THEORETICAL PROBLEMS

Country:	USA
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International Chemistry Olympiad
SLOVAKIA & CZECH REPUBLIC

BACK TO WHERE IT ALL BEGAN

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Instructions

- This theoretical exam booklet contains 58 pages.

- You may begin writing as soon as the **START** command is given.

- You have **5 hours** to complete the exam.

- All results and answers must be clearly written **in PEN in their respective designated areas** on the exam papers. Answers written outside the answer boxes will **NOT** be graded.

- You were provided with 3 sheets of scratch paper. If you need more, use the backside of the exam sheets. Remember that **nothing outside the designated areas will be graded**.

- The periodic table and visible light spectrum are not part of this booklet; they are provided separately.

- Use only the pen and calculator provided.

- **The official English version** of the exam booklet is available upon request and serves for clarification only.

- If you need to leave the exam room (to use the toilet or have a snack), wave the blue IChO card. The exam supervisor will come to accompany you.

- The supervisor will announce a 30-minute warning before the **STOP** command.

- You must stop your work immediately when the **STOP** command is announced. Failure to stop writing within 30 seconds will lead to nullification of your theoretical exam.

- After the **STOP** command has been given, place your exam booklet back in your exam envelope and wait at your seat. The exam supervisor will come to collect the envelope.

Physical constants and equations

Avogadro's constant:	$N_A = 6.022 \times 10^{23}\ \text{mol}^{-1}$
Universal gas constant:	$R = 8.314\ \text{J K}^{-1}\ \text{mol}^{-1}$
Speed of light:	$c = 2.998 \times 10^8\ \text{m s}^{-1}$
Planck's constant:	$h = 6.626 \times 10^{-34}\ \text{J s}$
Faraday constant:	$F = 9.6485 \times 10^4\ \text{C mol}^{-1}$
Standard pressure:	$p = 1\ \text{bar} = 10^5\ \text{Pa}$
Normal (atmospheric) pressure:	$p_{atm} = 1.01325 \times 10^5\ \text{Pa}$
Zero of the Celsius scale:	$273.15\ \text{K}$
Mass of electron:	$m_e = 9.109 \times 10^{-31}\ \text{kg}$
Unified atomic mass unit:	$u = 1.6605 \times 10^{-27}\ \text{kg}$
Ångström:	$1\ \text{Å} = 10^{-10}\ \text{m}$
Electronvolt:	$1\ \text{eV} = 1.602 \times 10^{-19}\ \text{J}$
Watt:	$1\ \text{W} = 1\ \text{J s}^{-1}$

Ideal gas equation:	$pV = nRT$
The first law of thermodynamics:	$\Delta U = q + W$
Power input for electrical device:	$P = U I$ where U is voltage and I electric current
Enthalpy:	$H = U + pV$
Gibbs free energy:	$G = H - TS$ $\Delta G^\circ = -RT \ln K = -zFE^\circ_{cell}$ $\Delta G = \Delta G^\circ + RT \ln Q$
Reaction quotient Q for a reaction $a\,\text{A} + b\,\text{B} \rightleftharpoons c\,\text{C} + d\,\text{D}$:	$Q = \dfrac{[\text{C}]^c[\text{D}]^d}{[\text{A}]^a[\text{B}]^b}$
Entropy change:	$\Delta S = \dfrac{q_{rev}}{T}$ where q_{rev} is heat for the reversible process
Heat change for temperature-independent c_m:	$\Delta q = n c_m \Delta T$ where c_m is molar heat capacity

Van 't Hoff equation:	$\dfrac{\mathrm{d}\ln K}{\mathrm{d}T} = \dfrac{\Delta_r H_m}{RT^2} \quad \Rightarrow \quad \ln\left(\dfrac{K_2}{K_1}\right) = -\dfrac{\Delta_r H_m}{R}\left(\dfrac{1}{T_2} - \dfrac{1}{T_1}\right)$
Henderson–Hasselbalch equation:	$pH = pK_a + \log\dfrac{[A^-]}{[HA]}$
Nernst–Peterson equation:	$E = E^\circ - \dfrac{RT}{zF}\ln Q$
Energy of a photon:	$E = \dfrac{hc}{\lambda}$
Relation between E in eV and in J:	$E/\mathrm{eV} = \dfrac{E/\mathrm{J}}{q_e/\mathrm{C}}$
Lambert–Beer law:	$A = \log\dfrac{I_0}{I} = \varepsilon l c$
Wavenumber:	$\tilde{\nu} = \dfrac{v}{c} = \dfrac{1}{2\pi c}\sqrt{\dfrac{k}{\mu}}$
Reduced mass μ for a molecule AX:	$\mu = \dfrac{m_A\, m_X}{m_A + m_X}$
Energy of harmonic oscillator:	$E_n = h v\left(n + \dfrac{1}{2}\right)$
Arrhenius equation:	$k = A\, e^{-\frac{E_a}{RT}}$

Rate laws in integrated form:

|	
Zero order:	$[A] = [A]_0 - kt$
First order:	$\ln[A] = \ln[A]_0 - kt$
Second order:	$\dfrac{1}{[A]} = \dfrac{1}{[A]_0} + kt$

Theoretical Problem 1	Question	1.1	1.2	1.3	1.4	1.5	1.6	Total
	Points	5	5	4	12	12	24	62
7% of the total	Score							

Problem 1. DNA

Palindromic sequences are an interesting class of DNA. In a palindromic double-stranded DNA (dsDNA) species, the sequence of one strand read in the $5' \rightarrow 3'$ direction matches the $5' \rightarrow 3'$ reading on the complementary strand. Hence, a palindromic dsDNA consists of two identical strands that are complementary to each other. An example is the so-called Drew–Dickerson dodecanucleotide (**1**):

5′-CGCGAATTCGCG-3′
| | | | | | | | | | | |
3′-GCGCTTAAGCGC-5′
(**1**)
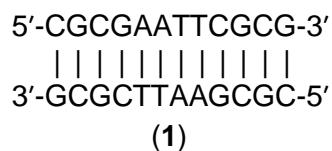
1.1 **CALCULATE** the number of different palindromic double-stranded DNA dodecanucleotides (i.e., dsDNA species with twelve base pairs) that exist.

1.2 **CALCULATE** the number of different palindromic double-stranded DNA undecanucleotides (i.e., dsDNA species with eleven base pairs) that exist.

The melting temperature of dsDNA, T_m is defined as the temperature at which 50% of the original amount of double stranded DNA dissociates into separate strands.

1.3 Consider the Drew–Dickerson dodecanucleotide (**1**). Assume that a G–C nucleobase pair contributes to the DNA duplex stability more than an A–T pair does. **CALCULATE** the probability that its T_m increases when a single randomly selected base pair is replaced by a G–C pair.

Let us analyze the thermodynamics of formation of double-stranded DNA from single strands, and its dependence on the length of the DNA and on the temperature. The equilibrium constant of association of single strands to form dsDNA differs for palindromic and non-palindromic dsDNA. A solution of dsDNA with the initial concentration of $c_{init} = 1.00 \times 10^{-6}$ mol / L was heated to T_m and equilibrium was reached.

1.4 **CALCULATE** the equilibrium constant of **association** of single strands at T_m for both non-palindromic and palindromic DNA.

Non-palindromic dsDNA Calculation:

$K =$

Palindromic dsDNA Calculation:

$K =$

The mean contributions to the Gibbs energy of association of two single strands to form dsDNA were estimated over a certain range of experimental conditions, and they amount to −6.07 kJ mol^{-1} per one G–C pair, and −1.30 kJ mol^{-1} per one A–T pair present in a dsDNA.

1.5 **CALCULATE** the number of base pairs there are in the **shortest** dsDNA oligonucleotide that has T_m above 330 K. At this T_m, consider the following values of the equilibrium constants of association of single strands to form a dsDNA: $K_{np} = 1.00 \times 10^6$ for a non-palindromic dsDNA, $K_p = 1.00 \times 10^5$ for a palindromic dsDNA. **TICK** whether the shortest oligonucleotide is palindromic or non-palindromic.


Calculation for the shortest number of base pairs:

The length needed for non-palindromic dsDNA:

The length needed for palindromic dsDNA:

The shortest oligonucleotide is
☐ palindromic (P)
☐ non-palindromic (NP).

Finally, let's leave the simplified idea of base pairs contributing individually to the **association** of DNA strands. The Gibbs energy of this process may be considered explicitly dependent on temperature. The dependence of the inverse T_m of the Drew–Dickerson dodecanucleotide (**1**) on the logarithm of the initial duplex concentration c_{init} is shown below. (***Note***: a standard concentration $c_0 = 1$ mol / L is introduced.)
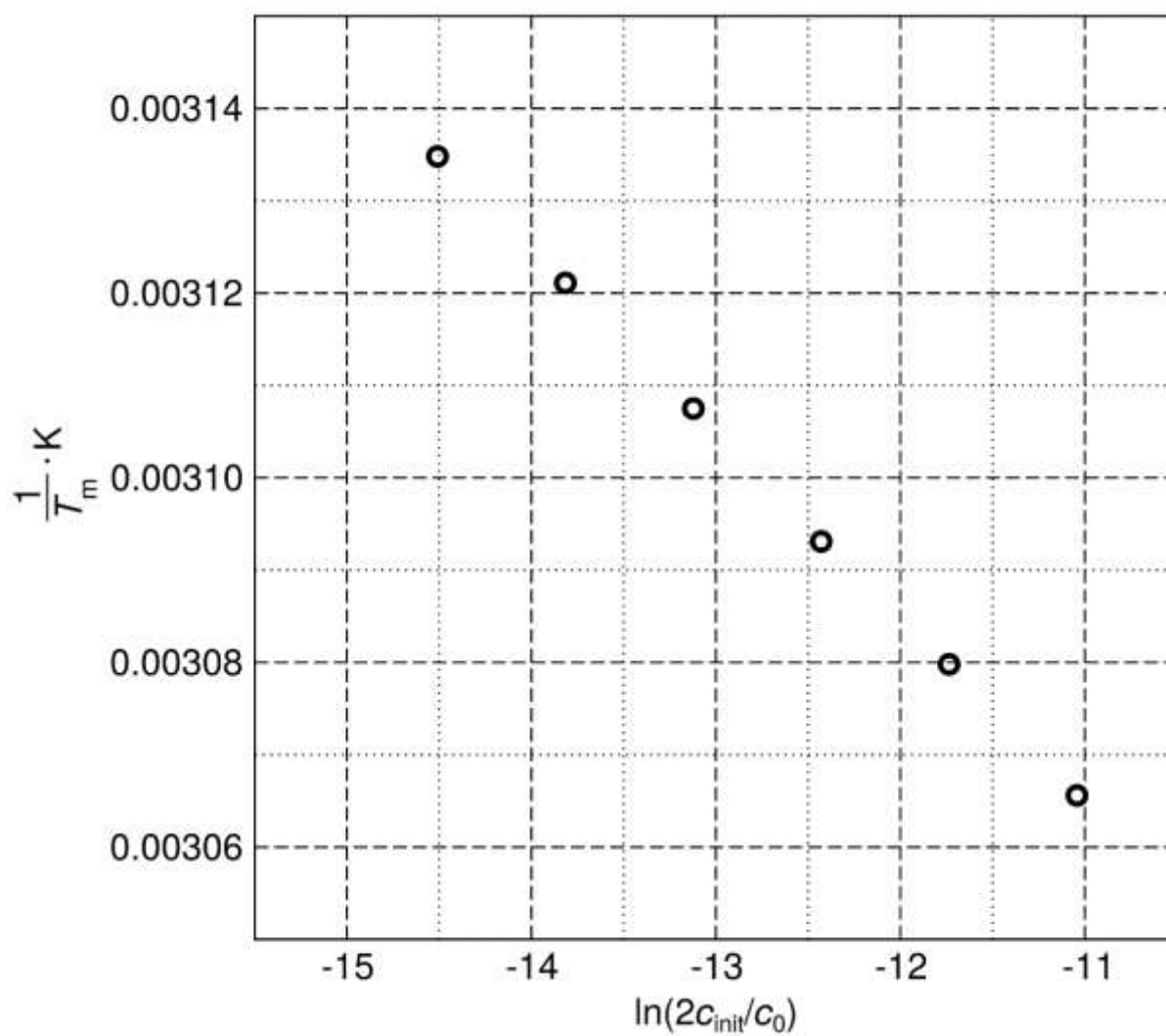
c_{init} (10^{-6} mol / L)	0.25	0.50	1.00	2.0	4.0	8.0
T_m (K)	319.0	320.4	321.8	323.3	324.7	326.2

