THE PREPARATORY PROBLEMS FROM THE INTERNATIONAL CHEMISTRY OLYMPIADS

Series 2

38th – 42nd IChOs
2006 – 2010

Edited by Anton Sirota

IChO International Information Centre
IUVENTA, Bratislava, 2017

THE PREPARATORY PROBLEMS FROM THE INTERNATIONAL CHEMISTRY OLYMPIADS, Series 2
The preparatory problems from the 38th – 42nd IChOs

Editor: Anton Sirota

IChO International Information Centre, Bratislava, Slovakia

ISBN 978-80-8072-171-8

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Issued by IUVENTA in 2017
with the financial support of the Ministry of Education of the Slovak Republic

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39th

International Chemistry Olympiad

PREPARATORY PROBLEMS

Edited by Anton Sirota

28 theoretical problems
6 practical problems

2007

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The original title page:

The 39th International Chemistry Olympiad

Chemistry: art, science and fun

PREPARATORY PROBLEMS

July 15-24, 2007

Moscow, Russia

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P r e f a c e

written by the editors from the Scientific Committee
(a shortened version)

We are happy to present you the Booklet of Preparatory problems. This year its structure was changed according to the recommendations of the International Steering Committee (ISC).

In the Booklet you will also find the list of level 3 areas organizers would like students to be acquainted with. Note that this is not a simple enumeration of level 3 topics from the Syllabus. It is rather an informal presentation of fields of advanced difficulty that will be addressed at the forthcoming Olympiad. We publish the list to make your preparation more effective.

Members of the Scientific Committee really did their best to prepare interesting tasks. The set covers all major parts of modern chemistry, though most of tasks can be solved by applying a basic knowledge of chemistry..Elaborating the tasks, we intended not only to announce particular chemistry fields, but also to make the material challenging and give you an idea of the structure and spirit of problems which you will see at the competition in July. We were also keen to provide you with sufficient material for training. Enjoy solving the tasks and please do not forget that **CHEMISTRY IS ART, SCIENCE, and FUN!**

Members of IChO-2007 Scientific Committee

LIST OF FIELDS OF ADVANCED DIFFICULTY

Problems	Field	Subfields
1	Periodic trends	–
2, 3	Chemical bonding, quantum mechanics	Superposition principle. Molecular orbitals. Periodic wave functions. Uncertainty principle.
4	Photochemistry	Energy diagram of a chemical reaction. Activation energy. Relationship between energy and wavelength of light.
	Quantum mechanics	Particle-in-a-box model.
5-7	Equilibrium	Surface tension. Gibbs energy and its dependence on pressure for pure substance. The temperature dependence of the saturated vapor pressure. Relationship between $\Delta_r G^\circ$ and equilibrium constant K. Using ΔG to predict direction of natural change. Dependence of $\Delta_r G$ on partial pressures of reactants and products. Le Chatelier's principle.
8	Phase diagrams, equations of state	Single component phase diagrams. Critical point. Van der Waals gas law.
9-11	Chemical kinetics	Determination of the reaction order. Rate-determining step. Steady-state approximation. Calculation of activation energy. Kinetic equations and kinetic curves. Autocatalysis. Enantiomeric enrichment. First-order reactions: Dependence of concentration on time, half-life. Carbon dating.
	Carbonyl compounds	Addition reactions. Stereochemistry: enantiomers.

12-14	Inorganic chemistry of elements	Fe(II) and Fe(III), redox processes, cyanide and tartrate complexes, hydroxides. MnO_4^- as an oxidizing agent in acidic media. As(III) and As(V), redox processes. Compounds of sulfur in lower oxidation states, oxidation with iodine. Zinc, sulfide and carbonate, their solubility. Phosphates, their thermal decomposition.
	Electrochemistry	Standard electrode potentials. Nernst equation. EMF. Direction of redox processes.
	Chemical equilibria	Acid-base and precipitation equilibria, calculation of pH, K_{sp} in complex mixtures.
	Analytical chemistry	Redox titration (direct and back-titration). Stoichiometric calculations.
	Carbonyl compounds	Nucleophilic addition of HSO_3^-.
15-17	Chemical bonding	VSEPR-concept (factors affecting distortion of an ideal polyhedron). Crystal Field Theory of coordination compounds. Calculation of Crystal Field Stabilization Energy.
	Solid state chemistry	Unit cell. Coordination number. Miller indices. Bragg's Law. Types of close packings. Calculation of density of packings. X-ray diffraction for f.c.c. lattice. NaCl, spinel, and perovskite structure.
	Equilibrium	Hard and Soft Acids and Bases (HSAB) concept. Hydrolysis, calculation of pH. Osmotic pressure. Free energy definition. Relationship between $\Delta G°$ and equilibrium constant K. Using ΔG to predict direction of natural change.
	Inorganic chemistry of elements	Group 14: oxocompounds ((+4) oxidation state of the elements). Group 15: oxoacids with the element having (+1), (+3) or (+5) oxidation states; structure of the acids; pK_a trends. Polymerization of oxoacids (oxoanions). Transition metals: tetrahedral and octahedral complexes of Co and Cr.
18-20	Carbonyl compounds	Aldehydes, ketones, carboxylic acid derivatives: properties, keto-enol tautomerism, enolates and enol derivatives.
	Condensations of carbonyl compounds	General principles, mechanism of base-catalyzed condensations.
	Concerted pericyclic reactions	General principles and common types of pericyclic processes.
21-24	Amino acids and peptides (without proteins)	Structure, sequencing, chemical properties of carboxyl, amino and functional side groups.

	Lipids	Structure, physical and chemical properties, synthesis and degradation.
	Bases, nucleosides and nucleotides: (without nucleic acids)	Structure and properties.
	Enzymes	Nomenclature, mechanisms of catalysis, specificity.
	Physico-chemical methods	^{1}H NMR and mass spectrometry.
25-27	Polymerization	Mechanisms, stages, kinetics, characteristics of obtained polymers
	Monomer structure and reactivity in polymerization	Inductive and mesomeric effects, ring strain, solvent effect, etc.
	Copolymers	Synthesis, architecture, distribution of units, properties.
	^{1}H NMR for studying polymers	Common ranges of chemical shifts of typical functional groups and simple fragments, integration of signals.
28	Quantum mechanics	Energy diagram of a chemical reaction. Tunneling. Relationship between frequency, energy and wavelength of light.

THE THIRTY NINTH INTERNATIONAL CHEMISTRY OLYMPIAD 15–24 JULY 2007, MOSCOW, RUSSIAN FEDERATION

PREPARATORY PROBLEMS

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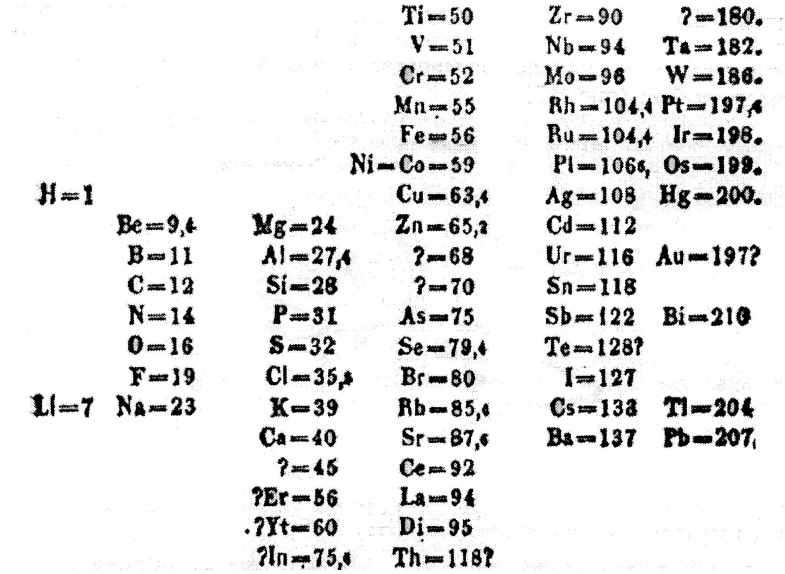
PREPARATORY THEORETICAL PROBLEMS

THEORETICAL PROBLEM 1

On the borders of the periodic system



			Ti=50	Zr=90	?=180.
			V=51	Nb=94	Ta=182.
			Cr=52	Mo=96	W=186.
			Mn=55	Rh=104,4	Pt=197,4
			Fe=56	Ru=104,4	Ir=198.
			Ni=Co=59	Pl=106,6	Os=199.
H=1			Cu=63,4	Ag=108	Hg=200.
	Be=9,4	Mg=24	Zn=65,2	Cd=112	
	B=11	Al=27,4	?=68	Ur=116	Au=197?
	C=12	Si=28	?=70	Sn=118	
	N=14	P=31	As=75	Sb=122	Bi=210
	O=16	S=32	Se=79,4	Te=128?	
	F=19	Cl=35,5	Br=80	I=127	
Li=7	Na=23	K=39	Rb=85,4	Cs=133	Tl=204
		Ca=40	Sr=87,6	Ba=137	Pb=207.
		?=45	Ce=92		
		?Er=56	La=94		
		?Yt=60	Di=95		
		?In=75,6	Th=118?		

The first Periodic system of the elements was proposed in 1869 by the Russian chemist D.I. Mendeleev, who arranged all the known chemical elements in the order of increasing atomic mass. In 1871 Mendeleev published the article «The natural system of the elements and its application to the prediction of properties of yet undiscovered elements » in the «Journal of the Russian Chemical Society». In that article Mendeleev described in detail the properties of three unknown elements that were ekaboron (Eb), ekaaluminum (Ea), and ekasilicon (Es). All of them were discovered in the next 15 years.

1.1 What are the present names of the three elements predicted by Mendeleev? Interestingly, all three names have a geographical origin.

The first Periodic system listed 66 elements only, of which three were unknown. In the present-day system there are 118 elements. The last, 118th element was discovered in 2005 during the collaborative studies by the Joint Institute for Nuclear Research (Russia) and the Livermore National Laboratory (USA). After the collisions of calcium-48 nuclei with the target containing californium-249 nuclei three cascades of α-decay were detected, that started from the 118th element with the mass number 294.

1.2 Write the balanced equations of the nuclear reactions of: i) the synthesis and ii) the α-decay of the 118th element.

1.3 To which group of the Periodic system does the 118th element belong? Give its electron configuration using a noble gas with the *spdf* notation.

1.4 Based on the properties of the same-group analogs of the 118th element and using extrapolation predict the following properties of the 118th element: i) melting point; ii) boiling point, iii) atomic radius, iv) first ionization energy, v) the formula of the oxide of the 118th element in its highest oxidation state.

SOLUTION OF PREPARATORY PROBLEM 1

1.1 In 1875 the French chemist Paul-Emile Lecoq de Boisbaudran studied the spectra of zinc ore and discovered the traces of a new element, which he called “gallium” from the Latin word "*Gallia*" meaning "*France*" and perhaps also from the Latin word "*gallus*" (the cock, a translation of Lecoq). In the same year Lecoq de Boisbaudran obtained the free metal by electrolysis of a solution of the hydroxide $Ga(OH)_3$ in KOH. When Mendeleev knew about this discovery he understood that the properties of gallium resemble those of ekaaluminum. Moreover, he wrote to Boisbaudran that he obtained the wrong value for the density of gallium (4.7 g cm^{-3}) whereas Mendeleev predicted the density to be 5.9 - 6.0 g cm^{-3}). Indeed, more accurate measurements gave the correct value 5.904 g cm^{-3}.

Scandium (from the Latin word "*Scandia*" meaning "*Scandinavia*") was discovered by Swedish chemist Lars Frederick Nilson in 1876 in the minerals euxenite and gadolinite, which had not yet been found anywhere except in Scandinavia. He and

his coworkers were actually looking for rare earth metals. By processing 10 kg of euxenite and other residues of rare-earth minerals, Nilson was able to prepare about 2 g of scandium oxide (scandia, Sc_2O_3) of high purity. Per Theodor Cleve found scandium oxide at about the same time. He noted that the new element was the element ekaboron predicted by Mendeleev in 1871.

Germanium (from the Latin word "*Germania*" meaning "*Germany*") was discovered in a mineral called argyrodite by Clemens Alexander Winkler in 1886. The properties of germanium became remarkably close to those predicted by Mendeleev.

1.2 Nuclear synthesis of the 118th element led to formation of three neutrons:

$$^{249}_{98}\mathrm{Cf} + {}^{48}_{20}\mathrm{Ca} \rightarrow {}^{294}_{118}118 + 3\,{}^{1}_{0}\mathrm{n}.$$

The α-decay of the obtained nuclide gave the nuclei of the 116th element:

$$^{294}_{118}118 \rightarrow {}^{290}_{116}116 + {}^{4}_{2}\mathrm{HeA}$$

1.3 The 118-th element completes the 7-th period. It belongs to the inert gases (group 18). Its electron configuration is [Rn] $5f^{14}\ 6d^{10}\ 7s^2\ 7p^6$.

1.4 For the extrapolation we will consider inert gases of the periods 3 – 6 because helium and neon differ significantly in their properties from other inert gases.

i) Melting points:

Z	T_m, K
18	84
36	116
54	161
86	202

The dependence of boiling point on atomic number is almost linear. Linear extrapolation gives $T_m(118) = 263$ K = –10 °C.

ii) Boiling points:

Z	T_b, K
18	87
36	120
54	165
86	211

On average, boiling points are 4 degrees higher than the corresponding melting points, hence we predict that $T_b(118) = 267$ K = –6 °C.

iii) Covalent atomic radii:

iv)

Z	*r*, nm
18	0.097
36	0.110
54	0.130
86	0.145

Linear extrapolation gives: $r(118) = 0.171$ nm.

iv) Ionization energies:

Z	*IE*, eV
18	15.8
36	14.0
54	12.1
86	10.7

Ionization energy is a non-linear function of atomic number. Linearization in coordinates ln *Z* – *IE* gives for $Z = 118$ the ionization energy $IE = 9.7$ eV.

Compare these data with the values predicted for the 118th element by American chemists 40 years ago: t_m = –15 °C, t_b = –10 °C, $r = 0.23$ nm, $I = 9.8$ eV.

Of course, these results obtained by extrapolation are approximate. Moreover, bulk properties such as melting and boiling points can be measured only for significant amounts of an element, whereas only three atoms of the 118-th element were obtained and they decayed during milliseconds. For this reason, our predictions may hardly be confirmed in future.

v) The highest oxidation state for the 118-th element is VIII, and the corresponding oxide should be RO_4 as for xenon (for radon neither oxide, nor any other compounds have been obtained).

THEORETICAL PROBLEM 2

Schrödinger cat and chemistry

Many chemical phenomena can be explained by physical theories. The main theory for chemistry is quantum mechanics, which gives the solid foundation for the observed chemical periodicity. One of the cornerstones of quantum mechanics is the superposition principle that says:

"If a quantum system can be found in the states 1 and 2 described by wavefunctions Ψ_1 and Ψ_2, it can also be found in a mixed state with the wavefunction

$$\Psi = c_1\Psi_1 + c_2\Psi_2,$$

where factors c_1 and c_2 characterize the contributions of the pure states 1 and 2 to the mixed state".

The sum or difference of some wave functions taken with certain factors is called a superposition (a linear combination) of these functions.

In a mixed state the quantum system exists in both pure states simultaneously. When you perform some measurement on the system being in the mixed state, this measurement transfers the system to one of the pure states. We can never predict the specific final state; it is determined by the probability laws. The probability of any of the final states after measurement is proportional to the square of the modulus of the corresponding factor:

$$p_1 \sim |c_1|^2, \; p_2 \sim |c_2|^2.$$

Of course, the probability to find the system in either of the states is unity:

$$p_1 + p_2 = 1.$$

The superposition principle is applicable to quantum systems only and is not valid when applied to macrosystems. To illustrate this idea, E. Schrödinger proposed the following mental experiment. Consider the Geiger counter which detects the entering electrons. The counter is connected to a device which breaks the glass with the poison when the particle enters the counter. Near the glass is a live cat. If the particle enters the counter, the cat is poisoned. But if the counter did not perform the measurement and is in the mixed state between the detected and undetected particle then the state of the cat is a superposition of life and death. Evidently, this is nonsense: the cat can be either alive or dead.

In chemistry, the superposition principle is used in the theories of hybridization, resonance, and molecular orbitals.

The superposition principle in theory of hybridization.

2.1 An sp^3-hybrid atomic orbital is a linear combination of one s and three p-orbitals:

$$\Psi_{sp^3} = c_1\Psi_s + c_2\Psi_{p_x} + c_3\Psi_{p_y} + c_4\Psi_{p_z} .$$

i) If we assume that all the orbitals make an equal contribution to a hybrid orbital, what are the absolute values of the coefficients c_1 – c_4?

ii) Similarly, find the absolute values of the coefficients c_1 – c_3 for an sp^2 hybrid orbital.

The superposition principle in molecular orbital theory.

2.2 The molecular orbital for the ground state of H_2^+ molecule ion has the form:

$$\Psi = \frac{1}{\sqrt{2}}\Psi_{1s}^{a} + \frac{1}{\sqrt{2}}\Psi_{1s}^{b},$$

where *a* and *b* denote hydrogen atoms. What is the probability to find an electron on the 1s-orbital of the atom *a*?

The superposition principle in theory of resonance

2.3 Covalent bonds have a partial ionic character. Thus the wavefunction of a hydrogen halide bond can be presented as a linear combination of two wavefunctions characterizing its ionic ($\Psi_{H^+Hal^-}$) and covalent ($\Psi_{H:Hal}$) states:

$$\Psi_{HHal} = c_{cov}\Psi_{H:Hal} + c_{ion}\Psi_{H^+Hal^-}$$

L. Pauling in his famous book «The nature of the chemical bond» (1947) claimed that in the HCl molecule the chemical bond is 17 % ionic in character. Find the absolute values of c_{cov} and c_{ion} for HCl.

One of the benzene wavefunctions can be presented as a linear combination of wavefunctions that correspond to two Kekule and three Dewar structures:

$$\Psi_{C_6H_6} = \sqrt{\frac{2}{5}}\Psi_{\bigcirc} + \sqrt{\frac{2}{5}}\Psi_{\bigcirc} + \frac{1}{\sqrt{15}}\Psi_{\bigcirc} + \frac{1}{\sqrt{15}}\Psi_{\bigcirc} - \frac{1}{\sqrt{15}}\Psi_{\bigcirc}$$

2.4 What is the total contribution of the Kekule structures to this electronic state of benzene?

In chemical reactions molecular structure changes over time so that the electronic state of a molecule is a function of time. In some cases structure of a molecule can be presented by a superposition of the initial and final states with time-dependent coefficients.

Let's assume that a molecule oscillates between two pure states, one with a wave function Ψ_1, and another with a wavefunction Ψ_2, with the frequency ω. Initially (t = 0) the molecule is in the pure first state and after a half-period ($t = \pi / \omega$) – in the second pure state.

2.5 Find the time-dependent coefficients of the superposition of these states describing the electronic structure of the molecule. Write the total wave function at a quarter of a period.

SOLUTION OF PREPARATORY PROBLEM 2

2.1 (i) All orbitals make equal contribution, hence $|c_1|^2 = |c_2|^2 = |c_3|^2 = |c_4|^2 = 1/4$, because the sum of squares of all modulus is unity. Therefore, $|c_1| = |c_2| = |c_3| = |c_4| = 1/2$.

(ii) For the sp^2-orbital $|c_1|^2 = |c_2|^2 = |c_3|^2 = 1/3$, hence $|c_1| = |c_2| = |c_3| = 1/\sqrt{3}$.

2.2 The probability of being found in a definite state is equal to the square of the modulus of the corresponding coefficient:

$$p_a = \left(\frac{1}{\sqrt{2}}\right)^2 = \frac{1}{2}.$$

This result is obvious because both hydrogen atoms are indistinguishable in H_2^+.

2.3 The probability of ionic state is 17 %:

$$|c_{ion}|^2 = 0.17,$$

Whence $|c_{ion}| = \sqrt{0.17} \approx 0.41$. Similarly, $|c_{cov}| = \sqrt{0.83} \approx 0.91$.

2.4 The total contribution of two Kekule structures is equal to the sum of squares of the moduli of all the corresponding coefficients in the linear combination:

$$p_{Kekule} = \left(\sqrt{\frac{2}{5}}\right)^2 + \left(\sqrt{\frac{2}{5}}\right)^2 = \frac{4}{5}.$$

It means that in a given state 80% of benzene molecules have one of the Kekule structures, and 20 % – one of the Dewar ones.

2.5
$$\Psi(x,t) = c_1(t)\,\Psi_1(x) + c_2(t)\,\Psi_2(x)$$

$c_1(t)$, $c_2(t)$ – are periodic functions of time with the boundary conditions $c_1(0) = 1$, $c_1(\pi/\omega) = 0$, $c_2(0) = 0$, $c_2(\pi/\omega) = 1$. It is natural to express these coefficients via the sine and cosine trigonometric functions:

$$c_1(t) = \cos\left(\frac{\omega t}{2}\right), \quad c_2(t) = \sin\left(\frac{\omega t}{2}\right)$$

After a quarter of a period, at $t = \pi/(2\omega)$, the total wave function is a superposition of both states with equal masses:

$$\Psi\left(x, \frac{\pi}{2\omega}\right) = \cos\left(\frac{\omega}{2}\frac{\pi}{2\omega}\right)\Psi_1(x) + \sin\left(\frac{\omega}{2}\frac{\pi}{2\omega}\right)\Psi_2(x) = \frac{1}{\sqrt{2}}\Psi_1(x) + \frac{1}{\sqrt{2}}\Psi_2(x)$$

THEORETICAL PROBLEM 3

Quantum uncertainty

One of the main quantum laws relates the uncertainties of position Δx and momentum Δp of quantum particles. The uncertainty product cannot be less than a fixed value – a half of Planck's constant:

$$\Delta x \cdot \Delta p \geq \frac{\hbar}{2}$$

where momentum is the product of mass and velocity: $p = m\,v$, the Planck's constant is $\hbar = 1.05 \times 10^{-34}$ J s.

3.1 Without performing calculations arrange the following particles in the order of increasing minimal uncertainty of velocity, Δv_{min}:

a) an electron in a H_2 molecule;

b) a H atom in a H_2 molecule;

c) a proton in the carbon nucleus;

d) a H_2 molecule within a nanotube;

e) a O_2 molecule in the room of 5 m width.

3.2 For the first and the last particles from the list above calculate Δv_{min}. Take the necessary reference data from handbooks or Internet.

———————

SOLUTION OF PREPARATORY PROBLEM 3

3.1 From uncertainty relation it follows:

$$\Delta v_{\min} = \frac{\hbar}{2\, m\, \Delta x}$$

Of all the particles listed above, a O_2 molecule, (e), has the largest mass and Δx and hence is characterized by smallest $\Delta v_{\min}$. In three other cases (b) – (d) the particles have a comparable mass – proton (b, c) and H_2 molecule, therefore uncertainty of velocity may be determined by localization length Δx. The uncertainty in position, Δx, is the largest for nanotube (about 1 nm), smaller by an order of magnitude for H_2 and is very small for the carbon nucleus, so that $\Delta v_{\min}$ increases in the following order: (d) < (b) < (c).

Consider now localization of an electron in a H_2 molecule. Electron mass is approximately 2000 smaller than that of proton, hence $\Delta v_{\min}$ for the electron is larger than in cases (b) and (d). But the size of the carbon nucleus is by 100 thousand times (5 orders of magnitude) smaller than diameter of H_2, therefore $\Delta v_{\min}$ for the proton in the carbon nucleus is larger than that for the electron in H_2.

The final sequence is as follows: (e) < (d) < (b) < (a) < (c).

3.2 For O_2 molecule in a room of 5 m width we get:

$$\Delta v_{\min} = \frac{1.05\times10^{-34}}{2\times\dfrac{0.032}{6.0\times10^{23}}\times5} = 2.0\times10^{-10}\ \text{m s}^{-1} = 2.0\ \text{Å/s}.$$

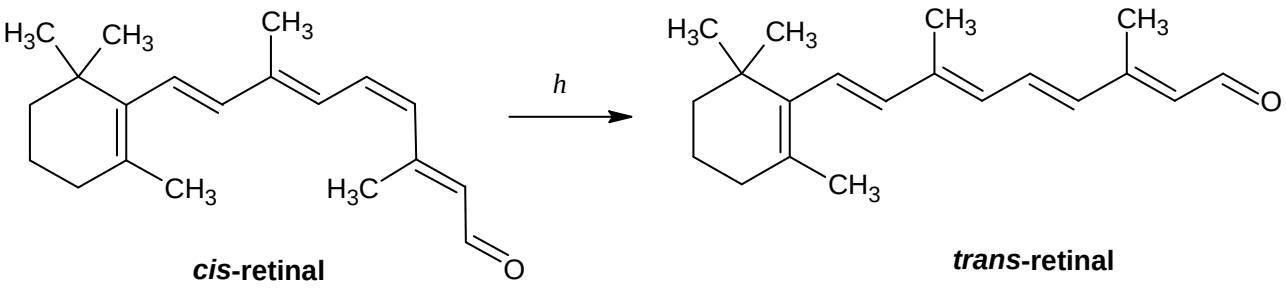
In the carbon nucleus the size of the proton localization area is equal to the nucleus diameter – about $4\cdot10^{-15}$ m.

$$\Delta v_{\min} = \frac{1.05\times10^{-34}}{2\times\dfrac{0.001}{6.0\times10^{23}}\times 4\times10^{-15}} = 7.9\times10^{6}\ \text{m s}^{-1} \approx 8000\ \text{km s}^{-1}.$$

THEORETICAL PROBLEM 4

Quantum chemistry of vision

The first step in the very complex mechanism of vision is the photoinduced *cis* → *trans* isomerization of the chromophore retinal embedded in rhodopsin molecules. Absorption of visible light by *cis*-retinal causes a change of the configuration of a double bond:



***cis*-retinal** ***trans*-retinal**

4.1 Show the double bond, which participates in the *cis-trans*-isomerization. Indicate the reaction coordinate.

4.2 Energies of the reactant and the product were found to be periodic functions of the reaction coordinate *x*:

$$E_{\text{cis}}(x) = 1.79 \times (1 - \cos(x)),$$

$$E_{\text{trans}}(x) = 1.94 + 0.54 \times \cos(x).$$

Energies are in eV (1 eV = 1.60×10^{-19} J = 96500 J mol^{-1}), $x = 0$ corresponds to the reactant, $x = \pi$ to the product. Draw the energy diagram for this reaction.

4.3 Determine the energy change for the reaction and its activation energy in kJ mol^{-1}.

4.4 What is the largest wavelength of light that can be absorbed by *cis*-retinal?

Let us apply the "particle-in-a-box" model to the electrons present in the conjugated system of *cis*-retinal. Energy levels of a particle of the mass *m* locked in an one-dimensional box with the width *l* are given by:

$$E_n = \frac{h^2 n^2}{8 m l^2}, \quad n = 1, 2, \ldots$$

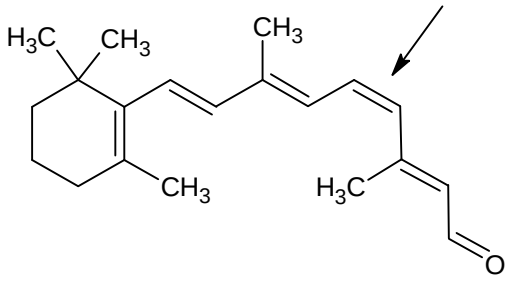
4.5 What is the number of electrons in the conjugated system of *cis*-retinal?

4.6 Based on your answers on questions 4.4 – 4.5 and using the formula above calculate *l*. How does this value compare with the structure of retinal molecule?

_____

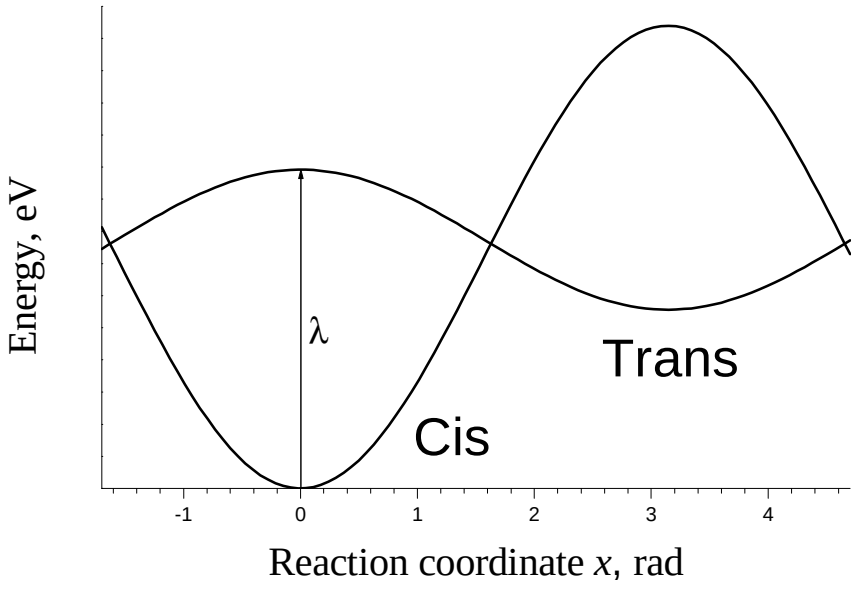
SOLUTION OF PREPARATORY PROBLEM 4

4.1 Reaction proceeds by rotation of a part of the molecule about the C_{11}–C_{12} bond:



The rotation angle is the reaction coordinate.

4.2



The energy change is the difference between the lowest energies of the *trans*- and *cis*-isomers:

$$Q = E_{\text{trans}}(\pi) - E_{\text{cis}}(0) = 1.40 - 0 = 1.40 \text{ eV} = 135 \text{ kJ mol}^{-1}.$$

Transition state of reaction is near the region of curve-crossing:

$$1.79 \times \left((1 - \cos(x)\right) = 1.94 + 0.54 \times \cos(x),$$

$$x = 1.64 = 0.521\pi = 93.7\ ^\circ.$$

Activation energy (reaction barrier) is defined by the energy difference between the transition state and the reagent:

$$E_{\text{A}} = E_{\text{cis}}(1.64) - E_{\text{cis}}(0) = 1.91 \text{ eV} = 184 \text{ kJ mol}^{-1}.$$

This barrier is rather high to be overcome at ambient temperature.

4.3 Maximal wavelength is determined by the energy difference between *trans*- and *cis*-retinal at $x = 0$:

$$\frac{h\,c}{\lambda} = E_{\text{trans}}(0) - E_{\text{cis}}(0) = 2.48 - 0 = 2.48 \text{ eV} = 3.97 \cdot 10^{-19} \text{ J}.$$

$$\lambda = \frac{h\,c}{\Delta E} = \frac{6.63 \times 10^{-34} \times 3.00 \times 10^{8}}{3.97 \times 10^{-19}} = 5.01 \times 10^{-7} \text{ m} = 501 \text{ nm}.$$

4.4 Conjugated electronic system of retinal contains 6 double bonds, that is, 12 π-electrons that occupy 6 lowest energy levels.

4.5 Absorption of light causes the transition from the highest occupied to the lowest unoccupied level:

$$E_7 - E_6 = \frac{h^2}{8 m l^2}\left(7^2 - 6^2\right) = \frac{13\,h^2}{8\,m\,l^2},$$

where electron mass is $m = 9.11 \times 10^{-31}$ kg. Hence,

$$l = \sqrt{\frac{13\,h^2}{8m\,\Delta E}} = 6.63 \times 10^{-34} \times \sqrt{\frac{13}{8 \times 9.11 \times 10^{31} \times 3.97 \times 10^{-19}}} = 1.41 \times 10^{-9}\ m = 1.41 \text{ nm}.$$

This value correlates well with the sum of bond lengths in the conjugated system – 6 double bonds and 5 ordinary bonds.

THEORETICAL PROBLEM 5

Nanoparticles and nanophases

Nanochemistry has sparked much excitement in the recent years and a large amount of research has been dedicated to understanding of nanomaterials. Single-walled carbon nanotubes (SWNTs) are a universally known example of such materials. SWNT can be thought of as a sheet of graphite rolled into a seamless cylinder ($d \approx 1.5$ nm). These cylindrical carbon "molecules" might provide components for molecular electronic devices of the future.

The properties of nanometer-scale materials are size- and shape-dependent.

Saturated vapor pressure of a small spherical particle (crystalline or liquid) is higher than that of the bulk phase of the same material. At equilibrium the molar Gibbs functions (G) of the condensed phase (G_{bulk}) and vapor (G_{vap}) are equal. Equation (1) determines the saturated vapor pressure, p, above a bulk phase

$$G_{bulk} = G_{vap} = G^\circ_{vap} + RT \ln p, \qquad (1)$$

G°_{vap} is the standard molar Gibbs energy of vapor at standard pressure $p = 1$ bar.

The substance inside a small spherical sample is under excess pressure, caused by surface tension:

$$\Delta P_{in} = \frac{2\sigma}{r}$$

r – the radius of the spherical sample, σ – the surface tension at the "condensed phase-vapor" interface. The increase of the internal pressure results in a change in the molar Gibbs energy of the substance inside the spherical sample. This molar Gibbs energy G^*_{sph} is larger than $G_{bulk.}$ The difference in the Gibbs energy of the spherical sample and the bulk phase is equal to $\Delta P_{in} V$:

$$G^*_{sph} = G_{bulk} + \Delta P_{in} V = G_{bulk} + \frac{2\sigma V}{r}, \qquad (2)$$

V is the molar volume of the liquid or solid substance. Therefore from equation (1)

$$G^*_{sph} = G_{bulk} + \frac{2\sigma V}{r} = G_{vap} = G^\circ_{vap} + RT \ln p^* \qquad (3)$$

p^* is the saturated vapor pressure of the spherical sample with the radius r.

5.1 The saturated vapor pressure of water at T = 298 K is 3.15×10^{-2} bar. Calculate the saturated vapor pressure of the spherical droplets of water with the radius of:

i) 1 μm,

ii) 1 nm.

The surface tension at the liquid-vapor interface of water is 0.072 J m^{-2}.

5.2 Assuming that the substance retains properties of a bulk while the difference between its saturated vapor pressure and the saturated pressure of the bulk is less than 1 %, what is the minimum radius of the spherical sample that can still be considered as a bulk phase? How many molecules of water are there in such a droplet?

5.3 Few droplets of mercury were put inside a SWNT maintained at 400 K. What is the minimum vapor pressure of mercury inside the tube? The saturated vapor pressure of bulk mercury is 1.38×10^{-3} bar, the density of mercury ρ(Hg) = 13.5 g cm^{-3}, the surface tension at the liquid-vapor interface of mercury is 0.484 J m^{-2} at the given temperature.

5.4 The boiling point of benzene at the standard atmospheric pressure is T_b = 353.3 K. The temperature dependence of the saturated vapor pressure of benzene near the boiling point is given by the equation

$$\ln p(T) = -\frac{\Delta H_{\text{vap}}}{R\,T} + const \qquad (4)$$

where ΔH_{vap} = 30720 J mol^{-1} is the enthalpy of vaporization of benzene. Estimate the boiling point (T*) of the finely dispersed liquid benzene at the standard atmospheric pressure if the sample consists of droplets with the radius r = 50 nm. The surface tension of benzene near the boiling point is 0.021 J m^{-2} and its density is 0.814 g cm^{-3}.

5.5 In general, properties of the bulk and nano-sized material composed by one and the same substance A are different. Which of the following thermodynamic constants will decrease when passing from the bulk to the nano-scaled material?

1) Solubility of A in any solvent;
2) the boiling temperature at atmospheric pressure;
3) the saturated vapor pressure over solid substance A;
4) the equilibrium constant of a chemical reaction, where A is a reagent;

5) the equilibrium constant of a chemical reaction, where A is a product.

SOLUTION OF PREPARATORY PROBLEM 5

5.1 From equations (1) and (3) one gets

$$\frac{2\sigma V}{r} = RT \ln\frac{p^*}{p}$$

$$p^* = p \exp\left(\frac{2\sigma V}{rRT}\right) \qquad (5)$$

Knowing p we get p^*.

For r = 1 μm: $p^* = 3.15\times10^{-2} \exp\left(\frac{2\times0.072\times18\times10^{-6}}{1.00\times10^{-6}\times\ 8.314\ \times\ 298}\right) = 3.15\times10^{-2}$ bar

For r = 1 nm: $p^* = 3.15\times10^{-2}\exp\left(\frac{2\times0.072\times18\times10^{-6}}{1.00\times10^{-9}\times\ 8.314\times298}\right) = 8.97\times10^{-2}$ bar

5.2 The minimum size of the spherical sample that can still be considered as a bulk phase can be calculated from the inequality

$$\exp\left(\frac{2\sigma V}{rRT}\right) \le 1.01,$$

$$\exp\left(\frac{2\times0.072\times18\times10^{-6}}{r\times8.314\times298}\right) \le 1.01$$

$$r \ge 1.05\times10^{-7} \text{ m} = 105 \text{ nm}.$$

r = 105 nm may be considered as the minimum radius.

The number of water molecules N in the drop with r = 105 nm can be calculated from the formula

$$N = \frac{4\pi r^3}{3V} N_A,$$

$V = 18\times10^{-6}$ m^3 is the molar volume of water, $N_A = 6.02\times10^{23}$ mol^{-1} is the Avogadro number.

$$N = \frac{4\pi(1.05\times10^{-7})^3}{3\times18\times10^{-6}}\times 6.02\times10^{23} = 1.62\times10^{8}$$

5.3 The maximum radius of the droplet is equal to the internal radius of the nanotube. The saturated pressure goes up while the radius of the droplet goes down. Therefore, the maximum radius corresponds to the minimum vapor pressure of mercury inside the tube. One has to calculate the saturated vapor pressure above the droplet with r = 0.75 nm (d = 1.5 nm). From eq. 5 one gets:

$$p^* = 1.38\times10^{-3}\exp\left(\frac{2\times 0.484\times\frac{200.5}{13.5}\times10^{-6}}{0.75\times10^{-9}\times 8.314\times 400}\right) = 0.440 \text{ bar}.$$

This pressure is approximately three hundred times higher than the one of the bulk liquid mercury.

Comment. The droplets of mercury are so small, that the whole basis of calculation is suspect. There is an experimental evidence of a validity of the equation at least for $r \geq 3$ nm. For smaller values it is believed that the orders of the magnitude of the vapor pressures are approximately correct.

5.4 The boiling temperature of the dispersed benzene is T^*. At this temperature the saturated vapor pressure p^* is equal to the atmospheric pressure 1 bar. So,

$$\ln p^*(T^*) = \ln\frac{p^*(T^*)}{p(T^*)} + \ln p(T^*) = 0$$

From equations (4) and (5)

$$\frac{2\sigma V}{rRT^*} - \frac{\Delta H_{vap}}{RT^*} + const = 0$$

The *const* can be calculated from the boiling point of bulk benzene:

$$\ln p(T_b) = -\frac{\Delta H_{vap}}{RT_b} + const = 0$$

$$const = \frac{\Delta H_{vap}}{RT_b}$$

Thus

$$\frac{2\sigma V}{rRT^*} - \frac{\Delta H_{vap}}{RT^*} + \frac{\Delta H_{vap}}{RT_b} = 0$$

$$T^* = T_b\left(1 - \frac{2\sigma V}{\Delta H_{vap} r}\right) = 353.3 \times \left(1 - \frac{2 \times 0.021 \times \frac{78}{0.814} \times 10^{-6}}{30720 \times 5 \times 10^{-8}}\right) = 352.4\ \text{K}$$

5.5 The molar Gibbs energy of liquid A increases when passing from the bulk phase to the small droplet (see equation 2).

Increase of the molar Gibbs energy leads to the decrease of the boiling temperature at atmospheric pressure and the equilibrium constant of the chemical reaction (A is a product).

The decrease of the boiling temperature was demonstrated above.

The equilibrium constant K can be calculated from the standard reaction Gibbs energy, $\Delta_r G^0$:

$$RT\ln K = -\Delta_r G^0 = -(G^0_{\text{prod}} - G^0_{\text{react}})$$

G^0_{prod}, G^0_{react} are molar Gibbs energies for products and reactants, respectively. If G^0_{prod} increases, the equilibrium constant K goes down.

THEORETICAL PROBLEM 6

In which direction does a chemical reaction proceed?

The natural tendency of any chemical reaction to proceed in a certain direction at constant temperature and pressure is determined by the sign of the Gibbs energy of the reaction, ΔG. This is the universal principle. If $\Delta G < 0$, the reaction can proceed predominantly in the forward direction (a product-favored reaction). If $\Delta G > 0$ the reaction can proceed predominantly in the reverse direction (a reactant-favored reaction). When $\Delta G = 0$ the reaction is at equilibrium.

The standard reaction Gibbs energy, $\Delta G°$, can be calculated from the tabulated Gibbs energies of formation of the reactants and products (see the Table).

6.1 Calculate the equilibrium constant of reaction (1) at 1627 °C. Can the reaction proceed predominantly in the forward direction if the initial partial pressure of O_2 is below 1.00 Torr?

$$2\ Ni(l) + O_2(g) = 2\ NiO(s) \qquad (1)$$

The standard Gibbs energy of the reaction

$$TiO_2(s) + 3\ C(s) = 2\ CO(g) + TiC(s) \qquad (2)$$

is positive at 727 °C.

6.2 Calculate the equilibrium pressure of CO at 727 °C.

What should be the reaction conditions to allow for the forward reaction to be the predominant process at this temperature if this is possible at all?

6.3 Calculate the standard Gibbs energy of the reaction

$$3\ H_2 + N_2 = 2\ NH_3 \qquad (3)$$

at 300 K. Can the forward reaction be the predominant process under the following conditions: $p(NH_3) = 1.0$ atm, $p(H_2) = 0.50$ atm, $p(N_2) = 3.0$ atm?

In fact the reaction does not occur at 300 K at a noticeable rate. Why?

Table 1. Gibbs energies of formation*

Substance	t, °C	$\Delta_f G^o$, kJ mol^{-1}
NiO	1627	–72.1
TiO_2	727	–757.8
TiC	727	–162.6
CO	727	–200.2
NH_3	27	–16.26

*The standard pressure – 1atm, JANAF Tables.

SOLUTION OF PREPARATORY PROBLEM 6

6.1 The standard Gibbs energy of the reaction (1) is equal to the Gibbs energy of formation of NiO, multiplied by two:

$$\Delta G^o_{1900} = 2 \times (-72.1) = -144.2 \text{ kJ mol}^{-1}$$

The equilibrium constant and the equilibrium partial pressure of oxygen at 1900 K are:

$$K = \frac{1}{p(\mathrm{O_2})} = \exp\left(-\frac{\Delta G^o}{RT}\right) = \exp\left(-\frac{144200}{8.314 \times 1900}\right) = 9215,$$

$$p(\mathrm{O_2}) = \frac{1}{K} = 1.085 \times 10^{-4} \text{ atm} = 0.0825 \text{ Torr}$$

If the oxygen pressure is above the equilibrium value, the reaction will proceed from the left to the right to reach the equilibrium state. So the answer is

$$0.0825 \text{ Torr} < p(\mathrm{O_2}) < 1.00 \text{ Torr}.$$

6.2 The reaction proceeds forward as long as ΔG, not ΔG° is negative! The following equation is valid for the reaction (2):

$$\Delta G = \Delta G^o + RT \ln p(\mathrm{CO})^2$$

(solid reactants and products are considered to be pure substances, they do not contribute to this equation). The reaction proceeds from the left to the right if $\Delta G < 0$:

$$\Delta G^o > -RT \ln p(\mathrm{CO})^2,$$

$$p(\mathrm{CO}) < \exp\left(-\frac{\Delta G^o}{2RT}\right)$$

Using the data from Table 1 we obtain:

$$\Delta G^\circ = -162.6 + 2 \times (-200.2) - (-757.8) = 194.8 \text{ kJ mol}^{-1}.$$

$$p(\mathrm{CO}) < \exp\left(-\frac{194800}{2 \times 8.314 \times 1000}\right) = 8.17 \times 10^{-6} \text{ atm}.$$

Therefore, if the partial pressure of CO in the system is below 8.17×10^{-6} atm, the reaction can predominantly proceed from the left to the right.

