

IChO 2018

Theory problems and solutions · Bratislava and Prague, Slovakia and Czech Republic · 8
theory problems with complete solutions

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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):



1.1 How many different palindromic double-stranded DNA dodecanucleotides (i. e. dsDNA species with twelve base pairs) exist?

1.2 How many different palindromic double-stranded DNA undecanucleotides (i.e., 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 of association of single strands to form dsDNA differs for palindromic and non-palindromic dsDNA.

A solution of dsDNA with the initial concentration of $c_{\text{init}} = 1.00 \times 10^{-6} \text{ mol dm}^{-3}$ was heated to T_m and equilibrium was reached.

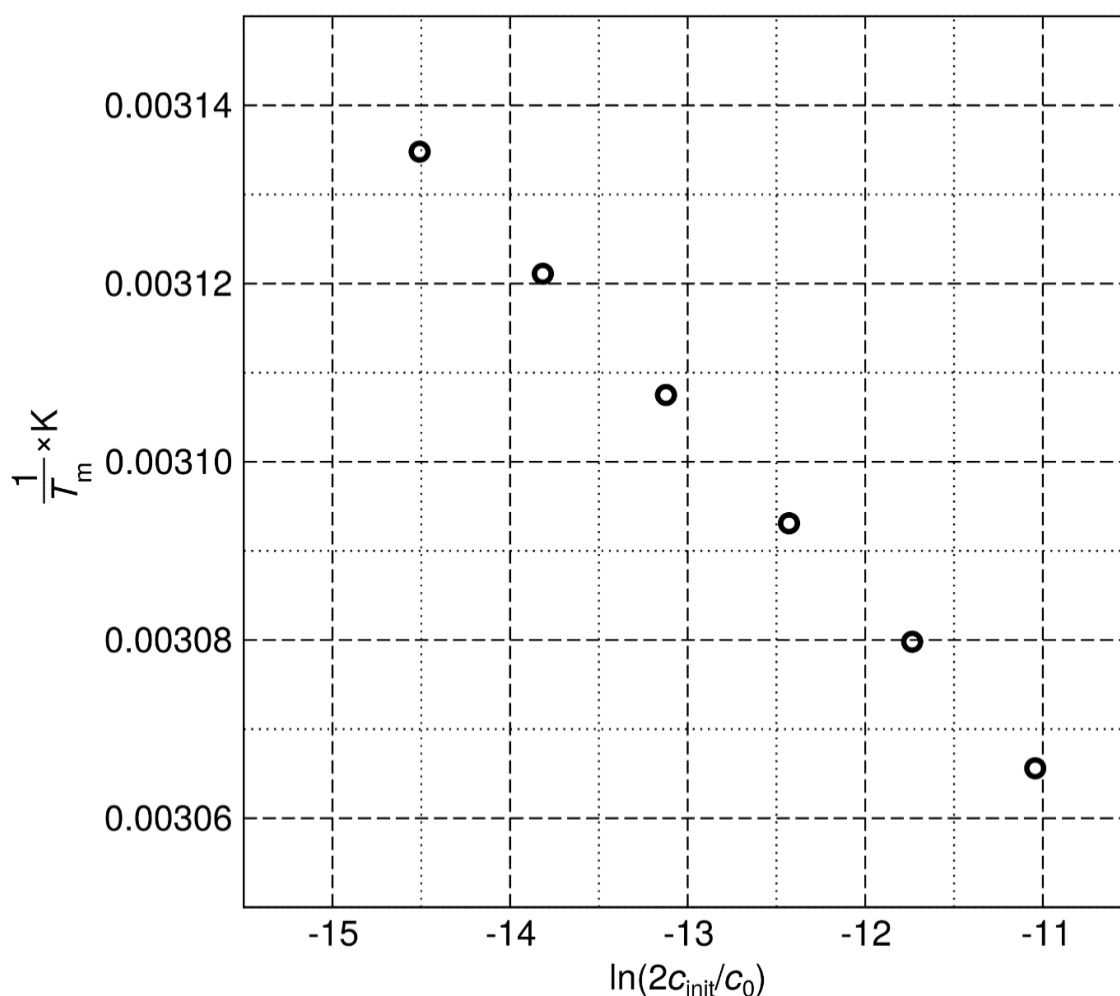
1.4 Calculate the equilibrium constant of **association** of single strands at T_m for both non-palindromic and palindromic DNA.

The mean contributions to the Gibbs energy of association of two single strands to form dsDNA were estimate over a certain range of experimental conditions, and they amount to $-6.07 \text{ kJ mol}^{-1}$ 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 , consider the following values of the equilibrium constant 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. Is the shortest oligonucleotide palindromic or non-palindromic?

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_{init} is shown below. (Note: a standard concentration $c_0 = 1 \text{ mol dm}^{-3}$ is introduced.)

$c_{init}/10^{-6} \text{ mol dm}^{-3}$	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



1.6 Calculate the standard enthalpy ΔH° and the standard entropy ΔS° of the association of DNA single strands to form the palindromic double-stranded Drew–Dickerson dodecanucleotide (1). Assume that ΔH° and ΔS° do not vary with temperature.

Official English text of the problem.

Answers

- 1.1: $\boxed{4096}$.
- 1.2: $\boxed{0}$.
- 1.3: $\boxed{\frac{1}{3} \approx 33.3\%}$.
- 1.4: $\boxed{K_{c,np} = 2.00 \times 10^6 \text{ dm}^3 \text{ mol}^{-1}}$ and $\boxed{K_{c,p} = 5.00 \times 10^5 \text{ dm}^3 \text{ mol}^{-1}}$. The dimensionless standard-state constants have the same numerical values when $c_0 = 1 \text{ mol dm}^{-3}$.
- 1.5: $\boxed{6 \text{ base pairs; palindromic, with all six pairs G-C}}$.
- 1.6: $\boxed{\Delta H^\circ \approx -416 \text{ kJ mol}^{-1}}$ and $\boxed{\Delta S^\circ \approx -1.18 \times 10^3 \text{ J mol}^{-1} \text{ K}^{-1}}$, per mole of duplex formed.

Solution

1.1

A palindromic DNA strand equals its reverse complement. Thus, if its bases are $b_1, \dots, b_{12}$,

$$b_i = \bar{b}_{13-i},$$

where the bar denotes the complementary base: A pairs with T, and G pairs with C.

The first six positions can each contain any of four bases. The last six positions are then fixed:

$$N = 4^6 = \boxed{4096}.$$

There is no division by two: the two strands of each palindromic duplex already have identical sequences when read $5' \rightarrow 3'$.

1.2

For an eleven-base strand, the central position would have to satisfy

$$b_6 = \bar{b}_6.$$

None of the four standard DNA bases is complementary to itself. Consequently, an odd-length DNA duplex cannot be palindromic:

$$\boxed{N = 0}.$$

1.3

The Drew–Dickerson duplex contains eight G–C pairs and four A–T pairs. Under the stated stability model, replacing an A–T pair with a G–C pair increases stability and hence $T_{m,i}$; replacing an existing G–C pair does not increase its contribution.

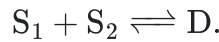
All twelve positions are equally likely to be selected, so

$$P(T_m \text{ increases}) = \frac{4}{12} = \boxed{\frac{1}{3} \approx 33.3\%}.$$

1.4

Let D denote a duplex and S_1, S_2 its complementary single strands. These are symbols for whole DNA strands, rather than elemental formulas.

For **non-palindromic DNA**, the strands are distinct:



At T_m , half the original duplex has dissociated:

$$[D] = \frac{c_{\text{init}}}{2}, \quad [S_1] = [S_2] = \frac{c_{\text{init}}}{2}.$$

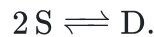
Therefore,

$$K_{c,\text{np}} = \frac{[D]}{[S_1][S_2]} = \frac{c_{\text{init}}/2}{(c_{\text{init}}/2)^2} = \frac{2}{c_{\text{init}}}.$$

Substitution gives

$$K_{c,\text{np}} = 2.00 \times 10^6 \text{ dm}^3 \text{ mol}^{-1}.$$

For **palindromic DNA**, both strands are the same species S :



Each dissociated duplex produces two molecules of S . Hence,

$$[D] = \frac{c_{\text{init}}}{2}, \quad [S] = 2 \left(\frac{c_{\text{init}}}{2} \right) = c_{\text{init}}.$$

Thus,

$$K_{c,\text{p}} = \frac{[D]}{[S]^2} = \frac{c_{\text{init}}/2}{c_{\text{init}}^2} = \frac{1}{2c_{\text{init}}},$$

giving

$$K_{c,\text{p}} = 5.00 \times 10^5 \text{ dm}^3 \text{ mol}^{-1}.$$

The dimensionless equilibrium constants used in thermodynamic logarithms are

$$K_{\text{np}} = \frac{2c_0}{c_{\text{init}}}, \quad K_{\text{p}} = \frac{c_0}{2c_{\text{init}}}.$$

These equal $c_0 K_c$, so their numerical values agree with those above when $c_0 = 1 \text{ mol dm}^{-3}$.

1.5

In the stated additive model,

$$\Delta G^\circ = -(6.07n_{\text{GC}} + 1.30n_{\text{AT}}) \text{ kJ mol}^{-1}.$$

At the melting temperature,

$$\Delta G^\circ = -RT_m \ln K.$$

For a fixed number of base pairs, the greatest stabilization—and therefore the greatest T_m in this model—is obtained when every pair is G–C. For an all-G–C duplex of n base pairs,

$$T_m = \frac{6070n}{R \ln K},$$

using $R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1}$.

For **non-palindromic DNA**, use the value specified in this part, $K_{np} = 10^6$:

$$T_m > 330 \text{ K} \implies n > \frac{(8.314)(330) \ln(10^6)}{6070} = 6.245.$$

Thus, the shortest possible non-palindromic duplex has **seven base pairs**.

For **palindromic DNA**, $K_p = 10^5$:

$$n > \frac{(8.314)(330) \ln(10^5)}{6070} = 5.204.$$

The smallest allowed even integer is **six**. Such an all-G–C palindrome exists: choose any three G/C bases as the first half of a strand, then use their reverse complement as the second half.

Its predicted melting temperature is

$$T_m = \frac{6(6070)}{(8.314) \ln(10^5)} \approx 380 \text{ K} > 330 \text{ K}.$$

Moreover, a six-base-pair palindrome containing any A–T pairs must contain at least two of them, because complementary positions occur in pairs. Its maximum stabilization would then be

$$4(6.07) + 2(1.30) = 26.88 \text{ kJ mol}^{-1},$$

below the required

$$R(330) \ln(10^5) \approx 31.59 \text{ kJ mol}^{-1}.$$

Therefore,

The shortest duplex is palindromic and contains six G–C base pairs.

1.6

For the palindromic duplex at its melting temperature, part 1.4 gives

$$K_p = \frac{c_0}{2c_{\text{init}}}.$$

Combining

$$\Delta G^\circ = \Delta H^\circ - T_m \Delta S^\circ$$

with

$$\Delta G^\circ = -RT_m \ln K_p = RT_m \ln \left(\frac{2c_{\text{init}}}{c_0} \right)$$

yields

$$\frac{\Delta H^\circ}{T_m} - \Delta S^\circ = R \ln \left(\frac{2c_{\text{init}}}{c_0} \right).$$

Therefore,

$$\boxed{\frac{1}{T_m} = \frac{R}{\Delta H^\circ} \ln \left(\frac{2c_{\text{init}}}{c_0} \right) + \frac{\Delta S^\circ}{\Delta H^\circ}}.$$

Thus, for the plotted variables

$$x = \ln \left(\frac{2c_{\text{init}}}{c_0} \right), \quad y = \frac{1}{T_m},$$

the slope and intercept are

$$m = \frac{R}{\Delta H^\circ}, \quad b = \frac{\Delta S^\circ}{\Delta H^\circ}.$$

A least-squares straight-line fit to all six tabulated points gives

$$m = -1.99660 \times 10^{-5} \text{ K}^{-1}, \quad b = 2.84523 \times 10^{-3} \text{ K}^{-1}.$$

Hence,

$$\Delta H^\circ = \frac{R}{m} = \frac{8.314}{-1.99660 \times 10^{-5}} \text{ J mol}^{-1} \approx -416.4 \text{ kJ mol}^{-1},$$

and

$$\Delta S^\circ = b\Delta H^\circ \approx (2.84523 \times 10^{-3})(-416.4 \times 10^3) \text{ J mol}^{-1} \text{ K}^{-1} \approx -1184.8 \text{ J mol}^{-1} \text{ K}^{-1}.$$

To sensible precision,

$$\boxed{\Delta H^\circ \approx -416 \text{ kJ mol}^{-1}}, \quad \boxed{\Delta S^\circ \approx -1.18 \times 10^3 \text{ J mol}^{-1} \text{ K}^{-1}}.$$

The negative enthalpy indicates exothermic duplex formation; the negative entropy is consistent with association and ordering of the strands.

The solution was checked against the official solution.

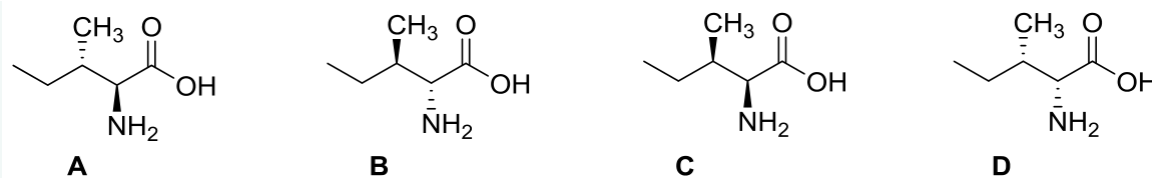
Problem 2: Repatriation of remains in the middle ages

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) ((2*S*, 3*S*)-2-amino-3-methylpentanoic acid) as an example. It isomerizes on the α -carbon and forms (2*R*, 3*S*)-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.

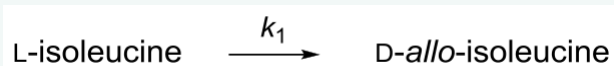


- ☐ $2S, 3R$ (L-*allo*-isoleucine)
- ☐ $2R, 3S$ (D-*allo*-isoleucine)
- ☐ $2S, 3S$ (L-isoleucine)
- ☐ $2R, 3R$ (D-isoleucine)

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 $G_{\text{m}}^{\circ} = 0 \text{ kJ mol}^{-1}$ determine the Gibbs free energies for all structures **A–D** from question 2.2 at 374 K.

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?

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



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

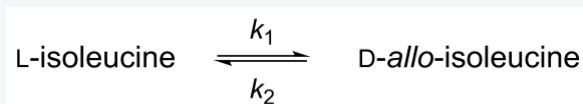
We can define a quantity *de* (diastereomeric excess):

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

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?

2.6 How long does it take to convert 10% of L-isoleucine to D-*allo*-isoleucine at 298 K?

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



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

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

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

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

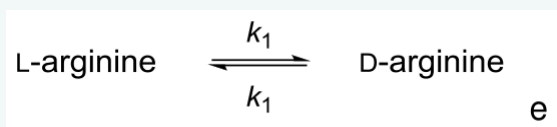
where $x(0)$ is the deviation from equilibrium at $t = 0 \text{ h}$.

2.7 Let us boil 1.00 mol dm^{-3} L-isoleucine solution for 1 943 hours at 374 K. The rate constant for the forward reaction is $k_1(374 \text{ K}) = 9.02 \times 10^{-5} \text{ h}^{-1}$, K_{ep} for L-isoleucine epimerization has the value of 1.38 (at 374 K). In the following calculation, shorten the concentration of L-isoleucine to $[L]$ and of D-*allo*-isoleucine to $[D]$. Evaluate (with three significant figures)

a) $[L]_{\text{eq}}$,

b) diastereomeric excess (*de*) after boiling.

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



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, immediately after his death, boiled in water (373 K) for a certain time. Let us try to estimate the boiling time with the help of chemical kinetics. We know that the rate constant k_1 of arginine racemization within the protein at 373 K and $\text{pH} = 7$ has the value of $5.10 \times 10^{-3} \text{ h}^{-1}$.

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 , 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.

Official English text of the problem.

Answers

- **2.1:** Select **only the fourth statement**: different specific optical rotations and different melting points.
- **2.2:**

Structure	Absolute configuration	Name	Stereochemical SMILES
A	(2 <i>S</i> , 3 <i>S</i>)	L-isoleucine	<chem>CC[C@H](C)[C@H](N)C(=O)O</chem>
B	(2 <i>R</i> , 3 <i>R</i>)	D-isoleucine	<chem>CC[C@@H](C)[C@@H](N)C(=O)O</chem>
C	(2 <i>S</i> , 3 <i>R</i>)	L- <i>allo</i> -isoleucine	<chem>CC[C@@H](C)[C@H](N)C(=O)O</chem>
D	(2 <i>R</i> , 3 <i>S</i>)	D- <i>allo</i> -isoleucine	<chem>CC[C@H](C)[C@@H](N)C(=O)O</chem>

Fill the four answer boxes, from top to bottom, with **C, D, A, B**.

- **2.3:** $G_m^\circ(A) = G_m^\circ(B) = 0 \text{ kJ mol}^{-1}$; $G_m^\circ(C) = G_m^\circ(D) = -1.00 \text{ kJ mol}^{-1}$.
- **2.4:** 64 stereoisomers.
- **2.5:** a) $1.00 \times 10^2\%$; b) 67.8%.
- **2.6:** $8.00 \times 10^7 \text{ h} \approx 9.13 \times 10^3 \text{ years}$.
- **2.7:** a) $0.420 \text{ mol dm}^{-3}$; b) 69.7%, retaining unrounded intermediate values.
- **2.8:** 6.1 h (calculated value 6.11286 h).

Solution

2.1 — Relationship between the stereoisomers

L-isoleucine is (2*S*, 3*S*), whereas D-*allo*-isoleucine is (2*R*, 3*S*). They differ at C2 but have the same configuration at C3. They are therefore **epimers**, a particular kind of diastereomer.

Diastereomers generally have different physical properties, including specific optical rotation and melting point. The equal-magnitude, opposite-sign optical rotations and identical melting points characteristic of an enantiomeric pair do not apply here. D-*allo*-isoleucine is chiral and optically active.

Thus, select **the fourth statement only**. The D/L designation does not itself specify the sign of optical rotation.

2.2 — Absolute configurations

Number the carboxyl carbon C1, the amino-bearing carbon C2, and the methyl-bearing carbon C3.

At **C2**, the Cahn–Ingold–Prelog priorities are



Nitrogen has priority over carbon. To distinguish the two carbon substituents, the carboxyl carbon is treated as attached to (O, O, O), whereas C3 is attached to (C, C, H).

At **C3**, the priorities are



The three carbon substituents have next-atom lists (N, C, H), (C, H, H), and (H, H, H), respectively.

With the lowest-priority group pointing away, clockwise $1 \rightarrow 2 \rightarrow 3$ gives *R*, and counterclockwise gives *S*. A solid wedge points toward the viewer; a dashed wedge points away.

For the orientations drawn:

- At C2, the solid amino bond gives *S*, and the dashed amino bond gives *R*.
- At C3, the solid methyl bond gives *R*, and the dashed methyl bond gives *S*.

Consequently,

$$\boxed{A = (2S, 3S), \quad B = (2R, 3R), \quad C = (2S, 3R), \quad D = (2R, 3S).}$$

Their names and stereochemical SMILES are given in the answer table. The required box order is **C, D, A, B**.

2.3 — Relative standard molar Gibbs energies

For the epimerization of L-isoleucine to D-*allo*-isoleucine,

$$\Delta_r G^\circ = G_m^\circ(\text{D-*allo*-isoleucine}) - G_m^\circ(\text{L-isoleucine}) = -RT \ln K_{\text{ep}}.$$

Using $R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1}$,

$$\Delta_r G^\circ = -(8.314)(374) \ln(1.38) = -1.00 \times 10^3 \text{ J mol}^{-1} = -1.00 \text{ kJ mol}^{-1}.$$

Structure A is L-isoleucine, whose reference value is zero. Structure D is D-*allo*-isoleucine, so its value is $-1.00 \text{ kJ mol}^{-1}$.