1.6 **CALCULATE** the standard enthalpy $\Delta H°$ and the standard entropy $\Delta S°$ for the association of DNA single strands to form the palindromic double-stranded Drew–Dickerson dodecanucleotide (**1**). Assume that $\Delta H°$ and $\Delta S°$ do not vary with temperature.

Calculation:

Theoretical Problem 2	Question	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	**Total**
	Points	1	4	4	2	6	10	17	14	**58**
8% of the total	Score									

Problem 2. Repatriation of remains in the middle ages

At ambient temperatures, racemization is a slow reaction. As such, it can be used for dating biological objects and, moreover, for studying their thermal history. Let us take L-isoleucine (L-Ile) ((2S,3S)-2-amino-3-methylpentanoic acid) as an example. It isomerizes at the α-carbon and forms (2R,3S)-2-amino-3-methylpentanoic acid, also known as D-*allo*-isoleucine. As the configuration changes on only one of the two stereogenic centers, this process is called epimerization rather than racemization.

2.1 **TICK** all true statements.

☐ D-*allo*-isoleucine and L-isoleucine have the same values of specific optical rotation but they have different melting points.

☐ D-*allo*-isoleucine has an identical absolute value of specific optical rotation as L-isoleucine but the sign is opposite. The melting point is the same for both isomers.

☐ D-*allo*-isoleucine and L-isoleucine have different values of specific optical rotation but they have the same melting points.

☐ D-*allo*-isoleucine and L-isoleucine have different values of specific optical rotation and different melting points.
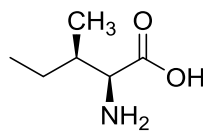
☐ D-*allo*-isoleucine is not optically active.

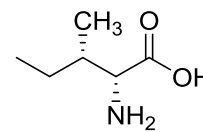**2.2** **ASSIGN** the absolute configurations for each stereoisomer of isoleucine.
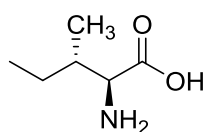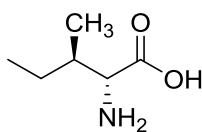
A   B   C   D

☐ 2S,3R (L-*allo*-isoleucine)

☐ 2R,3S (D-*allo*-isoleucine)

☐ 2S,3S (L-isoleucine)

☐ 2R,3R (D-isoleucine)

2.3 The equilibrium constant K_{ep} for L-isoleucine epimerization is 1.38 (at 374 K). If we set molar Gibbs free energy of L-isoleucine $G_m^\circ = 0$ kJ mol^{-1}, **DETERMINE** the Gibbs free energies for all structures **A–D** from question **2.2** at 374 K.

A	**kJ mol^{-1}**
B	**kJ mol^{-1}**
C	**kJ mol^{-1}**
D	**kJ mol^{-1}**

2.4 Taking into account stereoisomerism at all stereocenters, **CALCULATE** the maximum number of possible stereoisomers of the tripeptide Ile-Ile-Ile.

Number of stereoisomers:

At the start of the epimerization, we can neglect the reverse reaction. The epimerization then follows first-order kinetics:

$$\text{L-isoleucine} \xrightarrow{k_1} \text{D-}\textit{allo}\text{-isoleucine}$$
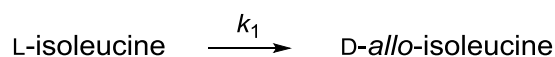
The value of the rate constant at 374 K is $k_1(374 \text{ K}) = 9.02 \times 10^{-5}$ h^{-1} and at 421 K it is $k_1(421 \text{ K}) = 1.18 \times 10^{-2}$ h^{-1}.

In the following calculation, abbreviate the concentration of L-isoleucine as [L] and D-*allo*-isoleucine as [D].

We can define a quantity *de* (diastereomeric excess):

$$de = \frac{[L] - [D]}{[L] + [D]} \times 100(\%).$$

2.5 Consider boiling L-isoleucine for 1,943 hours at 374 K. **CALCULATE** the value of *de* (with three significant figures) for L-isoleucine a) before boiling and b) after boiling.

a) **Before boiling calculation:**

de **(with three significant figures)=** %

b) **After boiling calculation:**
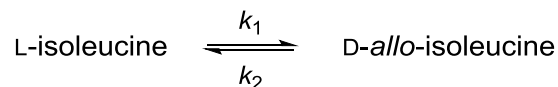
de **(with three significant figures)=** %

2.6 **CALCULATE** the time needed to convert 10% of L-isoleucine to D-*allo*-isoleucine at 298 K.

Calculation:

$t =$ **years**

In fact, the reverse reaction cannot be neglected. The correct kinetic scheme is expressed as

$$\text{L-isoleucine} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \text{D-}allo\text{-isoleucine}$$

Let us define the deviation of concentration from its equilibrium value $[L]_{eq}$ as:

$$x = [L] - [L]_{eq}$$

It is possible to derive that x evolves with time according to the following equation:

$$x = x(0) \times e^{-(k_1 + k_2)t}$$

where $x(0)$ is the deviation from equilibrium at $t = 0$ h.

2.7 A solution of 1.00 M L-isoleucine boils for 1,943 hours at 374 K. The rate constant for the forward reaction is $k_1(374\ K) = 9.02 \times 10^{-5}\ h^{-1}$, K_{ep} for L-isoleucine epimerization has the value of 1.38 (at 374 K). **CALCULATE** (with three significant figures) a) $[L]_{eq}$, b) diastereomeric excess (*de*) after boiling. In your calculation, abbreviate the concentration of L-isoleucine as [L] and D-*allo*-isoleucine as [D].
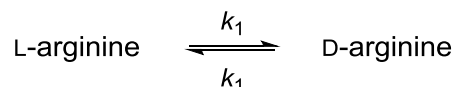
a) **Calculation**:

$[L]_{eq} =$ **mol / L**

b) Calculation:

de **(with three significant figures)=** **%**

Amino acids with a single chiral center undergo racemization, e.g. L-arginine racemizes:

$$\text{L-arginine} \xrightleftharpoons[k_1]{k_1} \text{D-arginine}$$

The time evolution of concentrations is governed by

$$\ln\frac{1 + \frac{[D]}{[L]}}{1 - \frac{[D]}{[L]}} = 2k_1 t + C$$

Here [D] and [L] are concentrations of D- and L-arginine at time t, k_1 is the rate constant, and the term C is set according to the initial concentrations.

Holy Roman Emperor Lothar III passed away during his journey to Sicily in 1137. To facilitate the repatriation of the remains, his body was boiled in water immediately after his death (373 K) for a certain time. The boiling time can be estimated with the aid of chemical kinetics. We know that the rate constant k_1 of arginine racemization within the protein at 373 K and pH = 7 has the value of 5.10×10^{-3} h^{-1}.

In order to analyze the isomeric composition of arginine in Lothar's bones, they were first hydrolyzed in a highly acidic environment for 4 hours at 383 K. The ratio of the optical isomers was $\frac{[D]}{[L]} = 0.090$. Lothar's wife Richenza was not boiled after her death. Her bones were hydrolyzed using the same procedure and in this case the ratio was $\frac{[D]}{[L]} = 0.059$. (**Note**: racemization also takes place during the hydrolysis, with the rate constant k_1', different from k_1).

2.8 **CALCULATE** the length of time Holy Roman Emperor Lothar III was boiled in water in 1137.

Note: The racemization of arginine is an extremely slow process at temperatures typically encountered in graves. As both bodies are only some 880 years old, we can neglect the natural racemization during this time.

Calculation:

$t_{boiling}$ =   h

Theoretical Problem 3	Question	3.1	3.2	3.3	3.4	3.5	3.6
	Points	2	6	7	3	7	8
	Score						
8% of the total	Question	3.7	3.8	3.9	3.10	3.11	**Total**
	Points	6	10	5	2	6	**62**
	Score						

Problem 3. Emerging electromobility

Modern transportation relies on burning fossil fuels. The efficiency of real combustion engines is inherently limited with a typical range between 20 and 40%.

3.1 **TICK** the factors that increase the efficiency of a heat engine:
☐ Increasing the friction in the mechanical parts of the engine
☐ Increasing the burning temperature of the fuel in the engine
☐ Narrowing the working temperature interval of the engine
☐ Increasing the working pressure of the gas

Hydrogen-based fuel cells are one way to improve engine efficiency in future vehicles.

3.2 The standard enthalpy of formation of liquid water is $\Delta_f H°(H_2O,l) = -285.84$ kJ mol^{-1}, and the standard combustion enthalpy of isooctane is $\Delta_c H°(C_8H_{18},l) = -5{,}065.08$ kJ mol^{-1} (both at 323.15 K). **CALCULATE** the values of specific (per unit of mass) combustion enthalpy at 323.15 K of pure liquid isooctane and pure gaseous hydrogen.

