THEORETICAL PROBLEMS

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<th>Country:</th>
<th>New Zealand</th>
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<td>Name as in passport:</td>
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<td>Student code:</td>
<td>NZL-2</td>
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<td>English</td>
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Instructions

- This theoretical exam booklet contains 57 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 designed 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 designed 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 by ½ minute or longer 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

For all calculations make sure you show your working! 😋

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: \( p_{\text{atm}} = 1.01325 \times 10^5 \text{ Pa} \)

Zero of the Celsius scale: 273.15 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 Å = 10\(^{-10}\) m

Electronvolt: 1 eV = 1.602 \times 10^{-19} \text{ J}

Watt: 1 W = 1 J s\(^{-1}\)

Ideal gas equation: \( pV = nRT \)

The first law of thermodynamics: \( \Delta U = q + W \)

Power input for electrical device: \( P = UI \)

where \( U \) is voltage and \( I \) electric current

Enthalpy: \( H = U + pV \)

Gibbs free energy: \( G = H - TS \)

\( \Delta G^0 = -RT \ln K = -zF_{\text{cell}}E_{\text{cell}} \)

\( \Delta G = \Delta G^0 + RT \ln Q \)

Reaction quotient \( Q \)

for a reaction \( a A + b B \rightleftharpoons c C + d D \):

\[ Q = \frac{[C]^c[D]^d}{[A]^a[B]^b} \]

Entropy change:

\( \Delta S = \frac{q_{\text{rev}}}{T} \)

where \( q_{\text{rev}} \) is heat for the reversible process

Heat change

for temperature-independent \( c_m \):

\( \Delta q = nc_m\Delta T \)
where \( c_m \) is molar heat capacity

Van 't Hoff equation:

\[
\frac{d \ln K}{dT} = \frac{\Delta_r H_m}{RT^2} \quad \Rightarrow \quad \ln \left(\frac{K_2}{K_1}\right) = -\frac{\Delta_r H_m}{R} \left(\frac{1}{T_2} - \frac{1}{T_1}\right)
\]

Henderson–Hasselbalch equation:

\[
pH = pK_a + \log \frac{[A^-]}{[HA]}
\]

Nernst–Peterson equation:

\[
E = E^0 - \frac{RT}{zF} \ln Q
\]

Energy of a photon:

\[
E = \frac{hc}{\lambda}
\]

Relation between \( E \) in eV and in J: 

\[
\frac{E}{\text{eV}} = \frac{E}{J} \frac{1}{q_e/C}
\]

Lambert–Beer law:

\[
A = \log \frac{I_0}{I} = \varepsilon c
\]

Wavenumber:

\[
\tilde{\nu} = \frac{\nu}{c} = \frac{1}{2\pi c} \sqrt{\frac{k}{\mu}}
\]

Reduced mass \( \mu \) for a molecule AX:

\[
\mu = \frac{m_A m_X}{m_A + m_X}
\]

Energy of harmonic oscillator:

\[
E_n = h\nu (n + \frac{1}{2})
\]

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:

\[
\frac{1}{[A]} = \frac{1}{[A]_0} + kt
\]
**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′→3′ direction matches the 5′→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):

\[
5\prime\text{-CGCGAATTCGCG-3}\prime \\
| | | | | | | | |
3\prime\text{-GCGCTTAAGCGC-5}\prime
\]  

(1)

1.1 How many different palindromic double-stranded DNA dodecanucleotides (that is, dsDNA species with twelve base pairs) exist?

1.2 How many different palindromic double-stranded DNA undecanucleotides (that is, dsDNA species with eleven base pairs) exist?
The melting temperature of dsDNA, $T_m$ is defined as the temperature at which 50% of the original amount of DNA double strands are dissociated 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. What is 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-helical DNA from single strands, and its dependence on the length of the DNA and on the temperature. The equilibrium constant for association of single strands to form dsDNA differs for palindromic and non-palindromic dsDNA. A solution of dsDNA with the initial concentration of $c_{\text{init}} = 1.00 \times 10^{-6}$ mol dm$^{-3}$ was heated to $T_m$ and equilibrium was reached.

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

Non-palindromic dsDNA

Calculation:
Palindromic dsDNA
Calculation:

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

1.5 How many base pairs are there in the shortest dsDNA oligonucleotide that has $T_m$ above 330 K? At this $T_m$, the equilibrium constant for association of single strands to form a dsDNA is $K_{np} = 1.00 \times 10^6$ for a non-palindromic dsDNA and $K_p = 1.00 \times 10^5$ for a palindromic dsDNA. Is the shortest oligonucleotide palindromic or non-palindromic?