Enantiomers have equal standard molar Gibbs energies in an achiral environment. A and B form one enantiomeric pair; C and D form the other. Therefore,

$$\boxed{G_m^\circ(\text{A}) = G_m^\circ(\text{B}) = 0 \text{ kJ mol}^{-1}}$$

and

$$\boxed{G_m^\circ(\text{C}) = G_m^\circ(\text{D}) = -1.00 \text{ kJ mol}^{-1}.$$

These are standard-state values; the equilibrium composition is accounted for separately by the activities in K_{ep} .

2.4 — Stereoisomers of Ile-Ile-Ile

Each isoleucine residue contributes two stereogenic carbon atoms. Formation of the two peptide bonds preserves these centres, giving

$$n = 3 \times 2 = 6$$

stereocentres.

For example, the all-L member, **L-isoleucyl-L-isoleucyl-L-isoleucine**, has SMILES:

CC[C@H](C)[C@H](N)C(=O)N[C@@H]([C@@H](C)CC)C(=O)N[C@@H]([C@@H](C)CC)C(=O)O

Each of the six centres can independently have either configuration. The distinct amino and carboxyl termini prevent an internal symmetry that would identify different assignments. Hence,

$$\boxed{N = 2^6 = 64}.$$

2.5 — Diastereomeric excess when the reverse reaction is neglected

Initially, the sample contains only L-isoleucine:

$$[D]_0 = 0, \quad [L]_0 = C_T,$$

where $C_T = [L] + [D]$ is conserved.

For irreversible first-order conversion,

$$[L](t) = C_T e^{-k_1 t}, \quad [D](t) = C_T (1 - e^{-k_1 t}).$$

Thus,

$$de(t) = (2e^{-k_1 t} - 1) \times 100\%.$$

a) Before boiling:

$$de(0) = (2 - 1) \times 100\% = \boxed{1.00 \times 10^2\%}.$$

b) After boiling:

$$k_1 t = (9.02 \times 10^{-5} \text{ h}^{-1})(1943 \text{ h}) = 0.1752586.$$

Therefore,

$$de = (2e^{-0.1752586} - 1) \times 100\% = 67.847993 \dots \%$$

To three significant figures,

$$\boxed{de = 67.8\%}.$$

2.6 — Time for 10% conversion at 298 K

First determine the activation energy using the Arrhenius equation:

$$\ln \frac{k_1(421)}{k_1(374)} = \frac{E_a}{R} \left(\frac{1}{374} - \frac{1}{421} \right).$$

Hence,

$$E_a = \frac{R \ln \left(\frac{1.18 \times 10^{-2}}{9.02 \times 10^{-5}} \right)}{\frac{1}{374 \text{ K}} - \frac{1}{421 \text{ K}}} = 1.3575 \dots \times 10^5 \text{ J mol}^{-1} \approx 136 \text{ kJ mol}^{-1}.$$

Assuming the same Arrhenius dependence down to 298 K, and retaining the unrounded activation energy,

$$k_1(298) = k_1(374) \exp \left[-\frac{E_a}{R} \left(\frac{1}{298 \text{ K}} - \frac{1}{374 \text{ K}} \right) \right].$$

This gives

$$k_1(298) = 1.31755 \dots \times 10^{-9} \text{ h}^{-1}.$$

Under the irreversible approximation used in this part, 10% conversion means

$$\frac{[L](t)}{[L]_0} = 0.900 = e^{-k_1 t}.$$

Therefore,

$$t = \frac{-\ln(0.900)}{1.31755 \dots \times 10^{-9} \text{ h}^{-1}} = 7.99668 \dots \times 10^7 \text{ h}.$$

Using 365 days per year,

$$t = 8.00 \times 10^7 \text{ h} \approx 9.13 \times 10^3 \text{ years}.$$

2.7 — Reversible epimerization

a) Equilibrium concentration

At equilibrium, the forward and reverse rates are equal:

$$k_1[\text{L}]_{\text{eq}} = k_2[\text{D}]_{\text{eq}}.$$

Consequently,

$$K_{\text{ep}} = \frac{[\text{D}]_{\text{eq}}}{[\text{L}]_{\text{eq}}} = \frac{k_1}{k_2}.$$

The total concentration remains

$$C_{\text{T}} = [\text{L}]_{\text{eq}} + [\text{D}]_{\text{eq}} = 1.00 \text{ mol dm}^{-3}.$$

Thus,

$$[\text{L}]_{\text{eq}} = \frac{C_{\text{T}}}{1 + K_{\text{ep}}} = \frac{1.00}{2.38} \text{ mol dm}^{-3} = 0.420168 \dots \text{ mol dm}^{-3},$$

so

$$[\text{L}]_{\text{eq}} = 0.420 \text{ mol dm}^{-3}.$$

b) Diastereomeric excess after boiling

The reverse rate constant is

$$k_2 = \frac{k_1}{K_{\text{ep}}} = \frac{9.02 \times 10^{-5}}{1.38} = 6.53623 \dots \times 10^{-5} \text{ h}^{-1}.$$

The supplied relaxation equation gives

$$[\text{L}](t) = [\text{L}]_{\text{eq}} + ([\text{L}]_0 - [\text{L}]_{\text{eq}})e^{-(k_1+k_2)t}.$$

Using $t = 1943 \text{ h}$, with intermediate quantities unrounded,

$$[\text{L}](t) = 0.8487494758 \dots \text{ mol dm}^{-3},$$

and

$$[\text{D}](t) = C_{\text{T}} - [\text{L}](t) = 0.1512505242 \dots \text{ mol dm}^{-3}.$$

Therefore,

$$de = \frac{0.8487494758 \dots - 0.1512505242 \dots}{1.00} \times 100\% = 69.749895 \dots \%.$$

The unrounded value lies just below the 69.75% rounding boundary. To three significant figures,

$$de = 69.7\%.$$

The reverse reaction leaves more L-isoleucine than the irreversible calculation, explaining the larger de .

2.8 — Boiling time of Lothar III

The interconverting enantiomers are **L-arginine**, with *S* configuration, and **D-arginine**, with *R* configuration. Their neutral free-amino-acid SMILES are:

- L-arginine: N[C@@H](CCCNC(=N)N)C(=O)O
- D-arginine: N[C@H](CCCNC(=N)N)C(=O)O

Define

$$r = \frac{[D]}{[L]}, \quad F(r) = \ln \frac{1+r}{1-r}.$$

The given kinetic law means that a period t at a constant rate coefficient k increases F by $2kt$. Thus, successive boiling and hydrolysis contributions add in F .

Take the two bodies to have the same initial stereochemical composition, corresponding to naturally occurring L-arginine, and neglect racemization during burial as instructed. If F_0 denotes their common initial value, then for Lothar,

$$F(0.090) = F_0 + 2k_1 t_b + 2k'_1(4 \text{ h}),$$

where t_b is the boiling time. For Richenza, who was not boiled,

$$F(0.059) = F_0 + 2k'_1(4 \text{ h}).$$

Subtracting eliminates both the initial contribution and the racemization caused by hydrolysis:

$$F(0.090) - F(0.059) = 2k_1 t_b.$$

Therefore,

$$t_b = \frac{\ln\left(\frac{1.090}{0.910}\right) - \ln\left(\frac{1.059}{0.941}\right)}{2(5.10 \times 10^{-3} \text{ h}^{-1})}.$$

Numerically,

$$t_b = \frac{0.1804883757 - 0.1181372060}{0.0102 \text{ h}^{-1}} = 6.11286 \dots \text{ h}.$$

At the precision supported by the measured ratios,

$$\boxed{t_b \approx 6.1 \text{ h}}.$$

The solution was checked against the official solution.

Problem 3: Emerging electro-mobility

Contemporary means of transportation rely on burning fossil fuels, although the efficiency of real combustion engines is inherently 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

Fuel cells represent a way to improve the engine efficiency for future vehicles. The engine efficiency can be improved by using hydrogen-based fuel cells.

3.2 The standard enthalpy of formation of liquid water is $\Delta_f H^\circ(\text{H}_2\text{O}, \text{l}) = -285.84 \text{ kJ mol}^{-1}$, and the standard combustion enthalpy of isooctane is $\Delta_c H^\circ(\text{C}_8\text{H}_{18}, \text{l}) = -5\,065.08 \text{ kJ mol}^{-1}$ (both at 323.15 K). Calculate the values of specific (per unit of mass) combustion enthalpy at 232.15 K of pure liquid isooctane and pure gaseous hydrogen.

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: $S^\circ(\text{H}_2\text{O}, \text{l}) = 70 \text{ J K}^{-1} \text{ mol}^{-1}$,

$$S^\circ(\text{H}_2, \text{g}) = 131 \text{ J K}^{-1} \text{ mol}^{-1},$$

$$S^\circ(\text{O}_2, \text{g}) = 205 \text{ J K}^{-1} \text{ mol}^{-1}.$$

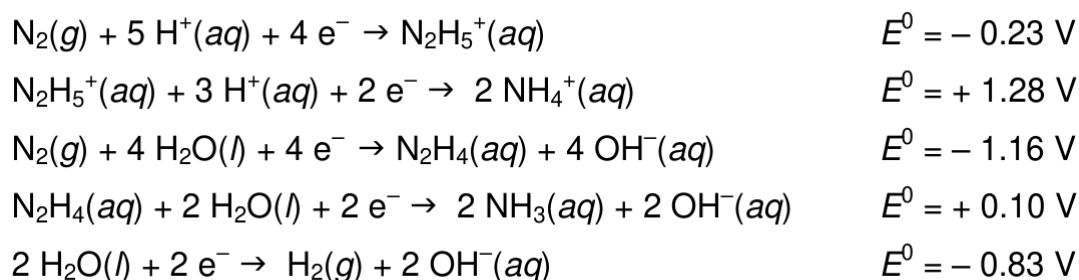
3.4 Determine the ideal thermodynamic efficiency (η) of a fuel cell producing liquid water at 353.15 K. At this temperature, the enthalpy of formation of water is $\Delta_f H^\circ(\text{H}_2\text{O}, \text{l}) = -281.64 \text{ kJ mol}^{-1}$ and the corresponding reaction Gibbs energy change is $\Delta_r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

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 produced hydrogen divided by its theoretical produced mass.

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 $\Delta_r G^\circ = -226 \text{ kJ mol}^{-1}$.

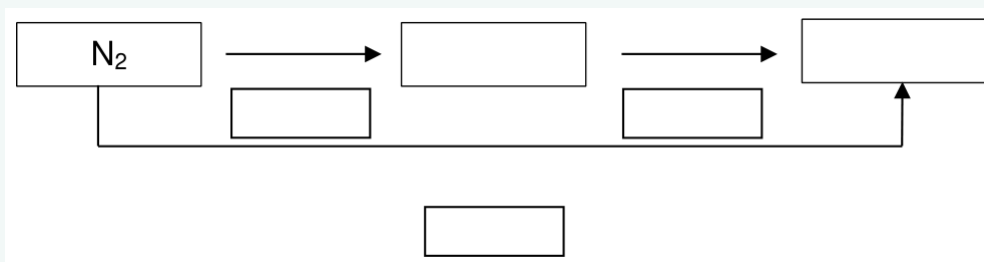
The low efficiency of hydrogen production and the safety issues connected with its storage impede spreading the hydrogen-based transportation technology. Hydrazine (N_2H_4) fuel cells might be a suitable alternative.

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

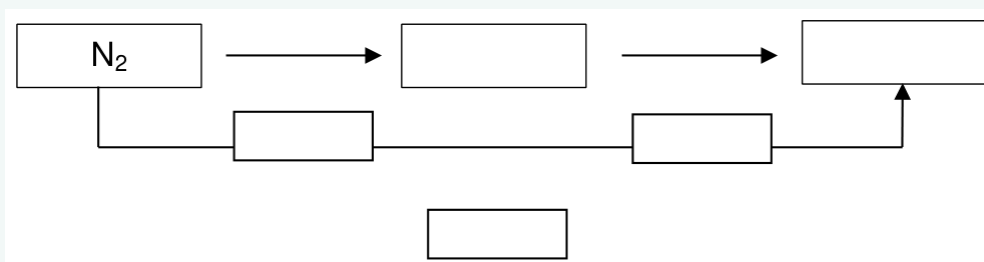


3.7 Fill in the following Latimer diagrams with the forms of hydrazine and ammonia prevailing at the given conditions and write the redox potential value for each arrow representing the electrochemical half-reaction. Record all the necessary calculations.

a) Acidic environment (pH = 0)



b) Basic environment (pH = 14)



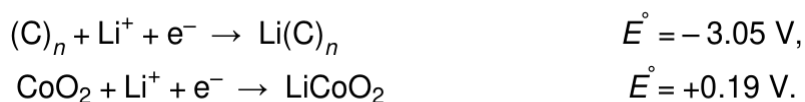
Due to the toxicity, odour and its environmental impact, it is extremely unfavourable to produce ammonia in fuel cells.

3.8 Write down the net reaction for the decomposition of hydrazine under basic conditions to:

- (i) ammonia and nitrogen,
- (ii) nitrogen and hydrogen.

Calculate the corresponding equilibrium constants at $T = 298.15 \text{ K}$.

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:



3.9 Using the formalism given above, write down the overall chemical reaction occurring in the battery during the **discharge** process. Give the oxidation states of the cobalt atom.

3.10 Tick the boxes to get the correct statements which are valid for the **discharge** of the lithium-based battery described in 3.9:

Li(C) _n electrode is	☐ cathode	☐ because lithium ions are reduced here.
	☐ anode	☐ because lithium atoms are oxidized here.
LiCoO ₂ electrode is	☐ cathode	☐ because cobalt ions are reduced here.

☐ anode

☐ because cobalt ions are oxidized here.

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 $mAh\ g^{-1}$) and the energy density (in $kWh\ kg^{-1}$) of such a model lithium ion battery related to the whole active battery mass.

Official English text of the problem.

Answers

- **3.1:** Tick **increasing the burning temperature** and **increasing the working pressure of the gas**, the latter through increased compression.
- **3.2:** Isooctane: $-44.34\ MJ\ kg^{-1}$; hydrogen: $-141.8\ MJ\ kg^{-1}$, using the supplied **323.15 K** data. Exact values at the printed **232.15 K** cannot be determined from the supplied information.
- **3.3:** $E^\circ = 1.207\ V \approx 1.21\ V$.
- **3.4:** $\eta = 80.2\%$.
- **3.5:** Theoretical hydrogen mass = $1.504 \times 10^3\ kg$; electrolysis yield = 72.5% .
- **3.6:** $m(H_2) = 6.92\ kg$.
- **3.7(a):** Middle box: hydrazinium, $N_2H_5^+$, $N[NH_3+]$; right box: ammonium, NH_4^+ , $[NH_4+]$. Successive arrow potentials: $-0.23\ V$, $+1.28\ V$; overall arrow: $+0.273\ V$.
- **3.7(b):** Middle box: hydrazine, N_2H_4 , NN ; right box: ammonia, NH_3 , N . Successive arrow potentials: $-1.16\ V$, $+0.10\ V$; overall arrow: $-0.740\ V$.
- **3.8(i):** $3\ N_2H_4(aq) \longrightarrow 4\ NH_3(aq) + N_2(g)$, with $K \approx 1.6 \times 10^{85}$.
- **3.8(ii):** $N_2H_4(aq) \longrightarrow N_2(g) + 2\ H_2(g)$, with $K \approx 2.1 \times 10^{22}$.
- **3.9:** $Li(C)_n + CoO_2 \longrightarrow (C)_n + LiCoO_2$. Cobalt changes from +4 in CoO_2 to +3 in $LiCoO_2$.
- **3.10:** $Li(C)_n$: **anode**, because lithium atoms are oxidized in the stated formalism. $LiCoO_2$: **cathode**, because cobalt ions are reduced.
- **3.11:** $E^\circ = 3.24\ V$; theoretical specific charge capacity $157.7\ mAh\ g^{-1} \approx 158\ mAh\ g^{-1}$; energy density $0.511\ kWh\ kg^{-1}$.

Solution

I use $F = 96485.3\ C\ mol^{-1}$, $R = 8.31446\ J\ K^{-1}\ mol^{-1}$, and conventional atomic molar masses.

The molecular and ionic species used in the solution are identified below. These SMILES specify connectivity and charge; physical states and electron transfer are specified separately in the equations.

Species	Name	SMILES
C_8H_{18}	Isooctane, 2,2,4-trimethylpentane	<chem>CC(C)(C)CC(C)C</chem>
H_2	Hydrogen	<chem>[H][H]</chem>

Species	Name	SMILES
O ₂	Oxygen	O=O
H ₂ O	Water	O
CO ₂	Carbon dioxide	O=C=O
N ₂	Nitrogen	N#N
N ₂ H ₄	Hydrazine	NN
N ₂ H ₅ ⁺	Hydrazinium ion	N[NH3+]
NH ₃	Ammonia	N
NH ₄ ⁺	Ammonium ion	[NH4+]
H ⁺	Hydrogen ion, proton	[H+]
OH ⁻	Hydroxide ion	[OH-]
Li ⁺	Lithium ion	[Li+]
Li	Lithium atom	[Li]
Co ⁴⁺	Cobalt(IV) ion, formal oxidation-state representation	[Co+4]
Co ³⁺	Cobalt(III) ion, formal oxidation-state representation	[Co+3]

Graphite, (C)_n; lithiated graphite, Li(C)_n; cobalt(IV) oxide, CoO₂; and lithium cobalt(III) oxide, LiCoO₂, are extended solids. A finite molecular SMILES cannot describe their full lattices or lithium intercalation. The cobalt-ion representations above do not describe the solid-state coordination geometry or imply free cobalt ions in solution.

3.1 — Factors affecting heat-engine efficiency

For a reversible heat engine operating between hot and cold reservoirs,

$$\eta_{\text{Carnot}} = 1 - \frac{T_c}{T_h},$$

where both temperatures are in kelvin.

Option	Selection	Reason
Increasing friction	Do not tick	Friction dissipates useful mechanical work.
Increasing the burning temperature	Tick	Raising the hot-side temperature can increase the attainable efficiency.
Narrowing the working temperature interval	Do not tick	Bringing the hot and cold temperatures closer reduces the attainable efficiency.
Increasing the working pressure	Tick	Increased compression raises working-gas pressure and can increase combustion-engine efficiency.

The compression effect can be illustrated by the ideal Otto-cycle relation

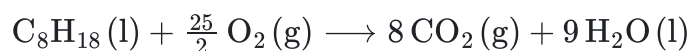
$$\eta_{\text{Otto}} = 1 - \frac{1}{r^{\gamma-1}},$$

where $r = V_{\text{max}}/V_{\text{min}}$ is the compression ratio and $\gamma = C_p/C_v > 1$. Increasing r increases efficiency. Thus the pressure option is selected, in the sense of a higher compression of the working gas.

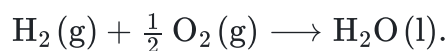
3.2 — Specific combustion enthalpies

The printed temperatures conflict: the enthalpies are supplied at 323.15 K, but the requested temperature is 232.15 K. The numerical calculation below uses the supplied 323.15 K data.

The balanced combustion equations, with liquid water as product, are



and



The second reaction is also the formation reaction of one mole of liquid water from its elements. Therefore,

$$\Delta_c H^\circ(\text{H}_2) = \Delta_f H^\circ(\text{H}_2\text{O}, \text{l}) = -285.84 \text{ kJ mol}^{-1}.$$

Specific combustion enthalpy is the molar combustion enthalpy divided by molar mass.

For isooctane,

$$M(\text{C}_8\text{H}_{18}) = 8(12.011) + 18(1.008) = 114.232 \text{ g mol}^{-1},$$
$$h_c^\circ = \frac{-5065.08}{114.232} = -44.3403 \text{ kJ g}^{-1} = \boxed{-44.34 \text{ MJ kg}^{-1}}.$$

For hydrogen,

$$M(\text{H}_2) = 2.016 \text{ g mol}^{-1},$$
$$h_c^\circ = \frac{-285.84}{2.016} = -141.786 \text{ kJ g}^{-1} = \boxed{-141.8 \text{ MJ kg}^{-1}}.$$

The negative signs denote exothermic combustion; the corresponding released-energy magnitudes are positive.