$\Delta_c H_s°(C_8H_{18}) =$

$\Delta_c H_s°(H_2) =$

3.3 **CALCULATE** the standard electromotive force (EMF) of a fuel cell using gaseous oxygen and hydrogen, both ideal gases at 100 kPa and 323.15 K, to produce liquid water. Use the following entropy data at 323.15 K: $S°(H_2O,l) = 70$ J K^{-1} mol^{-1}, $S°(H_2,g) = 131$ J K^{-1} mol^{-1}, $S°(O_2,g) = 205$ J K^{-1} mol^{-1}.

Calculations:

EMF =   **V**

3.4 **DETERMINE** the ideal thermodynamic efficiency (η) of a fuel cell producing liquid water at 353.15 K. At this temperature, the enthalpy of formation of water is $\Delta_fH°(H_2O,l) = -281.64$ kJ mol^{-1}, and the corresponding reaction Gibbs energy change is $\Delta_rG° = -225.85$ kJ mol^{-1}.

η =   **%**

3.5 A polymer membrane electrolysis facility operates at the voltage of 2.00 V and is powered by a 10.0 MW wind turbine plant which runs at full power from 10 pm to 6 am. The electrolysis yields 1,090 kg of pure hydrogen. **CALCULATE** the electrolysis yield defined as the mass of produced hydrogen divided by its theoretical produced mass.
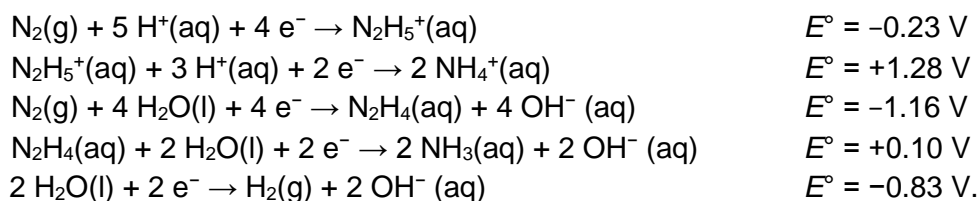
Calculations:

$\eta_{electrolysis} = $ _____ %

3.6 **CALCULATE** the mass of hydrogen required to drive the distance between Prague and Bratislava (330 km) at an average speed of 100 km h^{-1} in a car fitted with a 310 kW electric engine running at an average rate of 15% maximum power. Assume that the efficiency of the hydrogen cell producing electrical energy is 75%, the efficiency of the electric engine is 95%, and the Gibbs energy change for combustion of hydrogen fuel is $\Delta_r G$ = −226 kJ mol^{-1}.

Calculations:

m =   kg

The low efficiency of hydrogen production and the safety issues connected with its storage impede the spread of hydrogen-based transportation technology. Hydrazine (N_2H_4) fuel cells might be a suitable alternative.

The standard reduction potentials for aqueous hydrazine systems are:

$N_2(g) + 5\ H^+(aq) + 4\ e^- \rightarrow N_2H_5^+(aq)$	$E°$ = −0.23 V
$N_2H_5^+(aq) + 3\ H^+(aq) + 2\ e^- \rightarrow 2\ NH_4^+(aq)$	$E°$ = +1.28 V
$N_2(g) + 4\ H_2O(l) + 4\ e^- \rightarrow N_2H_4(aq) + 4\ OH^-\ (aq)$	$E°$ = −1.16 V
$N_2H_4(aq) + 2\ H_2O(l) + 2\ e^- \rightarrow 2\ NH_3(aq) + 2\ OH^-\ (aq)$	$E°$ = +0.10 V
$2\ H_2O(l) + 2\ e^- \rightarrow H_2(g) + 2\ OH^-\ (aq)$	$E°$ = −0.83 V.

3.7 **COMPLETE** the following Latimer diagrams with the forms of hydrazine and ammonia prevailing at the given conditions. **WRITE** the redox potential value for each arrow representing the electrochemical half-reaction. **SHOW** all the necessary calculations.

a) **Acidic environment (pH = 0)**

N_2
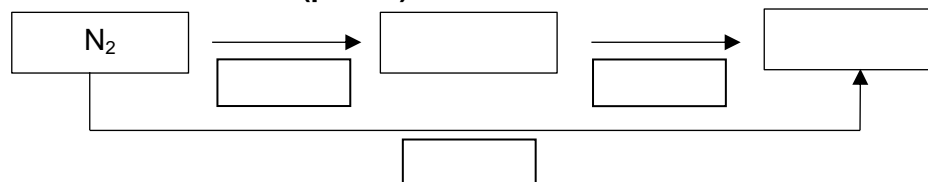
b) **Basic environment (pH = 14)**

N_2
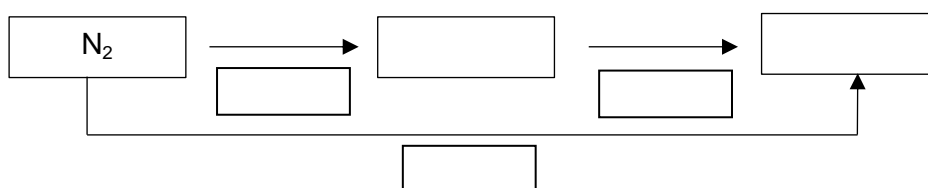
Calculations:

Due to the toxicity, odor, and its environmental impact, it is extremely unfavorable to produce ammonia in fuel cells.

3.8 **WRITE** the net reaction for the decomposition of hydrazine under basic conditions to (i) ammonia and nitrogen and (ii) nitrogen and hydrogen and **CALCULATE** the corresponding equilibrium constants at $T = 298.15$ K.

Equations for hydrazine decomposition:

   i.

   ii.

Calculations:
Hydrazine decomposition to NH_3 and N_2 in a basic environment:

$K =$

Hydrazine decomposition to H_2 and N_2 in a basic environment:

$K =$

Rechargeable lithium-based batteries are one alternative to fuel cells. Lithium-ion batteries commonly use graphite as one of the electrodes, where lithium clusters intercalate between the graphite sheets. The other electrode is made of lithium cobalt oxide, which can reversibly absorb lithium ions moving from one electrode to the other during the charge and discharge processes. The half-reactions relevant for the system can be formally written as:

$$(C)_n + Li^+ + e^- \rightarrow Li(C)_n \qquad\qquad E^\circ = -3.05 \text{ V},$$
$$CoO_2 + Li^+ + e^- \rightarrow LiCoO_2 \qquad\qquad E^\circ = +0.19 \text{ V}.$$
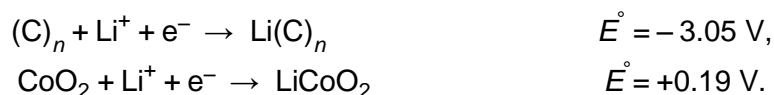
3.9 Using the formalism given above, **WRITE** the overall chemical reaction occurring in the battery during the **discharge** process. **WRITE** the oxidation states of the cobalt atom.

3.10 **TICK** the boxes indicating correct statements about the **discharge** of the lithium-based battery described in **3.9**:

$Li(C)_n$ electrode is the
☐ cathode
☐ anode

☐ because lithium ions are reduced there.
☐ because lithium atoms are oxidized there.

$LiCoO_2$ electrode is the
☐ cathode
☐ anode

☐ because cobalt ions are reduced there.
☐ because cobalt ions are oxidized there.

3.11 Assume that a C_6 unit, a CoO_2 unit, and Li atom form the active battery mass required to transfer one electron between the electrodes. Using the corresponding standard EMF, **CALCULATE** the theoretical specific reversible charge capacity (in mA h g^{-1}) and the energy density (in kW h kg^{-1}) of such a model lithium ion battery related to the whole active battery mass.

Calculations:

Charge capacity ($c_{q,s}$) =   **mA h g^{-1}**

Calculations:

Energy density (ρ_{el})=   **kW h kg^{-1}**

Theoretical Problem 4	Question	4.1	4.2	4.3	4.4	4.5	4.6	4.7	4.8	Total
	Points	2	5	1	2	7	2	3	2	24
6% of the total	Score									

# Problem 4. Column chromatography of radioactive copper

^{64}Cu for positron emission tomography is prepared by the bombardment of a zinc target with deuterium nuclei (further referred to as the activated target).

4.1 **WRITE** the balanced equation for ^{64}Zn bombardment with deuterium nuclei, giving ^{64}Cu. **WRITE** the corresponding atomic and mass numbers of all species, disregarding the charges.
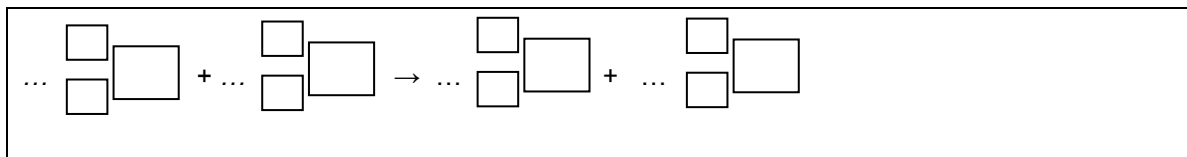
The activated target is dissolved in concentrated hydrochloric acid (HCl$_{(aq)}$) to give a mixture containing Cu^{2+} and Zn^{2+} ions and their respective chloro complexes.

4.2 **WRITE** the charges in the respective boxes:

$$Cu\square \quad [CuCl]\square \quad [CuCl_2]\square \quad [CuCl_3]\square \quad [CuCl_4]\square$$
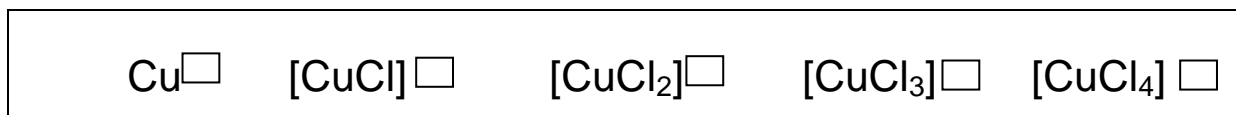
4.2 (continued) CALCULATE the mole fraction of negatively charged copper species with respect to the amount of copper prepared by zinc target activation. Assume $[Cl^-] = 4$ mol / L. For the overall complexation constants, β, see Table 1.