6.3 Using the data from Table 1, the following expression for ΔG of the reaction (3) is derived

$$\Delta G = \Delta G^o + RT \ln \frac{p(NH_3)^2}{p(H_2)^3 p(N_2)} = 2 \times (-16260) + (8.314 \times 300) \times \ln \frac{1.0^2}{0.50^3 \times 3.0} =$$

$$= -30100 \text{ J mol}^{-1} = -30.1 \text{ kJ mol}^{-1}.$$

At 300 K the reaction (3) is allowed to proceed from the left to the right only. However, formation of ammonia is extremely slow under these conditions due to the kinetic restrictions.

THEORETICAL PROBLEM 7

Le Chatelier's principle

Le Chatelier's principle states that

«Every system in the state of equilibrium when subjected to a perturbation responds in a way that tends to eliminate the effect» (P.W. Atkins "Physical Chemistry").

Let us see how this principle works. Let a chemical equilibrium be established in the following reaction between the ideal gases:

$$3\ H_2 + N_2 = 2\ NH_3 \qquad (1)$$

At the temperature of T = 400 K partial pressures of reactants and product are respectively: $p(H_2)$ = 0.376 bar, $p(N_2)$ = 0.125 bar, $p(NH_3)$ = 0.499 bar.

The equilibrium was disturbed. Let this disturbance be:

a) increase of the total pressure in the system at constant temperature,

b) increase of the amount of NH_3 in the system at constant total pressure and temperature,

c) small increase of the amount of N_2 in the system at constant total pressure and temperature,

d) small increase of the amount of H_2 in the system at constant total pressure and temperature.

7.1 Calculate the standard Gibbs energy for the reaction (1) at T = 400 K.

7.2 Write down the expression for the Gibbs energy of reaction (1) for any pressure of reactants and product after perturbation. This expression is called the isotherm of chemical reaction.

7.3 Using the equation of isotherm from question 7.2 determine in which direction the reaction (1) will predominantly proceed after the disturbance of equilibrium as indicated in (a) – (d).

7.4 Will the answers to question 3 change, if the initial equilibrium partial pressures in the system are: $p(H_2)$ = 0.111 bar, $p(N_2)$ = 0.700 bar, $p(NH_3)$ = 0.189 bar? Assume that temperature and total pressure in the system are the same as in questions 7.1 – 7.3.

SOLUTION OF PREPARATORY PROBLEM 7

7.1 $$\Delta G^o = -RT\ln K_p = -RT\ln\frac{p(\mathrm{NH_3})^2}{p(\mathrm{H_2})^3\,p(\mathrm{N_2})} \qquad (2)$$

$$\Delta G^o = -8.314\times 400\times\ln\frac{0.499^2}{0.376^3\times 0.125} = -12100\ \mathrm{J\ mol^{-1}} = -12.1\ \mathrm{kJ\ mol^{-1}}.$$

7.2 After perturbation, the Gibbs energy of the reaction is:

$$\Delta G = \Delta G^o + RT\ln\frac{p'(\mathrm{NH_3})^2}{p'(\mathrm{H_2})^3\,p'(\mathrm{N_2})} \qquad (3)$$

The apostrophe ‘ denotes the partial pressures at the non-equilibrium state. The sign of ΔG (positive or negative) determines the direction in which the equilibrium shifts after perturbation.

7.3, 7.4

Let us determine the sign of ΔG in all the considered cases. From equations (2) and (3), we get:

$$\frac{\Delta G}{RT} = 2\ln\frac{p'(\mathrm{NH_3})}{p(\mathrm{NH_3})} - 3\ln\frac{p'(\mathrm{H_2})}{p(\mathrm{H_2})} - \ln\frac{p'(\mathrm{N_2})}{p(\mathrm{N_2})} \qquad (4)$$

Reactants and product are ideal gases, so we can use the Dalton law. Molar fractions x can be calculated from the partial pressures:

$$p(\mathrm{NH_3}) = x_{\mathrm{NH_3}}P,\quad p(\mathrm{H_2}) = x_{\mathrm{H_2}}P,\quad p(\mathrm{N_2}) = x_{\mathrm{N_2}}P$$
$$x_{\mathrm{NH_3}} + x_{\mathrm{H_2}} + x_{\mathrm{N_2}} = 1 \qquad (5)$$

P is the total pressure in the system. Taking into account (5), equation (4) can be written in a form:

$$\frac{\Delta G}{RT} = 2\ln\frac{x'_{\mathrm{NH_3}}}{x_{\mathrm{NH_3}}} - 3\ln\frac{x'_{\mathrm{H_2}}}{x_{\mathrm{H_2}}} - \ln\frac{x'_{\mathrm{N_2}}}{x_{\mathrm{N_2}}} - 2\ln\frac{P'}{P} \qquad (6)$$

In the case (a), only the last term in the right hand side of the equation (6) is non-zero. Since the total pressure is increased $P' > P$, the right side of equation (6) is negative, $\Delta G < 0$. The increase of the total pressure will push the reaction towards

formation of additional amounts of ammonia. The reaction will proceed predominantly in the forward direction (a product-favored reaction).

In the case (b), only the last term on the right side of (6) is equal to zero. Molar fraction of ammonia increases, whereas molar fractions of hydrogen and nitrogen decrease:

$$\ln\frac{x'_{NH_3}}{x_{NH_3}} > 0, \quad \ln\frac{x'_{H_2}}{x_{H_2}} < 0, \quad \ln\frac{x'_{N_2}}{x_{N_2}} < 0\,.$$

The right side of (6) is positive and $\Delta G > 0$. In the case b), the reaction will proceed predominantly in the reverse direction towards formation of additional amounts of reactants.

In the case (c) similarly as in the case (b), all the molar fractions change after the addition of hydrogen to the system. After simple rearrangements of the equation (6) one gets

$$\frac{\Delta G}{RT} = -3\ln\frac{n'_{H_2}}{n_{H_2}} - 2\ln\frac{n_{H_2}+n_{N_2}+n_{NH_3}}{n'_{H_2}+n_{N_2}+n_{NH_3}}, \qquad (7)$$

where n is the number of moles of reactants or product. The first term in the right side of (7) is negative ($n'_{H_2} > n_{H_2}$) while the second one is positive.

Let us solve the inequality $\Delta G < 0$:

$$-2\ln\frac{n_{H_2}+n_{N_2}+n_{NH_3}}{n'_{H_2}+n_{N_2}+n_{NH_3}} < 3\ln\frac{n'_{H_2}}{n_{H_2}} \qquad (8)$$

Let $n'_{H_2} = n_{H_2} + \Delta_{H_2}$, where Δ_{H_2} is the number of moles of hydrogen added to the system. Since Δ_{H_2} is small, $\Delta_{H_2} = n_{H_2}$. The inequality (8) can be written in the form:

$$\left(1+\frac{\Delta_{H_2}}{n_{NH_3}+n_{N_2}+n_{H_2}}\right)^2 < \left(1+\frac{\Delta_{H_2}}{n_{H_2}}\right)^3$$

Terms with the second and third powers of Δ_{H_2} can be neglected, then:

$$\frac{2\,\Delta_{H_2}}{n_{NH_3}+n_{N_2}+n_{H_2}} < \frac{3\,\Delta_{H_2}}{n_{H_2}},$$

or

$$x_{H_2} < \frac{3}{2}$$

This inequality is always valid, since molar fractions are less than one. It means that in the case (c) $\Delta G < 0$, no matter what the initial composition of the mixture was. After addition of a small amount of hydrogen to the system the reaction will proceed predominantly in the direction of ammonia synthesis.

In the case (d) both hydrogen and nitrogen are reactants. Their roles in the reaction (1) are similar. It is reasonable to expect that in cases (c) and (d) the answer to the problem will be the same. However, let us look at equation (9) which is similar to equation (8):

$$\frac{\Delta G}{R\,T} = -\ln\frac{n'_{N_2}}{n_{N_2}} - 2\ln\frac{n_{H_2}+n_{N_2}+n_{NH_3}}{n_{H_2}+n'_{N_2}+n_{NH_3}}. \qquad (9)$$

In the right side of (9) the first term is negative ($n'_{N_2} > n_{N_2}$), while the second is positive.

Let us solve the inequality $\Delta G < 0$:

$$-2\ln\frac{n_{H_2}+n_{N_2}+n_{NH_3}}{n_{H_2}+n'_{N_2}+n_{NH_3}} < \ln\frac{n'_{N_2}}{n_{N_2}}. \qquad (10)$$

Denote $n'_{N_2} = n_{N_2} + \Delta_{N_2}$, then

$$\left(1+\frac{\Delta_{N_2}}{n_{NH_3}+n_{N_2}+n_{H_2}}\right)^2 < 1+\frac{\Delta_{N_2}}{n_{N_2}}.$$

Again, term with the second power of Δ_{N_2} can be neglected, and then:

$$\frac{2\,\Delta_{N_2}}{n_{NH_3}+n_{N_2}+n_{H_2}} < \frac{\Delta_{N_2}}{n_{N_2}},$$

thus,

$$x_{N_2} < \frac{1}{2}$$

If the molar fraction of nitrogen in the initial equilibrium mixture is less than 0.5 (question 7.3), the small increase of the amount of nitrogen will push the reaction towards the formation of ammonia. But if

$$x_{N_2} > \frac{1}{2}$$

(question 7.4) after the addition of nitrogen the reaction will proceed predominantly in the reverse direction towards formation of the reactants.

Thus, in some cases addition of the reactant can lead to the opposite results. This "strange conclusion" is in full accord with the Le Chatelier's principle!

THEORETICAL PROBLEM 8

Dmitry Ivanovič Mendelejev: What besides the periodic table?

The Russian chemist D. Mendeleev is known for his Periodic Table of elements. This discovery made him famous worldwide. Dmitry Mendeleev has carried out some other interesting studies as well. Consider two of them.

Mendeleev was the first who state that every substance has "the temperature of the absolute boiling". Above this temperature "the substance will stay in the gas phase no matter how high the pressure is". According to Mendeleev "the temperature of the absolute boiling of water" is 543 °C.

8.1 What is "the temperature of the absolute boiling"?

8.2 Indicate the temperature of the absolute boiling in the *P*-*T* phase diagram of water.

8.3 Calculate the temperature of the absolute boiling of water from the Van der Waals equation of state:

$$\left(p + \frac{a}{V^2}\right)(V - b) = R\,T\ ,$$

For H_2O, a = 5.464 l^2 atm mol^{-2}, b = 0.03049 l mol^{-1}.

In Russia many people believe that D. Mendeleev invented the recipe of the famous drink "Russian vodka". We have a chance to check this legend.

The fact is that in his Ph.D. thesis Mendeleev characterized some properties of the binary system "ethanol-water". He measured the density ρ of a series of binary solutions of various compositions w, where w(%) is the mass percent of ethanol in the mixture. The derivative $d\rho / dw$ is presented in Fig. 1 as a function of w. The curve markedly changes the slope three times. According to D. Mendeleev these three special points correspond to the compositions of the weakly bonded chemical compounds, "hydrates of ethanol".

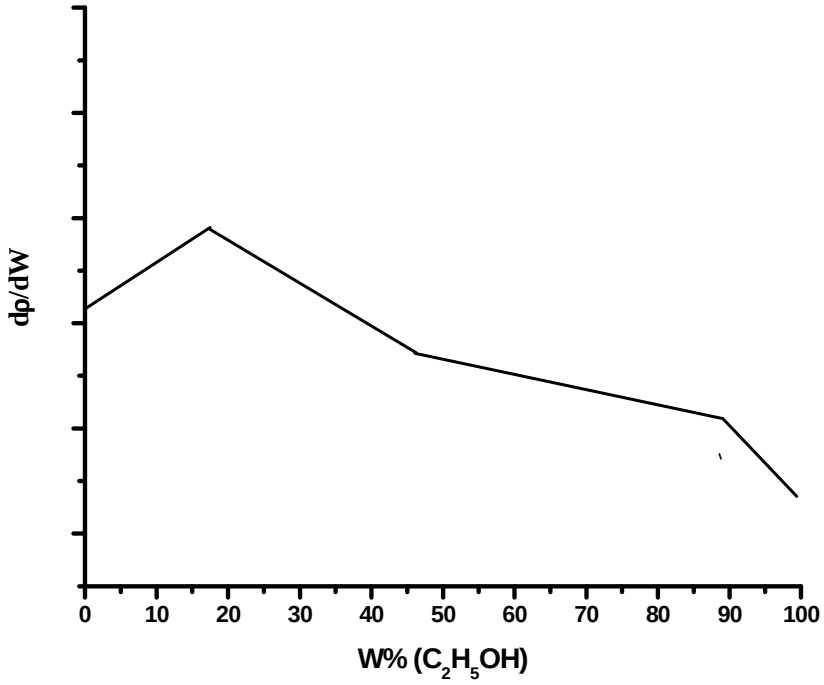


Fig. 1. Experimental results obtained by Mendeleev

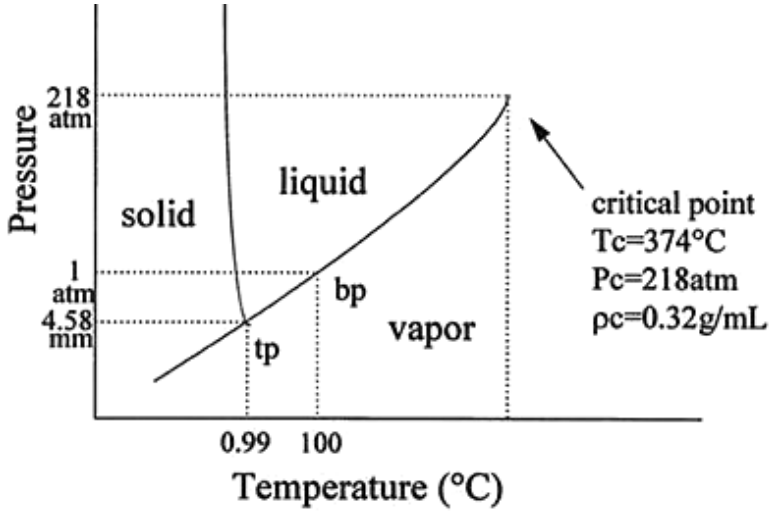
8.4 What are the chemical formulas of “the hydrates of the ethanol”?

8.5 Does the composition of any of the “hydrates” resemble the recipe of vodka (40 volume percent of C_2H_5OH)? The density of ethanol is 0.794 g cm^{-3}. Decide whether or not Dmitry Mendeleev took part in “the discovery of Russian vodka”.

SOLUTION OF PREPARATORY PROBLEM 8

8.1 At present temperature of the absolute boiling is called critical temperature. D. Mendeleev introduced the «temperature of the absolute boiling» in 1860. T. Andrews introduced his concepts of the critical temperature and the critical point in 1869.

8.2 On the phase diagram of water the line of phase equilibrium between liquid and vapor terminates at the critical point. The corresponding temperature is “the temperature of the absolute boiling” (see figure).



8.3 Critical temperature T_c can be calculated from the parameters *a* and *b* of the Van-der-Waals equation of state:

$$T_c = \frac{8a}{27Rb}$$

For H_2O this equation gives

$$T_c(H_2O) = \frac{8 \times 5.464 \times 101.3}{27 \times 8.314 \times 0.03049} = 647\,K = 374\,℃$$

One can see that Mendeleev overestimated the temperature of absolute boiling of water significantly. His value was 170 degrees above the real one.

8.4 From mass percent we calculate molar ratio:

$$\frac{n(C_2H_5OH)}{n(H_2O)} = \frac{\frac{w(\%)}{46}}{\frac{100 - w(\%)}{18}} = \frac{18w}{46(100 - w)}$$

There are three break points in the figure, namely at *w* = 17.5, 46 and 88 %. They correspond to the molar ratios $\frac{n(C_2H_5OH)}{n(H_2O)} = 1:12;\ 1:3;\ 3:1$. According to Mendeleev the binary solution consists of the weakly bonded associates of ethanol with water. The compositions of these “hydrates of ethanol” are given by the molar ratios mentioned above.

8.5 However, the special compositions found by Mendeleev have nothing in common with the recipe of vodka. The volume percent $V\%$ of the ethanol in vodka is 40. The corresponding mass percent is:

$$w\% = \frac{40 \times 0.794}{(40 \times 0.794) + (60 \times 1.000)} \times 100 = 34.6\%$$

There is nothing special in this part of the graph! From the point of view of physical chemistry there is nothing special in the recipe of vodka.

THEORETICAL PROBLEM 9

Kinetics of a free radical reaction

Pyrolysis is an important industrial process for conversion of coal to liquid fuels and chemical feedstocks. The structure of coal can be viewed as a three-dimensional network of polycyclic aromatic building blocks joined together by short aliphatic bridges. In model pyrolysis studies, α,ω-diphenylalkanes are sometimes used as model compounds for coal.

Thermal decomposition of 1,3-diphenylpropane gives toluene and styrene as the major products and ethylbenzene and other hydrocarbons as byproducts. The following mechanism of decomposition has been proposed (the first step is the slowest):

$$\underset{s}{PhCH_2CH_2CH_2Ph} \xrightarrow{k_1} \underset{1}{PhCH_2\bullet} + \underset{2}{PhCH_2CH_2\bullet} \qquad (1)$$

$$PhCH_2CH_2\bullet + PhCH_2CH_2CH_2Ph \xrightarrow{k_2} PhCH_2CH_3 + \underset{3}{Ph\overset{\bullet}{C}HCH_2CH_2Ph} \qquad (2)$$

$$PhCH_2\bullet + PhCH_2CH_2CH_2Ph \xrightarrow{k_3} \underset{P_1}{PhCH_3} + \underset{3}{Ph\overset{\bullet}{C}HCH_2CH_2Ph} \qquad (3)$$

$$\underset{3}{Ph\overset{\bullet}{C}HCH_2CH_2Ph} \xrightarrow{k_4} \underset{P_2}{PhCH=CH_2} + PhCH_2\bullet \qquad (4)$$

9.1 Applying the steady-state approximation for the radical **2**, derive the rate equation for the side reaction of ethylbenzene formation.

9.2 What is the ratio between the steady-state concentrations of the radicals **1** and **3**?

Additionally, two free radicals can recombine. The rate constant of recombination k_R is supposed to be the same for all radicals.

$$R_1\bullet + R_2\bullet \xrightarrow{k_R} R_1R_2$$

9.3 Why could we neglect these reactions in the steady-state equations in questions 9.1 and 9.2?

9.4 One of the radicals is present in the reaction mixture at much higher concentration than others. This radical is:

a) $PhC\dot{H}CH_2CH_2Ph$, because it is the most stable one;

b) $PhCH_2\bullet$, because the rate constant of β-scission reaction (4) is higher than the rate constant of chain propagation reaction (3);

c) $PhCH_2CH_2\bullet$, because it accumulates in the system.

9.5 Obtain the rate equation for toluene formation. Determine the reaction order. Express the effective activation energy via the activation energies of elementary steps.

SOLUTION OF PREPARATORY PROBLEM 9

9.1

$$\frac{d[2]}{dt} = 0 = k_1[S] - k_2[S][2]$$

$$r = k_2[S][2] = k_1[S]$$

9.2

$$\frac{d[2]}{dt} = 0 = k_1[S] - k_2[S][2]$$

$$r = k_2[S][2] = k_1[S]$$

$$\frac{d[1]}{dt} = 0 = k_1[S] - k_3[S][1] + k_4[3]$$

$$\frac{d[3]}{dt} = 0 = k_2[S][2] + k_3[S][1] - k_4[3] = k_1[S] + k_3[S][1] - k_4[3]$$

The first step is the slowest, therefore $k_1[S] << k_3[S][1]$, by neglecting $k_1[S]$ term, we get:

$$k_3[S][1] = k_4[3]$$

$$\frac{[1]}{[3]} = \frac{k_4}{k_3[S]}$$

9.3 Since the rate of radicals generation is small, the concentrations of radicals is low, and the rate of chain propagation which is proportional to the radical concentration is much higher than the rate of recombination which is proportional to the square of the radical concentration. This approximation is known as the long-chain approximation (many chain propagation steps occur before the radical recombinates).

9.4 The correct answer is (b).

9.5 The rate of free radicals generation must be equal to their recombination rate. Since the concentration of $PhCH_2^{\bullet}$ is much higher than those of other radicals, only the rate of two benzyl radicals recombination should be taken into account:

$$\frac{\mathrm{d[R]}}{\mathrm{d}t} = 0 = 2\,k_1[\mathrm{S}] - 2\,k_\mathrm{R}[1]^2$$

$$[1] = \sqrt{\frac{k_1[\mathrm{S}]}{k_\mathrm{R}}}$$

$$r = k_3[1][\mathrm{S}] = \frac{k_1^{1/2}\,k_3[\mathrm{S}]^{3/2}}{k_\mathrm{R}^{1/2}}$$

The total order is 1.5.

The effective rate constant:

$$k = \frac{k_1^{1/2}\,k_3}{k_\mathrm{R}^{1/2}}$$

The activation energy is:

$$E = \frac{E_1}{2} + E_3 - \frac{E_\mathrm{R}}{2} \approx \frac{E_1}{2} + E_3,$$

because activation energy of free radical recombination is close to zero.

THEORETICAL PROBLEM 10

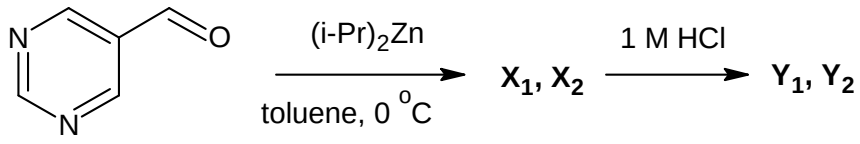
Asymmetric autocatalysis – amplification of chiral asymmetry

Living nature is homochiral: almost all natural amino acids have L-configuration, sugars – D-configuration. One of the possible explanations of this phenomenon is based on the concept of asymmetric autocatalysis. In some reactions chiral products can serve as catalysts of their own formation: the larger is the content of one of the enantiomers the faster is its synthesis.

The simplest equation for autocatalysis is: A + P $\rightarrow$ 2 P, where P is product. Reaction can be performed under various conditions: either in a closed system when reagents are mixed only once, or in an open system where reagent A is being continuously added to the mixture so that its concentration is maintained constant.

10.1 Write the kinetic equations and draw the kinetic curves for product P in the closed and open systems. Assume that the initial concentration of P is non-zero but small.

The first reaction of asymmetric autocatalysis was discovered in the early 1990-s. Addition of diisopropylzinc to pyrimidine-5-carbaldehyde in toluene leads to the mixture of enantiomers $\mathbf{X}_1$ and $\mathbf{X_2}$, which after hydrolysis is transformed to enantiomeric alcohols $\mathbf{Y_1}$ and $\mathbf{Y_2}$:



10.2 Draw the structure of enantiomeric pairs **X** and **Y**, and show the configuration of the stereocenter.

It turned out that the presence of small amounts of any product ($\mathbf{Y_1}$ or $\mathbf{Y_2}$) selectively accelerates the formation of that specific product which leads to enantiomeric enrichment of the reaction mixture. Suppose that the yield of each product is proportional to the square of its molar fraction in the mixture of alcohols prior to synthesis.

10.3 To 1 mmol of mixture $\mathbf{Y_1}$ and $\mathbf{Y_2}$, containing 55 % of $\mathbf{Y_1}$, 1 mmol of aldehyde and 1 mmol of diisopropylzinc are added several times. Assuming that total reaction

yield is 100 %, calculate how many times we should add the reagents to enrich the mixture of alcohols up to: a) 70 %, b) 90 %, c) 99 % of $\mathbf{Y_1}$.

Note. You need to write a small iteration program.

SOLUTION OF PREPARATORY PROBLEM 10

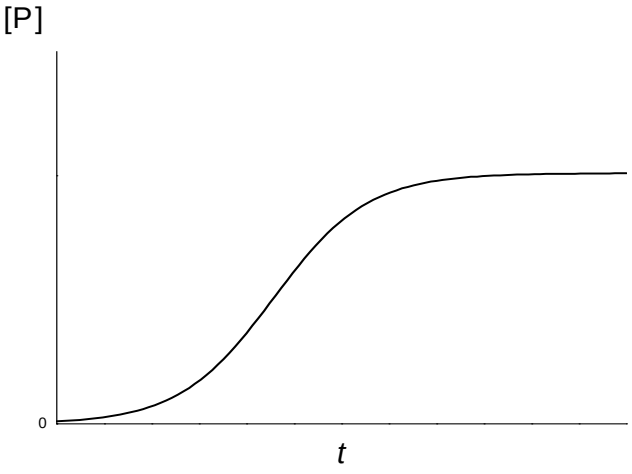
10.1 a) The closed system. The kinetic equation:

$$\frac{\mathrm{d[P]}}{\mathrm{d}t} = k\,[\mathrm{A}]\,[\mathrm{P}]$$

Taking into account the mass balance $[A] + [P] = [A]_0 + [P]_0$, we get:

$$\frac{\mathrm{d[P]}}{\mathrm{d}t} = k([\mathrm{A}]_0 + [\mathrm{P}]_0 - [\mathrm{P}])[\mathrm{P}]$$

At early stages the rate of P formation increases, but after some accumulation of the product reaction becomes more slow and finally its rate approaches zero.

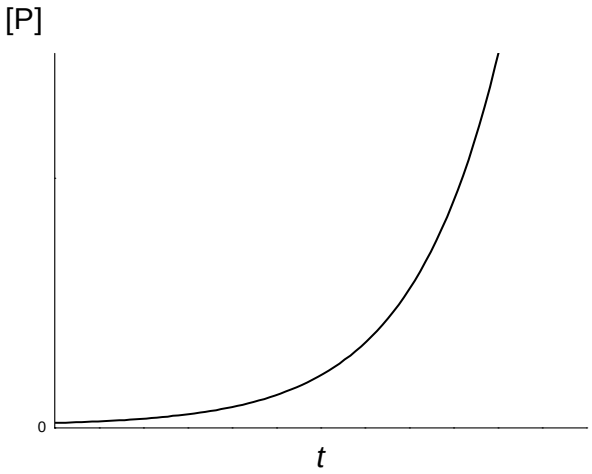


b) The open system. The kinetic equation:

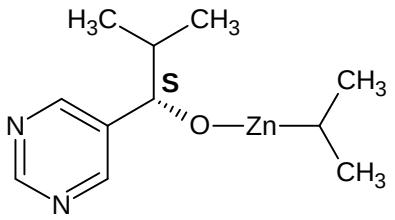
$$\frac{\mathrm{d[P]}}{\mathrm{d}t} = k\,[\mathrm{A}]_0[\mathrm{P}]$$

Both the rate of reaction and concentration [P] increase with time:

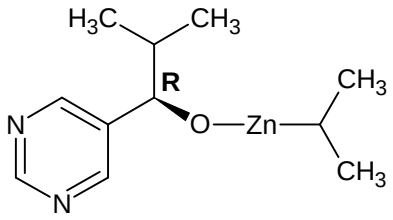
$$[P] = [P]_0 \exp(k[A]_0\, t)$$



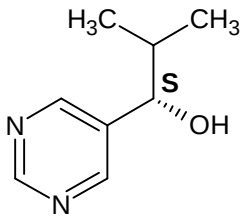
10.2 Diisopropylzinc is added across the C=O bond. Subsequent hydrolysis leads to a mixture of enantiomeric secondary alcohols:



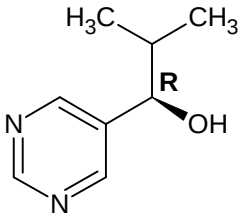
X1



X2



Y1



Y2

10.3 After the (n – 1)th addition the system will contain n mmol of mixture of alcohols. Let the fraction of (S)-isomer be a_n, and that of (R)-isomer – b_n. Let us add one more mmol of reagents. The yield of each alcohol is proportional to its fraction, hence

additionaly $\frac{a_n^2}{a_n^2+b_n^2}$ mmol of (S)- and $\frac{b_n^2}{a_n^2+b_n^2}$ mmol of (R)-isomer are formed. The new fraction of (S)-isomer is:

$$a_{n+1} = \frac{na_n + \frac{a_n^2}{a_n^2+b_n^2}}{n+1} = \frac{na_n + \frac{a_n^2}{a_n^2+(1-a_n)^2}}{n+1}$$

Now we need to solve the inequalities $a_{n+1} > 0.7; 0.9; 0.99$ with the initial condition $a_1 = 0.55$. It is easily done numerically. The iteration program can be written in any language. For example, the procedure in MathCad package has the form:

$$n := 436$$

$$r := \left| \begin{array}{l} a \leftarrow 0.55 \\ \text{for } x \in 1..n \\ \quad a \leftarrow \dfrac{a \cdot x + \dfrac{a^2}{a^2 + (1-a)^2}}{x+1} \end{array} \right.$$

$$r = 0.99001$$

Applying recurrence formula, we obtain: $a_9 > 0.7$, $a_{40} > 0.9$, $a_{437} > 0.99$.

Answer. a) $n = 8$; b) $n = 39$; c) $n = 436$.

THEORETICAL PROBLEM 11

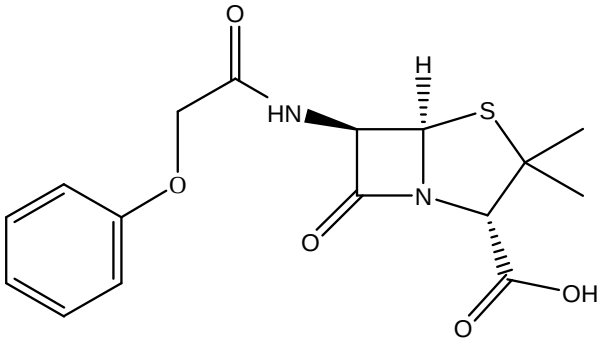
Radiocarbon dating

The carbon-14, a radioactive isotope of carbon, is often used to date archaeological, geological, and hydrogeological samples. The half-life of ^{14}C is $t_{1/2}$ = 5730 years, but in calculations of the age of samples, a different value of half-life, $t'_{1/2}$ = 5568 years, is used. The ^{14}C is produced from nitrogen in the atmosphere under the action of cosmic rays. It can be included in the organisms of plants and animals through the photosynthesis and the food chains. The radiocarbon content in living organisms is nearly constant with the activity of ^{14}C being 230 Bq per kg of carbon. After death of an organism, the carbon exchange stops and the ^{14}C content starts decreasing continually.

11.1 Give the balanced reaction equations of formation and decay of ^{14}C.

11.2 Activity of radiocarbon in a sample of cloth from an Egyptian pyramid corresponds to 480 disintegrations per hour per gram of carbon. What is the age of the cloth?

In another pyramid, a white powder was found. Analysis showed it was a pure phenoxymethylpenicillin (Penicillin V):



Commercial phenoxymethylpenicillin is produced by microorganisms cultured in a medium containing carbohydrates (lactose, glucose, sucrose), cornsteep liquor, mineral salts and phenoxyacetic acid.

It was decided to determine the radiocarbon content to estimate the age of the powder. The $^{14}C/^{12}C$ ratio determined from mass-spectrometry measurements amounts to 6.0×10^{-13}.

11.3 The archaeologists estimated the age of the powder from the radioactive decay law. What was the production date they obtained?

11.4 Explain this result. When was the powder produced in reality?

Constants were taken from:

Lloyd A. Currie. The Remarkable Metrological History of Radiocarbon Dating. // J. Res. Natl. Inst. Stand. Technol. 109, 185-217 (2004)

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SOLUTION OF PREPARATORY PROBLEM 11

11.1

$$^{14}_{7}\mathrm{N} + {}^{1}_{0}\mathrm{n} \rightarrow {}^{14}_{6}\mathrm{C} + {}^{1}_{1}\mathrm{H}$$

$$^{14}_{6}\mathrm{C} \xrightarrow{\beta^-} {}^{14}_{7}\mathrm{N}$$

11.2 Dependence of the activity (a) on time:

$$a = a_0 \mathrm{e}^{-\lambda t}$$

$$\ln\frac{a_0}{a} = \lambda t;$$

$$\lambda = \frac{\ln 2}{t'_{1/2}} = 1.245\times10^{-4}\ \text{years}^{-1}$$

$$t = \frac{\ln\dfrac{230}{480\times1000/3600}}{1.245\times10^{-4}} = 4380\ \text{years}$$

11.3 Activity 230 Bq/kg corresponds to the following ^{14}C / ^{12}C ratio:

$$a = N_A k \frac{m}{M(^{12}\mathrm{C})} w = N_A \frac{\ln 2}{t_{1/2}} \frac{m}{M(^{12}\mathrm{C})} w$$

(neglecting ^{13}C content)

$$w = \frac{a\, t_{1/2} M(^{12}\mathrm{C})}{N_A\, m \ln 2} = \frac{230\times5730\times365\times24\times3600\times12}{6.02\times10^{23}\times1000\times\ln 2} = 1.20\times10^{-12}$$

Since 6.0×10^{-13} / 1.20×10^{-12} = 1/2, one half-life time elapsed (we use the value 5568 year for the age determination). The archaeologists thought that the powder was made approximately in 3560 BC.

11.4 In fact, the phenoxyacetyl group is formed from phenoxyacetic acid synthesized in industry from the products of petroleum and coal processing. It does not contain radiocarbon. Only 8 carbon atoms of 16 are natural (formed from living matter), so the ^{14}C content is twice that in a natural part, and $w = 1.2\times10^{-12}$, that is the powder is present-day.

THEORETICAL PROBLEM 12

Iron determination

Iron is one of the most important elements necessary for the support of the vital functions of human organism. Its deficiency may cause anemia for treatment of which Fe(II) supplementation is usually employed. The therapeutic effect of Fe(III) compounds is much less pronounced.

Fe(II) is a fairly strong reducing agent which can be readily oxidized to Fe(III). Therefore methods for separate determination of Fe(II) and Fe(III) as well as for the determination of the total iron content are needed for quality control of pharmaceuticals. Here we will see how this problem can be solved.

12.1 Prior to determination of the total iron content it is usually transformed quantitatively either to Fe(II) or to Fe(III). Using standard redox potentials given below establish which of the oxidizing agents listed can oxidize Fe(II) to Fe(III) under standard conditions. Write down the balanced net ionic equations of corresponding reactions.

oxidized form	reduced form	$E°$, V
Fe^{3+}	Fe^{2+}	+0.77
HNO_3	NO (+ H_2O)	+0.96
H_2O_2 (+ H^+)	H_2O	+1.77
I_2	I^-	+0.54
Br_2	Br^-	+1.09

12.2 After oxidation of all the iron to Fe(III) its total amount can be determined by precipitation of iron in the form of $Fe(OH)_3$ followed by annealing of the precipitate to Fe_2O_3 and weighing.

a) Estimate the pH of aqueous $FeCl_3$ solution (c = 0.010 mol dm^{-3}). Assume that $Fe(OH_2)_6^{3+}$ cation is a monoprotic acid with the dissociation constant $K_a = 6.3\times10^{-3}$.

b) Calculate the pH necessary to start precipitation of $Fe(OH)_3$ from the solution above. Solubility product of $Fe(OH)_3$ is $K_{sp} = 6.3\times10^{-38}$.

c) At what pH value precipitation of $Fe(OH)_3$ from 100.0 cm^3 of $FeCl_3$ aqueous solution (c = 0.010 mol dm^{-3}) will be complete? Consider the precipitation as complete if no more than 0.2 mg Fe remains in solution.

Note. All the pH values should be estimated with accuracy of 0.1 units pH. Neglect the effect of ionic strength.

Fe(II) can be determined in the presence of Fe(III) by titration with $KMnO_4$ solution in acidic media. Since aqueous solutions of $KMnO_4$ tends to decompose slowly over time, the exact concentration of $KMnO_4$ has to be found immediately before determination of Fe(II). This is usually done by titration with $KMnO_4$ of a solution of a primary standard, a pure substance of known composition. Such standard solution can be prepared by dissolving an exact amount of the primary standard in water in a volumetric flask of an exactly known volume.

12.3 For the titration of 10.00 cm^3 of a primary standard solution containing 0.2483 g of As_2O_3 in 100.0 cm^3 of water 12.79 cm^3 of $KMnO_4$ solution were used, whereas for titration of 15.00 cm^3 of the solution containing 2.505 g Fe per liter 11.80 cm^3 of the same solution of $KMnO_4$ were used. What fraction of iron in the sample was present in the form of Fe(II)?

Tartaric acid was added to a solution containing Fe(II) and Fe(III). The solution was neutralized with aqueous ammonia and then excess KCN was added. The potential of the platinum electrode immersed in that solution was found to be +0.132 V against saturated calomel electrode.

12.4 Assuming that all iron in the last solution was present in the form of $Fe(CN)_6^{n-}$, calculate the fraction of iron present in the form of Fe(II) in the original sample. Standard redox potential of $Fe(CN)_6^{3-}$ / $Fe(CN)_6^{4-}$ is +0.364 V. Potential of saturated calomel electrode is +0.241 V. The temperature of the sample solution is 25 °C.

12.5 What concurrent reactions were prevented by the addition of tartaric acid and ammonia to the sample solution? Write down the net ionic equations of those reactions.

SOLUTION OF PREPARATORY PROBLEM 12

12.1 An oxidizing agent can convert Fe(II) to Fe(III) only if the corresponding redox potential is higher than that of the Fe(III) / Fe(II) couple. Therefore, all the oxidizing agents listed in Table with the exception of I_2 could be used:

$$3\ Fe^{2+} + NO_3^- + 4\ H^+ \rightarrow 3\ Fe^{3+} + NO + 2\ H_2O$$
$$2\ Fe^{2+} + H_2O_2 + 2\ H^+ \rightarrow 2\ Fe^{3+} + 2\ H_2O$$
$$2\ Fe^{2+} + Br_2 \rightarrow 2\ Fe^{3+} + 2\ Br^-$$

12.2 a) $Fe(H_2O)_6^{3+} \rightleftarrows Fe(H_2O)_5(OH)^{2+} + H^+$, $K_a = \dfrac{[Fe(H_2O)_5(OH)^{2+}][H^+]}{[Fe(H_2O)_6^{3+}]} = 6.3\times10^{-3}$

$[Fe(H_2O)_6]^{3+}$ (further referred to as $[Fe^{3+}]$) + $[Fe(H_2O)_5(OH)]^{2+}$ (further referred to as $[Fe(OH)^{2+}]$) = c(Fe) = 0.010 mol dm^{-3}, $[Fe(OH)]^{2+} = [H^+] = x$.

Therefore

$$6.3\times10^{-3} = \frac{x^2}{0.01-x} \Rightarrow x = 5.4\times10^{-3} = [H^+] \Rightarrow \text{pH} = \mathbf{2.3}$$

Note. In this case a simplified approach to calculate $[H^+]$ as $\sqrt{K_a\, c}$ leading to the pH value of 2.1 is not acceptable since the dissociation constant of $[Fe(OH_2)_6]^{3+}$ is large and x in the denominator of the expression above should not be neglected compared to c.

b) $K_{sp} = [Fe^{3+}][OH^-]^3 = 6.3\times10^{-38}$;

$[Fe^{3+}] + [Fe(OH)^{2+}] = c(Fe) = 0.010$;

$K_a = \dfrac{[Fe(OH)^{2+}][H^+]}{[Fe^{3+}]} \Rightarrow [Fe(OH)^{2+}] = [Fe^{3+}]\dfrac{K_a}{[H^+]} = [Fe^{3+}][OH^-]\,\beta$, where

$\beta = \dfrac{K_a}{K_w} = 6.3\times10^{11}$ and $K_w = [H^+][OH^-] = 1.0\times10^{-14}$.

A cubic equation relative to [OH^-] can be obtained from the equations above, which may be solved iteratively as follows.

Denote [Fe^{3+}] = x, [OH^-] = y, then

$x(1+\beta y) = c \Rightarrow x = \dfrac{c}{1+\beta y}$

$K_{sp} = x\,y^3 \Rightarrow y = \sqrt[3]{\dfrac{K_{sp}}{x}} \Rightarrow$ pH = – log K_w + log y.

Zeroth approximation: $y = 0 \Rightarrow x = \dfrac{c}{1+\beta y} = 0.010 \Rightarrow y = \sqrt[3]{\dfrac{K_{sp}}{x}} = 1.85\times10^{-12}$

$\Rightarrow$ pH = 2.27;

1st iteration: $y = 1.85\times10^{-12} \Rightarrow x = \dfrac{c}{1+\beta y} = 0.00462 \Rightarrow y = \sqrt[3]{\dfrac{K_{sp}}{x}} = 2.39\times10^{-12}$

$\Rightarrow$ pH = 2.38;

2nd iteration: $y = 2.39\times10^{-12} \Rightarrow x = \dfrac{c}{1+\beta y} = 0.00399 \Rightarrow y = \sqrt[3]{\dfrac{K_{sp}}{x}} = 2.51\times10^{-12}$

$\Rightarrow$ pH = 2.40 ≈ 2.4. Accuracy required obtained.

c) To be solved in a similar way with c(Fe) = $1\cdot10^{-6}$ mol dm^{-3}.
pH = 4.3 (after 4 iterations).

