

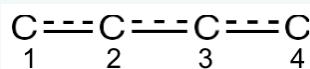
IChO 2019

Theory problems and solutions · Paris, France · 9 theory problems with complete solutions

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Problem 1: Infinite well and butadiene

The buta-1,3-diene molecule is often written $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$, with alternating single and double bonds. Nevertheless, its chemical reactivity is not consistent with this description and the π electrons are better described by a distribution along the three bonds:



This system can be modeled as a 1D box (*i.e.* infinite well) where the electrons are free. The energy of an electron in an infinite well of length L is:

$$E_n = \frac{n^2 h^2}{8m_e L^2}$$

where n is a non-zero positive integer.

1.1 Two different models are studied. Sketch at least the three lowest-energy levels E_n for each model in the respective diagrams, showing how the relative energy levels differ within and between models.

1.2 Place the π electrons for model 1 in the previous diagrams and express the total energy of the π system in model 1, as a function of h , m_e and d .

1.3 Place the π electrons for model 2 in the previous diagrams and express the total energy of the π system in model 2, as a function of h , m_e and d .

The conjugation energy is the total energy of the actual π system, minus the sum of the energies of ethylene molecules involving the same number of electrons.

1.4 Express the conjugation energy ΔE_c of butadiene, as a function of h , m_e and d .

Models 1 and 2 are too simplistic. A new model will be detailed in the following.

1.5 Draw three other resonance structures of butadiene using Lewis notation.

To take into account the size of carbon atoms, model 2 is now modified into model 3, as follows:

- the new length of the well is L and is located between the abscissa 0 and L ;
- the carbon atoms are located at the abscissas $L/8$; $3L/8$; $5L/8$ and $7L/8$.

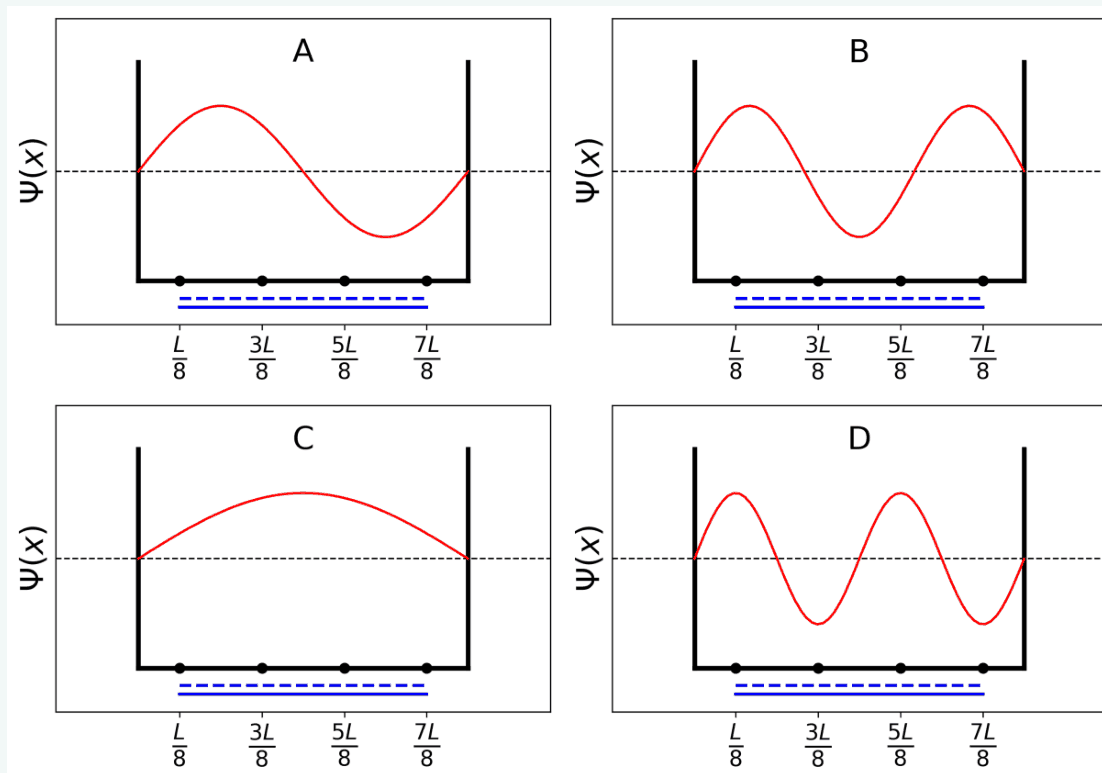
For each level n , the π wavefunction is:

$$\Psi_n(x) = \sqrt{\frac{2}{L}} \sin\left(\frac{n\pi x}{L}\right)$$

and the π electron density for a system with N π -electrons is:

$$\rho(x) = 2 \sum_{i=1}^{N/2} |\Psi_i(x)|^2$$

The four π wavefunctions, which correspond to the molecular orbitals of the π system, are depicted below (arbitrary order).



- 1.6 Sort the energies of the four π wavefunctions (E_A , E_B , E_C and E_D).
- 1.7 Give the labels (A, B, C or D) of the orbitals that are filled with electrons in butadiene.
- 1.8 Within model 3, give the values of the π wavefunctions ψ_n for occupied levels at positions 0, $L/4$ and $L/2$, for $n = 1$ and $n = 2$, as a function of L .
- 1.9 Within model 3, give the value of the π electron density at positions 0, $L/4$ and $L/2$.
- 1.10 Draw the π electron density between 0 and L .
- 1.11 Sort the following CC bonds (B1, B2, ..., B5) by increasing length, using the symbols = or <:
 - B1: C1–C2 in the butadiene molecule
 - B2: C2–C3 in the butadiene molecule
 - B3: C3–C4 in the butadiene molecule
 - B4: C–C in the ethane molecule
 - B5: C–C in the ethene molecule

Official English text of the problem.