Table 1. Overall complexation constants *β* of Cu species (charges were omitted in the formulas).

$$\beta_i = \frac{[CuCl_i]}{[Cu] \cdot [Cl]^i}$$

	i in [CuCl*ᵢ*]			
	1	2	3	4
βᵢ	2.36	1.49	0.690	0.055

Calculation:

Mole fraction =

(answer with 2 digits after decimal point)

The mixture containing Cu^{2+} and Zn^{2+} ions and their respective chloro complexes was separated with an anion exchange resin. Dry resin in OH^- form was dispersed in water, and the suspension was transferred into a column. To occupy all sites with Cl^- ions (i.e. to obtain resin in a Cl^- form), the resin was washed with hydrochloric acid and then with deionized water to wash out all the unbound Cl^- ions.

4.3 Assume everything was initially at laboratory temperature before washing with hydrochloric acid. **TICK** which statement is true about the column temperature during the washing with hydrochloric acid.

☐ There is no temperature change.

☐ The temperature decreases.

☐ The temperature increases.

The mixture containing Cu^{2+} and Zn^{2+} ions and their respective chloro complexes was transferred onto the resin-filled column. Hydrochloric acid solution was used as the eluent.

Using a simple experimental formula, average elution properties can be calculated for both copper species and zinc species on the column.

The retention volume V_R (the mobile phase volume at which 50% of the compound has been eluted from the column) can be calculated as follows:

$$V_R = D_g \times m_{resin,dry,OH\ form} + V_0$$

4.4 Using average mass distribution coefficients D_g (D_g(Cu species) = 17.4 mL g^{-1}, D_g(Zn species) = 78.5 mL g^{-1}), **CALCULATE** the retention volumes V_R in mL for both the copper and the zinc species. The mass of dry resin in OH^- form ($m_{resin,dry,OH\ form}$) is 3.72 g, and the void volume of the resin in the column (V_0) is 4.93 mL.

Calculation:
V_R(Cu species) =   mL (answer with 1 digit after the decimal point)
V_R(Zn species) =   mL (answer with 0 digit after the decimal point)

If you cannot find the answer, use a V_R(Cu species) of 49.9 mL and a V_R(Zn species) of 324 mL in further calculations.

Separation of two sets of species, **A** and **B**, can be considered complete if

$$V_{0.001}(A) - V_{0.999}(B) > 10 V_c$$

where $V_{0.001}$ is the mobile phase volume at which 0.1% of **A** has been eluted from the column, and $V_{0.999}$ is the mobile phase volume at which 99.9% of **B** has been eluted from the column.

$$V_{0.001}(A) = V_R(A) \times \left(1 - 6.91 \sqrt{d_p/L_c}\right)$$

$$V_{0.001}(B) = V_R(B) \times \left(1 - 6.91 \sqrt{d_p/L_c}\right)$$

$$V_{0.999}(B) = 2 V_R(B) - V_{0.001}(B)$$

4.5 **CALCULATE** and **TICK** whether the copper species was completely separated from the zinc species. The volume of the swollen resin in the column (V_c) is 10.21 mL, the resin particle diameter (d_p) is 0.125 mm, and the height of the wet resin in a swollen state in the column (L_c) is 13.0 cm.

$V_{0.001}(A) = \qquad$ mL

$V_{0.999}(B) = \qquad$ mL

It is possible to separate copper species from zinc species.

☐ **True**   ☐ **False**

4.6 The mass fraction of nitrogen in the dry resin was 4.83%. **CALCULATE** the theoretical value of the total ion exchange mass capacity of the dry resin used in this problem, $Q_{m,theor}$, in mmol g^{-1}. Assume tetraalkylammonium groups are the only ones responsible for ion exchange of the resin, and no other nitrogen containing groups are present.

$Q_{m,theor} = \qquad$ mmol g^{-1} **(answer with 2 digits after decimal point)**

If you cannot determine the answer, use a $Q_{m,theor}$ of 4.83 mmol g^{-1} for further calculations.

In reality, not all tetraalkylammonium groups are involved in the ion exchange. To determine the total ion exchange volume capacity, Q_v, a column filled with 3.72 g of dry resin converted to the Cl$^-$ form was washed with an excess of sodium sulfate solution. The eluent was collected in a 500 mL volumetric flask, which was then filled with water to the mark. An aliquot of 100 mL was potentiometrically titrated with 0.1027 mol / L silver nitrate. The silver nitrate solution volume at the equivalence point was 22.20 mL. The volume of the swollen resin in the column (V_c) is 10.21 mL.

4.7 **CALCULATE** the volume capacity, Q_v, of the swollen resin in mmol of active tetraalkylammonium groups per mL of the swollen resin.

$Q_v =$ **mmol / mL (answer with 2 digits after decimal point)**

If you cannot find the answer, use a Q_v of 1.00 mmol / mL for further calculations.

4.8 **CALCULATE** the mole fraction (x) of the tetraalkylammonium groups actively involved in the ion exchange.

$x =$ **(answer with 3 digits after decimal point)**

	Question	5.1	5.2	5.3	5.4	5.5	5.6	5.7	5.8	5.9
Theoretical Problem 5	Points	3	3	1	5	3	2	4	1	2
	Score									
8% of the total	Question	5.10	5.11	5.12	5.13	5.14	5.15	5.16	5.17	**Total**
	Points	5	7	3	2	6	1	1	1	**50**
	Score									

Problem 5. Bohemian garnet

Bohemian garnet (pyrope) is a famous Czech blood-colored semi-precious stone. The chemical composition of natural garnets is expressed by the general stoichiometric formula of $A_3B_2(SiO_4)_3$, where A^{II} is a divalent cation and B^{III} is a trivalent cation. Garnets have a cubic unit cell that contain 8 formula units. The structure comprises 3 types of polyhedra: the A^{II} cation occupies a dodecahedral position (it is surrounded by eight O atoms), the B^{III} cation occupies an octahedral position (it is surrounded by six O atoms) and Si^{IV} is surrounded by four O atoms arranged into a tetrahedron.

The most common garnet mineral is almandine with the formula of $Fe_3Al_2(SiO_4)_3$. Its unit cell parameter is $a = 11.50$ Å.

5.1 **CALCULATE** the theoretical density of almandine.

$\rho =$ **g / mL**

Bohemian garnet has a host material composition of $Mg_3Al_2(SiO_4)_3$. While pure $Mg_3Al_2(SiO_4)_3$ is colorless, the color of natural garnets comes from chromophores – transition metal cations that substitute the host material cations. The red color of the Bohemian garnet comes from trace amounts of Cr^{III} ions in the octahedral sites and Fe^{II} ions in the dodecahedral sites.

5.2 **DRAW** the splitting diagram for the $[Cr^{III}O_6]^{oct}$ d-orbitals and **POPULATE** with electrons.

5.3 **IDENTIFY** the 1st row transition metal(s) whose trivalent cation(s) M^{III}, when placed in an **octahedral** position, is/are diamagnetic in the low-spin arrangement and paramagnetic in the high-spin arrangement.

5.4 The figure below shows d-orbital splitting in the dodecahedral crystal field. **POPULATE** the orbitals with electrons for the $[Fe^{II}O_8]^{dod}$ chromophore for both existing arrangements.

a) high-spin arrangement   b) low-spin arrangement
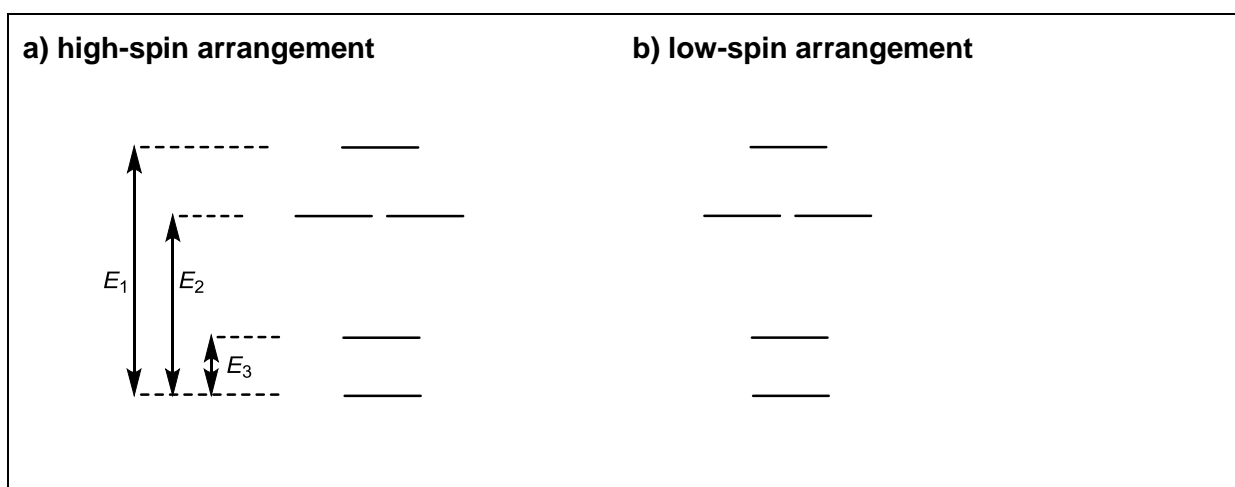
5.5 **DERIVE** the inequalities (e.g. $P < E_1 + E_2 + E_3$) for the pairing energy (P) magnitude in relation to energies E_1, E_2 and E_3 for both arrangements.

a) high-spin arrangement: P

b) low-spin arrangement: P

5.6 Assuming that $P > E_3$, **IDENTIFY** the 1st row transition metal(s) whose divalent cation M^{II}, when placed in dodecahedral position, is/are diamagnetic in the low-spin arrangement and paramagnetic in the high-spin arrangement.

