis of the compound **C** recovers the aldehyde function which reacts with amine affording the corresponding imine, the reduction of which with $NaBH_4$ produces the secondary amine **E**. The repetition of the reductive alkylation of amine with aldehyde furnishes the tertiary amine **F**. The hydrolysis of the ketal functionality in **F** yields the corresponding aldehyde molecular formula of which fulfils conditions. However, in the problem it is stated that **G** is tricyclic compound. It is possible if acid induces aldehyde attack of the proximal aromatic ring leading to 4-hydroxy-tetrahydroisoquinoline derivative **G**.



Analysis of the molecular formulae of **G** and **I** shows that the transformation of **G** to **I** corresponds to the removal of hydroxy group and the introduction of iodine atom into the molecule. The structure of (±)-α-noscapine demonstrates clearly that **I** reacts with bromophthalide by the C(1) atom of the isoquinoline fragment. We can conclude that the **G**-to-**H** step is the ionic reduction of the benzyl alcohol moiety to CH_2 group (the protonation of alcohol produces benzyl cation reaction of which with $NaBH_4$ yields CH_2 fragment) and the **H**-to-**I** step is the iodination of C(1) atom of isoquinoline core. It is known that α-iodoalkylamines exist as ionic compounds. In other words, the better presentation of the compound **I** is the corresponding salt but

structural formula with covalent C-I bond is also considered as a right answer. The last step is the C-C bond formation producing the target (±)-α-noscapine.

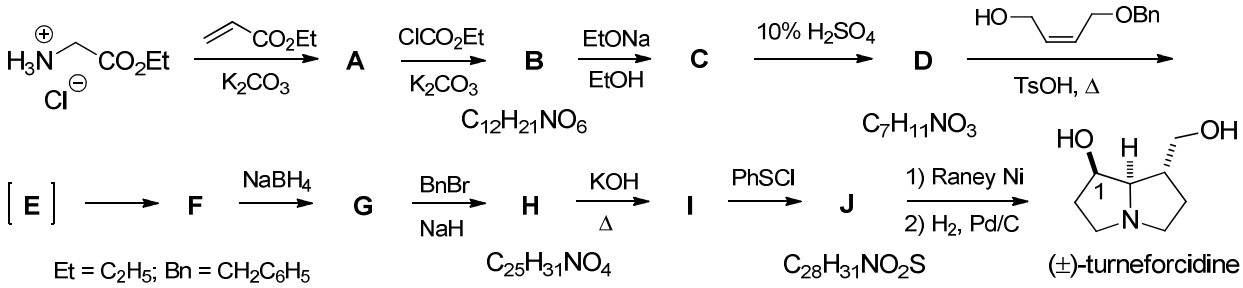


THEORETICAL PROBLEM 21

Pyrrolizidine alkaloids

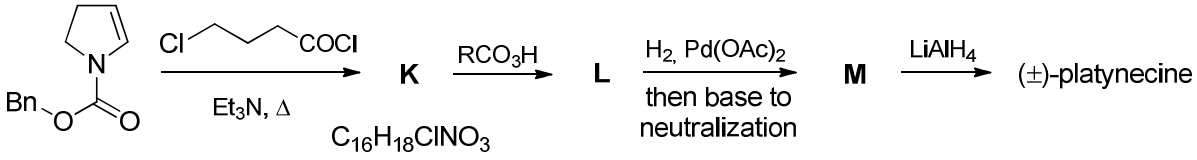
Pyrrolizidine alkaloids and their unnatural analogues occupy the important place in organic chemistry due to a broad variety of physiological activities. Polyhydroxylated pyrrolizidines form a sub-class of these alkaloids, members of which are often referred to as aza-sugars (or imino sugars) and inhibit various glycosidases that can be useful for the treatment of diabetes, influenza, HIV and other diseases. The synthesis of dihydroxypyrrolizidine alkaloid, (±)-turneforcidine, is given in the Scheme 1. In this scheme **E** is an unstable intermediate which spontaneously undergoes the Claisen rearrangement producing **F**.

Scheme 1



Epimer of turneforcidine at C(7) atom, (±)-platynecine, was synthesized by the reaction sequence given in Scheme 2. It is noteworthing that **K** is the product of [2+2]-cycloaddition.

Scheme 2



21.1 Decipher these schemes. Write down the structural formulae of compounds **A** – **M** as well as of (±)-platynecine.

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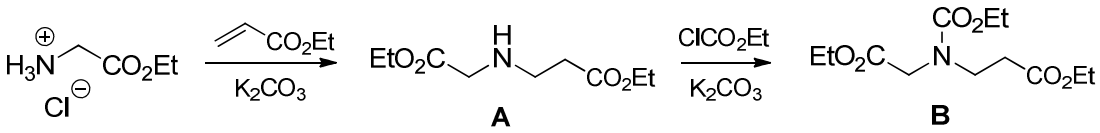
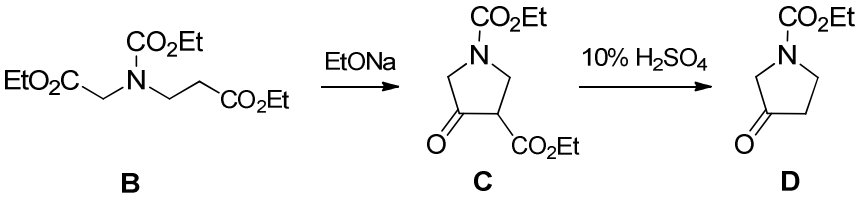
SOLUTION OF PREPARATORY PROBLEM 21

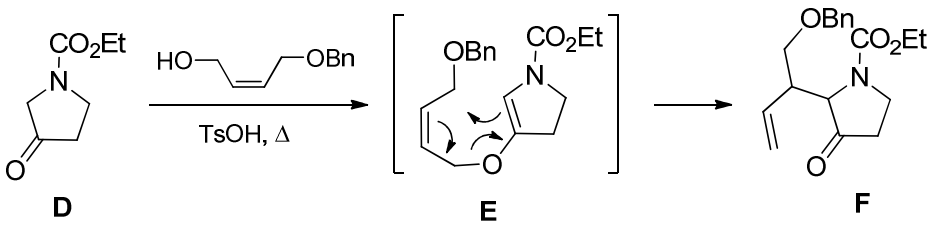
21.1 The molecular formula of compound **B** is a sum of molecular formulae of three reactants without 2 HCl. It is possible to conclude that **A** is the product of addition of ethyl ester of glycine to ethyl acrylate, and **B** is the product of acylation of **A** with ethyl chloroformate.



During next two steps molecule of **B** lost 5 carbon atoms, 10 hydrogen atoms and 3 oxygen atoms. It corresponds to the removal of ethoxy group, ethyl group and CO_2 molecule. The transformation of **B** to **C** is induced by EtONa. It is possible to suppose that this step is the intramolecular Claisen condensation furnishing 3-oxopyrrolidine-4-carboxylic acid (removal of ethanol). Its treatment with 10% sulfuric acid leads to hydrolysis of ester group (but not the less reactive carbamate) and decarboxylation. This supposition is consistent with the demand of synthesis of pyrrolizidine alkaloid consisting of two five-membered rings.

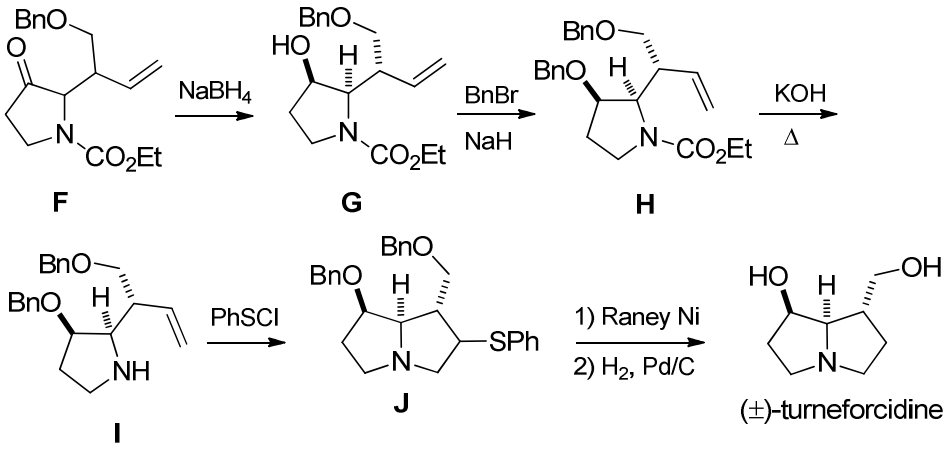


The intermediate **E** undergoes Claisen rearrangement, *i.e.*, it contains the fragment of allyl vinyl ether. This fragment can be prepared from the allyl alcohol and the ketone by the acid-catalyzed attack of the alcohol onto the carbonyl carbon affording an enol ether. The Claisen rearrangement produces pyrrolidone containing the substituted allyl group connected to C(2) or C(4) atom (depending on the regiochemistry of the enol moiety formation). Even we do not know that the enolization with the participation of C(2) atom is more preferable, we can conclude that the allyl group is connected with the C(2) atom from the necessity to prepare pyrrolizidine scaffold. It will be impossible (using the transformations given in the Scheme 1) if the allyl group is connected with the C(4) atom.



D **E** **F**

The reduction of ketone group with $NaBH_4$ produces the corresponding alcohol, alkylation of which with benzyl bromide gives rise to **H**. Its molecular formula coincides with the formula given in the Problem. Next step is the hydrolysis of carbamate (otherwise, it is impossible to form the second five-membered ring). Attack of electrophilic phenylsulfanyl chloride on the C=C bond is accompanied by the nucleophilic attack of the pyrrolidine nitrogen on the formed sulfonium ion furnishing pyrrolizidine system. The removal of the phenylsulfanyl group and the hydrogenolysis of Bn-O bonds accomplish the synthesis of (±)-turneforcidine. The relative stereochemistry of all stereocenters can be unambiguously deduced from the given stereochemistry for (±)-turneforcidine.



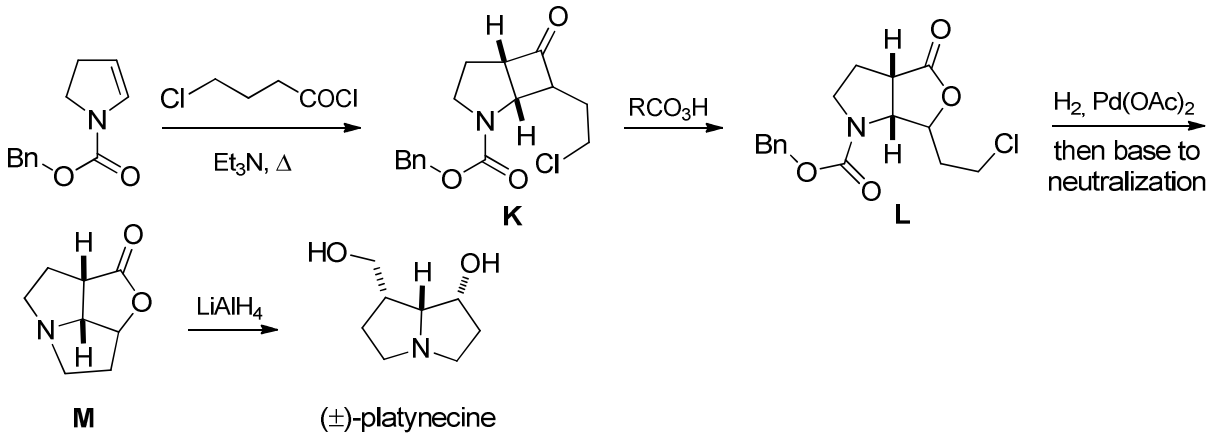
F **G** **H**

I **J** (±)-turneforcidine

The analysis of the scheme 2 shows that molecular formula of **K** is a sum of molecular formulae of reacting compounds without HCl. **K** is the product of [2+2]-cycloaddition. Evidently, the C=C bond of the pyrroline is involved in this process. The second partner (4-chlorobutyroyl chloride) has C=O bond. However, isomeric products of two possible [2+2]-cycloadditions between these moieties fail to form pyrrolizidine framework. However, elimination of HCl from acyl chloride can produce ketene which is able to form [2+2]-cycloadduct with pyrroline. Accounting for further

formation of the pyrrolizidine scaffold, the regiochemistry of the cycloaddition is unambiguous.

The transformation of **L** to **M** is the hydrogenolysis of the Bn–O bond followed by CO_2 elimination from the formed carbamic acid. During this step the NH moiety is formed. As the last step of the platynecine synthesis is the reduction, the NH moiety should cyclize affording pyrrolizidine immediately after formation. Platynecine is a diastereomer of turneforcidine, *i.e.*, platynecine contains the same substituents. This allows for concluding that the last step is the reduction of ester function producing two alcohols. In other words, the transformation of **K** to **L** is the oxidation of cyclobutanone fragment to the corresponding lactone. This reaction is known as the Baeyer-Villiger oxidation.



THEORETICAL PROBLEM 22

Delightful odor of truffle

For many people the taste and odor of truffles are so delightful that truffles cost more than their weight in gold. The compound **X** is responsible for the divine smell of the black truffle. The treatment of 0.108 g of compound **X** with the acidified solution of $HgSO_4$ leads to the formation of some precipitate **Z**. The treatment of the formed organic compound **A** with the excess of $[Ag(NH_3)_2]OH$ afforded 0.432 g of metallic silver. Gas formed as a result of the burning of 0.648 g of compound **X** was divided into two equal parts. One part was passed through the $Ba(OH)_2$ solution, 3.075 g of precipitate was formed. Another part was passed through NaOH solution. After some time the excess of $BaCl_2$ solution was added. It led to the formation of 3.171 g of precipitate.

22.1 Write down the structural formulae of compounds **X**, **Z**, **A**. Determine the weight of the precipitate **Z.** Assume that all reactions proceed with 100% yield.

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SOLUTION OF PREPARATORY PROBLEM 22

22.1 The difference between the weights of precipitates formed after direct reaction of gas with $Ba(OH)_2$ and ad a result of stepwise procedure (NaOH, after some time – $BaCl_2$) can be explained only by the presence of SO_2 in the gas mixture. Direct reaction with $Ba(OH)_2$ leads to formation of $BaCO_3$ and $BaSO_3$. When gas mixture was passed through NaOH solution, Na_2CO_3 and Na_2SO_3 were formed. Sodium sulfite is oxidized with time by oxygen from the air. So, the addition of $BaCl_2$ leads to the precipitation of $BaCO_3$ and $BaSO_4$. Therefore, (3.171 – 3.075) = 0.096 g corresponds to the 6 mmol of additional oxygen atoms, *i.e.* 6 × 2 = 12 mmol of SO_2 was present in the gas mixture. The first precipitate contains 1.773 g (9 mmol) of $BaCO_3$ and 1.302 g (6 mmol) of $BaSO_3$. The second precipitate is formed by 1.773 g of $BaCO_3$ and 1.398 g of $BaSO_4$. Therefore, 0.648 g of compound **X** contains 0.216 g (18 mmol) of carbon, 0.384 g (12 mmol) of sulfur and 0.648 – 0.216 – 0.384

= 0.048 g (48 mmol) of hydrogen. The brutto-formula of **X** is $C_3H_8S_2$. It is also the only possible molecular formula.

Formation of 0.432 g (4 mmol) of metallic silver shows that 2 mmol of aldehyde participated in the reaction. It corresponds to 1 mmol of CH_2O (compound **A**).

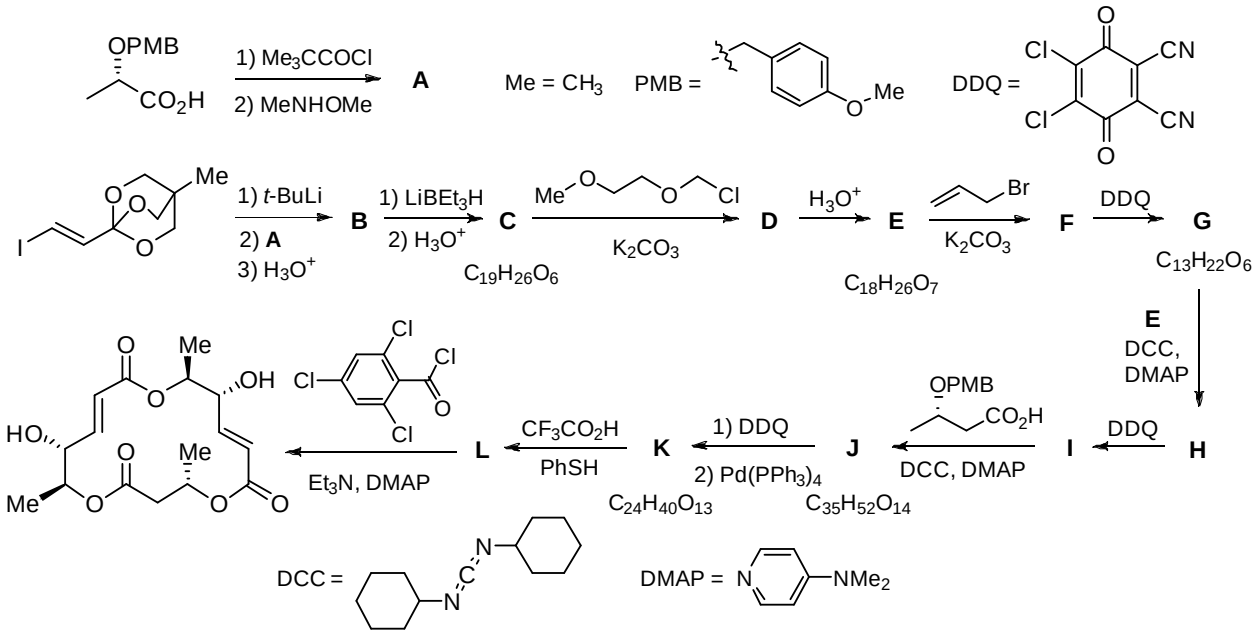
$$CH_2O + 4\ Ag(NH_3)_2OH = (NH_4)_2CO_3 + 4\ Ag + 6\ NH_3 + 2\ H_2O.$$

As a result, it is possible to conclude that compound **X** is bis(methylsulfanyl)-methane; thioketal of formaldehyde, $CH_3SCH_2SCH_3$. It is stable to acid hydrolysis but in the presence of Hg^{2+} salts it forms $Hg(SCH_3)_2$ (compound **Z**) and formaldehyde. 1 mmol of $Hg(SCH_3)_2$ is formed from 1 mmol of compound **X**. Molecular weight of this compound is 294.6. Therefore, weight of the precipitate **Z** is 294.6 mg (294 mg and 295 mg are also considered as right answers).

THEORETICAL PROBLEM 23

Synthesis of large rings. The magic or routine work?

The synthesis of large rings is a challenging problem of the synthetic organic chemistry. On the contrary, Nature solves this problem efficiently. Thus, various fungus produce macrolactone polyketides. One of them, Macrosphelide A, attracts attention as potent, orally bioavailable inhibitor of the interaction between cancer and endothelial cells. A number of syntheses of this molecule was reported. One of them was based on the utilization of lactic (2-hydroxypropionic) acid derivative according to Scheme below.



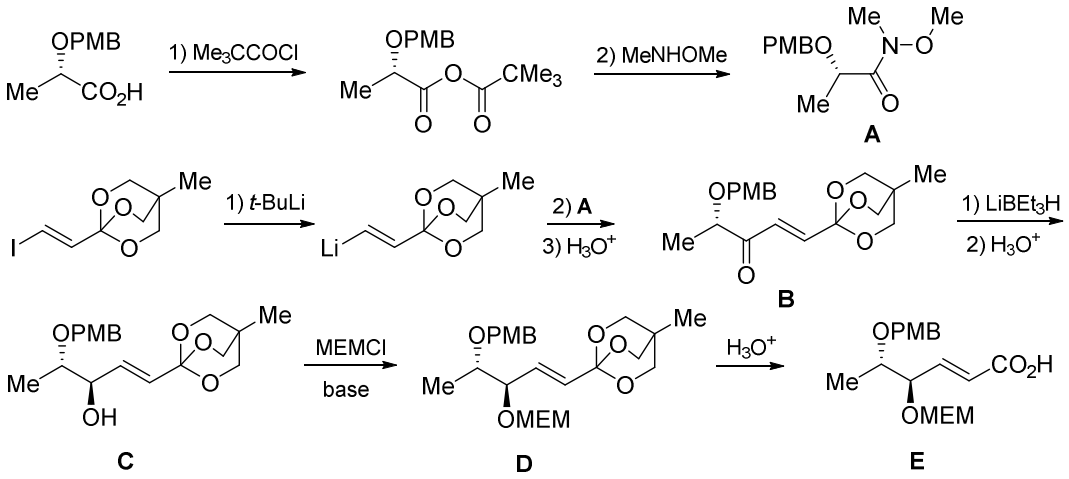
23.1 Decipher this scheme. Write down the structural formulae of compounds **A** - **L**.