Calculation of the number of base pairs:

The needed length of a non-palindromic dsDNA:
The needed length of a palindromic dsDNA:

- The shortest oligonucleotide is
  - ☐ palindromic (P)
  - ☐ non-palindromic (NP).
Finally, let us 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 $c_{\text{init}}$ is shown below. *(Note: The standard concentration is taken as $c_0 = 1 \text{ mol dm}^{-3}$)*

\[
\begin{array}{c|cccccccc}
\text{c}_{\text{init}} / 10^{-6} \text{ mol dm}^{-3} & 0.25 & 0.50 & 1.00 & 2.0 & 4.0 & 8.0 \\
T_m / K & 319.0 & 320.4 & 321.8 & 323.3 & 324.7 & 326.2 \\
\end{array}
\]
1.6 Calculate the standard enthalpy $\Delta H^\circ$ and the standard entropy $\Delta S^\circ$ of the association of DNA single strands to form the palindromic double-stranded Drew–Dickerson dodecanucleotide (1). Assume that $\Delta H^\circ$ and $\Delta S^\circ$ do not vary with temperature.

Calculation:
Theoretical Problem 2

<table>
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<tr>
<th>Theoretical Problem 2</th>
<th>Question</th>
<th>2.1</th>
<th>2.2</th>
<th>2.3</th>
<th>2.4</th>
<th>2.5</th>
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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 for studying their thermal history, for example L-isoleucine (L-Ile) ((2S,3S)-2-amino-3-methylpentanoic acid). It isomerizes on 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 centres, this process is called epimerization rather than racemization.

2.1 Choose 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.

☐ 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 has the value of 1.38 (at 374 K). If we set molar Gibbs free energy of $L$-isoleucine $G_m = 0 \text{ kJ mol}^{-1}$, determine the Gibbs free energies for all structures A–D from question 2.2.

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<th>kJ mol$^{-1}$</th>
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<td>A</td>
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<td>C</td>
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<tr>
<td>D</td>
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2.4 If we take into account stereoisomerism at all stereocentres, what is the maximum possible number of the stereoisomers of the tripeptide Ile-Ile-Ile?

The number of stereoisomers is

At the start of the epimerization the reverse reaction can be neglected. The epimerization then follows the first-order kinetics:

$L$-isoleucine $\xrightarrow{k_1} D$-allo-isoleucine

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

In the following calculation, shorten the concentration of L-isoleucine to [L] and of D-$allo$-isoleucine to [D].

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

$$de = \frac{[L] - [D]}{[L] + [D]} \times 100(\%).$$
2.5 Let us boil L-isoleucine for 1 943 hours at 374 K. What is the value of $de$ (with three significant figures) for L-isoleucine a) before boiling and b) after boiling?

a) Before boiling
Calculation:

\[ de = \% \text{ (3 sig figs)} \]

b) After boiling
Calculation:

\[ de = \% \text{ (3 sig figs)} \]
2.6 How long does it take to convert 10% of L-isoleucine to D-\textit{allo}-isoleucine at 298 K?

Calculation:

\[ t = \text{years} \]
In fact, the reverse reaction cannot be neglected. The correct kinetic scheme is expressed as

\[ \text{L-isoleucine} \xrightleftharpoons[k_2]{k_1} \text{D-allo-isoleucine} \]

Let us define the deviation of concentration from its equilibrium value \([L]_{eq}\)

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

It is possible to derive that \(x\) evolves with time according to the following equation (where \(x(0)\) is the deviation from equilibrium at \(t = 0\) h).

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

2.7 Let us boil 1.00 mol dm\(^{-3}\) L-isoleucine solution for 1943 hours at 374 K. The rate constant for the forward reaction is \(k_1(374 \text{ K}) = 9.02 \times 10^{-5} \text{ h}^{-1}\) and \(K_{ep}\) for L-isoleucine epimerization has the value of 1.38 (at 374 K).

In the following calculation, use \([L]\) for the concentration of L-isoleucine and \([D]\) for the concentration of D-allo-isoleucine.

Determine (with three significant figures)

a) \([L]_{eq}\),

b) diastereomeric excess (\(de\)) after boiling (see box on next page).

\[ \text{a) Calculation:} \]

\[ [L]_{eq} = \text{mol dm}^{-3} \]
b) Calculation:

\[ de = \text{\%} \]
Amino acids with a single chiral centre undergo racemization, e.g. L-arginine racemizes:

\[
\text{L-arginine} \rightleftharpoons \frac{k_1}{k_1} \text{D-arginine}
\]

The time evolution of concentrations is governed by

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

where [D] and [L] are concentrations of D- and L-arginine at time \( t \), \( k_1 \) is the rate constant, and the value of 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 (immediately after his death) boiled in water (373 K). Chemical kinetics can be used to estimate the boiling time. We know that the rate constant \( k_1 \) of arginine racemization within the protein at 373 K and pH = 7 has the value of \( 5.10 \times 10^{-3} \) h\(^{-1} \).