Answers

For **1.1–1.4**, assume that model 1 consists of **two independent wells, each of length d** , and model 2 consists of **one well of length $3d$** . The problem as printed does not define these models. Define

$$\varepsilon = \frac{h^2}{8m_e d^2}.$$

- **1.1** Each model-1 well has its first three levels at $\varepsilon, 4\varepsilon, 9\varepsilon$. Model 2 has its first three levels at $\varepsilon/9, 4\varepsilon/9, \varepsilon$. Use a common energy scale; model 2's third level coincides with model 1's first level.

- **1.2** Put two electrons with opposite spins in $n = 1$ of each separate well:

$$E_{\pi,1} = \frac{h^2}{2m_e d^2}.$$

- **1.3** Put two electrons in $n = 1$ and two in $n = 2$:

$$E_{\pi,2} = \frac{5h^2}{36m_e d^2}.$$

- **1.4**

$$\Delta E_c = -\frac{13h^2}{36m_e d^2}.$$

- **1.5** Three valid charge-separated resonance contributors of buta-1,3-diene are the C1-negative/C4-positive contributor, $[\text{CH}_2^-]\text{C}=\text{C}[\text{CH}_2^+]$; the C1-positive/C4-negative contributor, $[\text{CH}_2^+]\text{C}=\text{C}[\text{CH}_2^-]$; and the C1-negative/C2-positive contributor, $[\text{CH}_2^-]\text{C}=\text{C}[\text{CH}^+]$. Each negatively charged carbon has one lone pair.

- **1.6**

$$[E_C < E_A < E_B < E_D], \quad n_C = 1, n_A = 2, n_B = 3, n_D = 4.$$

- **1.7** $[C \text{ and } A]$, each containing two electrons.

- **1.8** The pairs (ψ_1, ψ_2) are

$$\begin{aligned} x = 0 &: (0, 0), \\ x = L/4 &: \left(\frac{1}{\sqrt{L}}, \sqrt{\frac{2}{L}} \right), \\ x = L/2 &: \left(\sqrt{\frac{2}{L}}, 0 \right). \end{aligned}$$

- **1.9**

$$\rho(0) = 0, \quad \rho(L/4) = \frac{6}{L}, \quad \rho(L/2) = \frac{4}{L}.$$

• 1.10

$$\rho(x) = \frac{4}{L} \left[\sin^2 \left(\frac{\pi x}{L} \right) + \sin^2 \left(\frac{2\pi x}{L} \right) \right].$$

The curve is symmetric about $L/2$, vanishes at both walls, has maxima $25/(4L)$ at approximately $0.290L$ and $0.710L$, and has a local minimum $4/L$ at $L/2$.

• 1.11

$$B5 < B1 = B3 < B2 < B4.$$

Solution

Buta-1,3-diene, commonly called butadiene, has SMILES C=CC=C. Its four sp^2 carbon atoms supply **four π electrons**. Within each well, a spatial energy level can accommodate two electrons with opposite spins.

1.1

For a well of any fixed length,

$$E_1 : E_2 : E_3 = 1 : 4 : 9.$$

Thus the energy levels become farther apart as n increases.

Using the assumed lengths d and $3d$,

$$E_n^{(1)} = n^2 \varepsilon, \quad E_n^{(2)} = \frac{n^2}{9} \varepsilon.$$

Level	Model 1: each separate well	Model 2: single well
$n = 1$	ε	$\varepsilon/9$
$n = 2$	4ε	$4\varepsilon/9$
$n = 3$	9ε	ε

For the drawing, use the same vertical energy scale and the same zero for both models. Draw two identical ladders for model 1, one for each localized electron pair, and one ladder for model 2.

The first two gaps in each model-1 ladder are 3ε and 5ε . The corresponding model-2 gaps are nine times smaller. In particular,

$$E_3^{(2)} = E_1^{(1)}.$$

1.2

Each localized well contains two electrons. Both occupy its lowest level, with opposite spins. Draw $\uparrow\downarrow$ on $n = 1$ in each well, leaving higher levels empty.

Adding the four one-electron energies,

$$E_{\pi,1} = 2E_1^{(1)} + 2E_1^{(1)} = 4 \frac{h^2}{8m_e d^2} = \boxed{\frac{h^2}{2m_e d^2}}.$$

1.3

In the single well, only two electrons can occupy $n = 1$, so the remaining two occupy $n = 2$. Draw $\uparrow\downarrow$ on each of these levels; $n = 3$ is empty.

Therefore,

$$\begin{aligned} E_{\pi,2} &= 2E_1^{(2)} + 2E_2^{(2)} \\ &= 2(1^2 + 2^2) \frac{h^2}{8m_e(3d)^2} \\ &= \boxed{\frac{5h^2}{36m_e d^2}}. \end{aligned}$$

1.4

Ethene, also called ethylene, has SMILES C=C and contains two π electrons. Two ethene molecules therefore provide the four-electron reference represented by model 1.

Using the definition in the question,

$$\begin{aligned} \Delta E_c &= E_{\pi,2} - E_{\pi,1} \\ &= \frac{5h^2}{36m_e d^2} - \frac{h^2}{2m_e d^2} \\ &= \boxed{-\frac{13h^2}{36m_e d^2}}. \end{aligned}$$

The negative sign denotes stabilization of the π system through delocalization within this model.

All these energies have units of joules when h , m_e , and d are expressed in SI units.

More generally, if the missing diagrams give each localized well length ℓ_1 and the delocalized well length ℓ_2 , the results are

$$E_{\pi,1} = \frac{h^2}{2m_e \ell_1^2}, \quad E_{\pi,2} = \frac{5h^2}{4m_e \ell_2^2},$$

and

$$\boxed{\Delta E_c = \frac{h^2}{8m_e} \left(\frac{10}{\ell_2^2} - \frac{4}{\ell_1^2} \right)}.$$

1.5

Number the carbon atoms from left to right as in the statement. Three possible additional Lewis resonance contributors are:

Contributor of buta-1,3-diene	Lewis skeleton	SMILES
R_1 : C1-negative/C4-positive	$\text{H}_2\text{C}^- - \text{CH}=\text{CH} - \text{CH}_2^+$	<chem>[CH2-]C=C[CH2+]</chem>
R_2 : C1-positive/C4-negative	$\text{H}_2\text{C}^+ - \text{CH}=\text{CH} - \text{CH}_2^-$	<chem>[CH2+]C=C[CH2-]</chem>
R_3 : C1-negative/C2-positive	$\text{H}_2\text{C}^- - \text{CH}^+ - \text{CH}=\text{CH}_2$	<chem>[CH2-][CH+]C=C</chem>

For the Lewis drawings, **place one lone pair on every negatively charged carbon**. Each positively charged carbon has three bonds, no lone pair, and an empty p orbital. Connect the contributors to the original structure using resonance double-headed arrows.