23.2 Write down the IUPAC name of compound **E**.

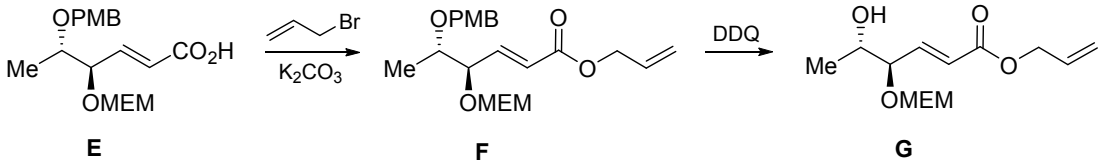
SOLUTION OF PREPARATORY PROBLEM 23

23.1 Macrospherolide A consists of two fragments of 4,5-dihydroxyhex-2-enoic acid. Molecule **E** participates twice during the synthesis of the final product. It is possible to conclude that **E** is some protected derivative of the above acid. Moreover, we can

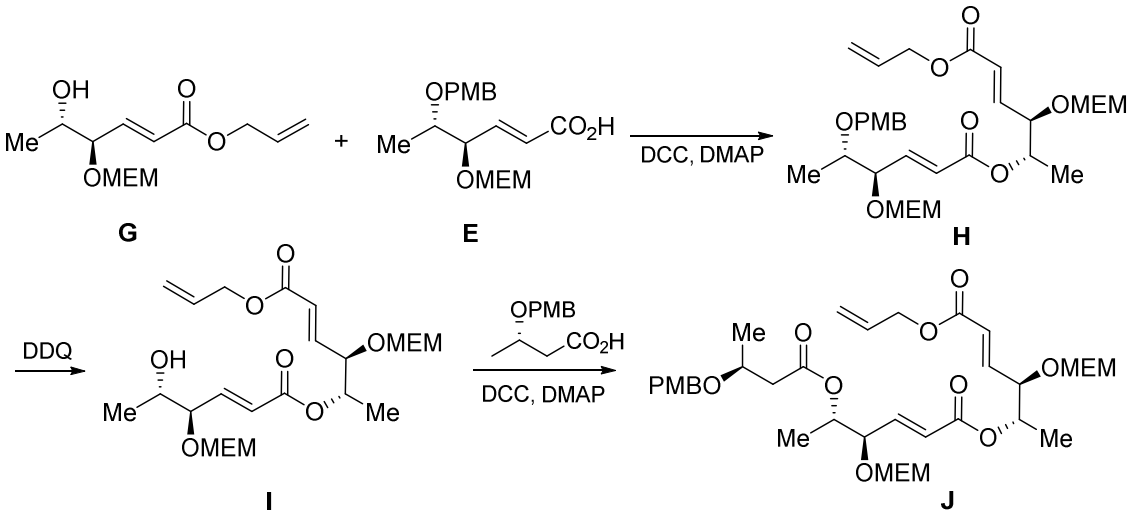
suppose that 2-(*p*-methoxybenzyloxy)propionic acid (its molecular formula is $C_{11}H_{14}O_4$) is the source of $CH_3CH(OH)CH(OH)$-fragment in **E**; another starting compound – *ortho*-ester with molecular formula $C_8H_{11}IO_3$ – provides the CH=CHC(O)-X fragment for the **E** formation. The analysis of molecular formulae of compounds **C** and **E** shows that **C**-to-**E** transformation proceeds with the loss of 1 carbon atom but with the introduction of 1 additional oxygen atom. During the alkylation of **C** with alkyl chloride we introduce 2-methoxyethoxymethyl substituent instead of H atom, *i.e.*, we add $C_4H_8O_2$. Therefore, at **D-**to**-E** step the molecule lost C_5H_8O. It is a step of the *ortho*-ester hydrolysis. In turn, **C**, obtained by the reduction of compound **B**, has 1 hydrogen atom more but 1 oxygen atom and 1 iodine atom less than two initial compounds together. Accounting for the presence of the dihydroxyalkenyl fragment in **E** we can conclude that **B**-to-**C** transformation is the reduction of the ketone fragment to the corresponding alcohol. Therefore, **B** is a product of condensation of the starting molecules affording *ortho*-ester of protected 5-hydroxy-4-oxohex-2-enoic acid. In other words, one can write the structure of **B** without knowledge of reactions used for the **B** synthesis. These reactions are the preparation of PMB-protected lactic acid amide (*via* intermediate formation of the mixed anhydride) and the attack of alkenyllithium, generated from alkenyl iodide by treatment with *t*-BuLi, onto this amide. This method of ketones synthesis was proposed by Weinreb and Nahm in 1981 (reactions of esters with RLi or RMgX fail to produce ketones in good yield as ketones are more reactive than starting esters; oppositely, Weinreb amides form stable chelates which decompose after aqueous treatment only). Finally, analysis of the structure of Macrosphelide A allows for concluding that the absolute configuration of chiral atom in starting lactic acid did not change during these reactions. It has (*S*)-configuration. The second stereocenter has (*R*)-configuration.



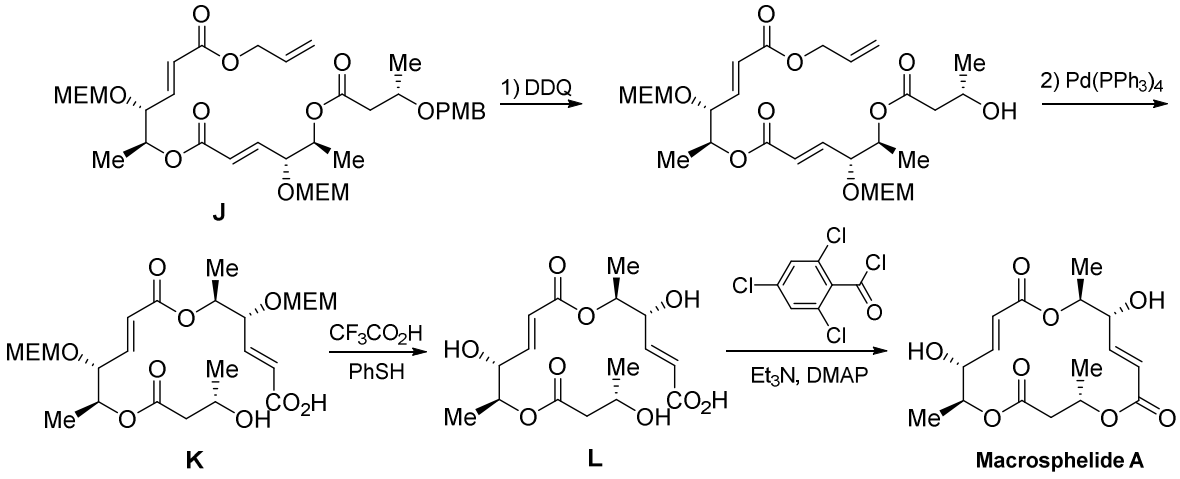
The reaction conditions for alkylation of **E** with allyl bromide show that it is the formation of ester but not the Friedel-Crafts alkylation of the activated benzene ring. Therefore, **F** is the allyl ester of the acid **E**. The comparison of its molecular formula ($C_{21}H_{30}O_7$) with that for **G** ($C_{13}H_{22}O_6$) shows that the **F**-to-**G** transformation proceeds with the loss of 8 carbon atoms, 8 hydrogen atoms and 1 oxygen atom. Accounting for the structure of **F**, we can conclude that this step is the removal of 4-methoxybenzyl group (its substitution by hydrogen atom).



The next step is the reaction of **G** with **E**. The molecule of **G** has hydroxy group; the molecule of **E** has unprotected carboxylic acid function. Macrospherolide **A** has the fragment of the corresponding ester (without protecting groups). Even if one does not know utilization of the given coupling agents, he can conclude that this step is the ester formation. Moreover, the comparison of molecular formulae confirms this supposition. The formation of the ester from **G** and **E** produces compound **H** with molecular formula of $C_{31}H_{46}O_{12}$. The treatment of **H** with DDQ leads to the removal of 4-methoxybenzyl group affording a free hydroxyl group (see above). Condensation of the alcohol **I** with 3-(*p*-methoxybenzyloxy)butyric acid produces the ester **J** with molecular formula of $C_{35}H_{52}O_{14}$ ($C_{23}H_{38}O_{11} + C_{12}H_{16}O_4 - H_2O$). This formula coincides with the formula given in the Problem.



Transformation of **J** to **K** is accompanied by the loss of 11 carbon atoms, 12 hydrogen atoms and 1 oxygen atom. The first step is the removal of 4-methoxybenzyl group (the same reagent as above). Therefore, the second step is the removal of C_3H_4 fragment. Analysis of structure of **J** shows that it is the removal of allyl group (its substitution by hydrogen atom; a common hydrolysis is inappropriate in this case due to the presence of other ester fragments). Synthesis of Macrospherolide A was accomplished by the removal of methoxyethoxymethyl protecting groups in **K** furnishing **L** which undergoes the Yamaguchi reagent-induced cyclization. Again, the knowledge of these reactions is not required to make these conclusions.



23.2 The IUPAC name of compound **E** is

(*E*,4*R*,5*S*)-5-(4-methoxybenzyloxy)-4-(2-methoxyethoxymethoxy)hex-2-enoic acid.

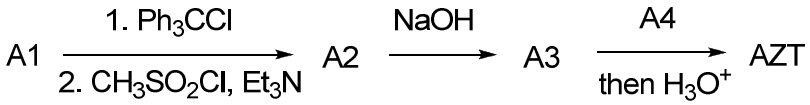
THEORETICAL PROBLEM 24

What Time is it in Baku or Cheating the Death

One looking at the puddle, sees in her dirt, and another – reflected in her star

Immanuel Kant

People use acronyms for convenience sake. Still, sometimes the meanings are not absolutely unambiguous. Thus, AZT generally standing for "Azerbaijan time" has acquired an alternative meaning in pharmacology denoting one of the most usable anti-HIV drugs. Nucleoside **A1**, a major component of nucleic acids, was used as a starting material in AZT synthesis. Under complete combustion with subsequent condensation of water **A1** gives a gas undergoing an 11-fold volume decrease when bubbled through the 1 M KOH solution.



24.1 What are the building blocks of nucleosides?

24.2 Deduce the structures of **A1** to **A4**. Note that:

- when arranged in any order the numbers of atoms in **A1** are not described by either arithmetic or geometric progression,
- all the synthetic steps are S_N-type reactions,
- **A4** is a binary compound (85.8 % N by mass),
- O is the heaviest element in both **A3** and **AZT**.

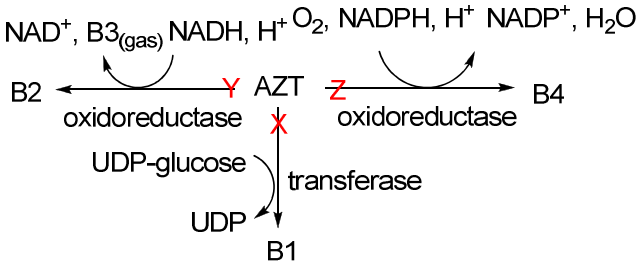
24.3 How many stereoisomers of **AZT** do exist?

24.4 Give the full wording for the pharmaceutical **AZT** acronym.

24.5 Propose the mechanism of **AZT** antiviral action.

Metabolism of **AZT** is diverse and includes several pathways (X, Y, and Z) shown in the hereunder scheme (all balanced equations). X, the major of these, leads to a higher soluble product **B1** excreted with urine. Y provides the cytotoxic product **B2** with the same

number of atoms as that in **AZT**. Z is found in patients infected with a specific bacteria, the product **B4** retaining the **AZT**-type activity.



24.6 Draw the structures of **B1**-**B4**.

"Dallas Buyers Club", a movie from 2013, received numerous awards including three Oscars. It is based on a true story describing ambiguous results of the first clinical **AZT** trials. The protagonist suffering from AIDS lacks a positive effect from **AZT** and switches over to drugs unauthorized by US FDA. One of the latter is based on the substance **D**.

D (51.17 % of C by weight) and nucleoside **N** (a major component of nucleic acids; 47.57 % of C by weight) differ by one atom only. Under complete combustion with subsequent condensation of water, the mixture of **D** and **N** of any composition gives gaseous products undergoing a 7-fold decrease of their total volume when bubbled through the 1 M KOH solution. It was found that **D** imitates AZT with respect to the mechanism of its action.

24.7 Calculate the number of C and N atoms in **D** without deciphering its structure.

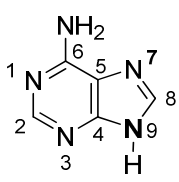
24.8 Draw the structures of **D** and **N**.

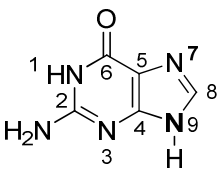
24.9 Do you support the “Dallas Buyers Club” principal character in his belief that **D** possesses a major clinical advantage over AZT? Comment why physicians used to administer AZT and **D** in a combination.

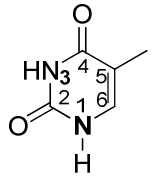
The compound **D** turns out to be a prodrug. Its active metabolite **M** (17.23 % P and 35.62 % O by mass) is produced by a number of manufacturers for research (non-clinical) purposes only.

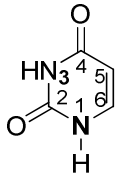
24.10 Draw the structure of **M**.

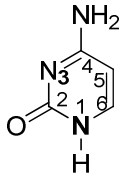
Note: *If you feel like watching the above movie, check the film rating system accepted in your country.*

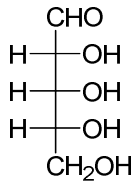

adenine


guanine


thymine


uracil


cytosine


D-ribose

SOLUTION OF PREPARATORY PROBLEM 24

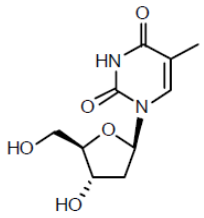
24.1 Nucleosides are glycosylamines with a nucleic acid base linked to a suitable sugar.

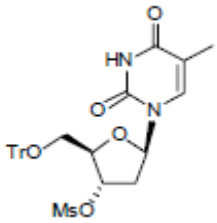
24.2 Since the wanted nucleoside is a major component of nucleic acids, all combinations with ribose or deoxyribose linked via glycosidic bond to one of the five common nitrogenous bases are to be considered. In any case, **A1** is composed of atoms of four elements, thus the combustion equation can be written as:

$$C_xH_yN_zO_t + (2x+y/2–t)/2\ O_2 = x\ CO_2 + y/2\ H_2O + z/2\ N_2$$

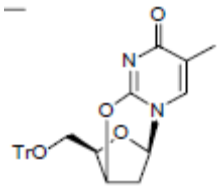
An 11-fold reduction of the gas amount when being passed through the alkali is due to absorption of carbon dioxide. Hence, $CO_2 : N_2 = 10 : 1$ or $C : N = x : z = 5 : 1$. This result excludes purine bases from further consideration. Both sugars (ribose and deoxyribose) contain 5 carbon atoms each. Thus, the nucleic base should also contain 5 carbon atoms to meet the integer relationship, and Thymine is the only option. The choice between deoxythymidine ($C_{10}H_{14}N_2O_5$) and methyluridine ($C_{10}H_{14}N_2O_6$) is decided in favor of the former, as no progression of the number of atoms in the molecule is possible. **A4** includes a light element. If one represents its composition as M_aN_b, then $0.858 = \frac{14.0 \times b}{M \times a + 14.0 \times b}$, and $M = \frac{2.32 \times b}{a}$ g mol^{-1}. LiN_3 is the only possible solution.

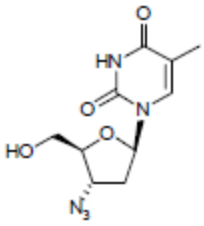
Note that the synthesis is a sequence of nucleophilic substitution steps. Deoxythymidine (**A1**) is transformed into **A2** (do not ignore the relative ease of substitution



is transformed into 

A2, (do not ignore the relative ease of substitution). **A3** is free of sulfur, which manifests in favor of intramolecular cyclization



. AZT synthesis is completed by 

AZT the azide formation and deprotection.

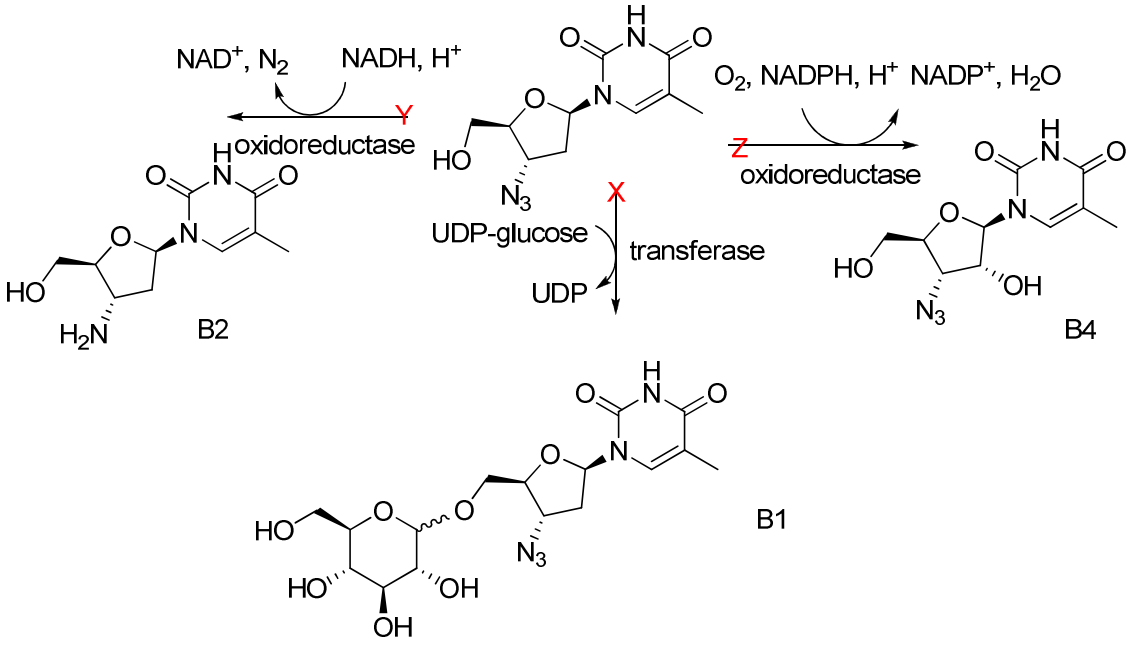
24.3 AZT molecule having 3 stereocenters, 8 isomers are theoretically possible.

24.4 AZT is used to denote azidothymidine. (International Nonproprietary Name – zidovudine.)

24.5 In the infected cells, DNA is actively produced on the virus RNA used as matrix. AZT inhibits the key enzyme of this process, HIV reverse transcriptase. The mechanism of termination of the DNA elongation is as follows. AZT, being a structural analogue of thymidine, is enzymatically converted to the corresponding 5`-triphosphate at the first stage. The latter is erroneously incorporated into the growing nucleic acid chain leading to termination due to the absence of a hydroxyl group in the 3`-position.

24.6 The pathway X is a conjugation with glucose, a classical way of xenobiotic hydrophilization for its subsequent excretion with urine or bile. Counting the number of atoms allows deciphering the pathway Y. **B3** turns out to be a diatomic gas, thus

suggesting reduction of the azide to the amine. Finally, the pathway Z is a mono-oxygenase reaction. Since the product retains its biological activity, the nitrous moiety important for the enzyme recognition is not affected. Thus, the product is a ribose derivative:



24.7 The absence of variations in volume ratio of the combustion gases before and after the absorption by the alkali solution with that of compounds **D** and **N** unambiguously indicates that the numbers of C and N atoms in these compounds are the same. The number of H atoms may differ in such compounds by an even value only. Hence, molecules of **D** and **N** differ by one oxygen atom, with **D** having notoriously less. From the equation (x – the number of C atoms):

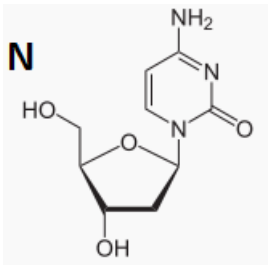
$$x\left(\frac{12.01\times 100}{47.57}-\frac{12.01\times 100}{51.17}\right)=16.00$$

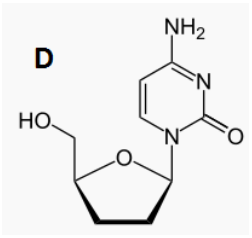
one finds x = 9. Using the trategy applied in i. 2, the number of nitrogens (z) in **D** is:

$$\frac{9+0.5\,z}{0.5\,z}=7,\ \text{hence}\ z=3\,.$$

24.8 The above results (9 carbon and 3 nitrogen atoms) allow establishing the nucleoside **N**. Only cytidine and deoxycytidine out of the nucleosides formed by the primary bases are in correlation the requirement. The given mass percent of carbon allows final assignment in favor of deoxycytidine. **D** has one oxygen atom less. Out of the four oxygens present in **N**, removal of only the hydroxyl group at the 3'-carbon atom

can provides for the mechanism of antiviral action identical to that of AZT (**D** – 2′,3′-dideoxycytidine, or zalcitabine).