In order to analyse the isomeric composition of arginine in Lothar’s bones, we need to start with transferring arginine into solution. Lothar’s bones were 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 that the racemization also takes place during the hydrolysis, with the rate constant, \( k_1' \) that is different from \( k_1 \)).

2.8 How long was the Holy Roman Emperor Lothar III 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 (see next page for calculation box).
Calculation:

\[ t_{\text{boiling}} = h \]
Problem 3. Emerging electro-mobility

Contemporary means of transportation rely on burning fossil fuels, although the efficiency of real combustion engines is limited, and typically ranges between 20 and 40%.

3.1 Mark the factors that can make the efficiency of a heat engine higher:
☐ 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 represent a way to improve the engine efficiency for future vehicles.

3.2 The standard enthalpy of formation of liquid water is ΔfH°(H\textsubscript{2}O,l) = −285.84 kJ mol\textsuperscript{-1}, and the standard combustion enthalpy of isooctane is ΔcH°(C\textsubscript{8}H\textsubscript{18},l) = −5 065.08 kJ mol\textsuperscript{-1} (both at 323.15 K). Calculate the values of specific combustion enthalpy (ΔcH\textsubscript{s}) of pure liquid isooctane, and pure gaseous hydrogen (per unit of mass).

\[
\Delta_c\text{H}_s\, ^\circ (C_8H_{18}) = \\
\Delta_c\text{H}_s\, ^\circ (H_2) =
\]
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 for 323.15 K:

\[ S^\circ_\text{(H}_2\text{O,l)} = 70 \text{ J K}^{-1} \text{ mol}^{-1}, \quad S^\circ_\text{(H}_2\text{,g)} = 131 \text{ J K}^{-1} \text{ mol}^{-1}, \quad S^\circ_\text{(O}_2\text{,g)} = 205 \text{ J K}^{-1} \text{ mol}^{-1}. \]

Calculations:

\[ \text{EMF} = \quad V \]

3.4 Determine the ideal thermodynamic efficiency (\( \eta \)) of a fuel cell producing liquid water at 353.15 K. At this temperature, the enthalpy of formation of water is \( \Delta^\circ H_\text{f}(\text{H}_2\text{O,l}) = -281.64 \text{ kJ mol}^{-1} \) and the corresponding reaction Gibbs energy change is \( \Delta^\circ G^\circ = -225.85 \text{ kJ mol}^{-1} \).

\[ \eta = \quad \% \]
3.5 A polymer membrane electrolyzer facility operates at the voltage of 2.00 V and is powered by a 10.0 MW wind turbine plant which was running at full power from 10 pm to 6 am. The electrolysis yielded 1 090 kg of pure hydrogen. Calculate the electrolysis yield defined as the mass of hydrogen produced divided by the theoretical mass produced.

Calculations:

\[ \eta_{\text{electrolysis}} = \% \]
3.6 Calculate the mass of hydrogen required to drive the distance between Prague and Bratislava (330 km) at the average speed of 100 km h\(^{-1}\) with a car fitted with a 310 kW electric engine running on average at a 15% rate of its 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 \(\Delta G = -226 \text{ kJ mol}^{-1}\).

Calculations:

\[
m = \text{kg}
\]

The low efficiency of hydrogen production and the safety issues connected with its storage impede spreading the hydrogen-based transportation technology. Hydrazine (N\(_2\)H\(_4\)) fuel cells might be a suitable alternative.

The following standard reduction potentials for aqueous hydrazine systems are available:

\[
\begin{align*}
\text{N}_2\text{(g)} + 5 \text{H}^+(\text{aq}) + 4 \text{e}^- &\rightarrow \text{N}_2\text{H}_5^+(\text{aq}) & E^\circ &= -0.23 \text{ V} \\
\text{N}_2\text{H}_5^+(\text{aq}) + 3 \text{H}^+(\text{aq}) + 2 \text{e}^- &\rightarrow 2 \text{NH}_4^+(\text{aq}) & E^\circ &= +1.28 \text{ V} \\
\text{N}_2\text{(g)} + 4 \text{H}_2\text{O(l)} + 4 \text{e}^- &\rightarrow \text{N}_2\text{H}_4(\text{aq}) + 4 \text{OH}^- (\text{aq}) & E^\circ &= -1.16 \text{ V} \\
\text{N}_2\text{H}_4(\text{aq}) + 2 \text{H}_2\text{O(l)} + 2 \text{e}^- &\rightarrow 2 \text{NH}_3(\text{aq}) + 2 \text{OH}^- (\text{aq}) & E^\circ &= +0.10 \text{ V} \\
2 \text{H}_2\text{O(l)} + 2 \text{e}^- &\rightarrow \text{H}_2(\text{g}) + 2 \text{OH}^- (\text{aq}) & E^\circ &= -0.83 \text{ V}.
\end{align*}
\]
3.7 Fill in the following Latimer diagrams with the forms of hydrazine and ammonia prevailing at the given conditions and write the redox potential value for each arrow representing the electrochemical half-reaction. Record all the necessary calculations in the box below.