The figures below show simplified absorption spectra of four colored minerals – blood-colored Bohemian garnet, green uvarovite, blue sapphire and yellow-orange citrine.
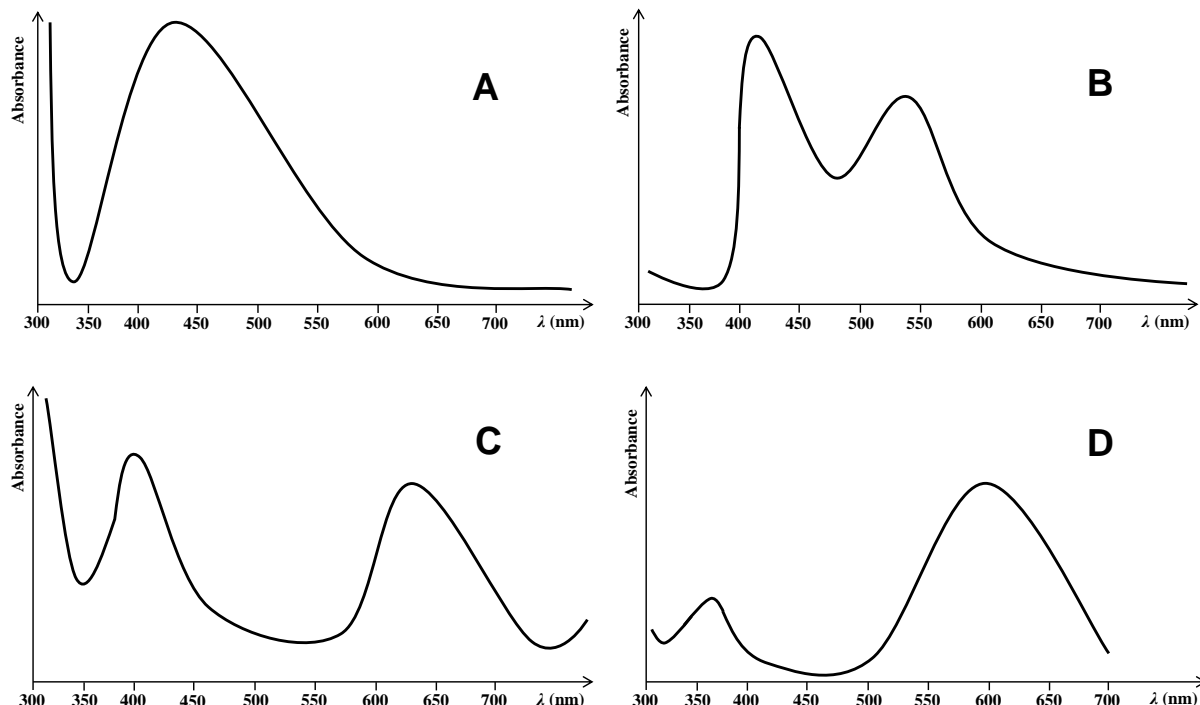
5.7 MATCH the spectra with the minerals.

Bohemian garnet:	Sapphire:
Uvarovite:	Citrine:

5.8 TICK how the Bohemian garnet appears when illuminated with monochromatic blue-green light.

☐ Red	☐ Blue	☐ Yellow-orange	☐ Black
☐ Yellow	☐ Blue-green	☐ Violet	☐ White

Andradite is another garnet mineral; its host material composition is $Ca_3Fe_2(SiO_4)_3$. A double cation substitution – Ti^{IV} for Fe^{III} in the octahedral position and Fe^{III} for Si^{IV} in the tetrahedral position – gives rise to black schorlomite. Its chemical composition can be expressed as $Ca_3[Fe,Ti]_2^{oct}([Si,Fe]^{tet}O_4)_3$.

5.9 CALCULATE the percentage of Si^{IV} ions in a sample of schorlomite that must be substituted with Fe^{III}, if we know that 5% of Fe^{III} ions in octahedral position are substituted with Ti^{IV}.

p =   **%**

The color of the mineral is caused by two chromophores: $[Fe^{III}O_6]^{oct}$ and $[Fe^{III}O_4]^{tet}$. The central ions of both chromophores have equal number of unpaired electrons.

5.10 DRAW the d-orbital splitting diagrams for both chromophores and **POPULATE** with electrons.

$[Fe^{III}O_6]^{oct}$:   **$[Fe^{III}O_4]^{tet}$:**

Tetrahedral field causes a smaller splitting than the octahedral field ($\Delta_{tet} = \frac{4}{9} \Delta_{oct}$). Surprisingly for the Fe^{III} ion, the energy of the first d–d transition (although very weak) for the octahedral chromophore is smaller ($11,000$ cm^{-1}) than for the tetrahedral one ($22,000$ cm^{-1}).

5.11 CALCULATE the size of pairing energy (P) and the sizes of Δ_{oct} and Δ_{tet} splitting. Assume that the pairing energy is equal in both chromophores.

P =   **cm^{-1}**

Δ_{oct} =   **cm^{-1}**

Δ_{tet} =   **cm^{-1}**

Synthetic garnet YAG (YttriumAluminiumGarnet), used in optoelectronics, has the composition of $Y_3Al_5O_{12}$. Its structure is derived from the general garnet structure $A_3B_2(SiO_4)_3$ by placing the ions Y^{III} and Al^{III} to the A, B and Si positions.

5.12 Based on your knowledge of the relative ionic radii, **DETERMINE** which cation occupies each position.

A:	B:	Si:

5.13 For use in LED technology, YAG is doped with Ce^{III}. **DETERMINE** the values of x and y in the formula of YAG in which 5% of yttrium atoms are substituted with cerium.

$Y_xCe_yAl_5O_{12}$

$x =$ $y =$

If you cannot calculate the answer, use an x value of 2.25 and a y value of 0.75 for future calculations.

5.14 Ce^{III}-doped YAG is prepared by annealing a mixture of Y_2O_3, Al_2O_3 and CeO_2 in an H_2 atmosphere. Using the formula from **5.13**, **WRITE** a balanced equation for this reaction with the smallest whole-number stoichiometric coefficients.

Doping the YAG structure with rare earth ions enables the production of lasers with emission wavelengths ranging from the UV to the mid-IR region. In the scheme below, simplified f–f energy transitions for selected rare earth ions are shown.
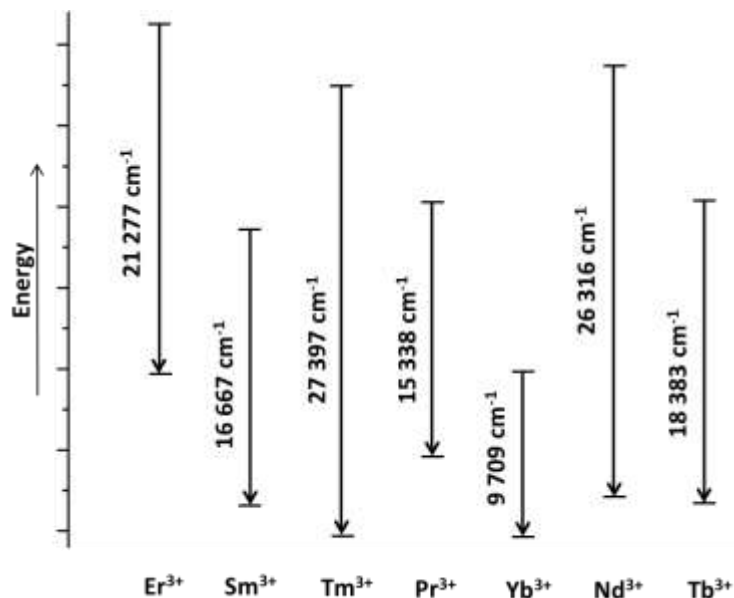
5.15 TICK which cation has a transition that corresponds to blue light emission.

□ Er^{3+}	□ Sm^{3+}	□ Tm^{3+}	□ Pr^{3+}
□ Yb^{3+}	□ Nd^{3+}	□ Tb^{3+}	

5.16 CALCULATE the emission wavelength of this light.

$λ =$ **nm**

5.17 According to legend, Noah used a stick with a garnet stone for illumination during his voyage. Assuming only the photoluminescence effect, **TICK** the color of the laser light emitted from his stick if the stone were the blood-colored Bohemian garnet.

□ Red	□ Blue	□ Yellow-orange	□ Black
□ Yellow	□ Blue-green	□ Violet	□ White

Theoretical Problem 6	Question	6.1	6.2	6.3	6.4	6.5	6.6	6.7	6.8	**Total**
	Points	18	4	8	3	4	12	16	3	**68**
7% of the total	Score									

Problem 6. Let's go 'shrooming!

Mushrooming is a Czech and Slovak traditional pastime. While some of our mushroom species are edible, some are inedible or even poisonous.

Inky cap (*Coprinopsis atramentaria*) is considered edible and delicious. It contains a natural compound called coprine (**E**), which can be easily synthesized from ethyl 3-chloropropanoate (**1**).
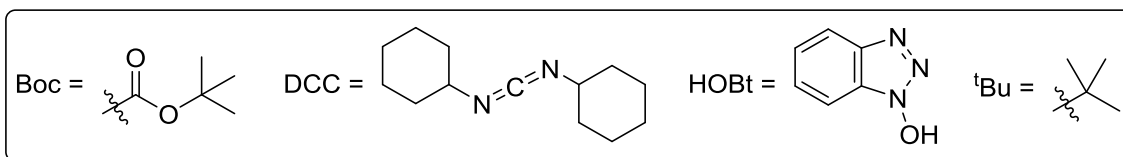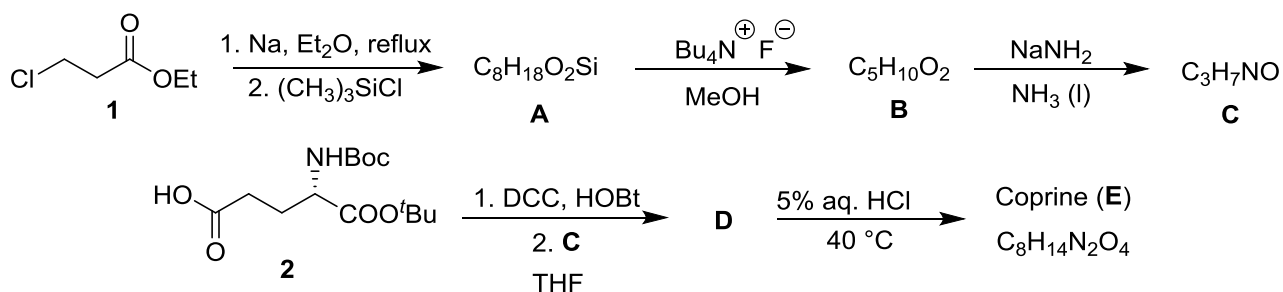
6.1 **DRAW** the structures of compounds **A**–**E** including stereochemistry when necessary. *Hint: The first reaction affording compound A proceeds via an organometallic compound which then cyclizes.*

A	B	C

D	E

In the human body, coprine undergoes hydrolysis to L-glutamic acid (**3**) and compounds **C** and **4**, which are responsible for its adverse side-effects. They inhibit the enzyme acetaldehyde dehydrogenase, which is involved in the metabolism of alcohol. When the enzyme is inhibited, acetaldehyde formed by alcohol dehydrogenase accumulates in the body, causing strong symptoms of hangover (the so-called "antabuse effect"). The active site of the enzyme contains a cysteine SH group, which is blocked either by compound **C** or **4**.
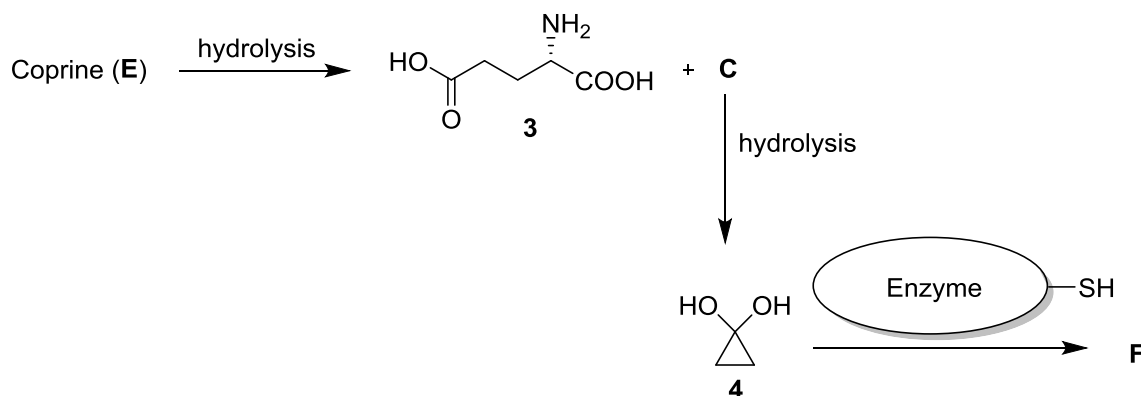

Enzyme = acetaldehyde dehydrogenase

6.2 Using the pictogram for acetaldehyde dehydrogenase above, **DRAW** the structure **F** of the enzyme inhibited by compound **4**.