24.9 Despite AZT and zalcitabine (ddC) have identical mechanisms of action, their clinical effects can vary significantly. For example, AZT (as shown in i. 6) can be metabolized to a cytotoxic amine compound, whereas ddC, of course, not. This may cause the non-identical safety profiles of drugs as well as the difference in patients` tolerance due to adverse effects. Moreover, mutant variants of reverse transcriptase exhibit different specificities for non-identical substrates (AZT and ddC), which also affects the relative clinical efficiency. Thus, in some cases the appearance of AZT-resistant HIV strains is overcome by ddC administration, since the virus mutant strains retain sensitivity to the latter drug. Therefore it is no surprise that a combination (AZT + ddC) is applied in real clinical practice. Besides, the absence of any significant clinical benefit from taking AZT by the main character of the movie could be due to the combination of drugs with alcohol.

24.10 The presence of phosphorus in **M** together with the knowledge received in i. 5 allow us classifying this metabolite as a nucleotide with the molar ratio of phosphorus and oxygen:

$$n(\mathrm{P}) : n(\mathrm{O}) = \frac{17.23}{30.97} : \frac{35.62}{16.00} = 1:4$$

Any ddC based nucleotide should have the general formula $C_9H_{n+13}N_3O_{3n+3}P_n$. Hence, the value of n is: $\frac{3n+3}{n} = 4$, so $n = 3$. The molar mass of **M** is equal to 539.2 g mol^{-1}, which is much higher than that of $C_9H_{16}N_3O_{12}P_3$ (451.2 g mol^{-1}). Considering **M** is a salt helps overcoming the contradiction. Then it contains a cation with the molar mass of:

$$A_r(\text{cation}) = \frac{539.2 + 4\times1.008 - 451.2}{4} = 23.01 \approx 23 \text{ a.m.u.}$$

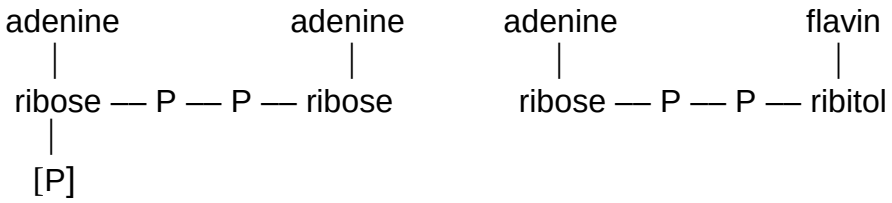
Hence **M** is tetrasodium ddC-triphosphate. Of course, in some cells (e.g., CD4-lymphocytes) mono-, di-, and trianionic ddC-triphosphates will be found at physiological pH values alongside with **M** (sometimes even in larger quantities). Also, high intracellular concentration of potassium ions compared to that sodium ions further extends the range of possible nucleotide salts. However, the chemical industry manufactures tetrasodium ddC-triphosphate for research objectives.

THEORETICAL PROBLEM 25

Number One Enzyme

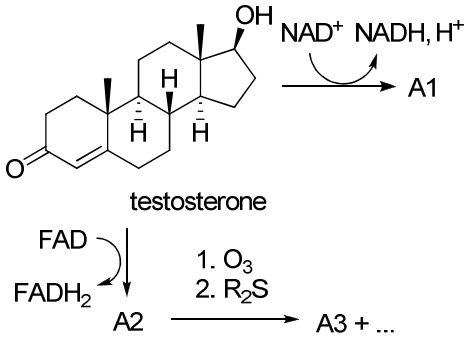
Enzymes rule over in biochemical processes. Enzyme Commission (EC) numbers have been proposed in order not to be lost in the vast variety of biocatalysts. This is a four-level classification based on the types of enzymatic reactions, each specific reaction being described by four numbers separated by periods. Number 1 of 6 top-level EC numbers is attributed to oxidoreductases, enzymes catalyzing oxidation/reduction reactions (transfer of H and O atoms or electrons from one substance to another). These reactions are of a great importance for both energy transformation and xenobiotic metabolism.

Changes of the oxidation state of a molecule can be achieved in different ways, which makes possible a more detailed classification of oxidoreductases. Many of these require a cofactor or coenzyme. Thus, *dehydrogenases* remove two hydrogen atoms from an organic substrate and pass them over to a suitable acceptor like nicotinamide adenine dinucleotide {phosphate} (NAD^+ {$NADP^+$}) or flavin adenine dinucleotide (FAD).



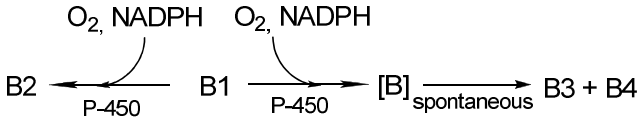
25.1 Write down the equation of ethanol oxidation involving NAD^+ as the coenzyme. Show the changes in the nicotinamide moiety.

25.2 Sometimes the route of dehydrogenase reaction is determined by the coenzyme/cofactor involved. Predict the structures of **A1**–**A3** in the following scheme if it is known that 1.00 g of **A3** gives 7.52 g of silver precipitate under Tollens` reagent treatment.



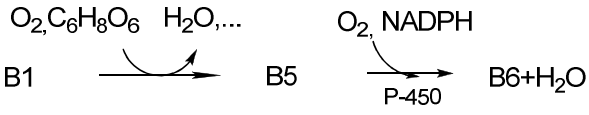
Oxygenases catalyze direct addition of oxygen atoms originating from O_2 to an organic substrate. These enzymes are further subdivided into *mono*- and *di-oxygenases* depending on the number of incorporated atoms (one and two, respectively). In the case of monooxygenases the other oxygen atom is reduced to water by an appropriate reactant. Cytochrome P-450-dependent monooxygenase is an exceptionally important representative of the class.

An aromatic compound **B1** contains 77.75 % C and 14.80 % O by mass. **B1** metabolism in rat liver microsomes develops in two ways (see on the hereunder scheme). **B2** reveals 4 signals in ^{1}H-NMR spectrum. **B2** and **B3** undergo color changes when added to 1% $FeCl_3$ solution, whereas the **B1** color is unaffected by such treatment. All of **B1** to **B4** are composed of the same elements. **B4** is a gas under STP.



25.3 Decipher **B1** to **B4**. Write down the balanced equations.

Under oxygen deficiency **B1** partially converts into **B5**, an isomer of **B2**. This transformation requires a vitamin as the oxygen acceptor. Further oxidation of **B5** leads to **B6** characterized by 2 signals in ^{1}H-NMR spectrum.



25.4 Draw the structures of **B5** and **B6** as well as of both forms of the vitamin.

Like dehydrogenases, o*xidases* remove hydrogen atoms from an organic substrate transferring these either to the molecular oxygen or **X**, which finally results in water formation in both cases. The phenol oxidation can be described by the following equation:

$$2\ \text{Phenol} + \mathbf{X} = \mathbf{Y} + 2\ H_2O$$

The reaction develops *via* a free radical intermediate and leads to a mixture of isomers of **Y** (77.4 % C by mass).

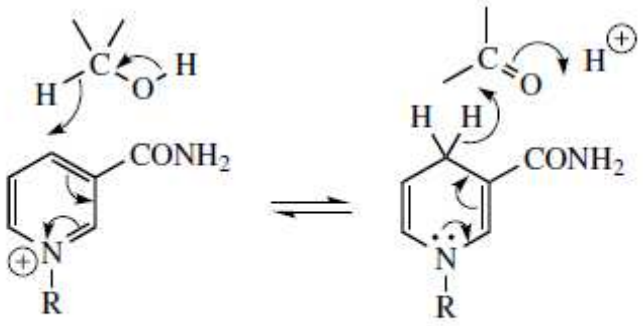
25.5 Decipher **X**. Draw the isomers of **Y** that show a sole peak in the phenolic region of ^{1}H-NMR spectra at low temperatures.

_____

SOLUTION OF PREPARATORY PROBLEM 25

25.1 Reaction: $CH_3CH_2OH + NAD^+ = CH_3CHO + NADH + H^+$.

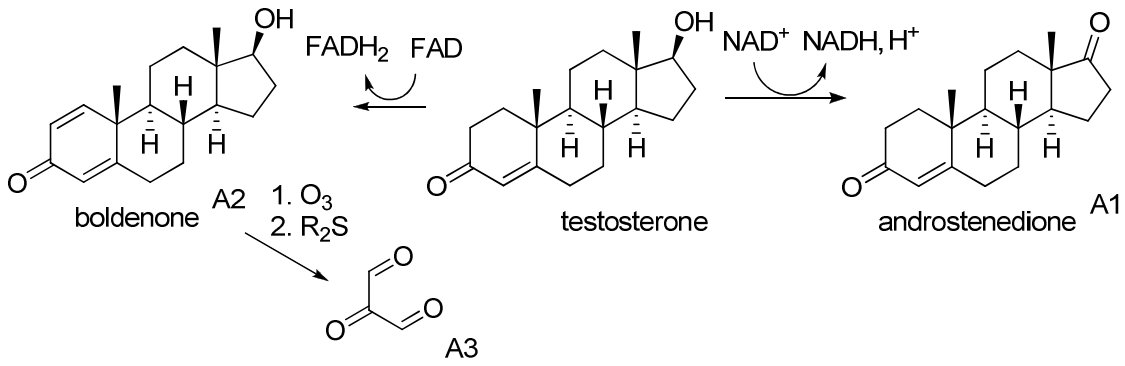
Only nicotinamide moiety of the coenzyme is affected as a result of the reaction:



NAD$^+$ NADP$^+$ NADH NADPH

25.2 Both enzymatic steps are oxidation (dehydrogenation) reactions. Generally, coenzymes reveal a “specialization”. Thus, the NAD-system is involved in dehydrogenation of polar bonds (discussed above with ethanol as an example), whereas the FAD-system in that of nonpolar bonds. Therefore, it is necessary to decide on the **A3** nature. Its equivalent in the silver mirror reaction is

$\frac{1.00}{7.52} \times 107.9 = 14.3$ g mol^{-1}. Usually oxidation of an aldehyde group provides 2 electrons. Then such a small equivalent can correspond to low molecular weight fragment only. Analyzing cleavage options, one comes to the following scheme (note, that intermediates of **A3** oxidation are easily decarboxylated):



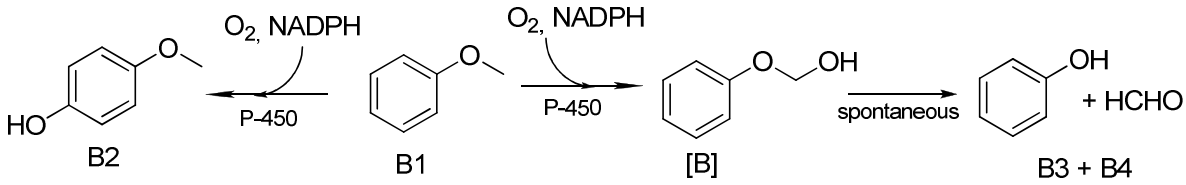
25.3 The rest of **B1** mass is attributed to hydrogen.

Then $C : H : O = \frac{77.75}{12.01} : \frac{100 - 77.75 - 14.80}{1.008} : \frac{14.80}{16.00} = 7 : 8 : 1.$

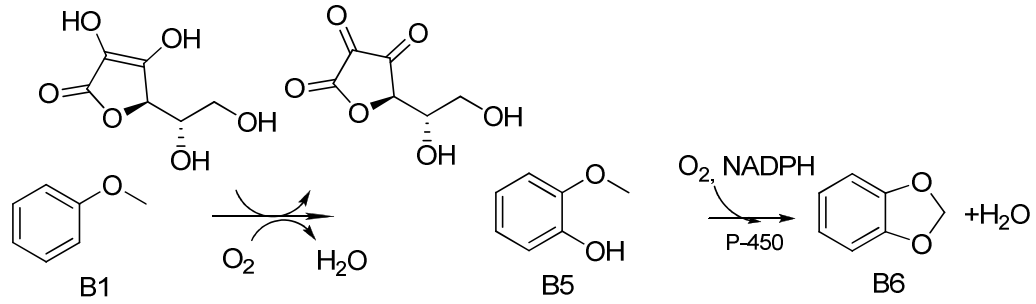
It is anisole (C_7H_8O) belonging to aromatics, still denying the probe for phenols. Monooxygenase reaction should lead to a product $C_7H_8O_2$, which, in turn, contains a phenolic hydroxyl. Among possible aromatic hydroxylation products, only 4-methoxyphenol (**B2**) contains the desired number of signals in the NMR spectrum. Intermediate **B** ($C_7H_8O_2$) spontaneously decomposes into the products of the same qualitative composition, which allows us identifying phenol (positive $FeCl_3$ test of **B3**) and formaldehyde (**B4** is a gas at STP). The overall equations for the two directions of the oxidative metabolism (do not forget, that the cofactor is an acceptor of the second oxygen atom) are:

$$C_7H_8O + O_2 + NADPH + H^+ = C_7H_8O_2 + NADP^+ + H_2O;$$

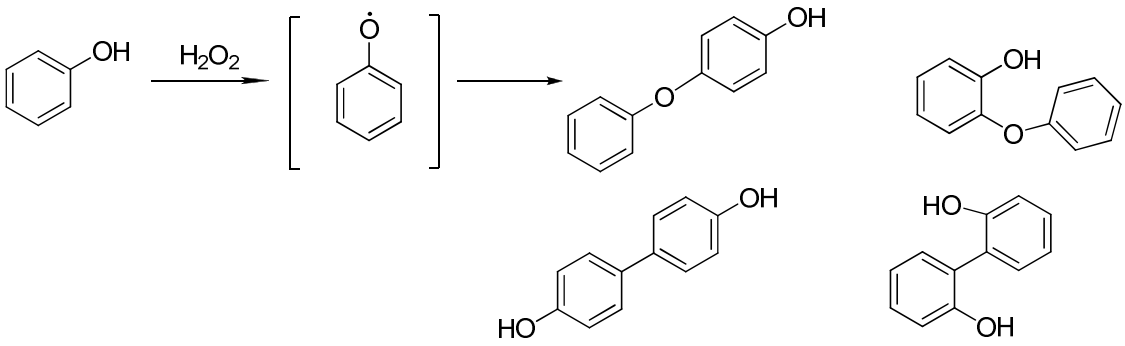
$$C_7H_8O + O_2 + NADPH + H^+ = C_6H_6O + CH_2O + NADP^+ + H_2O.$$



25.4 Careful consideration of the transformations allows us concluding that **B5** and **B6** have the composition of $C_7H_8O_2$ and $C_7H_6O_2$, respectively. So, **B5** can be either *meta*- or *ortho*- methoxyphenol. Opting for the latter is based on the high symmetry of the product **B6**, which can only be methylenedioxybenzene. Finally, ascorbic acid is the electron acceptor:



25.5 The reaction equation suggests that **Y** contains 12 carbon atoms with the molar mass of $\frac{12.01\times12}{0.774} = 186$ g mol^{-1}. With an account for the oxidative nature of the conversion, we get a unique meaningful solution for the equation in integers: **Y** = $C_{12}H_{10}O_2$. Checking the balance one finds that **X** = H_2O_2. So, it is a peroxidase reaction involving a phenolic free radical generation with the unpaired electron delocalized between the oxygen atom and the *ortho* / *para* ring positions. Accordingly, **Y** represents the dimer of such particles. Spectral data correspond to the following substances:



THEORETICAL PROBLEM 26

Holy War against Four Horsemen of the Apocalypse

For centuries the Caspian Sea is widely known for its oil fields. Nowadays it attracts ever increasing attention of researches as a treasury of biological resources, in particular, of algae which can be considered as virtually inexhaustible source of unique chemicals. These studies are in line with the global fight of Enlightened Humanity against the four Horsemen of the Apocalypse – Conquest, War, Famine, and Death.

Substances **X** and **Y** have been isolated from red algae *Asparagopsis armata*. These substances are rarely found in nature and belong to the same class of organic compounds. A sample of 1.000 g of **Y** was combusted in an excess of oxygen at high temperature followed by complete absorption of colorless gaseous (25°C, 1 atm) mixture of products with an excess of aqueous calcium hydroxide solution leading to 1.620 g of a white precipitate. Addition of the supernatant to an excess of silver nitrate solution provided 1.786 g of a colored precipitate.

It is also known that:

- cooling of **Y** combustion products from 150 down to 0°C does not result in any condensed phase;
- white precipitate is an individual compound;
- the molar masses of each of **X** and **Y** are less than 275 g mol^{-1};
- the number of atoms of any element in the molecules of **X** and **Y** does not exceed 3.

26.1 Without revealing the molecular formula, deduce which elements may be found in **Y**.

26.2 Without revealing the molecular formula of **Y**, write down the equation that includes numbers of atoms in the molecule as unknowns. Can this equation be of help in establishing the **Y** composition?

26.3 Determine the molecular formula of **Y** using all the data provided.

26.4 Will the substitution of silver nitrate by silver oxide in ammonia solution in the above experiment change the weight and color of the precipitate? To support the answer, calculate the solubility of AgBr ($K_s = 5.4 \cdot 10^{-13}$) in NH_3 solution (c = 1.0 mol dm^{-3} taking into account that the two first stepwise formation constants of silver-ammonia complexes are $10^{3.32}$ and $10^{3.92}$, respectively.

Subjecting 1.000 g of **X** to the described above analysis sequence results in a colored gaseous (250°C, 1 atm) mixture of products leading to 0.756 g of a white individual precipitate after passing the mixture through an excess of aqueous calcium hydroxide solution. Addition of silver nitrate solution to the supernatant also provides a colored precipitate.

It is known that molecules of **Y** and **X** differ by one element, **Y** having one atom more. **X** can exist as a mixture of enantiomers, whereas **Y** reveals geometric isomerism. Furthermore, **Y** reacts with 0.1 M aqueous KOH solution at room temperature.

26.5 Deduce the molecular formula and draw the structure of **X**.

26.6 Draw all possible geometric isomers of **Y**.

26.7 Based on theoretical considerations decide which of the Horsemen of the Apocalypse can be potentially defeated by **X** and **Y**?

Substance **Z** (41.00 % O by weight) belongs to the same class of compounds as **X** and **Y**. However, **Z** has been only detected in leaves of some plants, and never in algae. Combustion of a 1.000 g sample of **Z** in a large excess of oxygen followed by complete absorption of colorless gaseous (25°C, 1 atm) products with an excess of aqueous calcium hydroxide solution leads to 3.065 g of a white precipitate. By contrast, no precipitate formed when the supernatant from the previous test was added to an excess of silver oxide in ammonia solution.

It is also known that:

- one of the gaseous products of **Z** combustion has the density of 1.43 g dm^{-3} (measured at 34°C, 750 Torr);
- the number of atoms of any element in the molecule of **Z** does not exceed 3.

26.8 Find the molecular and structural formulae of **Z**.

Both **Z** and its sodium salt are highly toxic to all mammals.

26.9 Knowledge of the area of organisms producing **Z** as well as of its metabolic pathway in mammals can be considered as a weapon against some of the Horsemen of the Apocalypse. Comment which of these, in your mind.

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SOLUTION OF PREPARATORY PROBLEM 26

26.1 Since both **X** and **Y** are organic compounds, they contain carbon transformed into carbon dioxide under combustion in an excess of oxygen. CO_2 is then reacted with an excess of aqueous calcium hydroxide solution according to the equation:

$$Ca(OH)_2 + CO_2 \rightarrow CaCO_3\downarrow + H_2O$$

Thus, calcium carbonate is the white precipitate (individual compound). This eliminates from consideration a plenty of elements that might potentially be present in **Y**, including fluorine, chalcogens and phosphorus.

There is no nitrogen in **Y**, as soon as combustion products are absorbed completely by calcium hydroxide. Lack of condensation of any substance upon cooling of the combustion reaction products from 150 °C down to 0 °C strongly suggests that water is not one of these. In other words, all hydrogen atoms are bound to halogens (molecular hydrogen halides).