a) Acidic environment (pH = 0)

\[
\begin{array}{c}
\text{N}_2 \\
\rightarrow \\
\rightarrow \\
\rightarrow \\
\end{array}
\]

b) Basic environment (pH = 14)

\[
\begin{array}{c}
\text{N}_2 \\
\rightarrow \\
\rightarrow \\
\rightarrow \\
\end{array}
\]

Calculations:

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

3.8 Write down 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:
Calculations:
Hydrazine decomposition to NH₃ and N₂ in a basic environment:

\[ K = \] 

Hydrazine decomposition to H₂ and N₂ in a basic environment:

\[ K = \]

Rechargeable lithium-based batteries are an alternative to fuel cells. Lithium-ion batteries commonly use graphite for one of the electrodes, in which lithium clusters intercalate in 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:

\[
(C)_n + Li^+ + e^- \rightarrow Li(C)_n \quad E^\circ = -3.05 \text{ V},
\]
\[
CoO_2 + Li^+ + e^- \rightarrow LiCoO_2 \quad E^\circ = +0.19 \text{ V}.
\]

3.9 Using the symbols given in the equations above, write down the overall chemical reaction occurring in the battery during the **discharge** process. Give the oxidation states of the cobalt atom (*in the box on the next page*).
3.10 Tick the boxes to make the correct statements that are valid for the discharge of the lithium-based battery described in 3.9 above.

- Li(C)₆ electrode is the [ ] cathode because lithium ions are reduced here.
- Li(C)₆ electrode is the [ ] anode because lithium atoms are oxidized here.
- LiCoO₂ electrode is the [ ] cathode because cobalt ions are reduced here.
- LiCoO₂ electrode is the [ ] anode because cobalt ions are oxidized here.

3.11 Assume that a C₆ unit, a CoO₂ unit and a 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 \( (\rho_{el}) = \) kWh kg⁻¹
Problem 4. Column chromatography of radioactive copper

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

4.1 Write down the balanced equation for the $^{64}$Zn nucleus bombardment with deuterium nuclei, giving $^{64}$Cu. Specify the corresponding atomic and mass numbers of all species. Disregard the charges.

\[
\ldots + \ldots \rightarrow \ldots + \ldots
\]

The activated target is dissolved in concentrated hydrochloric acid to give a mixture containing Cu$^{2+}$ and Zn$^{2+}$ ions and their respective chlorido complexes.

4.2 Calculate the mole fraction of negatively charged copper species with respect to the amount of copper prepared by zinc target activation. Assume $[Cl^-] = 4 \text{ mol dm}^{-3}$. For the overall complexation constants, $\beta$, see Table 1 below.

Before you start the calculation, write down the charges in the upper right boxes:

\[
\begin{align*}
\text{Cu} & \quad [\text{CuCl}] & \quad [\text{CuCl}_2] & \quad [\text{CuCl}_3] & \quad [\text{CuCl}_4] \\
\end{align*}
\]

Table 1. Overall complexation constants $\beta$ of the Cu species (charges were omitted in the formula). $\beta_i = \frac{[\text{CuCl}_i]}{[\text{Cu}[\text{Cl}]^i}$

\[
\begin{array}{c|cccc}
    i & 1 & 2 & 3 & 4 \\
\hline
\beta_i & 2.36 & 1.49 & 0.690 & 0.055 \\
\end{array}
\]
Calculation:

Mole fraction =

(answer with 2 digits after decimal point)

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

4.3 Everything was initially at room temperature before washing with hydrochloric acid. Does the column temperature change during the washing with hydrochloric acid?

☐ No.
☐ Yes, the temperature decreases.
☐ Yes, the temperature increases.

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

Using the simple experimental equation below, you can calculate quantities that determine average elution properties of 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:

$$V_R = D_0 \times m_{\text{resin,dry}} + V_0$$
4.4 Using average mass distribution coefficients $D_g (D_g_{(Cu \ species)} = 17.4 \ \text{cm}^3 \ \text{g}^{-1},$ 
$D_g_{(Zn \ species)} = 78.5 \ \text{cm}^3 \ \text{g}^{-1})$, calculate the retention volumes $V_R$ in cm$^3$ of the copper species 
and the zinc species if the mass of dry resin is $m_{\text{resin,dry}} = 3.72 \ \text{g}$ and the void volume of a 
column $V_0 = 4.93 \ \text{cm}^3$.

\[
\begin{align*}
V_R(\text{Cu species}) &= \text{cm}^3 \ (\text{answer with 1 digit after the decimal point}) \\
V_R(\text{Zn species}) &= \text{cm}^3 \ (\text{answer with 0 digit after the decimal point})
\end{align*}
\]

If you cannot find the answer, use $V_R(\text{Cu species}) = 49.9 \ \text{cm}^3$ and $V_R(\text{Zn species}) = 324 \ \text{cm}^3$ for 
further calculations.