12.3 Determination of $KMnO_4$ concentration:

$$5\ As_2O_3 + 4\ MnO_4^- + 12\ H^+ + 9\ H_2O \rightarrow 10\ H_3AsO_4 + 4\ Mn^{2+}$$

$M(As_2O_3)$ = 197.8 g mol^{-1}

$c(As_2O_3) = \dfrac{0.2483}{0.1000\times197.8} = 0.01255$ mol dm^{-3}

$c(KMnO_4) = \dfrac{\frac{0.01255}{5}\times10.00}{12.79\times4} = 7.850\times10^{-3}$ mol dm^{-3}

Determination of Fe(II):

$$5\ Fe^{2+} + MnO_4^- + 8\ H^+ \rightarrow 5\ Fe^{3+} + Mn^{2+} + 4\ H_2O$$

A_r(Fe) = 55.85

$$c(\text{Fe(II)}) = \frac{7.850\times10^{-3}\times11.80}{15.00\ \times\ 5\ \times\ 55.85} = 1.724 \text{ mg cm}^{-3} = 1.724 \text{ g dm}^{-3}$$

$$w(\text{Fe(II)}) = \frac{1.724}{2.505}\times100\ = 68.8\ \textbf{\%}$$

12.4 From Nernst equation (at 25 °C)

$$E = E^{o} + \frac{0.059}{1}\log\frac{[\text{Fe(CN)}_6^{3-}]}{[\text{Fe(CN)}_6^{4-}]}$$

$$E = 0.132 + 0.241 = 0.373 \text{ V};\quad E^{\circ} = 0.364 \text{ V} \Rightarrow \log\frac{[\text{Fe(CN)}_6^{3-}]}{[\text{Fe(CN)}_6^{4-}]} = \frac{E - E^{o}}{0.059} = 0.153\ \Rightarrow$$

$$\frac{[\text{Fe(CN)}_6^{3-}]}{[\text{Fe(CN)}_6^{4-}]} = 1.42;\quad w(\text{Fe(II)}) = 1\ /\ (1+1.42)\times100\ \% = 41.3\ \textbf{\%}$$

12.5 Adding ammonia prevents formation of HCN in acidic medium:

$$CN^- + H^+ \rightarrow HCN$$

Adding tartaric acid leads to formation of stable Fe(III) and Fe(II) tartrate complexes and prevents:

(i) precipitation of $Fe(OH)_3$ and, possibly, $Fe(OH)_2$ with NH_3:

$$Fe^{3+} + 3\ H_2O + 3\ NH_3 \rightarrow Fe(OH)_3 + 3\ NH_4^+$$

$$Fe^{2+} + 2\ H_2O + 2\ NH_3 \rightarrow Fe(OH)_2 + 2\ NH_4^+$$

(ii) formation of insoluble mixed Fe(II) – Fe(III) cyanide (Berlin blue, Prussian blue, Turnbull's blue):

$$Fe^{3+} + Fe^{2+} + K^+ + 6\ CN^- \rightarrow KFe^{II}Fe^{III}(CN)_6$$

THEORETICAL PROBLEM 13

Sulfur determination

Compounds of sulfur in its lower oxidation states are present in many industrial wastes (metallurgy, production of paper, chemical) and are dangerous ecotoxicants. The prevalent forms of sulfur in lower oxidation states in solutions are S^{2-}, SO_3^{2-} and $S_2O_3^{2-}$ ions. Their content can be determined by redox titration under different conditions.

13.1 To a 20.00 cm^3 sample containing S^{2-}, SO_3^{2-} and $S_2O_3^{2-}$ an excess of $ZnCO_3$ suspended in water was added. Upon completion of the reaction the solution was filtered into a 50.00 cm^3 volumetric flask and diluted to the mark. To 20.00 cm^3 of the filtrate an excess of aqueous formaldehyde was added. The mixture was acidified with acetic acid and titrated with 5.20 cm^3 of iodine standard solution (c = 0.01000 mol dm^{-3}).

a) Write down the net ionic equations of the reactions taking place during the analysis.

b) Which ion, S^{2-}, SO_3^{2-} or $S_2O_3^{2-}$, can be determined by this method?

c) Calculate the concentration of this ion in ppm in the initial solution.

13.2 A 20.00 cm^3 of the sample of the iodine solution (c = 0.01000 mol dm^{-3}) was acidified with acetic acid and then combined with 15.00 cm^3 of the filtrate above. The mixture was titrated with 6.43 cm^3 of the standard sodium thiosulfate solution with a concentration of 0.01000 mol dm^{-3}.

a) Write down the net ionic equations of the reactions taking place during the analysis.

b) Which ion, S^{2-}, SO_3^{2-} or $S_2O_3^{2-}$, can be determined by this method taking into account the result of the previous experiment?

c) Calculate the concentration of this ion in ppm in the initial solution.

13.3 A 10.00 cm^3 sample of iodine solution (0.05000 mol dm^{-3}) was acidified with acetic acid and then 10.00 cm^3 of the original sample containing S^{2-}, SO_3^{2-} and $S_2O_3^{2-}$ were added. The mixture was titrated with 4.12 cm^3 of the standard sodium thiosulfate solution with a concentration of 0.05000 mol dm^{-3}.

a) Write down the net ionic equations of the reactions taking place during the analysis.

b) Which ion, S^{2-}, SO_3^{2-} or $S_2O_3^{2-}$, can be determined by this method taking into account the results of two previous determinations?

c) Calculate the concentration of this ion in ppm in the initial solution.

SOLUTION OF PREPARATORY PROBLEM 13

13.1 a) $ZnCO_3(s) + S^{2-} \rightarrow ZnS(s) + CO_3^{2-}$

$SO_3^{2-} + CH_2O + H^+ \rightarrow CH_2(OH)SO_3^-$

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

b) $S_2O_3^{2-}$

c) $n(S_2O_3^{2-}) = 2 \times 5.20 \times 0.01000 = 0.104$ mmol (in 20.00 cm^3 of the filtrate)

$c(S_2O_3^{2-}) = 0.104 / 20.00 \times 50.00 / 20.00 = 0.0130$ mol dm^{-3} (in the initial) = $= 0.01300 \times 112.13$ g $dm^{-3} = 1.46$ g dm^{-3} (1460 ppm)

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

$SO_3^{2-} + I_2 + H_2O \rightarrow SO_4^{2-} + 2\ H^+ + 2\ I^-$

b) SO_3^{2-}

c) $n(I_2)_{initial} = 20.00 \times 0.01000 = 0.2000$ mmol

$n(I_2)_{excessive} = 0.5 \times 6.43 \times 0.01000 = 0.0322$ mmol

$n(SO_3^{2-}) + 0.5\ n(S_2O_3^{2-}) = 0.2000 - 0.03215 = 0.1679$ mmol (in 15.00 cm^3 of the filtrate)

$n(SO_3^{2-}) = 0.1679 - 0.5 \times 0.1040 / 20.00 \times 15.00 = 0.1289$ mmol (in 15.00 cm^3 of the filtrate)

$c(SO_3^{2-}) = 0.1289 / 15.00 \times 50.00 / 20.00 = 0.0215$ mol dm^{-3} (in the initial) = 0.0215×80.07 g $dm^{-3} = 1.720$ g dm^{-3} (1720 ppm)

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

$SO_3^{2-} + I_2 + H_2O \rightarrow SO_4^{2-} + 2\ H^+ + 2\ I^-$

$S^{2-} + I_2 \rightarrow S + 2\ I^-$

b) S^{2-}

c) $n(I_2)_{initial} = 10.00 \times 0.05000 = 0.5000$ mmol

$n(I_2)_{excessive} = 0.5 \times 4.12 \times 0.05000 = 0.103$ mmol

$n(S^{2-}) + n(SO_3^{2-}) + 0.5\ n(S_2O_3^{2-}) = 0.5000 - 0.1030 = 0.3970$ mmol (in 10.00 cm^3 of the initial)

$n(S^{2-}) = 0.3970 - 10.00 \times 0.02148 - 10.00 \times 0.5 \times 0.01300 = 0.1172$ mmol (in 10.00 cm^3 of the initial)

$c(S^{2-}) = 0.1172 / 10.00 = 0.01172$ mol $dm^{-3} = 0.01172 \times 32.07$ g $dm^{-3} = 0.376$ g dm^{-3} (376 ppm)

THEORETICAL PROBLEM 14

Magnesium determination

To determine the amount of magnesium in a solution, a sample of the liquid was first acidified with HCl, then made slightly alkaline by addition of NH_3 and then combined with an excess $(NH_4)_2HPO_4$ in water. The precipitate of $MgNH_4PO_4$ formed was filtered off, washed with diluted aqueous NH_3, annealed at 1000 °C to constant mass and weighed.

Answer the following questions using numerical data given in the end of the text whenever necessary.

14.1 Write down the net ionic equation for the precipitation reaction taking place in course of the analysis.

14.2 Write down the equation for the reaction taking place in the course of annealing.

14.3 When determining the content of magnesium in a granulated medicine preparation calmagin 0.1532 g of the annealed precipitate were obtained from a 1.8005 g sample of calmagin. Calculate the mass percent of MgO in the preparation.

14.4 During the precipitation of $MgNH_4PO_4$ some impurities may coprecipitate such as $MgHPO_4$, $Mg(NH_4)_4(PO_4)_2$, $Mg_3(PO_4)_2$, $Mg(OH)_2$, $(NH_4)_2HPO_4$ and NH_4Cl. Some of these substances can undergo thermal decomposition at annealing. Write down the equations of the corresponding reactions.

14.5 Indicate if the presence of the impurities listed in Table below can lead to an error in the magnesium content as determined by the method described above. Put 0 in the Table if no error is expected, plus or minus sign if the error will be positive or negative, respectively.

Impurity	Error
$MgHPO_4$	
$Mg(NH_4)_4(PO_4)_2$	
$Mg_3(PO_4)_2$	
$Mg(OH)_2$	
$(NH_4)_2HPO_4$	
NH_4Cl	

14.6 At what maximum pH value the precipitation of $MgNH_4PO_4$ may be carried out to avoid simultaneous precipitation of $Mg(OH)_2$? Assume that the volume of the original sample was 200 cm^3 and the content of magnesium in it was 0.10 g.

14.7 To determine the solubility product (K_{sp}) of $MgNH_4PO_4$ a NaOH solution was added dropwise until the beginning of precipitation to a 100 cm^3 of a solution containing $MgCl_2$, NH_4Cl and NaH_2PO_4 with a concentration of 0.010 mol dm^{-3} each. The precipitation started at pH 6.48. Calculate K_{sp}. Neglect the volume change during the experiment.

Reference data

H_3PO_4	acidity constant	K_{a1}	7.1×10^{-3}
		K_{a2}	6.2×10^{-8}
		K_{a3}	5.0×10^{-13}
NH_3	basicity constant	K_b	1.8×10^{-5}
$Mg(OH)_2$	solubility product	K_{sp}	6.0×10^{-10}
H_2O	ionic product	K_w	1.0×10^{-14}

SOLUTION OF PREPARATORY PROBLEM 14

14.1 $Mg^{2+} + HPO_4^{2-} + NH_3 \rightarrow MgNH_4PO_4\,(s)$

14.2 $2\ MgNH_4PO_4 \rightarrow Mg_2P_2O_7 + 2\ NH_3 + H_2O$

14.3 $M_r(MgO) = 24.31 + 16.00 = 40.31$;

$M_r(Mg_2P_2O_7) = 2 \times 24.31 + 2 \times 30.97 + 7 \times 16.00 = 222.56$;

$$w(MgO) = \frac{2\times40.31}{222.56}\times\frac{0.1532}{1.8005}\times100\,\% = 3.08\ \%$$

14.4 $2\ MgHPO_4 \rightarrow Mg_2P_2O_7 + H_2O$

$Mg(NH_4)_4(PO_4)_2 \rightarrow Mg(PO_3)_2 + 4\ NH_3 + 2\ H_2O$

$(Mg_3(PO_4)_2 \rightarrow$ no changes)

$Mg(OH)_2 \rightarrow MgO + H_2O$

$(NH_4)_2HPO_4 \rightarrow HPO_3 + 2\ NH_3 + H_2O$

$NH_4Cl \rightarrow NH_3 + HCl$

14.5

Impurity	Error
$MgHPO_4$	0
$Mg(NH_4)_4(PO_4)_2$	+
$Mg_3(PO_4)_2$	–
$Mg(OH)_2$	–
$(NH_4)_2HPO_4$	+
NH_4Cl	0

The error is positive if the percentage (by mass) of magnesium in the annealing product is *lower* than that in $Mg_2P_2O_7$, negative if *higher* and equal to zero if the same or if the impurity completely volatilizes during annealing.

14.6 $pH = -\log [H^+] = -\log K_w + \log [OH^-]$

$$[OH^-] = \sqrt{\frac{K_{sp}(Mg(OH)_2)}{[Mg^{2+}]}}$$

$$[Mg^{2+}] = \frac{0.10\ g}{0.200\ dm^3 \times 24.31\ g\ mol^{-1}} \approx 2.1\times10^{-2}$$

$$[OH^-] = \sqrt{\frac{6.0\times10^{-10}}{2.1\times10^{-2}}} = 1.7\times10^{-4};\quad pOH = 3.8;\quad pH = 14.00 - 3.8 = 10.2$$

14.7 At $pH = 6.48$ $\quad [H^+] = 3.31\times10^{-7}$

$$[PO_4^{3-}] = c(PO_4)\cdot\frac{K_{a1}K_{a2}K_{a3}}{K_{a1}K_{a2}K_{a3} + K_{a1}K_{a2}[H^+] + K_{a1}[H^+]^2 + [H^+]^3} =$$

$$\frac{0.010 \times 7.1\times10^{-3} \times 6.2\times10^{-8} \times 5.0\times10^{-13}}{7.1\times10^{-3} \times 6.2\times10^{-8} \times \left(5.0\times10^{-13} + 3.31\times10^{-7}\right) + 7.1\times10^{-3} \times (3.31\times10^{-7})^2 + (3.31\times10^{-7})^3} =$$

$$= 2.4\times10^{-9}$$

$[NH_4^+] \approx c(NH_4^+) = 0.010\ mol\ dm^{-3}$

($pH << pK_a(NH_3) = pK_w - pK_b(NH_3) = 9.25$)

$[Mg^{2+}] = 0.010$

$$K_{sp} = [Mg^{2+}][NH_4^+][PO_4^{3-}] = 2.4\times10^{-13}$$

THEORETICAL PROBLEM 15

Inorganic phosphates: From solution to crystals

Inorganic acids containing phosphorus and oxygen and most of the salts of these acids are composed of oxygen tetrahedra, each with the phosphorus atom in the center. The tetrahedra can either be isolated or share an oxygen atom so being linked by means of P–O–P bridges.

15.1 a) Draw the structure of the anions present in the neutral salts of the following acids: H_3PO_4, H_3PO_3, H_3PO_2.

b) For the series of acids above, reveal the trends in:

1) acidity of the substances (compare the values of pK_{a1}),

2) O–P–O valence angle.

15.2 The formula of metaphosphoric acid can be written as $(HPO_3)_n$. This acid is composed of the phosphorus-oxygen tetrahedra either. Suggest the structure of this compound assuming the minimal number of phosphorus atoms in its molecule.

15.3 a) To estimate the relative charge of atoms in $P_nO_k^{(2k-5n)-}$ anion, let us define a special secondary parameter A_i of an atom i as the oxidation number of this atom, Z_i, divided by its coordination number, CN_i ,:

$$A_i = \frac{Z_i}{C\,N_i}.$$

The sum of the oxidation number (Z_N) of an atom N (for instance, phosphorus atom) and A_i values for the atoms forming the coordination environment (for instance, oxygen atoms) of the atom N gives the relative charge $Q(N)$ of the atom N:

$$Q(\mathrm{N}) = Z_N + \sum_{i=1}^{k} \frac{Z_i}{CN_i}.$$

Calculate $Q_m(\mathrm{P})$ for the PO_4 tetrahedron considering m = 1, 2, 3 and 4 of its oxygen atoms being shared with neighboring PO_4-tetrahedra.

b) Perform similar calculations for TO_4-tetrahedra linked through the common vertices, where

1) T = Si,

2) T = S.

15.4 Let us suppose that a tetrahedron with the minimal absolute value of Q_m(P) is the most stable towards hydrolysis.

a) Which value of *m* corresponds to the phosphorus-oxygen tetrahedron the most stable towards hydrolysis?

b) Which value of *m* corresponds to the TO_4 tetrahedron (T = Si, S) the most stable towards hydrolysis?

15.5 Isolated phosphorus-oxygen tetrahedra (without P–O–P bonding) can be found in crystalline substances. Mixed phosphates (V) M_aPO_b are known to be composed of PO_4 and MO_4 tetrahedra with each oxygen atom having the same number of M and P atoms coordinated to it.

a) Determine the *Q*(O) value for such compounds.

b) Suggest possible empirical formulas for such compounds.

15.6 Fluorapatite $Ca_5(PO_4)_3F$ is a constituent of human teeth. It can be synthesized using a double-diffusion method with a gelatin membrane separating solutions containing F^-, HPO_4^{2-}, and Ca^{2+} ions. The synthesis leads to a hybrid material – bioorganic polymer/inorganic phosphate, resembling tooth (or bone) tissue.

a) Give a reasonable composition of two solutions placed on different sides of the gelatin membrane, that allow preparation of fluorapatite as the target substance in this double-diffusion experiment.

	5 mM*) $Ca(NO_3)_2$	1 mM*) NaF	3 mM*) Na_2HPO_4
Solution 1			
Solution 2			

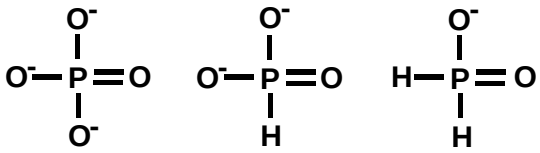
*) mM: c = mmol dm^{-3}

b) Write down the balanced equation of the reaction described above leading to fluorapatite.

c) Calculate the osmotic pressure acting on the membrane at the beginning of this experiment (25 ℃, activity of all ions is equ al to 1).

SOLUTION OF PREPARATORY PROBLEM 15

15.1 a)

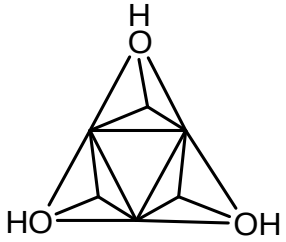


b)

1) Strength of the acids decreases from H_3PO_2 to H_3PO_4, i.e. pK_{a1} increases in this sequence. The explanation is based on the fact that one O-terminated side of each PO_n-tetrahedron with double bond P=O (shifting electron density from protons in P–OH groups due to inductive effect) acts on three P–OH groups in phosphoric acid and only on the sole P–OH group in the case of phosphinic (hypophosphorous) acid.

2) According to the Valence Shell Electron Pair Repulsion (VSEPR) theory O–P–O angle decreases in the same sequence. This is due to different polarity of P–O and P–H bonds (it is apparent from the values of Pauling's elektronegativity X_P for these three atoms X_P(H) = 2.20, X_P(P) = 2.19 and X_P(O) = 3.44). This fact stipulates partial negative charge δ– at oxygen atoms and almost δ = 0 in the case of hydrogen atoms. Thus, the P–O bonds endure higher repulsion from each other than from P–H bonds, and to a first approximation we can ignore the P–H bonds in our consideration. Then the following strong repulsive bonds for the above acids should be taken into account: one P=O and one P–OH for H_3PO_2, one P=O and two P–OH for H_3PO_3, and one P=O and three P–OH for H_3PO_4.

15.2 Three tetrahedra linked through the common vertices; protons are attached to one oxygen atoms in each tetrahedron so that $CN(O)_{OH} = 2$.



In a species with two phosphorus atoms two tetrahedra should share an edge which contradicts the initial assumption that each two adjacent tetrahedra have one shared oxygen atom. Thus, minimal amount of P-atoms is equal to three. It corresponds to *cyclo*-trimetaphosphoric acid.

15.3 a)

m	Q_m(P)
1	(–2/1)·3 + (–2/2)·1 + 5 = –2
2	(–2/1)·2 + (–2/2)·2 + 5 = –1
3	(–2/1)·1 + (–2/2)·3 + 5 = 0
4	(–2/1)·0 + (–2/2)·4 + 5 = +1

b) 1), 2)

m	Q_m(Si)	Q_m(S)
1	(–2/1)×3 + (–2/2)×1 + 4 = –3	(–2/1)×3 + (–2/2)×1 + 6 = –1
2	(–2/1)×2 + (–2/2)×2 + 4 = –2	(–2/1)×2 + (–2/2)×2 + 6 = 0
3	(–2/1)×1 + (–2/2)×3 + 4 = –1	(–2/1)×1 + (–2/2)×3 + 6 = +1
4	(–2/1)×0 + (–2/2)×4 + 4 = 0	(–2/1)×0 + (–2/2)×4 + 6 = +2

15.4 a) $m = 3$,

b) m(Si) = 4, m(S) = 2 according to the assumption.

15.5 a) Since the bonds between M and P are missing, the following equality is to be fulfilled: $CN_O \times b = (a+1) \times 4$, therefore $CN_O = (a+1) \times 4/b$.

The M to P ratio in an oxygen surrounding, n(M) : n(P), is a : 1, then, the number of atoms of M and P in the coordination sphere of O is:

$n(M) = a / (a+1) \times CN_O = a / (a+1) \times (a+1) \times 4 / b = 4\,a / b$, $\quad n(P) = 4/b$,

$Q(O) = (5/4) \times (4/b) + (Z/4) \times (4a/b) + (-2) = (-2\,b + 5 + Z\,a)/b$

where Z is the oxidation number of M.

The condition of the charge balance for M_aPO_b requires that $-2 \times b + 5 + Z \times a = 0$.

Therefore, Q(O) = 0.

b) According to the result above, $n(P) = 4/b$. Therefore, the number of phosphorus atoms in the oxygen coordination sphere, $n(P)$, can be 1, 2 or 4 since b is an integer. Note that stoichiometry «M_aPO» and «M_aPO_2», b =1 and 2 respectively, is not possible for a phosphorus atom in the oxidation state +5. Hence, $b = 4$.

From the condition of the charge balance, $-8 + 5 + Z \times a = 0$. Solving this equation in integers gives $Z = +3$ ($a = 1$) or $Z = +1$ ($a = 3$). Indeed, the empirical formulas MPO_4 and M_3PO_4 correspond to known compounds such as $AlPO_4$ and Li_3PO_4. Note that the condition of oxygen atom equivalence is fulfilled here.

15.6 a) Since Ca^{2+} ions when combined with either NaF or Na_2HPO_4 solutions give precipitates, it is advisable to separate solutions containing calcium cations and phosphate/fluoride anions with the membrane.

	$Ca(NO_3)_2$	NaF	Na_2HPO_4			$Ca(NO_3)_2$	NaF	Na_2HPO_4
Soln. 1	✓			or	Soln. 1		✓	✓
Soln. 2		✓	✓		Soln. 2	✓		

b) $10\ Ca(NO_3)_2 + 2\ NaF + 6\ Na_2HPO_4 + 6\ NaOH \rightarrow$

$\rightarrow Ca_{10}(PO_4)_6F_2\downarrow + 20\ NaNO_3 + 6\ H_2O$,

if the pH values of the solutions were adjusted to alkaline range prior to the experiment.

Or,

$10\ Ca(NO_3)_2 + 2\ NaF + 6\ Na_2HPO_4 \rightarrow Ca_{10}(PO_4)_6F_2\downarrow + 14\ NaNO_3 + 6\ HNO_3$,

without the pH adjustment. The equation gives a clear evidence of acidification. Note that this is not favorable for fluorapatite formation, since it is rather soluble in acidic solutions.

c) Dissociation of $Ca(NO_3)_2$ and Na_2HPO_4 gives 3 ions for calcium- and phosphorous-containing salts, and two ions in the case of NaF. Then, the overall concentration of ions at the right and the left sides of the membrane is:

$c = 5\times10^{-3}\times 3 + 2\times10^{-3} + 3\times10^{-3}\times 3 = (15 + 2 + 9)\times10^{-3} = 2.6\times10^{-2}$ mol dm^{-3} =

$= 26$ mol m^{-3}.

$$p = c\,R\,T = 26\ \text{mol m}^{-3}\times 8.31 \times 298 = 6.44\times10^4\ \text{Pa}.$$

THEORETICAL PROBLEM 16

Fruits, vegetables, atoms

When solving this problem none of the fruits or vegetables was destroyed!

In 1611 German mathematician and astronomer Johannes Kepler observed the stacking of cannonballs in a pyramid. He asserted there is the only way to fill the space the tightest possible with equal hard spheres, "…so that in no other arrangement could more pellets be stuffed into the same container". He was the first to formulate such a problem termed later as Kepler Conjecture. In 1998 Professor Thomas Hales announced a solution to the Kepler Conjecture, which was published in a series of papers in "Discrete and Computational Geometry" starting from 1997. He considered 150 more variants of space filling besides that asserted by Kepler. Hales' solution required about 250 pages in a printed version and a size of 3 Gb in computer files. Thus, the term of close-packing of spheres (c.p.s.) widely accepted in the field of solid state chemistry passed through the rigorous mathematical proof and remained valid.

We do not request that you provide an alternative solution to this problem. However, you can check with our help how the basic law of space filling is applicable to our everyday life.

16.1 In order to avoid smashing tomatoes during their transportation, it is useful to arrange them on a shelf in a uniform single layer. Let us consider two types of packing (Fig. 16.1).

a) Calculate the density of tomatoes packing (φ) for the case A and B as $\varphi = S_{tomato} / (S_{void} + S_{tomato})$.

b) Which type of the packing requires less shelf area?

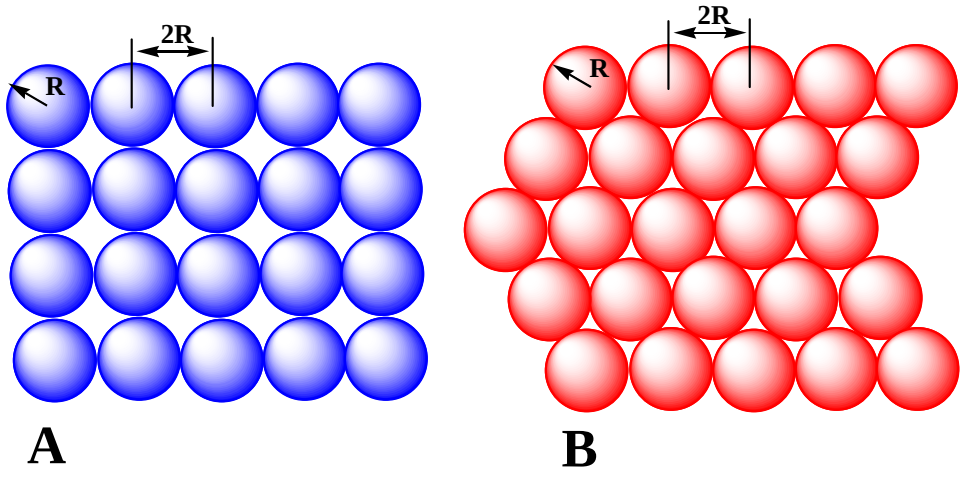


Fig. 16.1. Two possible types of packing tomatoes.

16.2 Hard vegetables such as potatoes or cabbage heads can be packed in containers. Consider several types of packing:

(1) The first layer is of the type A (see Fig. 16.1). The second layer is an exact copy of the first, a vegetable in the second layer is above another one in the first layer (such a packing is termed usually as simple cubic packing , or s.c.).

(2) The first layer is of the type A. In the second layer each vegetable is above a void space in the first layer (body centered cubic packing, or b.c.c.).

(3) The first layer is of the type B. The second layer is an exact copy of the first, a vegetable in the second layer is above another one in the first layer (hexagonal packing, or h.p.).

(4) The first layer is of the type B. In the second layer each vegetable is above a void space in the first layer (hexagonal close packing, or h.c.p.).

a) Calculate the densities of packing for the cases (1) – (4).

b) Which type of packing is more efficient in the sense of van filling?

c) There are two alternatives to arrange the third layer in the case B: i) by placing vegetables right above the vegetables of the first layer (that is to place them into the voids of the second layer) or ii) by arranging vegetables right above the voids of the first layer (see the case B in Fig. 2). Calculate the density of packing φ for the second alternative which is called the face centered cubic packing – f.c.c.

d) A farmer filled the third layer in the way of f.c.c. and now can not figure out where the voids and vegetables of the first layer are. How does the value of φ vary due to the faults in regular sequence of closed packed layers?

16.3 Assume now that the enterprising farmer decided to place peaches into the van with watermelons. His bright idea was to place peaches into the voids of watermelon packing.

a) Estimate the maximal value of the R_{peach} / $R_{watermelon}$ peach/watermelon radii ratio that allows to avoid peach smashing in cases of:

(1) cubic void within s.c.

(2) octahedral void within b.c.c.

(3) octahedral void within f.c.c.

b) How many peaches (maximum) per one watermelon can the farmer place using c.s., h.c.p., b.c.c. and f.c.c. types of packing?

c) What is the maximal φ value for c.s., b.c.c. and f.c.c. packings containing peaches in voids?

16.4 The fruits can go bad due to insufficient ventilation in the van.

a) In order to keep the voids in b.c.c. and f.c.c. packings the go-ahead farmer decided to put peaches only in the octahedral voids which are not linked by edges and faces. How many peaches per one watermelon can be packed in this case?

b) The enterprising farmer has got another idea: to feel all the octahedral voids in f.c.c. with peaches (you know about it), whereas (it's brilliant!) the tetrahedral voids with apples. How many apples per one watermelon can he arranged in this way?

Nature invents puzzles like the Kepler Conjecture. Opal is a natural stone composed of c.p.s.-packed SiO_2 microspheres. The main feature of opal is the distinguished shining (the so-called iridescence) when it is illuminated. This phenomenon is explained by the diffraction of visible light in accordance with Bragg's law:

$$\lambda = 2d \sin \theta$$

where λ is the wavelength of light, d is the distance between layers in c.p.s. of opal, 2θ is the angle between incident and diffracted beams (or, in other words, θ the inclination angle of the beam with respect to the surface of opal stone).

Opal is a prototype of photonic crystals, materials composed by closely packed microspheres with high refraction index. Optical spectra of photonic crystals demonstrate unusual features, for instance, photonic band gap (like electron band gap in semi-conductors). Photonic crystals are considered to be the main active elements in photonics, the information technology of the future.

16.5 a) Find the minimal values of Miller indices – (*h k l*) related to the first "permitted" reflection in f.c.c.

b) Calculate the wavelength of light if the first reflection is observed for $2\theta = 60°$. The radius of SiO_2 microspheres is equal to 450 nm. The dispersion of SiO_2 refraction index (that is, its dependence on wavelength) can be neglected.

SOLUTION OF PREPARATORY PROBLEM 16

16.1 a) Since tomatoes touch each other in layers **A** and **B**, regular *n*-polygons (where *n* is the number of the nearest neighbors) with touch points located in the middle of their sides define the square relevant to one tomato. Among *n*-polygons only squares and hexagons fill space without voids. Therefore, $\varphi = S_{tomat}/S_{polygon}$. *R* is the radius of vegetable or fruit (hereunder).

$$S_{square} = 4R^2, \quad S_{hexagon} = 2\sqrt{3}\,R^2. \quad S_{tomat} = \pi R^2.$$

$$\varphi_A = \frac{\pi}{4} >> 0.7854\,; \quad \varphi_B = \frac{\pi}{2\sqrt{3}} >> 0.9069$$

b) Type **B**.

16.2 a) The density of a packing can be estimated as the ratio of the volume of all tomatoes (*Z*) with the radius *R* filling the space inside of an arbitrarily chosen bulk polyhedron (P) of a certain volume V_P.

$$\varphi = \frac{4\pi Z R^3}{3 \times V_P}$$

Type of packing	s.c.	b.c.c.	h.p.	h.c.p.
P	Cube, $a = 2R$	Cube, $a = \frac{4\sqrt{3}}{3}R$	Rhombic prism, $h = 2R$, $L = 2R$	Rhombic prism $h = \frac{4\sqrt{6}}{3}R$, $L = 2R$
V_P	$8R^3$	$\frac{64\sqrt{3}}{9}R^3$	$4\sqrt{3}R^3$	$8\sqrt{2}R^3$
Z	$8\times(1/8) = 1$	$1+ 8\times(1/8) = 2$	$4\times(1/12)+4\times(1/6) = 1$	$1+4\times(1/12)+4\times(1/6) = 2$
Φ	0.5236	0.6802	0.6046	0.7405

b) The case **(4)** (h.c.p.) corresponds to the most efficient way to fill space.

c) Calculation for f.c.c.: P is a cube $a = 2\sqrt{2}R$, $Z = 6\times(1/2) + 8\times(1/8) = 4$, $V_P = 16\sqrt{2}R^3$.

$$\varphi_{\text{f.c.p.}} = \frac{16\pi}{3\times16\sqrt{2}} \approx 0.7405.$$

d) For c.p.s. φ does not depend on the type of the layer sequence.

16.3 a) In order to avoid peaches smashing the radius of a void should be less than the radius of a peach (r – radius of a peach, R – radius of a watermelon).

Type of packing	s.c.	b.c.c.	f.c.c.
The criterion of successful transportation	$2r < (a_{s.c.}\sqrt{3} - 2R)$	$2r < (a_{b.c.c.} - 2R)$	$2r < (a_{f.c.c.} - 2R)$
$r(\max)/R$	$(\sqrt{3} - 1) \approx 0.7321$	$(\frac{2\sqrt{3}}{3} - 1) \approx 0.1547$	$(\sqrt{2} - 1) \approx 0.4142$

b) The number of peaches cannot exceed that of corresponding voids:

Type of packing	s.c.	b.c.c.	h.c.p.	f.c.c.
Z_{peach}	1	$6\cdot1/2 + 12\cdot1/4 = 6$	2	$1 + 12\cdot1/4 = 4$
$Z_{peach}/Z_{watermelon}$	1	3	2	1

c) Let us calculate the maximal density according to the formula:

$$\varphi = \frac{4\pi R^3 Z_{watermelon}\left(1 + \frac{Z_{peach} r^3_{(max)}}{Z_{watermelon} R^3}\right)}{3 \times V_P}$$

Type of packing	s.c.	b.c.c.	f.c.c.
P	Cube, $a = 2R$	Cube, $a = \frac{4\sqrt{3}}{3} R$	Cube, $a = 2\sqrt{2}\,R$
V_P	$8R^3$	$\frac{64\sqrt{3}}{9}\,R^3$	$16\sqrt{2}\,R^3$
$Z_{peach}/Z_{watermelon}$	1	3	1
$1 + \frac{Z_{peach} r^3(\max)}{Z_{watermelon} R^3}$	1.3924	1.0111	1.0711
φ	0.721	0.6878	0.7931

16.4 a) In the case of b.c.c. ventilation of voids can be achieved by filling ¼ of voids: the network composed of octahedra linked by common apexes with ¼ watermelons which have no neighboring peaches. Similar calculation for f.c.c. gives ¼ (the same algorithm for void filling, for details see Appendix).

b) For f.c.c. $Z_{\text{apple}} = 8$ accounting for 4 watermelons (forming f.c.c. unit cell),

$$Z_{\text{apple}} / Z_{\text{watermelon}} = 2.$$

16.5 a) The rigorous condition for a diffraction maximum is: the product of inverse coordinates of diffracted planes $(\frac{h}{a}\frac{k}{a}\frac{l}{a})$ and coordinates of each microsphere in a cubic unit cell with side *a* has to be integer. In the case of f.c.c. there are three independent translations $(\frac{a}{2}\frac{a}{2}0)$, $(\frac{a}{2}0\frac{a}{2})$ and $(0\frac{a}{2}\frac{a}{2})$, then the condition of diffraction maximum is:

$h + k = 2\,n$, $k + l = 2\,m$, $h + l = 2\,q$, where m, n, q are integers. Hence, the reflection with $h\,k\,l$ =(1 1 1) satisfies the condition above.

b) $a = 2\sqrt{2}\,\text{r}$, $d_{\text{min}} = \dfrac{2\sqrt{2}\,\text{r}}{\sqrt{\text{h}^2+\text{k}^2+\text{l}^2}} = 2\sqrt{\dfrac{2}{3}} \times 450 \approx 734.85$ nm.

$\lambda = d_{\text{min}} \sin 30^{\text{o}} = 734.85 \times \dfrac{1}{2} \approx 367.42$ nm.

Appendix

How to achieve ventilation of partially filled b.c.c. and f.c.c. packings

b.c.c.

Filling the void at the center of a face in b.c.c., one should consider (from a viewpoint of symmetry) that the opposite face of the b.c.c. cell is occupied either. Filling any remaining void in the cell immediately leads to joining of octahedra by edges. Apparently, such a cell cannot be stacked with the other ones through a face but can be stacked via edges. Thus, filled cells are arranged within 0*xy* (and similar) plane in checkerboard order. Moving from plane to plane along coordinate axis, filled and empty cells arise alternately (like Na and Cl in rock salt structure) or they form columns. In each case above, watermelon/peach ratio will be the same, since the ratio (filled cells)/(empty cells) = 1:1 remains the same. Then,

$1_{cell} \times 1/2 \times 2 = 1$ peach is accounting for $2_{cell} \times 2 = 4$ watermelon, i.e. the optimal ratio peach/watermelon = 1/4. If all watermelons have 2 peach-neighbors in octahedral voids, then the ratio peach/watermelon = (the number of neighbors for a watermelon)/(the number of neighbors for a peach) = 2/6 = 1/3. However, this is impossible within the frame of b.c.c. type of packing.

Another glance on the transformation of c.p.s. layers during the filling of voids can be described as follows. Filling of octahedral voids immediately leads to the framework of octahedra joined by apexes like in ABX_3 perovskite structure. Here watermelons play roles of both A-cation and X-anion. From this consideration it is quite clear that further compaction of fruit-vegetable mixture is impossible without smashing. This means that we have reached the ultimate value of peach/watermelon ratio.

f.c.c.

Placing a peach at the origin of f.c.c. cell, one can find out that it is impossible to fill more voids. Then, the ratio peach/watermelon is equal to $1/Z_{f.c.c.} = 1/4$. Moving the origin of f.c.c. cell into the filled void, it is easy to show up the ABX_3 perovskite structure again with the same consequences related to further compaction of fruit-vegetable mixture.

THEORETICAL PROBLEM 17

Chameleonic cobalt

Information was always regarded as the most valuable product resulting from mankind activity. It is not striking that recognition of this fact was followed by numerous efforts aimed at information safety. Cryptography seemed to be a convenient way to reach such safety from unrecorded time. Cryptography cannot be detached from sympathetic ink that becomes visible only after special treatment, for instance, heating. History knows a number of recipes of such ink, among them that based on salts of cobalt(II). Being pale-pink in color, cobalt ink is virtually invisible when dried on paper. However, once heated with a candle flame, a letter written with such ink reveals hidden text colored in bright-blue.

We know other applications of cobalt(II) salts, less secret, but dependent on the color transition described above. Blue granules of silica-gel doped with Co(II) salt and placed into a desiccators to dry some product, become pink at last. This is the signal to regenerate silica-gel (just to dry, since it accumulates too much water). Similarly, a paper soaked with saturated solution of $CoCl_2$ turns blue in dry air due to formation of $CoCl_2 \cdot 4\ H_2O$, and changes its color back to pink $CoCl_2 \cdot 6\ H_2O$ in a humid environment. Apparently, the paper works as a humidity meter, hygrometer.

17.1 Using the thermodynamic data below, determine the threshold of air humidity (in %) specific to the response of such a hygrometer.

Compound	$-\Delta_f H^o_{298}$, kJ mol^{-1}	S^o_{298}, J mol^{-1} K^{-1}
$CoCl_2 \cdot 6\ H_2O(s)$	2113.0	346.0
$CoCl_2 \cdot 4\ H_2O(s)$	1538.6	211.4
$H_2O\ (l)$	285.8	70.1
$H_2O(g)$	241.8	188.7

The “pink (sometimes, violet) ↔ blue” color transition described above is related to the reconstruction of the coordination sphere of Co^{2+} ion: octahedron ↔ tetrahedron. The examples discussed in a previous section deal with the transition $[Co(H_2O)_6]_{oct}^{2+}$ ↔ $[Co(H_2O)_4]_{tetr}^{2+}$. As a rule, coordination compounds with tetrahedral geometry are less

abundant compared to octahedral ones. However, in particular case of Co^{2+} tetrahedral complexes competes with octahedral compounds.

17.2 To understand the reason behind such behavior, consider the following octahedral and tetrahedral complexes:

a) $[Cr(H_2O)_6]^{3+}$ and $[Cr(H_2O)_4]^{3+}$,

b) $[Co(H_2O)_6]^{2+}$ and $[Co(H_2O)_4]^{2+}$.

Draw diagrams for the case of an octahedral and a tetrahedral ligand field showing clearly the energy levels of all metal 3*d*-orbitals; indicate the *d*-orbital splitting parameter Δ. For each of the ions above use the appropriate diagram and fill it in with the electrons available in the metal *d*-subshell. Calculate the Crystal Field Stabilization Energy (CFSE) for each of the ions.

Compare the results and draw a conclusion.

17.3 The following reaction

$$[Co(H_2O)_6]^{2+} + 4\ X^- = [CoX_4]^{2-} + 6\ H_2O, \qquad (1)$$

where X^- = Cl^-, Br^-, I^-, SCN^-, is used in some textbooks to illustrate Le Chatelier's principle related to equilibrium shifting. If one adds an excess of salt containing X^-, the solution becomes blue, and under dilution with water it turns back pale-pink.

a) Predict the signs of the enthalpy ($\Delta_r H^o_{298}$) and entropy ($\Delta_r S^o_{298}$) changes for the reaction (1).

b) What effect does temperature produce on the equilibrium (1)?

c) Consider reaction (1) and KCl and KSCN as a source of ions X^- for it. Which salt present in the same molar concentration shifts the equilibrium (1) to the right in a greater extent? Explain using the principle of Hard and Soft Acids and Bases (HSAB).

17.4 Consider a similar equilibrium (2):

$$[CoX_2L_4] = [CoX_2L_2] + 2\ L. \qquad (2)$$

a) If L = pyridine (py), which ligand X (Cl^- or I^-) helps better shift the equilibrium (2) to the right? Explain using the principle of Hard and Soft Acids and Bases (HSAB).

b) If L = PH_3, which ligand X (Cl^- or I^-) helps better shift the equilibrium (2) to the right? Explain using the HSAB principle.

c) The coordination compound with the formula $[CoX_2L_2]$, where L = py, X = Cl^- exists in two forms colored blue and violet. The structure of the former is quite

apparent, whereas that of the latter is less obvious. For the violet form, draw a fragment of its structure large enough to show clearly the coordination mode of the cobalt ion.

With some knowledge of coordination chemistry of Co(II) described above, you may be able to account for the transformations described below.

NaOH solution is added dropwise to a solution of Co(II) under cooling (0 ℃), which results in a precipitate of blue color. If the precipitate is left at room temperature (25 ℃) for a while, it becomes pink. If an excess of alkali is further added to the precipitate, it dissolves giving blue solution.