It is known that HF and HCl are readily formed under combustion of organic compounds. In the case of HBr there is an equilibrium ($4\ HBr + O_2 = 2\ Br_2 + 2\ H_2O$), that is strongly shifted towards hydrogen bromide formation at elevated temperatures, whereas HI is readily oxidized providing colored gaseous mixture and products condensation upon cooling.

Thereby, silver bromide is supposed to be the colored precipitate:

$$CaBr_2 + 2\ AgNO_3 \rightarrow 2\ AgBr\downarrow + Ca(NO_3)_2$$

Further evidence comes from the fact that algae is commonly known as on the splendid natural sources of bromine and iodine. The results of calculation are summarized below.

compound	$n(CaCO_3)$, mol	n(AgBr), mol	n(C) : n(Br)
Y	1.62×10^{-2}	9.51×10^{-3}	17 : 10

It can be seen that there is no reasonable solution if a colored precipitate is an individual compound (within the constraints of the molar mass and number of atoms given). Consequently, the colored precipitate is a mixture of salts. Also one should bear silver chloride in mind, as it would be colored in the case of co-precipitation with bromide. Furthermore, it is impossible to exclude the presence of oxygen in **Y**. So, **Y** can be composed of C, H, O, Cl and Br atoms.

26.2 The expression $k = l + m$ can be written for any fragment $H_k(Hal_1)_l(Hal_2)_m$. Regardless of the even/odd nature of l and m, the equation does not allow us limiting the range of values k, l and m.

However, $k \leq 3$, and thus $l + m \leq 3$. Remembering the molar mass upper limit, one gets three possible combinations with bromine: 1 Br + 1 Cl (1), 1 Br + 2 Cl (2), 2 Br + 1 Cl (3).

26.3 Thorough inspection of the above variants (you have enough time for this!) leads to the "right" ratio of the number of moles of halogen and carbon in the case (1) for **Y**.

For an equimolar mixture of AgBr and AgCl:

$187.77\,x + 143.32\,x = 1.786$

where x is the amount of each halogen.

Therefore $x = 5.394 \times 10^{-3}$ mol and the molar ratio C : Br : Cl = 3 : 1 : 1.

Thus, **Y** necessarily contains the C_3H_2BrCl fragment. Since the mass of the sample is known, one can calculate its molecular weight followed by the number of oxygen atoms in the molecule.

$$n(\mathrm{O}) = \frac{\dfrac{1.000}{5.394 \times 10^{-3}} - 12.01 \times 3 - 1.008 \times 2 - 79.90 - 35.45}{16.00} = 2$$

The molecular formula of **Y** is $C_3H_2O_2BrCl$.

26.4 Let us consider the modified analysis of the compound. Silver bromide and iodide are not completely soluble even in concentrated ammonia, while silver chloride is not precipitated when an ammonia solution of silver oxide is used. A shift of the equilibrium towards formation of complex compounds in the solution undoubtedly changes the mass of the precipitate. Furthermore, due to the difference in the values of solubility products of AgBr and AgCl, the precipitate component ratio will change. This could be behind the color difference (even though not so sharp).

Calculations below provide for further proofs. One starts with mathematical expression for the equilibrium in the system together with the mass and charge balance equations denoting the desired solubility of s:

$$[Ag^+]\,[Br^-] = 5.4 \cdot 10^{-13}$$
$$[Ag^+]\,[NH_3] \times 10^{3.32} = [Ag(NH_3)^+]$$
$$[Ag(NH_3)^+]\,[NH_3] \times 10^{3.92} = [Ag(NH_3)_2{}^+]$$
$$[Ag(NH_3)^+] + [NH_3] + 2\,[Ag(NH_3)_2{}^+] = 1.0$$
$$[Ag^+] + [Ag(NH_3)^+] + [Ag(NH_3)_2{}^+] = [Br^-] = s$$

(For obvious reasons, the acid-base equilibria in concentrated ammonia solutions could be neglected.) Strict joint solution of the resulting system of equations leads to the value of $s = 3.0 \cdot 10^{-3}$ mol dm^{-3}.

The same answer can be obtained by making the reasonable assumption that $[NH_3] \approx c(NH_3) = 1.0$ mol dm^{-3}, because of the expected low solubility of salt. Then the equations would be simplified to the form:

$$[Ag^+] \times s = 5.4 \cdot 10^{-13};$$
$$[Ag^+] \times (1 + 10^{3.32} + 10^{3.92} \times 10^{3.32}) = s.$$

So, s is still $3.0 \cdot 10^{-3}$ mol dm^{-3}, and the assumptions made are valid.

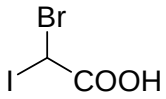
26.5 **Y** reacts with aqueous KOH solution (c = 0.1 mol dm^{-3}) at room temperature, which is due to the presence of the carboxyl group in its structure. Since both **X** and **Y** belong to the same class of organic compounds, **X** is also a carboxylic acid.

Therefore, the compounds differ qualitatively by halogen. The color of combustion products supports the iodine presence in **X**. The lacking atom in **X** should have an even valence, which suggests carbon for this position.

Since $7.55 \cdot 10^{-3}$ mol $CaCO_3$ obtained,

$$M(X) = \frac{2 \times 1.000}{0.00755} = 265 \text{ g mol}^{-1}$$

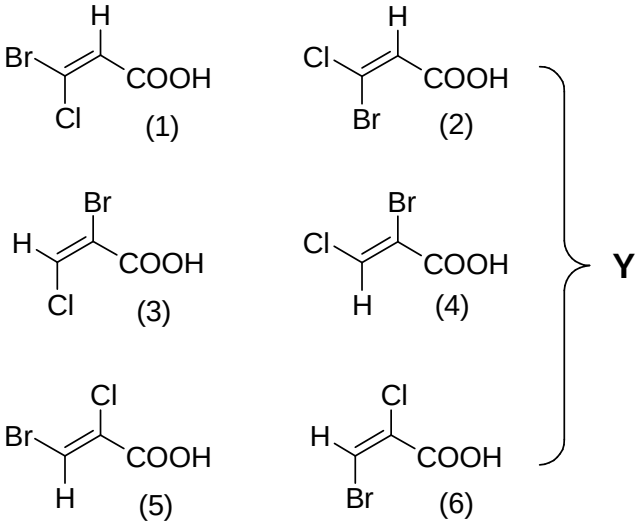
Hence its molecular formula is $C_2H_2O_2BrI$, and the structure is:



X

The validity of the structure is confirmed by chirality.

26.6 Six stereoisomers are possible for **Y** (a typical case when having four different substituents at a double bond):



26.7 It is difficult to imagine the use of chemical compounds to prevent large-scale conflicts and wars. Use of **X** and **Y** as food resources to beat the famine is unlikely either due to their suspected toxicity for mammals (both are rather strong acids with a strong necrotic effect on mucous membranes). At the same time the potential antibacterial and antiseptic properties of **X** and **Y** make them perspective in fighting the horses of Conquest and Death.

26.7 Assuming that the precipitate is an individual compound (calcium carbonate), let us calculate the molar ratio of carbon and oxygen in the molecule of **Z**.

$$n(\mathrm{C}) = \frac{3.065\ \mathrm{g}}{100.09\ \mathrm{g\,mol^{-1}}} = 3.062 \cdot 10^{-2}\ \mathrm{mol};$$

$$n(\mathrm{O}) = \frac{1.000\ \mathrm{g} \times 0.4100}{16.00\ \mathrm{g\,mol^{-1}}} = 2.563 \cdot 10^{-2}\ \mathrm{mol}$$

$$n(\mathrm{C}) : n(\mathrm{O}) = \frac{3.062 \cdot 10^{-2}\ \mathrm{mol}}{2.563 \cdot 10^{-2}\ \mathrm{mol}} = 1.195 : 1.000 \approx 1.2 : 1 \approx 6 : 5$$

However, the number of atoms of each element in **Z** should not exceed 3, so the initial guess is incorrect.

One can calculate the molar mass of **Z** gas:

$$M = \frac{\rho R T}{p} = \frac{1.43\ \mathrm{g\,dm^{-3}} \times\ 8.314\ \mathrm{J\,mol^{-1}\,K^{-1}} \times 307\ \mathrm{K}}{100.0\ \mathrm{kPa}} = 36.5\ \mathrm{g\,mol^{-1}}$$

This value corresponds to hydrogen chloride, which is further confirmed by the fact that there is no precipitation when supernatant (calcium chloride) is treated with an ammonia solution of silver oxide. However, the presence of chlorine in **Z** cannot explain the existence of at least two components in the precipitate. Hence, **Z** must contain fluorine or sulfur atoms (or both elements). Note that HF and SO_2 are gases at 25°C and 1 atm, and CaF_2 and/or $CaSO_3$ produced in the reactions can precipitate:

$$Ca(OH)_2 + 2\ HF \rightarrow CaF_2\downarrow + 2\ H_2O \quad (1)$$

$$Ca(OH)_2 + SO_2 \rightarrow CaSO_3\downarrow + H_2O \quad (2).$$

Since **Z** belongs to the class of carboxylic acids, it contains 2 or 3 oxygen atoms. Then, the possible values of its molecular mass are:

$$M(Z) = \frac{2 \times 16.00\ g\ mol^{-1}}{0.4100} = 78.0\ g\ mol^{-1} \quad or \quad \frac{3 \times 16.00\ g\ mol^{-1}}{0.4100} = 117.1\ g\ mol^{-1}$$

Calculation of the molecular masses of the following combinations of atoms: $M_r(CSClO_3H)$ = 128.5, $M_r(CSClO_2H)$ = 112.5, $M_r(CFClO_3H_2)$ = 116.5, and M_r $(CFClO_2H_2)$ = 100.5 shows that (S + Cl) combination is not suitable because of the upper limit on the molar mass. The (F + Cl) combination is also invalid, since the missing difference of mass cannot be attributed to any of atoms.

Our straightforward solution is deadlocked. The only way to escape consists in assuming that the density of 1.43 g dm^{-3} may correspond to hydrogen fluoride oligomerized in the gas phase. Then chlorine is excluded from consideration, and only two options remain: **Z** is composed of only fluorine atoms or both fluorine and sulfur atoms at a time. In the latter case, the molar mass of combination $CSFO_3H$ is equal to 112 g $mol^{-1}$and that of $CSFO_2H$ to 96 g mol^{-1}. The rest of the mass cannot be attributed to any atom.

Then, **Z** is composed of C, H, F, and O atoms. It contains either two or three oxygen atoms. The molar mass of the compound will be of 78.0 g mol^{-1} in the former case, and of 117.1 g mol^{-1} in the latter one. Analysis of possible combinations of atoms provides for molecular formula $C_2H_3FO_2$ in the former case, and CF_3O_3 or $C_4H_2FO_3$ in the latter one. $C_2H_3FO_2$ is the only correct answer from the chemical point of view. This variant is also supported by calculation of the precipitate mass.

Similarity between **Z, X,** and **Y** suggests the presence of a carboxyl group. Then the structural formula of **Z** can be deduced unambiguously: CH_2F-COOH (monofluoracetic acid).

26.9 According to some studies, monofluoroacetic acid and its sodium salt are responsible for the death of approximately 10 % of cattle in South Africa. Death occurs when animals eat the leaves of plants containing monofluoroacetate in high concentration. Thus, the understanding of biological processes associated with monofluoroacetic acid is important to combat Famine currently raging in several areas of the African continent as well as Death.

PRACTICAL PROBLEMS

PREPARATORY PROBLEM 27 (PRACTICAL)

Determination of nickel in nickel and copper-nickel alloys by complexometric titration

Nickel forms single-phase solid solutions with some metals such as copper, iron, and chromium. Nickel and copper feature unrestricted mutual solubility. Copper-nickel alloys, also referred to as cupronickels, possess different properties depending on their composition. The most used cupronickels contain 10 to 45 % of nickel.

The main properties of copper-rich alloys (70 – 90 % of copper) include high resistance to corrosion, electrical conductivity, ductileness, strength at elevated temperatures. These features make the alloys highly sought in various industrial applications: construction of sea water corrosion-resistant facilities including oil rig platforms (which is of particular importance for Azerbaijan!), condenser systems in desalination plants, cooling circuits, and ammunition. Small amounts of other elements are usually added for specific purposes; the two most popular alloys for marine applications contain up to 2 % iron and manganese. The alloy composed of copper with 45 % nickel content provide for almost exactly constant resistance regardless of temperature, and is thus used in the production of thermocouples and resistance wires in high precision resistors. The copper-nickel alloy containing 25 % nickel with an additive of 0.05 - 0.4 % manganese is commonly used in manufacturing coins and medals.

Precipitation of nickel as dimethylglyoximate followed by its weighing is widely used for accurate determination of this metal in steels and alloys. Nickel can also be assayed by treatment of a Ni^{2+} containing solution with KI and KCN followed by titration with silver nitrate.

Only metal ions (Zn(II), Cu(II), Ca(II) or Mg(II)) rapidly forming EDTA complexes can be determined by direct titration with EDTA. Since the EDTA complex of nickel(II) is formed slower, the back titration is used in the latter case: EDTA is added in an excess and the unreacted EDTA is back titrated with Ca(II) or Mg(II), the metals that also form

colored complexes with a suitable indicator (such as Eriochrome black T), still less stable than the nickel one.

In this task you will precipitate nickel from its ammonia solution with dimethylglyoxime in the presence of citric or tartaric acid as a masking agent* and then determine the metal content by complexometric titration with Eriochrome black T as the indicator.**

Notes.

*At this stage, gravimetric determination of nickel as dimethylglyoximate may be carried out. However, it requires drying to constant weight, which may be time consuming.

**The method gives best results with the alloys containing less than 0.5 mass % of Cu.

Chemicals and reagents

- Alloy sample, ~0.5 g, or a test solution (a solution containing about 1 g dm^{-3} of Ni^{2+}, 0.5 – 0.7 g dm^{-3}, Fe^{3+}, 5 – 6 g dm^{-3} Cu^{2+}),
- Diluted nitric acid (1 : 1, v/v),
- Diluted hydrochloric acid (1: 1, v/v),
- Diluted sulfuric acid (1 : 1, v/v),
- Citric acid or tartaric acid,
- Ammonia solution, concentrated,
- Dimethylglyoxime (10 g dm^{-3} in ethanol),
- Ammonium chloride, 10%,
- Sodium hydroxide (200 g dm^{-3}),
- Hydrogen peroxide solution, 3%,
- Eriochrome black T (as a mixture with NaCl, 1 : 100 w/w),
- Standard 0.05 mol dm^{-3} EDTA solution: Dissolve 18.61 g of solid ethylenediamine tetraacetate disodium dihydrate in 500 cm^3 of distilled water, place the mixture into a measuring flask and dilute to 1 dm^3.
- Ammonia – ammonium chloride buffer solution, pH 10: Dissolve 70 g of solid NH_4Cl in 600 cm^3 of concentrated (~15 mol dm^{-3}) ammonia and dilute to 1 dm^3 with distilled water.
- Magnesium sulfate solution (0.05 mol dm^{-3}): Dissolve 12.33 g of solid magnesium sulfate heptahydrate in 500 cm^3 of distilled water and dilute to 1 dm^3.

Equipment and glassware

- Analytical balance (± 0.0001 g),
- Glass beaker, 250 and 400 cm^3,
- Watch glass,
- Hotplate stirrer,
- Volumetric flask, 500 and 100 cm^3,
- Paper filters (3 ea.),
- Funnel,
- pH Indicator paper,
- Burette, 25 or 50 cm^3 (2 ea.),
- Funnels (to fill the burettes).
- Volumetric pipette, 10 cm^3,
- Erlenmeyer flask, 100 cm^3 (3 ea.),
- Graduated cylinders, 10 and 25 cm^3,
- Wash bottle with distilled water.

Procedure

A. Standardization of $MgSO_4$ solution

1. Fill a burette with the standard Na_2H_2EDTA solution. Transfer 5.00 cm^3 of the solution into the 100 cm^3 Erlenmeyer flask. Adjust pH to 10 with the ammonium buffer solution (3 – 4 cm^3). Add 20 – 30 mg of the Eriochrome black T indicator.
2. Fill the other burette with $MgSO_4$ solution. Titrate the prepared EDTA solution with $MgSO_4$ under continuous stirring until the blue color sharply turns into purple (the change must be irreversible). Record the volume of $MgSO_4$ solution consumed in titration. Repeat the titration until your get consistent results.

   The concentration of $MgSO_4$ solution (M) is found from the following equation:

$$c_1 = V_0 \cdot c_0 / V_1,$$

   where

   V_0 is the volume of Na_2H_2EDTA taken for titration, cm^3,

   V_1 is the volume of magnesium sulfate consumed in titration, cm^3,

   c_0 – the concentration of Na_2H_2EDTA solution.

B. Dissolution of the alloy sample (the experiment should be carried out under a fume hood)

*(Skip this stage and proceed to part **C** if you are analyzing a test solution rather than an actual alloy sample.)*

1. Accurately weigh out the alloy sample, place it into a 250 cm^3 beaker and carefully dissolve in 15 cm^3 of nitric acid (diluted with water, 1 : 1 v/v). Cover the beaker with the watch glass.
2. Gently heat the solution and boil it on a hot plate until dissolution is complete (the residual volume should be of about 5 cm^3). Transfer the solution into the 500 cm^3 volumetric flask, rinse the watch glass and the beaker with distilled water, add the wash water to the volumetric flask, and dilute to the mark using the wash bottle.
3. If the alloy sample cannot be totally dissolved (as it may contain W and/or Si), heat the mixture to dryness, add 10 cm^3 of HCl (1 : 1 v/v) and heat to dryness again. Dissolve the dry residue in 10 cm^3 of concentrated HCl and dilute it with 100 cm^3 of distilled water. Filter off the precipitated tungstic acid using two filters and a long-stem funnel. Wash the precipitate with hot diluted HCl solution (1 : 10 v/v) until no Ni^{2+} ions are detected in wash waters (test with dimethylglyoxime).
4. If the sample contains more than 0.1 mass % of Si, add 10 cm^3 of H_2SO_4 (1 : 1 v/v) and evaporate till abundant evolving of sulfuric acid fumes. Cool the slurry and carefully add about 10 cm^3 of cold water. Then add 100 cm^3 of hot water and dissolve the residue under heating. Filter off the precipitated silicic acid with filter paper and wash the precipitate with hot water. Transfer the filtrate obtained after W and/or Si separation to a 500 cm^3 volumetric flask and dilute to the mark.

C. Precipitation of nickel dimethylglyoximate

1. Transfer 50.00 cm^3 of the test solution into the 400 cm^3 beaker, adjust the volume with water to 200 cm^3 and add 6 – 8 g of solid tartaric or citric acid. Heat the solution on the hot plate until dissolution of the acid is complete. Neutralize the mixture to pH 4 – 5 with 5 – 10 cm^3 of ammonia solution (check against the pH indicator paper).
2. Add 25 cm^3 of the dimethylglyoxime solution in ethanol dropwise under intensive stirring, add 2 – 3 cm^3 of the concentrated ammonia solution to obtain pH 10 and then the other 2 – 3 cm^3 portion of the same solution to provide for NH_3 excess. You will observe the precipitation of nickel dimethylglyoximate.

3. If iron hydroxide precipitates as the solution turns alkaline, add more tartaric or citric acid.
4. Heat the solution with the precipitate on the hot plate until boiling (do not allow boiling!) and store it in a warm place for 40 – 50 min.
5. Filter the precipitate using the filter paper and wash it with 4 – 5 portions of hot distilled water. Then wash the precipitate off to the 400 cm^3 beaker, first with 30 – 50 cm^3 of HCl (1 : 1 v/v) and then hot water. If you failed dissolving the precipitate, heat the solution and slightly boil it with stirring.
6. Cool the solution down to room temperature, transfer to a 100 cm^3 volumetric flask and dilute to the mark with distilled water.

D. Determination of Ni^{2+}

1. Transfer 10.00 cm^3 of the prepared Ni^{2+} solution into the 100 cm^3 Erlenmeyer flask. Adjust pH to 10 with the ammonium buffer solution (4 – 6 cm^3) and add 10.00 cm^3 of the standard Na_2H_2EDTA solution from the burette. Add 20 – 30 mg of the Eriochrome black T indicator to obtain a blue colored solution.
2. Fill the burette with the standard $MgSO_4$ solution and take the initial reading of the burette. Titrate the blue nickel(II) solution with the standard $MgSO_4$ solution until the color becomes permanently purple. Take the final reading of the burette. Repeat the titration until your get consistent results.
3. Calculate the amount of Na_2H_2EDTA spent for Ni^{2+} titration based on the volumes of the Na_2H_2EDTA solution added and the $MgSO_4$ solution consumed in the titration.

