Worked solutions to preparatory problems

47th International Chemistry Olympiad (IChO-2015)

Moscow State University
Baku Branch
Azerbaijan

Please, send all the comments and questions to:
Vadim Eremin (vadim@educ.chem.msu.ru)
Sasha Gladilin (alexander.gladilin@simeon.ru)

Sent to head mentors February 16, 2015
Released on the web-site May 31, 2015

Contents

Theoretical problems

Problem 1.	Brayton cycle	3
Problem 2.	Liquefied natural gas	5
Problem 3.	Carnot cycle	6
Problem 4.	Quasi-equilibrium model	7
Problem 5.	The Second Law of thermodynamics applied to a chemical reaction	9
Problem 6.	Catalytic transformation of a single molecule on a single nanoparticle	11
Problem 7.	Esterification of a dicarboxylic acid	12
Problem 8.	Three elements	14
Problem 9.	Simple experiments with copper(II) chloride	15
Problem 10.	An element typical for Azerbaijan mud volcanoes expelled water	16
Problem 11.	The Prussian blue	17
Problem 12.	Substitution in square planar complexes	18
Problem 13.	Redox equilibria in aqueous solutions	19
Problem 14.	Determination of acetylsalicylic acid purity	20
Problem 15.	Chemical dosimeter	21
Problem 16.	Determination of water in oil	23
Problem 17.	Oxidation and inspiration	26
Problem 18.	Essential ozone	28
Problem 19.	Two in one	32
Problem 20.	Antitussive “narcotine”	33
Problem 21.	Pyrrolizidine alkaloids	35
Problem 22.	Delightful odor of truffle	37
Problem 23.	Synthesis of large rings. The magic or routine work?	38
Problem 24.	What Time is it in Baku or Cheating the Death	41
Problem 25.	Number One Enzyme	45
Problem 26.	Holy War against Four Horsemen of the Apocalypse	47

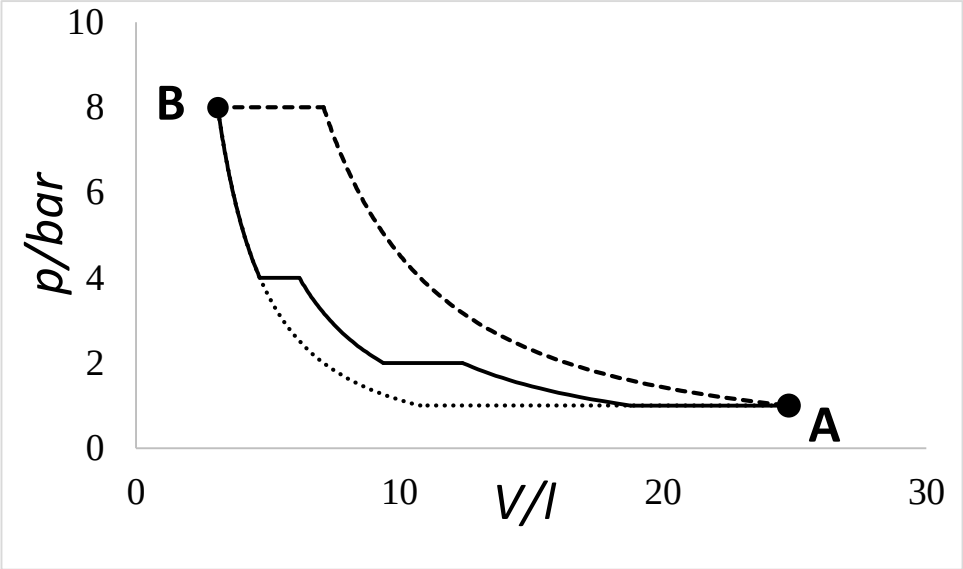
Practical problems

Problem 27.	Determination of nickel in nickel and copper-nickel alloys by complexometric titration	52
Problem 28.	Titrimetric determination of lead and silver in their mixture	54
Problem 29.	Complexometric determination of iron, chromium, and zinc in an alloy	54
Problem 30.	Synthesis of 3-(4-methylbenzoyl)propionic acid	56
Problem 31.	Synthesis of 4-(4-methylphenyl)-4-hydroxybutanoic acid	57
Problem 32.	Synthesis of diethyl ester of succinic acid	60
Problem 33.	Kinetic studies of Norfloxacin oxidation with permanganate in alkaline medium	61
Problem 34.	Temperature dependence of the reaction rate of disproportionation	63

Theoretical problems

Problem 1. Brayton cycle

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 $\frac{T^{5/3}}{p^{2/3}} = \text{const}$, or $\frac{T}{p^{2/5}} = \text{const}$. 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, $W = \frac{5}{2}\cdot 8.314 \cdot 298 \cdot \left(1 - \left(\frac{1}{8}\right)^{2/5}\right) = 3500$ J.

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

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

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

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.

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: $W = n\cdot\frac{5}{2}RT_2\left(1 - \left(\frac{1}{8}\right)^{2/5n}\right)$. After some calculations with different integer *n*, we find that *n* = 13.

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

Problem 2. Liquefied natural gas

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

2. Under 300 bar pressure at 298 K, 40000 m^3 have the mass $m = \frac{pVM}{RT} = \frac{300 \cdot 10^5 \cdot 40000 \cdot 0.016}{8.314 \cdot 298} = 7.75 \cdot 10^6$ kg, or 7750 tons. Thus, LNG has $\frac{16800}{7750} = 2.17$ times larger energy density.

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 $\Delta U = 7.2\ \text{kJ} \cdot \text{mol}^{-1}$. Thus, $\Delta H = \Delta U + RT = 8.1\ \text{kJ} \cdot \text{mol}^{-1}$.

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

5. Total heat obtained by methane is $Q = 50000 \cdot 3600 \cdot 24 \cdot 9 \cdot 30.5 = 1.19 \cdot 10^{12}$ J. It will lead to an increase of the internal energy per mole of methane by $\Delta U = \frac{Q}{m} \cdot M = \frac{1.19 \cdot 10^{12}}{16800000 / 3} \cdot 0.016 = 3.39$ $\text{kJ} \cdot \text{mol}^{-1}$. From the diagram, the initial internal energy at –159 °C is 0.1 $\text{kJ} \cdot \text{mol}^{-1}$. The abscise of the point corresponding to the final state on the diagram will thus be approximately 0.1 + 3.4 = 3.5 $\text{kJ} \cdot \text{mol}^{-1}$. 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.

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.

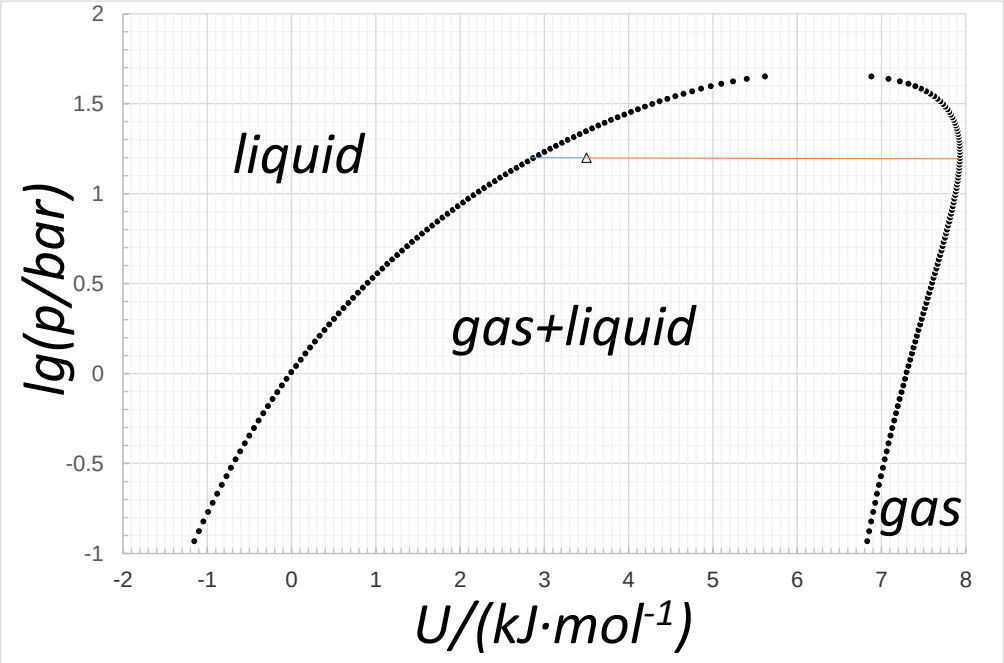


Figure. Graphical answer to question 5

Problem 3. Carnot cycle

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

2. $\eta = \dfrac{T_2 - T_1}{T_2} = \dfrac{390 - 298}{390} = 0.24$.