17.5 Write down equations corresponding to the transformations described above.

_____

SOLUTION OF PREPARATORY PROBLEM 17

17.1 $CoCl_2 \cdot 6\ H_2O(s) \rightleftarrows CoCl_2 \cdot 4\ H_2O(s) + 2\ H_2O(g)$

$\Delta_r H^o_{298} = 2 \times (-241.8) - 1538.6 - (-2113) = 90.8$ kJ

$\Delta_r S^o_{298} = 2 \times 188.7 + 211.4 - 346 = 242.8$ J K^{-1}

$\Delta_r G^o_{298} = 90800 - 298 \times 242.8 = 18.45$ kJ

$-RT \ln K_p = \Delta_r G^o_T$

$-RT \ln p^2_{H_2O} = \Delta_r G^o_T$

$$\lg p_{H_2O} = -\frac{\Delta_r G^o_{298}}{2 \times 2.3 \times 298 \times R} = -\frac{18450}{2.3 \times 2 \times 298 \times 8.31} = -1.62$$

$p_{H_2O} = 0.024$ atm

At 298 K, the pressure of saturated water vapor can be estimated from the equilibrium

$$H_2O(l) \rightleftarrows H_2O(g)$$

$\Delta_r H^o_{298} = -241.8 - (-285.8) = 44.0$ kJ

$\Delta_r S^o_{298}$ = 188.7 – 70.1 = 118.6 J K^{-1}

$\Delta_r G^o_{298}$ = 44000 – 298 × 118.6 = 8.66 kJ

$p^o_{H_2O}$ = 0.030 atm

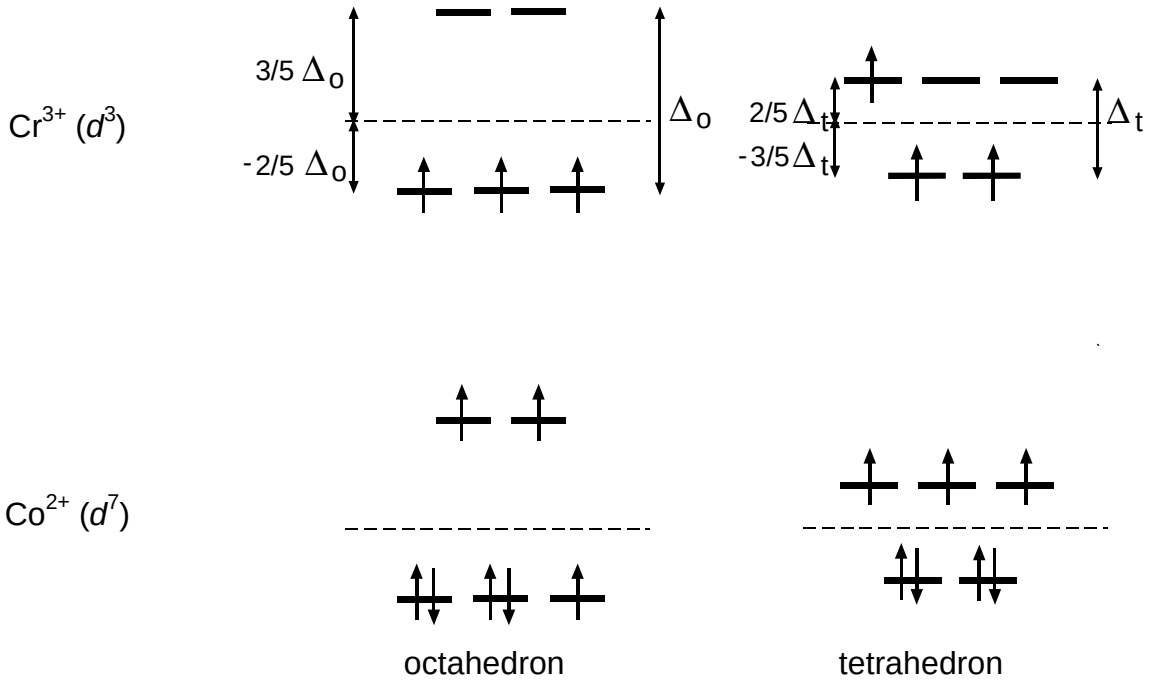
$$-RT \ln p^o_{H_2O} = \Delta_r G^o_T$$

$$\lg p^o_{H_2O} = -\frac{\Delta_r G^o_{298}}{2.3 \times 298 \times R} = -\frac{8660}{2.3 \times 298 \times 8.31} = -1.52$$

The threshold of relative humidity of air specific to the hygrometer response is

$$\frac{p_{H_2O}}{p^o_{H_2O}} = 0.024 / 0.030 = 0.80 \text{ or } 80\%$$

17.2 In a weak Crystal Filed (ligands are water molecules)



a) CFSE($[Cr(H_2O)_6]^{3+}$) = –6/5 Δ_o = – 1.2 Δ_o;
CFSE($[Cr(H_2O)_4]^{3+}$) = –4/5 Δ_t ≈ –16/45 Δ_o = – 0.36 Δ_o
(assuming that $\Delta_t \approx 4/9\ \Delta_o$);

b) CFSE ($[Co(H_2O)_6]^{2+}$) = – 4/5 Δ_o = – 0.8 Δ_o;
CFSE ($[Co(H_2O)_4]^{2+}$) = – 6/5 $\Delta_t \approx$ – 24/45 Δ_o = – 0.53 Δ_o
(assuming that $\Delta_t \approx 4/9\ \Delta_o$);

The value |CFSE(tetrahedron) – CFSE(octahedron)| becomes minimal just for the configuration d^7 (i.e. for Co^{2+}). The Crystal Field Theory assumes ionic bonding of ligand-central ion. That is true for the case of hard acid (a central ion) – hard base (a ligand) in terms of HSAB (see below). In the case of Co^{2+} ion (which is close to a soft acid) covalent contribution to chemical bonding of the central ion with a large polarizable ligand is an additional factor that stabilizes a tetrahedral complex.

17.3 a) We may expect that the entropy change for the reaction (1) $\Delta_r S^o_{298} > 0$, since the reaction is accompanied by an increase of the number of species. At the same time $\Delta_r G^o_{298}$ is slightly above zero (otherwise the reaction (1) would proceed from left to right completely). Therefore, $\Delta_r H^o_{298} > T\Delta_r S^o_{298} > 0$. This conclusion agrees well with CFSE calculations (see above).

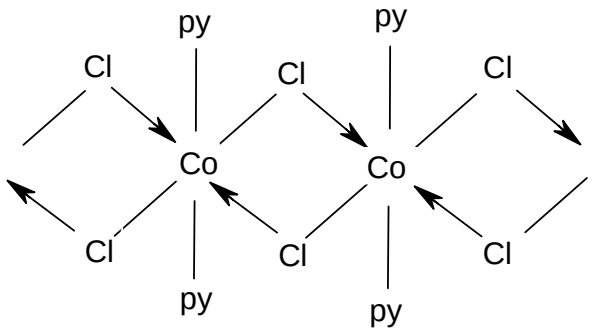
b) Heating shifts the equilibrium (1) to the right, since $\Delta_r H^o_{298} > 0$, and a pink solution turns its color to deep blue.

c) Since Co^{2+} is not a hard acid according to HSAB (rather it is an intermediate acid close to a soft one), it forms stable complexes with soft bases. Thiocyanate-ion SCN^- is a softer base compared to Cl^-, hence, <u>in the case of SCN^- the equilibrium (1) is largely shifted to the right</u>. This is used to discover Co^{2+} in solutions.

17.4 a) X = I^-. According to HSAB I^- is a softer base than Cl^-.

b) In both cases, i.e. for X = I^- and for X = Cl^-, the tetrahedral coordination compounds are stable. The reason lies in the fact that PH_3 is much softer base compared to pyridine. Then, softness of the secondary ligand is not the determining factor in stabilization of the tetrahedral complex.

c) Violet color of the compound corresponds to octahedral environment of Co ion. It is possible if the compound has a polymeric structure (bonding via Cl bridges):



17.5 $CoCl_2 + NaOH \rightarrow [Co(H_2O)_2(OH)_2]$ – blue precipitate

(in fact, the structure of hydroxides or basic salts of transition metals is quite complex, often polymeric in its nature, however, the color of the precipitate gives correct information concerning the coordination environment of Co ions having coordination number equal to 4)

$[Co(H_2O)_2(OH)_2] + 2\ H_2O \rightarrow [Co(H_2O)_4(OH)_2]$ (pink precipitate)

$[Co(H_2O)_4(OH)_2] + 2\ NaOH \rightarrow Na_2[Co(OH)_4]$ (blue solution) $+ 2\ H_2O$

THEORETICAL PROBLEM 18

The formose reaction

Aldehydes have a high and versatile reactivity serving as indispensable reagents in the organic synthesis. Carbon atom of the carbonyl group is an electrophilic center. In the aldol condensation reactions a nucleophilic enol (or enolate) attacks the electrophilic carbonyl group of the other aldehyde (or ketone) molecule.

18.1 Fill in blank boxes in the representative aldol condensation reaction, and mark by letters **E** or **N** the respective nucleophilic and electrophilic reaction centers which take part in the process

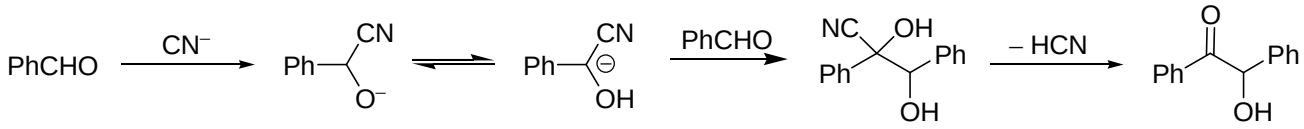
The aldehydes lacking α-hydrogen atoms are commonly believed to be unable to take part in the aldol reactions as a nucleophilic component, thus such aldehydes are apparently unable to undergo self-condensation.

18.2 Such aldehydes are commonly referred to as *non-enolizable*. Why? Give any three examples of such aldehydes.

Formaldehyde is the most famous among such aldehydes. It was discovered by one of the founding fathers of organic chemistry, Alexander M. Butlerov as early as in 1859. Studying the compound Butlerov discovered a very interesting transformation of aqueous formaldehyde in the presence of lime into sugary syrup. The other great chemist Emil Fischer studied this transformation in more detail about half a century later, and discovered that a complex mixture of racemic carbohydrates is actually formed. The mixture was given a name "*formose*"; the transformation since then is called *the formose reaction*. This reaction is very interesting due to its possible role in the generation of sugar molecules in a prebiotic Earth. Also it is quite promising from a practical viewpoint as a very inexpensive source of sugars for biotechnology given that formaldehyde is a readily accessible raw material which is produced in huge amounts from carbon and water.

18.3 Suggest a method for industrial preparation of formaldehyde from coal and water in no more than 3 stages.

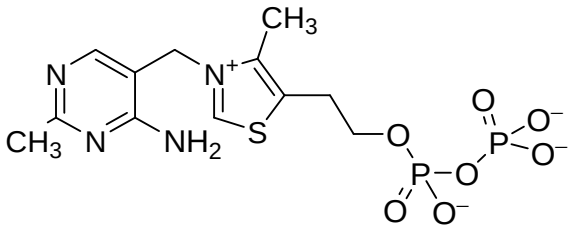
The way formaldehyde enters the condensation remained an enigma for a long time since Fischer's works. One of the possible keys to this problem is the so-called *Umpolung*. (Note: This German word is not usually translated in English due to lack of adequate and short translations.) The essence of this important synthetic notion can be illustrated using the benzoin condensation as an example:



18.4 Mark in structure of the product (benzoin) the fragments coming from benzaldehyde and put the letters **E** and **N** over electrophilic and nucleophilic centers.

The intermediate generation of a nucleophilic reagent from a compound ordinarily behaving as an electrophile (or vice versa) is referred to as the *Umpolung* principle in modern organic chemistry.

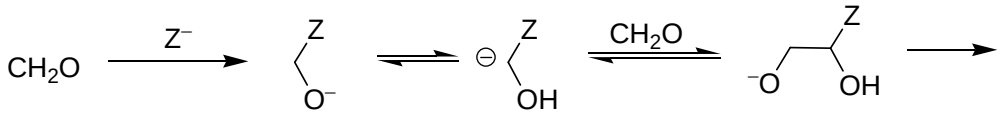
In order to avoid handling deadly cyanides, other compounds having similar CH-acidity, thiazolium salts, can be used. Such a non-trivial choice comes from a far-reaching analogy. One of such thiazolium salts, vitamin B_1 derivative, or thiamine pyrophosphate, is employed by Nature as a co-factor for trans-ketolases, that perform *in vivo* reactions closely resembling the benzoin condensation by transferring a carboxylic acid residue (acyl) as a nucleophilic rather than electrophilic reagent.



18.5 Mark in thiazolium the CH-acidic center equivalent to that in HCN. Draw the structure of the respective carbanion and show its resonance structures that account for the enhanced CH-acidity.

18.6 Alcohol addicts often suffer from an acute B_1 deficiency. Why?

A model of formose reaction has been studied. Formaldehyde in the presence of calcium hydroxide and vitamin B_1 (denoted as HZ in the Scheme below) gives the simplest ketotriose (dihydroxyacetone, DHA) in good yield.



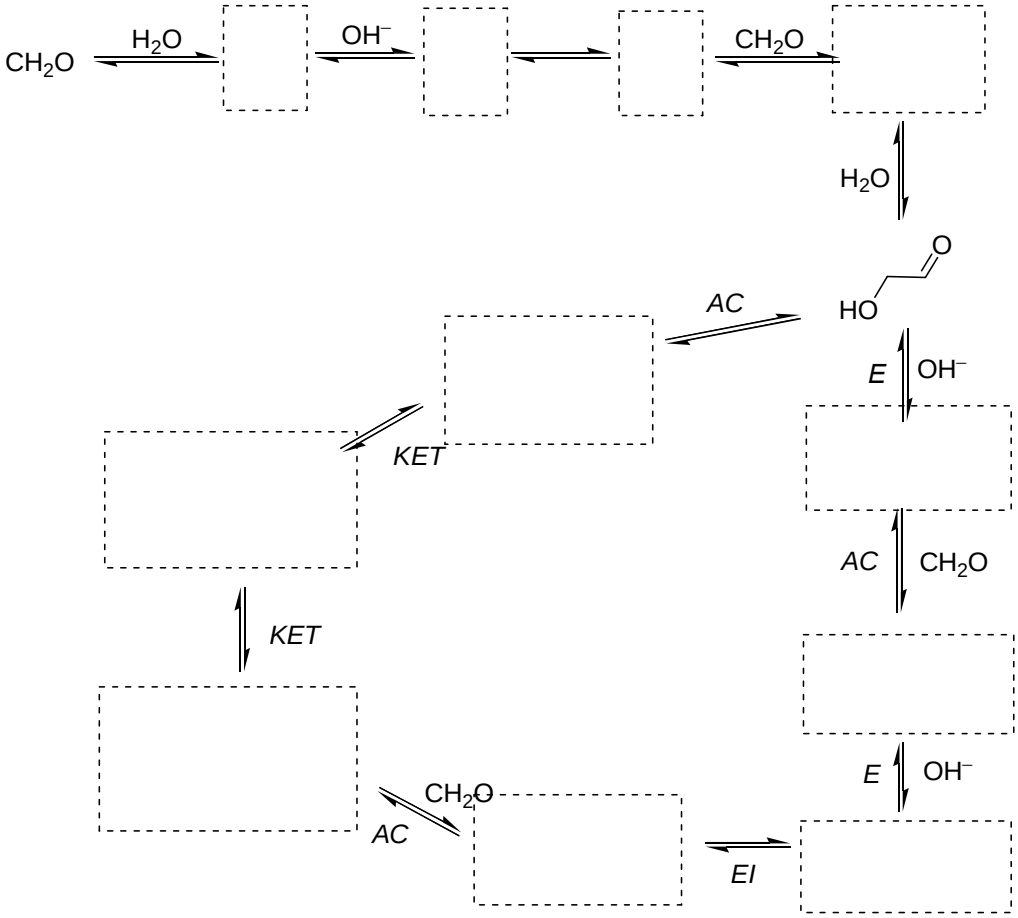
18.7 Complete this scheme to the final product.

With all these data at hand, we can try to crack the enigma of the real formose reaction. An essential clue is that the reaction of pure aqueous formaldehyde in the presence of lime is autocatalytic, which means that it is extremely slow at the beginning (there is an induction period), but once it starts it runs at an increasing rate until exhaustion of formaldehyde. Traces of *any* carbohydrate dramatically accelerate the reaction and immediately launch it if introduced within the induction period. The process involves a catalytic cycle consisting of aldol condensations (AC), keto-enol tautomerizations (KET), proton transfers leading to enolates (E), enolate or enol isomerizations (EI).

18.8 Fill in empty boxes on the simplified scheme of formose reaction below.

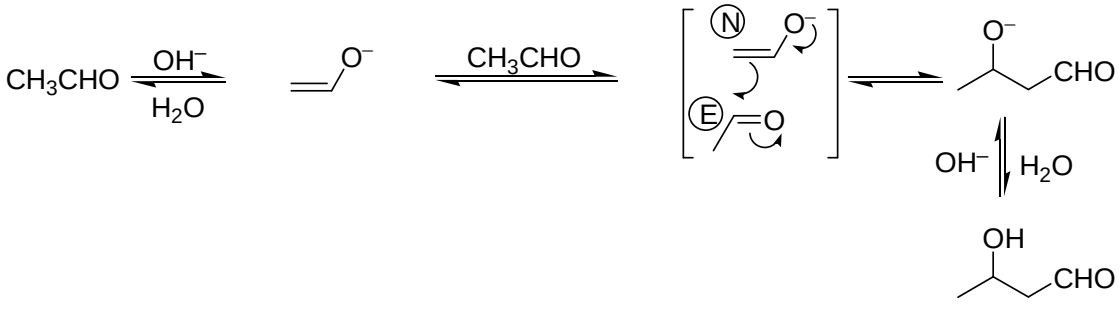
18.9 Show the step(s) involved in the induction period.

18.10 Show the catalytic cycle. What compound(s) serve(s) as catalyst(s)?



SOLUTION OF PREPARATORY PROBLEM 18

18.1 The base-catalyzed aldol condensation involves a highly reactive nucleophilic enolate-ion, which directly attacks the electrophilic carbonyl carbon of another aldehyde molecule giving β-hydroxyaldehyde (aldol).

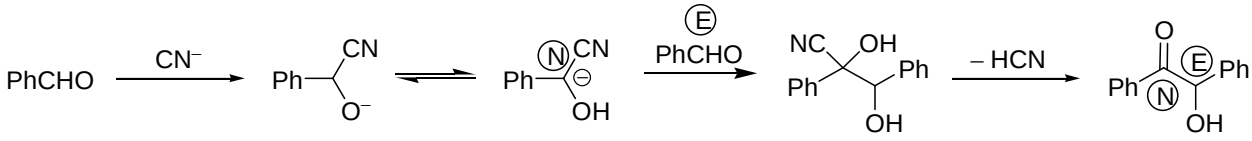


18.2 Non-enolizable are aldehydes lacking β-protons, that are those which cannot give enols or enolates. Among important non-enolizable aldehydes, besides formaldehyde are benzaldehyde PhCHO, trichloroacetic acid aldehyde (chloral) CCl_3CHO, glyoxal OHC–CHO, and many others.

18.3 Formaldehyde is produced by a 3-step process involving a) gasification of coal by the action of steam at high temperature to give the so-called *syngas*, which is used as feedstock for b) methanol synthesis using copper on zinc oxide catalyst at 250 ℃ and a pressure of 100 atm. Methanol is catal ytically dehydrogenized into formaldehyde over silver mesh at 650°.

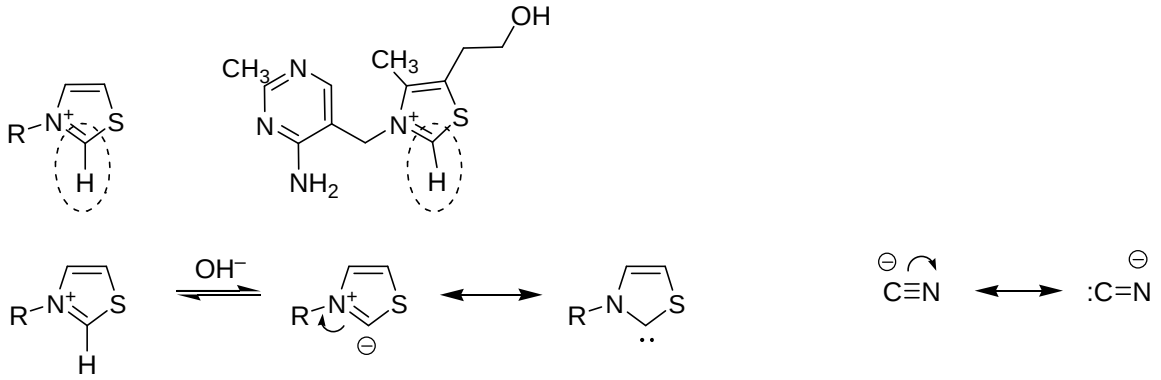
$$C + H_2O \longrightarrow CO + H_2 \longrightarrow CH_3OH \longrightarrow CH_2O$$

18.4 The main trick in the mechanism of benzoin condensation is the addition of nucleophilic catalyst to carbonyl group of a non-enolizable aldehyde. Central carbon of the adduct is no more sp^2-carbon, but rather sp^3-carbon bearing two substituents capable of delocalization of negative charge and thus rendering a reasonable CH-acidity. After deprotonation the resulting carbanion serves as a nucleophile attacking carbonyl group of the other aldehyde molecule. Elimination of nucleophilic catalyst (here, cyanide) regenerates carbonyl group. Thus, the net result is the transfer of PhCO (or generally RCO, acyl) residue from aldehyde.



18.5 Normally, acyl groups are transferred by electrophilic reagents (acid chlorides, anhydrides, and other carboxylic acid derivatives) to nucleophiles. The Umpolung principle shows the way how it can be done by using a pair of reagents of reverse reactivity.

The analogy between cyanide and thiazolium is profound and very interesting. Apparently, both HCN and thiazolium (with regard to C-2 atom) can be considered as derivatives of formic acid.

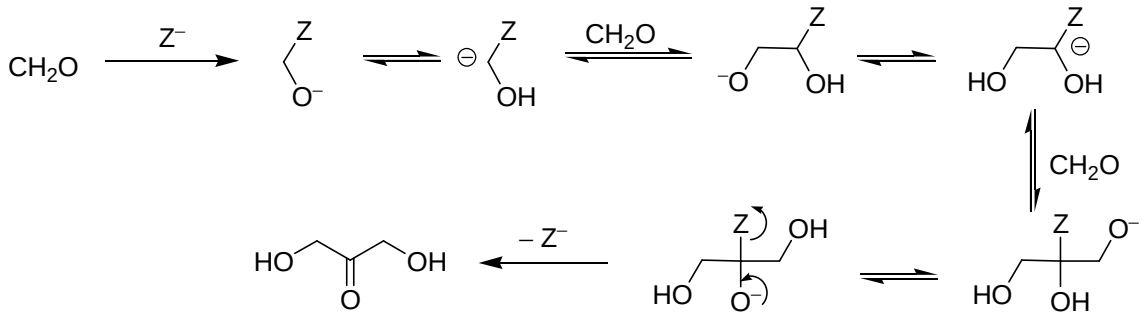


Resonance structures for thiazolium anion suggest that besides carbanionic form there is the only one other form, an electroneutral carbene! Indeed, this is a true carbene with 6-electron configuration of carbon atom, a lone pair and a vacant orbital. Recent research has shown that thiazolium anion and closely related anions of analogous heterocycles (e.g. imidazolium) are indeed stable (!) carbenes, which immediately found a lot of applications in organic chemistry and catalysis. These carbenes are nucleophilic due to two electron-rich heteroatoms connected to carbene center. Thus, it can be assumed that Nature employs a stable carbene in the transketolase catalysis.

Coming back to the analogy with cyanide, we see that cyanide has a second resonance form, isocyanide with carbene-like divalent carbon.

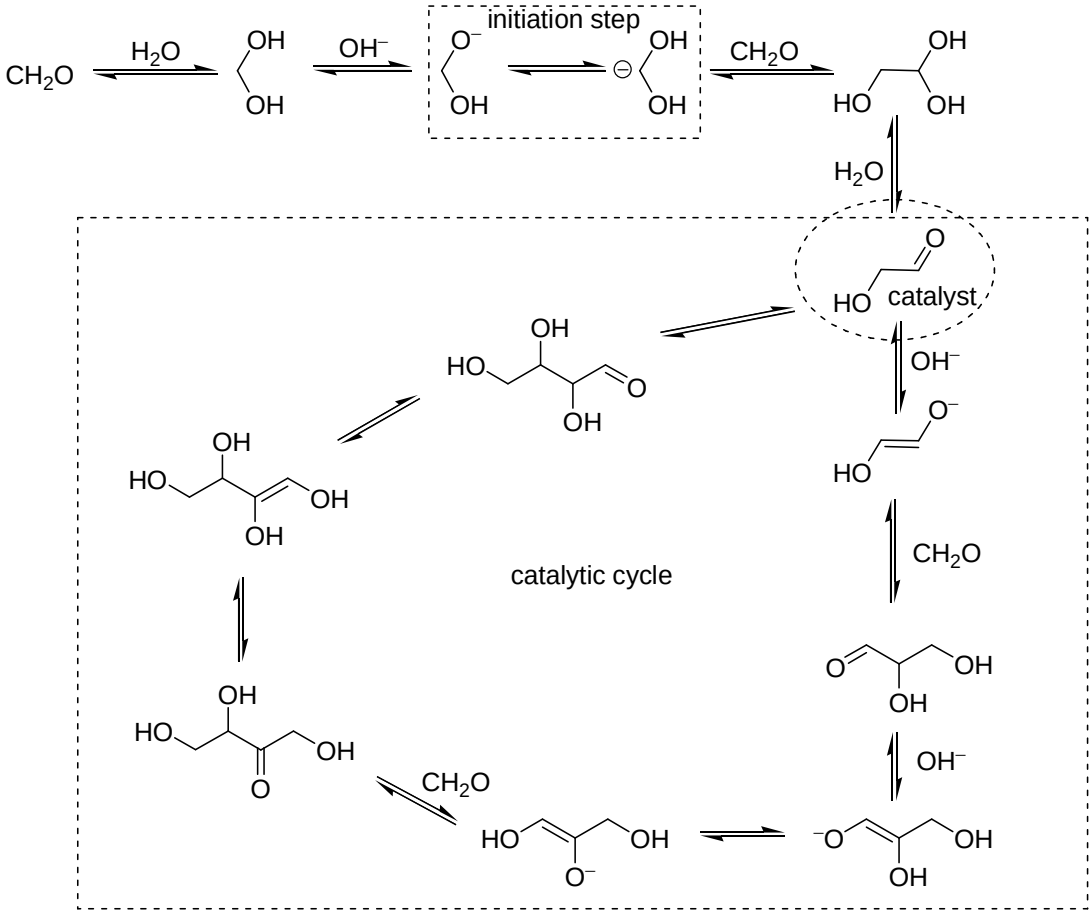
18.6 As shown above thiamine pyrophosphate, as other thiazolim salts, is very reactive towards aldehydes. In the organisms of heavy drunkards there is a lot of alcohol dehydrogenation product, acetaldehyde. This reactive aldehyde binds to thiamine thiazolium residue, thus stealing the vitamin from vital biochemical processes.

18.7 Continuation is straightforward to employ the same chemistry as in the steps already shown. Catalyst (thiazolium anion or thiazolidene, if we choose the carbene form) is regenerated at the last stage exactly as in the benzoin condensation.



(also 9 and 10) The Umpolung in the true formose reaction is apparently furnished by CH-acidic properties of the hydrated form of formaldehyde. Due to the lack of good mesomeric stabilization CH-acidity is much lower, and the deprotonation leading to nucleophilic carbanion is much less efficient. Therefore, the reaction is very slow at the beginning. The induction period is accounted for by very low concentration of carbanion. But as soon as some glyoxal is accumulated, a highly effective catalytic cycle is switched on. Within the catalytic cycle formaldehyde behaves as a normal electrophile.

18.8 – 18.10 (next page)



THEORETICAL PROBLEM 19

The analogy in organic chemistry

Though not strict but rather an intuitive concept, the analogy (structural, electronic, stereochemical) is widely used by chemists for reasoning. For example, organic chemists often predict new reagents or even reactions by analogy with known ones.

An important sort of analogy is heteroanalogy – the similarity of compounds or reactions differing by substitution of an atom or group by another atom or group having the same type of bonding.

Thus, heteroanalogues of aldehydes are iminium salts, e.g. a well-known Eschenmoser's salt $CH_2{=}NMe_2^+I^-$.

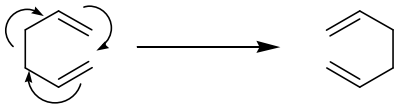
19.1 Which type of reagent is the cation of Eschenmoser's salt?

Electrophile ☐ nucleophile ☐ free radical ☐

Lewis acid ☐ oxidant ☐ protecting group ☐

19.2 Write by analogy the reaction of Eschenmoser's salt with acetone. Why does this reaction not require a catalyst?

Further we may consider a heteroanalogy concept with respect to reactions. For example, there is the Cope rearrangement, which takes place if 1,5-dienes are being heated. The reaction is a concerted movement of 6 electrons to involve two π-bonds and a σ-bond, a sigmatropic shift.

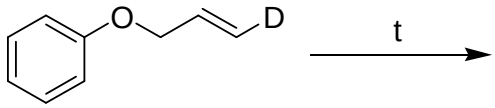


19.3 What products are formed on prolonged heating of 1,5-hexadiene substituted at C1 with one deuterium atom in inert atmosphere (possible isotope effects are to be neglected)?

If we take vinyl allyl ether $CH_2{=}CH{-}O{-}CH_2CH{=}CH_2$ in place of diene, the same sort of rearrangement takes place, but with a more interesting result leading to a compound of the other class, unsaturated ketone. Such hetero- (oxa-)analogue is usually called the

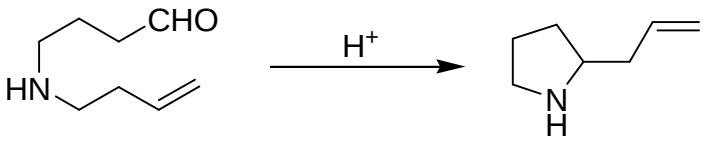
oxo-Cope rearrangement, or Claisen rearrangement. This reaction was discovered by a happy chance by great German chemist Ludwig Claisen.

19.4 Complete the reaction



The rearrangements of this sort are interesting because new reactive groups can form in a very simple process, and these newly-born groups can enter further reactions in the same reaction mixture without the isolation of intermediate compounds. Such chains of transformations are often called the domino-reactions, by analogy with a well-known trick when a long chain of standing dominoes is made to fall by a single click.

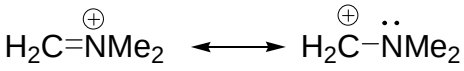
19.5 Your task would be to imagine how the following domino-process, which is initiated by a drop of strong acid and a dehydrating agent, such as $HC(OEt)_3$, takes place



Write the steps involved in this process.

SOLUTION OF PREPARATORY PROBLEM 19

19.1 Echenmoser's salt is an iminium salt, which involves a heteroanalogue of carbonyl group. Thus, Echenmoser's salt is an electrophile with electrophilic carbon center similar to the carbonyl carbon. Formally, it should behave as a stabilized carbenium ion, as is well seen by considering the resonance forms

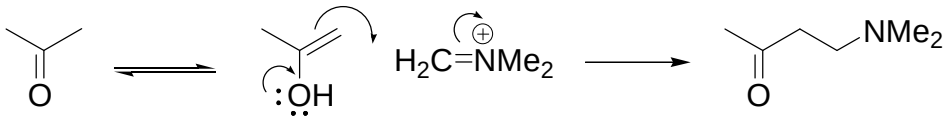


Due to very high π-donicity of dimethylamino group, the first form predominates, and thus nucleophilic properties, which may be attributed to the second form, are

virtually missing. It can be considered a Lewis acid, as any C-electrophile is, due to apparent ability to combine with bases, e.g. hydroxide ion or water.

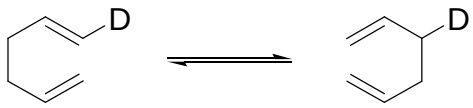
Thus, electrophile is the true answer, and Lewis acid and/or nucleophile can be regarded as valid additional answers.

19.2 No catalyst is required because iminium salt is already strongly polarized, and carbon atom is sufficiently electrophilic to attack carbonyl group without any additional activation by catalysts. In the reactions with aldehydes or ketones the iminium salt serves as a heteroanalogue of the *protonated carbonyl compound*, with the double carbon-nitrogen bond strongly polaryzed due to the positive charge at heteroatom. Therefore, the iminium salt is already reactive enough to take part in electrophilic attack at enol to form the so called Mannich base, which is itself a heteroanalogue of the aldols.



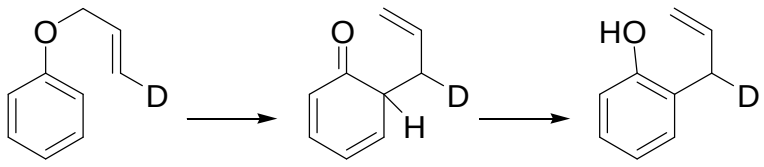
19.3 In the Cope rearrangement, it is highly important to realize that the reaction is an equilibrium, which is perfectly evident from the fact that the reactant and product are the same compound (or the same type of compound, if a substituted diene is used). Thus, the forward and the reverse transformations are the same reaction.

In the case of degenerate reaction (when reactant and product are the same, if isotope effects are neglected), it is evident that equilibrium constant is unity.



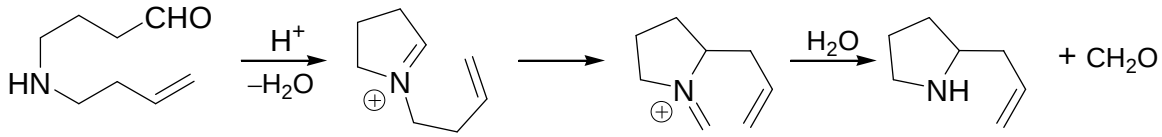
Thus, the result would be an equimolar mixture of 1- and 3-deuteriohexadiene-1,5.

19.4 Unlike the Cope rearrangement, oxo-Cope rearrangement involves two different compounds (belonging to different classes), thus the reversibility is not evident. In the case of allylic phenol ether hetero-hexadiene fragment is formed by allyloxy chain and one of the double bonds of benzene ring:



As the initial keto-form of phenol is immediately transformed into much more stable normal phenol (*enol*) form, the arrangement of double bonds for Cope-Claisen rearrangement disappears, and the whole reaction becomes irreversible.

19.5 The domino-reaction starts from the formation of a cyclic iminium salt similar to the Eschenmoser's salt, with triethyl-orthoformate serving as a dehydrating agent. In this salt there are two double bonds at a distance required for the Cope rearrangement, thus here we have the aza-Cope rearrangement. A new iminium salt is formed, which is readily hydrolyzed to liberate secondary amine and formaldehyde.



THEORETICAL PROBLEM 20

Keto-enol tautomerism

Aqueous or alcoholic solutions of ketones or aldehydes can be titrated by solutions of halogens or interhalides. In order to obtain reproducible results, the titration should be performed fast in the presence of buffer salts, such as $NaHCO_3$.

Thus, to 10 g of cyclohexanone in aqueous methanol were added 2.00 mmol $NaHCO_3$, and 1.00 cm^3 2.00 N methanolic solution of ICl. After thorough mixing an excess of aqueous NaI solution was added, followed by titration by 1.594 cm^3 of 1.00 N $Na_2S_2O_3$ using starch as indicator.

20.1 Write the reactions involved in the analysis.

20.2 What compound reacts with ICl? Estimate the content of this compound in cyclohexanone.

20.3 What is the role of buffer salt? What can happen if Na_2CO_3 is taken in place of $NaHCO_3$?

A colorless substance **A** with the empirical formula C_2H_2O shows in ^{13}C NMR only two signals at 94 and 159 ppm. The reactions of **A** with halogens or interhalides are instantaneous, but titration, as described above, is not useful as more than one mole halogen per mole **A** is consumed to give off heavy precipitates.

A readily reacts with aldehydes in the presence of either acidic or basic catalysts, to form products of 1:1, 1:2 or 1:3 stoichiometry (depending on reagent ratio). Such products are often colored, which is used in many well-known qualitative reactions for aldehyde-containing materials. For example, carbohydrates give red coloration when treated by **A** and a drop of HCl.

Under alkaline conditions **A** reacts with methyl iodide to give a mixture of products. With a large excess of MeI a single compound **B** is produced. **B** turned out to be identical to a known trimer of dimethylketene formed under the conditions of basic catalysis. On the other hand, if the reaction of **A** with excess MeI is performed in the presence of $NaHCO_3$ a different compound **C** is formed. This compound possesses a fine odor and has been identified as one of important constituents of rose flavor. In ^1H NMR compound **B** shows a single resonance, while **C** shows two sharp singlets with integral intensities ratio of 1:3.

The reaction of **A** with $NaHSO_3$ on heating gives colorless water-soluble material (brutto-formula $C_6H_5NaO_5S$) showing a purple coloration with $FeCl_3$ solution. The ^{13}C NMR spectrum in D_2O shows 4 signals at 157, 144,106,105 ppm.

The reaction of **A** with hydroxylamine gives a compound **D** (brutto-formula C_2H_3NO), which is cleanly reduced by H_2 over Raney-Ni catalyst to give a compound **E** (brutto-formula C_2H_3N) rapidly darkening in the air. The compound is poorly soluble in water, but readily dissolves in dilute HCl. Boiling of this solution gives back **A**.

20.4 Determine the structures of **A**, **B**, **C**, **D**, **E**.

20.5 Write the reactions mentioned in the text

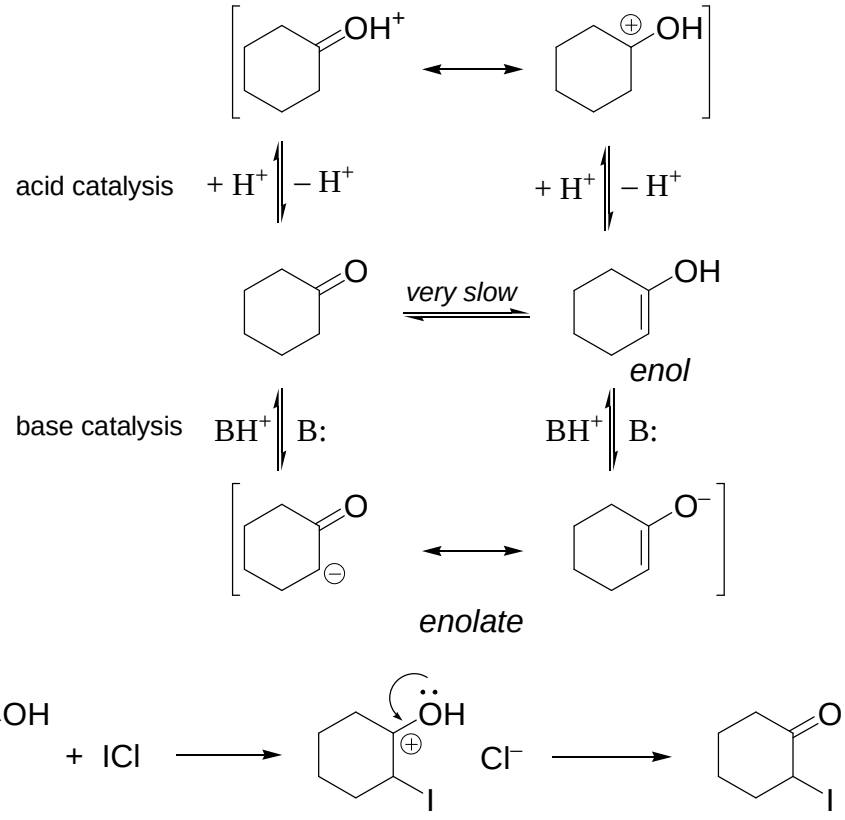
_____

SOLUTION OF PREPARATORY PROBLEM 20

20.1 - 20.3

Ketones do not react directly with halogens. Enolizable ketones and aldehydes contain the respective enols, which are unsaturated electron-rich compounds very reactive towards electrophiles. The reactions are very fast and quantitative. The transformation of ketone to enol is normally rather slow, but is effectively catalyzed by acids and bases. Thus, if the reaction with halogen is performed fast, only enol is consumed. In order to avoid catalyzed enolization the acid liberated during the addition should be neutralized by salt, which is not alkaline enough to switch on the base-catalyzed enolization.

Iodine chloride is more convenient as titration agent than bromine or iodine, as the former interhalide is more polar, and thus is more reactive towards the double bond.



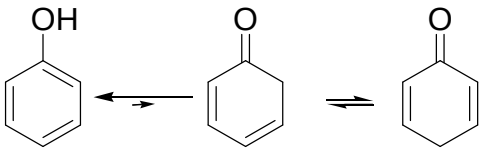
$ICl + I^- = I_2 + Cl^-$

$2S_2O_3^{2-} + I_2 = S_4O_6^{2-} + 2I^-$

Calculation of enol content should give the value of 1.18%. As has been shown by more accurate kinetic and spectroscopic investigations, this estimate is hugely overestimated. Real tautomerism constant for cyclohexanol is of the order p*K* = 5-6.

20.4 - 20.5

The content of enol in simple ketones is very low. However, there are some compounds for which the enol form is more stable, and even those with predominating enol form. One of the most important examples of such behavior are … phenols. Simple phenols practically do not show any properties characteristic of keto-form, because this form is not aromatic and thus very unstable in comparison with enol (phenol)

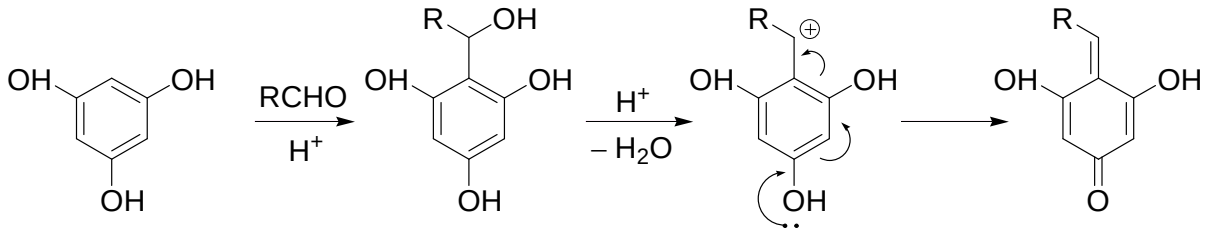


enol *keto-forms*

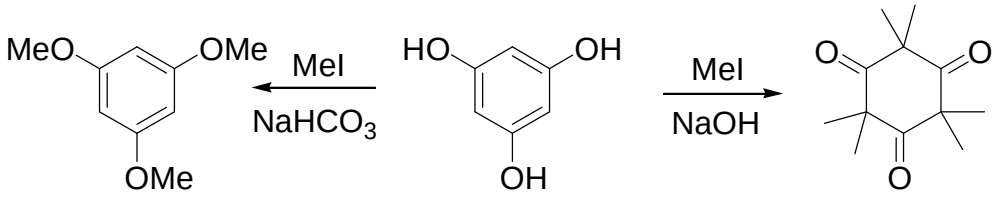
However, for some substituted phenols, as well as for polycyclic or heterocyclic phenols the presence of keto-form is well manifested. One of such examples is used in the second part of the task.

The transformations mentioned reveal the reactivity of carbonyl group (reactions with hydroxylamine, bisulfite, and condensation with aldehydes). From the empirical formula of bisulfite derivative it can be deduced that the compound has 6 carbon atoms, and all other empirical formulas are the results of factorization of divisible formulas. Thus, compound **A** is $C_6H_6O_3$ and is, according to ^{13}C NMR, a highly symmetrical compound. As it follows from apparent presence of keto-group this might be cyclohexatrione-1,3,5, or a fully enolized form of this compound 1,3,5-trihydroxybenzene, known as floroglucine.

Condensation with aldehydes gives normal aldols, which readily eliminate water to form quinoid structure, a well-known chromophore. Two or three aldehyde molecules can enter this reaction, and more complex structures can form if aldehyde bears some functional groups (such as e.g. carbohydrates or cinnamic aldehydes which are the building blocks of lignin).