Questions and Data Analysis

27.1 Write down the balanced chemical equations for the reactions occurring:

- when the sample of the alloy is dissolved in nitric acid;
- when the test solution is titrated with the magnesium sulfate solution.

27.2 Explain the role of citrate or tartrate when in the process leading to nickel dimethylglyoximate? Write down the corresponding chemical equations.

27.3 Explain the necessity of the nickel dimethylglyoximate precipitation. How do Cu and Mg present in the test mixture interfere with the determination of nickel? Write down appropriate chemical equations.

27.4 Explain why the pH value of the titrated solution should be kept below 10. In calculations, use the following constants of complex formation: $K[Ni(EDTA)]^{2-} = 4.2 \cdot 10^{18}$, $K([Mg(EDTA)]^{2-} = 4.9 \cdot 10^{8}$.

27.5 What is the most stable form of EDTA at pH 10? Compare the molar fractions of $HEDTA^{3-}$ and $EDTA^{4-}$. Note that H_4EDTA is a weak acid with the following acidity constants: $K_1 = 1.0 \cdot 10^{-2}$, $K_2 = 2.1 \cdot 10^{-3}$, $K_3 = 6.9 \cdot 10^{-7}$, $K_4 = 5.5 \cdot 10^{-11}$.

27.6 Derive the formulae for calculation of the Ni^{2+} concentration in the test solution. Calculate the mass fraction of Ni in the alloy.

SOLUTION OF PREPARATORY PROBLEM 27

27.1 $3\ Ni + 8\ HNO_3(diluted) \rightarrow 3\ Ni(NO_3)_2 + 2\ NO\uparrow + 4\ H_2O$

$EDTA^{4-} + Mg^{2+} \rightarrow MgEDTA^{2-}$

27.2 The alloy can contain iron; Fe^{3+} cation forms complexes with citrate and tartrate anions that can be used as masking agents. These complexes are water soluble, and their formation allows avoiding the precipitation of interfering iron(III) hydroxide that takes place in the basic medium required for the precipitation of nickel dimethylglyoximate:

$Fe^{3+} + 3\ OH^{-} \rightarrow Fe(OH)_3\downarrow$ (pH > 5)

27.3 Similar to nickel(II), Cu^{2+} and Mg^{2+} cations form stable complexes with EDTA. When the excess of EDTA is added directly to the dissolved alloy sample, the amount of EDTA spent for the titration is equal to the total amount of all the cations.

$$EDTA^{4-} + Mg^{2+} \rightarrow MgEDTA^{2-}$$

$$EDTA^{4-} + Cu^{2+} \rightarrow CuEDTA^{2-}$$

For this reason, isolation of Ni^{2+} by precipitation is necessary.

27.4 The complex of EDTA with nickel(II) is more stable and is formed first during titration, the complex of Mg^{2+} being formed afterwards. Hence the EDTA volume depends on the complexation of Mg^{2+} with the excess of EDTA. Since the formation

constant of Mg complex with EDTA is rather low, a higher pH value should be attained to provide for the complete complexation.

Quantitatively, the complex formation is governed by the conditional, or effective, formation constant:

$K'_f = K_f \ \alpha_{Y4-} \ \alpha_M$,

It depends on:

- α_{Y4-}, the molar fraction of fully deprotonated form of EDTA (Y^{4-}, increases at higher pH values), and
- α_M, the molar fraction of uncomplexed metal ion, which is influenced by competing reactions (like hydrolysis) taking place at the reaction pH.

  At pH > 10, the formation of insoluble magnesium hydroxide decreases the molar fraction of free Mg^{2+}. Thus, the value of pH 10 is considered optimal.

27.5 The molar fractions of the EDTA forms (Y^{4-}, HY^{3-}) are determined by the equations:

$$\alpha_{Y^{4-}} = \frac{[Y^{4-}]}{[EDTA]} \quad \alpha_{HY^{3-}} = \frac{[HY^{3-}]}{[EDTA]}$$

$[EDTA] = [H_4Y] + [H_3Y^-] + [H_2Y^{2-}] + [HY^{3-}] + [Y^{4-}]$.

At pH 10, concentrations of the first three forms of EDTA can be neglected, so:

$$\alpha_{Y^{4-}} = \frac{[Y^{4-}]}{[Y^{4-}]+[HY^{3-}]} \quad \text{or} \quad \alpha_{Y^{4-}} = \frac{K_4}{[H^+]+K_4} = 0.355, \qquad \alpha_{HY^{3-}} = \frac{[H^+]}{[H^+]+K_4} = 0.645.$$

$[HY^{3-}] > [Y^{4-}]$ at pH = 10.

27.6 Concentration of Ni in the sample solution taken for the precipitation (50 cm^3):

$$c_{Ni} = \frac{V_{EDTA}c_{EDTA} - V_{MgSO_4}c_{MgSO_4}}{V_a} ,$$

c_{Ni} is the concentration of nickel in the aliquot, mol dm^{-3},

V_{EDTA} is the volume of Na_2H_2EDTA solution taken for titration, cm^3,

c_{EDTA} is the concentration of the standard Na_2H_2EDTA solution, mol dm^{-3},

V_{MgSO4} is the volume of magnesium sulfate solution consumed in the back titration, cm^3,

c_{MgSO4} is the determined concentration of magnesium sulfate solution, mol dm^{-3}.

Mass of Ni in the test solution (or dissolved alloy solution):

$$m_{Ni} = \frac{c_{Ni} V_d}{V_s} V_0 \times M_{Ni},$$

taking into account the dilution (according to the protocol, V_d / V_s = 2)

$$m_{Ni} = 2 \times c_{Ni} V_0 \times M_{Ni},$$

V_0 is the volume of the graduated flask with Ni^{2+} (test solution or dissolved alloy), dm^3

V_s is the volume of the test solution or dissolved alloy solution taken for precipitation (50 cm^3),

V_d is the volume of the graduated flask with the dissolved nickel dimethylglyoximate precipitate (100 cm^3)

The mass fraction of Ni in the alloy:

$$w = \frac{m_{Ni}}{m_{alloy}} \times 100\ \%$$

PREPARATORY PROBLEM 28 (PRACTICAL)

Titrimetric determination of lead and silver in their mixture

Lead and silver are often both present in alloys (such as tin-lead-silver or lead-silver), which are successfully applied in bearing assembly, ballast, casting, step soldering, and radiation shielding. The alloys usually contain 30 – 90 % of lead and 1 – 5 % of silver. Redox titration was found to be a precise standardless method allowing determination of these metals.

In this work, you will determine lead and silver in a solution by redox titration.

Chemicals and reagents

- A sample of lead and silver containing alloy, or test solution simulating a dissolved alloy (a standard solution containing about 500 – 1000 mg Pb and 70 – 190 mg Ag in 0.1 dm^3),
- Ammonia aqueous solution (25% ammonium solution and water, 1 : 1 v/v),
- Oxalic acid, saturated solution at room temperature,
- Potassium permanganate, 0.0100 mol dm^{-3} standard solution,
- Sulfuric acid, solution c = 1 mol dm^{-3},
- Nitric acid, solution c = 4 mol dm^{-3},
- Ammonium iron(III) sulfate, saturated solution
- Ammonium thiocyanate, 0.0100 mol dm^{-3} standard solution.

Equipment and glassware

- Analytical balance (± 0.0001 g),
- Hot plate,
- Filter paper or glass filter,
- Burette, 25 cm^3 (2 ea.),
- Funnels (to fill the burettes),
- Volumetric pipette, 10.00 cm^3,
- Pipette filler,
- Erlenmeyer flask, 100 cm^3,
- Volumetric flask, 100 cm^3,
-

- Glass beaker, 100 and 250 cm^3,
- Graduated cylinders,
- Waste bottle for oxalate solution

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Procedure

A. Decomposition of the alloy sample

(Optional and may be omitted; if so, a model solution of metal salts is to be prepared; see *Chemicals and reagents* for the solution composition)

Take a precise weight of the metal (~250 mg) and place it in a beaker. Carefully add 5 cm^3 of concentrated nitric acid (to be done under a fume hood because of gaseous NO_2 evolvement). Heat the beaker slightly on the hot plate to provide for an effective dissolution. When the digestion is complete evaporate the solution to near dryness to remove the major part of the acid (avoid evaporating to dry salts, since hydrolysis may occur. If still so, add a minimal amount of HNO_3 to dissolve the residue). Allow the beaker cooling down to room temperature.

ATTENTION! *Nitric acid is very corrosive! You will have to deal with hot solutions in the above and subsequent steps. Be careful and beware of steam!*

B. Separation of lead

Using the hot plate, remove the excess of the acid by evaporating the solution obtained at stage **A** to dryness and dissolve the residue in water (skip this step if a model test solution is used rather than a real alloy solution). Bring the solution to boiling, then add about 10 cm^3 of the saturated solution of oxalic acid and observe a precipitate formation. Avoid large excess of oxalic acid. To partially dissolve the precipitate, add aqueous ammonia solution (1:1 v/v) dropwise.

ATTENTION! *The ammonia solution is corrosive and has a very strong smell! Keep the bottle stoppered when not in use*.

C. Determination of lead

Heat the solution above the precipitate on the hot plate to remove the excess of ammonia, and cool the mixture quickly under the running tap water. Filter the slurry through the glass filter. Keep the filtrate for next step. Wash the filter cake with cold water and then dissolve it in hot solution of HNO_3 (0.5 mol dm^{-3}) adding the acid in small portions. Collect the obtained solution in the 100 cm^3 volumetric flask and make it up to the mark with water. Titrate oxalate in the prepared solution (take 10.00 cm^3 aliquots) with 0.0100 mol dm^{-3} solution of potassium permanganate.

ATTENTION*! Oxalate solutions are toxic. Do not pour the solutions down a sink. Instead, dispose these in a special waste bottle*.

D. Determination of silver

Add 10 cm^3 of nitric acid solution (4 mol dm^{-3}) and 1 – 2 cm^3 of saturated iron(III) ammonium sulfate solution to the filtrate (from step **C**). Use burette to add the standard solution of ammonium thiocyanate until vanishing reddish-brown color is observed. Shake the flask and continue titrating until the color is stable.

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Questions and Data Analysis

28.1 Write down balanced chemical equations for the reactions that take place upon:

a) formation of the precipitate (step **B**),

b) partial dissolution of the precipitate in ammonia (step **B**),

c) dissolution of lead oxalate (step **C**),

d) oxalate titration with permanganate (step **C**).

28.2 Explain the role of iron(III) at step **D**.

28.3 Calculate the lead and silver content in the sample (starting alloy or test solution).

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SOLUTION OF PREPARATORY PROBLEM 28

28.1 Chemical equations:

a) $Pb^{2+} + C_2O_4^{2-} \rightarrow PbC_2O_4\downarrow$,

$PbC_2O_4\downarrow + C_2O_4^{2-} \rightarrow [Pb(C_2O_4)_2]^{2-}$ (excess of the precipitant),

$2\ Ag^{+} + C_2O_4^{2-} \rightarrow Ag_2C_2O_4\downarrow$

b) $Ag_2C_2O_4\downarrow + 4\ NH_3 \rightarrow 2\ [Ag(NH_3)_2]^{+} + C_2O_4^{2-}$

c) $PbC_2O_4\downarrow + 2\ H^{+} \rightarrow H_2C_2O_4 + Pb^{2+}$

d) $5\ H_2C_2O_4 + 2\ KMnO_4 \rightarrow 10\ CO_2 + 2\ MnSO_4 + K_2SO_4 + 8\ H_2O$

28.2 Step **D** describes the direct titrimetric determination of silver with ammonium thiocyanate. Iron(III) is a very sensitive indicator of the excess of thiocyanate ion:

$Fe^{3+} + SCN^{-} \rightarrow FeSCN^{2+}$ (reddish-brown; higher complexes are also formed)

PREPARATORY PROBLEM 29 (PRACTICAL)

Complexometric determination of iron, chromium, and zinc in an alloy

Ferrochrome is an alloy of iron and chromium mostly (over 80 % of world consumption) used in stainless steel production. To improve the corrosion resistance of steel it is often coated with zinc, the process being referred to as galvanization. It is of extreme importance to accurately control the contents of zinc, iron, and chromium in the resultant galvanized steel. Typically samples of steel are dissolved in concentrated nitric acid and the content of major components in the obtained solution is determined by different methods.

Analysis of multi-component systems is often hindered by the interference between the components. Various separation techniques (precipitation, extraction) or masking are the usual steps towards avoiding such interference. Still, nowadays researches are mainly focused at analytical methods allowing sequential determination of components in the same solution without any separation procedures. These methods are typically based on simple manipulations like changing the pH.

In this task you will apply one of such methods for sequential determination of iron(III), chromium(III) and zinc(II) simultaneously present in an aqueous solution.

Chemicals and reagents

- Test solution simulating a digested sample of galvanized steel (a standard solution containing Fe^{3+}, Zn^{2+} and Cr^{3+} ions within the concentration range of 0.1 – 0.3 mol dm^{-3}),
- Hydrochloric acid, 1 mol dm^{-3},
- Na_2H_2EDTA standard solution, 0.025 mol dm^{-3},
- Acetate buffer solution, pH 5.5 – 6.0, 1.7 mol dm^{-3} in acetate,
- Copper(II) sulfate standard solution, 0.025 mol dm^{-3},
- Ethanol, 96%,
- Distilled water,
- Indicators:
  - aqueous solution of 5-sulfosalicylic acid, 5% (w/w),
  - solution of 1-(2-pyridylazo)-2-naphthol (PAN) in ethanol, 0.1% (w/w),
  - universal pH indicator paper.

Equipment and glassware

- Hot plate,
- Funnels (to fill the burettes),
- Paper filters,
- Volumetric flask, 100 cm^3,
- Volumetric pipettes, 1 and 10 cm^3,
- Burette, 25 or 50 cm^3 (2 ea.),
- Erlenmeyer flask, 200 cm^3 (3 ea.),
- Graduated cylinder, 10 cm^3 (2 ea.),
- Glass dropper.

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Procedure

A. Sample preparation

Prepare 100 cm^3 of your working solution by a 10-fold dilution of the test solution provided. Use the 100 cm^3 volumetric flask and distilled water. The Fe^{3+}, Zn^{2+} and Cr^{3+} ions content in the working solution would be within the concentration range of 0.01 – 0.03 mol dm^{-3}.

B. Determination of Fe^{3+}

Place 10.00 cm^3 of the working solution into a 200 cm^3 Erlenmeyer flask, add about 20 cm^3 of distilled water and adjust the pH to 1 by adding about 5 cm^3 of 1 mol dm^{-3} HCl solution (check the pH value against the indicator paper). Finally, supplement 1 cm^3 of 5% aqueous solution of sulfosalicylic acid (the indicator) and mix thoroughly.

Titrate the flask contents with 0.025 mol dm^{-3} EDTA standard solution until the color changes from violet to yellow-green. Record the volume of the standard solution (V_1, cm^3). Repeat the titration as necessary.

C. Determination of Zn^{2+}

Adjust pH to 5 – 6 in the solution obtained in step **B** by adding 5 – 6 cm^3 of the acetate buffer solution, then add 3 – 5 drops of the PAN solution (the indicator), 2 cm^3 of ethanol (by cylinder) and mix thoroughly.

Titrate the flask contents with 0.025 mol dm^{-3} EDTA standard solution until the color changes from pink to yellow-green. Record the volume of the standard solution (V_2, cm^3). Repeat the titration when necessary.

D. Determination of Cr^{3+}

Direct titration of Cr^{3+} with EDTA solution is impossible because of the low rate of the complex formation. Thus, the method of a back titration is used: an excess of EDTA standard solution is introduced, and the unreacted EDTA is titrated with Cu^{2+}.

Supplement an excess of 0.025 mol dm^{-3} standard solution of EDTA (20 cm^3) to the solution obtained in step **C**, mix thoroughly and boil the mixture for 5 min. Add 3 - 5 drops of the PAN solution (the indicator) to the cooled mixture and mix thoroughly.

Titrate the flask contents with 0.025 mol dm^{-3} $CuSO_4$ standard solution until the color changes from wine-red to blue-violet. Record the volume of the standard solution (V_3, cm^3). Repeat the titration as necessary.

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Questions and Data Analysis

29.1 Write down balanced chemical equations for the reactions that take upon:

a) the sample of alloy is dissolved in concentrated nitric acid,

b) the working solution is titrated with Na_2H_2EDTA.

29.2 Derive the formulae for calculation of the Fe^{3+}, Zn^{2+} and Cr^{3+} concentration in the test solution. Calculate the concentrations of the ions.

29.3 Calculate the molar fraction of H_2EDTA^{2-} at pH 1. EDTA is a weak acid with the following acidity constants:

$K_1 = 1.0 \cdot 10^{-2}$, $K_2 = 2.1 \cdot 10^{-3}$, $K_3 = 6.9 \cdot 10^{-7}$, $K_4 = 5.5 \cdot 10^{-11}$.

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SOLUTION OF PREPARATORY PROBLEM 29

29.1 Chemical equations:

a) $Zn + 4\ HNO_{3(conc.)} \rightarrow Zn(NO_3)_2 + 2\ NO_2\uparrow + 2\ H_2O$

$Fe + 6\ HNO_{3(conc.)} \rightarrow Fe(NO_3)_3 + 3\ NO_2\uparrow + 3\ H_2O$

$Cr + 6\ HNO_{3(conc.)} \rightarrow Cr(NO_3)_3 + 3\ NO_2\uparrow + 3\ H_2O$

b) $Zn^{2+} + H_2EDTA^{2-} \rightarrow ZnEDTA^{2-} + 2\ H^+$

$Fe^{3+} + H_2EDTA^{2-} \rightarrow FeEDTA^{-} + 2\ H^+$

$Cr^{3+} + H_2EDTA^{2-} \rightarrow CrEDTA^{-} + 2\ H^+$

$Cu^{2+} + H_2EDTA^{2-} \rightarrow CuEDTA^{2-} + 2\ H^+$

29.2 $c(Fe^{3+}) = \dfrac{10 \times c\left(Na_2H_2EDTA\right) \times V_1\left(Na_2H_2EDTA\right)}{V_a}$

$c(Zn^{2+}) = \dfrac{10 \times c\left(Na_2H_2EDTA\right) \times V_2\left(Na_2H_2EDTA\right)}{V_a}$

$c(Cr^{3+}) = \dfrac{10 \times \left[20 \times c\left(Na_2H_2EDTA\right) - V_3\left(Cu^{2+}\right)\ c_3\left(Cu^{2+}\right)\right]}{V_a}$

29.3 For pH 1.0 and $K_1 = 1.0 \cdot 10^{-2}$, $K_2 = 2.1 \cdot 10^{-3}$, $K_3 = 6.9 \cdot 10^{-7}$, $K_4 = 5.5 \cdot 10^{-11}$:

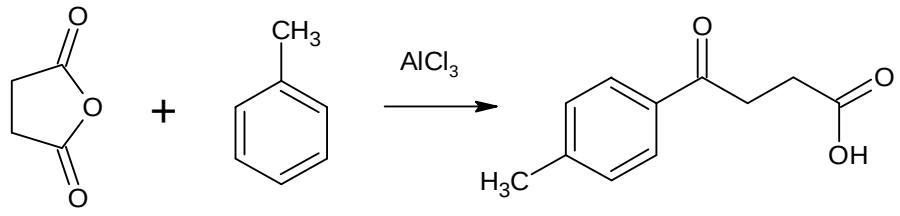
$$\alpha\left(H_2EDTA^{2-}\right) = \frac{K_1K_2\left[H^+\right]^2}{K_1K_2K_3K_4 + K_1K_2K_3\left[H^+\right] + K_1K_2\left[H^+\right]^2 + K_1\left[H^+\right]^3 + \left[H^+\right]^4} = 0.002$$

PREPARATORY PROBLEM 30 (PRACTICAL)

Synthesis of 3-(4-Methylbenzoyl)propionic acid

The Friedel-Crafts reactions are a family of processes (acylation, alkylation, and some other less important) developed by C. Friedel and J. Crafts in 1877 at the Sorbonne.

The Friedel-Crafts acylation allows introducing of an acyl group into the aromatic ring with a suitable acylating agent (acyl halide or carboxylic acid anhydride) and a strong Lewis acid as a catalyst. Nowadays it is an important synthetic method providing aromatic and alkyl-aromatic ketones, which are important intermediates in the production of pharmaceuticals, dyes and other valuable compounds.



The Friedel-Crafts alkylation is less sought, since may lead to a mixture of polyalkylated products. Remarkably, a solution comes from the Friedel-Crafts acylation, since the acylation products are readily reduced to the corresponding alkanes (e.g. via Clemmensen or Wolff-Kishner reactions).