3. Since $pV^{(1+R/C_V)} = p\left(\dfrac{RT}{p}\right)^{(1+R/C_V)} = \text{const}$, then $\dfrac{T^{(1+R/C_V)}}{p^{R/C_V}} = \text{const}$, or $\dfrac{T}{p^{R/(C_V+R)}} = \text{const}$. Thus, we can find C_V from the initial and final temperatures and pressures of the adiabate:

$$\ln\frac{T_2}{T_1} \Big/ \ln\frac{p_2}{p_1} = R/\left(C_V + R\right)$$

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

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

Problem 4. Quasi-equilibrium model

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

$$r_1 \approx r_{-1},$$

$$k_1[\mathrm{A}][\mathrm{B}] \approx k_{-1}[\mathrm{AB}]$$

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

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

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

$$k_{\text{eff}} = \frac{k_1 k_2}{k_{-1}} = 200\, M^{-1}\,\mathrm{s}^{-1}$$

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

$$2\mathrm{F} \rightleftarrows \mathrm{F}_2 \qquad (2a).$$

$$K_p = 1.7 \cdot 10^3 \text{ bar}^{-1} = \frac{p_{\mathrm{F}_2}}{p_{\mathrm{F}}^2};\ p_{\mathrm{F}} = 10^{-5} \text{ bar}$$

$$p_{\mathrm{F}_2} = 1.7 \cdot 10^{-7} \text{ bar}$$

Partial pressure of molecular fluorine near the surface is negligible.

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

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

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

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

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

within the desorbed flow. Then

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

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

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

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

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

or

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

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

$$\alpha \frac{p_{\mathrm{F_{Inc}}}}{(m_{\mathrm{F}})^{1/2}} \approx 2\frac{p_{\mathrm{PtF_2}}}{(m_{\mathrm{PtF_2}})^{1/2}}$$

The rate of gasification is

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

2.5. As it was shown in 2.4,

$$\alpha \frac{p_{\mathrm{F_{Inc}}}}{(m_{\mathrm{F}})^{1/2}} \approx 2\frac{p_{\mathrm{PtF_2}}}{(m_{\mathrm{PtF_2}})^{1/2}}$$

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

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

2.6. $r_{\mathrm{Pt}} = \frac{dn_{\mathrm{Pt}}}{dt} = \rho_{\mathrm{PtF_2}} + \rho_{\mathrm{PtF_4}} \approx \rho_{\mathrm{PtF_2}} \approx \frac{\alpha}{2}\rho_{\mathrm{F_{Inc}}}$

$$r_{\mathrm{Pt}} \approx \rho_{\mathrm{PtF_2}} \approx \frac{0.1}{2}\rho_{\mathrm{F,In}} = \frac{0.1}{2} \cdot \frac{p_{\mathrm{F_{In}}}}{(2\pi m_{\mathrm{F}} RT)^{1/2}} N_{\mathrm{A}} = \frac{0.1}{2} \cdot 2 \cdot 10^{18} = 10^{17} \text{ atoms/cm}^2/\text{s}$$

In 15 minutes,

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

will be gasified.

Problem 5. The Second Law of thermodynamics applied to a chemical reaction

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

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

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,

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

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

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

and

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

$[C]_{eq}$, $[B]_{eq}$, $[A]_{eq}$ 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

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

3.1. $(a')\quad \Delta G_{\text{Reaction}} = \Delta G^0_{\text{Reaction}} + RT\ln\dfrac{[\text{HBr}]^2}{[\text{H}_2][\text{Br}_2]}$

$(a'')\quad \Delta G_{\text{Reaction}} = \Delta G^0_{\text{Reaction}} + RT\ln\dfrac{[\text{HBr}][\text{Br}]}{[\text{H}][\text{Br}_2]}$

$(a''')\quad \Delta G_{\text{Reaction}} = \Delta G^0_{\text{Reaction}} + RT\ln[\text{CO}_2]$

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

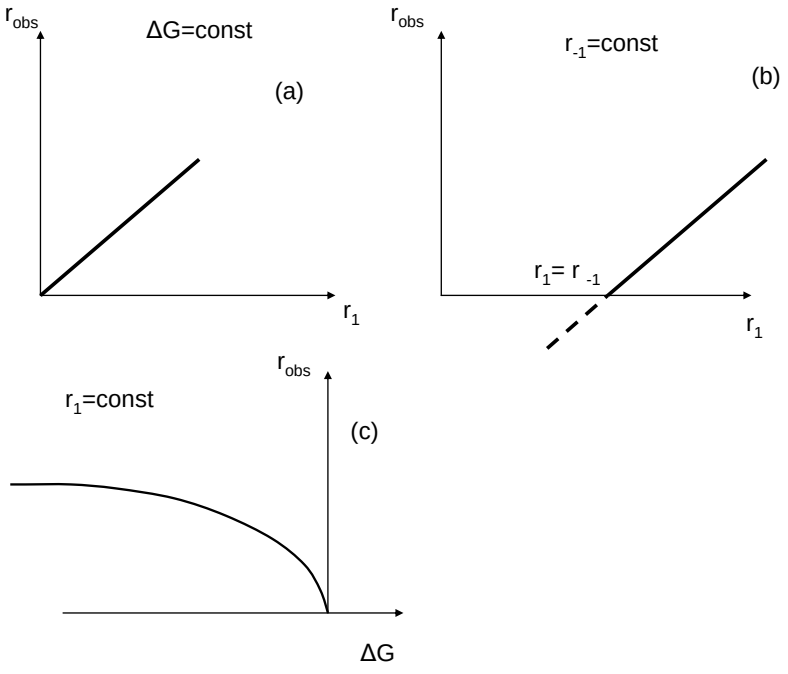
4.

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

$$\frac{r_{-1}}{r_1} = \frac{k_{-1}}{k_1}\frac{[\text{C}]}{[\text{A}][\text{B}]} = \frac{k_{-1}}{k_1}\frac{2}{0.5\cdot 1} = 0.5; \quad \frac{k_{-1}}{k_1} = 0.125\,\text{M}$$

$$\frac{k_1}{k_{-1}} = K = 8\ \text{M}^{-1}$$

5.



6. Table.

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

Problem 6. Catalytic transformation of a single molecule on a single nanoparticle

1. a) $V_{\text{Au nano}} = 4/3\pi R^3 = 1.13\cdot10^{-19}$ cm^3, $m_{\text{Au nano}} = 1.13\cdot10^{-19}$ cm^3 · 19.32 g/cm^3 = $2.18\cdot10^{-18}$ g, $N_{\text{Au atoms}} = 2.18\cdot10^{-18}$ g / 196.97 · $6.02\cdot10^{23}$ = 6675 atoms.

b) $f = V_{\text{surface}} / V_{\text{Au nano}} = (V_{\text{Au nano}} - V_{\text{core}}) / V_{\text{Au nano}} = 1 - (r^3(\text{core})/r^3(\text{Au nano})) = 1 - (3–0.7)^3/3^3 = 0.55$.

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:

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

3. 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 – were it from many molecules, the peaks would have variable heights depending on the number of molecules.

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

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

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

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

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

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

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

5.

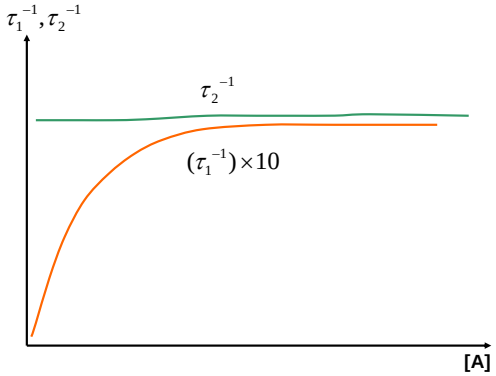


Fig. 3. $[\tau_2]^{-1}, [\tau_1]^{-1}$ *vs* [A]

$[\tau_2]^{-1}$ is independent of [A], $[\tau_1]^{-1}$ increases with the increase of [A] and approaches constant value when $K_{ad}[A] >> 1$ (see Answer 4)

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 4).