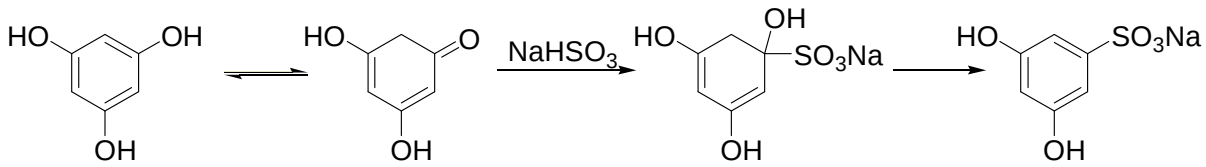


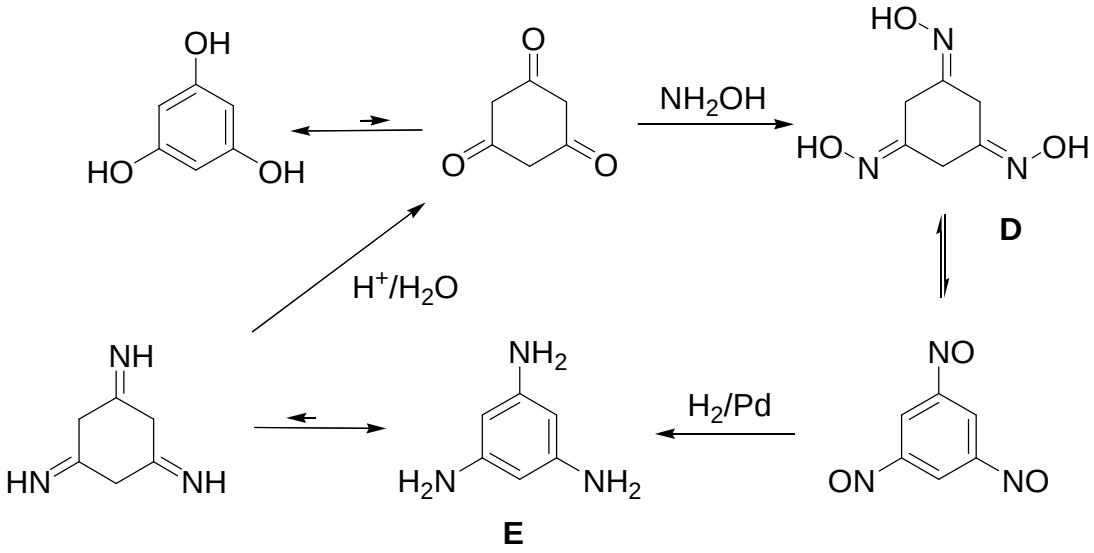
Methylation can give either permethylated enol or keto-forms, the former takes 3 methyls, the latter 6 methyls



C **A** **B**

Bisulfite derivative readily loses water to give 3,5-dihydroxybenzenesulfonic acid



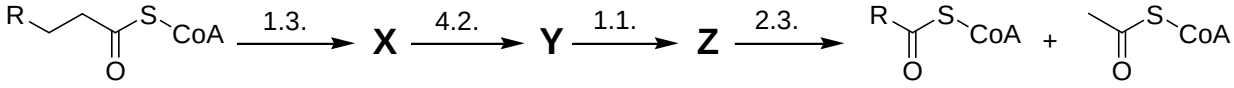


E

THEORETICAL PROBLEM 21

Unusual pathways of fatty acid oxidation: Alpha-oxidation

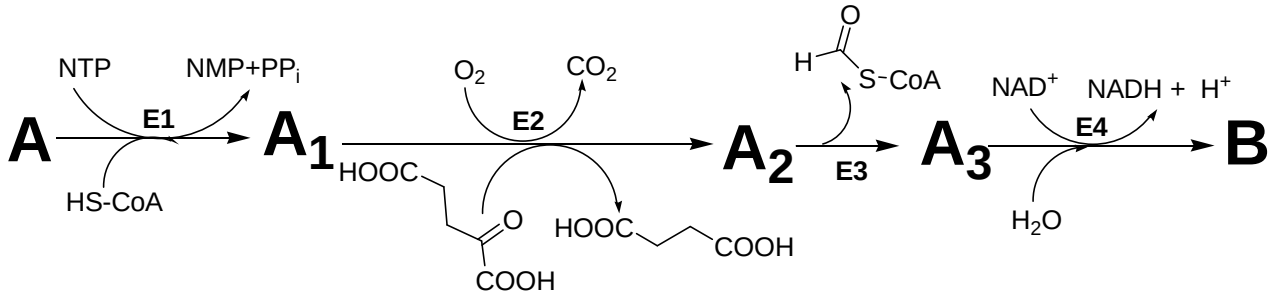
Oxidative destruction of fatty acids is a universal biochemical process inherent in all living systems. The so-called β–oxidation is the dominating pathway of fatty acid degradation in mitochondria. It can be described by the following scheme:



At all stages of β-oxidation, acyl residues are linked with coenzyme A by thioester bond. On the above scheme, classes and subclasses (numbers beyond the arrows) of enzymes catalyzing corresponding reactions are given in accordance with IUB classification. Note that substituent R remains unchanged within one cycle turnover.

21.1 Draw structures (without stereochemical details) of metabolites **X**, **Y** and **Z** using symbol “R” for the unchanged part of acyl residue.

Phytanic acid **A** is a saturated fatty acid which is found in nature as a mixture of two diastereomers. It is not involved in β-oxidation due to peculiar features of its structure. Nevertheless, mammals metabolize it into pristanic acid **B** with retention of configuration of chiral atoms. The latter process (usually referred to as α-oxidation) occurs in special cellar organelles, peroxisomes. Reaction equations on the scheme below illustrate metabolism of **A**:



NMP and NTP are mono– and triphosphates of ribonucleoside **N** (A, C, G or U), respectively, PP_i – pyrophosphate, CoA-SH – coenzyme A, NAD^+ and NADH – oxidized and reduced forms of nicotine amide adenine dinucleotide, respectively, **E1**-**E4** – enzymes catalyzing corresponding reactions.

Biosynthesis of $\mathbf{A_1}$ catalyzed by **E1** is a two-stage process. The intermediate formed contains phosphorus and oxygen in a molar ratio of 1 : 8.

21.2 From the list of reaction types given below, choose those which correspond to the stages catalyzed by **E1** and **E3.**

a) formation of an ester of ribonucleoside phosphate and carbonic acid,
b) transfer of a phosphoric acid residue on a substrate due to cleavage of high energy bond of another substrate (kinase reaction),
c) hydrolysis of an ester bond,
d) formation of a thioester of carbonic acid,
e) oxidative decarboxylation,
f) cleavage of a carbon-carbon bond.

21.3 Draw the intermediate of the **E1** catalyzed reaction considering the formula of phytanic acid as R–COOH, where R is a hydrocarbon residue.

B is further metabolized in a number of consecutive cycles of β-oxidation. Data on oxidative destruction of pristanic acid are given in the table below.

Stage	Cleavage Product(s)
Formation of pristanoyl CoA	No
The 1st cycle of β-oxidation	Propionyl CoA
The 2nd cycle of β-oxidation	Acetyl CoA
The 3rd cycle of β-oxidation	Propionyl CoA
The 4th cycle of β-oxidation	Acetyl CoA
The 5th cycle of β-oxidation	Propionyl CoA
The 6th cycle of β-oxidation	Acetyl CoA
The 7th cycle of β-oxidation	Propionyl CoA + Formyl CoA (final products of degradation)

21.4 Determine the empirical and molecular formulae of phytanic acid **A** without deciphering α-cycle and establishing structural formula of pristanic acid.

21.5 Draw structural formulae of **A** and **B** with stereochemical details. Take into account that all chiral centers in these fatty acids but that nearest to the carboxylic group exist in R-configuration only.

21.6 Explain why phytanic acid cannot be involved in β-oxidation.

The enzyme catalyzing the first reaction of β-oxidation cycle is stereospecific. Acyl CoA is transformed by this enzyme only in case the chiral center most distant from ω-carbon atom is in S-configuration. There exists a special enzyme, racemase AMCAR

marker of some oncologic pathologies), which transforms pristanic acid and some of its β-oxidation metabolites by catalyzing R → S transition in the chiral center most distant from ω-carbon atoms.

21.7 Suggest the mechanism of pristanoyl CoA racemization.

21.8 Draw (with stereochemical details) those metabolites of pristanic acid oxidation which are AMCAR substrates.

During α-oxidation of **A** in mammals, only one pair of diastereomers is formed in **E2** catalyzed reaction.

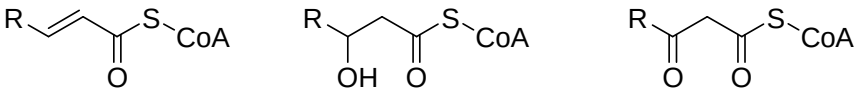
21.9 Based on sterical considerations, suggest configuration (R or S) of chiral centers in diastereomers **A2**.

SOLUTION OF PREPARATORY PROBLEM 21

21.1 According to IUB classification:

1.3. – oxidoreductases acting on the CH–CH group of donors;
4.2. – carbon-oxygen lyases (or hydrolases);
1.1. – oxidoreductases acting on the CH–OH group of donors;
2.3. – acyltransferases.

The 1st enzyme catalyzes dehydrogenation resulting in β-unsaturated acyl derivative (all the rest carbon atoms but carbonyl belong to R, and thus are not modified). Addition of water to this unsaturated acyl CoA leads to 3-hydroxyacyl CoA (formation of 2-hydroxyacyl CoA is not consistent with the final products given in the task). This is also confirmed by the subclass of the 3rd enzyme, which catalyzes oxidative transformation of a hydroxyl group into carbonyl one. The 4th enzyme leads to the final products of the cycle as a result of thioclastic degradation (transfer of R-CO fragment on a new CoA-SH molecule).



X **Y** **Z**

21.2 According to the task data, **E1** catalyzes two successive reactions. Based on the list of reaction types given, two variants are possible for the first stage: either formation of an ester bond of ribonucleoside phosphate and carbonic acid or kinase reaction. Then thioester of carbonic acid (phytanoyl CoA) is formed at the second stage. Two-stage character of **E1** catalyzed reaction is due to a positive change of Gibbs free energy of phytanoyl CoA formation. This process is possible if only it is conjugated with cleavage of high energy bond in NTP.

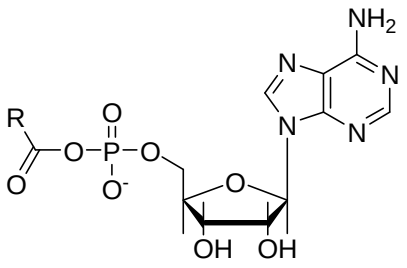
If the first stage is the kinase reaction, one product is possible: residue of phytanic acid linked with one phosphate. P:O ratio in this product would be 1:5. Thus, one can conclude that intermediate containing either NMP or NTP residue is formed. Note that NDP residue is not consistent with further phosphorus-containing products.

Finally, the reaction types are: **E1** – a), d); **E3** – f).

21.3 To decipher nucleotide in **E1** catalyzed reaction, a table with P:O molar ratios for all possible derivatives of ribonucleotide mono- and triphosphates is of help.

Intermediate contains	P:O molar ratio if the starting nucleotide contains as a base			
	Adenine	Guanine	Uracil	Cytosine
Monophosphate	1:8	1:9	1:10	1:9
Triphosphate	1:4.66	1:5	1:5.33	1:5

It is seen that the only possible variant is **E1**catalyzed transfer of adenosine monophosphate residue on phytanic acid molecule:

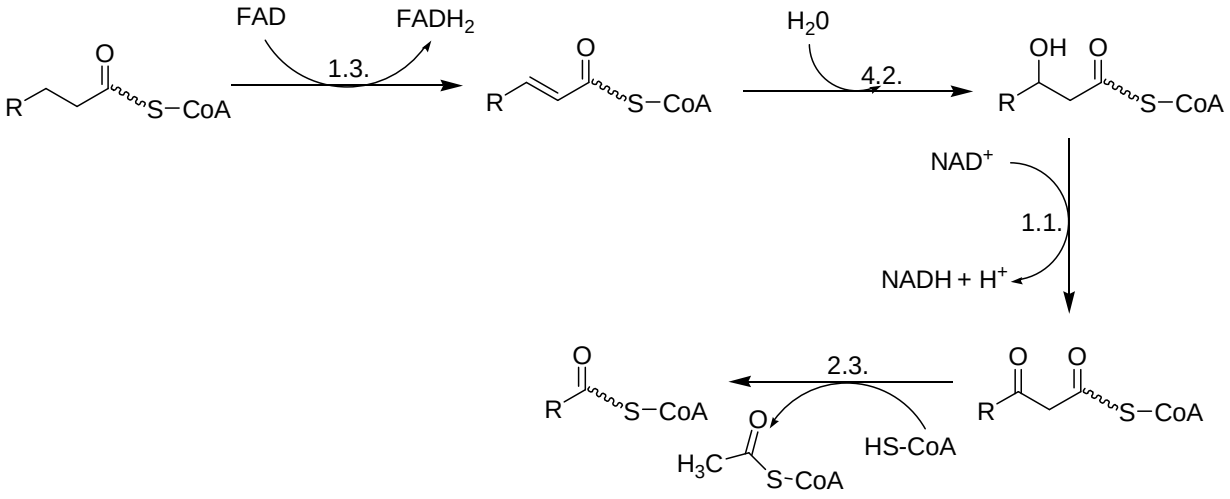


21.4 It is seen from the table in the task that the number of carbon atoms in prystanic acid is: 4·3 (propionyl CoA) + 3·2 (acetyl CoA) + 1 (formyl CoA) = 19.

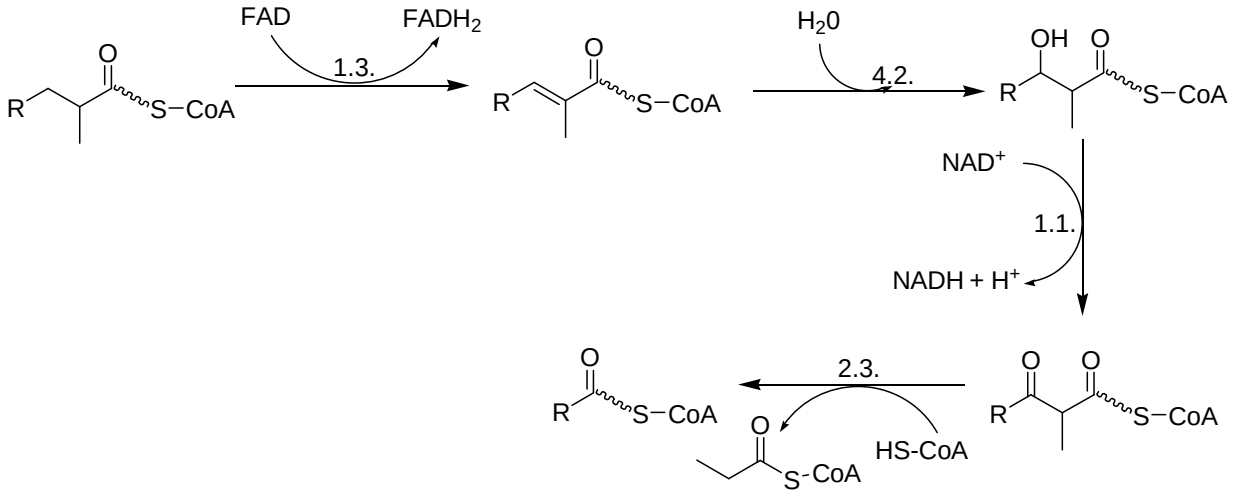
According to α-cycle reactions, **E3** catalyzed stage results in splitting off a monocarbon fragment attached to CoA. At the other stages including that catalyzed by **E2** no changes in the number of carbon atoms in phytanic acid metabolites is observed (note that reaction equations are given). Thus, **A** contains 19+1=20 carbon atoms.

For determination of the molecular formula of saturated phytanic acid: hydrogen – 20·2, oxygen – 2 (both in one carboxylic group). Finally, $C_{20}H_{40}O_2$. Note that it is given that phytanic acid can be represented as R–COOH, where R is hydrocarbon residue. Thus, R does not contain functional groups (including hydroxyl or carboxylic). Empirical formula: $C_{10}H_{20}O$.

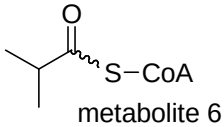
21.5 In the scheme of β–oxidation discussed in question 1, acetyl CoA is the product which is finally split off from a fatty acid:



Another metabolite, propionyl CoA, is elaborated as a result of every second cycle when prystanic acid is degraded. Propionyl CoA would be formed if a methyl group is linked with α-carbon atom. In this case α-carbon atom must also be linked with hydrogen atom which is removed at the first stage of the cycle. Thus, presence of the methyl group in this position does not prevent the fatty acid from being involved into β-oxidation, which is illustrated at the scheme below:

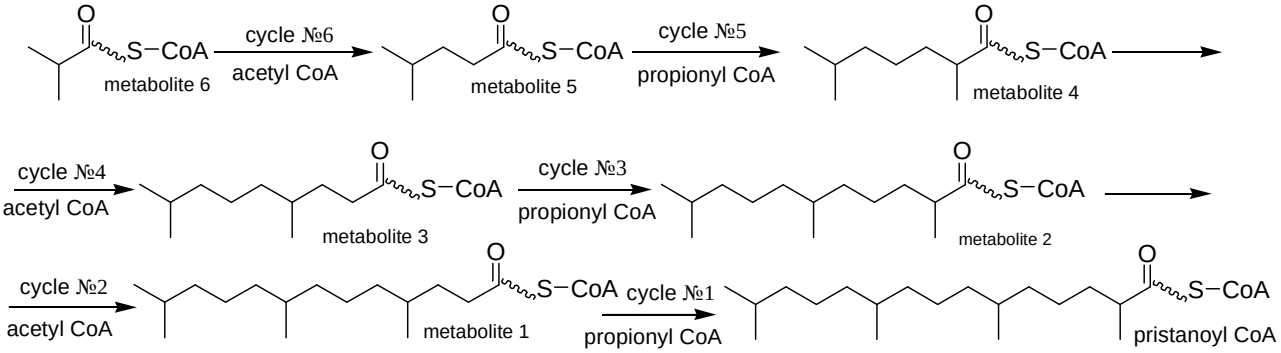


It is seen from the scheme that the final products of prystanic acid metabolism can be achieved if only R is substituted by H for the 7th β-oxidation cycle. Then, the product resulting from the 6th cycle would be:



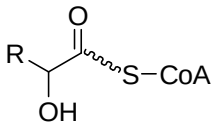
metabolite 6

Similarly, moving in the direction opposite to oxidative degradation of prystanic acid we have:

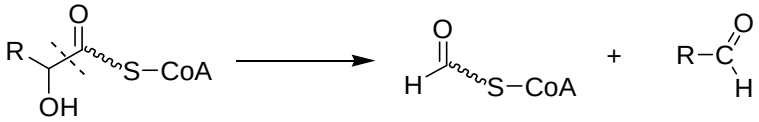


Once the structure of **B** is established, it is possible to clarify the scheme of α-oxidaion and determine the structure of **A**. Transition from **A** to $\mathbf{A_1}$ corresponds to formation of phytanoyl CoA. According to the matter balance for the second reaction, only one oxygen atom is incorporated into $\mathbf{A_1}$ to form $\mathbf{A_2}$. It is obvious that this oxygen atom is linked with α-carbon atom. This is supported by the name of

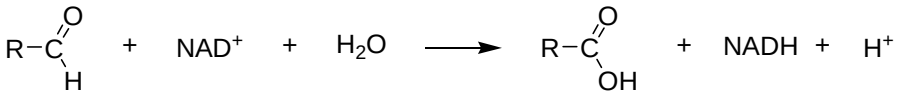
oxidation pathway, as well as by the fact that formyl CoA (and not acetyl CoA) is produced at the next stage. Thus, the general formula of **A_2** is:



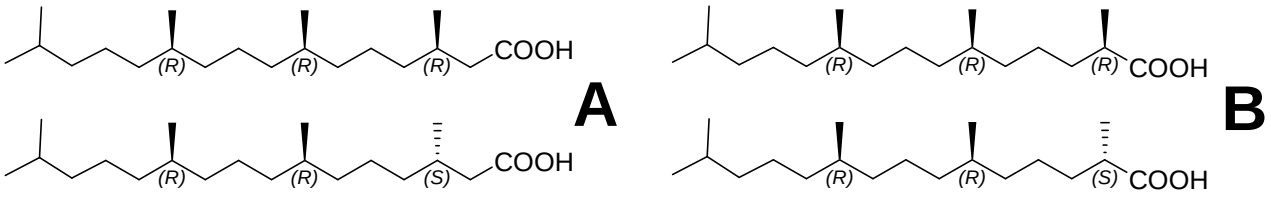
At the next step carbon-carbon bond is cleaved, which leads to formyl CoA and corresponding aldehyde **A_3**:



Carbonyl group is further oxidized to carboxyl allowing formation of **B** from **A_3**.

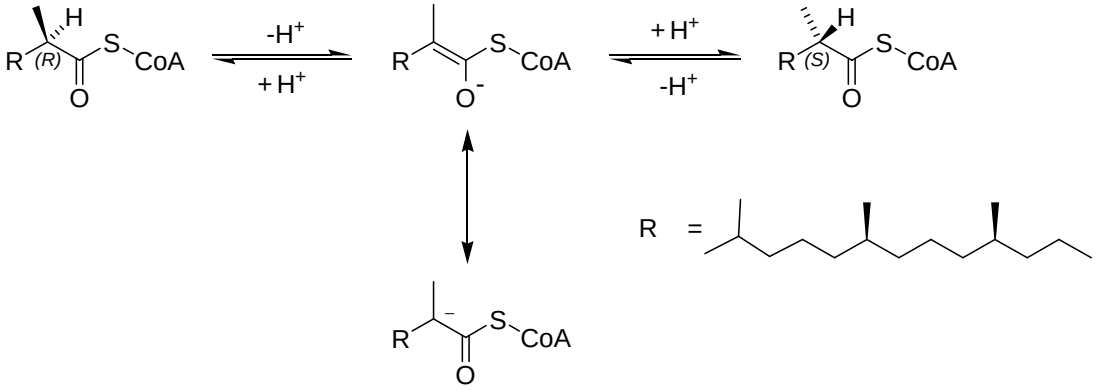


Taking into account configuration of chiral atoms in phytanic acids, existence of two natural diastereomers of phytanic acid and retention of configuration of chiral atoms during α–oxidation, one can finally deduce structures of **A** and **B**:



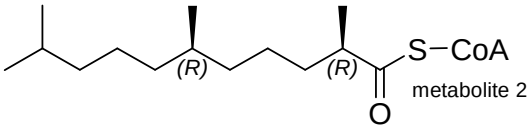
21.6 Phytanic acid is not oxidized according to β-scheme because of the methyl group in β–position, which makes impossible formation of keto-acyl derivative in the 3rd reaction of the cycle.

21.7

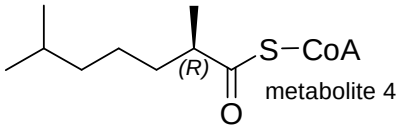


Thioesterification of pristanic acid increases the acidity of the C-2 hydrogen, which is sufficient to allow deprotonation and reprotonation.

21.8 It is seen that racemization affects substituents at α-position. Thus, two intermediates of pristanic acid degradation (metabolites 2 and 4, see the scheme above) can be AMCAR (α-methylacyl-CoA racemase) substrates.



metabolite 2



metabolite 4

21.9 Since only two stereoisomers of four possible are formed, hydroxylation of C-2 is stereospecific. It occurs from the side opposite to the methyl group, because the carbon atom is characterized by higher sterical availability from this side.

Configurations of chiral centers in diastereomers: 11R,7R,3R,2S and 11R,7R,3S, 2R.

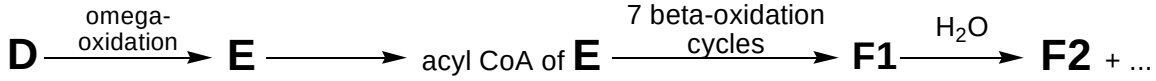
THEORETICAL PROBLEM 22

Unusual pathways of fatty acid oxidation: omega- and (omega-1)-oxidation

(To be solved after problem 21)

ω-Oxidation is one of metabolic pathways of fatty acids, though less common than β-oxidation. This unusual route starts with oxidation of the methyl group of a fatty acid to give new carboxyl group. The resulting dicarbonic acid is further involved into several β-oxidation cycles developing in the direction towards the carboxyl group initially present in the acid. All reactions of ω-oxidation are non-stereospecific.

Due to peculiar features of its structure, synthetic saturated fatty acid **D** can be involved in mammals into ω-oxidation only (neither in α- nor in β-oxidation). The resulting dicarbonic acid **E** is metabolized into corresponding acyl CoA, which is further subjected to seven consecutive cycles of β-oxidation to give seven acetyl CoA molecules. The formula of the remaining metabolite **F1** of the pathway is $C_{27}H_{39}N_7P_3SO_{19}^{5-}$. **F1** exists as anion at physiological pH values. Its hydrolysis leads to two products, one of which, substance **F2**, does not contain chiral carbon atoms.



22.1 Draw the structures of compounds **D**, **E**, **F2** and anion **F1** at pH 7. Show evidence to prove that the answer is unambiguous.

22.2 Explain why fatty acid **D** cannot be involved in both α- and β-oxidation.

22.3 Propose the structure (without stereochemical details) of synthetic fatty acid **G**, an isomer of compound **D**, which contains the same number of carbon atoms in the main chain and cannot be involved in both α- and β-oxidation for structural reasons.

(ω-1)-oxidation is another pathway of fatty acid degradation in mammals. It plays an important role in metabolism of prostaglandins and development of several genetic diseases. One (ω-1)-oxidation cycle includes five two-electron oxidation reactions of a fatty acid.

Fatty monocarbonic acid **H** that contains 75.97 % C, 12.78 % H, and 11.25 % O by mass is widespread in nature. It gives compound **J** as the final product of (ω-1)-oxidation cycle. Compound **I** (72.42 % C, 11.50 % H, 16.08 v% O by mass) is one of intermediates

of the pathway from **H** to **J**. ^{1}H NMR spectrum of **I** contains two singlets with different integral intensities and a number of multiplets. Integral intensity of any multiplet differs from those of singlets. One of the singlets is characterized by the maximal integral intensity among all the signals in the spectrum.

22.4 Draw the structures of **H** and **I**. Show evidence to prove that the answer is unambiguous.

22.5 Determine how many steps of two-electron oxidation of **H** are required to produce **I**, if it is known that the entire ω-pathway is a part of (ω-1)-pathway.

22.6 Draw the structure of **J**.

α-Oxidation is impossible for patients with hereditary pathology Adult Refsum Disease (ARD) due to genetically determined absence of an enzyme of this oxidation pathway. Metabolism of phytanic acid **A** (a mixture of two diastereomers enriched with R-epimer, i.e. R>S, see problem 21) in organisms of such patients leads to dicarbonic acid **C** (non-equivalent mixture of two enantiomers, R>S).

22.7 Determine how many steps of oxidation pathways given below are needed to obtain **C** from **A** in organisms of patients with ARD, if it is known that malonyl CoA is not released at the first β-oxidation cycle.

β-oxidation _____

ω-oxidation _____

(ω-1)-oxidation _____

AMCAR is the only epimerase involved in the process of oxidation of **A** to **C** (see problem 21 for detailed information on AMCAR).

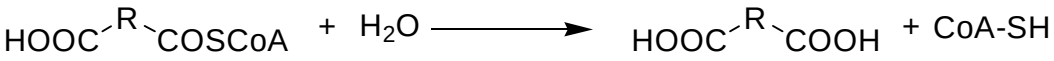
22.8 Draw formula(e) (with stereochemical details) of intermediate(s) of **A** oxidation in organisms of patients with ARD, that can be AMCAR substrates.

_____

SOLUTION OF PREPARATORY PROBLEM 22

22.1 Consideration of mechanisms of ω- and β-oxidation suggests that **F1** is an acyl CoA of a dicarbonic acid. Actually, the first carboxyl group was initially present in **D**, whereas the second one is formed as a result of the final β-oxidation cycle.

Taking into account the hydrolysis reaction:

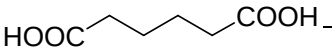
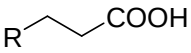
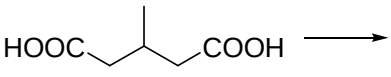
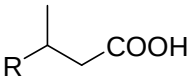
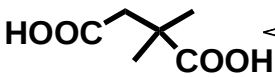
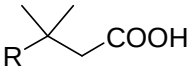
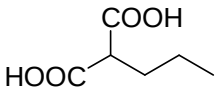
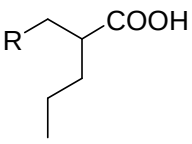
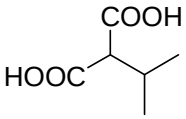
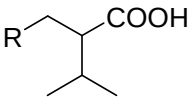


one can determine the formula of **F2** from the following calculations:

Formula of **F2** = Formula of anion **F1** + H_5 – Formula of non-ionized form of coenzyme A + H_2O = $C_{27}H_{39}N_7P_3SO_{19}$ + H_5 – $C_{21}H_{36}N_7P_3SO_{16}$ + H_2O = $C_6H_{10}O_4$.

Note that the second product of hydrolysis, coenzyme A, cannot be **F2** because it contains chiral carbon atoms.

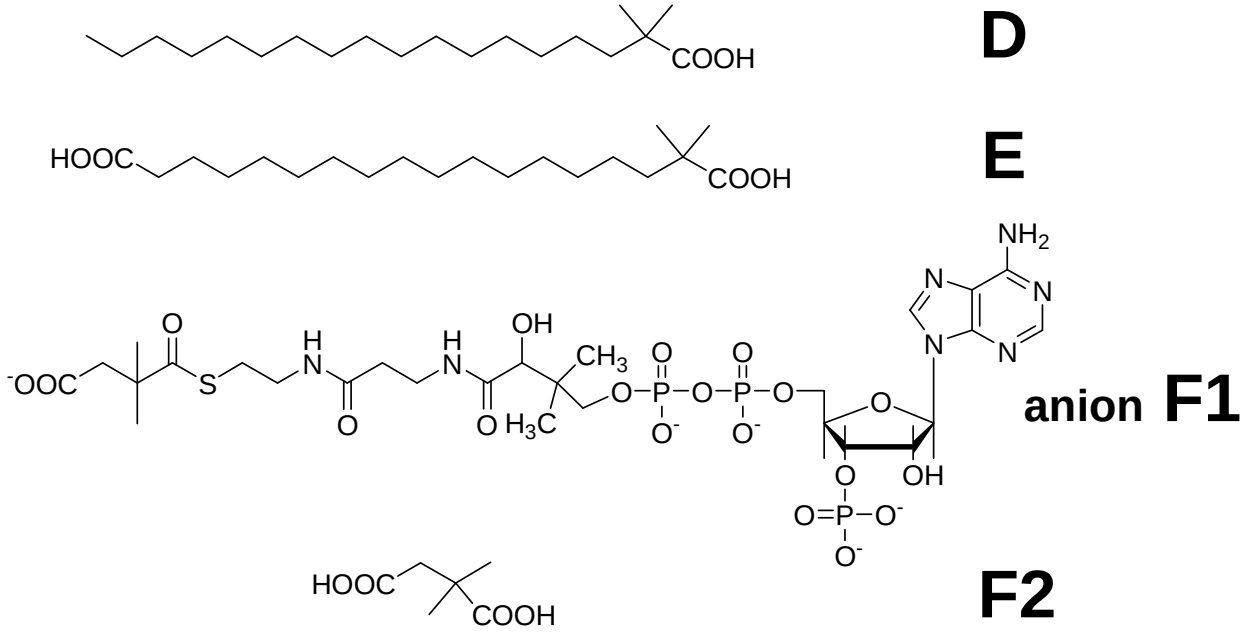
All possible structures of dicarbonic acids free of chiral carbon atoms and described by the formula $C_6H_{10}O_4$ are presented below, as well as fatty acids **D** corresponding to each variant of **F2**. Having in mind that **D** cannot be involved in either α- or β-oxidation, one can conclude that there is only one choice (highlighted in bold) meeting all above requirements.

F2	GENERAL FORMULA OF **D**	POSSIBILITY OF α-OXIDATION	POSSIBILITY OF β-OXIDATION
		YES	YES
		YES	NO
		NO	NO
		YES	NO
		NO	YES
		NO	YES

R - non-identical residues

Formulae of **D** and **E** are generated by addition of 14 carbon atoms (7 β-cycles) to the forth carbon atom in **F2**. There is no branching in the molecules except one at the α-carbon atom, since only acetyl CoA (and not propionyl CoA, *etc.*) molecules are released after every β-oxidation cycle.

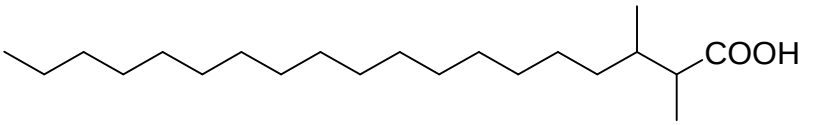
Thus,



22.2 **D** cannot be involved in α- or β-oxidation because it does not contain hydrogen atoms bound to α-carbon atom. This makes impossible formation of hydroxyl group and double bond, which are necessary for α- and β-pathways, respectively.

22.3 Fatty acid **D** and its isomer **G** contain 18 carbon atoms in their main chains. Thus, for **G** only two variants of branching are possible: either two methyl groups or one ethyl group. Possible structures of **G** with the ethyl group are equivalent with respect to oxidation pathways to phytanic and pristanic acids containing methyl substituents (see problem 22). We have found in question 1 of this problem that α- and β-oxidation pathways are restricted for fatty acids containing two substituents at the α-carbon atom. At the same time, α-pathway is possible if two substituents are bound to β-carbon atom (see solution of question 1). Thus, only a fatty acid containing methyl groups at both α- and β-carbon atoms is left in consideration. In this case β-oxidation is not possible for the same reason as for phytanic acid, whereas α-oxidation is restricted due to formation of ketone instead of aldehyde as an intermediate (a ketone group can not be oxidized to a carboxyl one *in vivo*).

Thus, the structure of **G** is:



G

22.4 Calculations to determine empirical formulae of compounds **H** and **I**:

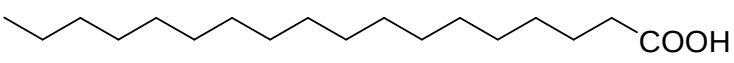
H: n(C): n(H) : n(O) = 75.97/12.01 : 12.78/1.01 : 11.25/16.00 = 9 : 18 : 1;

I: n(C) : n(H) : n(O) = 72.42/12.01 : 11.50/1.01 : 16.08/16.00 = 6 : 11.33 : 1.

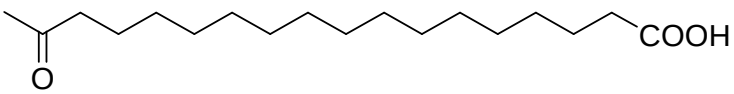
Empirical formula of **I** is $C_{18}H_{34}O_3$. Fatty acid **H** cannot contain less carbon atoms than its metabolite. It should also contain two oxygen atoms (monocarbonic acid). Thus, the molecular formula of **H** is $C_{18}H_{36}O_2$.

H is a saturated fatty acid. Formally, one oxygen atom substitutes two hydrogen atoms in **H** to give **I**. There are several options for such substitution, namely formation of: 1) carbonyl group; 2) epoxide; 3) unsaturated double bond and hydroxyl group at another carbon atom; 4) oxygen containing heterocycle. One of singlets corresponds to hydrogen atom of a carboxyl group (integral intensity is minimal). Thus, **I** is free of hydrogen atoms with the same intensity, and hydroxyl group, –CH–CH– fragment in epoxide cycle, and –CH– fragment in heterocycle are impossible. Carbonyl group is the only variant left, aldehyde group being impossible, since it produces a singlet with the same integral intensity as carboxyl group. Keto group is the final choice. This group should be located at [(ω)-1] carbon atom, because only in this case the methyl group would give a singlet with integral intensity three times higher than that of the carboxyl group. All multiplets give signals with integral intensity of 2 (higher than 1 and lower than 3). Thus, **H** is a linear fatty acid without branching (only nonequivalent CH_2 groups are present between terminal carbon atoms).

Finally,

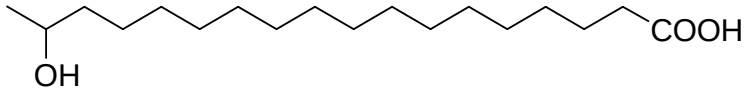


H



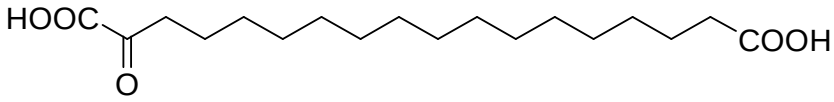
I

22.5 All reactions of ω-1-pathway are two-electron oxidations of a fatty acid. Reverse analysis shows that **I** is formed from the corresponding secondary alcohol.



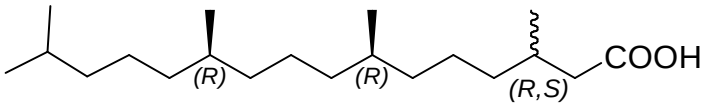
This alcohol is formed (do not forget two electrons) directly from stearic acid. (**H**) by oxygenase reaction Thus, **H** is converted into **I** in two steps.

22.6 Three steps are needed to metabolize **I** to the final product **J**, since (ω-1)-oxidation includes five consecutive steps. It is further needed to count the number of steps of ω-pathway, which allows formation of carboxyl group from the terminal methyl group. All steps of ω-pathway are also two-electron oxidations as it is a part of (ω-1)-pathway. At the first stage the fatty acid is transformed into primary alcohol by oxygenase reaction. The alcohol is then oxidized to aldehyde, and finally to carbonic acid (similar to (ω-1)-oxidation described above). Thus, ω-oxidation starts from **I** and includes the final product **J**. Finally,

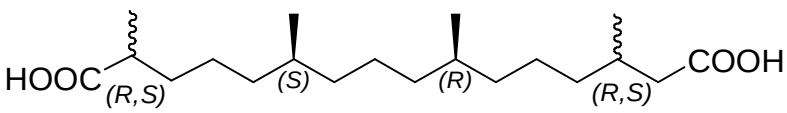


J

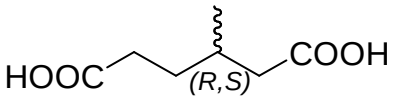
22.7 Structure of phytanic acid **A** (determined in problem 22):



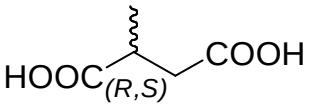
In organisms of patients with ARD, oxidation of this fatty acid from carboxyl terminus is impossible by any of known pathways. Therefore, degradation should start from ω-terminus. Presence of the methyl group at ω-1 carbon atom does not allow (ω-1)-oxidation. So, the first step is ω-oxidation, which leads to the following intermediate:



Repetitive ω-oxidation of the intermediate would lead to tricarbonic acid. Subsequent β-oxidation of this acid would give malonyl CoA, which is in contradiction with the task conditions. Thus, β-oxidation is the only possible pathway of further metabolism of the above dicarbonic acid. The number of β-cycles can be found by analyzing data on compounds **A** and **C**. Being a mixture of two enantiomers, **C** contains one chiral carbon atom. Only two metabolites of β-oxidation pathway are in agreement with this condition:

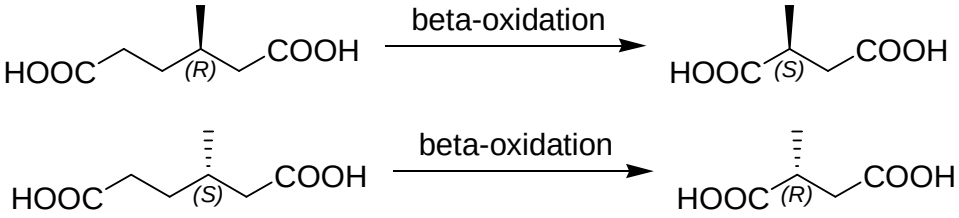


(1)



(2)

β-Oxidation of metabolite (1) leads to metabolite (2). This transformation is accompanied by inversion of the stereochemical configuration due to changes of the substituents priority.

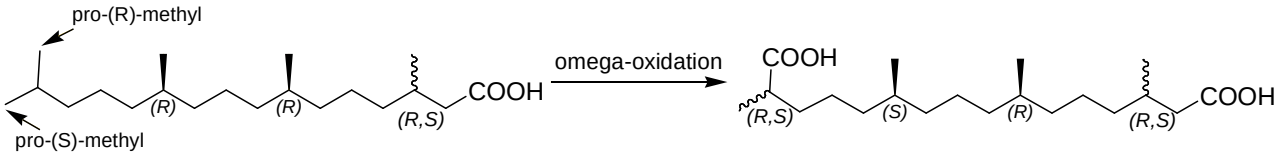


At the same time, five β-oxidation cycles of the dicarbonic acid (giving intermediate (1)) do not lead to inversion of the stereochemical configuration of the chiral carbon atom nearest to the initial carboxyl group. Since the R>S ratio is retained as a result of **A** metabolism to **C**, metabolite (1) is the final choice. Even an assumption that metabolite (2) is an AMCAR substrate will not allow treating this substance as appropriate (AMCAR will not alter the S>R ratio).

Thus, the number of steps needed on the way from **A** to **C**:

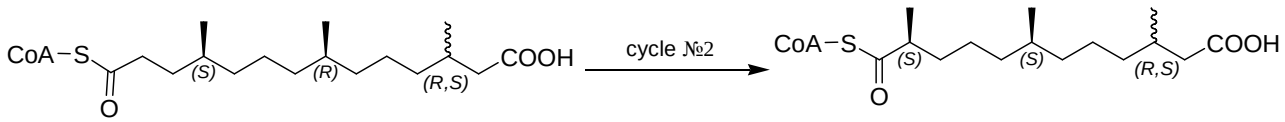
β-oxidation	five steps
ω-oxidation	one step
(ω-1)-oxidation	zero (the pathway impossible)

22.8 The enzyme catalyzing the first step of ω-oxidation is not stereospecific, thus a mixture of diastereomers will be obtained in the case of phytanic acid:

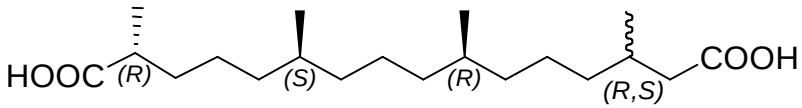


Therefore, acyl CoA formed by the product of ω-oxidation (15R-epimer) will be transformed by AMCAR into corresponding S-epimer.