F
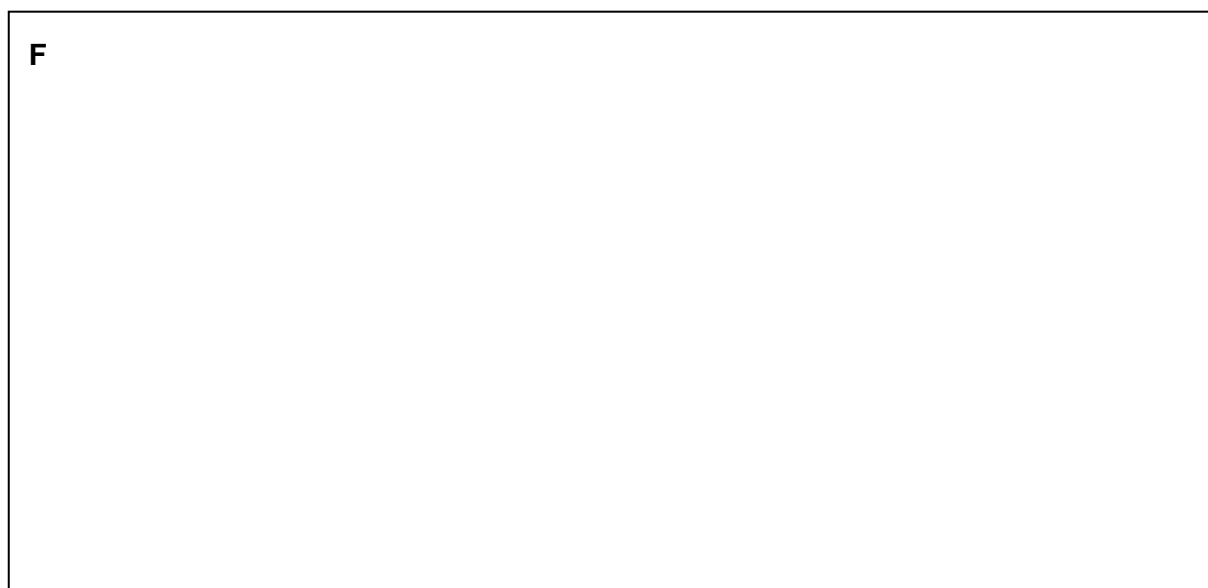
The antabuse effect got its name from antabuse (**5**), the most well-known drug for alcohol-addiction treatment. This drug can be synthesized according to the following scheme.
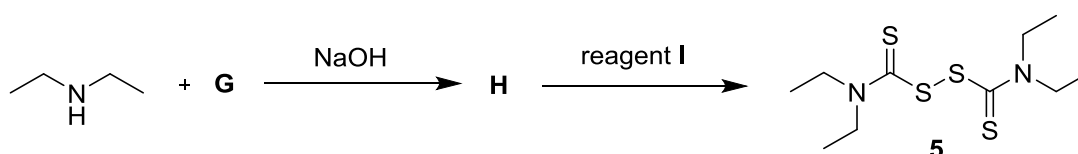
6.3 **DRAW** the structures of compounds **G** and **H**. *Hint: Compound **H** contains five carbon atoms.*

G	H

6.4 **TICK** all possible reagents from the following list which could be used as reagent **I**.

☐ *m*-chloroperbenzoic acid (*m*CPBA)   ☐ diluted H_2O_2

☐ Zn/CH_3COOH ☐ $NaBH_4$

☐ I_2 ☐ hot concentrated H_2SO_4

☐ K_2CO_3, H_2O ☐ $AlCl_3$

Antabuse inhibits acetaldehyde dehydrogenase in a similar way to compounds **C** and **4**.
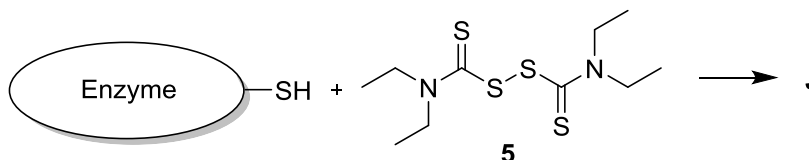
Enzyme = acetaldehyde dehydrogenase

6.5 Using the pictogram for acetaldehyde dehydrogenase above, **DRAW** the structure **J** of the enzyme inhibited by antabuse (**5**). *Hint: Three sulfur atoms should be in the structure.*

J

False morel (*Gyromitra esculenta*) is another interesting mushroom. Although it was considered edible in the past (*esculentus* means edible in Latin), there is clear evidence that this mushroom is poisonous due to the content of gyromitrin (**M**). This natural compound can be prepared from *N*-methylhydrazine (**6**):
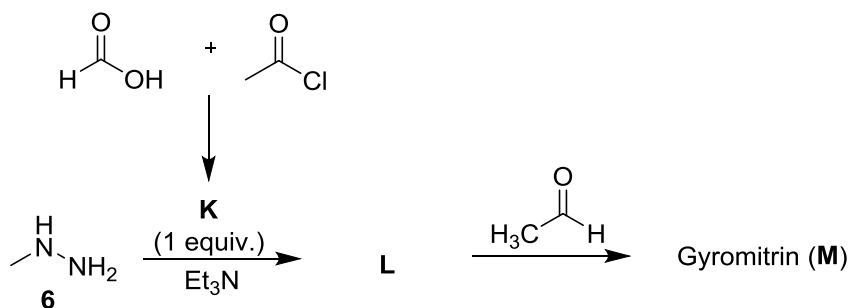
6.6 **DRAW** the structures of compounds **K**–**M**.

K	L	M

In the human body, gyromitrin (**M**) is hydrolyzed to *N*-methylhydrazine (**6**), which is strongly hepatotoxic. Gyromitrin (**M**) hydrolysis occurs as soon as it enters the acidic environment of the human stomach where both its amide and imine groups are hydrolyzed.

Let us focus on the hydrolysis of the amide moiety within the gyromitrin molecule. The vibrational wavenumber of the stretching mode of the relevant C−N bond is 1,293.0 cm^{-1} and the potential energy surface does not significantly alter its shape with isotope substitution effect.

6.7 **CALCULATE** the highest possible hypothetical kinetic isotope effect at the temperature of the human body, 37 °C, for the given hydrolysis reaction assuming that both relevant nitrogen and carbon atoms were simultaneously substituted, ^{14}N with the ^{15}N isotope and ^{12}C with the ^{13}C isotope. Consider that only the zero point vibrational energy affects the rate constants. Assume that the molar masses of all isotopes are integers. In all further steps consider five significant figures.

6.8 After making these isotopic changes, the rates of hydrolysis are not significantly different. **TICK** which of the following is <u>most likely</u> the rate determining step.

☐ Nucleophilic attack of water on a protonated amidic moiety

☐ C−N bond cleavage

☐ Protonation of the gyromitrin molecule

Theoretical Problem 7	Question	7.1	7.2	7.3	7.4	7.5	7.6	Total
	Points	10	6	15	9	11	6	57
7% of the total	Score							

Problem 7. Cidofovir

Cidofovir (**1**), originally designed and prepared by the group of Professor Holy in former Czechoslovakia, is a nucleotide analogue with antiviral activity. It is used to treat viral infections, mostly in patients with AIDS.
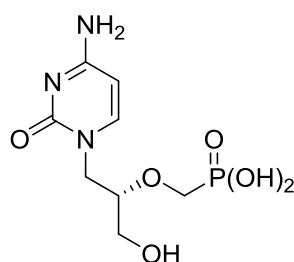
Cidofovir (**1**)

The key intermediate in the synthesis of cidofovir is optically pure diol **2**, which can be prepared from L-mannitol (**3**).
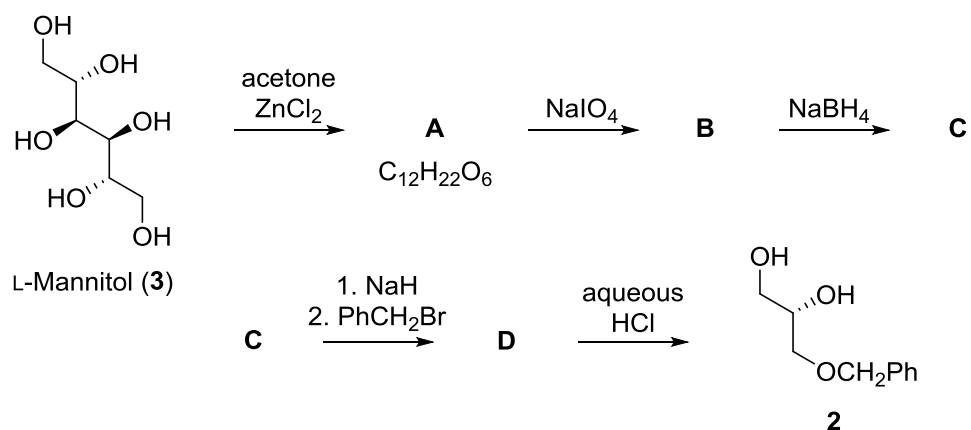
7.1 **DRAW** the structures of compounds **A–D**, including stereochemistry. One molecule of **A** produces two molecules of **B**.