Using the simple experimental equation, separation of two sets of species, A and B, can be 
considered complete if

\[
V_{0.001}(A) - V_{0.999}(B) > 10V_c
\]

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.

\[
\begin{align*}
V_{0.001}(A) &= V_R(A) \times \left(1 - 6.91 \sqrt{d_p/L_c}\right) \\
V_{0.001}(B) &= V_R(B) \times \left(1 - 6.91 \sqrt{d_p/L_c}\right) \\
V_{0.999}(B) &= 2V_R(B) - V_{0.001}(B)
\end{align*}
\]

4.5 Based on a calculation, decide whether the copper species were separated completely from 
the zinc species. The volume of the column filled with the swollen resin $V_c = 10.21 \ \text{cm}^3$, the 
resin particle diameter $d_p = 0.125 \ \text{mm}$, and the height of the wet resin in a swollen state in the 
column $L_c = 13.0 \ \text{cm}$.

\[
V_{0.001}(A) = \text{cm}^3 \ (\text{calculation box continues on next page})
\]
\[ V_{0.999}(B) = \text{cm}^3 \]

It is possible to separate copper species from zinc species.

☐ True  ☐ False

4.6 Assume tetraalkylammonium groups were the only ones responsible for ion exchange of the resin. No other nitrogen containing groups were present. 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, \( Q_{m,\text{theor}} \), in mmol g\(^{-1}\).

\[ Q_{m,\text{theor}} = \text{mmol g}^{-1} \quad \text{(answer with 2 digits after decimal point)} \]

If you cannot determine the answer, use \( Q_{m,\text{theor}} = 4.83 \text{ mmol g}^{-1} \) for further calculations.

In reality, not all tetraalkylammonium groups are involved in the ion exchange. To determine the total ion exchange volume capacity, \( Q_v \), the column filled with 3.72 g of dry resin converted to the Cl\(^-\) form was washed with the excess of sodium sulfate solution. The effluent was collected in a 500 cm\(^3\) volumetric flask, which was then filled with water to the mark. An aliquot of 100 cm\(^3\) was potentiometrically titrated with 0.1027 mol dm\(^{-3}\) silver nitrate. The silver nitrate solution volume at the equivalence point was 22.20 cm\(^3\). The volume of the column filled with the swollen resin, \( V_c \), was 10.21 cm\(^3\).

4.7 Calculate the \( Q_v \) of the swollen resin in mmol of active tetraalkylammonium groups per cm\(^3\) of the swollen resin.

\[ Q_v = \text{mmol cm}^{-3} \quad \text{(answer with 2 digits after decimal point)} \]

If you cannot determine the answer, use \( Q_v = 1.00 \text{ mmol cm}^{-3} \) for further calculations.
4.8 Calculate the mole fraction \( x \) of the tetraalkylammonium groups actively involved in the ion exchange.

\[
x = \quad \text{(answer with 3 digits after decimal point)}
\]
Problem 5. Bohemian garnet

Bohemian garnet (pyrope) is a famous Czech blood coloured 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 contains 8 formula units. The structure comprises 3 types of polyhedra: the $A^{II}$ cation occupies a dodecahedral position (it is surrounded with 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.

$\rho = \ldots \text{g cm}^{-3}$

The Bohemian garnet has the composition of $Mg_3Al_2(SiO_4)_3$. The pure compound is colourless and the colour of natural garnets comes from chromophores – transition metal cations that substitute the host material cations. The red colour 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 \([\text{Cr}^{III}\text{O}_6]^{\text{oct}}\) d-orbitals and fill it with electrons.

5.3 Identify the 1st transition row element(s) whose trivalent cation(s) \(M^{III}\) placed in an \textit{octahedral} position is/are diamagnetic in the low-spin arrangement and paramagnetic in the high-spin arrangement.

5.4 The figure below shows d-orbitals splitting in the dodecahedral crystal field. Fill in the electrons for the \([\text{Fe}^{II}\text{O}_8]^{\text{dod}}\) chromophore for both existing arrangements.

<table>
<thead>
<tr>
<th>a) high-spin arrangement</th>
<th>b) low-spin arrangement</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Diagram" /></td>
<td><img src="image2.png" alt="Diagram" /></td>
</tr>
</tbody>
</table>

5.5 Derive the inequalities (e.g. \(P < E_1 + E_2 + E_3\)) for the magnitude of the pairing energy \((P)\) in relation to energies \(E_1, E_2,\) and \(E_3\) for both arrangements.