Problem 7. Esterification of a dicarboxylic acid

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:

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

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 $x = \sqrt{K_1K_2}$: $\eta_{max} = \dfrac{1}{1+2\sqrt{\dfrac{K_2}{K_1}}}$. 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:

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

From the material balance with respect to water we get:

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

$$[\mathrm{E}] = \frac{[\mathrm{H_2O}]}{\sqrt{K_1K_2}} = [\mathrm{A}]\left(\frac{2}{\sqrt{K_1K_2}}+\frac{1}{K_2}\right)$$

The initial concentrations of ethanol and acid are:

$$[\mathrm{E}]_0 = [\mathrm{E}] + [\mathrm{M}] + 2[\mathrm{D}] = [\mathrm{A}]\left(\frac{2}{\sqrt{K_1K_2}}+\frac{1}{K_2}\right)+[\mathrm{A}]\sqrt{\frac{K_1}{K_2}}+2[\mathrm{A}],$$

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

And the optimal ratio is:

$$X = \frac{[\mathrm{E}]_0}{[\mathrm{A}]_0} = \frac{\dfrac{2}{\sqrt{K_1K_2}}+\dfrac{1}{K_2}+\sqrt{\dfrac{K_1}{K_2}}+2}{2+\sqrt{\dfrac{K_1}{K_2}}} = 1+\frac{1}{\sqrt{K_1K_2}}.$$

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

Answers.

1. $X = 1.05$.
2. $\eta_{max} = 1/3$.
3. $X = 1 + \frac{1}{\sqrt{K_1 K_2}}$, $\eta_{max} = \frac{1}{1 + 2\sqrt{\frac{K_2}{K_1}}}$.

Problem 8. Three elements

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:

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

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

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:

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

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,

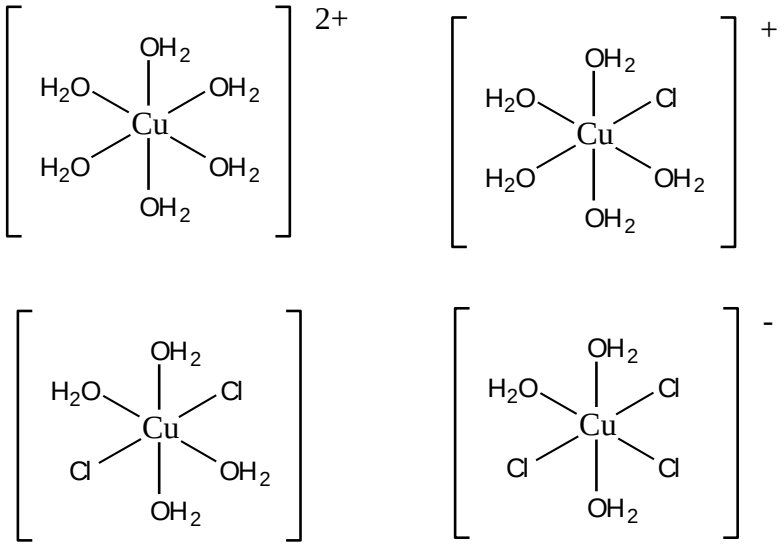
$$\omega(\text{C in } A_cC_a) = \frac{aM(\text{C})}{cM(\text{A}) + aM(\text{C})} = \frac{\frac{M(\text{C})}{c}}{\frac{M(\text{A})}{a} + \frac{M(\text{C})}{c}} = \frac{3.93}{1 + 3.93} = 0.798.$$

Problem 9. Simple experiments with copper(II) chloride

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:

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

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.

3. (a) $CuCl_2 + Zn = Cu\downarrow + ZnCl_2$ (red precipitate – copper),

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

(c) no noticeable changes,

(d) $CuCl_2 + Na_2S = CuS\downarrow + 2NaCl$ (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 (+1) and copper(+2).

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

$CuSO_4 + Zn = ZnSO_4 + Cu$

$Cu + Cl_2 = CuCl_2$.

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

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

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

Problem 10. An element typical for Azerbaijan mud volcanoes expelled water

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 $\Rightarrow$ Li, but it doesn't exist in +2 oxidation state.

n = 1.5 gives M(X) = 10.8 $\Rightarrow$ B. It's true as boron generally exists in +3 oxidation state. X is B.

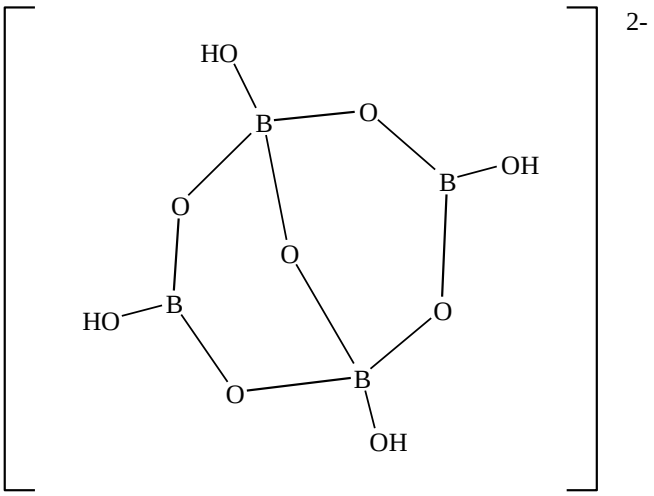
In water solution boron forms anionic oxo-species, the counter ion could be sodium as one of dominant ions in expelled water. The common boron mineral that contains sodium is borax $Na_2B_4O_7 \cdot 10H_2O$, it contains 11.3 wt.% of boron.

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

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: $m(Na_2B_4O_7 \cdot 10H_2O)$ = 250 / 0.113 = 2212 mg = 2.2 g.

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:

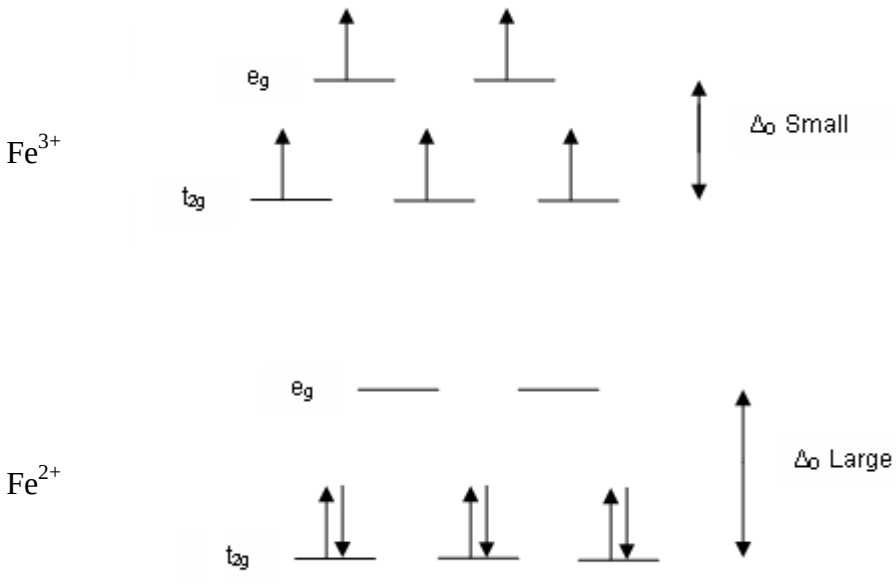


Problem 11. The Prussian blue

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

$$4Fe^{3+} + 3[Fe(CN)_6]^{4-} \rightarrow Fe^{3+}[Fe^{3+}Fe^{2+}(CN)_6]_3$$

2.



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.