Their electron-pair movements from the original $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$ structure are:

- For R_1 , move the $\text{C1}=\text{C2}$ π pair onto C1, and move the $\text{C3}=\text{C4}$ π pair into the $\text{C2}-\text{C3}$ bond.
- For R_2 , perform the mirror-image movements: move the $\text{C3}=\text{C4}$ π pair onto C4, and the $\text{C1}=\text{C2}$ π pair into $\text{C2}-\text{C3}$.
- For R_3 , move only the $\text{C1}=\text{C2}$ π pair onto C1.

Each structure preserves the atomic connectivity, total charge, and total electron count. These charge-separated contributors have smaller weights than the uncharged structure.

The SMILES specify connectivity and formal charges. For resonance, retain the same nuclear geometry throughout; no particular conformation is specified in the question.

1.6

The wavefunction

$$\psi_n(x) = \sqrt{\frac{2}{L}} \sin\left(\frac{n\pi x}{L}\right)$$

has $n - 1$ internal nodes. Counting the nodes in the diagrams gives:

Label	Internal nodes	n	Energy in units of $h^2/(8m_e L^2)$
C	0	1	1
A	1	2	4
B	2	3	9
D	3	4	16

Consequently,

$$E_C < E_A < E_B < E_D.$$

1.7

The four electrons occupy the two lowest orbitals, two electrons per orbital:



Orbitals B and D are empty in the ground state.

1.8

Substitute each position into the given wavefunction. The required sine values are

$$\sin 0 = 0, \quad \sin \frac{\pi}{4} = \frac{1}{\sqrt{2}}, \quad \sin \frac{\pi}{2} = 1, \quad \sin \pi = 0.$$

Thus:

Wavefunction	$x = 0$	$x = L/4$	$x = L/2$
$\psi_1(x)$	0	$\frac{1}{\sqrt{L}}$	$\sqrt{\frac{2}{L}}$

Wavefunction	$x = 0$	$x = L/4$	$x = L/2$
$\psi_2(x)$	0	$\sqrt{\frac{2}{L}}$	0

These wavefunctions have dimensions of length^{-1/2}.

1.9

For four electrons, $N/2 = 2$, so

$$\rho(x) = 2(|\psi_1(x)|^2 + |\psi_2(x)|^2).$$

Therefore,

$$\begin{aligned}\rho(0) &= 0, \\ \rho(L/4) &= 2\left(\frac{1}{L} + \frac{2}{L}\right) = \boxed{\frac{6}{L}},\end{aligned}$$

and

$$\rho(L/2) = 2\left(\frac{2}{L} + 0\right) = \boxed{\frac{4}{L}}.$$

This is an electron **number density per unit length**; its units are m^{-1} when L is in metres.

1.10

Substituting both occupied wavefunctions gives

$$\boxed{\rho(x) = \frac{4}{L} \left[\sin^2\left(\frac{\pi x}{L}\right) + \sin^2\left(\frac{2\pi x}{L}\right) \right]}.$$

For a precise sketch, label the horizontal axis x , from 0 to L , and the vertical axis $\rho(x)$. Draw a smooth curve with these features:

- It starts at $(0, 0)$ and ends at $(L, 0)$, with horizontal tangents at both walls.
- It is symmetric about $x = L/2$.
- It passes through $(L/4, 6/L)$ and $(3L/4, 6/L)$.
- It has a local minimum at $(L/2, 4/L)$, so the density remains positive at the centre.
- It has two equal maxima, one on either side of the centre.

To locate the maxima,

$$\rho'(x) = \frac{4\pi}{L^2} \sin\left(\frac{2\pi x}{L}\right) \left[1 + 4 \cos\left(\frac{2\pi x}{L}\right) \right].$$

The maxima satisfy

$$\cos\left(\frac{2\pi x}{L}\right) = -\frac{1}{4}.$$

Their positions are

$$x_{\max,1} = \frac{L}{2\pi} \arccos\left(-\frac{1}{4}\right) \approx 0.290L, \quad x_{\max,2} = L - x_{\max,1} \approx 0.710L.$$

At either maximum,

$$\sin^2\left(\frac{\pi x}{L}\right) = \frac{5}{8}, \quad \sin^2\left(\frac{2\pi x}{L}\right) = \frac{15}{16},$$

hence

$$\rho_{\max} = \frac{4}{L} \left(\frac{5}{8} + \frac{15}{16} \right) = \frac{25}{4L}.$$

The density also has the required normalization:

$$\int_0^L \rho(x) dx = \frac{4}{L} \left(\frac{L}{2} + \frac{L}{2} \right) = 4,$$

accounting for all four π electrons.

1.11

The outer bonds B1 and B3 are equivalent by symmetry. Their midpoints are $L/4$ and $3L/4$, where the model gives greater π -electron density than at the central-bond midpoint $L/2$.

Chemically, conjugation gives the central bond some double-bond character, while the outer bonds retain greater double-bond character than the central bond. The outer bonds have slightly less double-bond character than the localized double bond in ethene, $C=C$. The central bond has more bonding character than the single bond in ethane, CC .

Using the usual relationship between greater bond order and shorter bond length,

$$B5 < B1 = B3 < B2 < B4.$$

The solution was checked against the official solution.

Problem 2: Hydrogen production by water-splitting

Data:

Compound	H ₂ (g)	H ₂ O (l)	H ₂ O (g)	O ₂ (g)
$\Delta_f H^\circ$ (kJ mol ⁻¹)	0	-285.8	-241.8	0
S_m° (J mol ⁻¹ K ⁻¹)	130.6	69.9	188.7	205.2

Molecular hydrogen (H₂) can be used as an alternative to carbon dioxide-emitting fuels. Hence, lowering the cost and the environmental impact of its production is a major challenge. In this field, water-splitting is a promising candidate technology.