Chemicals and reagents

- Toluene (dry), 25 g,
- Succinic anhydride, 5 g,
- Aluminium chloride anhydrous, 13.3 g,
- Dichloromethane (Methylene chloride), 100 cm^3,
- Hexane, 75 cm^3,
- Hydrochloric acid, concentrated, 25 cm^3,
- Sodium sulfate, calcined, 20 g,
- Distilled water, 100 cm^3

Equipment and glassware

- Laboratory stand with clamps,
- Three-necked flask, 250 cm^3,
- Reflux condenser with breather tube,
- Dropping funnel, 100 cm^3,
- Magnetic stirrer with heating,
- Teflon magnetic stir bar,
- Hoses,
- Thermometer with a tapered joint,
- Tapered joint stopper,
- Ice bath,
- Graduated cylinder, 50 cm^3,
- Beaker, 100 cm^3,
- Separating funnel, 250 cm^3,
- Rotary evaporator,
- Paper filter,
- Fritted glass filter, porosity 2-3,
- Bunsen flask for vacuum filtration,
- Glass rod,
- Melting point apparatus,
- Capillary for melting point determination (2-3 ea.),
- Glass tube for capillary filling,
- Spatula,
- Teflon sleeves for tapered joints or vacuum grease,
- Analytical balances (± 0.001 g).

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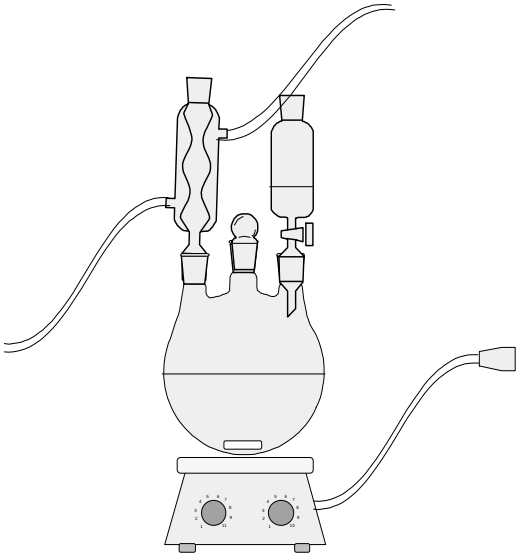
Procedure

A. Assembly of the apparatus

Assemble the apparatus as shown in the hereunder picture. Equip every joint with the Teflon sleeve or apply vacuum grease.



B. Preparation of the reagents and synthesis of the product

Fix the three-necked flask at the laboratory stand over the magnetic stirrer. Place 25 g of toluene and 5 g of succinic anhydride into the flask and equip it with the reflux condenser with a breather tube, the dropping funnel and the stir bar. Start stirring the mixture. Use the neck left open to add 13.3 g of the finely-powdered anhydrous aluminum chloride in portions at continuous stirring. When finished, fix the neck with the thermometer so that its tip is submerged into the reaction mixture. Switch on heating. Close the neck with the stopper and vigorously stir the reaction mixture for 1 h at 60 ℃.

C. Isolation of the product

Cool the flask down to room temperature and then place it in the ice bath. Fill the dropping funnel with 60 cm^3 of ice-cooled water. Add slowly (dropwise) all the water from the funnel to the reaction mixture at constant vigorous stirring. When finished, add dropwise 25 cm^3 of concentrated hydrochloric acid add 60 cm^3 of dichloromethane. Transfer the reaction mixture to the separatory funnel and tightly close it with the stopper.

Keep shaking the reaction mixture vigorously (turning the separatory funnel up and down) for a few minutes, and then allow the phase separation. Add extra 10 cm^3 of water and 10 cm^3 of dichloromethane if phase separation is not satisfactory. Segregate the well defined organic phase. For better extraction, add 20 cm^3 of dichloromethane to the aqueous phase and repeat separation as described above two times. Combine the

organic phases in the separatory funnel and wash with 30 cm^3 of water. Pour out the organic phase and dry it over calcined Na_2SO_4 1 hour. Filter the desiccant off using the paper filter or fritted glass filter. Evaporate the filtrate on the rotary evaporator to approximately 20% of the original volume.

D. Purification of the product

Transfer the residue left after the rotary evaporation into the beaker and add 30 cm^3 of hexane, which will initiate the crystallization process. Place the beaker in the ice bath for 20 min to complete crystallization. Filter out the precipitate using the fritted glass filter and wash the product three times with 15 cm^3 of hexane each.

E. Analysis of the product

Weigh the product. Calculate the yield.

Place the non-sealed end of the capillary into the product crystals, then turn it the sealed end down and throw several times down through a glass tube. Check that the sealed end side of the capillary is filled with the product. Apply the ready capillary to the melting point apparatus and record the melting point of the product. Compare the value with the reference data and draw a conclusion about the product purity.

Note. The resulting product, if pure, can be used as the starting compound in Problem 31.

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Questions

30.1 Is it possible to introduce two acyl groups in the ring via the Friedel-Crafts electrophilic substitution reaction? Propose the way to obtain 1,4-diacetylbenzene.

30.2. Compare the activity of phenol, *p*-nitrophenol and *p*-methoxyphenol in the O-acylation reaction in neutral medium (*e.g.* in THF). Suggest the reaction scheme of the most active compound (according to your choice) with propionic acid chloride.

30.3 Why is the Friedel-Crafts acylation more often used as compared to the Friedel-Crafts alkylation?

30.4 Which other reagents (besides that considered in the Problem) can be used in the Friedel-Crafts acylation?

30.5 Why are the ice-cooled water and concentrated hydrochloric acid added to the mixture once the reaction is complete?

30.6 Why aluminum chloride is taken in the two-fold excess?

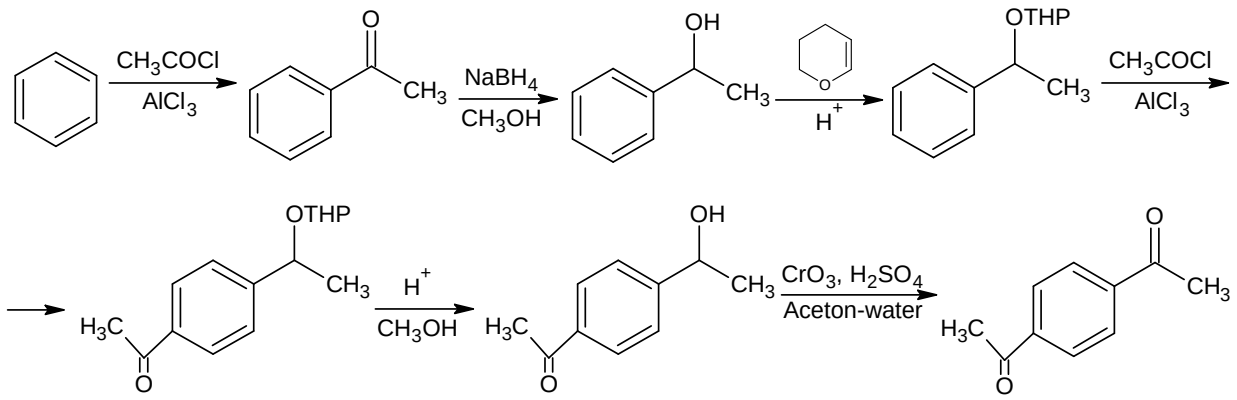
_____

SOLUTION OF PREPARATORY PROBLEM 30

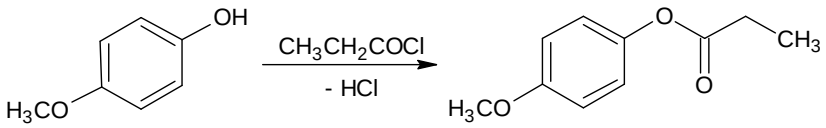
Product	Appearance	Melting/Boiling point, °C	n_D^{20}	Yield, %
3-(4-Methyl--benzoyl) propionic acid	Beige crystals (prisms)	126-127	-	6.6 g (68 %)

NMR reference data ($CDCl_3$)
2.42 (s,3H, CH_3), 2.81 (t, 2H, J=6.6 Hz, $C\underline{H_2}COOH$), 3.30 (t, 2H, J=6.6 Hz, $C\underline{H_2}CO$), 7.27 (d, 2H, 2H, J=8.0 Hz), 7.89 (d, 2H, 2H, J=8.1 Hz) [ArH]

30.1 No, because the first acyl group introduced into the ring exhibits the –M effect, thus deactivating the ring with respect to subsequent electrophilic substitution reactions. To advance on the way to diacylated product, one should temporarily change the first introduced acyl group so that its deactivation effect on the ring is minimized. Reduction of the monoacylated derivative with sodium borohydride followed by introduction of the trimethylsilyl or THP protection can be considered as examples. The synthetic sequence is continued by the second acylation, removal of the protection from the hydroxyl group, and finally by the oxidation of the hydroxyl group with any suitable reagent (PCC, PDC, manganese dioxide, etc.)



30.2 A reagent activity in O-acylation reaction depends on the electron density at the oxygen atom (nucleophilicity). As the electron pair of the phenolic oxygen is conjugated with the aromatic π-system, the electron density at this atom depends on the donor-acceptor properties of the ring substituents. Being an acceptor of electron density, the nitro group reveals the –M effect and depletes the ring and the phenolic oxygen. The methoxy group produces the +M effect, thus increasing the electron density in the ring and at the phenolic oxygen. Thus, the activity increases in the following order: *p*-nitrophenol < phenol < *p*-methoxyphenol.

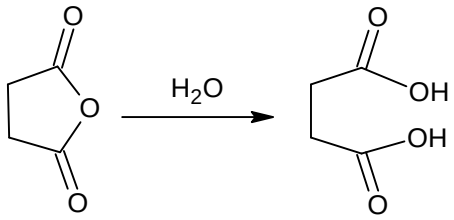


30.3 The Friedel-Crafts alkylation leads to a mixture of polyalkylation products. Besides, the reaction proceeds *via* carbcationic intermediates, which are subject to various rearrangements. As a result, the hydrocarbon skeleton of the starting alkylating agent undergoes isomerization. Thus, alkylation typically leads to a complex mixture of products, which both reduces the product yield and makes its isolation complicated.

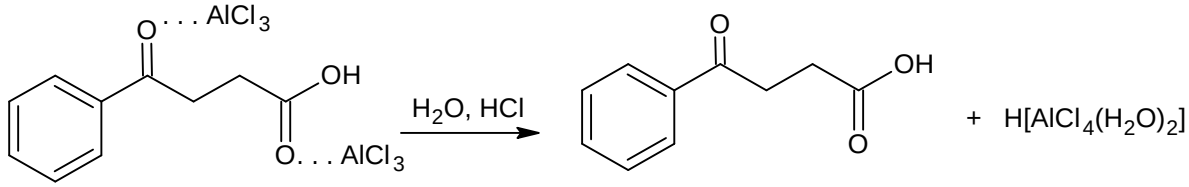
By contrast, the Friedel-Crafts acylation always affords a sole product of the known structure.

30.4 Acid halides are often used as acylating agent. Various Lewis acids (zinc chloride, ferric chloride, boron trifluoride, etc.) can be introduced in the reaction mixture instead of aluminum chloride.

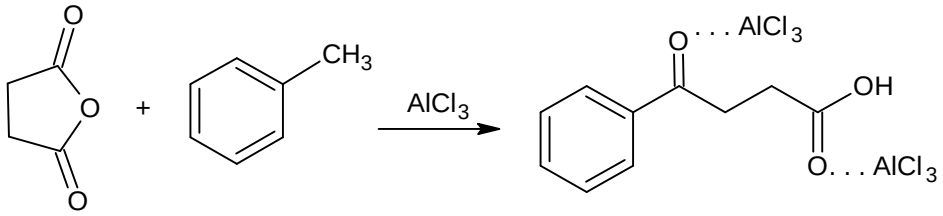
30.5 Water is added to decompose the unreacted anhydride, the reaction being exothermic:



Hydrochloric acid is added to destroy the complex of aluminum chloride with the reaction product and to remove aluminates in the form of $H[AlCl_4(OH_2)_2]$.



30.6 Aluminum chloride forms complexes with carbonyl and carboxyl groups. The answer comes from the fact that the product contains both of these groups.

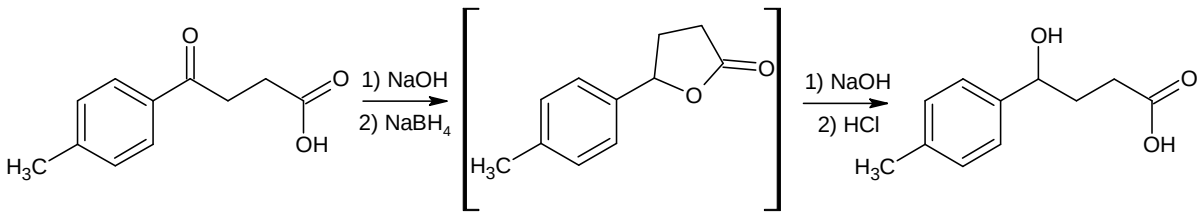


PREPARATORY PROBLEM 31 (PRACTICAL)

Synthesis of 4-(4-methylphenyl)-4-hydroxybutanoic acid

The intermediate oxidation state of carbon in carbonyl compounds specifies its ability to take part in oxidation-reduction reactions. Depending on the selected reaction conditions the reduction of a carbonyl group can lead either to alcohols (primary in the case of aldehydes and secondary in the case of ketones) or saturated hydrocarbons. The latter are typically formed as a result of hydrogenation at elevated temperature and high pressure, still can also be obtained under relatively mild conditions (e.g. via Clemmensen or Wolff-Kischner reactions).

Reduction of carbonyl compounds to alcohols can be successfully carried out by catalytic hydrogenation. Still, the preference is nowadays given to other chemical processes due to the simplicity of experimental procedures and accessibility of reagents. Hydride complexes of aluminum (or boron) and alkaline metals are indispensable in organic synthesis due to their high reducing ability in a wide range of temperatures and the possibility of choosing appropriate complexes applicable in solvents with different polarity. In this task you will get acquainted with one of such reagents, sodium borohydride.



Chemicals and reagents

- β-(4-methylbenzoyl)-propionic acid, 4 g,
- Sodium borohydride, 0.8 g,
- Sodium hydroxide, 2.5 mol dm^{-3} aqueous solution, 24 cm^3,
- Hydrochloric acid, 6 mol dm^{-3} aqueous solution, 20 cm^3,
- Distilled water, 100 cm^3.

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Equipment and glassware

- Laboratory stand with clamps,
- Three-necked flask, 250 cm^3,
- Reflux condenser with breather tube,
- Dropping funnel, 100 cm^3,
- Magnetic stirrer with heating,
- Teflon magnetic stir bar,
- Hoses,
- Thermometer with a tapered joint,
- Tapered joint stopper,
- Ice bath,
- Beaker, 100 cm^3 (2 ea.),
- pH indicator paper,
- Fritted glass filter, porosity 2 – 3,
- Glass rod,
- Melting point apparatus,
- Capillary for melting point determination (2-3 ea.),
- Glass tube for capillary filling,
- Spatula,
- Teflon sleeves for tapered joints or vacuum grease,
- Analytical balances (± 0.001 g)

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Procedure

A. Assembly of the apparatus

Assemble the apparatus as shown in the picture in Problem 30. Equip every joint with the Teflon sleeve or apply vacuum grease.

B. Preparation of the reagents and synthesis of the product

Prepare the solution of 0.8 g of sodium borohydride in 12 cm^3 of water and pre-cool it to 0 – 5 ℃. Fix the three-necked flask at the labo ratory stand over the magnetic stirrer. Weigh out and admeasure the required amounts of the reagents. Place 4 g of β-(4-methylbenzoyl)-propionic acid and 12 cm^3 of 2.5 mol dm^{-3} aqueous solution of NaOH

in the flask and equip it with the reflux condenser with a breather tube, the dropping funnel and the stir bar. Switch on stirring. Fix the unused neck with the thermometer so that its tip is submerged into the reaction mixture. Place the ice-water bath under the flask. When the reaction mixture gets cooled down to 0 – 5 ℃, quickly add with intensive stirring the pre-cooled sodium borohydride solution. Remove the ice-bath and let the reaction mixture warm up to room temperature. Gently heat up the mixture to boiling and keep refluxing for 40 min. Then add 12 cm^3 of 2.5 mol dm^{-3} aqueous solution of NaOH to the heated reaction mixture and continue refluxing for another 20 min.

C. Isolation of the product

Switch off the heating. Cool the flask down to room temperature and then place it in the ice-water bath containing sodium chloride. Fill the dropping funnel with 15 cm^3 of HCl solution (6 mol dm^{-3}) and add the acid solution slowly to the flask under vigorous stirring continuously monitoring the pH of the reaction mixture with the pH indicator paper (capture a drop of the reaction mixture with the glass rod through the neck of the flask and apply it to the test paper). **Important!** The temperature of the reaction mixture **must not** exceed 5 ℃. Instantly control the temperature keeping the tip of the thermometer submerged into the reaction mixture. Adjust the pH to 2 and observe precipitation of white crystals. Filter out the product using the fritted glass filter and wash it 2-4 times with ice-cold water until the pH of the filtrate attains 4 - 5. Air-dry the resulting white precipitate on a filter paper for a few hours. To accelerate the process the precipitate may be placed in a round-bottom flask and dried out on a rotary evaporator under reduced pressure. Control the dryness of the product by determining its melting point.

Place the non-sealed end of the capillary into the product crystals, then turn it the sealed end down and throw several times down through a longer glass tube. Check that the sealed end side of the capillary is filled with the product. Apply the ready capillary to the melting point apparatus and record the melting point of the product. Compare the value with the reference data and draw a conclusion about the product purity.

D. Analysis of the product

Weigh the product. Calculate the yield.

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Questions

31.1 What effects does an alkali produce on the starting materials and the reaction intermediates? Write down the equation of sodium borohydride reaction with water in neutral medium. Suggest the mechanism of the lactone disruption.

31.2 Why does addition of the acid at the final stage of the synthesis lead to the product precipitation?

31.3 Consider an alkylaldehyde and a dialkyl ketone. Which carbonyl group is more readily reduced with sodium borohydride? Justify your answer.

31.4 The reaction considered in this Problem serves as an example of the selective reduction of a keto group in the presence of a carboxyl one. Propose a way how a carboxyl group can be selectively reduced in the presence a carbonyl group.

31.5 A compound with the molecular formula $C_{17}H_{25}NO_2$ is produced when the starting compound is treated with cyclohexylamine (in equimolar amount to ketoacid) in methanol in the presence of catalytic amounts of a strong acid followed by the addition of sodium borohydride. Suggest the structures of the final and intermediate products as well as the mechanism of the first stage of the reaction.