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

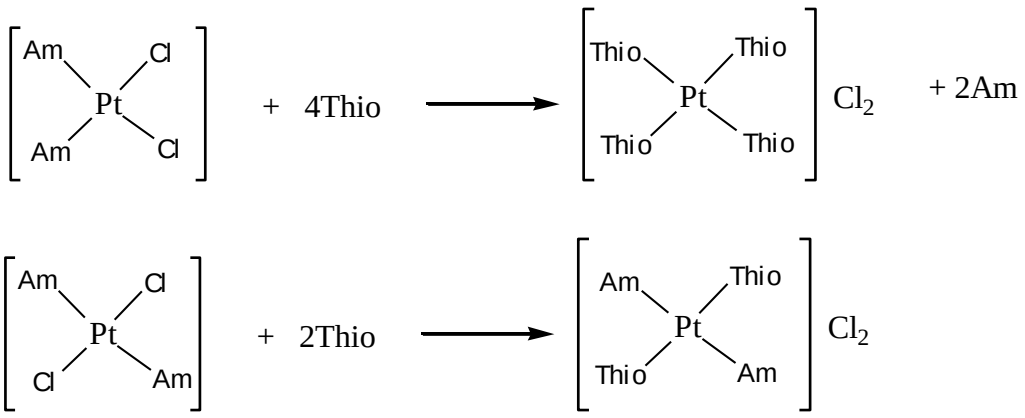
$$K^+ + Fe^{3+} + [Fe(CN)_6]^{4-} \rightarrow K^+[Fe^{3+}Fe^{2+}(CN)_6]$$

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

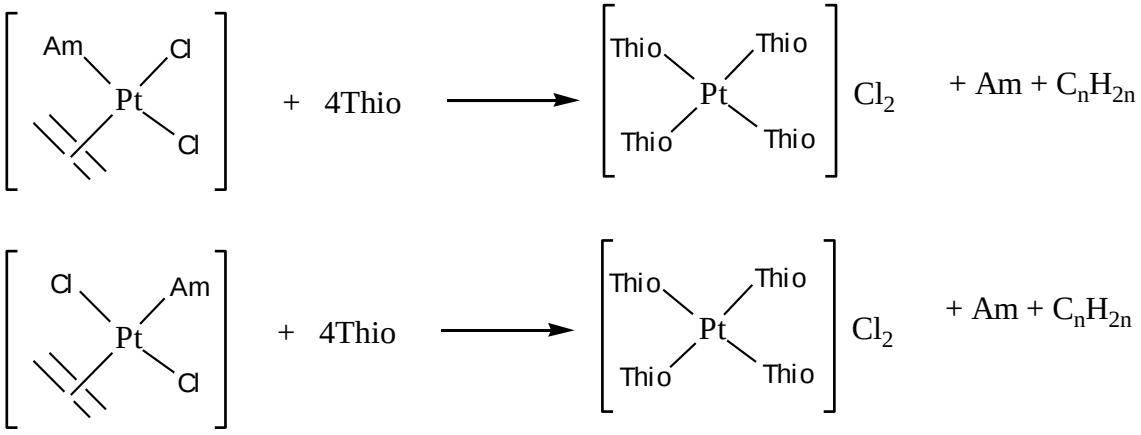
Problem 12. Substitution in square planar complexes

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

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.



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



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:

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

Problem 13. Redox equilibria in aqueous solutions

1) The aqua-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

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

$E° = 1.692 – 1.401 = 0.291$ V.

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

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

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

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

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

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

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

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

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

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

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

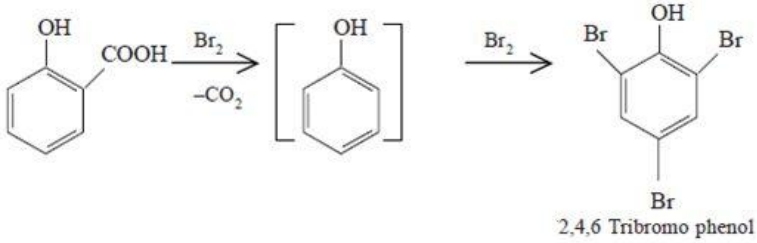
$1.763 – 0.059\ pH > 1.154$,

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

Problem 14. Determination of acetylsalicylic acid purity

1. $5KBr + KBrO_3 + 3H_2SO_4 = 3Br_2 + 3H_2O + 3K_2SO_4$

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



2,4,6 Tribromo phenol

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

$$\log K' = \frac{\left(E^{0\prime}_{2BrO_3^-/Br_2} - E^0_{Br_2/2Br^-}\right)}{0.059} * 10 = \frac{\left(E^0_{2BrO_3^-/Br_2} - 0.059\frac{12}{10} * pH - E^0_{Br_2/2Br^-}\right)}{0.059} * 10 = 0;$$

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

3. $Br_2 + NaAsO_2 + 2H_2O = 2HBr + NaH_2AsO_4$

4. $\nu(KBr) = 0.5950$ g / 119.00 g/mol = 5.00 mmol

$\nu(KBrO_3) = 0.1670$ g / 167.00 g/mol = 1.00 mmol → $\nu(Br_2)^{total}$ = 3.00 mmol in 100.0 mL and $\nu(Br_2)^{total}$ = 0.600 mmol in 20.00 mL.

$\nu(NaAsO_2) = \nu(Br_2) = 0.02015$ M * 9.93 mL = 0.200 mmol = excess of bromine

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

ν(salicylic acid) = 0.400 / 3 in aliquote (25 mL)

ν(salicylic acid) = 0.400 mmol* 10 / 3 in 250 mL

m(salicylic acid) = 0.400 mmol*10*138.12 g/mol / 1000 /3 = 0.1842 g

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

5. Impurity is present at a level greater than allowed.

Problem 15. Chemical dosimeter

1.1. A).

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

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

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

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

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

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

2.2. a) Concentration of iron(II) can be calculated from equation 2.1(a):

$12.3 \cdot 0.1000 \cdot 5 = 20 \cdot x$,

$x = 0.3075$ M.

b) Using equation 2.1(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 2.1(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:

$1 \cdot x = 0.0888 \cdot 4.6$,

$x = 0.4085$ M.

c) The initial amount of potassium permanganate is 7.15 mL·0.1000 M = 0.7150 mmol. So, from stoichiometry of 2.1(a) the amount of Fe^{2+} is

$\nu(Fe^{2+}) = 7.15 \cdot 0.1000 \cdot 5 = 3.5750$ 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.

ν(Fe total) $= 13.7 \cdot 0.4150 = 5.6855$ mmol.

Then, the amount of iron(III) is:

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

The iron concentrations are:

$c(Fe^{2+}) = 3.5750 / 5 = 0.7150$ M,

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

3.1. **a**–6–β^- **b**–9–β^- **c**–4–α **d**–5–β^- **e**–8–α

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

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

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

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

The radioactivity is (round to the integer number):

$A_{Ra} = \lambda_{Ra} N_{Ra} = 2.6636 \cdot 10^{21} \cdot 1.3635 \cdot 10^{-11} = 36$ GBq.

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

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

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

Total radioactivity is the sum of both values:

$A_{tot} = 3$ GBq.

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

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

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

$$\frac{ln2}{T_{1/2(total)}} = \frac{ln2}{T_{1/2(e\ capture)}} + \frac{ln2}{T_{1/2(\beta)}}$$

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

$$T_{1/2(total)} = \frac{T_{1/2(e-capture)} \cdot T_{1/2(\beta)}}{T_{1/2(e-capture)} + T_{1/2(\beta)}} = \frac{20{,}8 \cdot 32{,}6}{20{,}8 + 32{,}6} = 12{,}7\ hours$$

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:

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

$\ln 0.1 = -\lambda t$,

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

Problem 16. Determination of water in oil

1.1. Reductant – sulfur dioxide, oxidizer – iodine.

1.2. C)

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

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

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

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

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:

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

Reaction of hydrogen iodide with peroxides:

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

Hydroperoxides produce equivalent amounts of iodine and water. The Karl 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:

$$R{-}CO{-}O{-}O{-}CO{-}R + 2HI \rightarrow 2RCOOH + I_2.$$

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

3.1. a) First, calculate the amounts of iodine and sulphur dioxide.

$\nu(I_2) = 49 / (2 \cdot 127) = 0.193$ mol, $\nu(SO_2) = 38.5 / 64 = 0.6$ mol.

Iodine is completely consumed. One molecule of iodine reacts with one molecule of sulphur oxide, so the theoretical titre is (in mg/mL):

$m(H_2O) = 0.193 / 1000 \cdot 18 = 3.5$ mg / mL.

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 / mL.

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:

$\nu(I_2) = 0.01 / 32 / 2$ mol.

Multiplying this value by the molar mass of water, the value of overstatement can be calculated (in milligrams):

$m(H_2O) = \nu(I_2) \cdot M(H_2O) = 2.8$ mg.

The total mass of determined water is therefore:

$m(H_2O) = 7.5 \cdot 3.3 = 24.8$ 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:

$\omega(H_2O) = 22.0$ mg / 1.00 g $\cdot$ 100% = 2.20%.

3.2. a) In oxidation of iodine two electrons are involved. Then, using the Faraday equation water content (mass %) is calculated:

$m(H_2O) = MQ / (nF) = 18 \cdot 375.3 / (2 \cdot 96500) = 0.0035$ g.