2.1 Write down the balanced equation of liquid water splitting reaction using a stoichiometric coefficient of 1 for water.

2.2 Using only the provided thermodynamic data, this justify numerically whether reaction is thermodynamically favorable at 298 K.

Water splitting can be performed electrochemically using two electrodes in an acidic water bath, connected by a generator (Fig. 1). Gas bubbles are formed at both electrodes.

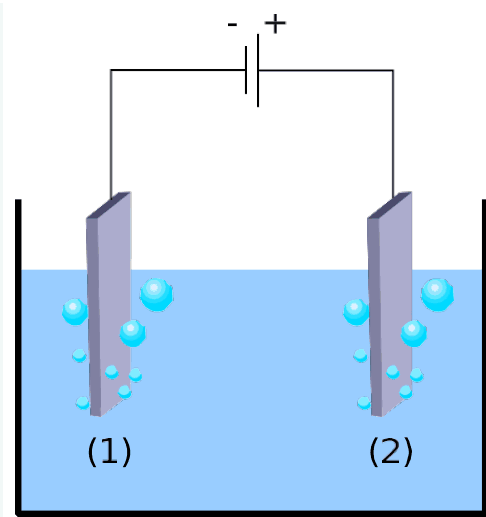


Fig. 1. Water-splitting electrochemical cell.

2.3 Write down the balanced net electrochemical half reactions occurring at each electrode.

2.4 Using only the provided thermodynamic data (or question 2), derive the condition on the applied voltage $\Delta E_{\text{applied}}$ between electrodes, compared to value ΔE_{th} (to determine), for the process to be thermodynamically favorable at 298 K, when all reactants and products are in their standard state. Tick the right condition and give the numerical value with 3 decimal places.

Experimentally, a higher voltage is needed to observe water splitting. For a given Pt cathode, the minimum voltage necessary to observe water splitting, ΔE_{min} , depends on the nature of the anode, as displayed in the table below:

Anode	ΔE_{min} (V)
IrO _x	1.6
NiO _x	1.7
CoO _x	1.7
Fe ₂ O ₃	1.9

The difference between ΔE_{min} and ΔE_{th} is responsible for losses in the device.

2.5 Give the expression of the device power efficiency η_{elec} (fraction of the power used for water splitting) as a function of ΔE_{th} and ΔE_{min} . Assuming an identical current value I , calculate the water electrolysis power efficiency when a Pt cathode and a Fe₂O₃ anode are used. Give the most efficient anode.

An alternative to water electrolysis is direct photocatalytic water-splitting. It uses a semiconductor that can be activated by absorbing light.

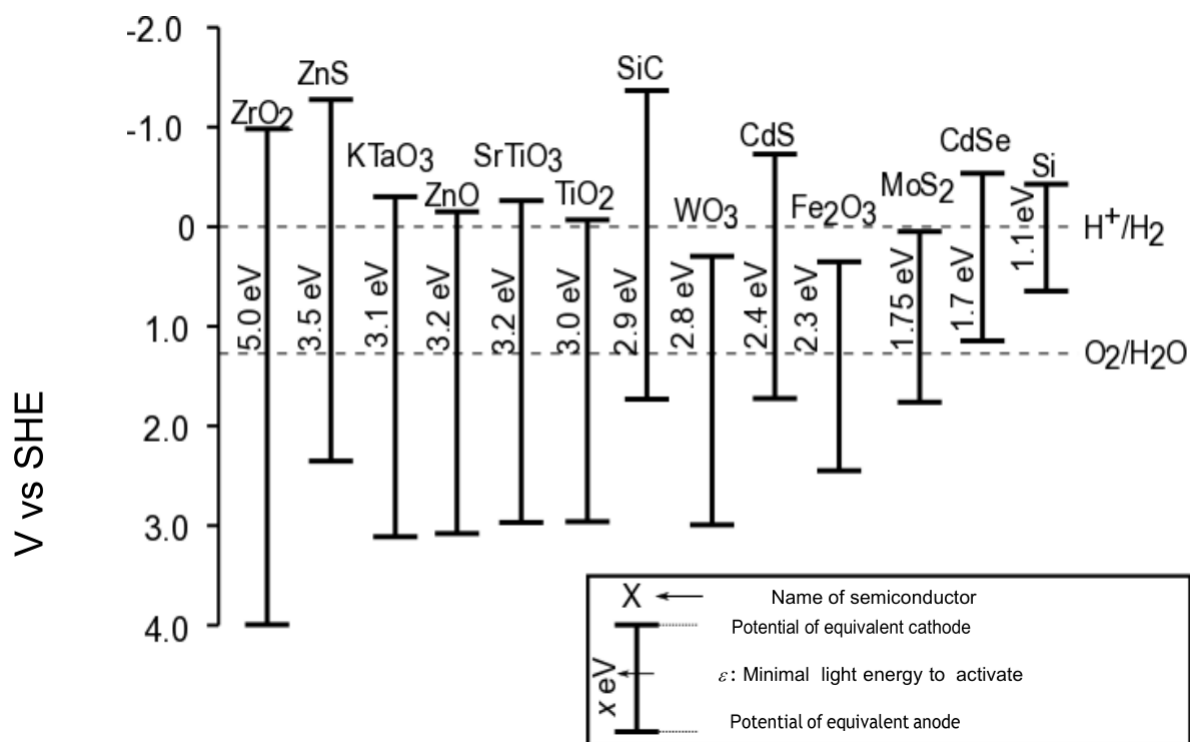


Fig. 2: Activation condition and equivalent electrode potentials of different semiconductors. Dashed lines correspond to water oxidation and reduction potentials. SHE = Standard Hydrogen Electrode