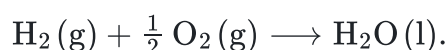
An exact temperature correction would require Kirchhoff's law,

$$\Delta_c H^\circ(232.15) = \Delta_c H^\circ(323.15) + \int_{323.15}^{232.15} \Delta_r C_p^\circ(T) dT,$$

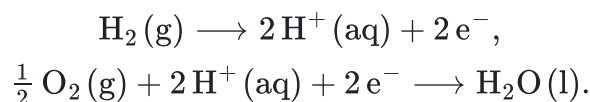
together with any necessary phase-change corrections. Those data are not supplied.

3.3 — Standard hydrogen–oxygen fuel-cell EMF

For one mole of hydrogen, the net reaction is



For example, it can be resolved into the balanced half-reactions



Thus $n = 2$ moles of electrons are transferred per mole of hydrogen.

The reaction entropy is

$$\begin{aligned}\Delta_r S^\circ &= S^\circ(\text{H}_2\text{O}, \text{l}) - S^\circ(\text{H}_2, \text{g}) - \frac{1}{2}S^\circ(\text{O}_2, \text{g}) \\ &= 70 - 131 - \frac{205}{2} \\ &= -163.5 \text{ J K}^{-1} \text{ mol}^{-1}.\end{aligned}$$

Consequently,

$$\begin{aligned}\Delta_r G^\circ &= \Delta_r H^\circ - T\Delta_r S^\circ \\ &= -285.84 - (323.15)(-0.1635) \\ &= -233.005 \text{ kJ mol}^{-1}.\end{aligned}$$

Using $\Delta_r G^\circ = -nFE^\circ$,

$$E^\circ = \frac{233005 \text{ J mol}^{-1}}{2(96485.3 \text{ C mol}^{-1})} = \boxed{1.207 \text{ V}}.$$

Each gas is at the standard pressure of 100 kPa, and pure liquid water has unit activity, so no Nernst correction is required.

3.4 — Ideal thermodynamic fuel-cell efficiency

The maximum electrical work is $-\Delta_r G^\circ$, while the combustion-energy input on the stated liquid-water basis is $-\Delta_r H^\circ$. Therefore,

$$\eta = \frac{-\Delta_r G^\circ}{-\Delta_r H^\circ} = \frac{225.85}{281.64} = 0.80191.$$

Hence,

$$\boxed{\eta = 80.2\%}.$$

3.5 — Electrolysis yield

The net electrolysis reaction is



Producing one mole of hydrogen requires two moles of electrons.

The operating time is

$$t = 8.00 \text{ h} = 28800 \text{ s}.$$

The electrical energy supplied is

$$W_{\text{el}} = Pt = (10.0 \times 10^6 \text{ W})(28800 \text{ s}) = 2.88 \times 10^{11} \text{ J}.$$

Since $W_{\text{el}} = UQ$,

$$Q = \frac{W_{\text{el}}}{U} = \frac{2.88 \times 10^{11}}{2.00} = 1.44 \times 10^{11} \text{ C}.$$

The theoretical hydrogen amount is

$$n_{\text{theor}}(\text{H}_2) = \frac{Q}{2F} = \frac{1.44 \times 10^{11}}{2(96485.3)} = 7.4623 \times 10^5 \text{ mol}.$$

Thus,

$$m_{\text{theor}} = (7.4623 \times 10^5)(2.016 \times 10^{-3}) = 1504.4 \text{ kg}.$$

The required mass yield is

$$Y = \frac{m_{\text{actual}}}{m_{\text{theor}}} = \frac{1090}{1504.4} = 0.72454,$$

or

$$\boxed{Y = 72.5\%}.$$

3.6 — Hydrogen needed for the journey

The travel time is

$$t = \frac{330 \text{ km}}{100 \text{ km h}^{-1}} = 3.30 \text{ h} = 11880 \text{ s}.$$

The average mechanical output power is

$$P_{\text{mech}} = 0.15(310) = 46.5 \text{ kW}.$$

The required mechanical work is therefore

$$W_{\text{mech}} = (46.5 \text{ kJ s}^{-1})(11880 \text{ s}) = 552420 \text{ kJ}.$$

Using the supplied Gibbs energy as the reversible electrical energy per mole, the useful mechanical energy obtained per mole of hydrogen is

$$w_{\text{mech,m}} = \eta_{\text{cell}}\eta_{\text{motor}} |\Delta_r G| = (0.75)(0.95)(226) = 161.025 \text{ kJ mol}^{-1}.$$

Hence,

$$n(\text{H}_2) = \frac{552420}{161.025} = 3430.65 \text{ mol},$$

$$m(\text{H}_2) = (3430.65)(2.016 \times 10^{-3}) = \boxed{6.92 \text{ kg}}.$$

The Gibbs-energy value already represents reversible electrical work; the thermodynamic factor from 3.4 is not applied again.

3.7 — Latimer diagrams

When consecutive reduction half-reactions are added, their Gibbs energies add. Since

$$\Delta G_i^\circ = -n_i F E_i^\circ,$$

the combined potential is

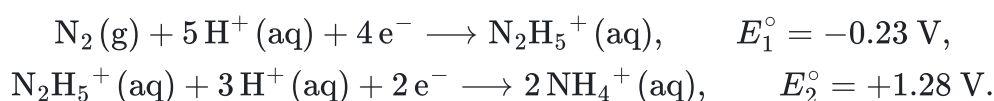
$$E_{\text{overall}}^\circ = \frac{n_1 E_1^\circ + n_2 E_2^\circ}{n_1 + n_2}.$$

The potentials must therefore be weighted by electron numbers.

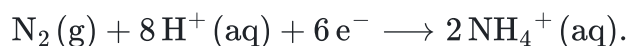
(a) Acidic environment, pH = 0

The prevailing forms represented by the supplied acidic half-reactions are hydrazinium, N_2H_5^+ , and ammonium, NH_4^+ . Their protonated forms are favoured in strongly acidic solution.

The half-reactions are



Adding gives



Thus,

$$E_{\text{overall}}^{\circ} = \frac{4(-0.23) + 2(+1.28)}{6} = \boxed{+0.273 \text{ V}}.$$

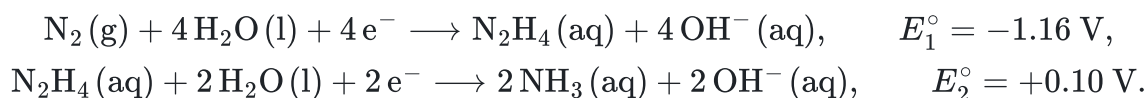
Fill the diagram precisely as follows:

- Left box: nitrogen, N_2 , already printed.
- Middle box: N_2H_5^+ .
- Right box: NH_4^+ .
- First horizontal arrow: -0.23 V .
- Second horizontal arrow: $+1.28 \text{ V}$.
- Lower bypass arrow from the left box to the right box: $+0.273 \text{ V}$.

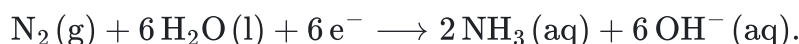
(b) Basic environment, pH = 14

Under strongly basic conditions, the corresponding prevailing forms are neutral hydrazine, N_2H_4 , and ammonia, NH_3 .

The half-reactions are



Adding gives



Therefore,

$$E_{\text{overall}}^{\circ} = \frac{4(-1.16) + 2(+0.10)}{6} = \boxed{-0.740 \text{ V}}.$$

Fill the diagram as follows:

- Left box: nitrogen, N_2 , already printed.
- Middle box: N_2H_4 .
- Right box: NH_3 .
- First horizontal arrow: -1.16 V .
- Second horizontal arrow: $+0.10 \text{ V}$.
- Lower bypass arrow: -0.740 V .

3.8 — Hydrazine decomposition and equilibrium constants

For a reaction assembled from oxidation and reduction half-reactions,

$$E_{\text{cell}}^{\circ} = E_{\text{cathode,red}}^{\circ} - E_{\text{anode,red}}^{\circ}.$$

Combining

$$\Delta_{\text{r}}G^{\circ} = -nFE_{\text{cell}}^{\circ}$$

with

$$\Delta_{\text{r}}G^{\circ} = -RT \ln K$$

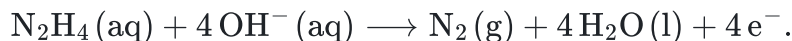
gives

$$\ln K = \frac{nFE_{\text{cell}}^{\circ}}{RT}.$$

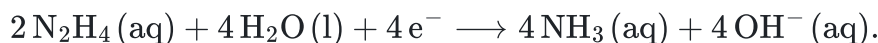
The value of n , and consequently K , refers to the balanced reaction exactly as written.

(i) Decomposition to ammonia and nitrogen

Reverse the nitrogen-to-hydrazine reduction half-reaction:



Multiply the hydrazine-to-ammonia reduction half-reaction by two:



After cancellation,



This is disproportionation: some hydrazine nitrogen is oxidized from oxidation state -2 to 0 , while the remainder is reduced from -2 to -3 .

For the integer-balanced reaction above, $n = 4$, and

$$E_{\text{cell}}^{\circ} = 0.10 - (-1.16) = 1.26 \text{ V}.$$

At 298.15 K,

$$\ln K = \frac{4(96485.3)(1.26)}{(8.31446)(298.15)} = 196.166.$$

Equivalently,

$$\log_{10} K = 85.194,$$

so

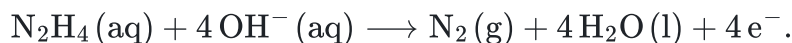
$$K \approx 1.6 \times 10^{85}.$$

For ideal gases, its dimensionless activity expression is

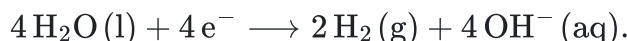
$$K = \frac{a_{\text{NH}_3}^4 (p_{\text{N}_2}/p^{\circ})}{a_{\text{N}_2\text{H}_4}^3}.$$

(ii) Decomposition to nitrogen and hydrogen

Use the same hydrazine oxidation half-reaction:



Multiply the supplied water-to-hydrogen reduction half-reaction by two:



The net reaction is



Again $n = 4$, while

$$E_{\text{cell}}^{\circ} = -0.83 - (-1.16) = 0.33 \text{ V}.$$

Therefore,

$$\ln K = \frac{4(96485.3)(0.33)}{(8.31446)(298.15)} = 51.3767,$$

$$\log_{10} K = 22.3126,$$

and

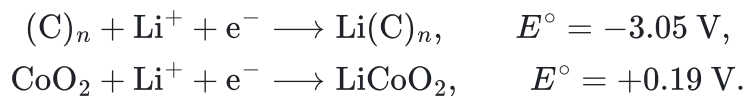
$$\boxed{K \approx 2.1 \times 10^{22}}.$$

The corresponding dimensionless activity expression is

$$K = \frac{(p_{\text{N}_2}/p^\circ)(p_{\text{H}_2}/p^\circ)^2}{a_{\text{N}_2\text{H}_4}}.$$

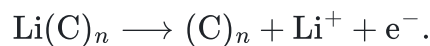
3.9 — Battery discharge reaction and cobalt oxidation states

The supplied reduction potentials are

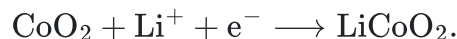


During spontaneous discharge, the half-reaction with the higher reduction potential proceeds as reduction. The graphite half-reaction is reversed.

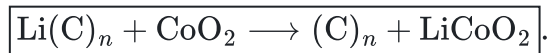
Oxidation:



Reduction:



Adding and cancelling the lithium ion and electron gives



For cobalt in CoO_2 ,

$$x + 2(-2) = 0 \implies x = +4.$$

For cobalt in LiCoO_2 ,

$$(+1) + x + 2(-2) = 0 \implies x = +3.$$

Thus cobalt is reduced from **cobalt(IV) to cobalt(III)** during discharge.

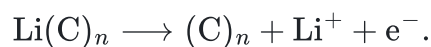
3.10 — Electrode identification

Oxidation occurs at the anode, and reduction occurs at the cathode.

For the $\text{Li}(\text{C})_n$ **electrode**, tick:

- **anode;**
- **because lithium atoms are oxidized here.**

These selections follow the problem's formal representation



For the LiCoO_2 **electrode**, tick:

- **cathode;**
- **because cobalt ions are reduced here.**

Cobalt changes from +4 to +3 as lithium is inserted into the cobalt-oxide electrode. Electrons flow through the external circuit from the lithiated-graphite electrode to the cobalt-oxide electrode.

3.11 — Specific charge capacity and energy density

The standard discharge EMF is

$$E^{\circ} = E_{\text{cathode,red}}^{\circ} - E_{\text{anode,red}}^{\circ} = 0.19 - (-3.05) = \boxed{3.24 \text{ V}}.$$

The active mass associated with transferring one mole of electrons contains one mole each of C_6 , CoO_2 , and lithium atoms:

$$\begin{aligned} M_{\text{active}} &= 6(12.011) + 58.933 + 2(15.999) + 6.94 \\ &= 169.937 \text{ g mol}^{-1}. \end{aligned}$$

The lithium mass is counted once, and both electrodes' active materials are included.

One mole of electrons carries charge F . Because

$$1 \text{ mAh} = 3.6 \text{ C},$$

the theoretical specific reversible charge capacity is

$$\begin{aligned} q_{\text{sp}} &= \frac{F}{M_{\text{active}}} \frac{1 \text{ mAh}}{3.6 \text{ C}} \\ &= \frac{96485.3}{3.6(169.937)} \\ &= \boxed{157.7 \text{ mAh g}^{-1}}. \end{aligned}$$

Numerically, this is also 157.7 Ah kg^{-1} . Thus the specific reversible energy is

$$\begin{aligned} w_{\text{sp}} &= E^{\circ} q_{\text{sp}} \\ &= (3.24 \text{ V})(157.7 \text{ Ah kg}^{-1}) \\ &= 511.0 \text{ Wh kg}^{-1} \\ &= \boxed{0.511 \text{ kWh kg}^{-1}}. \end{aligned}$$

The solution was checked against the official solution.

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 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.

The activated target is dissolved in concentrated hydrochloric acid ($\text{HCl}(\text{aq})$) 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 $[\text{Cl}^{-}] = 4 \text{ mol dm}^{-3}$. For the overall complexation constants, β , see Table 1.

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

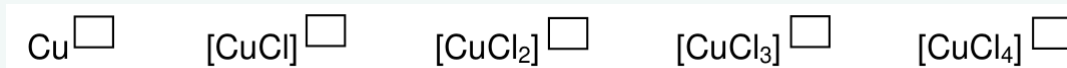


Table 1. Overall complexation constants β of Cu species (charges were omitted in the formula).

$$\beta_i = \frac{[\text{CuCl}_i]}{[\text{Cu}] \times [\text{Cl}]^i}$$

i in $[\text{CuCl}_i]$	1	2	3	4
β_i	2.36	1,49	0.690	0.055

The mixture containing Cu^{2+} and Zn^{2+} ions and their respective chlorido 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 Everything was initially at laboratory 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 formula 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:

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

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

(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 formula, separation of two sets of species, **A** and **B**, can be considered complete if

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

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.

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

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

$$V_{0.999}(\mathbf{B}) = 2V_{\mathbf{R}}(\mathbf{B}) - V_{0.001}(\mathbf{B})$$

4.5 Based on a calculation, decide whether copper species were separated completely from 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 $L_c = 13.0 \text{ cm}$.

4.6 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} . Consider 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%.

(If you cannot find 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 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 $0.1027 \text{ mol dm}^{-3}$ 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.

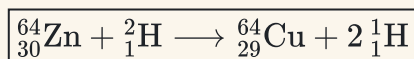
(If you cannot find the answer, use $Q_v = 1.00 \text{ mmol cm}^{-3}$ for further calculations.)

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

Official English text of the problem.

Answers

- **4.1**



Two protons are emitted.

- **4.2** Fill the boxes, from left to right, with 2+, +, 0, −, 2−. The mole fraction of negatively charged copper species is

$$x_- = 0.629 \quad (62.9\%).$$

- **4.3** Select "Yes, the temperature increases."
- **4.4**

$$V_{\mathbf{R}}(\text{Cu}) = 69.7 \text{ cm}^3, \quad V_{\mathbf{R}}(\text{Zn}) = 297 \text{ cm}^3.$$

- 4.5 Yes, separation is complete according to the given criterion:

$$V_{0.001}(\text{Zn}) - V_{0.999}(\text{Cu}) = 148.7 \text{ cm}^3 > 102.1 \text{ cm}^3.$$

- 4.6

$$Q_{\text{m,theor}} = 3.45 \text{ mmol g}^{-1}.$$

- 4.7

$$Q_v = 1.117 \text{ mmol cm}^{-3}.$$

- 4.8

$$x = 0.889 \quad (88.9\%).$$

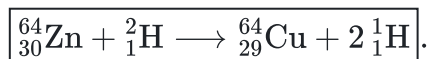
Solution

4.1

Both the mass number A and atomic number Z must balance. The reactants have

$$A_{\text{total}} = 64 + 2 = 66, \quad Z_{\text{total}} = 30 + 1 = 31.$$

After formation of ${}^{64}_{29}\text{Cu}$, the remaining particles must therefore carry a total mass number of 2 and atomic number of 2. These are two protons:



Species	Name	Atomic number Z	Mass number A
${}^{64}_{30}\text{Zn}$	Zinc-64 nucleus	30	64
${}^2_1\text{H}$	Deuteron	1	2
${}^{64}_{29}\text{Cu}$	Copper-64 nucleus	29	64
${}^1_1\text{H}$	Proton	1	1

The isotope atom SMILES are zinc-64 [${}^{64}\text{Zn}$] and copper-64 [${}^{64}\text{Cu}$]; the deuteron and proton can be represented as [$2\text{H}+$] and [$1\text{H}+$]. The metal SMILES identify isotopes as atoms; they do not represent the bare nuclei or encode the nuclear reaction.

4.2

Copper remains in oxidation state +2. Each chlorido ligand contributes charge -1 , so a complex containing i chlorido ligands has charge $2 - i$.

Thus the boxes should contain, from left to right,

$$2+, \quad +, \quad 0, \quad -, \quad 2-.$$

The species and their relative concentrations are:

Species	Name	SMILES	Concentration relative to $[\text{Cu}^{2+}]$
Cu^{2+}	Copper(II) ion	[Cu+2]	1
$[\text{CuCl}]^+$	Chloridocopper(II) ion	[Cu+2]<-[Cl-]	$2.36(4) = 9.44$

Species	Name	SMILES	Concentration relative to $[\text{Cu}^{2+}]$
$[\text{CuCl}_2]$	Dichloridocopper(II)	$[\text{Cu}+2](<-[\text{Cl}-])<-[\text{Cl}-]$	$1.49(4)^2 = 23.84$
$[\text{CuCl}_3]^-$	Trichloridocuprate(II) ion	$[\text{Cu}+2](<-[\text{Cl}-])<-[\text{Cl}-])<-[\text{Cl}-]$	$0.690(4)^3 = 44.16$
$[\text{CuCl}_4]^{2-}$	Tetrachloridocuprate(II) ion	$[\text{Cu}+2](<-[\text{Cl}-])<-[\text{Cl}-])<-[\text{Cl}-])<-[\text{Cl}-]$	$0.055(4)^4 = 14.08$

Here chloride is Cl^- , SMILES $[\text{Cl}-]$. The arrows in these extended SMILES denote ligand-to-metal dative bonds. Solvent ligands are omitted, as in the problem; these representations do not establish coordination geometries. The other uncomplexed metal ion in the mixture is zinc(II), Zn^{2+} , SMILES $[\text{Zn}+2]$.

Because the given constants are **overall** complexation constants,

$$c_{\text{Cu,total}} = [\text{Cu}^{2+}] \left(1 + \sum_{i=1}^4 \beta_i [\text{Cl}^-]^i \right).$$

Every species contains one copper atom. Consequently, the required mole fraction is the sum of the concentrations of the two anionic complexes divided by the total copper concentration:

$$\begin{aligned}
 x_- &= \frac{[[\text{CuCl}_3]^-] + [[\text{CuCl}_4]^{2-}]}{c_{\text{Cu,total}}} \\
 &= \frac{0.690(4)^3 + 0.055(4)^4}{1 + 2.36(4) + 1.49(4)^2 + 0.690(4)^3 + 0.055(4)^4} \\
 &= \frac{44.16 + 14.08}{1 + 9.44 + 23.84 + 44.16 + 14.08} \\
 &= \frac{58.24}{92.52} = 0.6294855.
 \end{aligned}$$

Therefore,

$$\boxed{x_- = 0.629 \approx 62.9\%}.$$

4.3

During conversion of the resin to its chloride form, chloride becomes the counterion at the exchange sites. Hydrogen ions from hydrochloric acid neutralize the hydroxide counterions:



This neutralization is exothermic, so the column temperature increases.