$\omega(H_2O) = 0.035 / 10 \cdot 100\% = 0.35\%$.

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 – $C_{12}H_{22}O_{11}$):

$$\chi(H_2O) = \frac{\frac{0.05}{18}}{\frac{0.05}{18} + \frac{0.95}{342}} \cdot 100\% = 50\%.$$

Problem 17. Oxidation and inspiration

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**).

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*.

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.

Problem 18. Essential ozone

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:

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.

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):

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.

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 $C_{10}H_{16}O$,

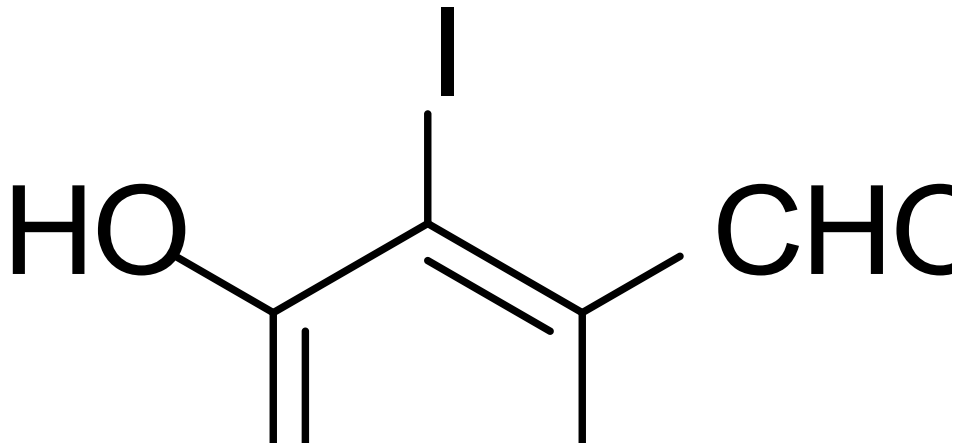
i.e. formula of **K** differs from formula of **I** by 1 oxygen atom. The **I**-to-**J** is anti-Markovnikov hydration of C=C bond; next step is alcohol-to-ketone oxidation. From formula of **K** it is possible to conclude that only one C=C bond was hydrated during the first step. $LiN(SiMe_3)_2$ is 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.

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.

Problem 19. Two in one

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**.

Problem 20. Antitussive “narcotine”

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-hydroxytetrahydroisoquinoline 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.

Problem 21. Pyrrolizidine alkaloids

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.

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.

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.

Problem 22. Delightful odor of truffle

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 an oxygen from 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).

Problem 23. Synthesis of large rings. The magic or routine work?

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.

2. The IUPAC name of compound **E** is
(*E*,4*R*,5*S*)-5-(4-methoxybenzyloxy)-4-(2-methoxyethoxymethoxy)hex-2-enoic acid.

Problem 24. What Time is it in Baku or Cheating the Death

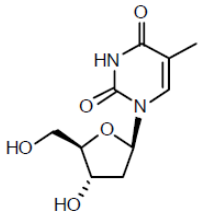
1. Nucleosides are glycosylamines with a nucleic acid base linked to a suitable sugar.

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:

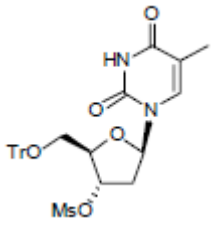
$$C_xH_yN_zO_t + (2x+y/2–t)/2\ O_2 = xCO_2 + y/2H_2O + z/2N_2.$$

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 $0.858 = \frac{14.0 \cdot b}{M \cdot a + 14.0 \cdot b}$, and $M = \frac{2.32 \cdot b}{a}$ g/mol. LiN_3 is the only possible solution.

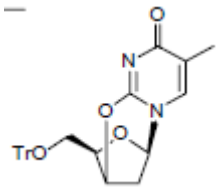
Note that the synthesis is a sequence of nucleophilic substitution steps. Deoxythymidine (**A1**)



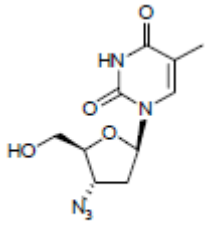
is transformed into



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



. AZT synthesis is completed by



AZT

the azide formation and deprotection.

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

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

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.

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 monooxygenase 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:

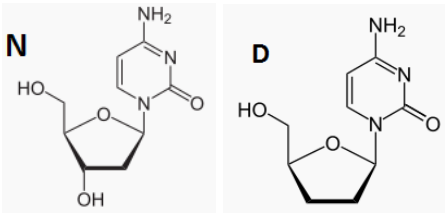
7. The absence of variations in volume ratio of the combustion gases before and after the absorption by the alkali solution with that of compounds **D** and **N** unambiguously indicates that the numbers of C and N atoms in these compounds are the same. The number of H atoms may differ in such compounds 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):

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

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

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

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).



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.

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:

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

.

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, which is much higher than that of $C_9H_{16}N_3O_{12}P_3$ (451.2 g/mol). Considering **M** is a salt helps overcoming the contradiction. Then it contains a cation with the molar mass of:

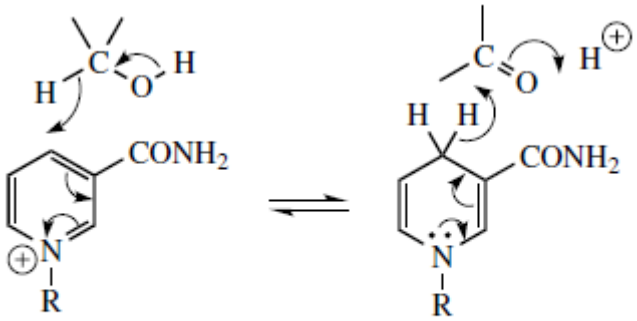
$$A_r(cation) = \frac{539.2 + 4 \cdot 1.008 - 451.2}{4} = 23.01 \approx 23\ a.m.u.$$

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.

Problem 25. Number One Enzyme

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

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 $\frac{1.00}{7.52} \cdot 107.9 = 14.3$ g/mol. 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):

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:

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

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

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:

5. The reaction equation suggests that **Y** contains 12 carbon atoms with the molar mass of $\frac{12.01 \cdot 12}{0.774} = 186$ g/mol. 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:

Problem 26. Holy War against Four Horsemen of the Apocalypse

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 ($4HBr + O_2 = 2Br_2 + 2H_2O$), 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:

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

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	$1.62 \cdot 10^{-2}$	$9.51 \cdot 10^{-3}$	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.

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 limiit, one gets three possible combinations with bromine: **1Br + 1Cl** (1), **1Br + 2Cl** (2), **2Br + 1Cl** (3).

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:

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

where x is the amount of each halogen.

Therefore $x = 5.394 \cdot 10^{-3}$ 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.

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

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

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*:

$$[Ag^+]\cdot[Br^-] = 5.4\cdot10^{-13};$$
$$[Ag^+]\cdot[NH_3]\cdot10^{3.32} = [Ag(NH_3)^+];$$
$$[Ag(NH_3)^+]\cdot[NH_3]\cdot10^{3.92} = [Ag(NH_3)_2{}^+];$$
$$[Ag(NH_3)^+]+[NH_3]+2\cdot[Ag(NH_3)_2{}^+] = 1.0;$$
$$[Ag^+]+[Ag(NH_3)^+]+[Ag(NH_3)_2{}^+] = [Br^-] = s.$$

(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 mM.

The same answer can be obtained by making the reasonable assumption that $[NH_3] \approx C(NH_3)$ = 1.0 M, because of the expected low solubility of salt. Then the equations would be simplified to the form:

$$[Ag^+]\cdot s = 5.4\cdot10^{-13};$$
$$[Ag^+]\cdot(1+10^{3.32}+10^{3.92}\cdot10^{3.32}) = s.$$

So, *s* is still $3.0\cdot10^{-3}$ M, and the assumptions made are valid.

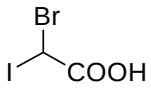
5. **Y** reacts with 0.1 M aqueous KOH solution at room temperature, which is due to the presence of the carboxyl group in its structure. Since both **X** and **Y** belong to the same class of organic compounds, **X** is also a carboxylic acid.