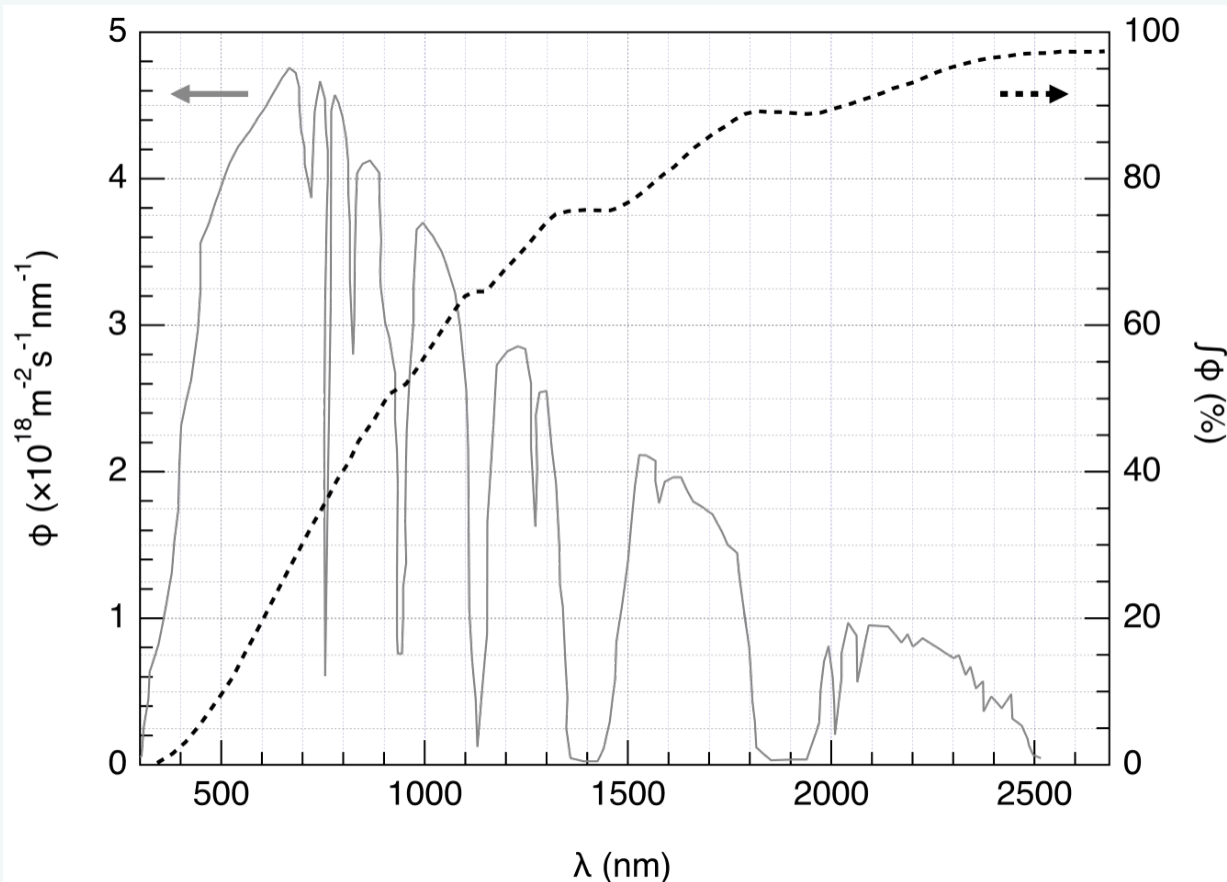


Fig. 3 – Left axis: Spectral distribution of the solar photon flux Φ . The photon flux is the number of photons per unit area per unit time arriving on the semiconductor. Right axis and dashed line: cumulative photon flux (i.e. fraction of the photon flux with smaller wavelength).

2.6 Estimate the fraction of the solar photon flux that can activate the following semiconductors: TiO_2 , CdS , Si . State explicitly the equations and units used for the computation.

The activation of the semi-conductor results in a modification of the surface potentials, so that it can be seen as two electrodes of different potentials.

2.7 Using the data in Fig 2, choose the semiconductor(s) in the following list that, once activated, can play both roles of anode and cathode for water-splitting reaction.

2.8 Give the semiconductor that, used as both cathode and anode, is expected to be the most efficient for water splitting upon a given solar shining.

The evolution of H_2 and O_2 when a semiconductor is irradiated by simulated solar light at $T = 25^\circ\text{C}$ at p_{atm} was recently studied. Using an incident power light of $P = 1.0 \text{ kW m}^{-2}$ and a photoelectrode with a $S = 16 \text{ mm}^2$ surface, the production of $V = 0.37 \text{ cm}^3$ of $\text{H}_2(\text{g})$ was measured after $\Delta t = 1$ hour of reaction.

2.9 Calculate the power efficiency η_{direct} of the conversion.

Two modes of converting solar energy to hydrogen can thus be compared: direct photocatalysis, and indirect photo-electrolysis combining a photovoltaic panel with an electrolyzer. The efficiency of photovoltaic panels on the market is around $\eta_{\text{panels}} = 20\%$.

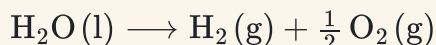
2.10 Compare the power efficiencies of the two modes, η_{direct} and η_{indirect} , using Fe_2O_3 and Pt electrodes for the electrolysis.

Official English text of the problem.

Answers

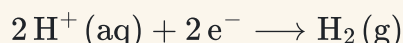
Molecular and ionic species used below are water, SMILES O ; dihydrogen, SMILES $[\text{H}][\text{H}]$; dioxygen, SMILES $\text{O}=\text{O}$; and the hydrogen ion (proton), SMILES $[\text{H}^+]$. These SMILES do not specify physical phase, aqueous solvation, or the triplet spin state of dioxygen. The electrode and semiconductor materials are extended solids, for which a molecular SMILES does not specify the crystal structure.

- **2.1**

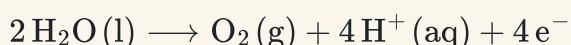


- **2.2** $\Delta_r G^\circ(298 \text{ K}) = +237.1 \text{ kJ mol}^{-1}$. The reaction is **not thermodynamically favorable under standard conditions**.

- **2.3** Electrode **(1)** is the negative cathode:



Electrode **(2)** is the positive anode:



- 2.4

$$\Delta E_{\text{applied}} > \Delta E_{\text{th}}, \quad \Delta E_{\text{th}} = 1.229 \text{ V}$$

Equality is the reversible limit, with no net thermodynamic driving force.