The relevant species are the hydrogen ion $[\text{H}^+]$, hydroxide ion $[\text{OH}^-]$, and water O. Aqueous hydrochloric acid is represented by its dissociated ions, $[\text{H}^+] \cdot [\text{Cl}^-]$.

Select **"Yes, the temperature increases."**

4.4

Apply the supplied relation separately to the copper and zinc species:

$$V_{\text{R}} = D_{\text{g}} m_{\text{resin,dry,OH form}} + V_0.$$

For copper,

$$\begin{aligned}V_R(\text{Cu}) &= (17.4 \text{ cm}^3 \text{ g}^{-1})(3.72 \text{ g}) + 4.93 \text{ cm}^3 \\&= 69.658 \text{ cm}^3 \\&\approx \boxed{69.7 \text{ cm}^3}.\end{aligned}$$

For zinc,

$$\begin{aligned}V_R(\text{Zn}) &= (78.5 \text{ cm}^3 \text{ g}^{-1})(3.72 \text{ g}) + 4.93 \text{ cm}^3 \\&= 296.95 \text{ cm}^3 \\&\approx \boxed{297 \text{ cm}^3}.\end{aligned}$$

Thus copper elutes earlier and zinc later.

4.5

The later-eluting species must be identified as **A**, so

$$\mathbf{A} = \text{zinc species}, \quad \mathbf{B} = \text{copper species}.$$

First express the particle diameter and column height in the same units:

$$d_p = 0.125 \text{ mm} = 0.0125 \text{ cm}, \quad L_c = 13.0 \text{ cm}.$$

Define the dimensionless factor

$$f = 6.91 \sqrt{\frac{d_p}{L_c}} = 6.91 \sqrt{\frac{0.0125}{13.0}} = 0.214270.$$

Using the unrounded retention volumes from 4.4,

$$\begin{aligned}V_{0.001}(\text{Zn}) &= 296.95(1 - 0.214270) \text{ cm}^3 \\&= 233.3225 \text{ cm}^3,\end{aligned}$$

and

$$\begin{aligned}V_{0.001}(\text{Cu}) &= 69.658(1 - 0.214270) \text{ cm}^3 \\&= 54.7324 \text{ cm}^3.\end{aligned}$$

Therefore,

$$\begin{aligned}V_{0.999}(\text{Cu}) &= 2V_R(\text{Cu}) - V_{0.001}(\text{Cu}) \\&= 2(69.658) - 54.7324 \\&= 84.5836 \text{ cm}^3.\end{aligned}$$

The separation gap is

$$V_{0.001}(\text{Zn}) - V_{0.999}(\text{Cu}) = 233.3225 - 84.5836 = 148.7389 \text{ cm}^3.$$

The required minimum is

$$10V_c = 10(10.21) = 102.1 \text{ cm}^3.$$

Since

$$\boxed{148.7 \text{ cm}^3 > 102.1 \text{ cm}^3},$$

the separation is complete according to the supplied experimental criterion.

4.6

A tetraalkylammonium exchange site, R_4N^+ , contains one nitrogen atom and carries one positive charge. Its generic structural SMILES is [*][N+]([*])([*])[*], where each wildcard denotes an unspecified alkyl substituent; the substituents include attachment to the resin. The exact polymer structure is not given.

Since all nitrogen belongs to these groups, one mole of nitrogen corresponds to one mole of theoretical exchange sites.

Using the standard nitrogen molar mass $M(N) = 14.01 \text{ g mol}^{-1}$,

$$\begin{aligned} Q_{\text{m,theor}} &= \frac{w_N}{M(N)} \\ &= \frac{0.0483}{14.01 \text{ g mol}^{-1}} \\ &= 0.00344754 \text{ mol g}^{-1} \\ &= \boxed{3.45 \text{ mmol g}^{-1}}. \end{aligned}$$

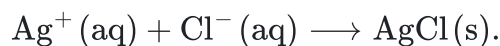
This is the capacity if every tetraalkylammonium group participates in ion exchange.

4.7

Excess sulfate displaces the exchangeable chloride counterions. Each active tetraalkylammonium group initially holds one chloride ion, so

$$n_{\text{active groups}} = n_{\text{displaced chloride}}.$$

The chloride is determined by precipitation with silver(I):



The stoichiometric ratio is 1 : 1.

The relevant species are sulfate ion [O-]S(=O)(=O)[O-], silver(I) ion [Ag+], and silver chloride [Ag+] . [Cl-]. The reagents are sodium sulfate [Na+] . [Na+] . [O-]S(=O)(=O)[O-] and silver nitrate [Ag+] . [O-][N+](=O)[O-]. These dotted SMILES identify ionic components; silver chloride forms an extended solid lattice.

The amount of chloride in the 100 cm^3 aliquot is

$$\begin{aligned} n_{\text{aliquot}}(\text{Cl}^-) &= c(\text{AgNO}_3)V_{\text{eq}} \\ &= (0.1027 \text{ mol dm}^{-3})(22.20 \times 10^{-3} \text{ dm}^3) \\ &= 2.27994 \times 10^{-3} \text{ mol} \\ &= 2.27994 \text{ mmol}. \end{aligned}$$

The entire 500 cm^3 solution contains five times this amount:

$$n_{\text{active groups}} = \frac{500}{100}(2.27994) = 11.3997 \text{ mmol}.$$

Hence the capacity per unit swollen-resin volume is

$$\begin{aligned}
 Q_v &= \frac{n_{\text{active groups}}}{V_c} \\
 &= \frac{11.3997 \text{ mmol}}{10.21 \text{ cm}^3} \\
 &= \boxed{1.117 \text{ mmol cm}^{-3}}.
 \end{aligned}$$

4.8

The total amount of tetraalkylammonium groups in the original 3.72 g of dry resin is

$$\begin{aligned}
 n_{\text{total groups}} &= m_{\text{resin}} Q_{m,\text{theor}} \\
 &= (3.72 \text{ g})(3.447537 \text{ mmol g}^{-1}) \\
 &= 12.82484 \text{ mmol}.
 \end{aligned}$$

The active fraction is therefore

$$\begin{aligned}
 x &= \frac{n_{\text{active groups}}}{n_{\text{total groups}}} \\
 &= \frac{Q_v V_c}{Q_{m,\text{theor}} m_{\text{resin}}} \\
 &= \frac{11.3997}{12.82484} \\
 &= 0.8888766.
 \end{aligned}$$

Thus,

$$x = 0.889, \quad \text{or } 88.9\%.$$

The solution was checked against the official solution.

Problem 5: Bohemian garnet

The dodecahedral splitting diagram referred to in 5.4 and the formula defining x, y in 5.13 are not printed in this version of the problem.

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 $A_3B_2(\text{SiO}_4)_3$, 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 with six O atoms) and Si^{IV} is surrounded with four O atoms arranged into a tetrahedron.

The most common garnet mineral is almandine with the formula of $\text{Fe}_3\text{Al}_2(\text{SiO}_4)_3$. Its unit cell parameter is $a = 11.50 \text{ \AA}$.

5.1 Calculate the theoretical density of almandine.

The Bohemian garnet has the composition of $\text{Mg}_3\text{Al}_2(\text{SiO}_4)_3$. 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 $[\text{Cr}^{\text{III}}\text{O}_6]^{\text{oct}}$ d-orbitals and fill it with electrons.

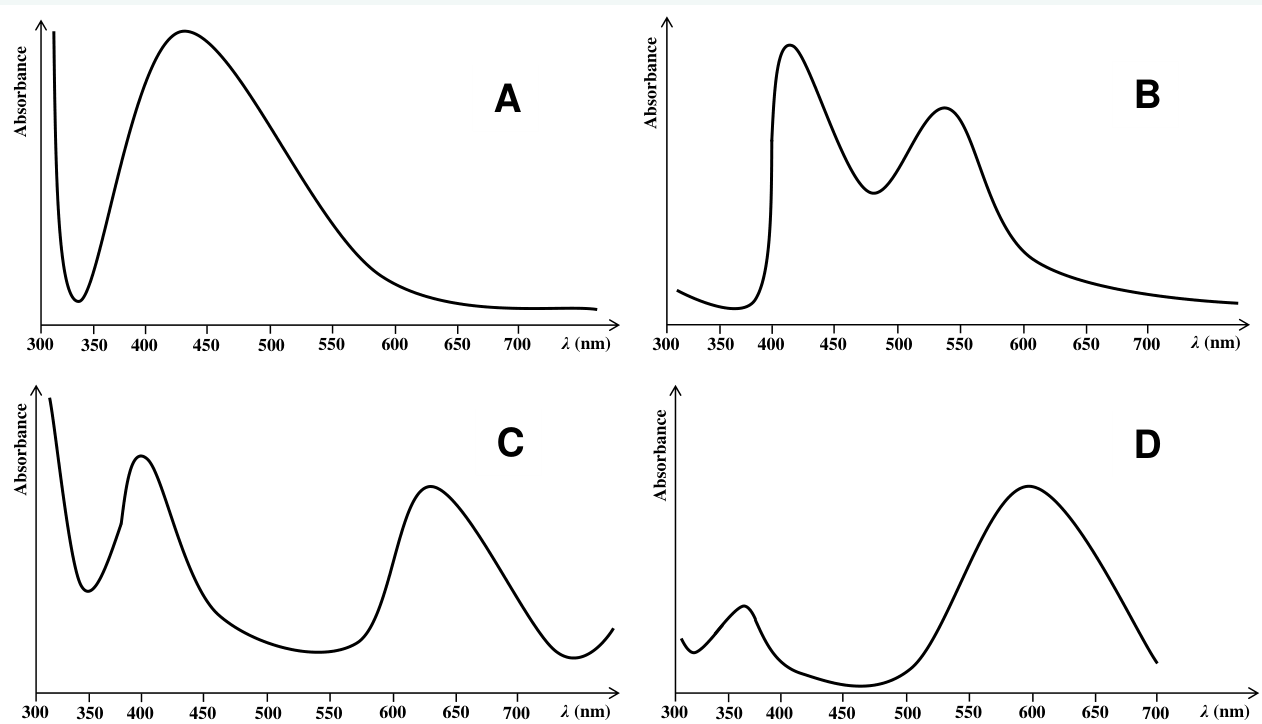
5.3 Identify the 1st transition row element(s) whose trivalent cation(s) M^{III} placed in an **octahedral** position is/are diamagnetic in the low-spin arrangement and paramagnetic in the high-spin arrangement.

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

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.

5.6 Assuming that $P > E_3$, identify the 1st transition row element(s) whose divalent cation M^{II} placed in dodecahedral position 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.

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 $\text{Ca}_3[\text{Fe}, \text{Ti}]_2^{\text{oct}}([\text{Si}, \text{Fe}]^{\text{tet}}\text{O}_4)_3$.

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 position are substituted with Ti^{IV} .

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

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

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 ($11\,000\text{ cm}^{-1}$) than for the tetrahedral one ($22\,000\text{ cm}^{-1}$).

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.

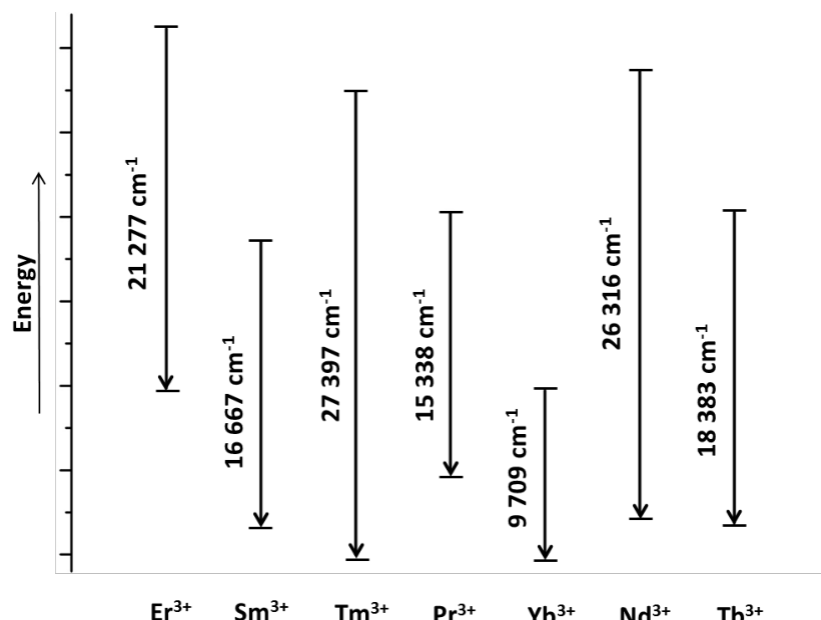
Synthetic garnet YAG (Yttrium Aluminium Garnet), used in optoelectronics, has the composition of $\text{Y}_3\text{Al}_5\text{O}_{12}$. Its structure is derived from the general garnet structure $\text{A}_3\text{B}_2(\text{SiO}_4)_3$ by placing the ions Y^{III} and Al^{III} to the A, B and Si positions.

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

5.13 For the 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. (If you don't get result, use $x = 2.25$ and $y = 0.75$.)

5.14 The Ce^{III} -doped YAG is prepared by annealing the mixture of Y_2O_3 , Al_2O_3 and CeO_2 in H_2 atmosphere. Use 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-earths 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-earths ions are shown.



5.15 Which cation has a transition which 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.

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

Official English text of the problem.

Answers

For **5.4–5.6**, use the usual dodecahedral level order

$$\varepsilon_a < \varepsilon_b < \varepsilon_c = \varepsilon_d < \varepsilon_e,$$

with adjacent gaps g_L, g_M, g_H , from bottom to top. The missing diagram prevents confirmation of their correspondence to E_1, E_2, E_3 .

- 5.1:** $\rho = 4.348 \text{ g cm}^{-3}$.
- 5.2:** Chromium(III), Cr^{3+} , $[\text{Cr}^{3+}]$: d^3 , configuration $t_{2g}^3 e_g^0$, with three unpaired electrons.
- 5.3:** **Cobalt**, through cobalt(III), Co^{3+} , $[\text{Co}^{3+}]$: low-spin t_{2g}^6 , high-spin $t_{2g}^4 e_g^2$.
- 5.4:** Iron(II), Fe^{2+} , $[\text{Fe}^{2+}]$, is d^6 . Lower-spin: $a^2 b^2 c^1 d^1 e^0$, two unpaired electrons. High-spin: $a^2 b^1 c^1 d^1 e^1$, four unpaired electrons.
- 5.5:** Lower-spin when $P < g_M + g_H$; high-spin when $P > g_M + g_H$. If E_1, E_2, E_3 run from bottom to top, the threshold is $E_2 + E_3$; if they run from top to bottom, it is $E_1 + E_2$.

- **5.6:** The possible diamagnetic lower-spin ions are titanium(II), [Ti+2], chromium(II), [Cr+2], and nickel(II), [Ni+2], requiring $P < g_L$, $P < g_M$, and $P < g_H$, respectively. The condition $P > E_3$ excludes the ion associated with that gap. **For bottom-to-top E_1, E_2, E_3 , the answer is titanium and chromium; for top-to-bottom numbering, it is chromium and nickel.**
- **5.7:** A: citrine; B: Bohemian garnet; C: uvarovite; D: sapphire.
- **5.8:** Black, in the intended absorption model.
- **5.9:** 3.33% of the silicon(IV) sites.
- **5.10:** Iron(III), Fe^{3+} , [Fe+3], is high-spin d^5 in both sites: octahedral $t_{2g}^3 e_g^2$, tetrahedral $e^2 t_2^3$. Both have five unpaired electrons.
- **5.11:** In spectroscopic units,

$$\frac{P}{hc} = 30\,800\text{ cm}^{-1}, \quad \frac{\Delta_{\text{oct}}}{hc} = 19\,800\text{ cm}^{-1}, \quad \frac{\Delta_{\text{tet}}}{hc} = 8\,800\text{ cm}^{-1}.$$
- **5.12:** Yttrium(III), [Y+3], occupies the eight-coordinate A sites. Aluminium(III), [Al+3], occupies both the six-coordinate B sites and the four-coordinate Si sites.
- **5.13:** Taking the formula as $\text{Y}_x\text{Ce}_y\text{Al}_5\text{O}_{12}$, $x = 2.85$, $y = 0.15$. The substituent is cerium(III), [Ce+3].
- **5.14:**

$$57\text{Y}_2\text{O}_3 + 100\text{Al}_2\text{O}_3 + 6\text{CeO}_2 + 3\text{H}_2 \longrightarrow 40\text{Y}_2 \cdot 85\text{Ce}_0 \cdot 15\text{Al}_5\text{O}_{12} + 3\text{H}_2\text{O}.$$

The molecular reactant and product are hydrogen [H][H] and water o.
- **5.15:** Er^{3+} , erbium(III), [Er+3].
- **5.16:** $\lambda = 470.0\text{ nm}$.
- **5.17:** Blue-green, taking the emitted light to correspond to the same electronic transition that the garnet absorbs.

Solution

The garnets and metal oxides are extended crystalline solids, so a molecular SMILES would not describe their structures. The atomic-ion SMILES above identify the relevant ions but do not encode their coordination geometry or the shared oxygen lattice. The oxygen sites are formally oxide ions, O^{2-} , [O-2].

5.1 — Density of almandine

Using standard atomic masses,

$$\begin{aligned} M(\text{Fe}_3\text{Al}_2(\text{SiO}_4)_3) &= 3M(\text{Fe}) + 2M(\text{Al}) + 3M(\text{Si}) + 12M(\text{O}) \\ &= 497.74\text{ g mol}^{-1}. \end{aligned}$$

Each unit cell contains eight formula units, so

$$m_{\text{cell}} = \frac{8M}{N_A}.$$

The cell volume is

$$V_{\text{cell}} = a^3 = (11.50 \times 10^{-8} \text{ cm})^3 = 1.520875 \times 10^{-21} \text{ cm}^3.$$

Therefore,

$$\rho = \frac{8(497.74 \text{ g mol}^{-1})}{(6.02214076 \times 10^{23} \text{ mol}^{-1})(1.520875 \times 10^{-21} \text{ cm}^3)} = \boxed{4.348 \text{ g cm}^{-3}}.$$

5.2 — Octahedral chromium(III)

Chromium(III) has three d electrons. In an octahedral field, the three t_{2g} orbitals lie below the two e_g orbitals. Hund's rule places one electron in each lower orbital.

The required drawing has:

Level	Orbitals	Electron filling
Upper e_g	$d_{z^2}, d_{x^2-y^2}$	Both empty
Lower t_{2g}	d_{xy}, d_{xz}, d_{yz}	$\uparrow, \uparrow, \uparrow$

Thus,

$$\boxed{t_{2g}^3 e_g^0}, \quad S = \frac{3}{2}.$$

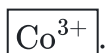
The six oxygen neighbours lie along the three mutually perpendicular coordination axes. This geometry is not represented by the central-ion SMILES.

5.3 — Octahedral trivalent ion with a diamagnetic low-spin state

The required configuration is d^6 :

- Low-spin: all six electrons occupy t_{2g} , producing three pairs.
- High-spin: $t_{2g}^4 e_g^2$, producing four unpaired electrons.

For a first-row trivalent ion, d^6 corresponds to cobalt(III):



A d^0 ion would be diamagnetic in either arrangement and therefore would not satisfy the question.

5.4 — Dodecahedral iron(II)

Iron(II) has six d electrons.

Because the answer-sheet diagram is missing, describe the usual dodecahedral scheme by energy order: a lowest singlet a , a second singlet b , a degenerate pair c, d , and a highest singlet e .