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 $7.55\cdot10^{-3}$ mol $CaCO_3$ obtained,

$$M\ (X) = \frac{2\cdot1.000}{0.00755} = 265\ \text{g/mol}$$

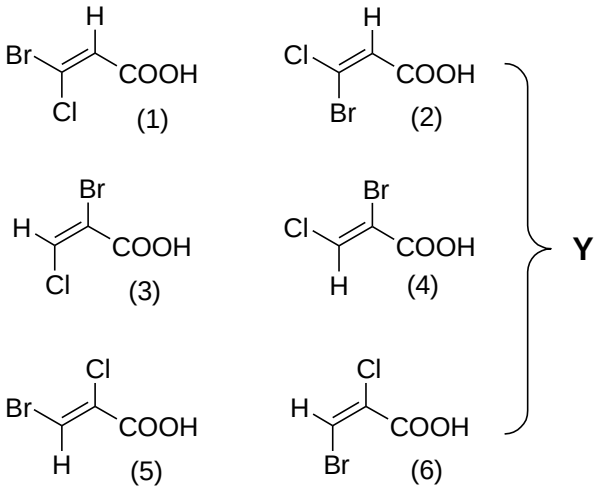
Hence its molecular formula is $C_2H_2O_2BrI$, and the structure is:



X

The validity of the structure is confirmed by chirality.

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



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.

8. 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**.

$$n(C) = \frac{3.065\ \text{g}}{100.09\ \text{g/mol}} = 3.062 \cdot 10^{-2}\ \text{mol};\ n(O) = \frac{1.000\ \text{g} \cdot 0.4100}{16.00\ \text{g/mol}} = 2.563 \cdot 10^{-2}\ \text{mol}$$

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

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:

$$M = \frac{\rho \cdot R \cdot T}{p} = \frac{1.43\text{g/L} \cdot 8.31\text{J/(mol} \cdot \text{K)} \cdot 307\text{K}}{100.0\ \text{kPa}} = 36.5\ \text{g/mol}$$

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:

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

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

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:

$$M\,(Z) = \frac{2 \cdot 16.00}{0.4100} = 78.0\,\frac{g}{mol} \;\; or \;\; \frac{3 \cdot 16.00}{0.4100} = 117.1\;g/mol$$

Calculation of the molecular masses of the following combinations of atoms: $M(CSClO_3H)$ = 128.5, $M(CSClO_2H)$ = 112.5, $M(CFClO_3H_2)$ = 116.5, and $M(CFClO_2H_2)$ = 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/L 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 and that of $CSFO_2H$ to 96 g/mol. 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 in the former case, and of 117.1 g/mol 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).

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

Problem 27. Determination of nickel in nickel and copper-nickel alloys by complexometric titration

1. $3Ni + 8HNO_3(diluted) \rightarrow 3Ni(NO_3)_2 + 2NO\uparrow + 4H_2O$

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

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:

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

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.

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:

$K'_f = K_f\, \alpha_{Y^{4-}} \alpha_M$,

It depends on:

- $\alpha_{Y^{4-}}$, 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.

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

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

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

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

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

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

6. Concentration of Ni in the sample solution taken for the precipitation (50 mL):

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

C_{Ni} is the concentration of nickel in the aliquot, M,

V_{EDTA} is the volume of Na_2H_2EDTA solution taken for titration, mL,

C_{EDTA} is the concentration of the standard Na_2H_2EDTA solution, M,

V_{MgSO_4} is the volume of magnesium sulfate solution consumed in the back titration, mL,

C_{MgSO_4} is the determined concentration of magnesium sulfate solution, M.

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

$$m_{Ni} = \frac{C_{Ni} \cdot V_d}{V_s} V_0 \cdot M_{Ni},$$

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

$$m_{Ni} = 2 \cdot C_{Ni} V_0 \cdot M_{Ni},$$

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

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

V_d is the volume of the graduated flask with the dissolved nickel dimethylglyoximate precipitate (100 mL)

The mass fraction of Ni in the alloy:

$$\omega = \frac{m_{\text{Ni}}}{m_{\text{alloy}}} \cdot 100\%$$

Problem 28. Titrimetric determination of lead and silver in their mixture

1. Chemical equations:

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

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

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

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

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

d) $5H_2C_2O_4 + 2KMnO_4 + 3H_2SO_4 = 10CO_2\uparrow + 2MnSO_4 + K_2SO_4 + 8H_2O$

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:

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

Problem 29. Complexometric determination of iron, chromium, and zinc in an alloy

1. Chemical equations:

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

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

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

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

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

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

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

2. $C(Fe^{3+}) = 10 \times C(Na_2H_2EDTA) \times V_1(Na_2H_2EDTA) / V_a$

$C(Zn^{2+}) = 10 \times C(Na_2H_2EDTA) \times V_2(Na_2H_2EDTA) / V_a$

$C(Cr^{3+}) = 10 \times [20 \times C(Na_2H_2EDTA) - V_3(Cu^{2+}) \times C(Cu^{2+})] / V_a$

3. For pH 1.0 and $K_1 = 1.0\times10^{-2}$, $K_2 = 2.1\times10^{-3}$, $K_3 = 6.9\times10^{-7}$, $K_4 = 5.5\times10^{-11}$:

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

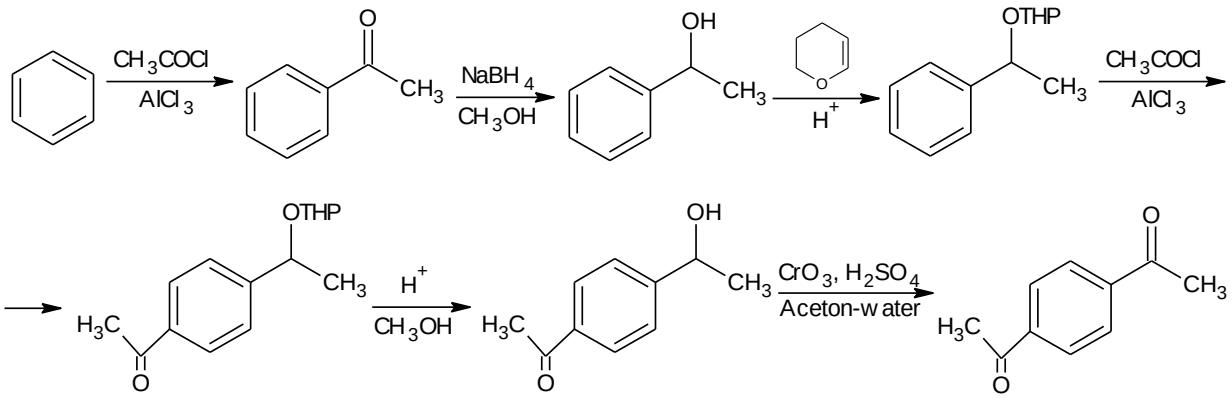
Problems 30-32. Characteristics and yields of the products

Problem ##	Product	Appearance	Melting/Boiling point, °C	n_D^{20}	Yield, %
30	3-(4-Methylbenzoyl) propionic acid	Beige crystals (prisms)	126-127	-	6.6 g (68%)
31	4-(4-Methylphenyl)-4-hydroxybutanoic acid	White crystals	97 -99 °C	-	3.0 g (72%)
32	Diethyl ester of succinic acid	Colorless liquid	105°C at 15 mm Hg	1.4256	23 g (87 %)

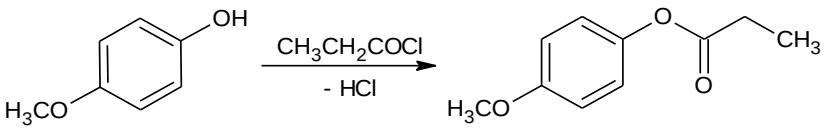
Problem ##	NMR reference data ($CDCl_3$)
30	2.42 (s,3H, CH_3), 2.81 (t, 2H, J=6.6 Hz, $C\underline{H_2}COOH$), 3.30 (t, 2H, J=6.6 Hz, $C\underline{H_2}CO$), 7.27 (d, 2H, 2H, J=8.0 Hz), 7.89 (d, 2H, 2H, J=8.1 Hz) [ArH]
31	2.07 (m, 2H, CH_2), 2.35 (s,3H, CH_3), 2.48 (t, 2H, J=7.3 Hz, CH_2), 4.75(t, 2H, J=7.3 Hz, $C\underline{H}OH$), 7.17 (d, 2H, 2H, J=8.0 Hz), 7.24 (d, 2H, 2H, J=8.0 Hz) [ArH]
32	1.23 (t, 6H, J=7.1 Hz, CH_3), 2.59 (s, 4H, CH_2CO), 4.12 (q, 2H, J=7.1 Hz, $C\underline{H_2}CH_3$)

Problem 30. Synthesis of 3-(4-Methylbenzoyl)propionic acid

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.)