As can be seen from the above scheme, ω-oxidation alters the absolute configuration of C-11 due to the changes in substituents priority, which makes AMCAR catalyzed reaction prior to the third β-oxidation cycle unnecessary. Similar considerations are true for C-7, the absolute configuration of which is changed after second β-oxidation cycle:



Thus, the only AMCAR substrate is:



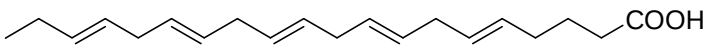
THEORETICAL PROBLEM 23

Unusual pathways of fatty acid oxidation: peroxidation

Peroxidation of lipids, in particular of those found in biomembranes and lipoproteins, is considered as an important stage in the development of numerous diseases including atherosclerosis. Lipids containing residues of polyunsaturated fatty acids (PUFA) are most liable to oxidation of this type.

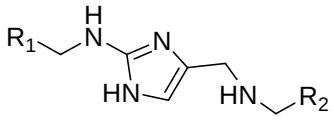
X is one of the final products of peroxidation of any polyunsaturated acids in mammals. **X** can by also obtained by reductive ozonolysis of PUFA.

23.1 Write down the overall reaction of exhaustive ozonolysis of timnodonic acid with subsequent treatment of the reaction mixture with dimethyl sulfide.



timnodonic acid (without stereochemical information)

X reveals high reaction ability towards various biomolecules including proteins. In particular, it interacts non-enzymatically with amino acid residues of albumin, an important transport protein of serum. As a result, side groups of two canonical amino acids are cross-linked. The linker formed in this reaction is depicted below (R_1 and R_2 are fragments of polypeptide chain of the protein):

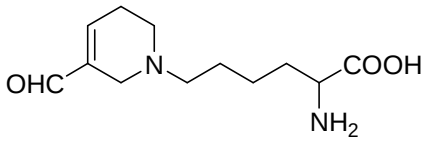


23.2 Draw (with stereochemical details) the structures of **X** and canonical amino acids, side groups of which are involved in the cross-linking.

23.3 Suggest mechanism of the linker formation, if it is known that only water molecules are released during the cross-linking.

Y is another product of peroxidation of lipids. It contains the same number of carbon atoms as **X** and interacts with both proteins and nucleic acids.

Interaction of **Y** with lysine residues present in a protein results in formation of residues of non-canonical amino acid N^{ε}-(3-formyl-3,4-dehydropiperidino) lysine (FDP-lysine):

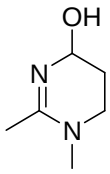


23.4 Draw the structure of **Y**, taking into account that equimolar amount of water is released upon FDP-lysine formation.

23.5 Suggest mechanism of formation of FDP-lysine residue if the starting lysine residue is a part of a protein. Note that Michael reaction is one of the steps of the pathway.

Interaction of **Y** with nucleoside **Z** found in nucleic acids results in an adduct, nucleoside **Z1**. Mass spectrum of **Z1** obtained by using fast atom bombardment mass spectrometry (FAB-MS) contains two major peaks corresponding to monoprotonated fragments ($M+H^+$), *m*/*z* values being equal to 191 and 307.

23.6 Draw the structure of **Z**, if its reaction with **Y** gives solely product **Z1**. **Z1** contains a base, a fragment of which is given below:

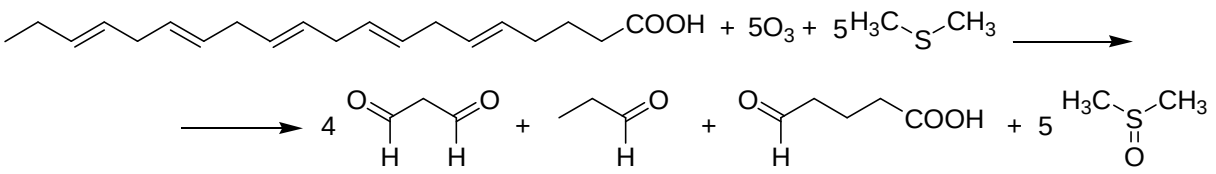


23.7 Draw the structure of **Z1**.

———————————

SOLUTION OF PREPARATORY PROBLEM 23

23.1



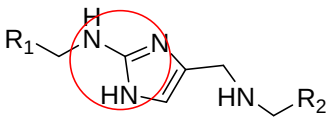
23.2 Since **X** is formed as a result of reductive ozonolysis of PUFA, it contains atoms of only three elements: carbon, hydrogen and oxygen. Hence, all four nitrogen atoms found in the linker originate from side groups of two amino acids (note that there is no way to insert peptide bond –NH–CO– into the linker).

There exist six canonical amino acids containing nitrogen in the side group: asparagine, glutamine, lysine, histidine, arginine and tryptophan.

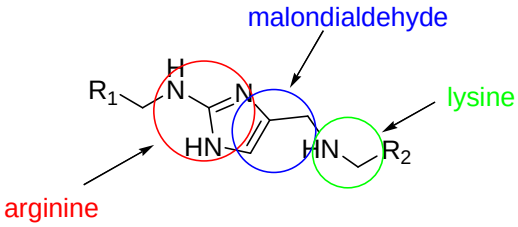
Tryptophan can not be inserted into the linker. Glutamine and asparagine should be rejected for the same reason as peptide bonds: the linker does not contain CO-groups connected with nitrogen atoms and R_1 and R_2 residues (amide reduction to amine as a result of non-enzymatic reaction with aldehyde is impossible).

There are two reasons allowing discrimination of histidine, though imidazole fragment can be easily seen in the linker. First, there is no space left for substance **X** which contains three or five carbon atoms. And second, origin of the rest two nitrogen atoms separated by imidazole group is absolutely unclear.

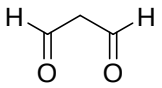
Lysine and arginine are only amino acids left for consideration. These amino acids provide for two combinations: Arg-Arg and Arg-Lys (Lys-Lys can be omitted since it would grant only two nitrogen atoms to the linker). Thus, arginine is definitely one of canonical amino acids. Guanidine group of arginine is found in the linker according to the following picture:



The remaining nitrogen atom can originate from lysine only, since it is connected with two CH_2-groups (if it were the second arginine, another guanidine group should at least be partially found in the linker). Finally:

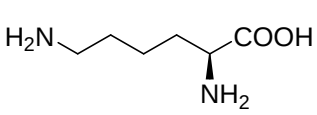


X unambiguously corresponds to malonic dialdehyde (see the above picture). The other product of timnodonic acid ozonolysis, propanal, also contains three carbon atoms. Still, it can not be **X**, since sole carbonyl group is insufficient for cross-linking. Also, propanal is not formed by peroxidation of most PUFA.

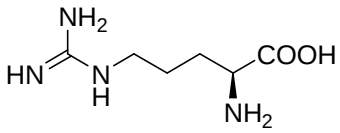


X

Structures of L-lysise and L-arginine (L isomers since amino acids found in proteins):

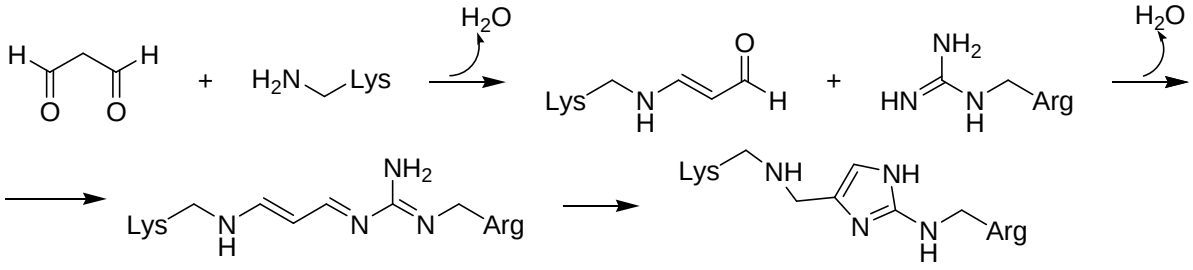


L-lysine



L-arginine

23.3 Mechanism of the linker formation (for easier representation R_1 is substituted by Arg, and R_2 by Lys):

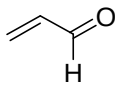


23.4 It is seen that the adduct of lysine with **Y** contains six extra carbon atoms as compared to the starting amino acid. **Y** contains three carbon atoms (as **X** does). Thus, attachment of two **Y** molecules to lysine is needed to form FDP-lysine.

Since equimolar amount of water is being released, the brutto-formula of **Y** is:

Y = (FDP-lysine – lysine + H_2O)/2 = ($C_{12}H_{20}O_3N_2$ – $C_6H_{14}O_2N_2$ + H_2O)/2 = C_3H_4O.

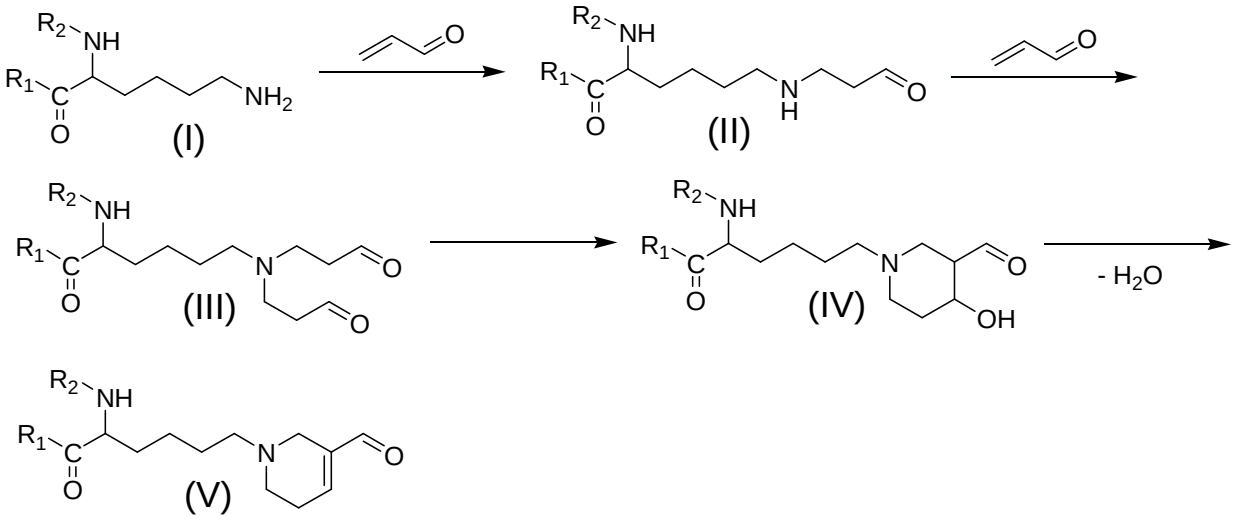
FDP-lysine contains carbonyl group, which strongly suggests that **Y** is an aldehyde (it was shown in question 1 that aldehydes are common products of peroxidation of lipids). Then **Y** is acrolein (only vinyl group can be the substituent C_2H_3 attached to carbonyl group).



Y

Methyl ketene CH_3–CH=C=O also meets the formula C_3H_4O. Still, this variant is hardly possible because of chemical properties of the substance. For instance, there are no methyl groups in the adduct, which would have inevitably been found in the case of methyl ketene.

23.5



At the first stage, nucleophilic addition of free ε-amino group of lysine to the double bond (C-3) of acrolein leads to a derivative of secondary amine (**II**) with retention of carbonyl group. **II** interacts with the second acrolein molecule according to Michael reaction to give **III**, which transforms into **IV** as a result of aldol condensation. Subsequent dehydration (croton condensation) finally gives FDP-lysine residue (**V)**.

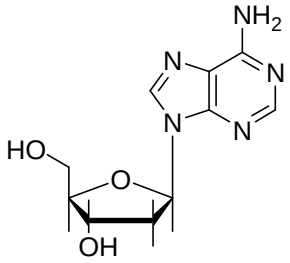
23.6 Both peaks in the mass spectrum of **Z1** correspond to monoprotonated fragments of it. Let us determine which fragment is missing in the species corresponding to the peak with lower *m/z* value. Difference in *m/z* values is: 307 – 191 = 116. Analysis of this data along with nucleoside structure strongly suggests deoxyribose residue,

indicating that the most vulnerable N-glycoside bond is subjected to fragmentation (ribose residue as well as other conventional bases have different molecular masses). Thus, **Z** is a deoxyribonucleoside found in DNA.

Molecular mass of the other component of **Z1** is equal to 191. Since deoxyribose residue is intact (according to FAB-MS data), it is a conventional base modified by **Y**. The following table is of use for determination of the base (note that the reaction of **Z** with **Y** gives solely product **Z1**).

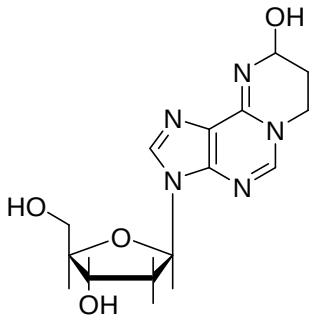
The number (*N*) of acrolein residues (molecular mass of 56) in the adduct	1	2	3
Molecular mass of the base in **Z** (191 – *N*·56)	135	79	23

Only adenine (*M* = 135, *N* = 1) is in agreement with the data in the table. Finally, **Z** is deoxyadenine:



Z

23.7 The fragment given in the task can be inserted into deoxyadenine molecule only as shown below:



Z1

Since the substances react in equimolar quantities, there are no other modifications of the base but that given in the task.

THEORETICAL PROBLEM 24

Biologically active peptides and their metabolic pathways

(*Hint*: for calculations round all values of atomic masses of elements to integers)

Angiotensins (Ang) form a class of biologically active oligopeptides with numerous significant effects on human organism. They play an important role in regulating blood pressure, maintaining water-saline balance and performing intellectual and amnestic functions.

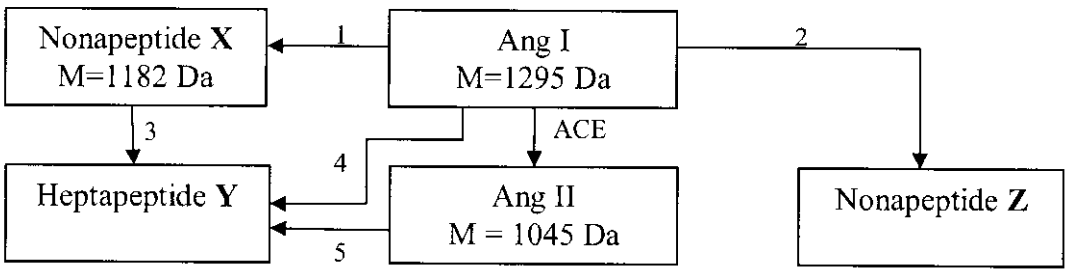
Decapeptide angiotensin I (Ang I) is the initial oligopeptide, a precursor of all members of the class. Complete acidic hydrolysis of Ang I leads to the mixture of nine amino acids: aspartic acid, arginine, valine, histidine, isoleucine, leucine, proline, tyrosine and phenylalanine.

Asparagine is hydrolyzed to form aspartic acid under the conditions required for complete hydrolysis of peptides.

24.1 Write down the equation of the acidic hydrolysis of asparagine.

Enzymes of several groups are involved in the metabolism of angiotensins. The first group includes amino peptidases (AMA and AMN), which cut off amino acids or peptide fragments from N-terminus of oligopeptides. The second group is represented by carboxypeptidases (Angiotensin-converting enzyme, ACE and its homolog ACE2), which cut off amino acids or peptide fragments from C-terminus of oligopeptides. The third group includes peptidases (neutral endopeptidase (NEP) and prolyl endopeptidase (PEP)), which split peptide bonds formed by specific amino acids residues.

Ang I is metabolized in man according to the scheme below:



1 – 5 are peptidases catalyzing corresponding reactions. Each of these peptidases catalyzes hydrolysis of only one peptide bond. One and the same peptidase may be encoded by different numbers.

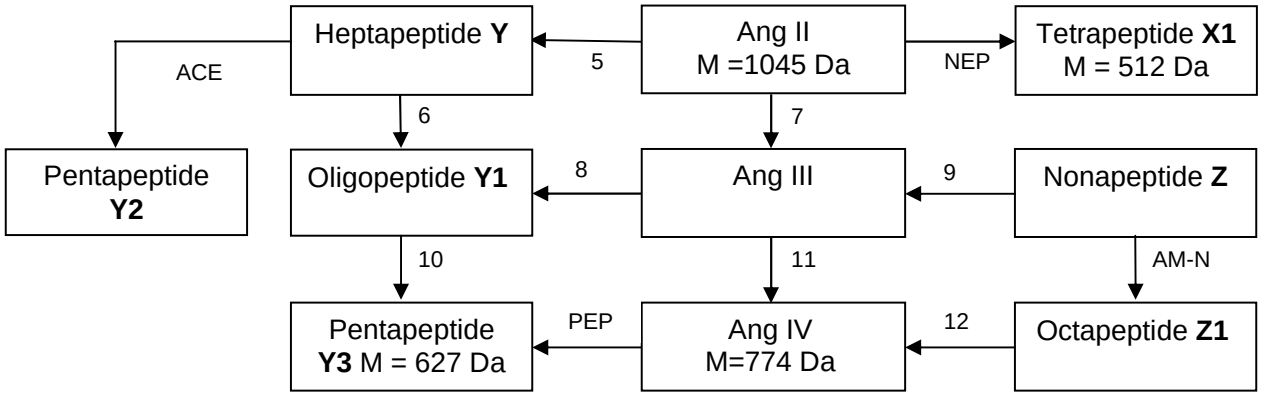
To name angiotensins, a special nomenclature has been developed. Amino acid residues of Ang I are enumerated from N- to C-termini. Since all angiotensins contain fragments of Ang I, the word «angiotensin» in their names is followed by Arabic numerals in parenthesis, indicating the positions of N- and C-terminal residues they occupied in Ang I. For instance, Ang I should be named according to the nomenclature as «angiotensin (1-10)».

24.2 Write down all possible variants of amino acids and/or oligopeptides, which can be cut off as a result of Ang II formation from Ang I.

24.3 Name oligopeptides **X**, **Y** and **Z** according to the Angiotensin nomenclature. Determine whether enzymes 1-3 are amino or carboxypeptidases.

24.4 Determine the gross amino acid content of Ang I. Show evidence to prove that the answer is unambiguous.

Metabolic pathways of Ang I derivatives are summarized in the following scheme:



6 – 12 are peptidases catalyzing corresponding reactions. One and the same peptidase may be encoded by different numbers.

Pancreatic proteinase trypsin catalyzes hydrolysis of peptide bonds formed by carboxyl groups of arginine or lysine. **Z1** has the highest molecular mass among all peptides formed as a result of trypsin catalyzed proteolysis of Ang I.

24.5 Determine which fragments are cut off as a result of the transformation from Ang II to Ang IV.

PEP selectively cleaves peptide bonds formed by carboxyl group of proline.

24.6 Determine the C-terminal amino acid in Ang II and structure of the dipeptide released when heptapeptide Y is treated with ACE.

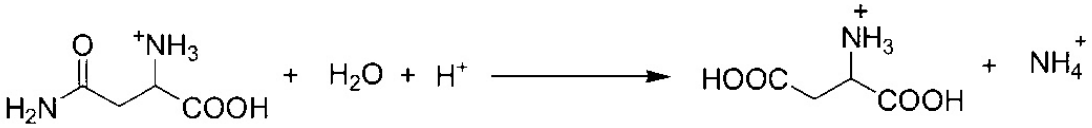
Pancreatic proteinase chymotrypsin catalyzes hydrolysis of peptide bonds formed by carboxyl groups of aromatic amino acids phenylalanine, tyrosine or tryptophane. Quite often chymotrypsin also reveals specificity towards leucine, which is close to the mentioned above amino acids in hydrophobicity. Only two tetrapeptides are formed when Ang II is treated with chymotrypsin.

24.7 Write down the finally established exact amino acid sequence of Ang I.

24.8 Name oligopeptides **X1**, **Y1** and **Z1** according to the Angiotensin nomenclature.

SOLUTION OF PREPARATORY PROBLEM 24

24.1



24.2 **X** and **Z** are nonapeptides. To pass from Ang I to these substances one terminal amino acid should be cut off in each case. Ang I is an acyclic peptide having two ends, thus N- and C-terminal residues are affected in these reactions. Heptapeptide **Y** is formed from Ang II, which is definitely not a nonapeptide (only two nonapeptides are possible, and these are **X** and **Z**). Thus, Ang II is an octapeptide. Since ACE is a carboxypeptidase, **Y** can be either Ang (1 – 7) or Ang (2 – 8). The fact that **Y** is formed directly from Ang I through one step process allows attributing **Y** to Ang (1 – 7).

By the other reaction **Y** is formed directly from **X**. Thus, the latter comprises **Y** in its structure and has the same N-terminal amino acid as Ang I and **Y**. Then nonapeptide **X** is formed as a result of cleavage of C-terminal peptide bond in Ang I.

The molecular mass of the leaving amino acid is: 1295 – 1182 + 18 = 131, which corresponds to either leucine or isoleucine.

Ang II is formed from Ang I as a result of cutting off two C-terminal amino acids. The molecular mass of 9th (from the N-terminus) amino acid in Ang I is: 1182 – 1045 + 18 = 155, which corresponds to histidine.

Finally, two dipeptides are possible as leaving fragments: His-Leu and His-Ile.

24.3 **X** – Ang (1 – 9)

Y – Ang (1 – 7).

Z – Ang (2 – 10), since is being formed by cutting off N-terminal amino acid.

2 - Amino peptidase;

1 and 3 - Carboxypeptidase.

24.4 Gross amino acid content of Ang I can be determined from its molecular mass using the following calculations:

M(Ang I) – sum of molar masses of amino acids formed as a result of hydrolysis + 9 *M*(H_2O) = molar mass of the repeating amino acid (this is correct only if Ang I does not contain Asn).

If Ang I contains Asn, the calculated above value of molecular mass will be different from the molecular mass of the repeating amino acid by 1 g mol^{-1} (in case 1 residue of Asn present) or 2 g mol^{-1} (in case 2 residues of Asn present). This deviation is due to the difference of the molecular masses of Asn and Asp (132 and 133 g mol^{-1}, respectively).

Calculations:

M_r (repeating-amino acid) = 1295 – (155 + 2·131 + 133 + 174 + 117 + 181 + 115 + + 165 – 18·9) = 155.

The value corresponds to histidine as the repeating amino acid and Asp. Thus, the gross amino acid content of Ang I is:

2 His : 1 Asp : 1 Arg : 1 Ile : 1 Leu : 1 Phe : 1 Pro : 1 Tyr.

24.5 **Z1** is formed in two ways: from Ang I in the trypsin catalyzed reaction and from nonapeptide Z (Ang (2-10)) in the AM-N (N-peptidase) catalyzed reaction. Thus, **Z1** is Ang (3-10), whereas Arg is the 2nd amino acid residue in Ang I.

Studying the transformation of Ang II to Ang IV, we come to the conclusion that Ang III is a heptapeptide (pay attention to the reactions catalyzed by enzymes 7, 8, 10). Since Ang IV is formed from heptapeptide Ang III and further hydrolyzed to pentapeptide Y3, it is a hexapeptide. Taking into account that Ang IV is formed from both Ang (3-10) and Ang (1-8), we finally attribute Ang IV to Ang (3-8). Thus, on the way from Ang II to Ang IV the 1st and 2nd amino acids residues are consecutively cut off. The 2nd residue was earlier found to be Arg. The first residue can be easily determined from the difference of relative molecular masses of Ang II and Ang IV: 1045 – 774 – 174 + 2·18 = 133, which corresponds to Asp.

24.6 PEP cuts off the 8th amino acid residue from Ang (3-8), revealing that proline is the 7th residue in Ang I. Relative molecular mass of the 8th eighth amino acid in Ang I is: 774 – 627 + 18 = 165, which corresponds to Phe.

Heptapeptide **Y** is Ang (1 – 7). ACE catalyzed hydrolysis can lead only to one pentapeptide, Ang (1 – 5). Relative molecular mass of the 6th amino acid which is released from **Y** as a part of the dipeptide, is: 1045 – 664 – 165 – 115 + 3·18 = 155, which corresponds to His.

Thus, C-terminal amino acid of Ang II is Phe, and dipeptide released from **Y** is His-Pro.

24.7 Only two tetrapeptides are formed when octapeptide Ang II is treated with chymotrypsin. This means that one the following amino acids: Tyr, Phe or Leu is among the first 7 amino acids and occupies the 4th position. Phe was earlier established as the 8th amino acid, and can be thus omitted from subsequent considerations. If the 4th position is occupied by Leu, Tyr should be either the 3rd or 5th residue (the 10th position is already occupied by either Leu or Ile, see answer to question 2), which will result in a complicated mixture of products of chymotrypsin catalyzed hydrolysis. Thus, the 4th amino acid is Tyr. For similar reasons, Leu can be placed in the 3rd or 5th position. So, it is Leu that occupies the 10th position.

There are only two positions (the 3rd and 5th) and two amino acids (Val and Ile) left. Exact assignment can be done by calculating possible molecular masses of tetrapeptides formed as a result of Ang II treatment with NEP.

Variant 1.

Val – 3, Ile – 5: M_r(angiotensin (1 – 4)) = 133 + 174 + 117 + 181 – 3·18 = 551;

M(angiotensin (5 – 8)) = 131 + 155 + 115 + 165 – 3·18 = 512;

Variant 2.

Val – 5, Ile – 3: M_r (angiotensin (1-4)) = 133 + 174 + 131 + 181 – 3·18 = 565;

M_r (angiotensin (5-8)) = 117 + 155 + 115 + 165 – 3·18 = 498.

It is seen that Variant 1 is in agreement with the task conditions. Finally, Ang I structure:

Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu

24.8 **X1** – Ang (5 – 8);

Y1 – Ang (2 – 7);

Z1 – Ang (3 – 10)

THEORETICAL PROBLEM 25

Radical polymerization

Radical polymerization is one of the most common methods of polymer synthesis. It involves the following stages:

Initiation – the stage at which active particles usually referred to as radicals appear as a result of particular chemical reaction and/or changes of physical properties of the system (heating, irradiation).

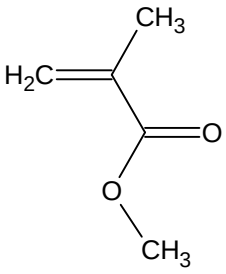
Chain propagation – consecutive addition of monomer molecules to a radical resulting in formation of new radicals of bigger size. Usually the rate constant of propagation is considered to be independent of polymerization degree of a growing radical (assumption of equal reactivity).

Chain termination – the stage at which chain growth is stopped due to bimolecular interaction of radicals. Recombination and disproportionation are possible ways of chain termination.

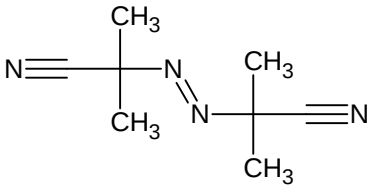
Chain transfer – the stage at which an inactive polymer molecule is formed due to interaction of a propagating radical with a chain transfer agent. This process is accompanied by transformation of the transfer agent into new radical. The latter can either initiate growth of a new polymer chain or terminate the chain. Molecules of the monomer, solvent or special additives can act as chain transfer agents.

To obtain poly-(methyl methacrylate) (poly-MMA), its monomer (9.4 g) was heated to 60 °C in the presence of 0.1 g of α,α'-azodiisobutyronitrile (AIBN) and 0.5 g of α-chlorotoluene. The density of the reaction mixture is 0.91 g cm^{-3}. The rate constants of elementary stages are: $k_{in} = 7.2\times10^{-4}$ s^{-1} (initiation), $k_p = 7.1\times10^{2}$ l mol^{-1} s^{-1} (propagation), $k_t = 2.6\times10^{7}$ l mol^{-1} s^{-1} (termination). Initiation efficiency is $f_{in} = 0.8$. Constants of chain transfer are: $C_A = 4.2\times10^{-4}$ (to α-chlorotoluene) and $C_M = 1.0\times10^{-5}$ (to the monomer).

Hint: chain transfer constant is defined as the ratio of the rate constants of chain transfer to a given species and chain propagation ($C = k_{tr} / k_p$).



MMA



AIBN

25.1 Write down reaction equations for initiation, chain propagation, chain termination, and chain transfer in the above given system.

25.2 Write down reaction equation(s) which decrease(s) initiation efficiency f_{in}.

25.3 Write rate equations for:

a) generation of active radicals

b) monomer consumption

c) changes of the concentration of radicals

25.4 Express equilibrium concentration of radicals under steady-state conditions as a function of kinetic parameters of elementary stages.

25.5 Express the rate of monomer consumption (rate of polymerization) as a function of immediate concentrations of the monomer and initiator and kinetic parameters of elementary stages. Find the order of polymerization reaction on the monomer and initiator.

Polymer obtained in the described above system at low conversion (less than 10% of the monomer consumed) possesses a number-average degree of polymerization P_n of 125.

25.6 Determine the value of the rate constant of termination via disproportionation. Arrange the following processes in the decreasing order of their influence on P_n value.

a) chain termination

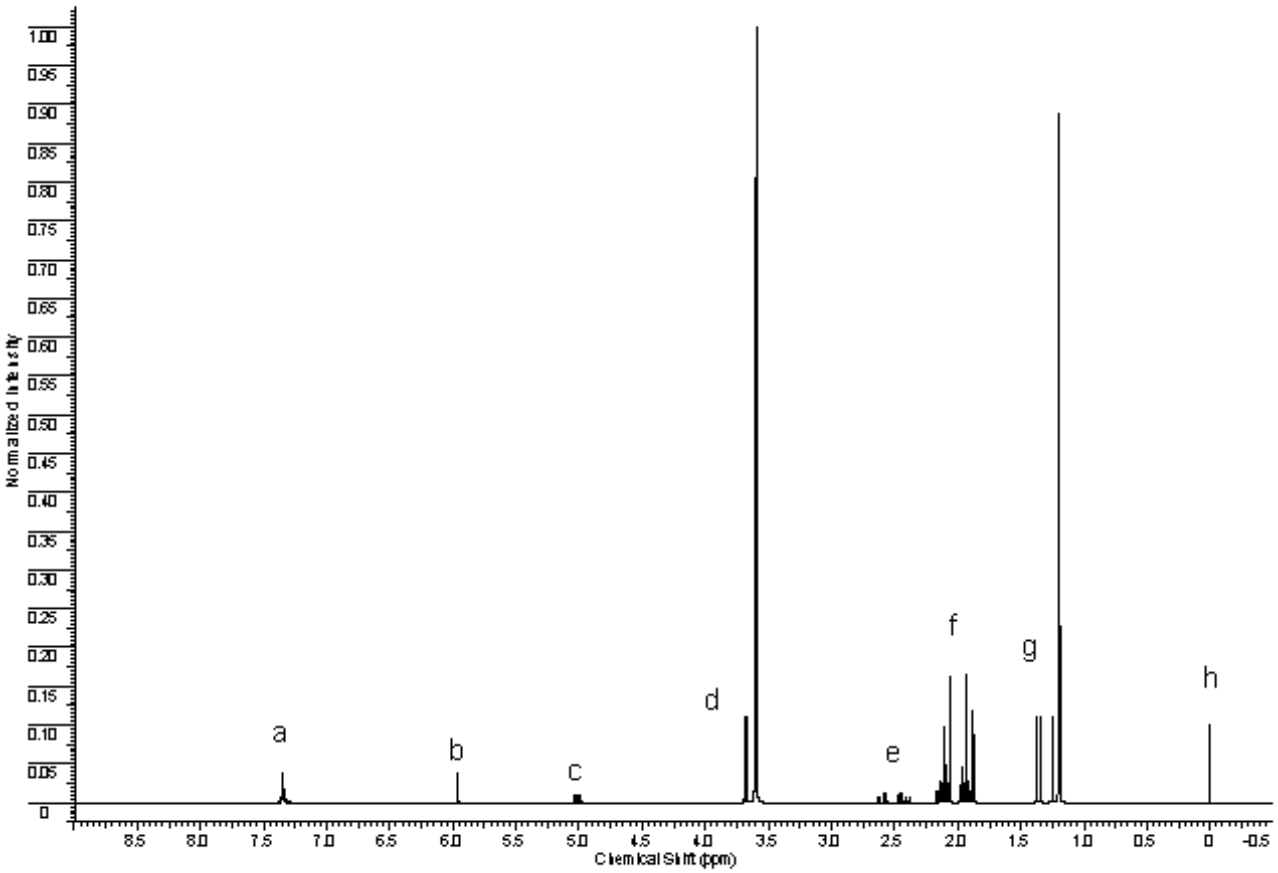
b) chain transfer to monomer

c) chain transfer to α-chlorotoluene

^{1}H NMR spectrum of a polymer obtained according to the above procedure is given hereunder.

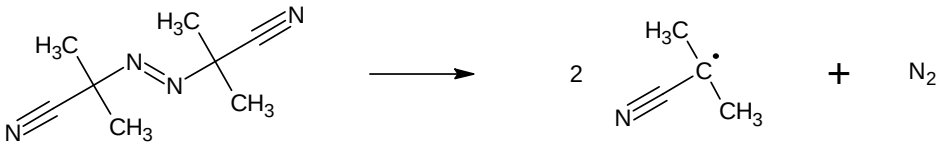
25.7 Deduce the structure of the polymer using integral intensities of characteristic peaks given in the table.

Signal	Integral intensity
a	5.0
b	1.0
c	1.0
d	42
e	2.0
f	27
g	39
h	4.5

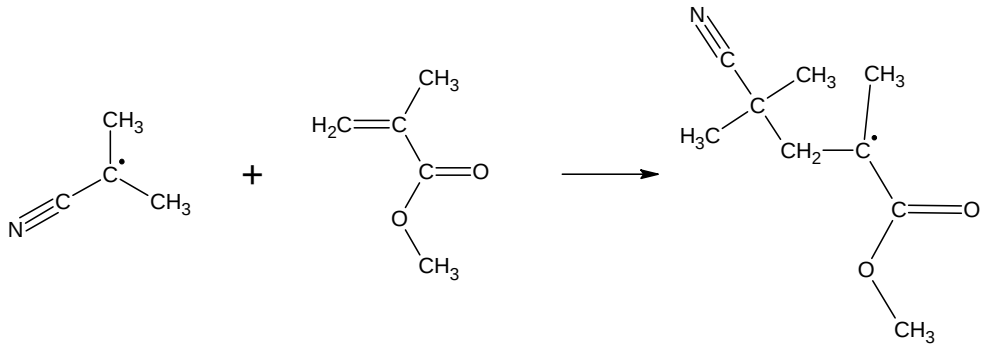


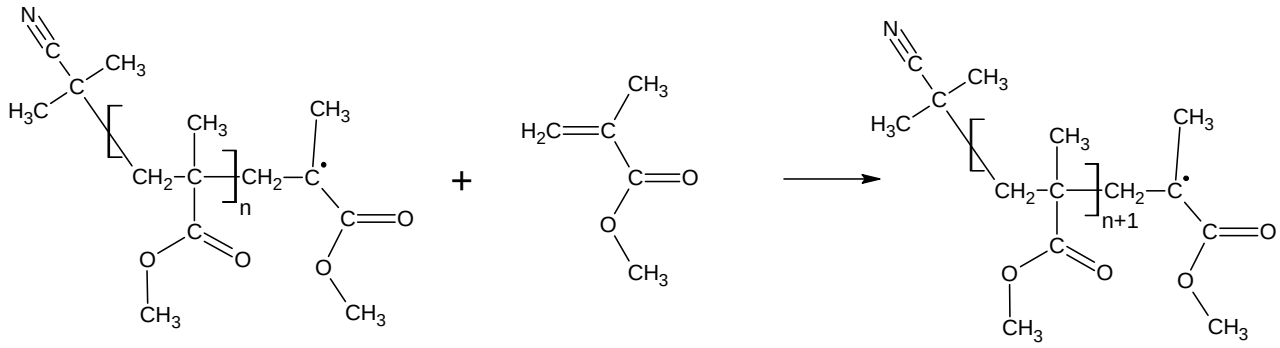
SOLUTION OF PREPARATORY PROBLEM 25

25.1 Initiation:

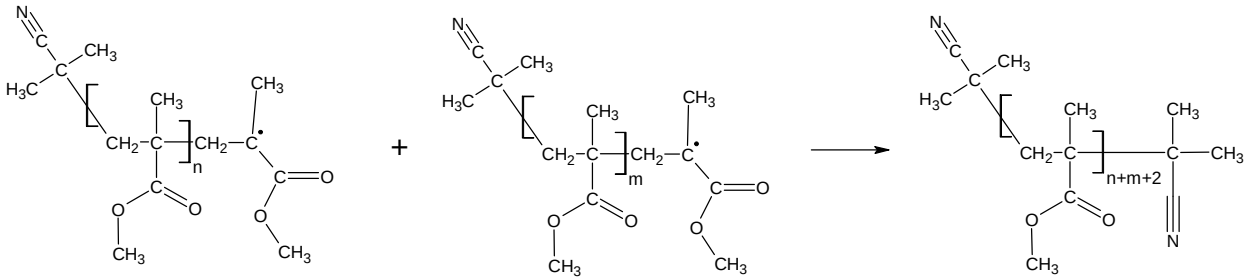


Chain propagation:

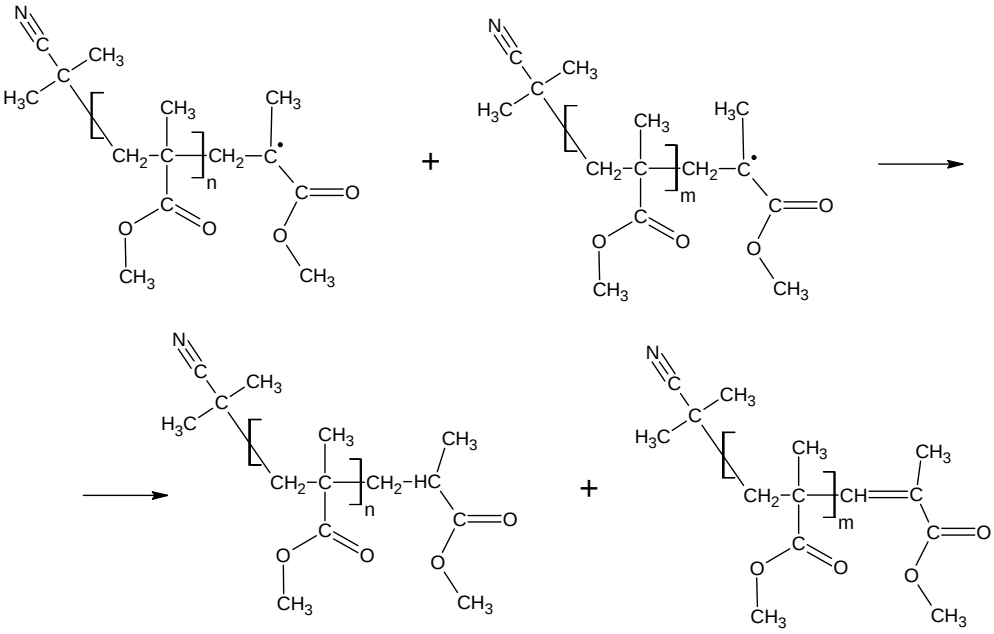




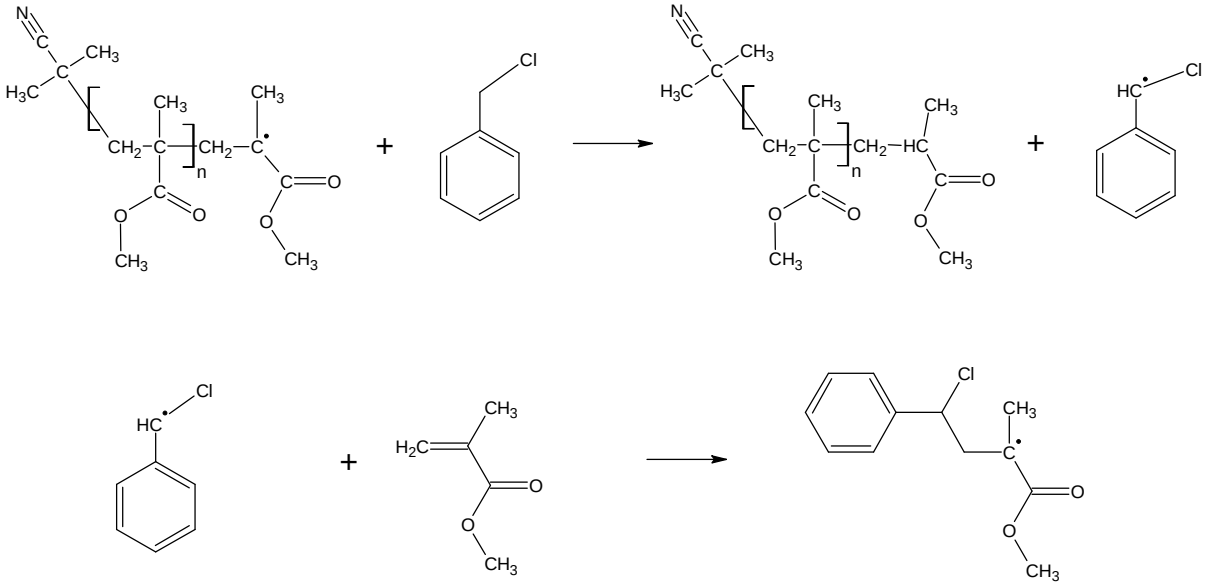
Chain termination via recombination:



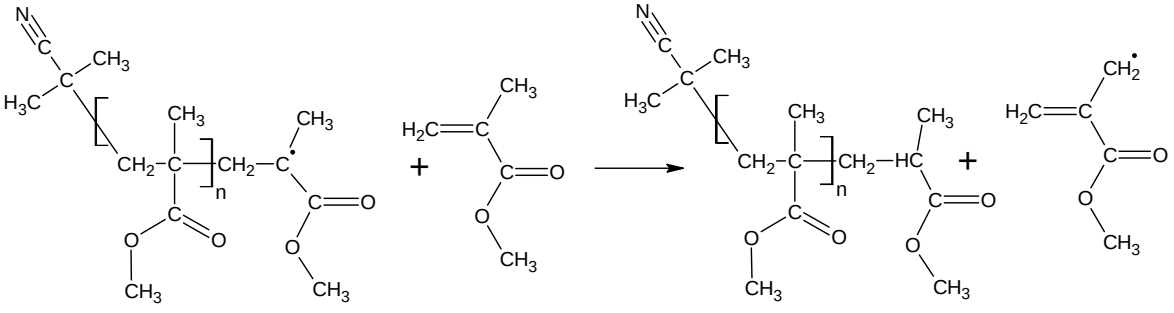
Chain termination via disproportionation:



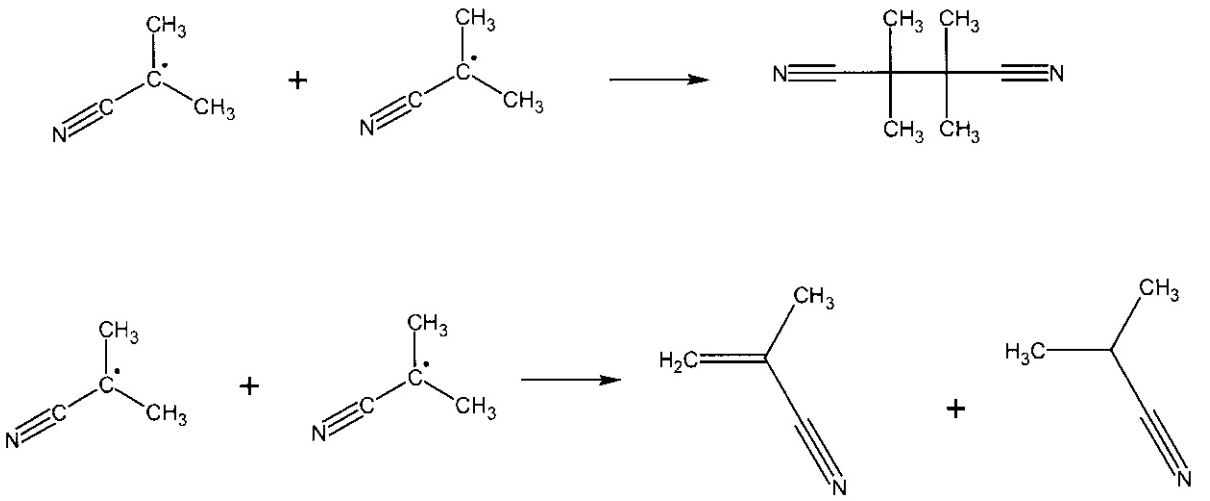
Chain transfer to α-chlorotoluene:



Chain transfer to the monomer:



25.2



25.3 Generation of active radicals:

$$\frac{\mathrm{d}[\mathrm{P}^{\times}]}{\mathrm{d}t} = 2 \times k_{\mathrm{in}} \times f_{\mathrm{in}} \times [\mathrm{In}]$$

Monomer consumption:

$$\frac{\mathrm{d}[\mathrm{M}]}{\mathrm{d}t} = -k_{\mathrm{p}} \times [\mathrm{P}^{\times}] \times [\mathrm{M}]$$

Change of concentration of radicals:

$$\frac{\mathrm{d}[\mathrm{P}^{\times}]}{\mathrm{d}t} = 2 \times k_{\mathrm{in}} \times f_{\mathrm{in}} \times [\mathrm{In}] - 2\,k_{\mathrm{t}} \times [\mathrm{P}^{\times}]^2$$

25.4

$$\frac{\mathrm{d}[\mathrm{P}^{\times}]}{\mathrm{d}t} = 2 \times k_{\mathrm{in}} \times f_{\mathrm{in}} \times [\mathrm{In}] - 2\,k_{\mathrm{t}} \times [\mathrm{P}^{\times}]^2 = 0$$

$$[\mathrm{P}^{\times}] = \left(\frac{k_{\mathrm{in}} \times f_{\mathrm{in}} \times [\mathrm{In}]}{k_{\mathrm{t}}} \right)^{1/2}$$

25.5

$$-\frac{\mathrm{d}[\mathrm{M}]}{\mathrm{d}t} = k_{\mathrm{p}} \times [\mathrm{P}^{\times}] \times [\mathrm{M}] = k_{\mathrm{p}} \times \left(\frac{k_{\mathrm{in}} \times f_{\mathrm{in}} \times [\mathrm{In}]}{k_{\mathrm{t}}} \right)^{1/2} \times [\mathrm{M}]$$

Thus the order of the reaction is 1 on the monomer, ½ on the initiator.