The required fillings are:

Level, highest first	Lower-spin arrangement	High-spin arrangement
e	Empty	$\uparrow$
c, d	$\uparrow, \uparrow$	$\uparrow, \uparrow$
b	$\uparrow\downarrow$	$\uparrow$
a	$\uparrow\downarrow$	$\uparrow\downarrow$

Consequently,

$$\begin{aligned}\text{Lower-spin: } a^2 b^2 c^1 d^1, \quad S &= 1, \\ \text{High-spin: } a^2 b^1 c^1 d^1 e^1, \quad S &= 2.\end{aligned}$$

Both are paramagnetic. Pairing the two electrons within just one of the degenerate c, d orbitals would add pairing energy without lowering their orbital energy, so it is unfavourable.

5.5 — Pairing-energy inequalities

Define

$$g_L = \varepsilon_b - \varepsilon_a, \quad g_M = \varepsilon_c - \varepsilon_b, \quad g_H = \varepsilon_e - \varepsilon_c.$$

Counting one pairing penalty P for every doubly occupied orbital gives

$$U_{\text{LS}} = 2\varepsilon_a + 2\varepsilon_b + 2\varepsilon_c + 2P$$

and

$$U_{\text{HS}} = 2\varepsilon_a + \varepsilon_b + 2\varepsilon_c + \varepsilon_e + P.$$

Their difference is

$$U_{\text{HS}} - U_{\text{LS}} = \varepsilon_e - \varepsilon_b - P = g_M + g_H - P.$$

Thus,

$P < g_M + g_H$	: lower-spin arrangement,
$P > g_M + g_H$	: high-spin arrangement.

At equality, the two arrangements have equal energy in this model.

The physical threshold is therefore **the separation between the highest and second-lowest orbitals**.

Its expression in the missing diagram's symbols is:

Gap labelling, bottom to top	Lower-spin condition	High-spin condition
E_1, E_2, E_3	$P < E_2 + E_3$	$P > E_2 + E_3$
E_3, E_2, E_1	$P < E_1 + E_2$	$P > E_1 + E_2$

5.6 — Diamagnetic divalent ions in the dodecahedral field

An odd number of electrons cannot give a diamagnetic ion. For the even electron counts, the possible closed lower levels are:

Ion	d count	Diamagnetic filling	Condition for that filling
Titanium(II), Ti^{2+}	d^2	a^2	$P < g_L$
Chromium(II), Cr^{2+}	d^4	$a^2 b^2$	$P < g_M$
Nickel(II), Ni^{2+}	d^8	$a^2 b^2 c^2 d^2$	$P < g_H$

Each has a paramagnetic high-spin arrangement. The d^6 ion remains paramagnetic in its lower-spin arrangement, as established in 5.4; a d^{10} ion remains diamagnetic.

The stated condition $P > E_3$ excludes whichever closed-shell arrangement requires $P < E_3$:

- If $E_3 = g_H$, the answer is **titanium and chromium**.
- If $E_3 = g_L$, the answer is **chromium and nickel**.
- If $E_3 = g_M$, the answer is **titanium and nickel**.

The original diagram is needed to select the intended case without assuming its labels.

5.7 — Assignment of absorption spectra

The observed colour comes from visible wavelengths that are comparatively weakly absorbed.

Spectrum	Mineral	Reason
A	Citrine	Strong absorption in the violet–blue region leaves predominantly yellow–orange light.
B	Bohemian garnet	Strong blue and green absorption, with much weaker red absorption, produces a red appearance.
C	Uvarovite	Absorption in violet/blue and red regions leaves a transmission window in the green.
D	Sapphire	Strong absorption around the yellow–orange/red region leaves blue light relatively unabsorbed.

5.8 — Garnet under monochromatic blue-green illumination

Blue-green light falls in a strongly absorbed region of the garnet spectrum. Under the intended ordinary-colour model, little light emerges, and there is no incident red component to provide the usual red appearance.

The answer is therefore

Black.

5.9 — Coupled substitution in schorlomite

Replacing iron(III), Fe^{3+} , with titanium(IV), Ti^{4+} , $[\text{Ti}^{4+}]$, increases the positive charge by one per substitution.

Replacing silicon(IV), Si^{4+} , $[\text{Si}^{4+}]$, with iron(III) decreases it by one. Charge neutrality therefore requires equal **numbers** of these two substitutions.

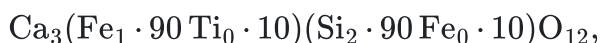
There are two octahedral iron sites and three tetrahedral silicon sites per formula unit. Thus,

$$n(\text{octahedral substitutions}) = 0.05 \times 2 = 0.10.$$

The same 0.10 tetrahedral sites must be substituted, giving

$$\frac{0.10}{3} \times 100\% = 3.33\%.$$

The corresponding site composition can be written



where the first parenthesis describes octahedral sites and the second describes tetrahedral sites.

5.10 — Iron(III) in octahedral and tetrahedral sites

Iron(III) is d^5 . The weak oxygen-ligand field, especially in tetrahedral coordination, gives the high-spin arrangement. Both chromophores consequently have five unpaired electrons, consistent with the statement.

For the **octahedral** chromophore, draw:

Level	Filling
Upper e_g , two orbitals	$\uparrow, \uparrow$

Level	Filling
Lower t_{2g} , three orbitals	$\uparrow, \uparrow, \uparrow$

Hence,

$$t_{2g}^3 e_g^2.$$

For the **tetrahedral** chromophore, the order reverses: the two e orbitals are lower, and the three t_2 orbitals are higher.

Level	Filling
Upper t_2 , three orbitals	$\uparrow, \uparrow, \uparrow$
Lower e , two orbitals	$\uparrow, \uparrow$

Hence,

$$e^2 t_2^3.$$

Both have $S = 5/2$. The tetrahedral drawing represents four oxygen neighbours at the vertices of a tetrahedron; the octahedral drawing represents six neighbours along the coordination axes.

5.11 — Pairing energy and crystal-field splittings

In each high-spin d^5 ground state, every orbital contains one electron. The relevant excitation transfers an electron from an upper orbital into a lower orbital, where it must form a pair.

This lowers the one-electron orbital energy by Δ , but costs pairing energy P . Its net energy is therefore

$$E_{\text{transition}} = P - \Delta.$$

For the octahedral ion, the configuration changes as

$$t_{2g}^3 e_g^2 \longrightarrow t_{2g}^4 e_g^1.$$

For the tetrahedral ion,

$$e^2 t_2^3 \longrightarrow e^3 t_2^2.$$

Each excited configuration has three unpaired electrons rather than five. The change in total spin explains why these transitions are weak.

Define spectroscopic energies

$$\tilde{P} = \frac{P}{hc}, \quad \tilde{\Delta} = \frac{\Delta}{hc}.$$

The given transitions require

$$\begin{aligned} \tilde{P} - \tilde{\Delta}_{\text{oct}} &= 11\,000 \text{ cm}^{-1}, \\ \tilde{P} - \tilde{\Delta}_{\text{tet}} &= 22\,000 \text{ cm}^{-1}, \end{aligned}$$

with

$$\tilde{\Delta}_{\text{tet}} = \frac{4}{9} \tilde{\Delta}_{\text{oct}}.$$

Subtracting the first equation from the second,

$$\left(1 - \frac{4}{9}\right) \tilde{\Delta}_{\text{oct}} = 11\,000 \text{ cm}^{-1}.$$

Therefore,

$$\boxed{\tilde{\Delta}_{\text{oct}} = 19\,800 \text{ cm}^{-1}},$$

$$\boxed{\tilde{\Delta}_{\text{tet}} = 8\,800 \text{ cm}^{-1}},$$

and

$$\boxed{\tilde{P} = 11\,000 + 19\,800 = 30\,800 \text{ cm}^{-1}}.$$

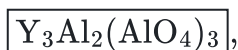
Since P exceeds both splittings, the assumed high-spin ground states are consistent.

5.12 — Cation positions in YAG

Yttrium(III) is substantially larger than aluminium(III). It therefore occupies the larger, eight-coordinate dodecahedral A sites.

Aluminium(III) occupies both the six-coordinate octahedral B sites and the four-coordinate tetrahedral sites normally occupied by silicon.

The site assignment is



equivalent to $\text{Y}_3\text{Al}_5\text{O}_{12}$.

5.13 — Five-percent cerium substitution

Interpreting the missing formula as $\text{Y}_x\text{Ce}_y\text{Al}_5\text{O}_{12}$, there are three yttrium-type sites per formula unit:

$$x + y = 3.$$

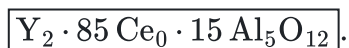
Replacing 5% of them with cerium(III) gives

$$y = 0.05(3) = 0.15, \quad x = 3 - 0.15 = 2.85.$$

Thus,

$$\boxed{x = 2.85, \quad y = 0.15},$$

and the composition is

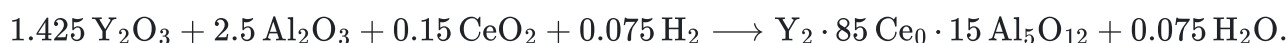


The substitution is isovalent, so it requires no compensating charge defect.

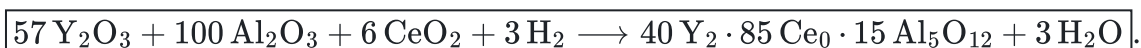
5.14 — Preparation of cerium-doped YAG

The reactants are yttrium(III) oxide, aluminium oxide, cerium(IV) oxide, and hydrogen. Cerium is reduced from +4 in CeO_2 to +3 in the garnet, while hydrogen forms water.

For one formula unit, the balance is



Multiplication by 40 gives



Both sides contain 114 Y, 200 Al, 6 Ce, 483 O, and 6 H atoms. The coefficients have no common divisor. In particular, the yttrium oxide coefficient is $57/40$ times the product coefficient, so 40 is the smallest permitted positive integer product coefficient.

The molecular species are hydrogen, H_2 , $[\text{H}][\text{H}]$, and water, H_2O , o.

5.15 — Blue-emitting cation

Blue light near 450–495 nm corresponds approximately to

$$20\,200\text{--}22\,200\text{ cm}^{-1}.$$

The diagram's $21\,277\text{ cm}^{-1}$ transition lies in this interval and belongs to

$$\boxed{\text{Er}^{3+}}.$$

5.16 — Emission wavelength

Wavelength and wavenumber are reciprocals:

$$\lambda = \frac{1}{\tilde{\nu}}.$$

Thus,

$$\lambda = \frac{1}{21\,277\text{ cm}^{-1}} = 4.69991 \times 10^{-5}\text{ cm} = 469.991\text{ nm}.$$

Therefore,

$$\boxed{\lambda \approx 470.0\text{ nm}}.$$

5.17 — Photoluminescence colour

In the intended interpretation, the emission reverses the electronic transition responsible for absorption.

The garnet appears blood-red under white illumination because it absorbs the complementary blue-green component strongly. Reversing that absorption transition emits photons of the corresponding blue-green energy.

The intended answer is therefore

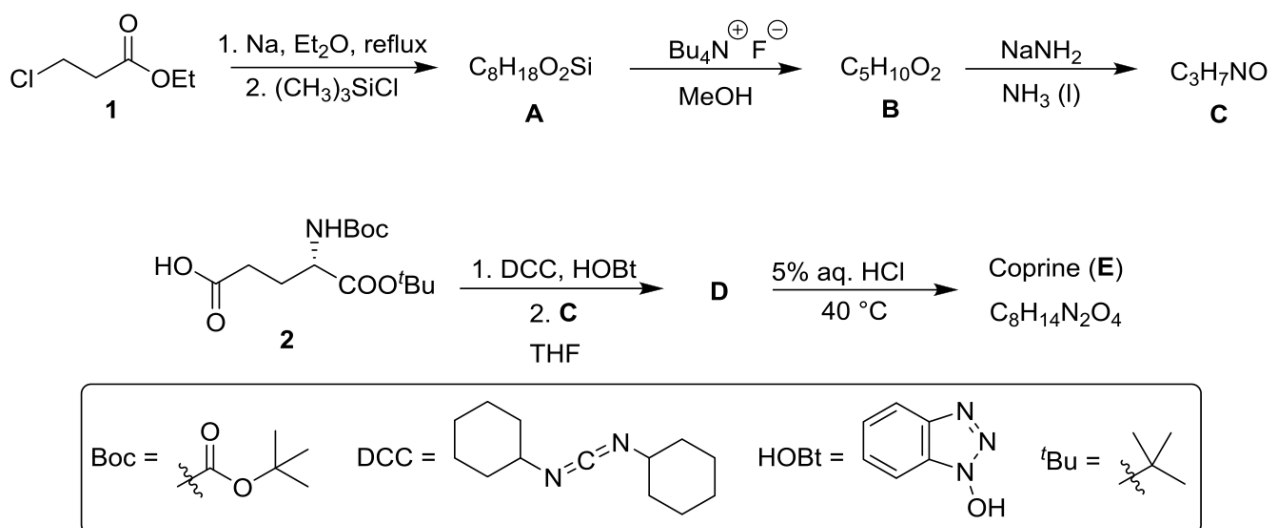
$$\boxed{\text{Blue-green}}.$$

The solution was checked against the official solution.

Problem 6: Let's go mushrooming

Mushrooming belongs to Czech and Slovak traditional pastimes. While some of our mushroom species are edible, some are inedible or even poisonous.

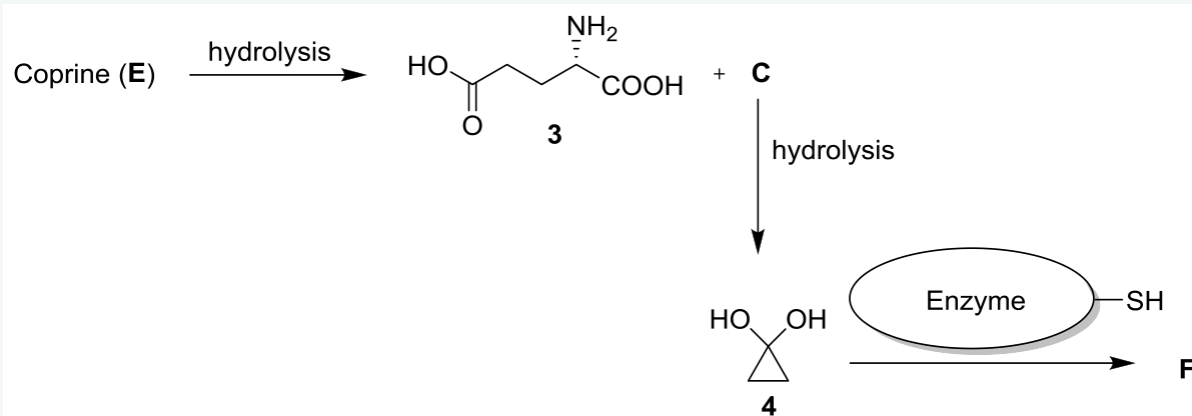
Inky cap (*Coprinopsis atramentaria*) is considered edible and delicious. It contains a natural compound called coprine (**E**), which can be easily synthesized from ethyl 3-chloropropanoate (**1**).



6.1 Draw the formulae of compounds **A–E** including stereochemistry when necessary.

Hint: The first reaction affording compound **A** proceeds via an organometallic compound which then cyclizes.

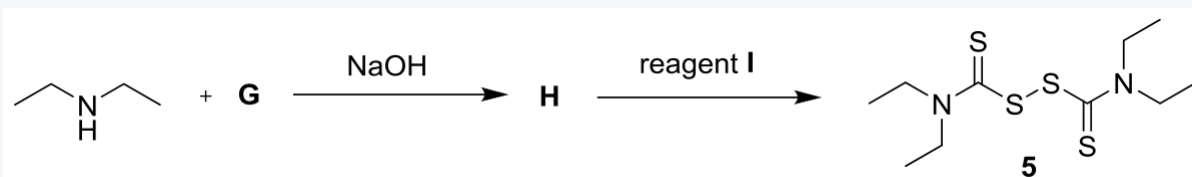
In the human body, coprine undergoes hydrolysis to L-glutamic acid (**3**) and compounds **C** and **4**, which are responsible for the coprine adverse side-effects. They inhibit the enzyme acetaldehyde dehydrogenase, which is involved in the metabolism of alcohol. When the enzyme is inhibited, acetaldehyde formed by alcohol dehydrogenase accumulates in the body, causing strong symptoms of hangover (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**.

The antabuse effect got its name after antabuse (**5**), the most known drug used in alcohol-addiction treatment. This drug can be synthesized according to the following scheme.



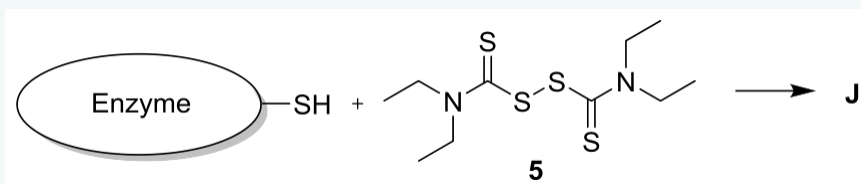
6.3 Draw the formulae of compounds **G** and **H**.

Hint: Compound H contains five carbon atoms.

6.4 Mark all possible reagents which could be used for **I** from the following list.

☐ <i>m</i> -chloroperbenzoic acid (mCPBA)	☐ diluted H_2O_2
☐ $\text{Zn} / \text{CH}_3\text{COOH}$	☐ NaBH_4
☐ I_2	☐ hot concentrated H_2SO_4
☐ $\text{K}_2\text{CO}_3, \text{H}_2\text{O}$	☐ AlCl_3

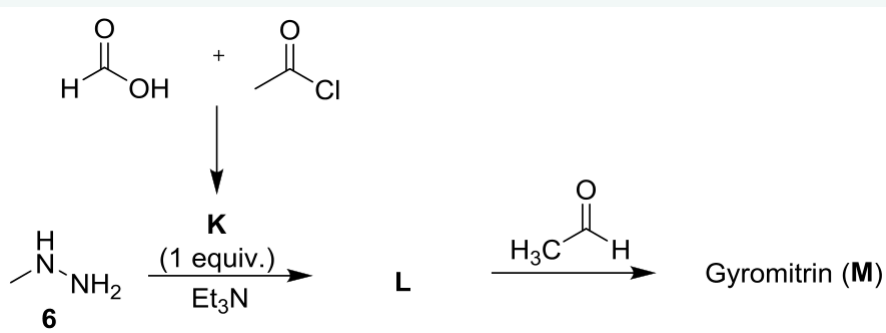
The way antabuse inhibits acetaldehyde dehydrogenase is similar to the effect of compounds **C** and **4**.



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.*

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 formulae of compounds **K – M**.

In human body, gyromitrin (**M**) hydrolyzes and provides *N*-methylhydrazine (**6**), which is strongly hepatotoxic. Gyromitrin (**M**) hydrolysis occurs as soon as it enters the acidic environment in 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 amounts to $1\,293.0\text{ cm}^{-1}$ 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 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 steps consider five significant digits.

6.8 After making these isotopic changes, the rates of hydrolysis are not significantly different. Which of the following is the *most likely* the rate determining step?

- ☐ Nucleophilic attack of water on a protonated amidic moiety
- ☐ C—N bond cleavage
- ☐ Protonation of the gyromitrin molecule

Official English text of the problem.

Answers

In the enzyme-adduct SMILES, * represents the rest of the enzyme attached to the active-site cysteine sulfur.

• 6.1

Compound	Identification	SMILES
A	1-Ethoxy-1-(trimethylsilyloxy)cyclopropane	<chem>CCOC1(O[Si](C)(C)C)CC1</chem>
B	1-Ethoxycyclopropan-1-ol	<chem>CCOC1(O)CC1</chem>
C	1-Aminocyclopropan-1-ol	<chem>NC1(O)CC1</chem>
D	N^α -Boc-protected coprine α -tert-butyl ester; amino-acid centre S'	<chem>CC(C)(C)OC(=O)N[C@@H](CCC(=O)NC1(O)CC1)C(=O)OC(C)(C)C</chem>
E	Coprine, N^5 -(1-hydroxycyclopropyl)-L-glutamine; amino-acid centre S'	<chem>N[C@@H](CCC(=O)NC1(O)CC1)C(=O)O</chem>

- **6.2 F** is the enzyme-bound cyclopropanone hemithioketal, *SC1(O)CC1. The same cyclopropane carbon bears OH and S—Enzyme.
- **6.3 G** is carbon disulfide, S=C=S. **H** is sodium N,N -diethyldithiocarbamate, CCN(CC)C(=S)[S-].[Na+].
- **6.4** Select:
 - m -chloroperbenzoic acid, O=C(OO)c1cccc(Cl)c1;
 - diluted hydrogen peroxide, OO;
 - iodine, I I.