- 2.5

$$\eta_{\text{elec}} = \frac{\Delta E_{\text{th}}}{\Delta E_{\text{min}}}$$

For Pt/Fe₂O₃, $\eta_{\text{elec}} \approx 64.7\%$. The most efficient anode is **iridium oxide**, IrO_x, giving approximately 76.8%.

- 2.6

Semiconductor	Maximum activating wavelength	Activating fraction of photon flux
Titanium dioxide, TiO ₂	413 nm	approximately 4%
Cadmium sulfide, CdS	517 nm	approximately 12%
Silicon, Si	1127 nm	approximately 65%

- 2.7 Among all the materials in Fig. 2, those capable of both half-reactions are

$$\text{ZrO}_2, \text{ZnS}, \text{KTaO}_3, \text{ZnO}, \text{SrTiO}_3, \text{TiO}_2, \text{SiC}, \text{CdS}.$$

- 2.8 Cadmium sulfide, CdS.

- 2.9

$$\eta_{\text{direct}} \approx 6.2\%$$

using $p_{\text{atm}} = 1 \text{ atm}$.

- 2.10

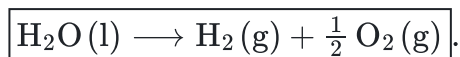
$$\eta_{\text{indirect}} = \eta_{\text{panels}} \eta_{\text{elec}} \approx 12.9\%$$

The indirect route is approximately **2.1 times as efficient** as the measured direct route.

Solution

2.1 — Overall water-splitting reaction

Liquid water forms gaseous hydrogen and oxygen. With the coefficient of water fixed at one, atom balance gives



All molar reaction quantities below refer to this equation: one mole of liquid water consumed and one mole of hydrogen produced.

2.2 — Thermodynamic favorability at 298 K

The standard reaction enthalpy is

$$\begin{aligned}
\Delta_r H^\circ &= \Delta_f H^\circ(\text{H}_2(\text{g})) + \frac{1}{2} \Delta_f H^\circ(\text{O}_2(\text{g})) - \Delta_f H^\circ(\text{H}_2\text{O}(\text{l})) \\
&= 0 + \frac{1}{2}(0) - (-285.8) \\
&= +285.8 \text{ kJ mol}^{-1}.
\end{aligned}$$

The standard reaction entropy is

$$\begin{aligned}
\Delta_r S^\circ &= 130.6 + \frac{1}{2}(205.2) - 69.9 \\
&= +163.3 \text{ J mol}^{-1} \text{ K}^{-1} \\
&= +0.1633 \text{ kJ mol}^{-1} \text{ K}^{-1}.
\end{aligned}$$

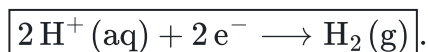
Therefore,

$$\begin{aligned}
\Delta_r G^\circ &= \Delta_r H^\circ - T \Delta_r S^\circ \\
&= 285.8 - 298(0.1633) \\
&= \boxed{+237.1366 \text{ kJ mol}^{-1}}.
\end{aligned}$$

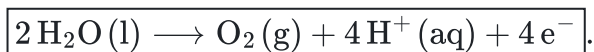
Since $\Delta_r G^\circ > 0$, standard-state water splitting is thermodynamically unfavorable at 298 K. Energy must be supplied to drive it.

2.3 — Electrode half-reactions

In Fig. 1, electrode **(1)** is connected to the generator's negative terminal. It receives electrons and is the **cathode**, where hydrogen ions are reduced:



Electrode **(2)** is connected to the positive terminal. It is the **anode**, where water is oxidized:



Multiplying the cathode reaction by two and adding cancels both electrons and hydrogen ions:



Dividing by two reproduces the equation in 2.1.

2.4 — Thermodynamic threshold voltage

Producing one mole of hydrogen transfers two moles of electrons, corresponding to charge

$$q = 2F,$$

where $F = 96485 \text{ C mol}^{-1}$.

The reversible electrical energy required per mole is therefore

$$2F \Delta E_{\text{th}} = \Delta_r G^\circ.$$

Using $1 \text{ V} = 1 \text{ J C}^{-1}$,

$$\begin{aligned}
\Delta E_{\text{th}} &= \frac{237136.6 \text{ J mol}^{-1}}{2(96485 \text{ C mol}^{-1})} \\
&= 1.22888 \text{ V} \\
&= \boxed{1.229 \text{ V}}.
\end{aligned}$$

With an applied voltage supplying electrical work, the net free-energy change per mole is

$$\Delta G_{\text{net}} = \Delta_r G^\circ - 2F\Delta E_{\text{applied}}.$$

For a thermodynamic driving force in the water-splitting direction,

$$\Delta G_{\text{net}} < 0,$$

so the condition to select is

$$\Delta E_{\text{applied}} > \Delta E_{\text{th}}.$$

At equality, electrolysis is at its reversible threshold.

2.5 — Electrolyzer power efficiency

At current I , the electrical input power at the observed minimum voltage is

$$P_{\text{input}} = I\Delta E_{\text{min}}.$$

The useful power associated with the Gibbs-energy increase of the products is

$$P_{\text{useful}} = I\Delta E_{\text{th}}.$$

Thus,

$$\eta_{\text{elec}} = \frac{I\Delta E_{\text{th}}}{I\Delta E_{\text{min}}} = \frac{\Delta E_{\text{th}}}{\Delta E_{\text{min}}}.$$

For a platinum cathode and iron(III) oxide anode,

$$\eta_{\text{elec}} = \frac{1.22888}{1.9} = 0.6468 \approx \boxed{64.7\%}.$$

The most efficient anode has the lowest ΔE_{min} . The table gives this as iridium oxide, IrO_x :

$$\eta_{\text{elec}}(\text{IrO}_x) = \frac{1.22888}{1.6} = 0.7680 \approx \boxed{76.8\%}.$$