<table>
<thead>
<tr>
<th>a) high-spin arrangement:</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>b) low-spin arrangement:</td>
<td>(P)</td>
</tr>
</tbody>
</table>
5.6 Assuming that \( P > E_3 \), identify the 1st transition row element(s) whose divalent cation \( M^{II} \), when placed in the dodecahedral crystal field, is diamagnetic in the low-spin arrangement and paramagnetic in the high-spin arrangement.

The figures below show simplified absorption spectra of four coloured minerals: blood-coloured Bohemian garnet, green uvarovite, blue sapphire and yellow-orange citrine.

5.7 Match the spectra with the minerals.

<table>
<thead>
<tr>
<th>Bohemian garnet:</th>
<th>Sapphire:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uvarovite:</td>
<td>Citrine:</td>
</tr>
</tbody>
</table>

5.8 If illuminated with monochromatic blue-green light, how will the Bohemian garnet look?

- Red
- Blue
- Yellow-orange
- Black
- Yellow
- Blue-green
- Violet
- White
Andradite is another garnet mineral; its chemical composition is $\text{Ca}_3\text{Fe}_2(\text{SiO}_4)_3$. 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 $\text{Ca}_3[\text{Fe,Ti}]_{\text{oct}}^2([\text{Si,Fe}]_{\text{tet}}^4\text{O}_4)_3$.

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 positions are substituted with Ti$^{IV}$.

$$p = \%$$

The colour of the mineral is caused by two chromophores: $[\text{Fe}^{III}\text{O}_6]_{\text{oct}}$ and $[\text{Fe}^{III}\text{O}_4]_{\text{tet}}$. The central ions of both chromophores have equal number of unpaired electrons.

5.10 Draw the d-orbital splitting diagrams for both chromophores and fill in the electrons.

$[\text{Fe}^{III}\text{O}_6]_{\text{oct}}$:      $[\text{Fe}^{III}\text{O}_4]_{\text{tet}}$: 

A tetrahedral field causes a smaller splitting than the octahedral field ($\Delta_{\text{tet}} = \frac{4}{9} \Delta_{\text{oct}}$). 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 $\Delta_{\text{oct}}$ and $\Delta_{\text{tet}}$ splitting. Assume that the pairing energy is the same for both chromophores.

Calculation box continues on the next page
Synthetic garnet YAG (Yttrium Aluminium Garnet), used in optoelectronics, has the composition of Y₃Al₅O₁₂. Its structure is derived from the general garnet structure A₃B₂(SiO₄)₃ by placing the ions Y³⁺ and Al³⁺ to the A, B and Si positions.

5.12 Based on your knowledge of the relative ion radii, determine which cation occupies which position.

A:  B:  Si:

5.13 For the use in LED technology, YAG is doped with Ce³⁺. Determine the values of x and y in the formula of YAG in which 5% of yttrium atoms are substituted with cerium.

\[ Y_xCe_yAl_5O_{12} \]

\( x = \quad y = \)

If you don’t get a result, use \( x = 2.25 \) and \( y = 0.75 \)

5.14 The Ce³⁺-doped YAG is prepared by annealing the mixture of \( Y_2O_3 \), \( Al_2O_3 \) and \( CeO_2 \) in an \( H_2 \) atmosphere. Using the formula from 5.13, write down 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 of selected rare-earth ions are shown.

5.15 Which cation has a transition that corresponds to the emission of blue light.

- Er\(^{3+}\)
- Sm\(^{3+}\)
- Tm\(^{3+}\)
- Pr\(^{3+}\)
- Yb\(^{3+}\)
- Nd\(^{3+}\)
- Tb\(^{3+}\)

5.16 Calculate the emission wavelength of this light.

\[ \lambda = \text{nm} \]

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

- Red
- Blue
- Yellow-orange
- Black
- Yellow
- Blue-green
- Violet
- White
Problem 6. Let’s go mushrooming

Mushrooming belongs to Czech and Slovak traditional pastimes. While some mushroom species are edible, others 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).

![Chemical structures and reactions](image.png)

6.1 Draw the structures of compounds A–E including stereochemistry when appropriate. *Hint: The first reaction producing compound A proceeds via an organometallic compound which then cyclizes.*
In the human body, coprine undergoes hydrolysis to L-glutamic acid (3) and compounds C and 4. These compounds are responsible for the coprine adverse side-effects because 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 (so called antabuse effect).

The active site of the enzyme contains a cysteine SH group, which is blocked either by compound C or 4.