25.6 Number-average degree of polymerization P_n can be expressed as a ratio of the number of polymerized monomer units to that of polymer chains appeared during the same time interval. The latter value is equal to ½ of the number of polymer end groups not involved in the polymerization process (inactive end groups of the polymer).

$$P_{\mathrm{n}} = \frac{\Delta n(\mathrm{M})}{0.5 \times \Delta n(\mathrm{tails})}$$

Different stages either increase or remain unchanged the number of end groups. Namely,

Initiation: + 1 end group per each radical formed,

Propagation: 0 end groups,

Chain transfer: + 2 end groups,

Disproportionation: + 1 end group,

Recombination: + 0 end groups.

Thus,

$$P_{\mathrm{n}} = \frac{R_{\mathrm{p}} \times \mathrm{d}t}{0.5\,(R_{\mathrm{i}} + R_{\mathrm{t,d}} + 2R_{\mathrm{tr}}) \times \mathrm{d}t} = \frac{R_{\mathrm{p}}}{0.5\,(R_{\mathrm{i}} + R_{\mathrm{t,d}} + 2R_{\mathrm{tr}})},$$

where R_{p}, R_{i}, $R_{\mathrm{t,d}}$, R_{tr} are rates of propagation, initiation, disproportionation and chain transfer, respectively.

$$R_{\mathrm{i}} = 2 f_{\mathrm{in}} \times k_{\mathrm{in}} \times [\mathrm{In}] = 2 \times (k_{\mathrm{t,d}} + k_{\mathrm{t,c}}) \times [P^{\times}]^2$$

$$R_{\mathrm{t,d}} = 2 k_{\mathrm{t,d}} \times [P^{\times}]^2$$

$$R_{\mathrm{tr}} = k_{\mathrm{tr}}^{\mathrm{M}}\,[P^{\times}]\,[M] \times k_{\mathrm{tr}}^{\mathrm{A}}\,[P^{\times}][A]\ ,$$

where $k_{\mathrm{tr}}^{\mathrm{M}}$ and $k_{\mathrm{tr}}^{\mathrm{A}}$ are rate constants of chain transfer to monomer and compound A, respectively (in this task compound A is α-chlorotoluene). (According to transfer constant definition, $k_{\mathrm{tr}}^{\mathrm{M}} = C_{\mathrm{M}} \times k_{\mathrm{p}}$ and $k_{\mathrm{tr}}^{\mathrm{A}} = C_{\mathrm{A}} \times k_{\mathrm{p}}$.)

$$R_{\mathrm{p}} = k_{\mathrm{p}} \times [M][P^{\times}]$$

Using expressions for the corresponding rates in the equation for P_n and carrying out transformations, we come to:

$$\frac{1}{P_{\mathrm{n}}} = \frac{(2 k_{\mathrm{t,d}} + k_{\mathrm{t,c}})}{k_{\mathrm{p}}[\mathrm{M}]} \left(\frac{k_{\mathrm{in}} \times f_{\mathrm{in}}[\mathrm{In}]}{k_{\mathrm{t,d}} + k_{\mathrm{t,c}}} \right)^{1/2} + C_{\mathrm{M}} + C_{\mathrm{A}} \frac{[\mathrm{A}]}{[\mathrm{M}]}$$

with $k_{t,d}$ and $k_{t,c}$ denoting rate constants for termination via disproportionation and recombination, respectively.

Monomer concentration [M]:
9.4 g / (100.1 g mol^{-1}) / (10 g / 0.91 g cm^{-3}) = 8.5 mol dm^{-3}.
Concentration of the initiator [In]:
0.1 g / (164.2 g mol^{-1}) / (10 g / 0.91 g cm^{-3}) = 0.055 mol dm^{-3}.
Concentration of the chain transfer agent [A]:
0.5 g / (98.96 g mol^{-1}) / (10 g / 0.91 g cm^{-3}) = 0.46 mol dm^{-3}.
Other values are given in task.

Substituting the 2nd and 3rd items with numerals, we get:

$$\frac{1}{P_n} = \frac{(2k_{t,d} + k_{t,c})}{k_p[M]} \left(\frac{k_{in} \times f_{in}[In]}{k_{t,d} + k_{t,c}} \right)^{1/2} + 1.0 \times 10^{-5} + 2.26 \times 10^{-5}$$

As disproportionation and recombination are described by similar kinetic equations (differing only in the values of rate constants), one can substitute the sum $k_{t,d} + k_{t,c}$ with the observed rate constant of chain termination k_t. Then,

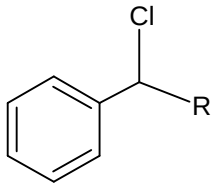
$$\frac{1}{P_n} = \frac{(k_{t,d} + k_t)}{k_p[M]} \left(\frac{k_{in} \times f_{in}[In]}{k_{t,d} + k_{t,c}} \right)^{1/2} + 1.0 \times 10^{-5} + 2.26 \times 10^{-5} =$$
$$= (k_{t,d} + 2.6 \times 10^7) \times 1.8 \times 10^{-10} + 1.0 \times 10^{-5} + 2.26 \times 10^{-5}$$

Substituting P_n = 125, we get: $\boldsymbol{k_{t,d} = 1.8 \cdot 10^7}$ **dm^3 mol^{-1} s^{-1}.**

The first item makes the maximal contribution to the $1/P_n$ value, whereas those of the second and third items are comparable (the second item is slightly less than the third). So, contributions of the processes to the observed value of P_n decrease in the following order:

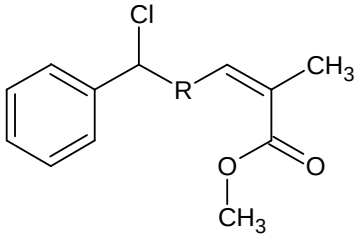
chain termination >> chain transfer to chlorotoluene > chain transfer to monomer.

25.7 Signal ***a*** corresponds to protons of an aromatic ring. This suggests that benzene ring can be found at least at one end of the polymer, which is due to chain transfer to chlorotoluene. So, one or both ends have the following structure



Then, either peak ***b*** or peak ***c*** should be assigned to the proton of the chloromethyl group (this is supported by the values of chemical shifts of ***b*** and ***c*** and by the ratios ***b/c*** and ***a/c*** both being equal to 1:5).

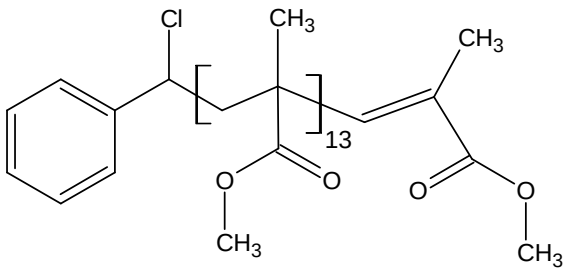
If chlorotoluene residues are found at both ends of the polymer, the molecular formula of the polymer may be written as follows: $(C_7H_6Cl)–(C_5H_8O_2)_n–(C_7H_6Cl)$. Ratio of the total integral intensities of peaks ***a*** and (***b*** or ***c***) to the total integral intensities of peaks (***c*** or ***b***) + ***d*** + ***e*** + ***f*** + ***g*** (peak of TMS ***h*** is omitted) is equal to 6:111. Thus, the total signal of $(C_5H_8O_2)_n$ corresponds to 111·12/6 = 222 protons. Dividing this value by the number of protons in one repeated unit (8), one obtains the polymerization degree of 27.75. Polymerization degree being an integer number, the deviation of 0.25 exceeds possible round-off error. So, the polymer has the chlorotoluene residue only at one of its ends. Moreover, there is only one proton in the weak field area (at 5 ppm), which is seen from the ratio of integral intensities ***a*** : ***b*** : ***c***. This chemical shift can hardly be ascribed to aromatic protons. It may rather correspond to the proton located near a double bond. Analysis of all possible variants of chain termination and transfer allows concluding that the structure fitting best of all to all ratios of peak intensities is formed as a result of disproportionation. Then, the polymer structure is:



its brutto-formula being:

either $(C_7H_6Cl)–(C_5H_8O_2)_n–(C_5H_7O_2)$ or $(C_7H_6Cl)–(C_{5n+5}H_{8n+7}O_{2n+2})$.

From the ratio of intensities of ***a*** + (***b*** or ***c***) to those of (***c*** or ***b***) + ***d*** + ***e*** + ***f*** + ***g*** = 6:111 one concludes that the peak of ($C_{5n+5}H_{8n+7}O_{2n+2}$) corresponds to 111·6/6 = 111 protons. So, 8*n* + 7 = 111, or *n* = 13. Finally, the polymer structure is:

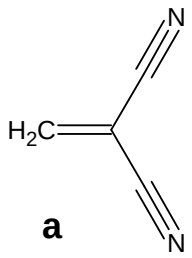


THEORETICAL PROBLEM 26

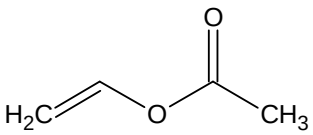
Ionic polymerization

Polymerization may be initiated by ionic species. Depending on the charge on the end group of a propagating chain, cationic and anionic polymerization types are distinguished. Ionic as well as radical polymerization involves the stages of initiation, propagation, termination and chain transfer. Cationic polymerization is initiated by strong acids and other electrophilic compounds, whereas anionic by strong bases and electron donors.

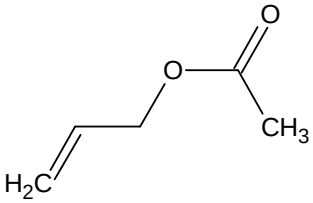
26.1 For each monomer given below, choose polymerization type(s) (radical, anionic, cationic) which it can be involved in.



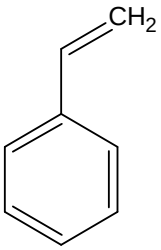
a



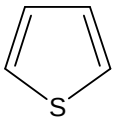
b



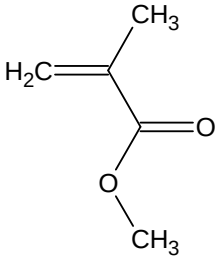
c



d

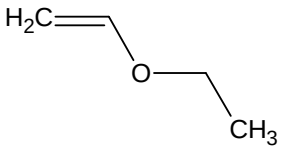


e

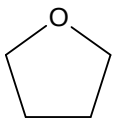


f

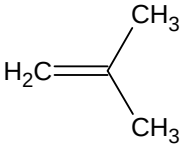
g



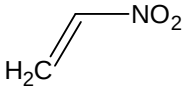
h



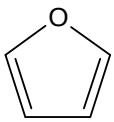
i



j

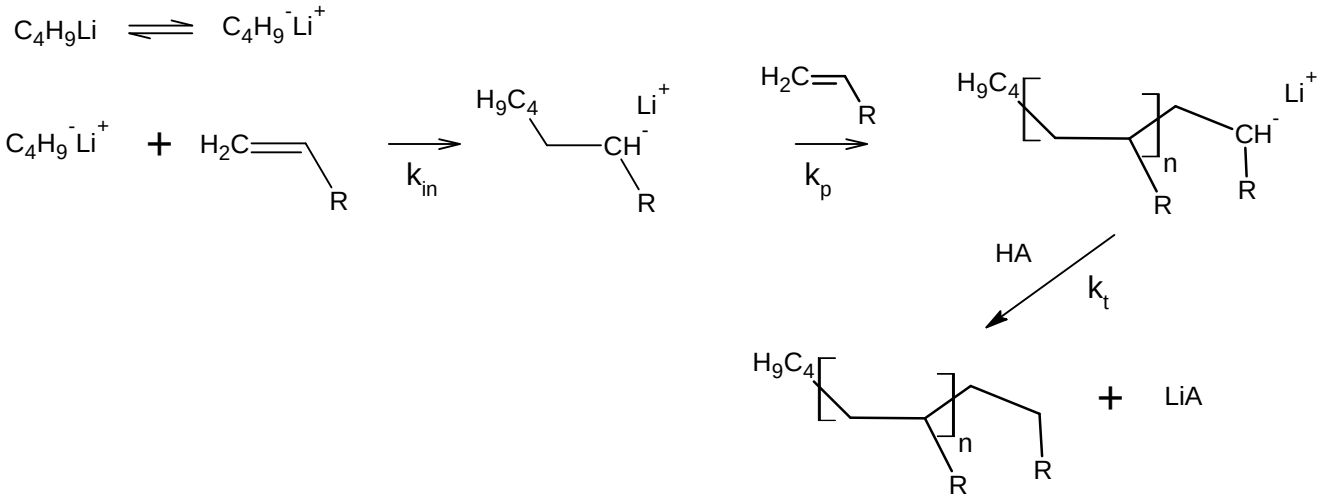


k



l

Anionic polymerization initiated by metal alkyls can be described by the following kinetic scheme, which includes stages of initiation, chain propagation and chain termination. The latter occurs as a result of carbanion reaction with a terminating agent, acid HA.



26.2 a) Write down the rate equation for monomer consumption, expressing concentrations of monomer and active chains (macroanions) as [M] and [M$^-$], respectively.

b) Anionic polymerization allows synthesis of nearly monodisperse polymer. Based on this fact, compare qualitatively rate constants of initiation and chain propagation.

c) Calculate molecular mass of the polymer obtained as a result of polymerization of 100 g of styrene in 600 cm^3 of 1,4-dioxane in the presence of 0.234 g of naphthalene and 0.042 g of metallic sodium, if 58.9 % of the monomer was consumed during polymerization.

Polymerization is a perspective approach towards design of chain molecules of various shape and size. Still chain termination can be regarded as a drawback of the method, since it leads to species not capable of attaching new monomer units.

26.3 a) What chain termination processes are probable for radical and anionic polymerization? Fill in the table.

Type of chain termination	Radical polymerization	Anionic polymerization
Disproportionation		
Recombination		
Chain transfer to solvent		
Chain transfer to monomer		

b) Explain why a polymer obtained by anionic polymerization has narrower molecular mass distribution than that obtained by radical polymerization.

c) The following solvents are used as a medium for anionic polymerization: (a) benzene; (b) 1,4-dioxane; (c) tetrahydrofuran; (d) 1,2-dimethoxyethane. Arrange the solvents in the order of increasing polymerization rate.

d) Compare the rates of anionic polymerization with sodium, potassium and cesium naphthalenides used as initiators.

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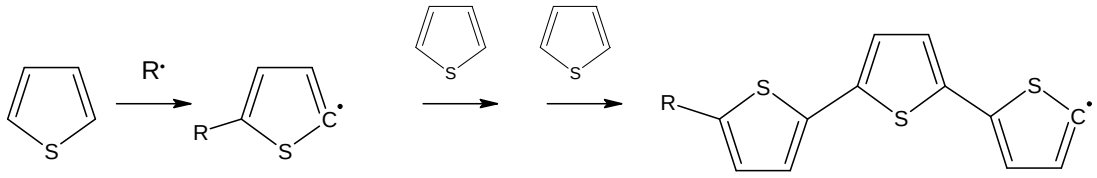
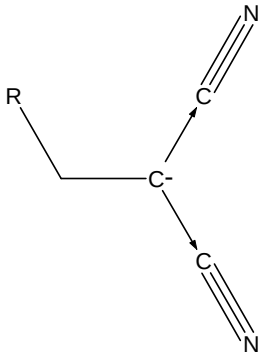
SOLUTION OF PREPARATORY PROBLEM 26

26.1 All compounds containing double bonds (including cyclic unsaturated compounds thiophene (***e***) and pyrrole (***l***)) can be polymerized according to radical mechanism. In case of aromatic heterocycles, the radical on a propagating chain is stabilized by interaction with the conjugated system of double bonds:

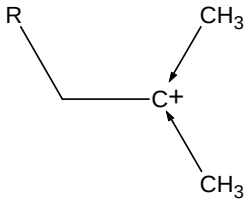


Thus, radical polymerization is possible for compounds **a** - **f**, **h**, **j** - **l**.

Electron acceptors, such as nitrile (***a***), carbonyl (***f***), or nitro (***k***) groups stabilize negatively charged macroions (see structure below). Compounds containing such groups can be polymerized according to anionic mechanism.



On the contrary, compounds containing electron donor substituents close to double bond (isobutylene (**j**)**)** form stable carbocations. Such compounds are polymerized according to cationic mechanism.

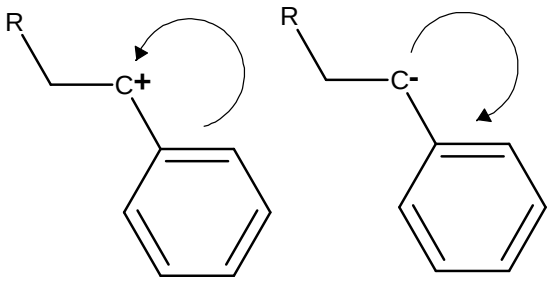


Vinyl ethers can also be involved in cationic polymerization. In this case alkoxyl group stabilizes the macrocation due to its positive mesomeric effect.

Highly strained epoxy cycle can be opened as a result of carbanion formation. Thus, (***e***) may be a monomer in anionic ring-opening polymerization. Interaction of epoxides with strong acids leads to ring-opening and carbocation formation, which allows polymerization of epoxides according to cationic mechanism.

Tetrahydrofuran (***i***) is not involved in anionic polymerization, since the cycle in its molecule is less strained and is not altered by bases. Still, strong acids can protonate ether oxygen in THF causing cleavage of C–O bond. As a result, carbocation is formed which initiates cationic ring-opening polymerization.

Mesomeric effect of phenyl substituent stabilizes both carbocation and carbanion, so styrene (***d***) can be polymerized according to both ionic mechanisms.



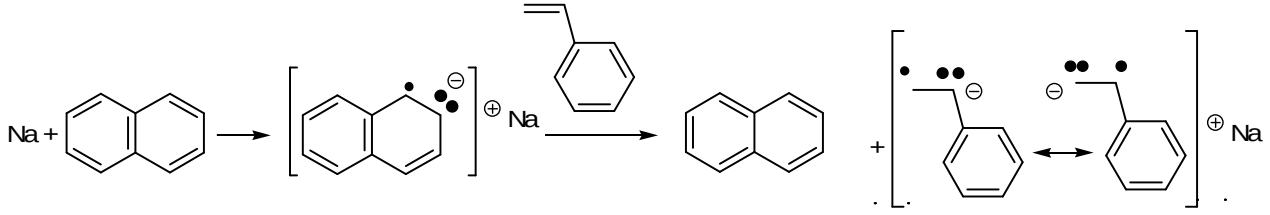
Thus, Anionic polymerization is possible for compounds **a**, **d**, **f**, **g**, **k**,

Cationic polymerization is possible for compounds **d**, **h**, **j**.

26.2 a) $r_P = -\frac{d[M]}{dt} = k_p \times [M^-] \times [M]$

b) All chains of monodisperse polymer are of equal length, which is possible if all the chains are initiated at one and the same time and then propagate simultaneously. Thus, initiation must occur much faster than propagation, $k_{in} >> k_p$.

c) Interaction of naphthalene and sodium in dioxane gives rise to anion-radical of sodium naphthalenide, which further produces styrene anion due to one-electron reduction of styrene:



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This process initiates anionic polymerization of styrene. To find the relationship between the degree of polymerization (P_n) and the fraction of a monomer consumed (q), one needs to write the balance equation for the monomer (express the total monomer concentration via current concentrations of the monomer, macroanions and initiator):

$$[M]_0 = [M] + P_n([M^-] + [In]) = [M] + P_n\,[In]_0$$

$[In]_0$ is the initial concentration of sodium naphthalenide.

Now one can express [M] as a function of q:

$$q = \frac{[M]_0 - [M]}{[M]_0} = 1 - \frac{[M]}{[M]_0} \Rightarrow [M] = [M]_0(1-q) \Rightarrow [M]_0 = [M]_0(1-q) + P_n[In]_0$$

And finally, $P_n = \frac{[M]_0 q}{[In]_0}$

Monomer concentration $[M]_0 = \frac{100}{0.600 \times 104} = 1.60$ mol dm^{-3}.

Initiator concentration $[In]_0 = \frac{0.234}{0.600 \times 128} = 3.05 \times 10^{-3}$ mol dm^{-3}.

Substituting these values, one gets

$$P_n = \frac{q\,[M]_0}{[In]_0} = \frac{0.589 \times 1.60}{3.05 \times 10^{-3}} = 309,$$

Molecular mass of the synthesized polymer is $P_n \times 104 = 32100$ g mol^{-1}.

26.3 a)

Type of chain termination	Radical polymerization	Anionic polymerization
Disproportionation	+	Improbable for most monomers
Recombination	+	–
Chain transfer to solvent	+	Possible in some solvents, e.g. in liquid ammonia. Trace amounts of water and acids in the reaction mixture may also terminate chain propagation.
Chain transfer to monomer	+	–

b) In contrast to radical, anionic polymerization may proceed almost without chain termination. Thus, active centers at chain ends are retained until the process is completed. In this case, all chains are of almost the same length, which stipulates narrow molecular mass distribution.

c) Rate of anionic polymerization depends on the strength of interaction between propagating carbanion and counter ion. Lower ability of a solvent to interact with the counterion may result in diminished polymerization rate. Benzene is characterized by the lowest ability to solvate ions of alkaline metals. 1,4-Dioxane possesses a symmetrical structure and zero dipole moment. As a result it also solvates ions of alkaline metals marginally, its solvating ability being slightly higher than that of benzene. Tetrahydrofuran having one oxygen atom is characterized by higher polarity, and thus solvates ions of alkaline metals with higher efficiency than dioxane. Dimethoxyethane molecule is flexible and possesses two ether functions, which allows formation of chelates with ions of alkaline metals.

   Thus, rate of anionic polymerization increases in the following order:

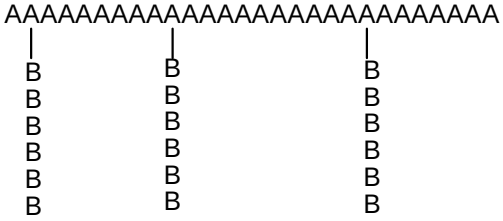
   benzene < 1,4-dioxane < tetrahydrofuran < dimethoxyethane

d) Strong electrostatic interaction between cation of alkaline metal and macroanion diminishes propagation rate in the case of anionic polymerization. Value of the constant of this interaction depends on the size of a counter ion, cations with bigger radius being subjected to weaker interaction. Ionic radii increase in the order of $Na^+ < K^+ < Cs^+$. The rate of anionic polymerization changes in the same order.

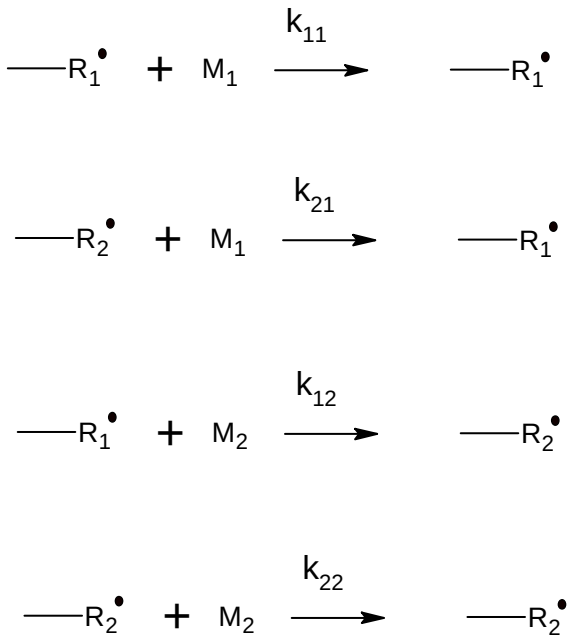
THEORETICAL PROBLEM 27

Co-polymerization

To synthesize macromolecules with complex architecture one can use various approaches: apply different types of polymerization, vary initiators, solvents and reaction conditions, copolymerize different monomers, as well as modify the obtained polymers. Some examples of copolymers are given in the table hereunder.

Type of a copolymer	Schematic structure	Abbreviation
Block	AAAAAAAAAAAABBBBBBBBBBBBB	poly(A)-block-poly(B)
Alternating	ABABABABABABABAB	poly(A-alt-B), poly(AB)
Statistical	AABABAABBBAABBBABAABABAAB	poly(A-stat-B)
Graft		poly(A)-graft-poly(B)
Gradient	AAAAABAAABAABBABABBBBABBBB	poly(A-grad-B)

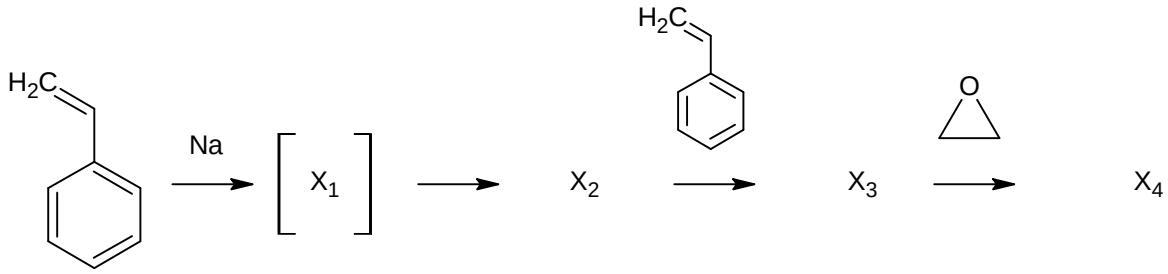
While developing copolymerization technique it is important to take into account relative reactivity of monomers. Kinetics of copolymerization can be described by a set of elementary reactions with corresponding rate constants. In the case of binary radical copolymerization four elementary reactions of chain propagation should be considered (end-unit model) (see next page):



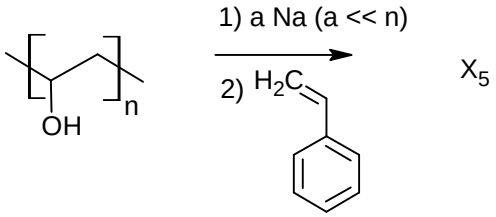
Relative reactivity of monomers in copolymerization is characterized by the ratio of the rate constants of their addition to a given macroradical: $r_1 = \frac{k_{11}}{k_{12}}$, and $r_2 = \frac{k_{22}}{k_{21}}$. These ratios are referred to as copolymerization constants (*r* value is always between zero and unity). For instance, for styrene and maleic acid anhydride the copolymerization constants are 0.04 and 0.01, respectively. Sometimes, the same approach is applied to define constants of binary ionic copolymerization.

27.1 Complete equations of polymerization reactions below and draw structures of compounds X_1 – X_7. Give both detailed and short formulas of all copolymers. In short formulas represent styrene units as St, ethylene oxide units as EO, vinyl alcohol units as VA, and maleic anhydride units as MA. Use abbreviations from the above table when necessary.

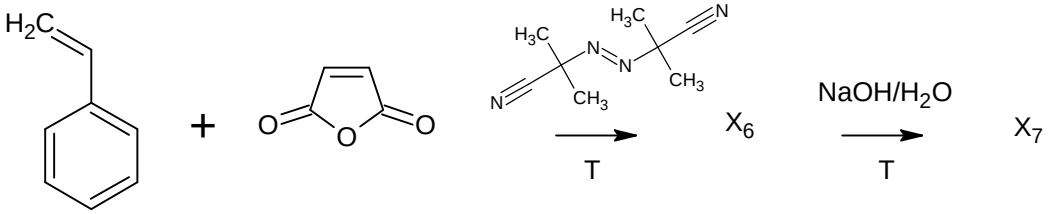
a)



b)



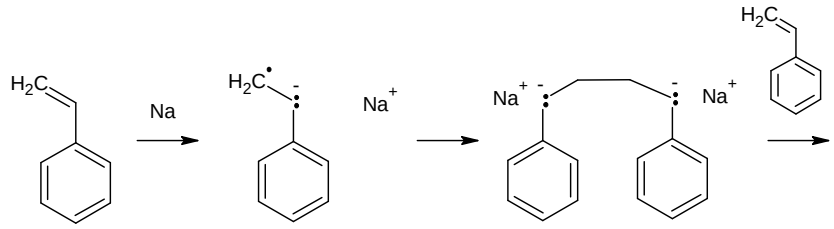
c)



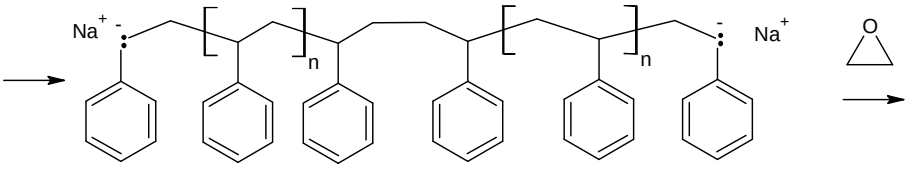
27.2 Calculate the average length of a chain of units A in the polymer obtained by radical copolymerization of equimolar mixture of two monomers of the same reactivity.

SOLUTION OF PREPARATORY PROBLEM 27

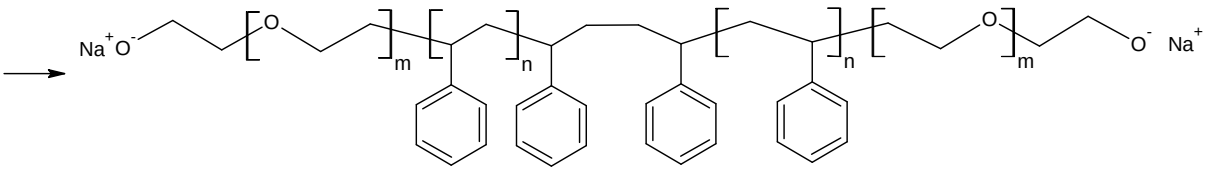
27.1 a)



X_1 X_2



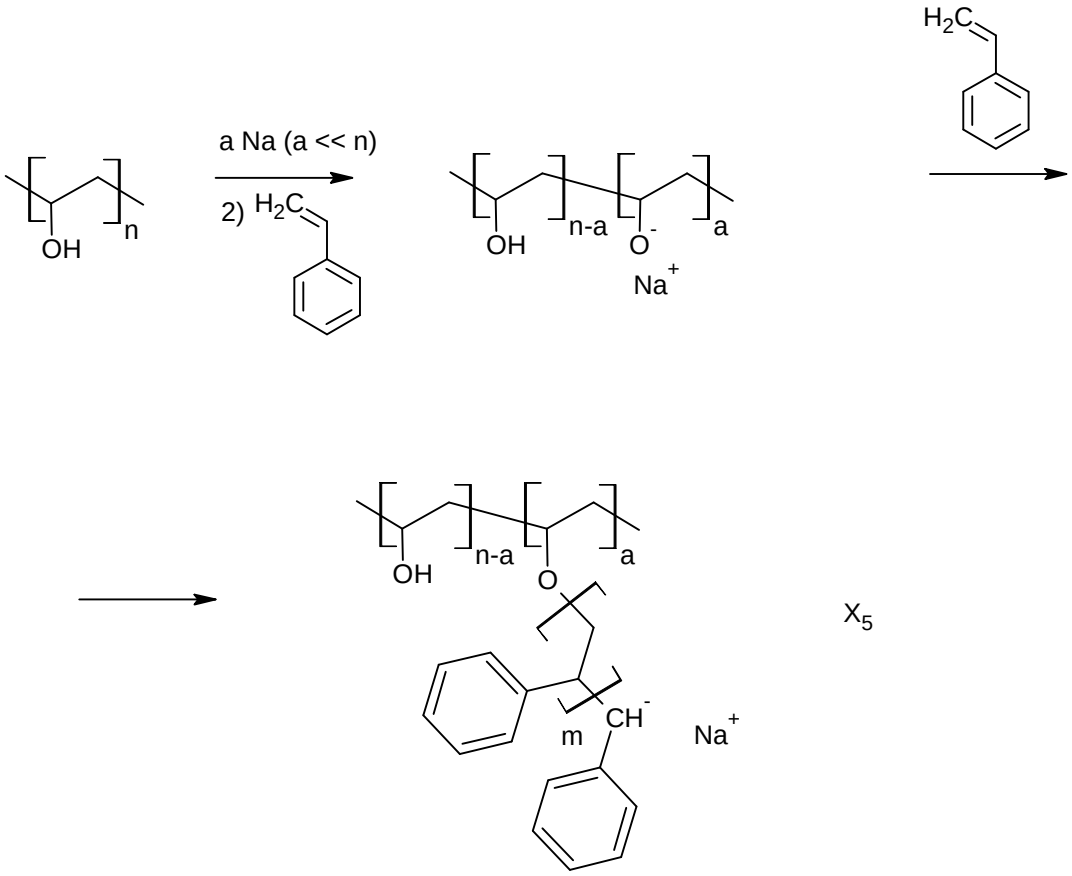
X_3



X_4

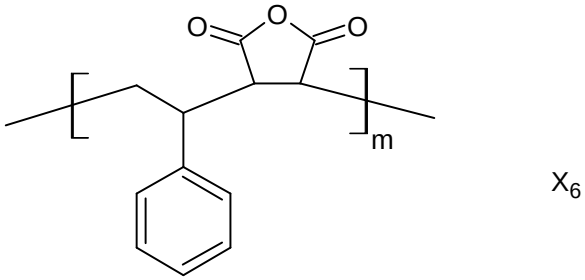
X_4 : poly(EO)-block-poly(St)-block-poly(EO)

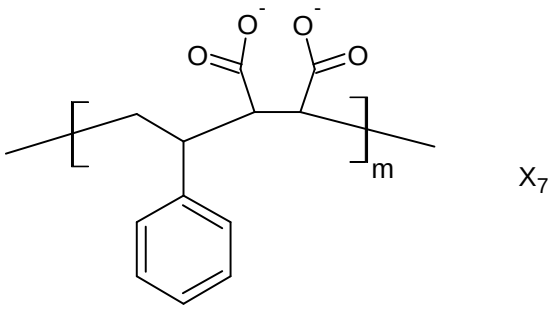
b)



X_5 : poly(VA)-graft-poly(St)

c)





X_6 : poly(St-alt-MA)

X_7 : poly(St-alt-Ma) (here Ma is used for maleate)

27.2 Monomers possess equal reactivity ($r_1 = r_2 = 1$). Thus, fraction of units A in the polymer is the same as that of monomers in the reaction mixture and is equal to ½. Besides, distribution of units along the chain is random. So we conclude that fractions of dyads AA, AB, BA and BB are equal (¼).

Solution 1.

Let us consider a long polymeric chain of *N* units. It contains *N*/2 of units A (with accuracy to one unit). The total number of dyads AB and BA is (*N*–1)/2, as there are *N*–1 dyads in the whole chain. The number of blocks in the chain exceeds the total number of dyads AB and BA by 1, and is equal to (*N*+1)/2, half of the blocks being composed of A. Thus, there are (*N*+1)/4 blocks of A in the chain. Then the average number of A units per block is: ((*N*+1)/2) : ((*N*+1)/4) ≈ (*N*/2) : (*N*/4) = 2.

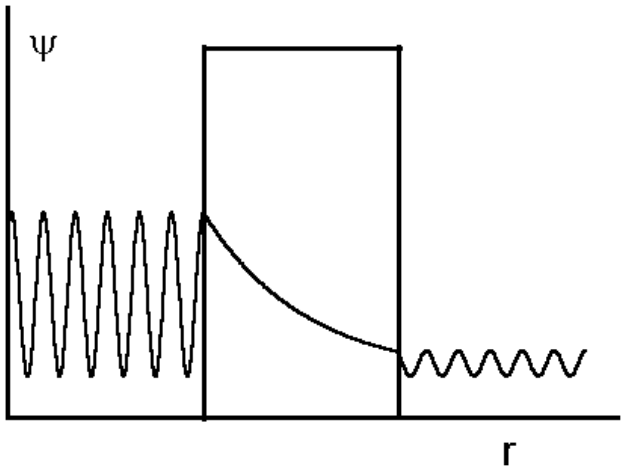
Solution 2.

Average lengths of blocks composed of A and B are equal due to symmetry of problem with respect to permutation (A, B). In the chain containing *N* units there are (*N*+1)/2 ≈ *N*/2 blocks (see calculations in solution 1). Thus, the average length of block is *N*:(*N*/2) = 2.

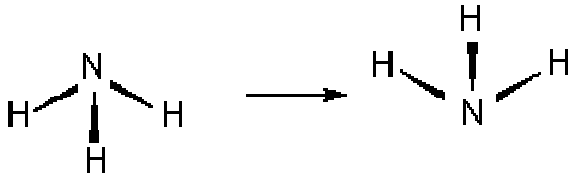
THEORETICAL PROBLEM 28

Tunneling in chemistry

Tunneling through energy barriers is a purely quantum-mechanical effect. It is explained by the fact that wave functions can differ from zero even in the classically forbidden areas where energy of a particle is less than an energy barrier:



Inversion of ammonia is a widely known example of tunneling:



In this process the molecule of ammonia is turned out like an umbrella against a strong wind. The tunneling frequency is 24 GHz, and the energy barrier separating two states is 25 kJ mol^{-1}.

28.1 Draw the reaction energy profile (plot of energy vs. reaction coordinate) for the inversion of ammonia. What is the reaction coordinate? What coordinate corresponds to the maximum of energy?

28.2 In which region of the electromagnetic spectrum can the tunneling of ammonia be observed?

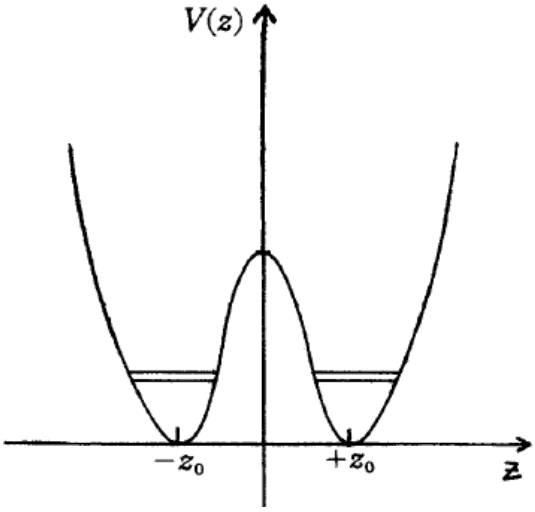
28.3 Find the energy difference corresponding to the tunneling frequency. What is the ratio of this energy to the barrier height?

28.4 How would the tunneling frequency change if we substitute some hydrogen atoms by deuterium ones? Explain.

_____

SOLUTION OF PREPARATORY PROBLEM 28

28.1 Energy profile is the symmetric double-well curve, where the minima correspond to stable pyramidal geometries of ammonia and the maximum – to the unstable planar geometry.



The reaction coordinate is the bond angle ∠HNH. In the planar geometry corresponding to the maximum of energy ∠HNH = 120°.

28.2 The wavelength for the tunneling transition is

$$\lambda = \frac{c}{v} = \frac{3.00\times10^{10}\ \text{cm s}^{-1}}{24\times10^{9}\ \text{s}^{-1}} = 1.25\ \text{cm}.$$

This wavelength corresponds to radiowaves.

28.3 The transition energy per 1 mol is:

$$E = h\,v\,N_A = 6.63\times10^{-34}\times(24\times10^{9})\times(6\times10^{23}) = 10 \text{ J mol}^{-1},$$

which accounts for 10 / 25000 = 0.0004, or 0.040 % of the energy barrier.

28.4 Tunneling of the heavier particles is less probable, hence the tunneling frequency for deuterated ammonia is smaller than that for NH_3.

PRACTICAL PROBLEMS

PREPARATORY PROBLEM 29 (PRACTICAL)

Titrimetric determination of Fe in different oxidation states

Some methods of iron determination in the oxidation states II and III are discussed in Problem 12**.** You are invited to test one more approach to solving that problem in practice.

Reagents and solutions required

- KIO_3 reagent grade, solid
- Ascorbic acid, solid
- KI aqueous solution, 5%
- HCl conc. aqueous solution and solution with c = 2 mol dm^{-3}
- HNO_3, conc. aqueous solution,
- Sulfosalicylic acid, 25% aqueous solution,
- NH_3, 10% aqueous solution,
- EDTA, standard aqueous solution, concentration about 0.05 mol dm^{-3} (the exact concentration will be given)

1. Preparation of a primary standard solution of KIO_3

1.1. Calculate with the accuracy of 0.0001 g the mass of KIO_3 necessary for the preparation of 200.0 cm^3 of KIO_3 solution (c = 0.01000 mol dm^{-3})

1.2. Using analytical balance weigh out accurately a portion of KIO_3. The mass of the portion may differ from the calculated one no more than by 0.05 g and it should be measured with an accuracy of 0.0001 g.