2.6 — Fraction of sunlight capable of activation

A photon activates the semiconductor if its energy reaches the minimum activation energy ε :

$$E_\gamma = h\nu = \frac{hc}{\lambda} \geq \varepsilon.$$

Hence the activating wavelengths satisfy

$$\lambda \leq \lambda_{\text{max}} = \frac{hc}{\varepsilon}.$$

Using

$$h = 6.626 \times 10^{-34} \text{ J s}, \quad c = 2.998 \times 10^8 \text{ m s}^{-1},$$

and

$$1 \text{ eV} = 1.602 \times 10^{-19} \text{ J},$$

the convenient numerical form is

$$\lambda_{\text{max}} [\text{nm}] = \frac{1239.84}{\varepsilon [\text{eV}]}.$$

From Fig. 2:

$$\begin{aligned}\text{TiO}_2 : \quad \varepsilon &= 3.0 \text{ eV}, & \lambda_{\max} &= \frac{1239.84}{3.0} = 413 \text{ nm}, \\ \text{CdS} : \quad \varepsilon &= 2.4 \text{ eV}, & \lambda_{\max} &= \frac{1239.84}{2.4} = 517 \text{ nm}, \\ \text{Si} : \quad \varepsilon &= 1.1 \text{ eV}, & \lambda_{\max} &= \frac{1239.84}{1.1} = 1127 \text{ nm}.\end{aligned}$$

If $\Phi(\lambda)$ is the spectral photon flux in photons $\text{m}^{-2} \text{s}^{-1} \text{nm}^{-1}$, the activating fraction is

$$f = \frac{\int_0^{\lambda_{\max}} \Phi(\lambda) d\lambda}{\int_0^{\infty} \Phi(\lambda) d\lambda}.$$

Both integrals have units photons $\text{m}^{-2} \text{s}^{-1}$, so f is dimensionless. This fraction is given directly by the dashed cumulative curve in Fig. 3.

Reading that curve at the three threshold wavelengths gives approximately

$$\boxed{f_{\text{TiO}_2} \approx 4\%, \quad f_{\text{CdS}} \approx 12\%, \quad f_{\text{Si}} \approx 65\%.$$

These are fractions of **photon flux**, rather than fractions of incident radiant power.

2.7 — Semiconductors capable of both half-reactions

For hydrogen evolution, the equivalent cathode must have a potential more negative than the hydrogen-ion/hydrogen couple:

$$E_{\text{cathode}} < E_{\text{H}^+/\text{H}_2}^\circ = 0 \text{ V} \quad \text{vs SHE.}$$

For oxygen evolution, the equivalent anode must have a potential more positive than the oxygen/water couple:

$$E_{\text{anode}} > E_{\text{O}_2/\text{H}_2\text{O}}^\circ \approx +1.229 \text{ V} \quad \text{vs SHE.}$$

Thus, the semiconductor's potential interval must span **both** dashed lines in Fig. 2. Because the numerical potential increases downward in the figure, its upper endpoint must lie above the hydrogen line and its lower endpoint below the oxygen line.

Materials in Fig. 2	Hydrogen evolution possible?	Oxygen evolution possible?	Both possible?
ZrO ₂ , ZnS, KTaO ₃ , ZnO, SrTiO ₃ , TiO ₂ , SiC, CdS	Yes	Yes	Yes
WO ₃ , Fe ₂ O ₃ , MoS ₂	No: equivalent cathode potential is too positive	Yes	No
CdSe, Si	Yes	No: equivalent anode potential is insufficiently positive	No

The complete qualifying set is therefore zirconium dioxide, zinc sulfide, potassium tantalate, zinc oxide, strontium titanate, titanium dioxide, silicon carbide, and cadmium sulfide.

2.8 — Most efficient semiconductor under the stated model

The semiconductor must first satisfy both potential conditions in 2.7. Among the qualifying materials, cadmium sulfide has the smallest activation energy:

$$\varepsilon_{\text{CdS}} = 2.4 \text{ eV}.$$

It therefore has the longest activation cutoff wavelength and can use the largest fraction of the incident solar photon flux among those materials. Under the comparison implied by the problem,

the expected most efficient semiconductor is CdS.

Although silicon absorbs a larger fraction of solar photons, its equivalent anode potential does not permit water oxidation, so it cannot serve both roles.

2.9 — Direct solar-to-hydrogen efficiency

For consistency with the efficiency definition in 2.5, the useful chemical energy is the Gibbs-energy increase, $\Delta_r G^\circ$, per mole of hydrogen produced.

Treat the hydrogen as an ideal gas. Using

$$p_{\text{atm}} = 101325 \text{ Pa}, \quad T = 298.15 \text{ K}, \quad R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1},$$

and converting the volume,

$$V = 0.37 \text{ cm}^3 = 3.7 \times 10^{-7} \text{ m}^3,$$

gives

$$\begin{aligned} n(\text{H}_2) &= \frac{p_{\text{atm}} V}{RT} \\ &= \frac{(101325)(3.7 \times 10^{-7})}{(8.314)(298.15)} \\ &= 1.51 \times 10^{-5} \text{ mol}. \end{aligned}$$

The useful chemical energy produced is

$$\begin{aligned} E_{\text{chemical}} &= n(\text{H}_2) \Delta_r G^\circ \\ &= (1.512 \times 10^{-5})(237136.6) \\ &\approx 3.59 \text{ J}. \end{aligned}$$

The incident irradiance, area, and exposure time are

$$P = 1.0 \times 10^3 \text{ W m}^{-2}, \quad S = 16 \times 10^{-6} \text{ m}^2, \quad \Delta t = 3600 \text{ s}.$$

Therefore,

$$E_{\text{incident}} = PS\Delta t = (1.0 \times 10^3)(16 \times 10^{-6})(3600) = 57.6 \text{ J}.$$

The ratio of average powers equals the ratio of energies over the same interval:

$$\begin{aligned} \eta_{\text{direct}} &= \frac{n(\text{H}_2) \Delta_r G^\circ}{PS\Delta t} \\ &= \frac{3.59}{57.6} \\ &= 0.0623. \end{aligned}$$

Thus,

$$\eta_{\text{direct}} \approx 6.2\%.$$

2.10 — Comparison with photovoltaic-powered electrolysis

The indirect route consists of two successive conversions: sunlight to electricity, then electricity to chemical energy. Its overall efficiency is the product:

$$\eta_{\text{indirect}} = \eta_{\text{panels}} \eta_{\text{elec}}$$

For the stated photovoltaic panels and platinum/iron(III) oxide electrolyzer,

$$\begin{aligned}\eta_{\text{indirect}} &= 0.20 \left(\frac{1.22888}{1.9} \right) \\ &= 0.1294 \\ &\approx \boxed{12.9\%}.\end{aligned}$$

Consequently,

$$\frac{\eta_{\text{indirect}}}{\eta_{\text{direct}}} = \frac{0.1294}{0.0623} \approx 2.1.$$

Under the supplied conditions, the indirect route is approximately twice as efficient as the measured direct photocatalytic route.