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.



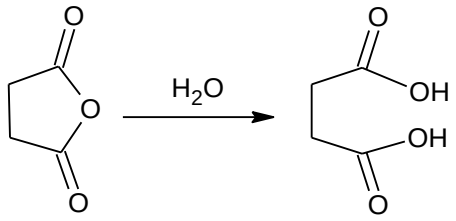
3. The Friedel-Crafts alkylation leads to a mixture of polyalkylation products. Besides, the reaction proceeds *via* carbocationic intermediates, which are subject to various rearrangements. As a result, the hydrocarbon skeleton of the starting alkylating agent undergoes isomerization. Thus,

alkylation typically leads to a complex mixture of products, which both reduces the product yield and makes its isolation complicated.

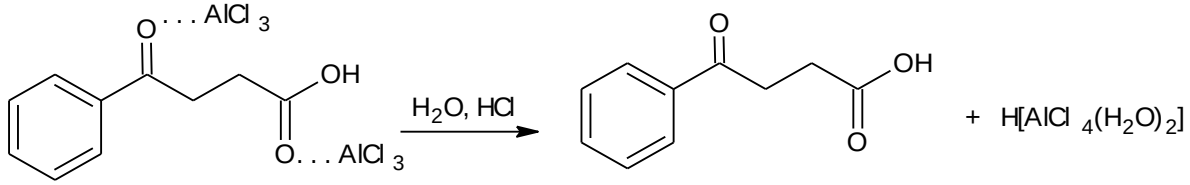
By contrast, the Friedel-Crafts acylation always affords a sole product of the known structure.

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.

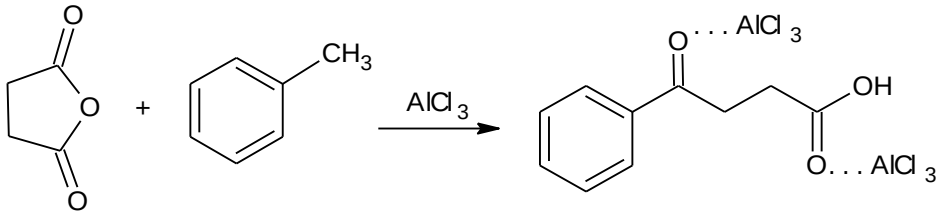
5. Water is added to decompose the unreacted anhydride, the reaction being exothermic:



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



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



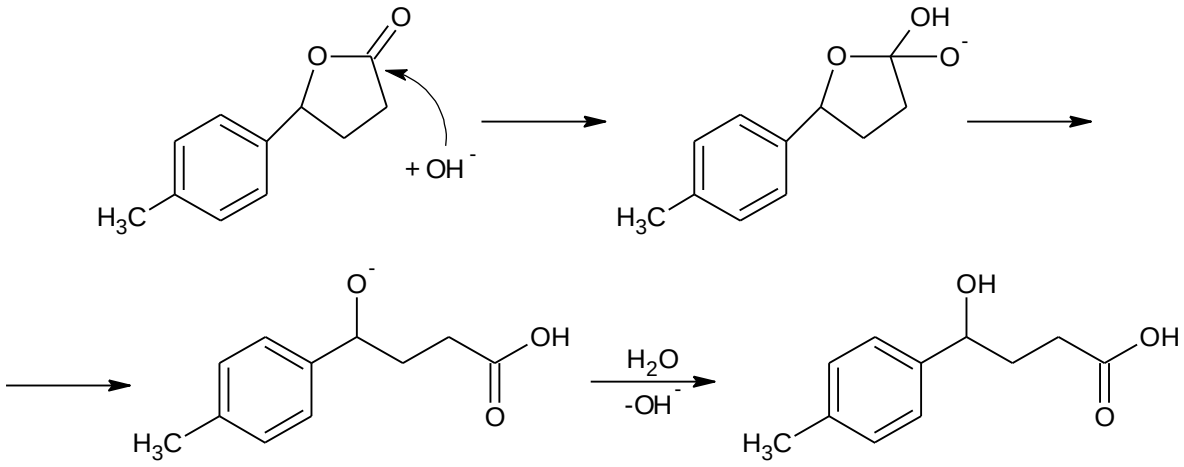
Problem 31. Synthesis of 4-(4-methylphenyl)-4-hydroxybutanoic acid

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:

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

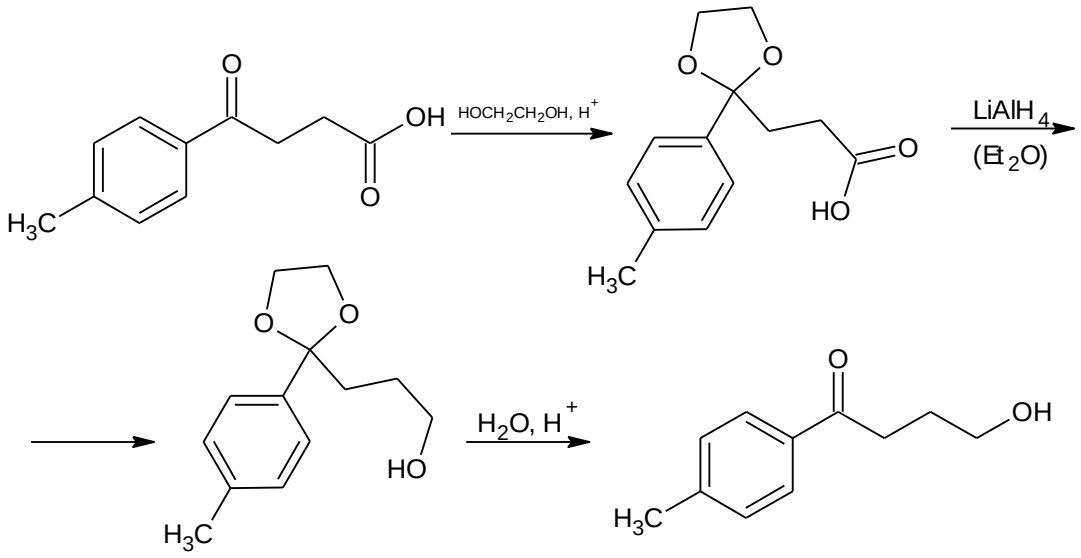
The mechanism of the lactone disruption is as follows:



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.

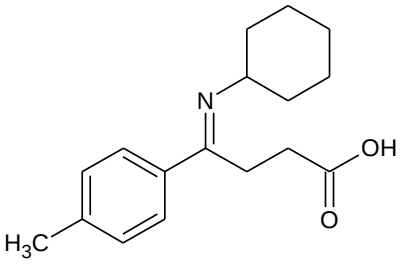
3. Readiness to reduction correlates with the value of the partial positive charge (δ +) on the carbon atom in the carbonyl group. Both alkyl groups in ketones produce the +I-effect on the carbonyl carbon atom. At the same time, there is only one group of this type in aldehydes. Thus, the value of δ+ on the carbon atom is higher in the case of the aldehyde group, and it is more readily reduced with sodium borohydride.

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.

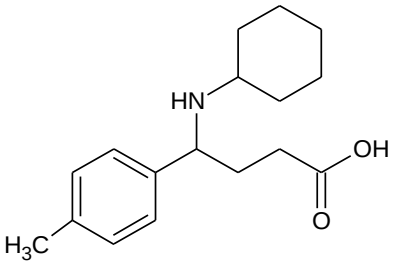


5. The combination of nucleophilic addition of an amine with subsequent reduction is referred to as reductive amination. The nucleophilic amine is attached to the carbonyl group affording the imine, which is further reduced to the amine with sodium borohydride.