SOLUTION OF PREPARATORY PROBLEM 31

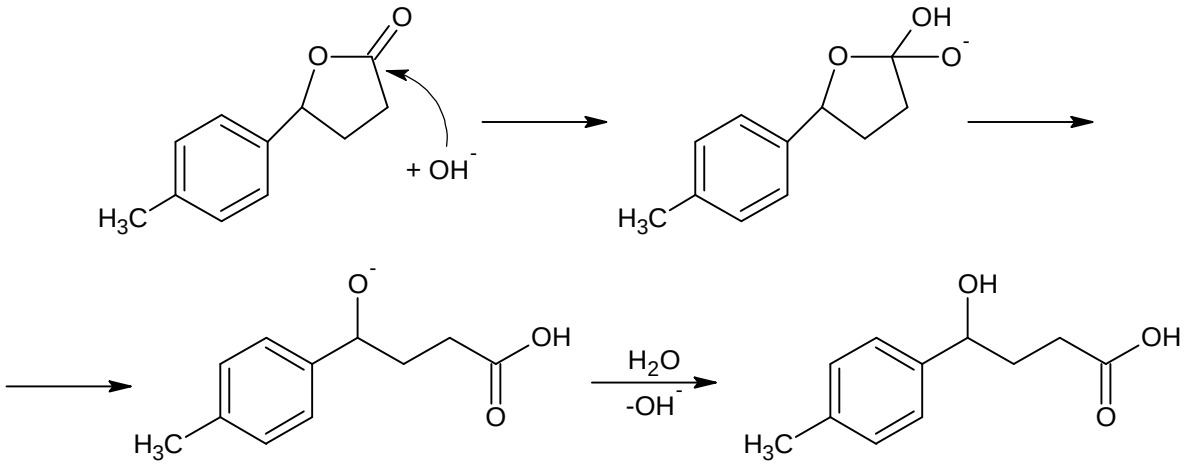
Product	Appearance	Melting/Boiling point, °C	n_D^{20}	Yield, %
4-(4-Methylphenyl)-4-hydroxybutanoic acid	White crystals	97 - 99 °C	-	3.0 g (72%)

NMR reference data ($CDCl_3$)
2.07 (m, 2H, CH_2), 2.35 (s,3H, CH_3), 2.48 (t, 2H, J=7.3 Hz, CH_2), 4.75(t, 2H, J=7.3 Hz, CHOH), 7.17 (d, 2H, 2H, J=8.0 Hz), 7.24 (d, 2H, 2H, J=8.0 Hz) [ArH]

31.1 Transformation of the acid in readily soluble anionic form is the main reason behind carrying out the reaction in alkaline medium (the protonated acid is practically insoluble in water). Also, sodium borohydride is stable in alkaline medium, whereas it undergoes decomposition with hydrogen evolution in neutral and especially in acidic medium. In neutral medium, the reaction equation is written down as:

$$NaBH_4 + 4\ H_2O \rightarrow Na[B(OH)_4] + 4\ H_2$$

The mechanism of the lactone disruption is as follows:

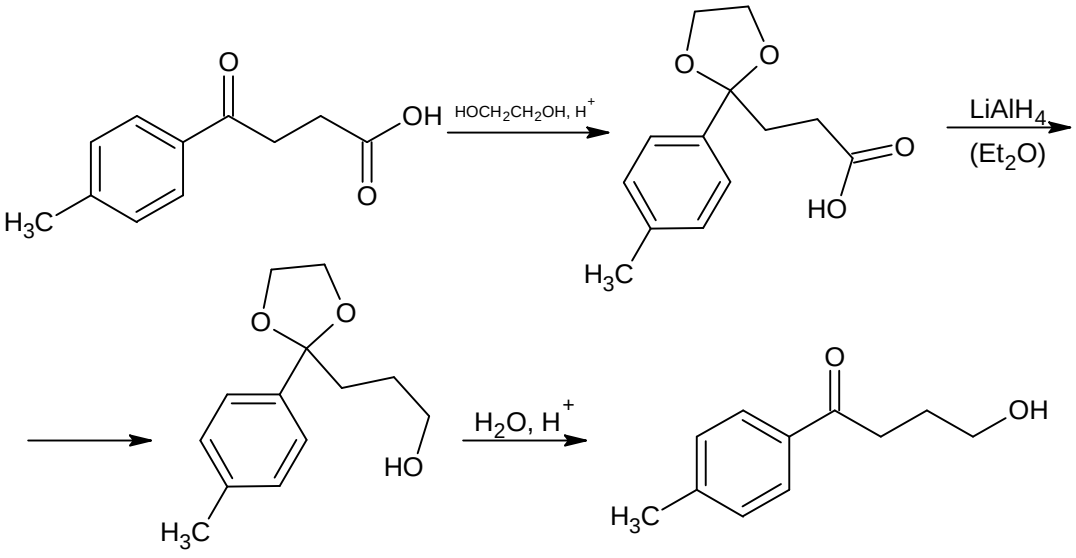


31.2 4-(4-Methylphenyl)-4-hydroxybutanoic acid is a weak acid. Its solubility in water in the non-dissociated form is low. By contrast, the solubility of the anionic form is considerably higher, since its negative charge effectively interacts with the solvent. The anionic form predominates in the alkaline medium. Addition of a strong acid leads to the carboxylate protonation, and the non-dissociated acid precipitates.

31.3 Readiness to reduction correlates with the value of the partial positive charge (δ+) on the carbon atom in the carbonyl group. Both alkyl groups in ketones produce the

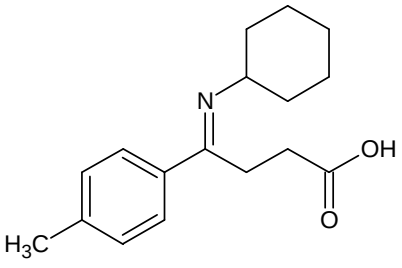
+I effect on the carbonyl carbon atom. At the same time, there is only one group of this type in aldehydes. Thus, the value of δ+ on the carbon atom is higher in the case of the aldehyde group, and it is more readily reduced with sodium borohydride.

31.4 Reduction of a carboxyl group in the presence of a carbonyl one turns out to be a much more complicated task. The carbonyl group should be first protected, *e.g.* by the formation of a cyclic acetal as a result of the reaction with ethylene glycol in acidic medium. Then a strong reagent (*e.g.* lithium aluminum hydride) is applied to reduce the carboxyl group. Finally, the protecting group is removed under mild acidic conditions.

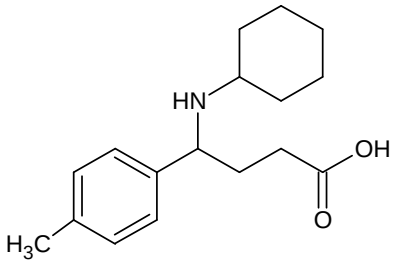


31.5 The combination of nucleophilic addition of an amine with subsequent reduction is referred to as reductive amination. The nucleophilic amine is attached to the carbonyl group affording the imine, which is further reduced to the amine with sodium borohydride.

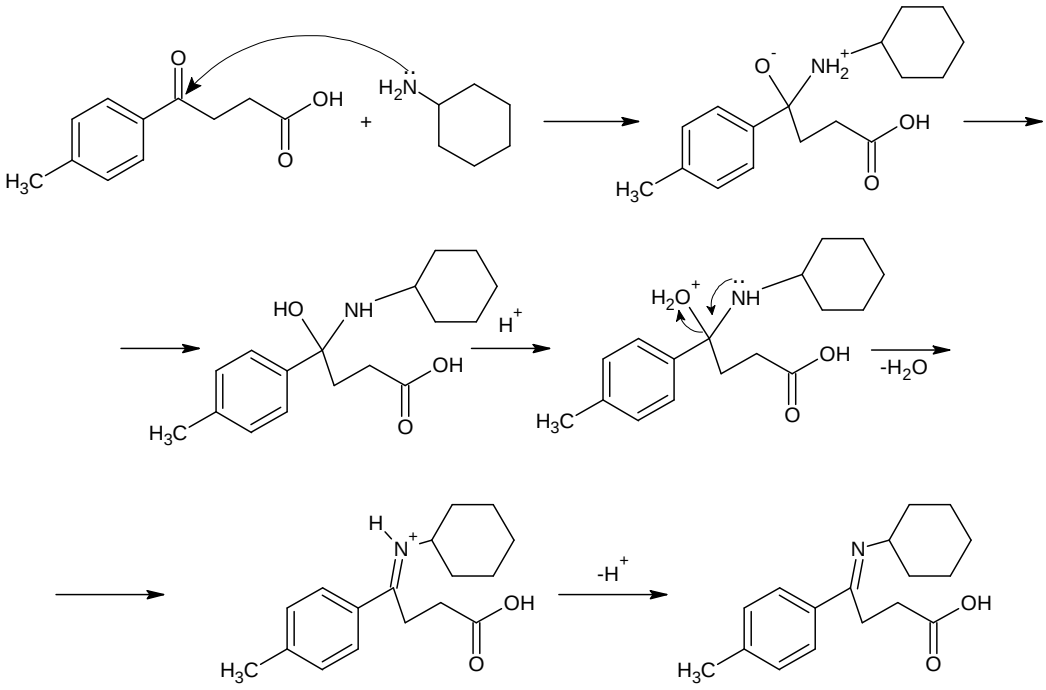
The intermediate product



The final product



The reaction mechanism:

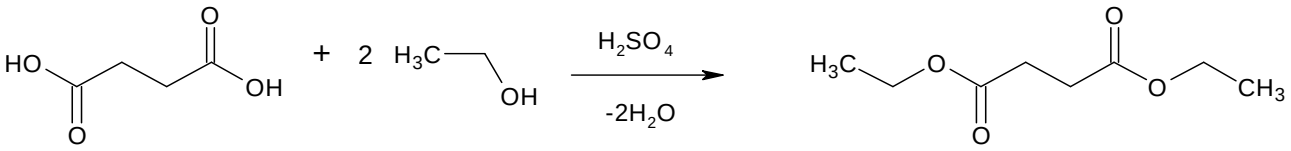


PREPARATORY PROBLEM 32 (PRACTICAL)

Synthesis of diethyl ester of succinic acid

Esters are widespread in nature. In particular, these compounds are responsible for pleasant aromas of flowers, fruits and berries. Low molecular weight esters, flammable liquids with low boiling points, are applied as solvents for varnishes and paints, flavoring additives in food industry, etc. Esters of higher monocarboxylic acids and higher alcohols are referred to as waxes. Fats and vegetable oils, vitally important storage compounds, are esters of polyhydric alcohol glycerol and higher carboxylic acids.

Several synthetic schemes are available for ester preparation. The acid catalyzed esterification of a carboxylic acid and an alcohol is among the most used in laboratory practice. Since the reaction is reversible, special attention should be given to shifting the equilibrium towards the ester formation. This can be achieved by either introduction of dehydrating agents or removal of the products (ester and/or water) from the reaction mixture. In the case of starting compounds with relatively low boiling points azeotropic removal of water is possible. In this work you will follow the latter approach to ester synthesis.



Chemicals and reagents

- Succinic acid, 18 g,
- Ethanol (absolute), 55 cm^3,
- Toluene (dry), 24 cm^3,
- Sulfuric acid (concentrated), 0.5 cm^3,
- Potassium carbonate (calcined), 25 g

Equipment and glassware

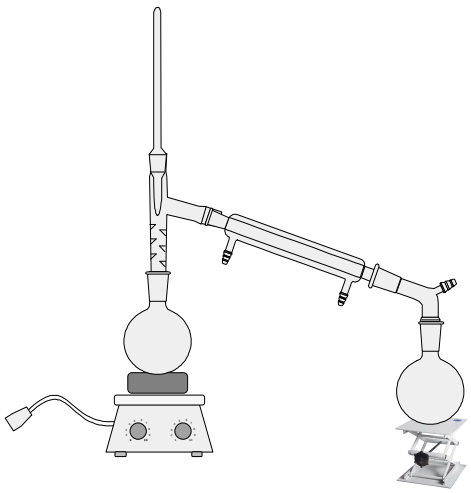
- 24 mL,Graduated cylinders, 5 and 50 cm^3,
- Round-bottom flask, 250 cm^3,
- Long Vigreux distilling column with a downward condenser,

- Vacuum adapter
- Hoses for the condenser,
- Glass capillaries or boiling granules,
- Receiver flask, 100 cm^3,
- Thermometer with a tapered joint,
- Magnetic stirrer with heating or hot plate,
- Claisen flask (150 cm^3) with a downward condenser,
- Capillary for Claisen flask,
- Filter paper or fritted glass filter,
- Beaker, 100 cm^3,
- Three-way vacuum adapter,
- Receiver, 50 cm^3 (3 ea.),
- Water-jet air pump,
- Manometer,
- Analytical balances (± 0.001 g),
- Refractometer,
- Teflon sleeves for tapered joints or vacuum grease,
- Spatula,
- Pressure nomogram.

Procedure

A. Assembly of the apparatus

Assemble the apparatus as shown in the hereunder picture. Equip every joint with the Teflon sleeve or apply vacuum grease.



Note: the tip of the thermometer should be positioned slightly below the outlet to the condenser.

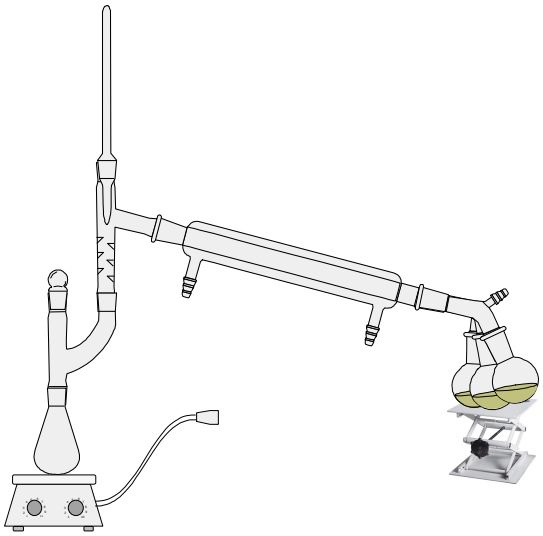
B. Preparation of the reagents and synthesis of the product

Weigh out and admeasure the required amounts of succinic acid (18 g), absolute ethanol (55 cm^3), toluene (24 cm^3), and concentrated sulfuric acid (0.5 cm^3). Place all the materials into a 250 cm^3 round-bottom flask.

Heat the reaction mixture constantly monitoring the temperature. The fraction with the azeotropic mixture of the alcohol, water and toluene should start distilling off at 74 – 80℃. Collect the distillate in the 100 cm^3 receiver flask and terminate distillation (turn off the heater plate and disconnect the receiver flask with the collected distillate). Add 25 g of calcined K_2CO_3 to the receiver flask to dry the distillate. Shake the flask and leave it for 1 hour. Then separate the liquid from the desiccant by filtration through any filter enlisted in the “Equipment and glassware” section. Place the dried distillate back to the reaction mixture in the round-bottom flask, switch on heating and collect once again the fraction with the azeotropic mixture of the alcohol, water and toluene distilled off at 80 ℃.

C. Vacuum distillation of the residue

Label and take weights of all empty 50 cm^3 receiver flasks. Transfer the residue from the round-bottom flask to the Claisen flask and add glass capillaries or boiling granules. Assemble the apparatus for vacuum distillation as shown in the hereunder picture. Equip every joint with the Teflon sleeve or apply vacuum grease. Connect the vacuum line to the vacuum adapter.



Distill the residue under vacuum using the water-jet pump. Collect the fractions into the receiver flasks. Maintain the rate of distillation of about 1 - 2 drops of the distillate per second. Once the temperature reaches 103 ℃ (as read on the thermometer) at 15 mm Hg, collect about 10 drops in the first receiver flask and change it to the second one by turning the adaptor. Collect the fraction up to 107 ℃ at 15 mm Hg. Then change to the third receiver flask and switch off the heating. Let the apparatus cool down before disconnecting the vacuum line and letting air in.

Note. Use the pressure nomogram to recalculate the temperatures if you observe pressure other than 15 mm Hg.

Record the pressure and the temperature of distillation.

Attention!
Never use flat-bottomed flasks as receivers!
Always wear protective glasses or mask when doing vacuum distillation!

D. Analysis of the product

Weigh the receiver flask with the required fraction and find the mass of the product. Calculate the yield.

Determine the refractive index n_D^{20} of the product using the refractometer. If you perform the measurement at a different temperature, reduce the obtained value to 20 ^oC.

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Questions

32.1 What is the role of toluene in the above process?

32.2 Write down the reaction mechanism.

32.3 Suppose ^{18}O-labeled ethyl alcohol and ^{18}O-labeled *tert*-butyl alcohols are involved into the reactions instead of unlabeled ethyl alcohol. Which compound(s) will be the ^{18}O atom found in when the reactions with the labeled alcohols are complete? Prove your choice.

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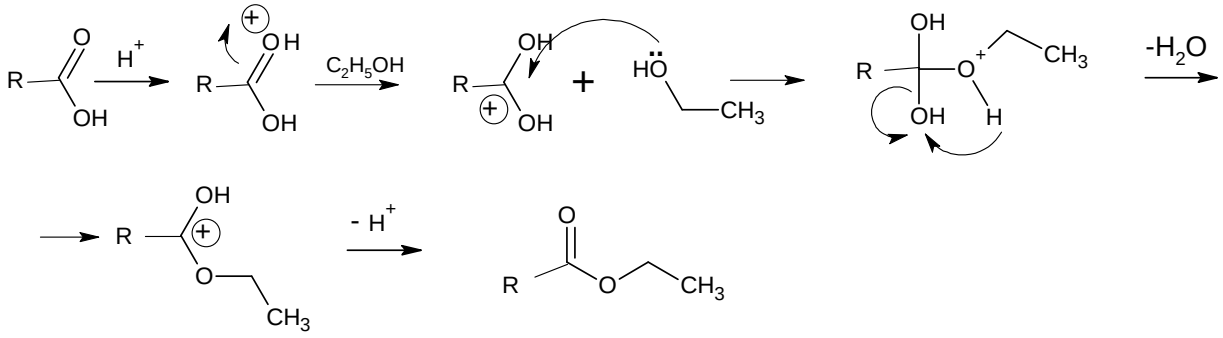
SOLUTION OF PREPARATORY PROBLEM 32

Product	Appearance	Melting/Boiling point, °C	n_D^{20}	Yield, %
Diethyl ester of succinic acid	Colorless liquid	105℃ at 15 mm Hg	1.4256	23 g (87 %)

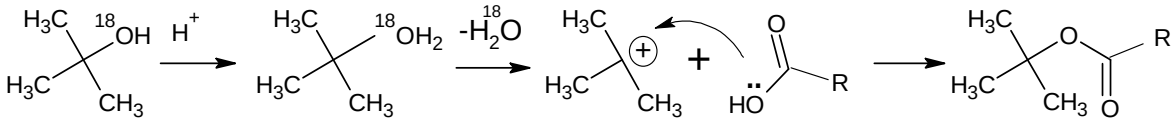
NMR reference data ($CDCl_3$)
1.23 (t, 6H, J=7.1 Hz, CH_3), 2.59 (s, 4H, CH_2CO), 4.12 (q, 2H, J=7.1 Hz, $C\underline{H_2}C\underline{H_3}$)

32.1 Toluene forms a ternary azeotrope with water and ethanol with the boiling temperature of 75 ℃. The boiling point of diethyl succinate is 218 ℃. The difference in the temperatures allows removing water from the reaction mixture, thus shifting the equilibrium towards the reaction product formation.

32.2

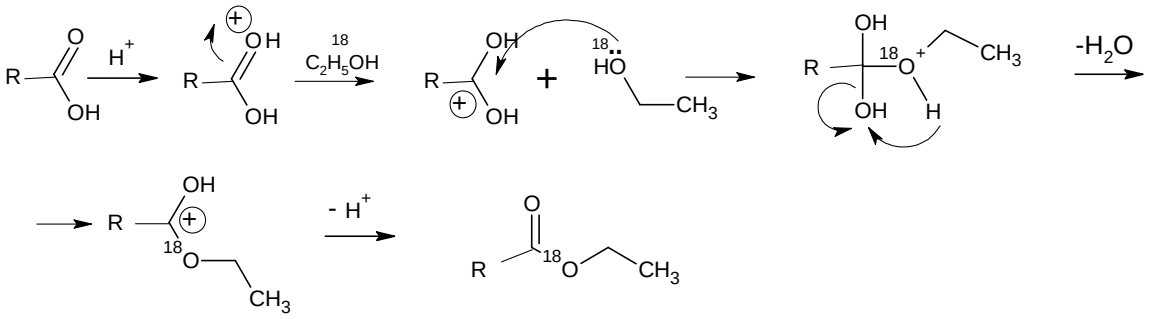


32.3 The *tert*-butyl alcohol molecule is protonated first, which is followed by a water molecule release. As a result, a relatively stable *tert*-butyl cation reacts with the acid molecule. Consequently, the isotopic label will be found in the H_2O molecule:



In the other case it is the acid molecule which is protonated first at the oxygen atom. Then one of the C-O bonds is cleaved giving the carbocation, which further

attacks the alcohol molecule followed by the proton elimination. Thus, the isotopic label remains in the ester molecule:

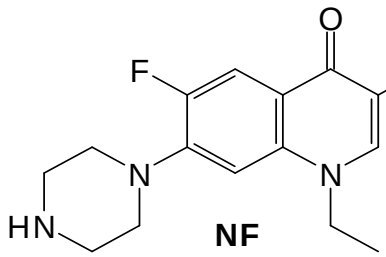


PREPARATORY PROBLEM 33 (PRACTICAL)

Kinetic studies of Norfloxacin oxidation with permanganate in alkaline medium

Norfloxacin [1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid] is a synthetic fluoroquinolone antibacterial agent of broad spectrum characterized by high activity against many gram-positive and gram-negative bacteria. As a result of constantly increasing administration, fluoroquinolones are expected to enter environment via waste waters. These substances are capable of bringing serious harm to aquatic life even if present in marginal concentrations mainly by giving rise to drug-resistant bacteria. Development of advanced oxidation processes leading to transformation of fluoroquinolones in water is an important task of contemporary chemistry.

Recently it was found that Norfloxacin (NF) can be oxidized by potassium permanganate in alkaline medium according to the following reaction:



NF

$$+ 2\ MnO_4^- + 2\ OH^- = \mathbf{A} + 2\ MnO_4^{2-} + H_2O$$

Product of oxidation

According to the mass action law, the reaction rate can be expressed as:

$$r = k\,[NF]^{\nu_1}\,[MnO_4^-]^{\nu_2}\,[OH^-]^{\nu_3}$$

where [NF], [MnO_4^-], [OH^-] are the concentrations of Norfloxacin, permanganate and alkali, respectively, and ν_1, ν_2, ν_3 are reaction orders with respect to the corresponding reagents.