6.2 Using the pictogram for acetaldehyde dehydrogenase above, draw structure F of the enzyme inhibited by compound 4.
The antabuse effect got its name after antabuse (5), the drug used in alcohol-addiction treatment. This drug can be synthesized according to the following scheme.

\[
\text{NH} + G \xrightarrow{\text{NaOH}} H \xrightarrow{\text{reagent I}} 5
\]

6.3 Draw structures of compounds \( \text{G} \) and \( \text{H}. \text{Hint: Compound H contains five carbon atoms.} \)

\[
\text{G} \quad \text{H}
\]

6.4 Mark any of the following which could be reagent I.

- ☐ \( m\text{-chloroperbenzoic acid (mCPBA)} \)
- ☐ \( \text{diluted } \text{H}_2\text{O}_2 \)
- ☐ \( \text{Zn}/\text{CH}_3\text{COOH} \)
- ☐ \( \text{NaBH}_4 \)
- ☐ \( \text{I}_2 \)
- ☐ \( \text{hot concentrated } \text{H}_2\text{SO}_4 \)
- ☐ \( \text{K}_2\text{CO}_3, \text{H}_2\text{O} \)
- ☐ \( \text{AlCl}_3 \)

The way antabuse inhibits acetaldehyde dehydrogenase is similar to compounds \( \text{C} \) and \( \text{4} \).

\[
\text{Enzyme} \xrightarrow{\text{SH}} + 5 \xrightarrow{} \text{J}
\]

Enzyme = acetaldehyde dehydrogenase

6.5 Using the pictogram for acetaldehyde dehydrogenase above, draw structure \( \text{J} \) of the enzyme inhibited by antabuse (5). \text{Hint: The structure should show three sulfur atoms.}
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 it is poisonous due to it containing gyromitrin (M). This compound can be prepared from *N*-methylhydrazine (6):

\[
\begin{align*}
\text{H}_2\text{O} & \quad \text{+} \quad \text{Cl}\text{O} \quad \downarrow \quad \text{K} \\
\text{N} \quad \text{NH}_2 & \quad \text{(1 equiv.)} \quad \text{Et}_3\text{N} \quad \rightarrow \quad \text{L} \\
\text{O} & \quad \quad \quad \quad \quad \text{H}_3\text{C} \quad \text{H} \quad \quad \quad \text{Gyromitrin (M)}
\end{align*}
\]

6.6 Draw the structures of compounds K–M.

\[
\begin{array}{c|c|c}
\text{K} & \text{L} & \text{M} \\
\end{array}
\]

In the human body, gyromitrin (M) hydrolyzes and provides *N*-methylhydrazine (6), which is strongly hepatotoxic. Hydrolysis of both the amide and imide groups in gyromitrin (M) occurs as soon as it enters the acidic environment in the human stomach.

Let us focus on the hydrolysis of the amide group within the gyromitrin molecule. The vibrational wavenumber of the stretching mode of the relevant C–N bond is 1293.0 cm\(^{-1}\). The potential energy surface does not significantly alter its shape with an isotope substitution effect.

6.7 Calculate the highest possible hypothetical kinetic isotope effect, at a temperature of 37 °C, for the hydrolysis reaction. Assume that both relevant nitrogen and carbon atoms are simultaneously substituted: \(^{14}\text{N}\) with the \(^{15}\text{N}\) isotope and \(^{12}\text{C}\) with the \(^{13}\text{C}\) isotope. Assume that only the zero point vibrational energy affects the rate constants and that the molar masses of all isotopes are integers. In all further steps use five significant figures. The box continues on the next page.
6.8 After making these isotopic changes, the rates of hydrolysis are not significantly different. Which of the following is the most likely rate-determining step?

☐ Nucleophilic attack of water on a protonated amide group

☐ C–N bond cleavage

☐ Protonation of the gyromitrin molecule
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.

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

A \[
\text{C}_{12}\text{H}_{22}\text{O}_6
\]

B

C

D
7.2 Draw the structures of all alternative stereoisomers of L-mannitol (3) which when used in the same reaction sequence give rise to the same product 2.

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 scheme on the previous page is shown below. Refer to this when entering answers.

- **E**
  - $C_{30}H_{30}O_4$

- **F**

- **G**

- **H**

- **I**
  - $C_{15}H_{27}O_5PS$
Phosphonate 4 can be prepared by the sequence of reactions shown:

\[
\begin{align*}
\text{O} & \quad \text{Br} \quad J \quad \rightarrow \quad K \quad \xrightarrow{1. \text{EtONa}} \quad L \quad \xrightarrow{2. \text{H}^+} \quad 4 \\
\text{TsCl} & \quad \text{NEt}_3
\end{align*}
\]

7.4 Draw the structures of compounds J–L.
The reaction of compound 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 group in compound O reacts with bromotrimethylsilane to provide cidofovir (1).