A ($C_{12}H_{22}O_6$)	B
C	**D**

7.2 **DRAW** the structures of **all** alternative stereoisomers of compound **3** which could be used in the same reaction sequence to afford **only** the same product **2**.
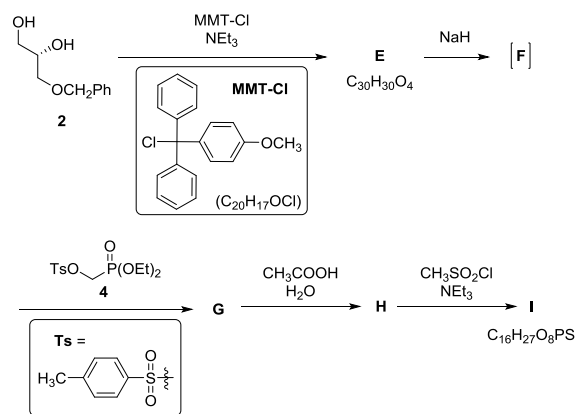
Relevant stereoisomers of compound 3
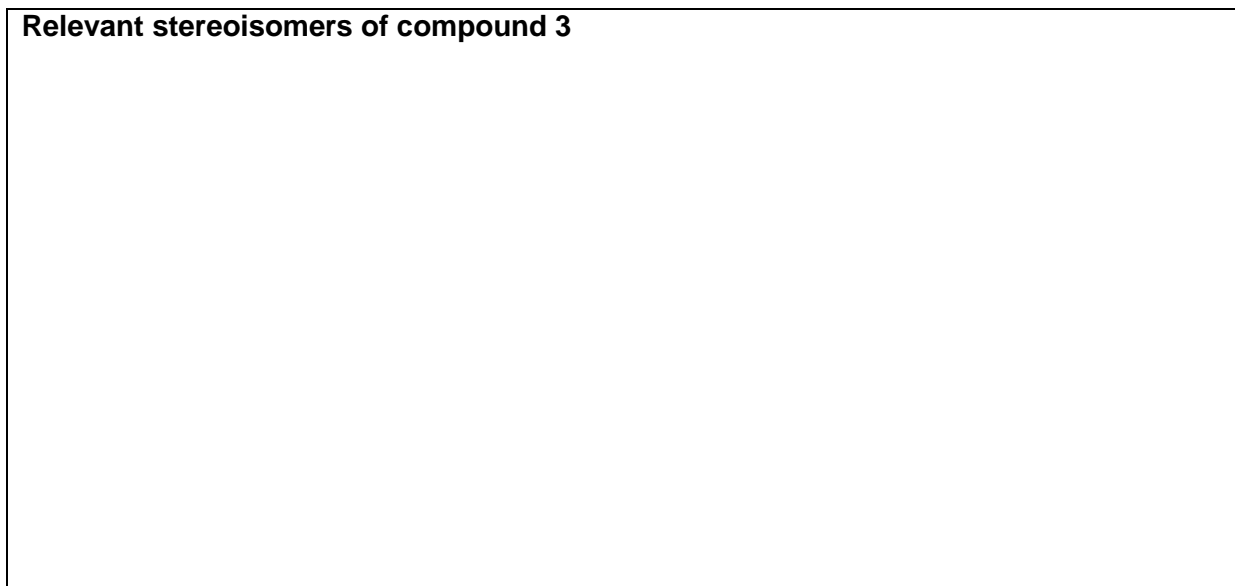
Diol **2** is further modified to provide compound **I**. The synthesis of phosphonate **4** used to convert compound **F** to **G** will be discussed later.
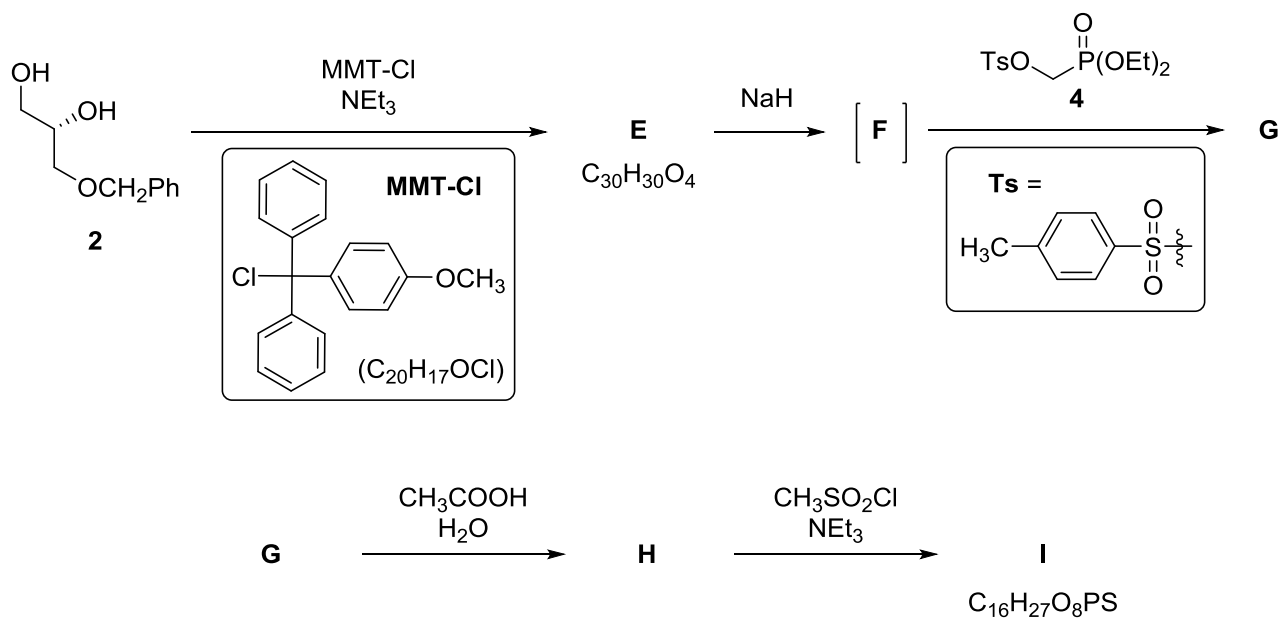
7.3 **DRAW** the structures of compounds **E–I**, including stereochemistry. Use the abbreviation MMT for the (4-methoxyphenyl)diphenylmethyl group.

The same scheme as on the previous page, for easier reference.	**E** **(C$_{30}$H$_{30}$O$_4$)**

F	**G**

H	**I** **(C$_{16}$H$_{27}$O$_8$PS)**

Phosphonate **4** can be prepared according to the following scheme:
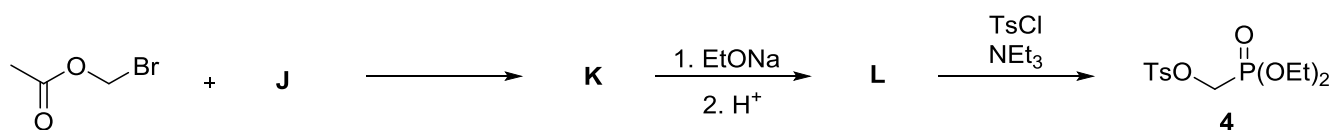
7.4 **DRAW** the structures of compounds **J–L**.

J	K
L	

The reaction of **I** (from question 7.3) with cytosine (**5**) leads to a 3:1 mixture of isomeric compounds **M** and **N**. The formation of these two products may be understood by realizing that cytosine (**5**) can also exist as an aromatic tautomer **P**. The reaction of **M** with cyclohexa-1,4-diene and palladium hydroxide on carbon leads to compound **O**. The phosphonic ester moiety in compound **O** reacts with bromotrimethylsilane to provide cidofovir (**1**).
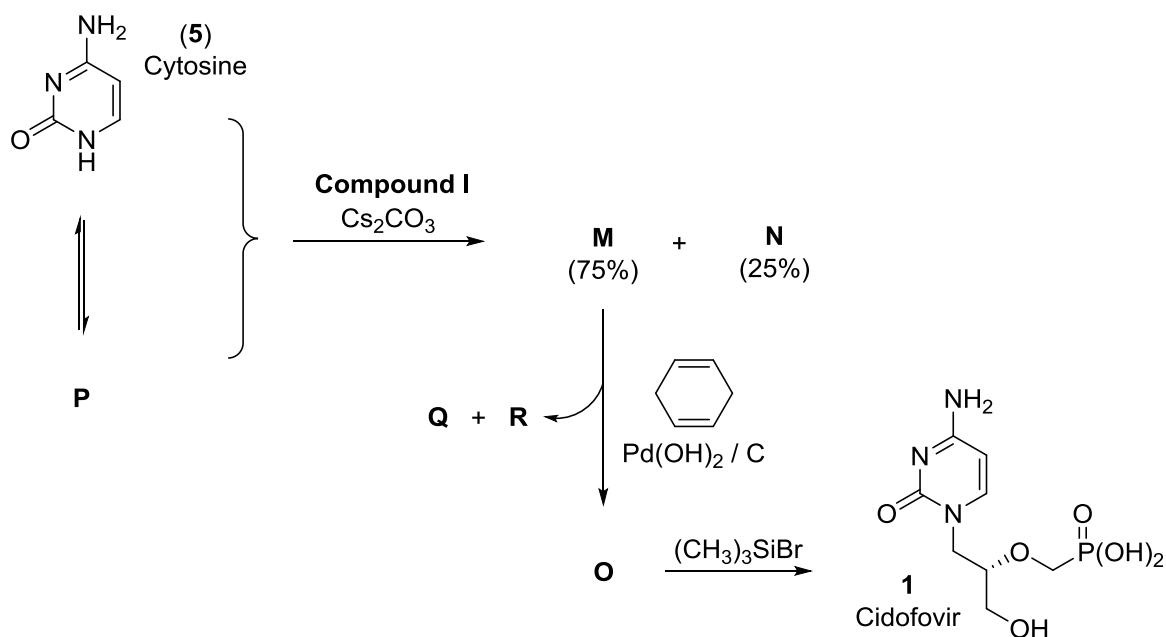
7.5 **DRAW** the two isomers, **M** and **N**; compound **O**; and aromatic tautomer **P** of cysteine **(5)**. For **M**, **N**, and **O**, include all appropriate stereochemistry. Transformation of **M** to **O** is the removal of a protecting group.

M (75%)	N (25%)

O	P

7.6 **DRAW** the structures of the two simple organic side products **Q** and **R** formed during the conversion of **M** to **O**.