In this task you will determine the reaction orders with respect to the involved reagents following the reaction progress photometrically at 525 nm, the wavelength of maximum absorbance of permanganate.

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Chemicals and reagents

- Potassium permanganate,
- Sodium hydroxide,

- Sodium perchlorate,
- Norfloxacin

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Equipment and glassware

- Analytical balance (± 0.0001 g),
- Visible spectrophotometer (or photometer with fixed wavelength of 525 nm) equipped with thermostated cell holder,
- Spectrophotometer cells with 3.5 cm optical path length (you will need to recalculate concentrations of the reagents if you use cells with different optical path length),
- Tissue to clear cell surfaces,
- Thermostat,
- PC (or other computing techniques) with Microsoft Excel software (English version),
- Volumetric flasks, 100 cm^3 (4 ea.),
- Graduated cylinder, 100 cm^3,
- Volumetric pipettes, 1, 2, 5, and 10 cm^3,
- Pipette filler,
- Spatula

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Procedure

A. Preparation of stock solutions

Read the procedure to the end and calculate the concentrations of stock solutions of potassium permanganate, sodium hydroxide, sodium perchlorate, and Norfloxacin that will allow easy preparation of the reaction mixtures to be analyzed. Prepare the stock solutions of potassium permanganate, sodium hydroxide and sodium perchlorate in the volumetric flasks according to standard procedures. Norfloxacin suffers from poor solubility in water at neutral pH values, thus first dissolve it in a small amount (about 6 cm^3) of 0.3 mol dm^{-3} alkali solution (in the volumetric flask) and then add water to attain the required concentration. Do not forget to account for the amount of alkali introduced with the Norfloxacin solution when preparing the reaction mixtures. Close the flasks containing the stock solutions with stoppers and place them into the thermostat pre-adjusted to 25 ^oC.

Note. Norfloxacin is commercially available as a pure reagent. Also, it can be found as an ingredient in medicines. In the latter case, it is recommended to check that the other ingredients do not interfere with Norfloxacin when it is being oxidized by potassium permanganate.

B. General design of the task

The experimental work consists of three parts as can be seen from the hereunder table:

- Part 1: Concentration of $KMnO_4$ is varied, concentrations of all other reagents being constant (lines 1 to 5);
- Part 2: Norfloxacin (NF) concentration is varied, concentrations of all other reagents being constant (lines 6 to 10);
- Part 3: Concentration of NaOH is varied, concentrations of all other reagents being constant (lines 11 to 16).

Line	$c(MnO_4^-)\cdot\times10^4$ (mol dm^{-3})	$c(NF)\cdot\times10^3$ (mol dm^{-3})	$c(OH^-)\times\cdot10^2$ (mol dm^{-3})	$c(ClO_4^-)\times\cdot10^2$ (mol dm^{-3})	k_{obs}
1	0.4	1.0	5.0	5.0	
2	0.8	1.0	5.0	5.0	
3	1.0	1.0	5.0	5.0	
4	2.0	1.0	5.0	5.0	
5	4.0	1.0	5.0	5.0	
6	1.0	0.8	5.0	5.0	
7	1.0	1.0	5.0	5.0	
8	1.0	4.0	5.0	5.0	
9	1.0	6.0	5.0	5.0	
10	1.0	8.0	5.0	5.0	
11	1.0	1.0	1.0	5.0	
12	1.0	1.0	2.0	5.0	
13	1.0	1.0	5.0	5.0	
14	1.0	1.0	6.0	5.0	
15	1.0	1.0	8.0	5.0	
16	1.0	1.0	10.0	5.0	

C. Determination of the reaction orders

1. Adjust the temperature of the thermostated cell unit to 25 ^{o}C.
2. Place the flasks with the stock solutions in the thermostat and let the solutions attain the desired temperature. Check the temperatures inside the flasks from time to time with the thermometer. Always carefully wash the thermometer with water before placing it in the next flask.
3. When ready with the temperature of the solutions, use the spectrophotometer cell to prepare the mixture containing $KMnO_4$, NaOH, and $NaClO_4$ in concentrations as indicated in the corresponding line in the Table. Add the Norfloxacin solution last (note that its introduction initiates the reaction) and promptly place the cell into the thermostated cell holder.

Note. If a thermostated cell holder is not available, fulfill the task at room temperature having in mind that temperature alterations will produce only slight effect on the results of kinetic studies.

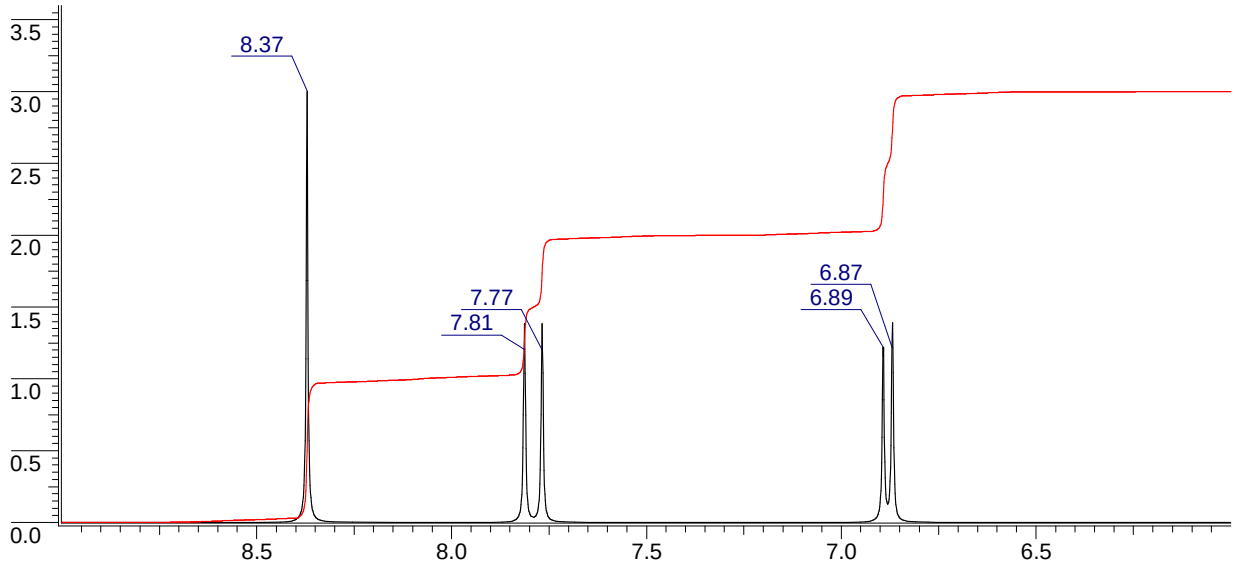
4. Immediately start recording the absorbance at the wavelength of 525 nm. Continue measuring till the absorbance remains constant (A_∞).
5. Plot the obtained data as the dependence of $\log(A_t - A_\infty)$ on time (A_t is the reaction mixture absorbance at time t).
6. Carefully wash the cell with plenty of water, dry the cell and wipe the walls with clean tissue.
7. Use the initial straight part of the curve to calculate the observed rate constant of Norfloxacin oxidation. Write down the value in the Table.
8. Repeat steps 3-7 for all the lines of the Table.

———

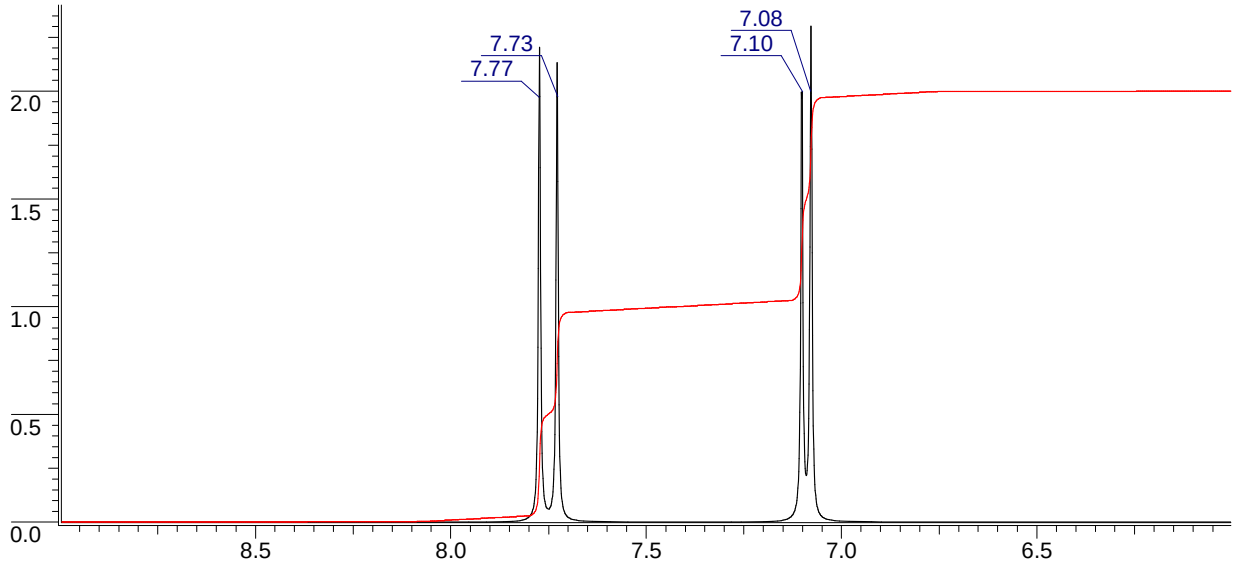
D. Questions and Data Analysis

33.1 Propose the structure of the oxidized product **A** based on data given below:

- mass spectrum of the product A have peaks with m/z = 335, 321, and 64;
- NMR spectra (aromatic region) of Norfloxacin and the product A are as follows:



^{1}H NMR spectrum (300 MHz, 5 % NaOD/D_2O, aromatic region) of Norfloxacin



^{1}H NMR spectrum (300 MHz, 5% NaOD/D_2O, aromatic region) of the product **A**.

33.2 Explain the ^{1}H NMR spectral pattern of Norfloxacin in the aromatic region.

33.3 Propose coordinates allowing determination of the reaction order with respect to a reagent.

33.4 Using the found values of k_{obs} and compositions of the mixtures, sketch the necessary plots and determine the reaction orders with respect to permanganate, Norfloxacin, and alkali.

Note. You are expected to fulfill this item by using the English version of Microsoft Excel software.

33.5 Write down the expression for calculation of the rate of Norfloxacin oxidation with permanganate.

The mechanism of Norfloxacin oxidation by alkaline manganese(VII) is given hereunder (**B** and **C** are intermediates of the process).

$$MnO_4^- + OH^- \overset{K_1}{\rightleftharpoons} [MnO_4OH]^{2-}$$

$$NF + [MnO_4OH]^{2-} \overset{K_2}{\rightleftharpoons} \mathbf{B}$$

$$\mathbf{B} \xrightarrow[\text{slow}]{k_1} \mathbf{C} + MnO_4^{2-} + H_2O$$

$$\mathbf{C} + [MnO_4OH]^{2-} \xrightarrow[\text{fast}]{k_2} \mathbf{A} + MnO_4^{2-}$$

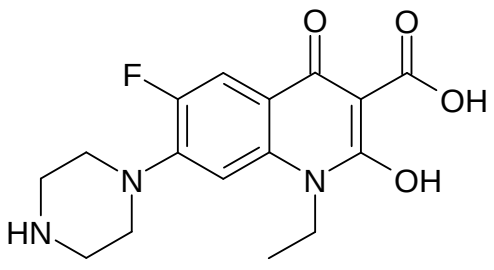
33.6 Propose the structures of **B** and **C**. Note that **C** is a radical.

33.7 Propose the expression for the rate of Norfloxacin oxidation with permanganate according to the above scheme.

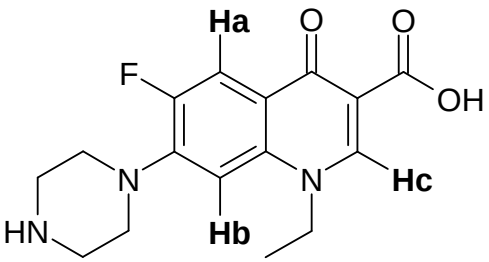
SOLUTION OF PREPARATORY PROBLEM 33

33.1

A =



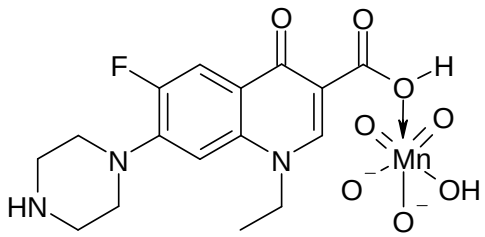
33.2



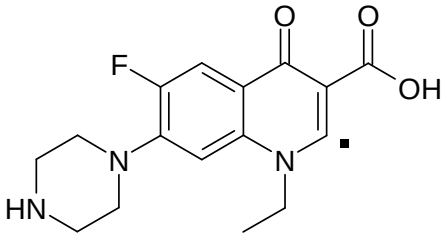
6.88 (d; $^4J_{H\text{-}F}$ = 6.9 Hz; 1H; $\mathbf{H_b}$); 7.79 (d; $^3J_{H\text{-}F}$ = 13.6 Hz; 1H; $\mathbf{H_a}$); 8.37 (s; 1H; $\mathbf{H_c}$)

33.6

B =



C =



33.7 $$\text{rate} = -\frac{\mathrm{d}[MnO_4^-]}{\mathrm{d}t} = \frac{k_1 K_1 K_2 [NF]\,[MnO_4^-]_0\,[OH^-]}{1 + K_1[OH^-] + K_1 K_2 [OH^-][NF]}$$

(use the quasi-equilibrium approximation for the first two reactions and material balance with respect to $[MnO_4^-]$, for details see Naik et al., *Ind. Eng. Chem. Res.* 2009, 48, 2548 – 2555).

PREPARATORY PROBLEM 34 (PRACTICAL)

Temperature dependence of the reaction rate of disproportionation

Autocatalytic reaction is a chemical process in which at least one of the reactants turns out to be also a product. The rate equations for autocatalytic reactions are fundamentally nonlinear. Oxidation of oxalic acid with permanganate is one of famous examples of such reactions. When no manganese(II) ions are added into the system, the reaction initially proceeds slowly. Still, at a particular moment the rate gradually increases because the product autocatalyzes the reaction. Addition of a few crystals of $MnSO_4$ greatly accelerates the reduction of purple permanganate affording a grayish-brown complex ion **A**. This complex ion is characterized by an extremely low stability in water and practically immediately starts decomposing via disproportionation giving colorless products.

The progress of the disproportionation reaction can be followed photometrically at the wavelength of 405 nm corresponding to the maximum absorbance of the trioxalomanganesate ion. Since potassium permanganate is rapidly and quantitatively consumed in the reaction and all the rest substances found in the reaction mixture are colorless, the measured value of the absorbance (A) is proportional to the complex ion concentration (c) according to Beer-Lambert-Bouguer law:

$$A = \varepsilon c l$$

where ε is the molar extinction coefficient and l is the optical path length.

Chemicals and reagents

- Potassium permanganate,
- Manganese(II) sulphate,
- Oxalic acid,

Equipment and glassware

- Analytical balance (± 0.0001 g),
- Visible spectrophotometer (or photometer with fixed wavelength of 405 nm) equipped with thermostated cell holder,
- Spectrophotometer cells,
- Tissue to clear cell surfaces,

- Thermostat,
- Thermometer,
- PC (or other computing techniques) with Microsoft Excel software (English version),
- Volumetric flask, 100 cm^3, with a tight stopper (4 ea.),
- Graduated cylinder, 100 cm^3,
- Volumetric pipettes, 5 and 10 cm^3,
- Pipette filler,
- Spatula.

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Procedure

A. Preparation of stock solutions

Read the procedure to the end and calculate the concentrations of stock solutions of potassium permanganate, manganese(II) sulfate, and oxalic acid that will allow easy preparation of the reaction mixture to be analyzed. Prepare the stock solutions of potassium permanganate, manganese(II) sulfate, and oxalic acid in the volumetric flasks according to standard procedures.

B. General design of the task

The reactions are carried out at five different temperatures, always with the same concentrations of the reagents manganese(II) sulfate (0.012 mol dm^{-3}), oxalic acid (0.085 mol dm^{-3}), and potassium permanganate (0.002 mol dm^{-3}). The disproportionation progress is always followed photometrically at the wavelength of 405 nm by detecting the decrease of the complex ion concentration. The reactions are first conducted at a temperature between 20 and 25 ^oC. When changing to new conditions, the temperature is always increased by about 10 ^oC. Carefully fix the actual temperatures studied. This will be of importance in order to get reliable results when analyzing the experimental data.

C. Determination of the temperature dependence of the reaction rate

1. Prepare the mixture containing $MnSO_4$ and oxalic acid in the required concentrations in the volumetric flask.

2. Adjust the temperature of the thermostated cell unit and that of the thermostat to the required temperature. Place the flasks with the reaction mixture and potassium permanganate stock solution in the thermostat and let the mixture and the solution attain the desired temperature. Check the temperatures inside the flasks from time to time with the thermometer. Always carefully wash the thermometer with water before placing it in the next flask.
3. When ready with temperatures, add the required amount of potassium permanganate stock solution and mix well for 2 - 3 s. Transfer the mixture promptly to the photometer cell, place the cell into the cell holder and immediately start recording the absorbance.

   Note. The thermostated cell holder is desirable, still can be omitted, since the reaction is completed within a short period of time. As a result, the temperature alterations will produce only slight effect on the results of kinetic studies.

4. Continue recording the absorbance till the reaction mixture turns colorless.
5. Carefully wash the cell with plenty of water, dry the cell and wipe the walls with clean tissue.
6. Repeat the steps 2-5 for the other four temperatures.

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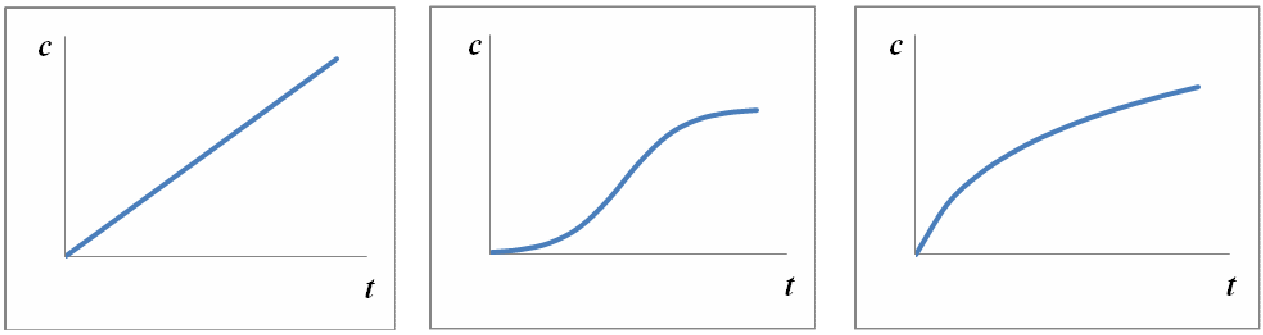
D. Questions and Data Analysis

34.1 Choose the plot which corresponds to the autocatalytic reaction (c is the product concentration, and t is time)



a **b** **c**

34.2 Propose the formula of the ion **A** if it known that its charge is –3 and it contains 17.22 % of manganese.

34.3 Write down the equation of the formation of **A**.

34.4 Write down the equation of the disproportionation of **A**.

34.5 Graphically determine the general reaction order by testing the first and second order coordinates and choosing which of these provide for the best fit.

34.6 For each temperature studied, draw a plot in the coordinates chosen in i. 2 and determine the value of the rate constant. Hint: use the initial section of plot.

34.7 Calculate the activation energy of the disproportionation reaction.

Note. You are expected to fulfill ii. 34.5 – 34.7 by using the English version of Microsoft Excel software.

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SOLUTION OF PREPARATORY PROBLEM 34

34.1 Plot b.

34.2 A = $[Mn(C_2O_4)_3]^{3-}$

34.3 $Mn^{2+} + 6\ H_2C_2O_4 + MnO_4^- = [Mn(C_2O_4)_3]^{3-} + 4\ H_2O + 4\ H^+$.

34.4 $2\ [Mn(C_2O_4)_3]^{3-} + 6\ H^+ = 2\ MnC_2O_4 + 2\ CO_2 + 3\ H_2C_2O_4$.