Do not select hot concentrated sulfuric acid: it promotes decomposition of the dithiocarbamate.

- **6.5 J** is the enzyme–diethyldithiocarbamate mixed disulfide, *SSC(=S)N(CC)CC. Draw Enzyme—S—S—C(=S)—N(Et)₂.

- 6.6

Compound	Identification	SMILES
K	Acetic formic anhydride, the mixed anhydride of acetic and formic acids	<chem>CC(=O)OC=O</chem>
L	<i>N</i> -Amino- <i>N</i> -methylformamide	<chem>CN(N)C=O</chem>
M	Gyromitrin, acetaldehyde <i>N</i> -methyl- <i>N</i> -formylhydrazone	<chem>CC=NN(C)C=O</chem>

The supplied scheme does not specify the hydrazone's *E/Z* geometry.

- 6.7

$$\left(\frac{k_{\text{light}}}{k_{\text{heavy}}} \right)_{\text{max}} \approx 1.12$$

Five-significant-digit intermediate rounding gives **1.1165**; retaining guard digits gives **1.1166**.

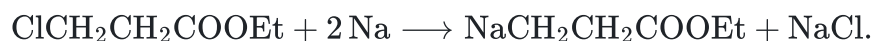
- 6.8 Select **nucleophilic attack of water on a protonated amidic moiety**.

Solution

Throughout the equations, **Et** denotes ethyl and **Enz** denotes the enzyme residue bonded to its active-site sulfur. Neutral organic structures are used for the hydrolysis and deprotection balances; protonation in acidic solution does not change the identified connectivity.

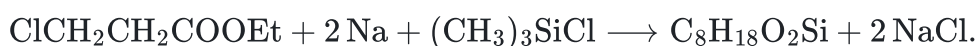
6.1 — Synthesis of coprine

Formation of A. Starting material **1** is ethyl 3-chloropropanoate, CCOC(=O)CCC1. Sodium generates its organosodium derivative:



The intermediate, ethyl 3-sodiopropanoate, has the ionic SMILES CCOC(=O)[C-]([Na+]). Its terminal carbanion attacks the ester carbonyl intramolecularly. The carbonyl π electrons move onto oxygen, producing a three-membered ring: sodium 1-ethoxycyclopropan-1-olate, CCOC1([O-])CC1.[Na+].

Chlorotrimethylsilane, C[Si](C)(C)Cl, traps this alkoxide at oxygen, giving **A**. The overall balance is



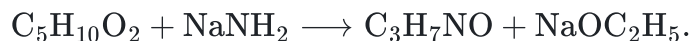
Sodium chloride is [Na+].[Cl-]. The structure of **A** contains the required eight carbons: three in the ring, two in ethoxy, and three attached to silicon.

Formation of B. Fluoride, [F-], attacks silicon and removes the trimethylsilyl protecting group. Methanol, CO, supplies the proton for the liberated oxygen. A balanced net ionic representation is



The silicon-containing product is fluorotrimethylsilane, C[Si](C)(C)F; methoxide is [O-]. Thus **B** is the ethyl hemiketal of cyclopropanone, with **OH** and **OEt** on the same ring carbon.

Formation of C. Sodium amide, [Na+].[NH2-], in liquid ammonia, **N**, replaces the ethoxy group by an amino group. The formal overall balance is



Sodium ethoxide is CC([O-])[Na+]. The transformation can proceed through cyclopropanone, O=C1CC1, followed by nitrogen addition and proton transfer. Consequently, **C** is the corresponding hemiaminal, 1-aminocyclopropan-1-ol.

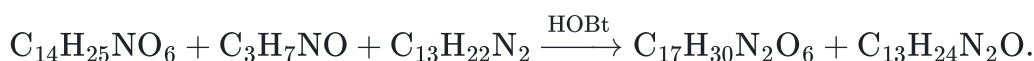
Formation of D. Compound **2** is *N*-Boc-L-glutamic acid α-tert-butyl ester:



Its side-chain carboxyl group is free, whereas its α-amino and α-carboxyl groups are protected. Coupling therefore joins the side-chain carboxyl group to the amino group of **C**, giving **D**.

Dicyclohexylcarbodiimide, DCC, C1CCCCC1N=C=NC1CCCCC1, becomes 1,3-dicyclohexylurea, O=C(NC1CCCCC1)NC1CCCCC1. HOBt, 1-hydroxybenzotriazole, O[n1nnc2ccccc21], assists acyl activation; tetrahydrofuran, C1CCOC1, is the solvent.

The balanced overall coupling, in molecular formulas, is



The reactants are **2**, **C**, and DCC; the products are **D** and dicyclohexylurea. DCC formally accepts the elements of water released during amide formation.

Formation of E. Aqueous hydrogen chloride, C1, removes both acid-labile protecting groups. The Boc group releases carbon dioxide, O=C=O; tert-butyl cleavage can be balanced using 2-methylpropene, C=C(C)C:

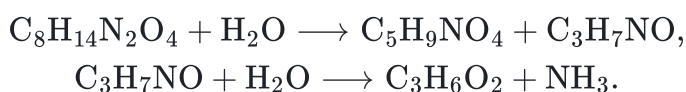


This gives coprine **E**, with a free α-amino group and α-carboxyl group.

The amino-acid stereocentre retains the *S* configuration supplied in **2**. None of these steps requires breaking a bond at that stereocentre. The substituted cyclopropane carbon is not stereogenic because its two ring paths are identical.

6.2 — Inhibition by compound 4

The stated hydrolyses are balanced as follows:



The products of the first equation are L-glutamic acid **3**, N[C@@H](CCC(=O)O)C(=O)O, and **C**. The second produces cyclopropane-1,1-diol **4**, OC1(O)CC1, and ammonia. Water is O.

Compound **4** is the hydrate of cyclopropanone:



The enzyme thiol, represented by *S, adds to cyclopropanone. Sulfur forms a bond to the carbonyl carbon, the carbonyl π bond opens toward oxygen, and proton transfer gives the hemithioketal **F**.

The net balance starting from the hydrate is

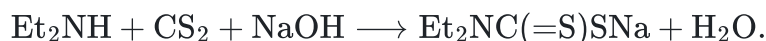


Here the product formula denotes **F**, *SC1(O)CC1. For the requested drawing, retain the enzyme oval and connect it through sulfur to one vertex of a cyclopropane triangle. Attach an OH group to that same vertex. The cyclopropane ring remains intact.

6.3 — Identification of G and H

Diethylamine, CCNCC, already contains four carbons. Carbon disulfide **G** supplies the fifth carbon required in **H**.

The amine attacks the electrophilic carbon of carbon disulfide, and sodium hydroxide, [Na+].[OH-], removes the nitrogen-bound proton:



Thus **H** is sodium *N,N*-diethyldithiocarbamate. Its four ethyl-group carbons and one thiocarbonyl carbon account for the five-carbon hint.

6.4 — Suitable oxidants

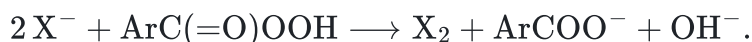
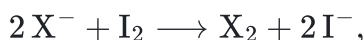
Antabuse **5** is disulfiram, tetraethylthiuram disulfide:



Let X^- denote the *N,N*-diethyldithiocarbamate anion, CCN(CC)C(=S)[S-], and let X_2 denote disulfiram, whose two units are joined by an S—S bond. The required oxidation half-reaction is

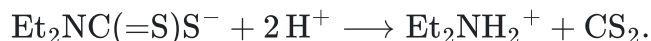


The three suitable reagents give the following balanced net ionic equations:



In the last equation, Ar is 3-chlorophenyl, so the oxidant is mCPBA. The ionic by-products are iodide, [I-]; hydroxide, [OH-]; and 3-chlorobenzoate, O=C([O-])c1cccc(Cl)c1.

Hot concentrated sulfuric acid is unsuitable. Sulfuric acid, OS(=O)(=O)O, strongly acidifies the dithiocarbamate. The resulting *N,N*-diethyldithiocarbamic acid, CCN(CC)C(=S)S, is susceptible to cleavage into diethylamine and carbon disulfide; heating promotes this destruction. Including protonation of the liberated amine gives



The protonated amine is diethylammonium, CC[NH2+]CC. Therefore, sulfuric acid's oxidizing character does not make hot concentrated sulfuric acid a suitable reagent for preserving and coupling this substrate.

The other unselected reagents also do not accomplish the required oxidation:

Reagent	Name and SMILES	Reason
Zn / CH ₃ COOH	Zinc <chem>[Zn]</chem> ; acetic acid <chem>CC(=O)O</chem>	A reducing system
NaBH ₄	Sodium borohydride <chem>[Na+].[BH4-]</chem>	A reducing agent
K ₂ CO ₃ , H ₂ O	Potassium carbonate <chem>[K+].[K+].[O-]C(=O)[O-]</chem> ; water <chem>O</chem>	Supplies basic conditions, not the required oxidation

Reagent	Name and SMILES	Reason
AlCl ₃	Aluminium chloride C1[Al](Cl)Cl	A Lewis acid, not the required oxidant

6.5 — Inhibition by disulfiram

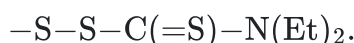
The enzyme's cysteine sulfur attacks one sulfur of disulfiram's disulfide bond. Cleavage of that bond releases a diethyldithiocarbamate unit and leaves the enzyme in a mixed disulfide.

A balanced neutral-form equation is



The second product is the dithiocarbamic acid identified above.

For **J**, draw the enzyme oval followed by



Its three sulfur atoms are the original cysteine sulfur, the sulfur joining it to the thiocarbonyl carbon, and the thiocarbonyl sulfur. This matches `*SSC(=S)N(CC)CC`.

6.6 — Synthesis of gyromitrin

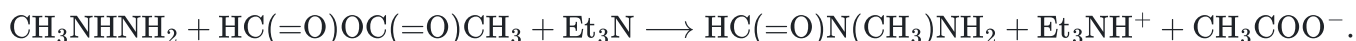
Formation of K. Formic acid, $\text{O}=\text{CO}$, reacts with acetyl chloride, $\text{CC}(=\text{O})\text{Cl}$, to produce the mixed anhydride **K**:



This mixed anhydride provides an activated formyl group.

Formation of L. *N*-Methylhydrazine **6**, `CNN`, is formylated at the methyl-bearing nitrogen, giving **L**. The terminal NH_2 group must remain available for the subsequent aldehyde condensation.

Triethylamine, `CCN(CC)CC`, captures the acid formed. A combined balance is



The salt by-product is triethylammonium acetate, `CC[NH+](CC)CC.CC(=O)[O-]`.

Formation of M. The remaining terminal amino group condenses with acetaldehyde, also called ethanal, $\text{CC}=\text{O}$, eliminating water:



The product is gyromitrin **M**. It contains both the formamide group and the hydrazone $\text{C}=\text{N}$ group described in the text. The reaction scheme specifies its connectivity but does not establish its *E/Z* configuration.

Hydrolysis of both groups has the overall balance



Thus the products are formic acid, *N*-methylhydrazine, and acetaldehyde.

6.7 — Maximum hypothetical kinetic isotope effect

For a harmonic bond-stretching vibration,

$$\tilde{\nu} = \frac{1}{2\pi c} \sqrt{\frac{f}{\mu}},$$

where f is the force constant and μ is the reduced mass. The unchanged potential-energy surface means that f is unchanged by isotopic substitution.

The reduced masses are

$$\mu_{\text{light}} = \frac{12 \times 14}{12 + 14} \text{ u} = 6.4615 \text{ u},$$

$$\mu_{\text{heavy}} = \frac{13 \times 15}{13 + 15} \text{ u} = 6.9643 \text{ u}.$$

Therefore,

$$\frac{\tilde{\nu}_{\text{heavy}}}{\tilde{\nu}_{\text{light}}} = \sqrt{\frac{\mu_{\text{light}}}{\mu_{\text{heavy}}}} = 0.96323,$$

and

$$\tilde{\nu}_{\text{heavy}} = (1293.0)(0.96323) = 1245.5 \text{ cm}^{-1}.$$

The molar zero-point energy of this mode is

$$E_0 = \frac{1}{2} N_A h c \tilde{\nu}.$$

The **maximum** effect occurs when the relevant stretching vibration is completely lost at the transition state. Its isotope-dependent zero-point-energy difference then contributes fully to the difference in activation energies:

$$\Delta E_{\text{heavy}}^{\ddagger} - \Delta E_{\text{light}}^{\ddagger} = E_{0,\text{light}} - E_{0,\text{heavy}}.$$

Using standard constants to five significant digits,

$$h = 6.6261 \times 10^{-34} \text{ J s},$$

$$c = 2.9979 \times 10^{10} \text{ cm s}^{-1},$$

$$N_A = 6.0221 \times 10^{23} \text{ mol}^{-1},$$

$$R = 8.3145 \text{ J mol}^{-1} \text{ K}^{-1},$$

the difference, using the rounded intermediate wavenumber, is

$$\begin{aligned} \Delta E_0 &= \frac{1}{2} N_A h c (1293.0 - 1245.5) \text{ cm}^{-1} \\ &= 284.11 \text{ J mol}^{-1}. \end{aligned}$$

The temperature is

$$T = 37 + 273.15 = 310.15 \text{ K},$$

so

$$RT = 2578.7 \text{ J mol}^{-1}.$$

Since only zero-point energies are to affect the rate constants,

$$\begin{aligned} \left(\frac{k_{\text{light}}}{k_{\text{heavy}}} \right)_{\text{max}} &= \exp \left(\frac{\Delta E_0}{RT} \right) \\ &= \exp(0.11018) \\ &= \boxed{1.1165}. \end{aligned}$$

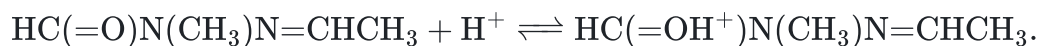
Thus the light molecule can hydrolyze approximately **12% faster** in this limiting model.

Retaining guard digits throughout instead gives $\Delta E_0 = 284.38 \text{ J mol}^{-1}$ and a five-significant-digit ratio of 1.1166. The difference is solely intermediate rounding.

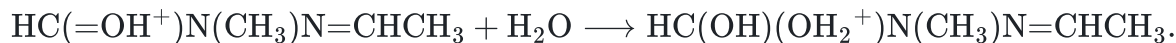
6.8 — Most likely rate-determining step

The best choice is **nucleophilic attack of water on the protonated amide**.

Carbonyl protonation is normally a rapid pre-equilibrium. The relevant protonated species is O-protonated gyromitrin, $\text{CC}=\text{NN}(\text{C})\text{C}=[\text{OH}^+]$:



Water then attacks the activated carbonyl carbon:



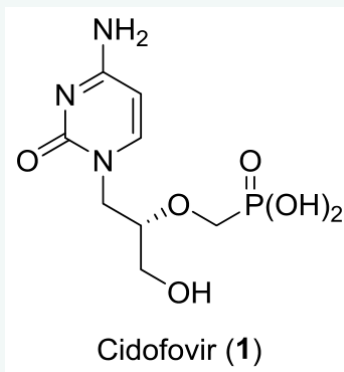
The product of this addition is the protonated tetrahedral intermediate, $\text{CC}=\text{NN}(\text{C})\text{C}(\text{O})[\text{OH}_2^+]$.

During this addition, the amide C—N bond remains intact. A small isotope effect is therefore consistent with addition being rate determining. Substantial C—N cleavage in the rate-determining step would be expected to produce a more pronounced primary isotope effect. Among the choices, water addition is consequently the most likely slow step.

The solution was checked against the official solution.

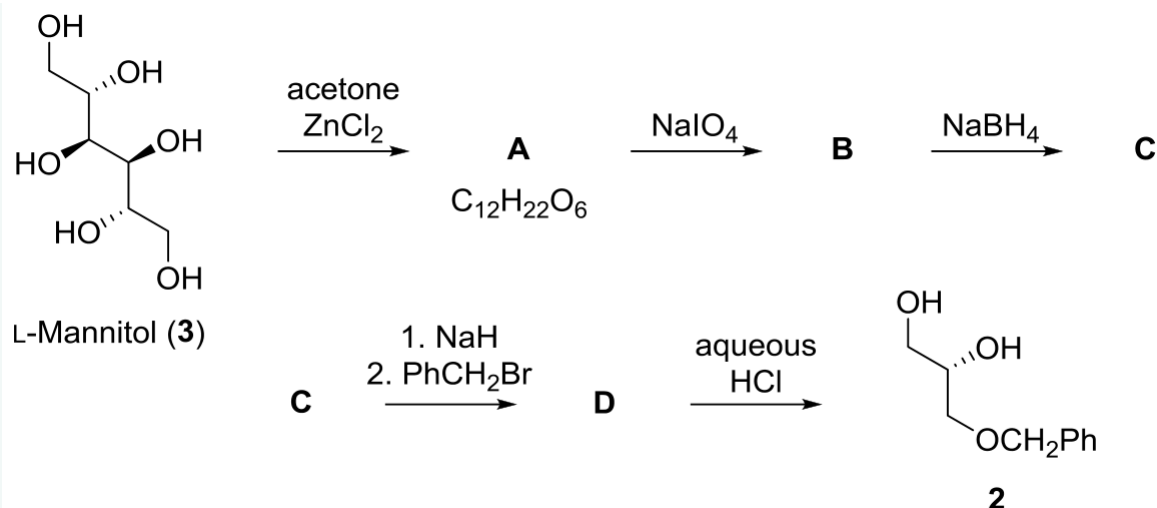
Problem 7: Cidofovir

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**)

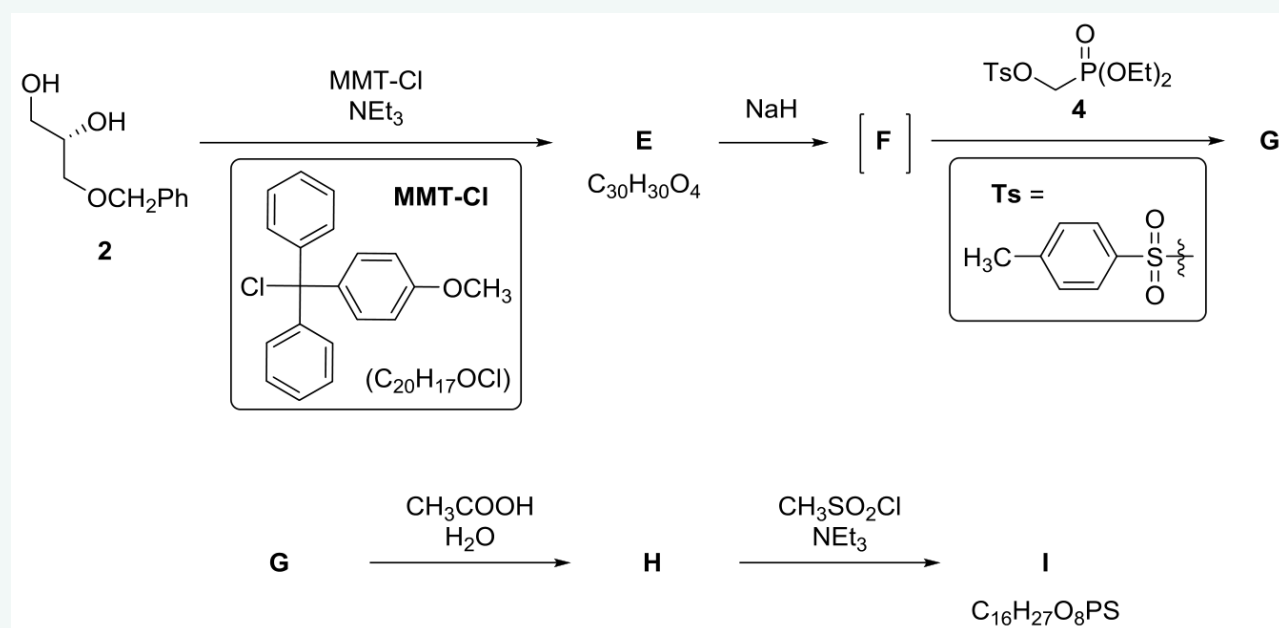
The key intermediate in the synthesis of cidofovir is optically pure diol **2**, which can be prepared from L-mannitol (**3**).