7.5 Draw structures of the two isomers M, N, and of compound O, including stereochemistry. Transformation of M to O involves the removal of a protecting group. Draw the structure of the aromatic tautomer P of cytosine (5).
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
Problem 8. Caryophyllene

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

\[
\text{β-Caryophyllene (3)}
\]

The synthesis of β-caryophyllene starts from a single enantiomer 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 reaction with tosyl chloride, providing B. Basic cyclization of this compound affords C. Finally, the reaction of C with ylide D provides β-caryophyllene.

\[
\begin{align*}
\text{C}_{10}\text{H}_{14}\text{O} & \xrightarrow{\text{Ph}_{3}\text{C}^{+}\text{ClO}_{4}^{-} (\text{cat.})} \text{1} \xrightarrow{\text{OCH}_{3}} \text{1} \xrightarrow{\text{OH}} \text{2} \xrightarrow{\text{TsCl, pyridine}} \text{B} \xrightarrow{\text{t-BuOK}} \text{C} \xrightarrow{\text{n-BuLi}} \text{D} \\
& \text{β-Caryophyllene (3)}
\end{align*}
\]

This scheme is repeated on the next page for easy reference when constructing your answers.
8.1 Draw structures of compounds A–D, including the appropriate stereochemistry.

*Hint: In transformation A → 2, the silyl ketene acetal acts as a nucleophile.*
The double bond in the ring in 2 and in 3 above has a trans configuration. Despite being significantly strained, these compounds have reasonable stability due to the ring having eight carbons as this is the smallest ring that can accommodate a trans double bond. trans-Cyclooctene (4) can be prepared according to the following scheme:

\[
\text{E} \rightarrow \text{LiPPh}_2 \rightarrow \text{LiPPh}_2 \xrightarrow{\text{THF}} \text{F} \xrightarrow{\text{H}_2\text{O}_2/\text{AcOH}} \text{G} \xrightarrow{\text{NaH}} \text{4} + \text{enantiomer}
\]

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.

<table>
<thead>
<tr>
<th>E</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>achiral</td>
</tr>
<tr>
<td>☐</td>
<td>single enantiomer</td>
</tr>
<tr>
<td>☐</td>
<td>racemic mixture</td>
</tr>
<tr>
<td>☐</td>
<td>mixture of diastereoisomers</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
</tr>
<tr>
<td>☐</td>
</tr>
<tr>
<td>☐</td>
</tr>
<tr>
<td>☐</td>
</tr>
</tbody>
</table>
8.3 Draw the structure of the enantiomer of cycloalkene 4.

![Structure of cycloalkene 4]

The two double bonds in β-caryophyllene display different reactivity. Due to ring strain, the double bond in the ring (endocyclic) is more reactive than the other one (exocyclic).

\[ \text{Ha + Hb} \xrightarrow{\text{CH}_3\text{COOOH} \ (1 \text{ equiv.})} \beta\text{-Caryophyllene (3)} \]

\[ \xrightarrow{\text{1. } \text{O}_3 \ (1 \text{ equiv.})} \xrightarrow{\text{2. } \text{Me}_2\text{S or Zn}} \]

\[ \xrightarrow{\text{1. } \text{BH}_3\text{-THF} \ (1/3 \text{ equiv.})} \xrightarrow{\text{2. } \text{H}_2\text{O}_2, \text{NaOH}} \text{Ja + Jb} \]

8.4 On the next page, draw structures of compounds \text{Ha + Hb, I and Ja + Jb}, including the appropriate stereochemistry. \textit{Hint: Ha + Hb and Ja + Jb are pairs of diastereomers.}
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ha + Hb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ja + Jb</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Interestingly, the reactivity of the double bonds is reversed when isocaryophyllene (5) is used instead of \(\beta\)-caryophyllene (3).

\[
\begin{align*}
\text{5} & \xrightarrow{1. \text{BH}_3 \text{THF} (1/3 \text{ equiv.})} \xrightarrow{2. \text{H}_2\text{O}_2, \text{NaOH}} \text{Ka + Kb}
\end{align*}
\]

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

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

\[
\begin{align*}
\text{3} & \xrightarrow{\oplus \text{PPh}_3 \cdot \text{CD}_2} \xrightarrow{\ominus \text{D}_2\text{O}, \text{NaOD} \text{ reflux}} \text{6} & \xrightarrow{\ominus \text{C}_{14}\text{H}_{28}\text{D}_2\text{O}} \text{L} \quad \frac{1}{2} \quad \text{M}
\end{align*}
\]

8.6 Draw the structures of compounds L and M on the next page.
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. These undergo hydration to give the target alcohols Na and Nb. Alternatively, 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 on the next page.
8.8 Draw the structures of diastereomers Na + Nb.