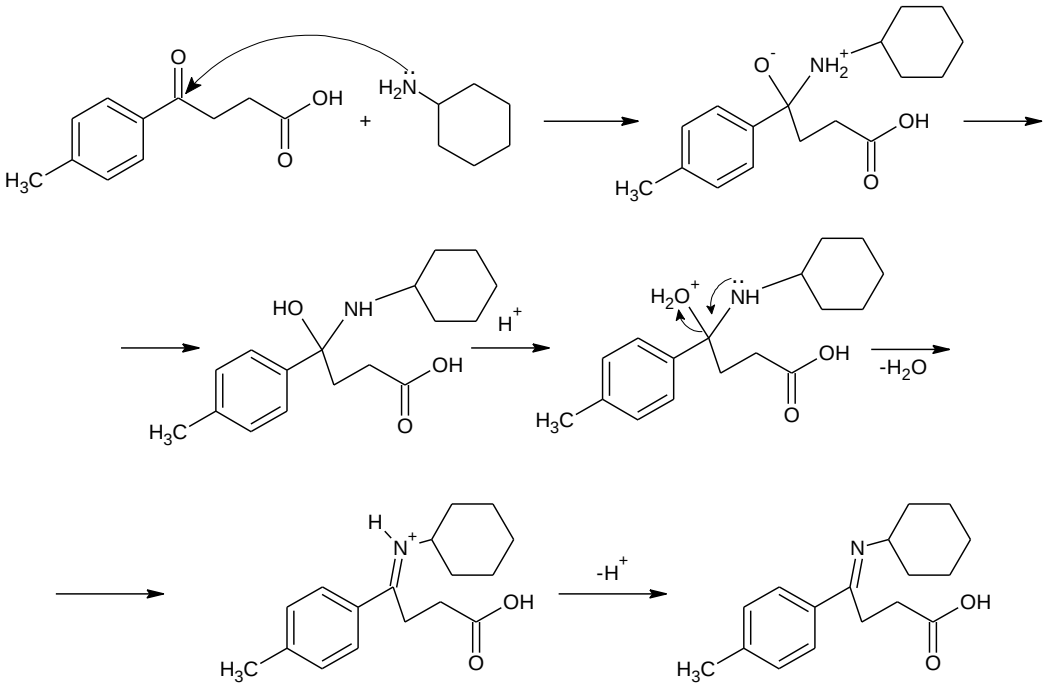
The intermediate product:



The final product:

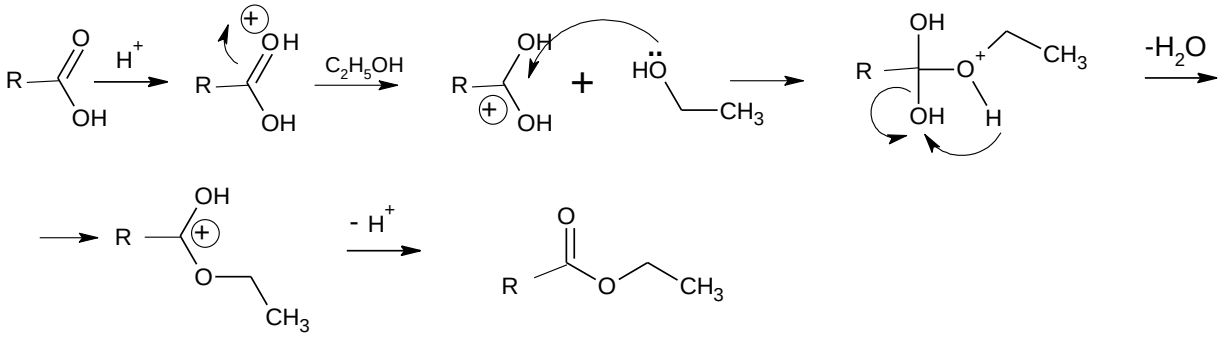


The reaction mechanism:

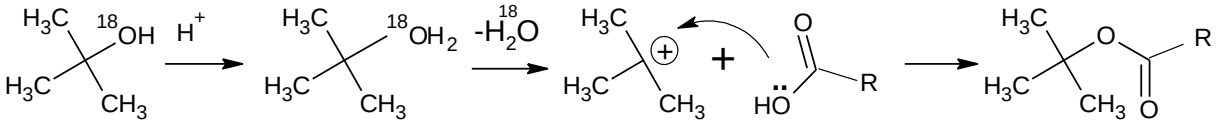


Problem 32. Synthesis of diethyl ester of succinic acid

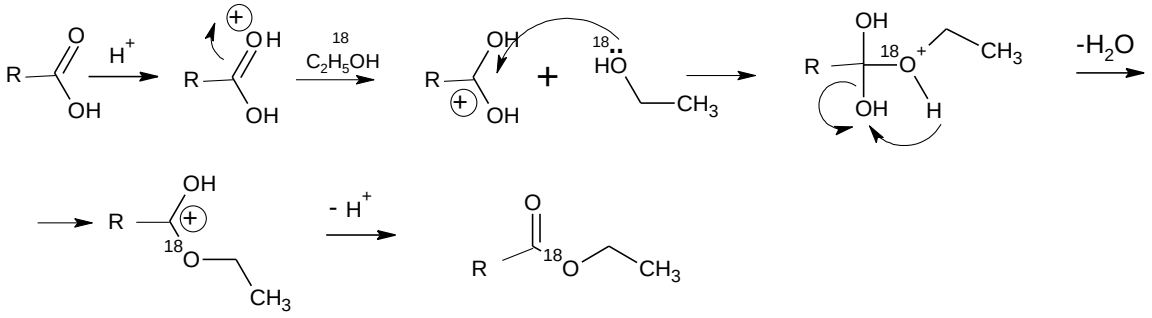
1. Toluene forms a ternary azeotrope with water and ethanol with the boiling temperature of 75°C. The boiling point of diethyl succinate is 218°C. The difference in the temperatures allows removing water from the reaction mixture, thus shifting the equilibrium towards the reaction product formation.

2. 

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:



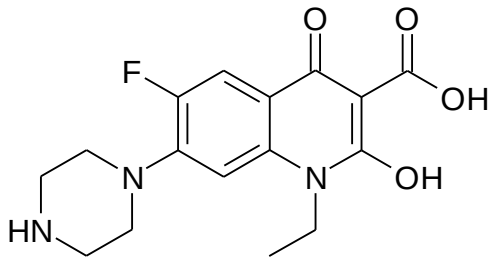
In the other case it is the acid molecule which is protonated first at the oxygen atom. Then one of the C-O bonds is cleaved giving the carbocation, which further attacks the alcohol molecule followed by the proton elimination. Thus, the isotopic label remains in the ester molecule:



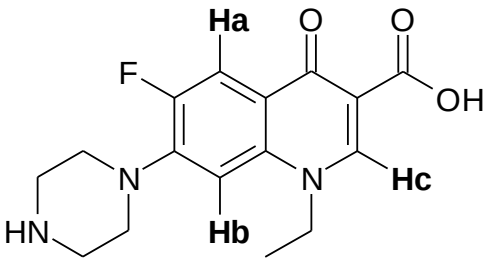
Problem 33. Kinetic studies of Norfloxacin oxidation with permanganate in alkaline medium

1a.

A =

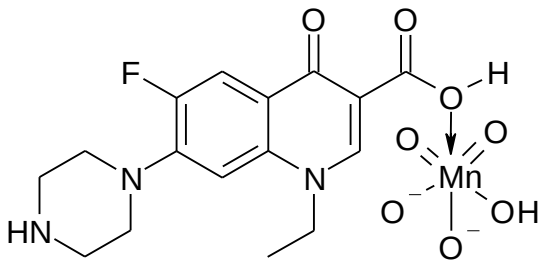


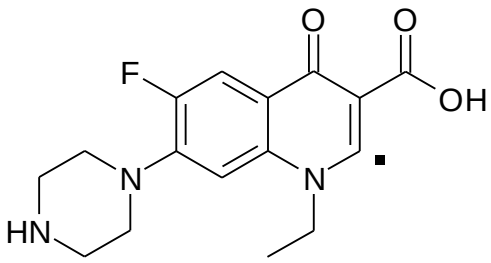
1b.



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; $\mathbf{H_c}$)

5a.

B = 

C = 

5b. $\text{rate} = -\frac{d[\text{MnO}_4^-]}{dt} = \frac{k_1 K_1 K_2 [\text{NF}][\text{MnO}_4^-]_0[\text{OH}^-]}{1 + K_1[\text{OH}^-] + K_1 K_2 [\text{OH}^-][\text{NF}]}$

(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).

Problem 34. Temperature dependence of the reaction rate of disproportionation

1. Plot b.

2. **A** = $[Mn(C_2O_4)_3]^{3-}$

3. $Mn^{2+} + 6H_2C_2O_4 + MnO_4^- = [Mn(C_2O_4)_3]^{3-} + 4H_2O + 4H^+$.

4. $2[Mn(C_2O_4)_3]^{3-} + 6H^+ = 2MnC_2O_4 + 2CO_2 + 3H_2C_2O_4$.