7.1 Draw the structures of compounds **A–D**, including stereochemistry. One molecule of **A** produces two molecules of **B**.

7.2 Draw the structural formulae of all alternative stereoisomers of compound **3** which could be used in the same reaction sequence to afford only 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.

Official English text of the problem.

Answers

- 7.1.** The four compounds are:

Compound	Name	Stereochemical SMILES
A	1,2:5,6-Di-O-isopropylidene-L-mannitol	<chem>CC1(C)OC[C@H]([C@H](O)[C@H](O)[C@H]2COC(C)(C)O2)O1</chem>
B	(4S)-2,2-Dimethyl-1,3-dioxolane-4-carbaldehyde	<chem>CC1(C)OC[C@H](C=O)O1</chem>
C	[(4R)-2,2-Dimethyl-1,3-dioxolan-4-yl]methanol, or (R)-solketal	<chem>CC1(C)OC[C@H](CO)O1</chem>
D	(4R)-4-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolane	<chem>CC1(C)OC[C@H](COCc2ccccc2)O1</chem>

- 7.2. There are **two distinct alternative stereoisomers**:

Name	Absolute configuration along the hexitol chain	Stereochemical SMILES
L-Altritol	(2 <i>S</i> , 3 <i>R</i> , 4 <i>S</i> , 5 <i>S</i>)	<chem>OC[C@H](O)[C@H](O)[C@H](O)[C@H](O)CO</chem>
L-Iditol	(2 <i>S</i> , 3 <i>R</i> , 4 <i>R</i> , 5 <i>S</i>)	<chem>OC[C@H](O)[C@H](O)[C@H](O)[C@H](O)CO</chem>

To draw their Fischer projections, place CH₂OH at both ends of a vertical chain. From C2 to C5, put the hydroxyl groups **right-left-left-left** for L-altritol and **right-left-right-left** for L-iditol. Put hydrogen opposite each hydroxyl group.

- 7.3. MMT denotes the (4-methoxyphenyl)diphenylmethyl group. It is expanded in the SMILES to keep the strings chemically valid.

Compound	Name	Stereochemical SMILES
E	(2R)-3-(Benzyloxy)-1-(MMT-oxy)propan-2-ol	<chem>COC1CCC(C(OC[C@H](O)COCc2ccccc2)(c2ccccc2)c2ccccc2)CC1</chem>
F	Sodium (2R)-3-(benzyloxy)-1-(MMT-oxy)propan-2-olate	<chem>COC1CCC(C(OC[C@H]([O-])COCc2ccccc2)(c2ccccc2)c2ccccc2)CC1.[Na+]</chem>
G	Diethyl {[(2R)-3-(benzyloxy)-1-(MMT-oxy)propan-2-yl]oxymethyl}phosphonate	<chem>COC1CCC(C(OC[C@H](OCP(=O)(OCC)OCC)COCc2ccccc2)(c2ccccc2)c2ccccc2)CC1</chem>
H	Diethyl {[(2S)-3-(benzyloxy)-1-hydroxypropan-2-yl]oxymethyl}phosphonate	<chem>OC[C@H](OCP(=O)(OCC)OCC)COCc1ccccc1</chem>
I	Diethyl {[(2R)-3-(benzyloxy)-1-(methanesulfonyloxy)propan-2-yl]oxymethyl}phosphonate	<chem>CS(=O)(=O)OC[C@H](OCP(=O)(OCC)OCC)COCc1ccccc1</chem>

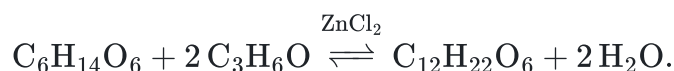
Solution

7.1. Identification of A–D

Number the original hexitol chain C1–C6. L-Mannitol (**3**) is (2*S*, 3*S*, 4*S*, 5*S*)-hexane-1,2,3,4,5,6-hexol, SMILES OC[C@H](O)[C@H](O)[C@@H](O)[C@@H](O)CO.

Formation of A: protection of the two terminal diols.

Acetone, CC(=O)C, forms cyclic ketals with vicinal diols. The molecular formula of **A** corresponds to incorporation of two acetone molecules with loss of two water molecules:



To leave a cleavable central diol and subsequently produce two identical three-carbon fragments, the protected pairs must be **01/02** and **05/06**. Thus **A** contains two five-membered acetonide rings, each with an O-C(CH3)2-O bridge. The hydroxyl groups at C3 and C4 remain free.

No stereogenic carbon undergoes substitution or epimerization. The original spatial configurations are retained.

Formation of B: periodate cleavage.

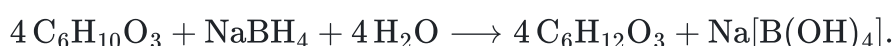
The free C3–C4 vicinal diol forms a periodate ester and undergoes oxidative cleavage of the C3–C4 bond. Each of these carbons becomes an aldehyde carbon:



The two halves have the same absolute configuration, so one molecule of **A** gives two molecules of **B**, the **(S)-glyceraldehyde acetonide** listed above. Its original terminal CH_2OH group and adjacent oxygen remain incorporated in the acetonide ring.

Formation of C: reduction of the aldehyde.

Sodium borohydride reduces the aldehyde substituent of **B** to CH_2OH, while leaving the acetonide intact. A balanced net equation, including aqueous protonation/work-up, is



This gives **C**, (*R*)-solketal. No new stereocentre is formed: the aldehyde carbon becomes a methylene carbon.

The descriptor changes from *S* in **B** to *R* in **C** because reduction changes the CIP priority order of the two carbon substituents. It does **not** represent inversion at the existing stereocentre.

Formation of D: benzylation of the free alcohol.

Sodium hydride deprotonates the sole free hydroxyl group of **C**, releasing hydrogen. The resulting alkoxide attacks benzyl bromide, BrCc1ccccc1, at its benzylic carbon by an *S_N2* reaction.

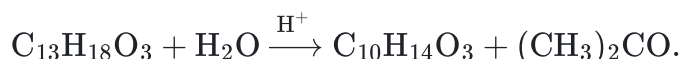
Using **R** for the protected glycerol residue, the combined balanced equation is



Consequently, **D** is obtained by replacing the exocyclic CH_2OH group of **C** with CH_2OCH_2Ph. Its acetonide and stereochemical arrangement remain intact.

Hydrolysis of D to verify product 2.

Aqueous hydrochloric acid hydrolyses the acetonide, restoring the primary and secondary hydroxyl groups:



The benzyl ether remains in place. The product is **(2S)-3-(benzyloxy)propane-1,2-diol (2)**, SMILES OC[C@H](O)COCc1ccccc1, exactly the stereoisomer shown in the question.

For a drawing matching the supplied orientation, place the CH_2OH arm above the stereocentre and the $\text{CH}_2\text{OCH}_2\text{Ph}$ arm below it; draw the central hydroxyl bond as a hashed wedge pointing behind the page.

7.2. Alternative starting stereoisomers

Only the original stereocentres at **C2 and C5 survive** the sequence. The centres at C3 and C4 are destroyed when periodate converts those carbons into aldehyde groups.

For both halves to give exclusively the specified product **2**, C2 and C5 must therefore both retain the configurations present in L-mannitol: $2S$ and $5S$. The configurations at C3 and C4 may be chosen independently:

C2	C3	C4	C5	Identity
<i>S</i>	<i>S</i>	<i>S</i>	<i>S</i>	Original L-mannitol
<i>S</i>	<i>R</i>	<i>S</i>	<i>S</i>	L-Altritol
<i>S</i>	<i>S</i>	<i>R</i>	<i>S</i>	The same L-altritol, numbered from the opposite end
<i>S</i>	<i>R</i>	<i>R</i>	<i>S</i>	L-Iditol

The two mixed configurations in the middle rows describe the **same molecule**, because the terminal groups are identical and the chain can be numbered from either end.

Thus there are exactly **two additional starting stereoisomers**, L-altritol and L-iditol. Their terminal acetonide-protected fragments become identical to **B** after cleavage, regardless of the configurations of the two carbons being cleaved.

7.3. Identification of E–I

Throughout this sequence, the carbon skeleton and the spatial arrangement at its stereocentre are preserved. To draw every intermediate in the orientation used for **2**, keep the upper primary carbon arm and lower benzyl-protected carbon arm in the plane, and keep the bond from the central carbon to oxygen pointing behind the plane.

Formation of E: selective primary hydroxyl protection.

The bulky MMT group protects the less hindered **primary hydroxyl group**. The secondary hydroxyl group remains free.

MMT chloride is (4-methoxyphenyl)diphenylmethyl chloride, SMILES COc1ccc(C(C1)(c2ccccc2)c2ccccc2)cc1. Triethylamine captures the hydrogen chloride produced:



Therefore **E** has the connectivity



with the stereochemistry specified in its SMILES.

The formula check is



consistent with the stated formula of **E**.

Formation of **F**: secondary alkoxide formation.

Sodium hydride removes the proton of the remaining secondary hydroxyl group:

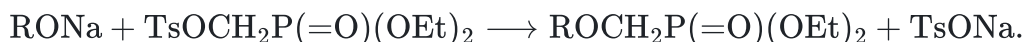


Thus **F** is the sodium alkoxide of **E**. Its central substituent is O^- , with Na^+ as counterion. The ionic SMILES does not prescribe a particular sodium coordination, solvation or aggregation state.

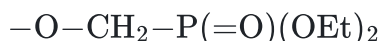
Formation of **G**: phosphonomethylation at oxygen.

Reagent **4** is **diethyl (tosyloxymethyl)phosphonate**, SMILES CCOP(=O)(COS(=O)(=O)c1ccc(C)cc1)OCC.

The alkoxide oxygen of **F** attacks the methylene carbon bearing the tosylate leaving group:



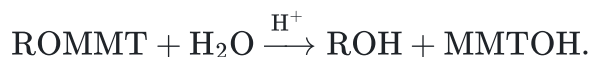
This installs the central substituent



and gives **G**. The new bond is formed between the alkoxide oxygen and the reagent's methylene carbon. No bond at the existing stereogenic carbon is displaced.

Formation of **H**: removal of MMT.

Aqueous acetic acid cleaves the acid-labile MMT ether, restoring the primary alcohol:



The benzyl ether and diethyl phosphonate groups remain intact. Thus **H** has the connectivity

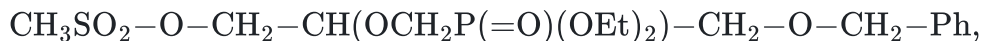


Formation of **I**: mesylation of the primary alcohol.

Methanesulfonyl chloride, CS(=O)(=O)Cl, converts the primary hydroxyl group of **H** into its methanesulfonate ester. Triethylamine captures the hydrogen chloride:

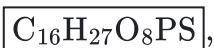


The product therefore has the connectivity



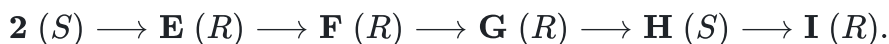
with the stereochemistry of **I** given in the answer table.

Starting from $\text{C}_{15}\text{H}_{25}\text{O}_6\text{P}$ for **H**, replacing the hydroxyl hydrogen by SO_2CH_3 gives



matching the supplied formula.

The absolute descriptors along this sequence are



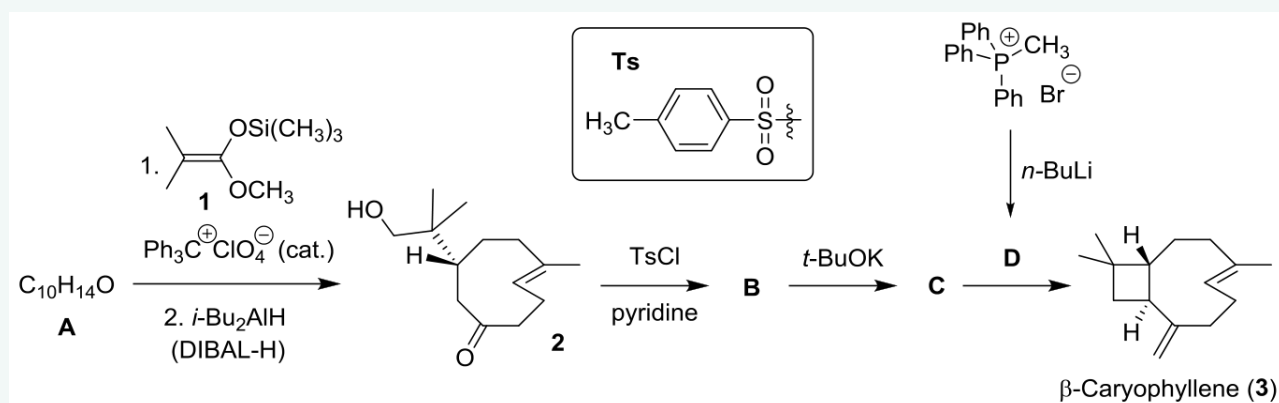
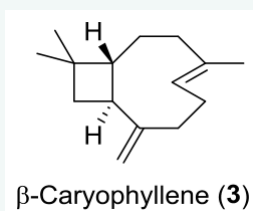
These changes in *R/S* labels arise solely from changes in CIP priorities. **There is no inversion or loss of configuration at the surviving stereocentre.**

The answers were checked against the official answers published by the organisers.

Problem 8: Caryophyllene

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

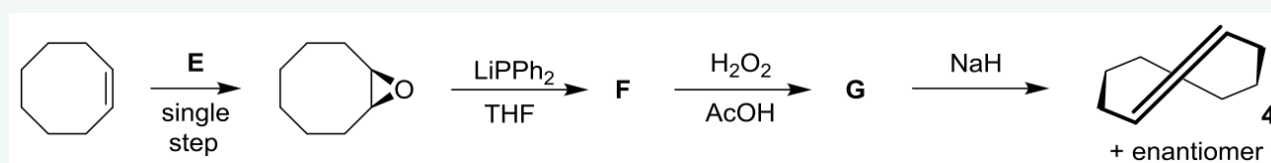
The synthesis of β -caryophyllene starts from a single enantiomer of dienone **A**. The reaction of **A** with silyl ketene acetal **1**, followed by immediate reduction and aqueous work-up affords ketone **2**. This intermediate then undergoes reaction with tosyl chloride, providing **B**. Basic cyclization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



8.1 Draw the structures of compounds **A–D**, including the appropriate stereochemistry.

Hint: In transformation $A \rightarrow 2$, the silyl ketene acetal acts as a nucleophile.

Due to the large ring size, both compounds **2** and **3** are stable, even though they contain a double bond in the *trans* configuration. *trans*-Cyclooctene (**4**) is the smallest ring that can accommodate a *trans* double bond. It can be prepared according to the following scheme:

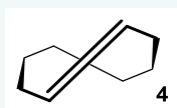


8.2 Draw the structures of reagent **E** and intermediates **F** and **G**, including the appropriate stereochemistry. For **F** and **G**, tick the box indicating the stereochemical outcome.

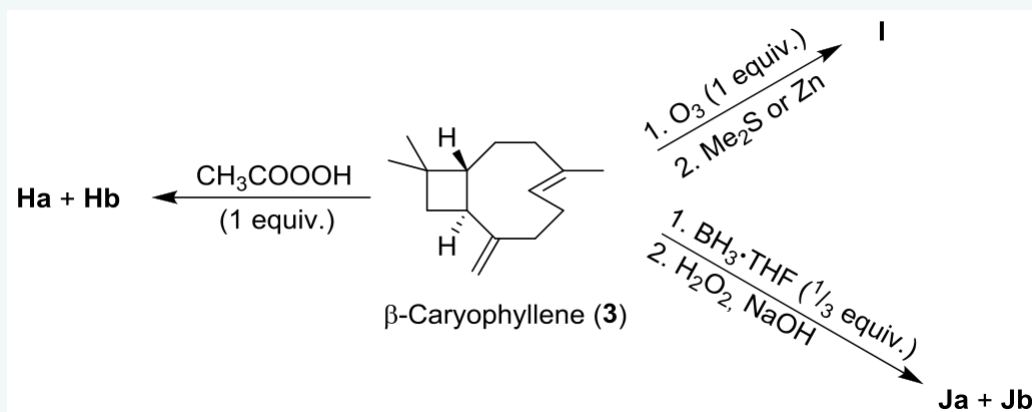
Mark the correct answer:

□ achiral, □ single enantiomer, □ racemic mixture, □ mixture of diastereoisomers

8.3 Draw the structure of the enantiomer of cycloalkene **4**.

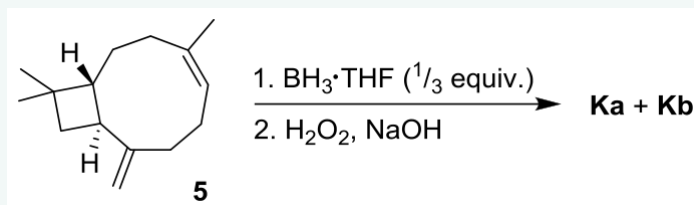


The two double bonds in β -caryophyllene display different reactivity: the double bond in the ring (endocyclic) is more reactive than the other one (exocyclic) due to the ring strain.



8.4 Draw the structures of compounds **Ha + Hb**, **I** and **Ja + Jb**, including the appropriate stereochemistry. *Hint: Ha + Hb and Ja + Jb are pairs of diastereomers.*

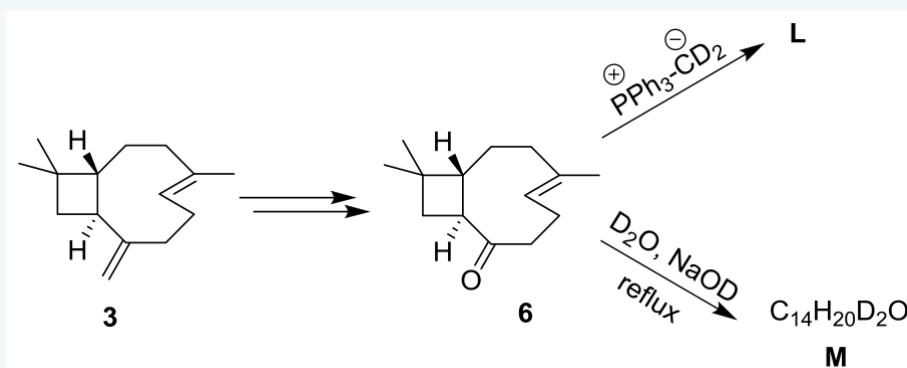
Interestingly, the reactivity of the double bonds is reversed when isocaryophyllene (**5**) is used instead of β -caryophyllene (**3**).



8.5 Draw the structures of compounds **Ka** and **Kb**.

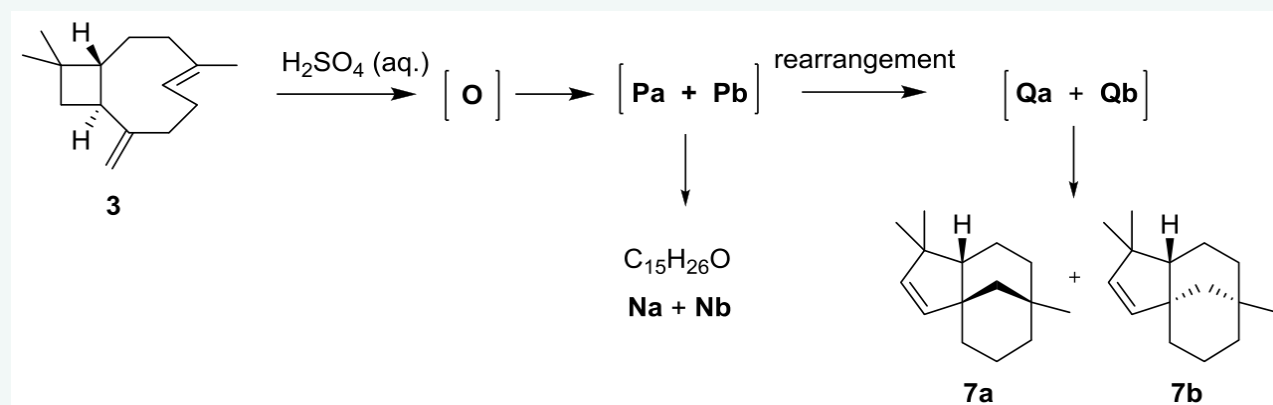
Hint: Ka + Kb are a pair of diastereomers.