Q (from cyclohexadiene)	R (from the protecting group)

Theoretical Problem 8	Question	8.1	8.2	8.3	8.4	8.5	8.6	8.7	8.8	Total
	Points	14	14	2	16	6	8	9	6	75
9% of the total	Score									

Problem 8. Caryophyllene

β-Caryophyllene (**3**) is a naturally occurring sesquiterpene present in the clove tree and in some traditional Czech and Slovak plants, such as the hop plant or small-leaf linden.

The synthesis of β-caryophyllene starts from a single isomer of dienone **A**. The reaction of **A** with silyl ketene acetal **1** followed by immediate reduction and aqueous work-up affords ketone **2**. This intermediate then undergoes further reaction with tosyl chloride, providing **B**. Basic cyclization of this compound affords **C**. Finally, the reaction of **C** with ylide **D** provides β-caryophyllene.
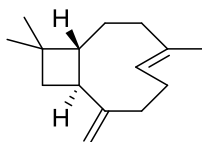

β-Caryophyllene (**3**)

β-Caryophyllene (3)
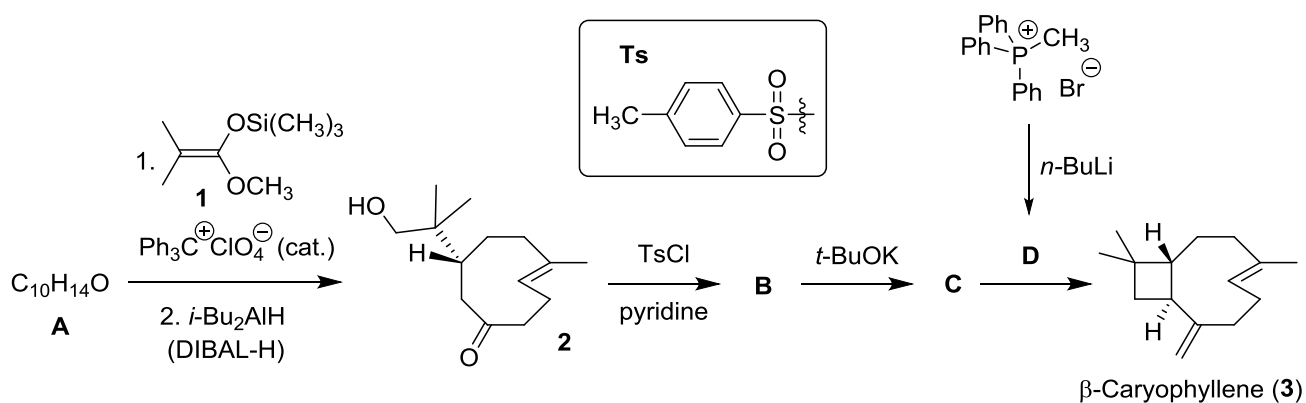
8.1 **DRAW** the structures of compounds **A–D**, including the appropriate stereochemistry. *Hint: In transformation **A** → **2**, the silyl ketene acetal acts as a nucleophile.*

A (C₁₀H₁₄O)	B
C	D

One of the double bonds in **2** as well as in **3** has a *trans* configuration and the scaffold is stable enough due to the large ring size. *trans*-Cyclooctene (**4**) is the smallest ring that can accommodate a *trans* double bond. It can be prepared according to the following scheme:
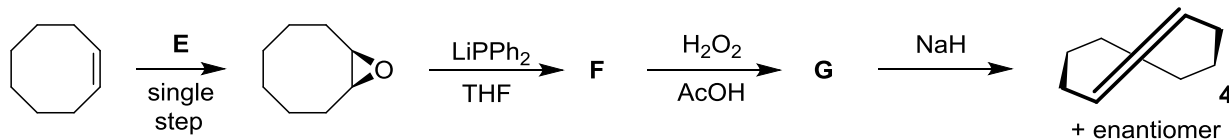

8.2   **DRAW** the structure of reagent **E** and intermediates **F** and **G**, including the appropriate stereochemistry. For **F** and **G**, **TICK** the box indicating the stereochemical outcome.

| E	F
	☐ achiral
	☐ single enantiomer
	☐ racemic mixture
	☐ mixture of diastereoisomers
G	
☐ achiral	
☐ single enantiomer	
☐ racemic mixture	
☐ mixture of diastereoisomers	

8.3 DRAW the structure of the enantiomer of cycloalkene **4**.
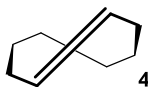
Enantiomer of 4

The two double bonds in β-caryophyllene display different reactivity: the double bond in the ring (endocyclic) is more reactive than the other one (exocyclic) due to ring strain.
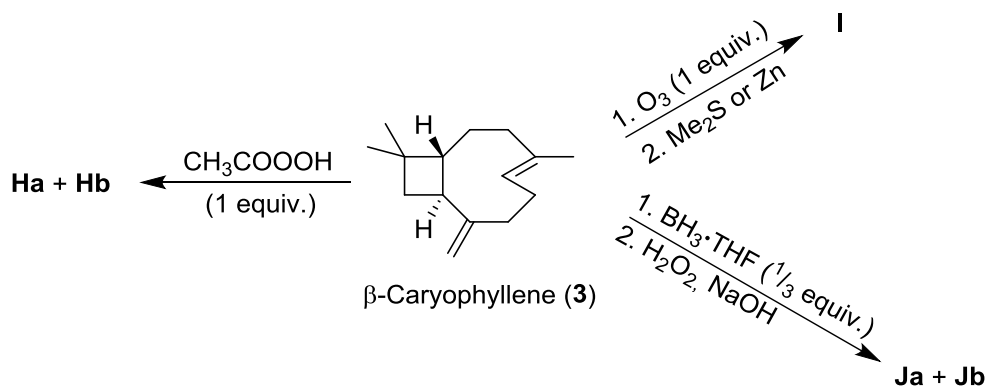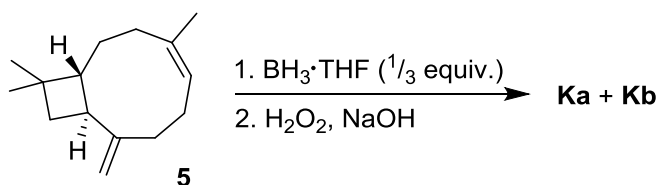
8.4 **DRAW** the structures of compounds **Ha + Hb**, **I** and **Ja + Jb**, including all appropriate stereochemistry. *Hint: **Ha + Hb** and **Ja + Jb** are pairs of diastereomers.*

Ha + Hb
I

Ja + Jb

Interestingly, the reactivity of the double bonds is reversed when isocaryophyllene (**5**) is used instead of β-caryophyllene (**3**).
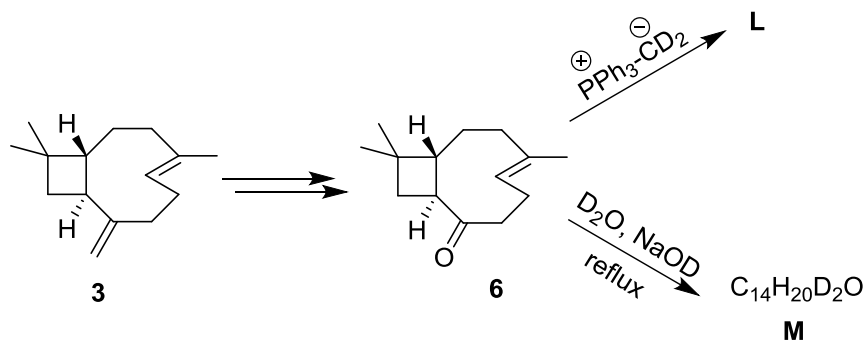

1. BH₃·THF (¹/₃ equiv.)
2. H₂O₂, NaOH

Ka + Kb

5

8.5 **DRAW** the structures of compounds **Ka** and **Kb**. *Hint: **Ka** + **Kb** are a pair of diastereomers.*

Ka + Kb

Isotopically labelled compounds are invaluable tools for reaction mechanism investigation, structure determination, and mass or NMR spectroscopy studies. Let us have a look at the synthesis of some labelled analogues of β-caryophyllene.

8.6 **DRAW** the structures of compounds **L** and **M**, including all appropriate stereochemistry.

L	M (C$_{14}$H$_{20}$D$_2$O)

β-Caryophyllene (**3**) undergoes acid-catalyzed cyclization, which leads to a complex mixture of products. Among them, the pair of diastereomers **Na + Nb** and the pair of diastereomers **7a + 7b** are the most abundant. The reaction starts with protonation of the more reactive internal double bond affording cation **O**. This cyclizes without the cleavage of a carbon-carbon single bond to yield diastereomeric tricyclic cations **Pa** and **Pb**, which undergo hydration to give the target alcohols **Na** and **Nb**. Alternatively, the cations **Pa** and **Pb** rearrange with the cleavage of a carbon-carbon single bond to cations **Qa** and **Qb**, which deprotonate to compounds **7a** and **7b**.
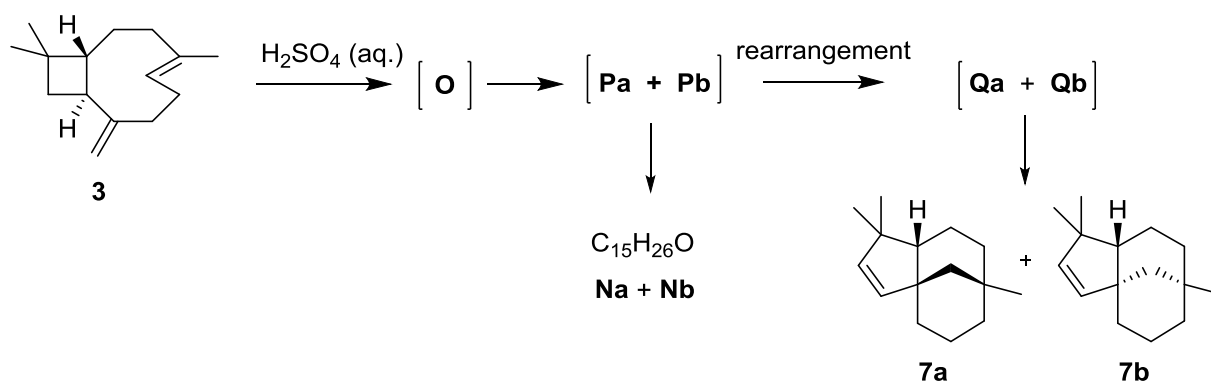
8.7 **DRAW** the structures of the **three** intermediates **O**, **Pa**, **Qa** leading to the diastereomer **7a**, including all appropriate stereochemistry.

O	Pa
Qa	

8.8 DRAW the structures of diastereomers **Na** + **Nb**.

Na + Nb   (C$_{15}$H$_{26}$O)