1.3. Transfer the portion into 200.0 cm^3 volumetric flask, dissolve it in water, dilute to the mark and mix.

1.4. Calculate the exact concentration (in mol dm^{-3}) of the solution prepared.

2. Preparation of the titrant solution (ascorbic acid)

2.1. Calculate with the accuracy of 0.01 g the mass of ascorbic acid necessary for preparation of 200 cm^3 of its aqueous solution with c = 0.1 mol dm^{-3}.

2.2. Using technical balance weigh out a portion of ascorbic acid. Its mass may differ from the calculated one no more than by 0.05 g.

2.3 Dissolve the portion in ~200 cm^3 of water, mix well, transfer the solution into a vessel and close it tightly with a stopper.

3. Standardization of the ascorbic acid solution

3.1. Fill in a burette with the ascorbic acid solution.

3.2. With a pipette transfer 10.00 cm^3 of standard KIO_3 solution into a 100 cm^3 Erlenmeyer flask, add 20 cm^3 of 5% KI solution and 5 cm^3 HCl aqueous solution with c = 2 mol dm^{-3}

3.3. Titrate the mixture with the ascorbic acid solution until the iodine color disappears.

Note. When titrating iodine with solutions of reducing agents, starch is usually added as an indicator. Here it is not recommended to do so because the reaction rate decreases significantly in presence of starch.

3.4. Repeat the titration until three titrant volumes differ no more than by 0.10 cm^3.

3.5. Calculate the average titrant volume.

3.6. Calculate the concentration of the ascorbic acid in the solution in mol dm^{-3}.

Questions

29.1 Write down the balanced equations of all the reactions taking place during standardization of ascorbic acid solution. Ascorbic acid $C_6H_8O_6$ is being oxidized to dehydroascorbic acid $C_6H_6O_6$.

29.2 KIO_3 in presence of excess of KI can be used as a primary standard for HCl standardization as well. The method is similar to that described above with the exception that no HCl is added to the titrated solution in this case. Which compound(s) can be used as an indicator(s) for that titration:

□ - starch,

□ - sulfosalicylic acid,

□ - methyl orange,

□ - methyl orange + $Na_2S_2O_3$ (in excess).

4. Determination of Fe(III) by ascorbimetric titration

4.1. From your instructor you obtain a sample solution containing Fe(II) and Fe(III) in a 100.0 cm^3 volumetric flask. Dilute the solution to the mark with water and mix.

4.2. Fill in the burette with the standardized ascorbic acid solution.

4.3. Measure with a pipette 10.00 cm^3 of the sample solution into a 100 cm^3 Erlenmeyer flask, add 40 cm^3 of water and heat nearly to boiling.

4.4. Into the hot solution add 4 – 5 drops of 25% sulfosalicylic acid solution as an indicator.

4.5. Titrate the solution with the ascorbic acid solution until the violet color disappears. During the titration and especially near the end point the solution must be hot. You may need to heat it additionally, if necessary. Near the end point the ascorbic acid solution should be added slowly.

4.6. Repeat the titrations until three titrant volumes differ no more than by 0.10 cm^3.

4.7. Calculate the average titrant volume.

4.8. Calculate the mass of Fe(III) in the sample solution under investigation.

Note. Ascorbic acid, especially in aqueous solutions, is instable and oxidizes with oxygen from the air. Therefore the standardization of ascorbic acid solution and ascorbimetric determination of Fe(III) must be carried out during one workday.

Questions

29.3 Write down the balanced equations of all the reactions taking place during Fe(III) determination. Ascorbic acid $C_6H_8O_6$ is being oxidized to dehydroascorbic acid $C_6H_6O_6$.

29.4 In what media does ascorbic acid exhibit its reducing properties most markedly?

□ - in acidic,

□ - in neutral.

□ - in alkaline,

□ - reducing properties of ascorbic acid do not depend on the pH.

5. Determination of total iron by complexometric titration

5.1. Fill in the burette with an EDTA standard solution.

5.2. With a pipette transfer 10.00 cm^3 of the sample solution into a 100 cm^3 Erlenmeyer flask. Add 5 cm^3 of conc. HCl and 2 cm^3 of conc. HNO_3 to oxidize Fe(II) present in the sample to Fe(III). Cover the flask with a watch glass, heat until boiling and continue heating for 3 – 5 min avoiding splashing.

5.3. Cool down the solution and neutralize it carefully adding 10% NH_3 aqueous solution dropwise until color changes from lemon yellow to yellowish brown and slight turbidity persists.

5.4. Add 1 – 2 drops of HCl solution (2 mol dm^{-3}) to dissolve the precipitate, then add 0.5 cm^3 of the HCl solution more, dilute up to 50 cm^3 with distilled water and heat nearly to boiling.

5.5. Into the hot solution add 4 – 5 drops of 25% sulfosalicylic acid solution as an indicator.

5.6. Titrate the solution until color changes from violet to clear yellow. During the titration and especially near the end point the solution must be hot. You may need to heat it additionally, if necessary. Near the end point the EDTA solution should be added slowly.

5.7. Repeat the titrations until three titrant volumes differ no more than by 0.10 cm^3.

5.8. Calculate the average titrant volume.

5.9. Calculate the total mass of iron in the sample solution given to you.

5.10. Calculate the mass of Fe(II) as a difference between the results obtained in 5.9 and 4.8.

Questions

29.5 Write down the balanced equations of all the reactions taking place during total Fe determination.

29.6 One of the crucial items in the Fe(III) determination by complexometric titration is strict maintenance of solution acidity. What are the reasons for that?

□
- If the acidity is too low, $Fe(OH)_3$ precipitates.
- If the acidity is too high, complex of Fe(III) with sulfosalicylic acid does not form.
- If the acidity is too high, complex of Fe(III) with EDTA acid does not form.
- If the acidity is too low and/or too high, the titrant decomposes.

SOLUTION OF PREPARATORY PROBLEM 29

Section 3:

29.1 $IO_3^- + 5\ I^- + 6\ H^+ \rightarrow 3\ I_2 + 3\ H_2O$

$I_2 + C_6H_8O_6 \rightarrow 2\ I^- + C_6H_6O_6 + 2\ H^+$

29.2 Methyl orange + $Na_2S_2O_3$ (in excess)

Section 4:

29.3 $2\ Fe^{3+} + C_6H_8O_6 \rightarrow 2\ Fe^{2+} + C_6H_6O_6 + 2\ H^+$

29.4 In alkaline media

Section 5:

29.5 $3\ Fe^{2+} + NO_3^- + 4\ H^+ \rightarrow 3\ Fe^{3+} + NO + H_2O$

$Fe^{3+} + Y^{4-}$ (EDTA anion) $\rightarrow FeY^-$

29.6 - at too low acidity $Fe(OH)_3$ precipitates,
- at too high acidity complex of Fe(III) with sulfosalicylic acid does not form,
- at too high acidity complex of Fe(III) with EDTA acid does not form.

PREPARATORY PROBLEM 30 (PRACTICAL)

Asymmetric autocatalysis – the numerical experiment

Nature exhibits a curious asymmetry between the left and the right, which is generally called 'chiral asymmetry'. Indeed, living organisms contain mostly L-amino acids and D-carbohydrates. One of the possible explanations of this phenomenon is based on the idea of autocatalysis. Chiral (asymmetric) autocatalysis is a reaction in which every chiral product serves as the catalyst of its own formation. In such reactions small initial excess of one of the enantiomers can increase exponentially in time.

Consider the kinetic scheme explaining this phenomenon. Two Enantiomers, X_L and X_D, are reversibly formed from achiral reagents T and S:

$$S + T \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_L \qquad (1)$$

$$S + T \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X_D \qquad (2)$$

$$S + T + X_L \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} 2\,X_L \qquad (3)$$

$$S + T + X_D \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} 2\,X_D \qquad (4)$$

$$X_L + X_D \xrightarrow{k_3} P \qquad (5)$$

Enantiomers react with each other giving the product P. The reactions take place in an open system, where constant concentrations of reagents S and T are maintained.

The system of rate equations can be solved numerically using any of the mathematical packages, for example Mathematica, MathCad, etc. Alternatively, you may use the program KINET posted on the official website www.icho39.chem.msu.ru. Let us assume the following values of rate constants (in arbitrary units): $k_1 = 0.5$, $k_{-1} = 0.1$, $k_2 = 0.5$, $k_{-2} = 0.2$, $k_3 = 0.5$.

Procedure

For numerical solution of the systems of differential equations mathematical packages use different commands. In Mathematica it is done by the function NDSolve. The arguments are the list of equations, initial conditions and a time interval. For example, the system of equations

$$a'(t) = -a(t)\, p(t)$$
$$p'(t) = a(t)\, p(t) - 2\, p(t)$$

with the initial conditions $a(0) = 2$, $p(0) = 0.5$ in a time interval from $t = 0$ to $t = 10$ is solved numerically by the command:

```
sol=NDSolve [{a ' [t] ==-a [t] *p [t], p ' [t] == a [t] *p [t]-2*p [t], a [0] == 2, p [0] == 0.5},
        {a, p}, {t, 0,10}]
```

The obtained solution is presented on the graph by the command Plot:

```
Plot [Evaluate [{a [t], p [t]}/.sol, {t, 0,10}], PlotRange-> All]
```

Questions

30.1 Compare equations 1 and 2 or 3 and 4 in the Scheme above. Why are the rate constants identical for enantiomers X_L and X_D?

30.2 The control parameter for this problem is the product of concentrations of reagents. Solve the system of kinetic equations numerically and draw on one graph the kinetic curves for X_L and X_D using the initial conditions: $[X_L]_0 = 0$, $[X_D]_0 = 0.01$. Consider two opposite cases: [S] [T] is small, [S] [T] is large. By varying the parameter [S] [T] determine its "break" value at which the shape of kinetic curve(s) changes drastically.

30.3 At fixed value [S] [T] = 5 study the influence of initial chiral asymmetry on kinetic curves. Consider two cases: $[X_D]_0 = 0.001$, $[X_D]_0 = 0.1$.

Let us determine which elementary reactions are essential for chiral asymmetry amplification.

30.4 Consider the role of reversibility. For this purpose, given the same initial concentrations compare kinetic curves for two mechanisms: with reversible ($k_{-1} \neq 0$; $k_{-2} \neq 0$) and with irreversible formation of the enantiomers ($k_{-1} = k_{-2} = 0$).

30.5 Consider the simplified scheme in which the first two reactions are absent. Whether an amplification of chiral asymmetry is possible in such system?

30.6 Compare the open and closed systems. You have already treated the open system. In the closed system the reagents S and T are no more introduced to a reaction

vessel during reaction, therefore they should be included in the system of kinetic equations. Whether or not amplification of chiral asymmetry is possible in a closed system?

Draw the conclusions. What conditions are necessary for amplification of chiral asymmetry to be observed? What elementary stages appear to be essential for it?

SOLUTION OF PREPARATORY PROBLEM 30

30.3 The more the initial chiral asymmetry the earlier kinetic curves separate from each other.

30.4 Reversible stages are not necessary for amplification of chiral asymmetry.

30.5 These reactions are not necessary for amplification of chiral asymmetry.

30.6 In a closed system amplification of chiral asymmetry is not possible. In an open system the essential stages are (3) – (5).

PREPARATORY PROBLEM 31 (PRACTICAL)

Oscillating reactions

Introduction

In 1921 W. Bray published an article describing the oscillating reaction of oxidation of hydrogen peroxide with potassium iodate. However thorough investigation of oscillating reaction mechanisms has begun only in 1951, when B.P. Belousov discovered oscillations of concentrations of reduced and oxidized forms of cerium catalyzing oxidation of citric acid by bromate-ion. Later it was shown that oscillating reactions are possible in other redox systems. A.M. Zhabotinsky investigated the oxidation of malonic acid by bromate-ion in the presence of manganese ions. This reaction mechanism is very sophisticated and includes dozens of intermediate compounds.

We will investigate an oscillating reaction taking place in the malonic acid-iodate ion system in the presence of manganese salt and hydrogen peroxide.

Reagents and equipment

- KIO_3 reagent grade, solid,
- 40 % H_2O_2,
- KIO_3,
- conc. H_2SO_4,
- $C_3H_4O_4$, malonic acid,
- $MnSO_4 \cdot 5\ H_2O$,
- starch,
- KI, solution,
- $AgNO_3$, solution,
- analytical balance,
- weighing dishes,
- flat-bottom flasks or beakers (250 - 500 cm^3), 4 pcs,
- stop-watch.

Procedure

Prepare three solutions (may be prepared in advance):

1) solution of 80 cm^3 40 % H_2O_2 in 120 cm^3 of water,

2) solution of 8.7 g KIO_3 and 0.9 cm^3 conc. H_2SO_4 in 190 cm^3 of water,

3) solution of 3 g $C_3H_4O_4$, 2.4 g $MnSO_4 \cdot 5\ H_2O$ and 0.06 g starch in 195 cm^3 of water.

Mix the solutions in the same vessel and observe the oscillating process. Evaluate the oscillation period and its change in time.

Divide the mixture into two parts and place them into beakers.

To one of the parts add $AgNO_3$ solution (first – several drops, then ~3 cm^3). Observe changes of the oscillation period. Note the color of the solution upon completion of the oscillation reaction.

To the other part add KI solution (several drops). Observe changes of the oscillation period.

Questions

31.1 Oxidation of malonic acid by potassium iodate is an autocatalytic process. Write down the net equation of the reaction. Which product is the catalyst of the oscillating process? Explain the effect of silver nitrate.

31.2 B. P. Belousov used bromate-ion as an oxidizing agent. Suggest what would happen if we substitute iodate-ion by bromate-ion in the reaction with malonic acid. What role does hydrogen peroxide play in the oxidation of malonic acid with iodate-ion?

31.3 It is well known, that one of the stages of the oscillating process is formation of iodomalonic acid with its subsequent decomposition. How can we explain the fact that potassium iodide inhibits the reaction?

31.4 B. P. Belousov used the Ce^{4+}/Ce^{3+} redox couple to study oscillating reactions. Is it possible to use the following transient metal redox couples as a catalyst: Co^{3+}/Co^{2+}, Fe^{3+}/Fe^{2+}, Tl^{3+}/Tl^{1+}?

$E^o(Co^{3+}/Co^{2+}) = 1.81$ V, $E^o(Ce^{4+}/Ce^{3+}) = 1.61$ V,
$E^o(Mn^{3+}/Mn^{2+}) = 1.51$ V, $E^o(Fe^{3+}/Fe^{2+}) = 0.77$ V?

SOLUTION OF PREPARATORY PROBLEM 31

31.1 The reaction mechanism is very complex and consists of many steps and parallel ways. The net equation of the reaction is

$KIO_3 + CH_2(COOH)_2 \rightarrow KI + HCOOH + 2\ CO_2 + H_2O$, (1)

The steps are:

$IO_3^- + 5\ I^- + 6\ H^+ \rightarrow 3\ I_2 + 3\ H_2O$ (2)

$I_2 + 5\ H_2O_2 \rightarrow 2\ HIO_3 + 4\ H_2O$ (3)

Thus, iodine derivatives are the catalysts of the oscillating process.

The addition of $AgNO_3$ eliminates I^- ion from reaction, so oscillations become slower and then stop.

31.2 BrO_3^- is a stronger oxidizing agent than IO_3^-, so oscillation frequency will increase and visual observation would become more difficult. H_2O_2 oxidizes I_2 to IO_3^- ion.

31.3 I^- ion interacts with one of the reagents according to equation (2), so adding I^- will decrease the oscillation frequency and increase the oscillation period.

31.4 Transition metal ions participate in oscillation reaction:

$10\ Mn^{2+} + 2\ IO_3^- + 12\ H^+ \rightarrow I_2 + 10\ Mn^{3+} + 6\ H_2O$ (4)

and next

$6\ Mn^{3+} + CH_2(COOH)_2 + 2\ H_2O \rightarrow 6\ Mn^{3+} + HCOOH + 2\ CO_2 + 6\ H^+$ (5)

or

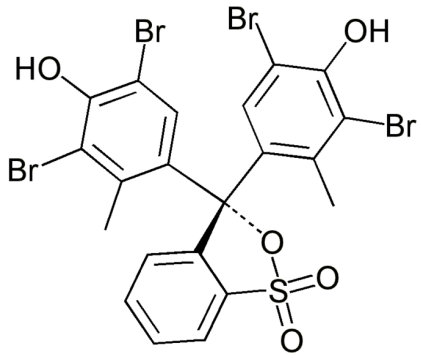
$4\ Mn^{3+} + ICH(COOH)_2 + 2\ H_2O \rightarrow 4\ Mn^{3+} + HCOOH + 2\ CO_2 + 5\ H^+ + I^-$ (6).

Co^{2+} is not oxidized by iodate-ion, Fe^{3+} is not a strong oxidizing agent and does not oxidize malonic acid. Redox process $Tl^{3+} \rightarrow Tl^+$ involves two-electron transfer so it is very slow.

PREPARATORY PROBLEM 32 (PRACTICAL)

Determination of the acidity constant of bromocresol blue (3′,3″,5′,5″-tetrabromo-m-cresolsulfonephthalein, bcb)

Bromocresol blue (BCB)



is an organic dye, an acid-base indicator, a weak diprotic acid (H_2A). In aqueous solutions in the pH range of 3-6 BCB changes its color from yellow to blue due to dissociation of the second proton:

$$HA^- \text{ (yellow)} \rightleftarrows A^{2-} \text{ (blue)} + H^+$$

On the base of the absorbance of BCB solution measured as a function of the pH one can calculate the second acidity constant of BCB, pK_{a2}.

Reagents and solutions required

- Bromocresol blue, 0.25% solution in 50% aqueous ethanol,
- Mixture of acids for preparation of buffer solutions: an aqueous solution containing H_3PO_4, and H_3BO_3 with a concentration 0.04 mol dm^{-3} each,
- NaOH, solutions with concentrations of 0.2 mol dm^{-3} and 2 mol dm^{-3},
- HCl, solution (c = 2 mol dm^{-3}).

1. Choice of the wavelength for the K_{a2} determination

1.1 Into each of two 50.0 cm^3 volumetric flasks place 1.00 cm^3 of the BCB solution and 10.00 cm^3 of the mixture of acids (see reagent list). Then add 1.00 cm^3 of NaOH solution (c = 0.2 mol dm^{-3}) into the first and 6.00 cm^3 of NaOH solution (c = 2 mol dm^{-3}) into the second flask. Dilute the solutions to the mark with water and mix.

1.2 Measure the pH of the solutions prepared. The first one must have the pH in the range of 2 – 3, the second one in the range within 7 – 8. Under such conditions all BCB is in the form of either HA^- or A^{2-} respectively. If either of the pH is different from the required, adjust it by adding few drops of HCl solution (2 mol dm^{-3}) or NaOH solution (2 mol dm^{-3}).

1.3 Measure the absorption spectra of the solutions in the range of 400 – 700 nm; 5 – 10 data points would be sufficient.

1.4 Choose the wavelength at which the absorbances of the solutions differ most greatly. Usually that wavelength corresponds to the maximum of absorbance of one of the species or close to it. Further carry out all the measurements at that wavelength.

2. Preparation of series of BCB solutions, measuring their absorbance and the pH

2.1 Into each of twelve 50 cm^3 volumetric flasks place 1.00 cm^3 of BCB solution and 10.00 cm^3 of the mixture of acids. Then add NaOH solution (c = 0.2 mol dm^{-3}) to each flask in the amount indicated in Table below:

Flask number	Solution NaOH, cm^3
1	0.75
2	1.50
3	2.50
4	2.75
5	3.00
6	3.25
7	3.50
8	3.75
9	4.00
10	4.25
11	5.25
12	6.25

Dilute the solutions to the mark with water and mix.

Note. It is of essential importance that the concentrations of BCB be strictly the same in all the solutions. When preparing the solutions pay especial attention to that requirement!

2.2 For each solution measure the pH and the absorbance at the chosen wavelength.

2.3 Using the data obtained calculate logK_{a2} for each of the solutions unless fraction of either of the species involved in the acid-base equilibrium is negligible.

2.4 Calculate the average logK_{a2} value.

Questions

Denote as:

$[HA^-]$, $[A^{2-}]$, c – equilibrium concentrations of the corresponding BCB forms and its total concentration, respectively;

l – cuvette length;

K_{a2} – acidity constant of HA^-;

ε_{HA}, ε_A – extinction coefficients of the corresponding forms at the chosen wavelength;

A_{HA}, A_A, A – absorbances of BCB solution containing only HA^-, only A^{2-} and their mixture, respectively.

32.1 Write down the equations for A_{HA}, A_A and A as functions of $[HA^-]$, $[A^{2-}]$ and c.

32.2 Express A as a function of A_{HA}, A_A and $[H^+]$.

32.3 Write down the equation for calculation of K_{a2} from A_{HA}, A_A, A and $[H^+]$.

32.4 Consider the wavelength at which $\varepsilon_{HA} = \varepsilon_A$. It is called the isosbestic point.

a) Is it possible to determine K_a of a dye by measuring the absorbance at the isosbestic point?

b) What analytical information can be obtained from such measurement?

SOLUTION OF PREPARATORY PROBLEM 32

32.1 $A_{HA} = \varepsilon_{HA} l\, c$ $\quad A_A = \varepsilon_A l\, c$ $\quad A = (\varepsilon_{HA}[HA^-] + \varepsilon_A[A^{2-}])l$

32.2 $[HA^-] = c\dfrac{[H^+]}{[H^+] + K_{a2}}$ $\quad [A^{2-}] = c\dfrac{K_{a2}}{[H^+] + K_{a2}}$

Therefore (see expressions above)

$$A = A_{HA}\frac{[H^+]}{[H^+]+K_{a2}} + A_A\frac{K_{a2}}{[H^+]+K_{a2}}$$

32.3 $$A - A_{HA} = (A_A - A_{HA})\frac{K_{a2}}{[H^+]+K_{a2}}$$

$$A_A - A = (A_A - A_{HA})\frac{[H^+]}{[H^+]+K_{a2}}$$

Thus,

$$K_{a2} = [H^+]\frac{A - A_{HA}}{A_A - A}$$

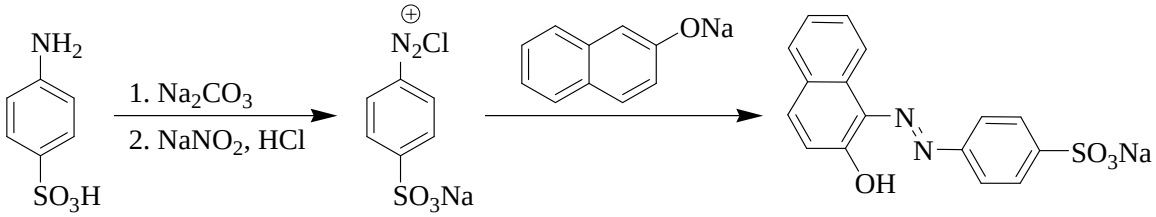
32.4 a) No. If $\varepsilon_{HA} = \varepsilon_A$ (= ε), then at any pH $A = (\varepsilon[HA^-]+\varepsilon[A^{2-}])l = \varepsilon\, l\, c = A_{HA} = A_A$. Calculation of K_{a2} is not possible.

b) Total concentration (c) of the dye.

PREPARATORY PROBLEM 33 (PRACTICAL)

Acid orange 7

A very popular azo-dye known under dozens of trade names and widely used in textile, leather, food, cosmetics, as well as other industries, Acid Orange 7 (Acid Orange II, Persian Orange, listed in the Color Index as No. 15510) can be readily obtained by azo-coupling of diazotized sulphanilic acid with 2-naphtholate



Materials and hardware

- Sulfanylic acid, solid,
- 2-Naphthol, solid,
- sodium carbonate, solid,
- sodium nitrite, solid,
- sodium hydroxide, 5% aqueous solution,
- hydrochloric acid, conc.
- ice.
- glass beakers (150, 200, 500 cm^3),
- thermometer,
- spatulas,
- magnetic stirrer,
- heating plate,
- vacuum filtration apparatus,
- desiccator.

The diazotization

Sulfanylic acid (8.66 g, 0.05 mol) is dissolved in the solution of 3 g of sodium carbonate in 50 cm^3 water in a 150 cm^3 glass beaker placed on a magnetic stirrer. 15 cm^3 of concentrated HCl are added to this solution at vigorous stirring. After cooling to room temperature, the beaker is immersed in an ice bath (a couple of ice chunks can be added

to the mixture to ensure good cooling) and the mixture is further cooled to 0 ℃. A solution of $NaNO_2$ (3.45 g, 0.05 mol) in 20 cm^3 of water is added dropwise (***warning!*** this operation should be done in a hood because of evolution of nitrogen oxides). The rate of addition should be controlled to keep the temperature near 0 ℃ as accurately as possible (***warning!*** even a 2° – 3° increase leads to side-reactions which may lead to the formation of phenols giving unwanted azo-dyes which dramatically worsen the purity of color of the target dye). During the addition white precipitate of diazonium salt (diazotized sulfanylate is a betaine, an inner salt with zero net charge, therefore it is not well soluble in water) may sometimes form. The results of diazocoupling do not depend on whether the diazonium salt is in solution or suspension.

After addition of all nitrite solution, stirring is continued for 10 – 15 min (***warning!*** temperature should be carefully controlled!). The diazonium salt solution (or suspension) should be used immediately after preparation.

The azocoupling

2-Naphthol (7.21 g, 0.05 mol) is dissolved in 40 cm^3 of 5% NaOH solution. This solution is mixed with solution of 12.5 g Na_2CO_3 in 100 cm^3 water in a 500 cm^3 beaker. The resulting solution should be transparent, if any precipitate or suspension persists, it should be filtered off. The solution of naphtholate is cooled to 0 ℃ by ice (an ice bath plus a few ice chunks inside). The diazonium salt solution is slowly poured to naphtholate solution under vigorous stirring by a spatula or a glass rod. Attention should be paid to keep the temperature below 8 ℃ throughout the addi tion. Afterwards, the mixture is left for an hour, preferably on a magnetic stirrer. The dye partially precipitates as golden plates.

After an hour, the solution is heated to completely dissolve the precipitate, filtered hot (*note*: this filtration can be omitted if a hot filtration funnel is not available), and saturated by 50 g of sodium chloride (50 g) while hot (it is necessary to keep temperature above 50 ℃ during saturation, so the beaker should be placed on a heating plate). Dye precipitate formed by salting-out is filtered off by vacuum filtration from hot solution (*note:* if the temperature of solution being filtered drops below 50 ℃, sodium chloride partially co-precipitates with the dye). The dye is dried in a desiccator over $CaCl_2$. Orange solid, yield 25 g.

The quality of dye can be controlled by the UV/Vis spectroscopy. In aqueous solution λ_{max} 487 nm ($\log\varepsilon = 4.87$).

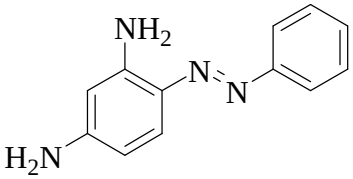
Questions

33.1 Under the name *tropaeolin 000* the dye is used as an acid-base indicator in aqueous solutions. Guess in which region of pH this dye changes its color:

☐ strongly acidic (pH<2); ☐ acidic (pH 2 – 6.5); ☐ neutral (pH 6.5 – 7.5) ☐ mildly alkaline (pH 7.5 – 9); ☐ strongly alkaline (pH 9 – 14).

33.2 Write the reaction equation which accounts for the color change.

33.3 Write the reaction equation of an azocoupling required to obtain *chrysoidine* dye.



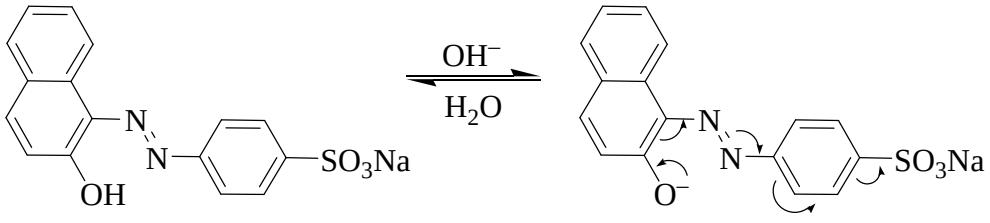
33.4 Which pH region should be chosen for this azocoupling:

☐ strongly basic, ☐ weakly basic, ☐ weakly acidic, ☐ strongly acidic?

SOLUTION OF PREPARATORY PROBLEM 33

33.1 - 33.2

The most apparent functional group in the dye molecule which can account for pH-dependent changes is a phenolic hydroxyl. Thus, the compound is a weak acid, which can be deprotonated under weakly alkaline conditions. Actually, pH-range in which the transformation takes place is within 7.5 – 8.5. As phenolate oxygen is a stronger donor than hydroxy-group, the color deepens upon the addition of a base (from yellow-orange to reddish).

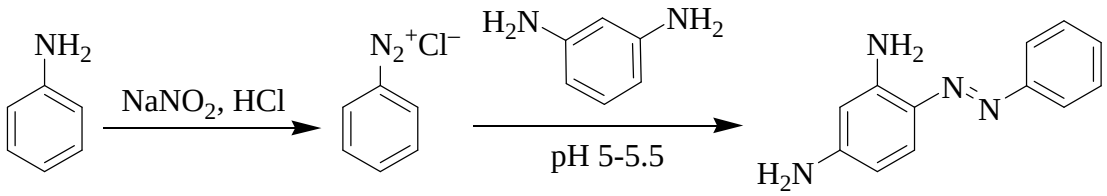


However, somebody might take into consideration that all azo-dyes are protonated at nitrogen atom of the azo-group under strongly acidic conditions. In fact, only those azo-dyes which contain amino groups are useful as indicators in the acidic region, but phenolic dyes should also be protonated below pH 1, though this transition is not practically useful. *Therefore*, *this idea can only be regarded as a secondary optional answer*.

33.3 - 33.4

When choosing how to correctly assemble some azo-dye molecule, the most important criterion is a weak electrophilicity of diazonium salts which can react only with such electron-rich benzene derivatives as amines or phenolates. Therefore, in the case of chrisoidine the choice is unambiguous to involve the coupling between benzenediazonium and *m*-phenylenediamine. The orientation rules suggest the only possible site for the attack (position 6). Position 2 is not attacked due to sterical hindrance.

The azo-coupling with amines is usually done under mildly acidic conditions.



PREPARATORY PROBLEM 34 (PRACTICAL)

Determination of molecular mass of a protein using gel filtration

Gel filtration is a simple and reliable chromatographic method for separating molecules according to their size. Within a fractionation range chosen, molecules are eluted in a decreasing order of their size. Versatility of the method makes it applicable for purification and characterization of biological substances of all classes, including macromolecules not readily fractionated by other techniques.

Some gel forming organic polymers with a 3D network structure (usually referred to as gel filtration media, GFM) possess properties of molecular sieves and can separate molecules according to their size and shape. A chromatography column should be filled with swollen gel and equilibrated with corresponding buffer solution. The separation mechanism is non-adsorptive and independent of the eluent system used, thus being fairly gentle. Liquid inside porous gel beads of GFM is the stationary phase, whereas eluent solution outside the beads is the mobile one.

In a column, all sample molecules can be present in the liquid between the beads. The total volume of such “outside” liquid is referred to as *the void volume* in gel filtration and is equal to about 30% of the column volume. Sample molecules are partitioned between the eluent (the mobile phase) and the accessible part of bead pores (the stationary phase). This partitioning acts to establish a *dynamic equilibrium* of sample molecules between the mobile and stationary phases and is driven exclusively by diffusion. The mobile phase transports the sample molecules down the column. The molecules present in the pores are "stationary" and not subjected to transportation. Migration rate of a sample zone depends on the fraction of sample molecules present in the mobile phase. Separation of individual macromolecules can only be achieved in the case of their partial access to the pores of the GFM. *Applicable sample volume* is restricted to 0.5 – 5% of that of the column, since no concentration effect is active in gel filtration. *Flow rate* is kept low to avoid peak broadening due to incomplete mass transfer, whereas columns used are long to allow optimum resolution.

Materials

- Blue dextran (molecular mass, MW = 2 MDa), 4 mg

Proteins:

- Ovalbumin (MW = 43 kDa), 1.5 mg
- Cytochrome C (MW = 13 kDa), 0.4 mg
- Bovine serum albumin (BSA) (MW = 67 kDa), 2.2 mg
- Chymotrypsinogen (MW = 25 kDa), 1 mg
- Hemoglobin (MW = 64.5 kDa), 1.5 mg
- HCl, 230 cm^3 of aqueous solution, (c = 0.1 mol dm^{-3})
- KCl, solid, 22.35 g
- Buffer: Tris (2-Amino-2-(hydroxymethyl)propane-1,3-diol; 6.05 g
- GFM: Toyopearl HW-50 (or HW-55), fine, 70 cm^3

If the above mentioned proteins are partially inaccessible, those missing can be substituted by proteins with close MW, but not proteases. Toyopearl may be also replaced by a GFM with similar properties.

Apparatus

70 cm^3 chromatography column; packing reservoir; stand; peristaltic pump; UV-cord connected to plotter; Eppendorf centrifuge; analytical balances; water-jet pump; one 1000 cm^3 measuring cylinder; one 250 cm^3 volumetric flask; one big Buchner funnel with glass filter; one 1000 cm^3 Bunsen flask; one 1000 cm^3 round-bottom flask; one 100 μdm^3 micropipette with tips; one 1000 μdm^3 micropipette with tips; one 2 cm^3 syringe connected to 20 cm tubing; four Eppendorf tubes; one 100 cm^3 measuring cylinder; one 200 cm^3 flask; one 100 cm^3 beaker; big steel spatula; small spatula; glass rod; filter paper.

Note: A UV-cord can be substituted by a UV-visible spectrophotometer and measuring test tubes.

Procedure

Step 1. Preparation of buffer solution

To prepare Tris buffer solution (c = 0.2 mol dm^{-3}), dissolve 6.05 g of Tris in 250 cm^3 of distilled water in the 250 cm^3 volumetric flask. Mix 125 cm^3 of the Tris solution and 230 cm^3 of HCl solution (0.1 mol dm^{-3}) in the 1000 cm^3 measuring cylinder. Add distilled water

to 800 cm^3. Add 22.35 g of KCl to the Tris-HCl solution and stir thoroughly until the salt completely dissolves. Add water to 1000 cm^3 (the final concentration of KCl is 0.3 mol dm^{-3})

Step 2: Preparation of a chromatographic column

Packaging the column is one of the most important stages in chromatography, as it determines the separation quality to a great extent. The column should be packed uniformly, and the upper and lower gel surfaces should be strictly horizontal.

1. Equilibrate gel material to room temperature.

2. Gently shake the bottle to make an even slurry.

3. Pour 70 cm^3 of gel slurry into a beaker and dilute with buffer to 100 cm^3.

4. Stir with a glass rod to make a homogeneous suspension free from aggregates.

5. Add eluent buffer solution to the column to check for leaks, wet the walls of the column and remove air from the bed support. (It is better to fill the column bottom-up using the water-jet pump). Drain buffer leaving about 1 cm above the gel surface. For columns with bottom glass porous filter, a filter paper circle with a diameter equal to the inner column diameter should be placed on the glass filter to prevent from gel leakage from the column.

6. Mount the column vertically and attach the addition packing reservoir firmly to the column. It should be twice shorter than the column.

7. Wash the gel with three portions (of about 100 – 120 cm^3) of Tris-buffer solution on Buchner funnel with glass filter attached to 1000 cm^3 Bunsen flask using water-jet pump. Try not to dry Toyopearl. After each washing disconnect the water-jet pump when the upper gel surface just starts turning dry. Then add next portion of buffer, stir with big steel spatula to make a homogeneous suspension, and subject to suction.

8. Transfer the gel from the funnel into 1000 cm^3 round – bottom flask, add 50 cm^3 of buffer solution and connect the flask to water-jet pump using a connector. Vacuum degassing should proceed for at least 5 min.

9. Re-suspend and pour the gel slurry into the column in one continuous motion. Pouring down a glass rod held against the wall of the column prevents from air bubbles (Fig.1). Try gel slurry to flow along the column wall.

10. Carefully fill the reservoir to the top with buffer solution, disturbing the gel as little as possible. Connect the reservoir with the peristaltic pump, which should in turn be joined to buffer stock in the 200 cm^3 flask. Turn on the pump and open the column outlet.

11. Buffer solution should be pumped through the column until the gel stops settling. After two bed volumes remove the gel reservoir and insert flow adaptor.

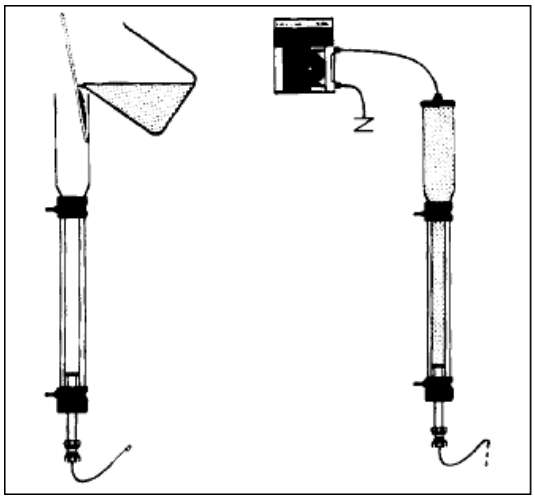


Fig. 1. Packaging the column with GFM.

Step 3: Preparation of solutions

Weigh blue dextran and proteins using balance and small spatula. Prepare solution of Blue dextran by dissolving it in 1 cm^3 of Tris-buffer solution in an Eppendorf tube. Prepare two solutions of standard proteins in Eppendorf tubes. The first solution contains Ovalbumin, Cytochrome C, 0.07 cm^3 of blue dextran solution and 0.93 cm^3 of Tris-buffer solution. The second solution contains Bovine serum albumin, Chymotrypsinogen, 0.07 cm^3 of blue dextran solution and 0.93 cm^3 of Tris-buffer solution. Prepare solution of Hemoglobin (unknown protein) in 1 cm^3 of Tris-buffer solution. Centrifuge two solutions with standard proteins and the solution of unknown protein for 5 min.

Step 4: Application of samples

1. Apply sample solutions carefully, trying not to disturb the gel. To make it easier, filter paper circle could be placed at the top of gel (still take into account possible protein absorption on the paper). Remove flow adaptor, disconnect the peristaltic pump and open the column outlet. Let the buffer soak into the gel (the gel surface should be free of buffer but not dry) and close the column outlet. Add sample solution slowly using pipette with wide tip or 2 cm^3 syringe connected to 20 cm tubing, open the column outlet and allow the

solution flow inside the gel. Close the column outlet and add buffer solution (about 1 cm^3) slowly and carefully (as during the sample application). Open the column outlet and let the buffer soak in the gel. Repeat the procedure. This allows the sample solution flowing deeper inside the gel and prevents from backward diffusion. Close the column outlet and carefully make a buffer layer with height of about 2 cm over the gel.

2. Connect the peristaltic pump to the column inlet and the UV-cord to the column outlet (the tube length should be as short as possible) and start elution.

Step 5: Column chromatography

1. Carry out calibration of the column in two steps:

A) Apply the first solution of standard proteins containing Blue dextran, Ovalbumin and Cytochrome C to the column. Start elution with the rate of about 1 – 2 cm^3/min, collecting the eluate into 100 cm^3 measuring cylinder. The elution process is monitored by following the eluate absorbance at 280 nm, which is registered by the UV-cord. Measure Elution volumes for Blue dextran and proteins using cylinder (record the volumes corresponding to maxima of the eluate absorbance).

Note: in the case of using a spectrophotometer and test-tubes, the procedure should be modified as follows. Collect the eluate in a measuring cylinder up to 25% of the column volume. Then continue collecting the eluate in test-tubes in portions of 1 mL. Determine the eluate absorbance at 280 nm in each test-tube by using a spectrophotometer and record the total volumes corresponding to maxima of the eluate absorbance).

After the three peaks are registered, the column should be washed with the buffer solution until the total elution volume becomes equal to that of the column.

B) Apply the second solution of standard proteins and proceed as described above.

2. Apply the solution of unknown protein. After the peak is registered, stop the peristaltic pump, close column outlet and turn off the UV-cord.

Questions

34.1 Correlate chromatographic peaks with substances you applied to the column. Complete the table:

Standard solution number	Number of a peak (in the order of its appearance)		
	1	2	3
1			
2			

34.2 What is the void volume of your column? Explain.

34.3 Calculate the volume of the chromatographic column.

34.4 Calculate the availability coefficient K_{av} for all proteins using formula

$$K_{av} = \frac{V_r - V_0}{V_c - V_0}$$

V_r is elution volume for sample molecule, V_o is the void volume, V_c is the column volume.

34.5 Plot the calibration curve as the dependence of K_{av} on log(MW) using the data obtained for four standard proteins.

34.6 Determine molecular mass of the unknown protein.

34.7 Another important characteristic of a column is *the exclusion limit*, M_r, which is defined as the molecular mass of the smallest molecule excluded from the pores. Calculate this parameter by finding the intercept of the extrapolated linear part of the calibration curve with the log(MW) axis.

34.8 Estimate the elution volume for low molecular mass substances if applied to the column under consideration. Provide an explanation.

———————

SOLUTION OF PREPARATORY PROBLEM 34

34.1

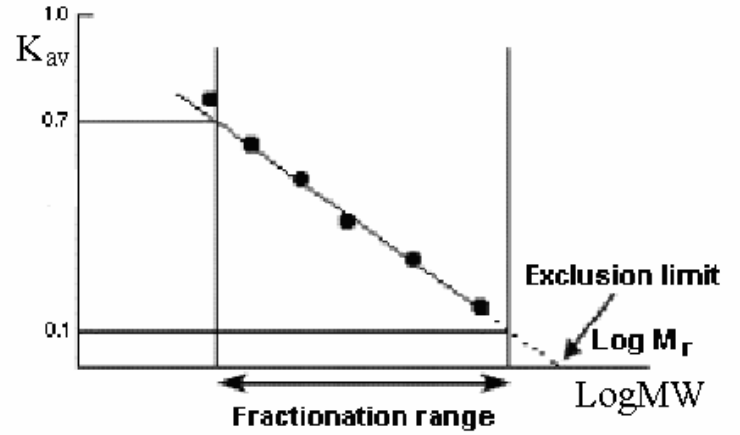
Standard solution number	Number of a peak (in the order of its appearance)		
	1	2	3
1	Blue dextran	Ovalbumin	Cytochrome C
2	Blue dextran	Bovine serum albumin	Chymotrypsinogen

34.2 The void volume of the column under consideration is equal to the elution volume of Blue dextran, since molecules of this substance can not penetrate into beads pores due to their size, thus moving between gel particles with the eluent front.

34.3 The volume of the chromatographic column is calculated as the volume of a cylinder using inner column diameter and height of the packed gel bed.

34.5 - 34.7

A typical plot is given below.



34.8 Elution volume for low molecular mass substances is approximately equal to the column volume as all pores are accessible to such substances.