Isotope-labelled compounds are invaluable tools for reaction mechanism investigation, structure determination, and mass 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 the appropriate stereochemistry.

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, including the appropriate stereochemistry, of the **three** intermediates **O**, **Pa**, **Qa** leading to the diastereomer **7a**, including the appropriate stereochemistry.

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

Official English text of the problem.

Answers

For precise structural descriptions, use these **carbon labels**, independently of the bold compound numbers:

- The nine-membered ring is $C1 - C2 - C3 - C4 - C5 - C6 - C7 - C8 - C9 - C1$.
- The cyclobutane is $C1 - C9 - C10 - C11 - C1$.
- $C12$ is the methyl on $C4$; $C13$ is the exocyclic methylene carbon on $C8$; $C14, C15$ are the methyls on $C11$.

Thus **3**, β -caryophyllene, is the $(1R, 4E, 9S)$ compound:

[C@@H]12CC/C(C)=C/CCC(=C)[C@H]1CC2(C)C

The names and descriptions below retain these carbon labels unless a complete tricyclic systematic name is given. Labels a/b within the epoxide and hydroboration pairs are arbitrary.

• 8.1

Compound	Identification	SMILES
A	$(2Z, 6E)$ -6-Methylcyclonona-2,6-dien-1-one, in the single planar enantiomer corresponding to the depicted synthesis	<chem>O=C1/C=C\CC/C(C)=C/CC1</chem>

Compound	Identification	SMILES
B	The primary O-tosylate of 2 , with its existing stereochemistry retained	<chem>[C@H]1(C(C)(C)C(=O)C(=O)C2CCC(C)CC2)CC/C(C)=C/CCC(=O)C1</chem>
C	Caryophyllene-derived <i>C</i> 8 ketone; identical to compound 6	<chem>[C@H]12CC/C(C)=C/CCC(=O)[C@H]1CC2(C)C</chem>
D	Methylenetriphenylphosphorane, represented in its ylide form	<chem>[CH2-][P+](c1ccccc1)(c1ccccc1)c1ccccc1</chem>

Ordinary SMILES specifies the two alkene geometries of **A**, but does not distinguish its planar enantiomers. The required drawing is described in Solution 8.1.

• 8.2

E: Peracetic acid, an acceptable peroxyacid epoxidizing reagent: CC(=O)OO.

F: *trans*-2-(Diphenylphosphanyl)cyclooctan-1-ol, **racemic mixture**:

- (1*R*, 2*R*): O[C@H]1[C@H](P(c2ccccc2)c2ccccc2)CCCCC1
- (1*S*, 2*S*): O[C@@H]1[C@@H](P(c2ccccc2)c2ccccc2)CCCCC1

In dry THF, before protonation, **F** is its lithium alkoxide; see Solution 8.2.

G: *trans*-2-(Diphenylphosphoryl)cyclooctan-1-ol, **racemic mixture**:

- (1*R*, 2*R*): O[C@H]1[C@H](P(=O)(c2ccccc2)c2ccccc2)CCCCC1
- (1*S*, 2*S*): O[C@@H]1[C@@H](P(=O)(c2ccccc2)c2ccccc2)CCCCC1

• 8.3

The answer is the **opposite planar enantiomer of (*E*)-cyclooctene**, obtained by reflecting the complete drawing of **4** left-to-right, including its perspective bonds.

SMILES: C1CC/C=C/CCC1

Both planar enantiomers have this ordinary SMILES. Their opposite ring handedness must be shown geometrically.

• 8.4

Compound	Identification	SMILES
Ha	<i>C</i> 4, <i>C</i> 5-epoxide of β-caryophyllene; new configurations 4 <i>S</i> , 5 <i>S</i>	<chem>[C@H]12CC[C@@]3(C)[C@H](CCC(=C)[C@H]1CC2(C)C)O3</chem>
Hb	The other <i>C</i> 4, <i>C</i> 5-epoxide; new configurations 4 <i>R</i> , 5 <i>R</i>	<chem>[C@H]12CC[C@]3(C)[C@@H](CCC(=C)[C@H]1CC2(C)C)O3</chem>
I	4-[(1 <i>S</i> , 2 <i>R</i>)-3,3-Dimethyl-2-(3-oxobutyl)cyclobutyl]pent-4-enal, the endocyclic ozonolysis product	<chem>[C@H]1(CCC(C)=O)[C@@H](C(CCC=O)=C)CC1(C)C</chem>
Ja	<i>C</i> 5-alcohol from internal hydroboration–oxidation; new configurations 4 <i>R</i> , 5 <i>S</i>	<chem>[C@H]12CC[C@@H](C)[C@@H](O)CCC(=C)[C@H]1CC2(C)C</chem>

Compound	Identification	SMILES
Jb	The other <i>C</i> 5-alcohol; new configurations 4 <i>S</i> , 5 <i>R</i>	<chem>[C@@H]12CC[C@H](C)[C@H](O)CCC(=C)[C@H]1CC2(C)C</chem>

All retain the original configurations at *C*1, *C*9. The exocyclic methylene survives all three reactions.

• 8.5

Ka and **Kb** are the two *C*8 epimers of the primary alcohol obtained by converting the exocyclic =CH₂ of isocaryophyllene into –CH₂OH. The internal *Z* alkene remains intact.

Compound	New configuration	SMILES
Ka , isocaryophyllene-derived <i>C</i> 13 alcohol	<i>C</i> 8 = <i>S</i>	<chem>[C@@H]12CC/C(C)=C\CC[C@H](CO)[C@H]1CC2(C)C</chem>
Kb , its <i>C</i> 8 epimer	<i>C</i> 8 = <i>R</i>	<chem>[C@@H]12CC/C(C)=C\CC[C@@H](CO)[C@H]1CC2(C)C</chem>

• 8.6

Compound	Identification	SMILES
L	β-Caryophyllene with exocyclic =CD ₂ , formula C ₁₅ H ₂₂ D ₂	<chem>[C@@H]12CC/C(C)=C/CCC(=C([2H])[2H])[C@H]1CC2(C)C</chem>
M	<i>C</i> 7, <i>C</i> 7'-dideuterated ketone 6 , formula C ₁₄ H ₂₀ D ₂ O	<chem>[C@@H]12CC/C(C)=C/CC([2H])([2H])C(=O)[C@H]1CC2(C)C</chem>

• 8.7

Intermediate	Identification	SMILES
O	<i>C</i> 4 carbocation formed by protonation at <i>C</i> 5: (1 <i>R</i> ,9 <i>S</i>)-4,11,11-trimethyl-8-methylidenebicyclo[7.2.0]undecan-4-ylum	<chem>[C@@H]12CC[C+](C)CCCC(=C)[C@H]1CC2(C)C</chem>
Pa	<i>C</i> 4 – <i>C</i> 13-cyclized <i>C</i> 8 carbocation: (2 <i>R</i> ,5 <i>R</i> ,8 <i>S</i>)-4,4,8-trimethyltricyclo[6.3.1.0 ^{2,5}]dodecan-1-ylum	<chem>[C@@H]12CC[C@]3(C)CCC[C+](C3)[C@H]1CC2(C)C</chem>
Qa	Rearranged <i>C</i> 9 carbocation: (1 <i>S</i> ,5 <i>S</i> ,8 <i>S</i>)-4,4,8-trimethyltricyclo[6.3.1.0 ^{1,5}]dodecan-2-ylum	<chem>[C@@H]12CC[C@]3(C)CCC[C@]1(C3)[CH+]CC2(C)C</chem>

• 8.8

Both products are stereoisomers of **4,4,8-trimethyltricyclo[6.3.1.0^{2,5}]dodecan-1-ol**, the caryolan-1-ol framework.

Compound	Configurations in this tricyclic name	SMILES
Na	(1 <i>R</i> , 2 <i>S</i> , 5 <i>R</i> , 8 <i>S</i>)	[C@@H]12CC[C@]3(C)CCC[C@@](O)(C3)[C@H]1CC2(C)C
Nb	(1 <i>S</i> , 2 <i>S</i> , 5 <i>R</i> , 8 <i>R</i>)	[C@@H]12CC[C@@]3(C)CCC[C@](O)(C3)[C@H]1CC2(C)C

Solution

8.1 — Conjugate addition, cyclobutane formation, and methylenation

The silyl ketene acetal **1** is the trimethylsilyl ketene acetal of methyl isobutyrate:



Its carbon bearing the two methyl groups is nucleophilic. In **2**, that carbon has become *C*11, attached to *C*1, two methyl groups, and a hydroxymethyl group.

Consequently, disconnecting the *C*1 — *C*11 bond identifies **A** as an α,β-unsaturated ketone whose conjugated double bond is *C*9 = *C*1. The other alkene, *C*4 = *C*5, is already present.

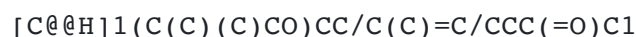
For the requested drawing of **A**:

1. Start with the nine-membered ring drawn in **2**.
2. Remove the complete —C(CH₃)₂CH₂OH substituent from *C*1.
3. Replace *C*1 — *C*9 by a **cis**, or *Z*, double bond.
4. Retain the internal *E* alkene and the ring handedness corresponding to the depicted enantiomeric series.

Numbering the monocyclic ketone from its carbonyl gives (2*Z*, 6*E*)-6-methylcyclonona-2,6-dien-1-one. Its formula is C₁₀H₁₄O, as required. Its chirality is associated with the folded trans-cycloalkene ring, rather than a tetrahedral stereogenic carbon.

The first reaction is a **Mukaiyama–Michael addition**. The ketene acetal attacks the β-carbon *C*1; the ketone-derived oxygen is initially present in a silylated enol intermediate. Immediate DIBAL-H reduction converts the ester-derived group into —CH₂OH. Aqueous work-up restores the ketone.

The resulting hydroxy ketone **2** is:

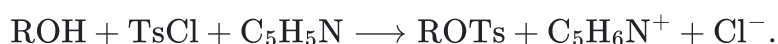


A balanced net organic equation, using [H] for a formal reducing-hydrogen equivalent, is



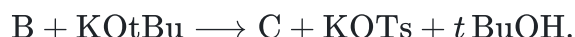
The four reducing-hydrogen equivalents correspond to the two hydride transfers and protonation steps needed to reduce an ester to a primary alcohol.

Tosyl chloride converts the primary alcohol into **B**. No bond to a stereogenic carbon is broken, so the existing configuration is retained:



Here ROH is **2**, and ROTs is **B**.

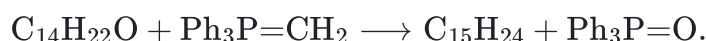
Potassium tert-butoxide then removes an α -hydrogen from **C**9. The resulting enolate attacks the primary carbon **C**10 intramolecularly, displacing tosylate and forming the **C**9 – **C**10 bond. This closes the four-membered ring **C**1 – **C**9 – **C**10 – **C**11, giving **C** with the trans ring-junction stereochemistry shown in the final product:



Finally, deprotonation of methyltriphenylphosphonium bromide gives **D**:



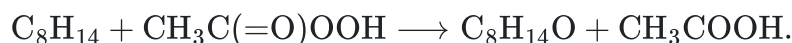
The Wittig reaction replaces the **C**8 carbonyl oxygen by CH_2 :



The phosphorus-containing product is triphenylphosphine oxide, $\text{O}=\text{P}(\text{c1ccccc1})(\text{c1ccccc1})\text{c1ccccc1}$.

8.2 — Epoxide opening and stereospecific elimination

The starting alkene is cis-cyclooctene, $\text{C1CC/C=C\CCCC1}$. A peroxyacid such as peracetic acid **E** epoxidizes it in one step:



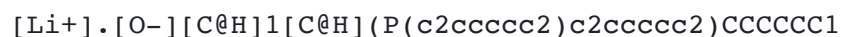
The product is meso-1,2-epoxycyclooctane:



Lithium diphenylphosphide opens the epoxide by backside attack. The carbon–oxygen bond at the attacked carbon breaks, so the phosphorus group and the remaining oxygen substituent are **trans**.

The two epoxide carbons are enantiotopic. Attack at either gives one member of the (*R*, *R*)/(*S*, *S*) pair. Since the reagents are achiral, **F** is **racemic**.

Strictly, the immediate product in dry THF is lithium trans-2-(diphenylphosphanyl)cyclooctan-1-olate. One enantiomer is



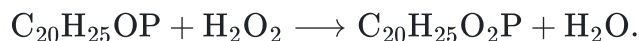
and the other has both @ symbols changed to @@. Its formation is balanced by



Protonation, available in the subsequent acetic-acid-containing medium, gives the alcohol **F**:



Hydrogen peroxide oxidizes the phosphine to the phosphine oxide **G**, without changing the carbon configurations:



Thus **G** is **also racemic**. Phosphorus introduces no additional stereogenic centre because its two phenyl substituents are identical.

Sodium hydride deprotonates the alcohol. The alkoxide attacks phosphorus, and the resulting cyclic elimination arrangement fragments to the *E* alkene. The net equation is



The phosphorus product is sodium diphenylphosphinate:

[Na+].[O-]P(=O)(c1cccc1)c1cccc1

The two enantiomers of **G** give the two planar enantiomers of trans-cyclooctene.

8.3 — Enantiomer of trans-cyclooctene

The double bond remains *E*. What changes is the handedness of the ring passing around that double bond.

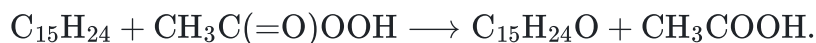
An exact drawing instruction is to **reflect every feature of the supplied drawing in a vertical mirror line**, including the bold perspective bonds. This produces the opposite planar enantiomer.

The ordinary SMILES C1CC/C=C/CCC1 encodes the connectivity and *E* geometry, but not this conformational handedness.

8.4 — Selective reactions of the internal double bond

The problem specifies that the strained internal *C4* = *C5* double bond reacts preferentially.

Epoxidation. Peracetic acid transfers oxygen to the alkene in a concerted, stereospecific reaction:



Approach from the two faces gives **Ha** and **Hb**. The two bonds to the newly introduced oxygen form from the same face. The original *E*-alkene relationship is therefore preserved in the epoxide: the two ring continuations remain trans across the epoxide.

The new configurations are *4S*, *5S* in the listed **Ha** and *4R*, *5R* in **Hb**. Because the pre-existing *C1*, *C9* configurations remain fixed, the products are diastereomers.

Ozonolysis. Cleavage of *C4* = *C5* gives:

- a ketone at *C4*, because that alkene carbon bears a methyl group;
- an aldehyde at *C5*, because that alkene carbon bears hydrogen.

The nine-membered ring opens, while the cyclobutane and exocyclic methylene remain intact. This gives **I**. With dimethyl sulfide as reductant, the balanced net equation is



Hydroboration–oxidation. Boron attaches preferentially to the less substituted carbon *C5*, and hydrogen attaches to *C4*. Addition is syn. Oxidation replaces the carbon–boron bond by a carbon–oxygen bond with retention at carbon.

Thus the added *C4*-hydrogen and *C5*-OH are syn. Addition from the two alkene faces gives **Ja** and **Jb**, with the configurations listed above.

One borane molecule has three B–H bonds, so $\frac{1}{3}$ equivalent supplies one hydroboration per substrate molecule. A balanced net equation in basic aqueous solution is



8.5 — Hydroboration of isocaryophyllene

Isocaryophyllene **5** has the internal *Z* alkene:

[C@@H]12CC/C(C)=C\CCC(=C)[C@H]1CC2(C)C

Here the exocyclic double bond reacts preferentially. Boron adds to terminal *C*13, and hydrogen adds to *C*8. Oxidation therefore gives a **primary hydroxymethyl group**, $-\text{CH}_2\text{OH}$, attached to *C*8.

Only *C*8 becomes a new stereogenic centre. Addition from its two faces gives **Ka** and **Kb**, which have opposite *C*8 configurations while retaining the original ring-junction configurations and the *Z* internal alkene.

The net balance is again



now with **5** as substrate and **Ka/Kb** as products.

8.6 — Deuterium incorporation

Formation of L. The reagent is dideuteriomethylenetriphenylphosphorane:



Its carbon becomes the exocyclic carbon of the Wittig product. Both deuterium atoms therefore appear on *C*13:



The existing alkene geometry and ring-junction stereochemistry remain unchanged.

Formation of M. Base-catalyzed enolization exchanges the two α -hydrogens on the methylene *C*7. Repeated deprotonation and deuteration in excess heavy water gives *C*7*D*₂.

The other α -position, *C*9, is the constrained ring junction. Enolization there would require a severely strained junction geometry; its hydrogen is retained in the specified product. Thus the two deuteriums are both on *C*7, rather than distributed over the two α -carbons.

The exchange balance is

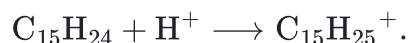


This gives exactly the formula printed for **M**.

8.7 — Carbocation cyclization and rearrangement

All three requested cations have formula $\text{C}_{15}\text{H}_{25}^+$.

Formation of O. Protonation occurs at *C*5 of the internal alkene, placing the positive charge on methyl-substituted *C*4. This gives the tertiary carbocation **O**:



The exocyclic *C*8 = *C*13 double bond remains available for intramolecular attack.

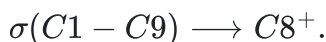
Formation of Pa. The exocyclic alkene attacks the *C*4 carbocation through its terminal carbon *C*13:

- the new bond is *C*4 – *C*13;
- *C*8 = *C*13 becomes a single bond;
- the positive charge moves to *C*8.

No carbon–carbon single bond breaks in this step. The newly formed methylene bridge gives the tricyclic caryolane framework.

The two possible configurations at newly tetrahedral $C4$ give **Pa** and **Pb**. The configuration of **Pa** is selected by the requirement that the subsequent rearrangement give the forward-pointing bridge drawn in **7a**.

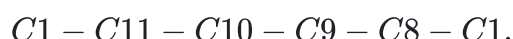
Formation of Qa. The adjacent cyclobutane undergoes a Wagner–Meerwein rearrangement:



Precisely:

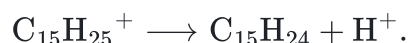
- $C1 - C9$ breaks;
- $C1 - C8$ forms;
- the positive charge moves from $C8$ to $C9$.

This expands the cyclobutane into the five-membered ring



The migration retains the spatial configuration at the migrating end. Some R/S descriptors change because the CIP priorities change, without inversion of the carried-through stereochemistry.

Finally, loss of a proton from $C10$ forms $C9 = C10$, giving **7a** and regenerating acid:



The resulting **7a**, (1*S*,5*S*,8*S*)-4,4,8-trimethyltricyclo[6.3.1.0^{1,5}]dodec-2-ene, is



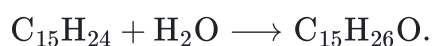
This reproduces the alkene position and the forward methylene bridge in the supplied drawing.

8.8 — Hydration of Pa and Pb

Water attacks the $C8$ carbocation of **Pa** or **Pb**. Deprotonation of the resulting oxonium ion gives **Na** or **Nb**:



The overall acid-catalyzed hydration is therefore



The original cyclobutane remains intact. Both products contain:

- the new $C4 - C13$ bond;
- the $C4 - C13 - C8$ methylene bridge;
- OH on $C8$;
- the original stereochemical arrangement at $C1, C9$.

For the requested pair, the two new bridgehead configurations at $C4, C8$ are reversed together. In a schematic drawing of the large ring, the methylene bridge occupies one face, while the $C4$ -methyl and $C8$ -OH point toward the opposite face. Reversing these new stereochemical features gives the other diastereomer, while the original ring-junction stereochemistry is retained.

The answers were checked against the official answers published by the organisers.