The solution was checked against the official solution.

Problem 3: About silver chloride

Data at 298 K:

$$pK_{s1}(\text{AgCl}) = 9.7 ; \quad pK_{s2}(\text{Ag}_2\text{CrO}_4) = 12$$

Formation constant of the complex $[\text{Ag}(\text{NH}_3)_n]^+$: $\beta_n = 10^{7.2}$

Potentials against the standard hydrogen electrode:

Standard potential of $\text{Ag}^+/\text{Ag}(\text{s})$: $E^\circ(\text{Ag}^+/\text{Ag}(\text{s})) = 0.80 \text{ V}$

Apparent potential of $\text{O}_2(\text{aq})/\text{HO}^-(\text{aq})$ (in seawater): $E'(\text{O}_2(\text{aq})/\text{HO}^-(\text{aq})) = 0.75 \text{ V}$

Part A: Quotes from a chemistry lesson by Louis Joseph Gay-Lussac

The following quotes from a chemistry lesson by Louis Joseph Gay-Lussac (French chemist and physicist, 1778–1850) deal with some properties of silver chloride.

Quote A: "I will now talk about silver chloride, a milk-white solid. It is easily obtained by pouring hydrochloric acid into an aqueous solution of silver nitrate."

Quote B: "This salt has no taste since it is insoluble."

Quote C: "This compound is completely insoluble in alcohol and even in acids, except in concentrated hydrochloric acid which dissolves it readily."

Quote D: "On the other hand, silver chloride is highly soluble in aqueous solution of ammonia."

Quote E: "Then, we can make silver chloride appear again by adding an acid which reacts with ammonia."

Quote F: "If you take a bowl made of silver to evaporate salty seawater, you will get impure sodium chloride, mixed with a milk-white solid."

3.1 Quote A: Write the balanced chemical equation of $\text{AgCl}(\text{s})$ synthesis.

3.2 Quote B: Calculate the solubility s of $\text{AgCl}(\text{s})$ in water at 298 K in mol dm^{-3} .

3.3 Quote C: In a highly concentrated solution of chloride ions, a well-defined complex of stoichiometry 1:2 is formed. On the following qualitative axis (with pCl increasing from left to right), place in each domain the silver-containing species that is predominant (or exists, for solids). pCl values at frontiers are not expected.

Quote D: When ammonia is added to silver chloride, a well-defined complex of stoichiometry n is formed.

3.4 Write the balanced equation corresponding to the synthesis of the complex $[\text{Ag}(\text{NH}_3)_n]^+$ from silver chloride and calculate the corresponding equilibrium constant.

3.5 Ammonia is added to 0.1 mol of silver chloride in 1 dm^3 of water until the last grain of solid disappears. At this moment, $[\text{NH}_3] = 1.78 \text{ mol dm}^{-3}$. Determine the stoichiometry of the complex neglecting dilution effects.

3.6 Write the balanced chemical equation corresponding to quote E.

3.7 Assuming that seawater is slightly basic and rich in dioxygen, and that silver metal can reduce dioxygen in such conditions, write a balanced chemical equation corresponding to the formation of the solid mentioned in quote F. A stoichiometric coefficient of 1 will be chosen for dioxygen. Calculate its equilibrium constant at 298 K.

Part B: The Mohr method

The Mohr method is based on the colorimetric titration of Cl^- by Ag^+ in the presence of potassium chromate ($2 \text{ K}^+, \text{CrO}_4^{2-}$). Three drops ($\sim 0.5 \text{ cm}^3$) of a K_2CrO_4 solution at about $c = 7.76 \times 10^{-3} \text{ mol dm}^{-3}$ are added to $V_0 = 20.00 \text{ cm}^3$ of a sodium chloride solution of unknown concentration c_{Cl} . This solution is then titrated by silver nitrate ($\text{Ag}^+, \text{NO}_3^-$) at $c = 0.050 \text{ mol dm}^{-3}$, which immediately leads to the formation of solid A. A red precipitate (solid B) appears at $V_{\text{Ag}} = 4.30 \text{ cm}^3$.

3.8 Write the balanced equations of the two reactions occurring during the experiment. Calculate the corresponding equilibrium constants.

3.9 Identify the solids.

3.10 Calculate the unknown concentration $c(\text{Cl}^-)$ of chloride ions in the sodium chloride solution.

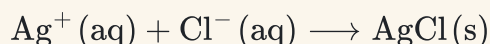
3.11 Calculate the minimal volume $V_{\text{Ag}}(\text{min})$ for which $\text{AgCl}(\text{s})$ precipitates.

3.12 Calculate the residual concentration $[\text{Cl}^-]_{\text{res}}$ of chloride ions when silver chromate begins to precipitate. Justify why CrO_4^{2-} is a good titration endpoint indicator by comparing two values.

Official English text of the problem.

Answers

- **3.1**



- **3.2** $s = 1.4 \times 10^{-5} \text{ mol dm}^{-3}$.

- **3.3** From left to right, as pCl increases: **dichloridoargentate(I)**, $[\text{AgCl}_2]^-$; **solid silver chloride**, AgCl(s) ; **silver(I) ion**, Ag^+ .

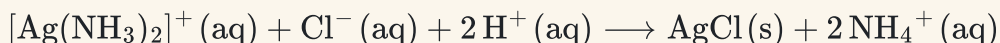
- **3.4**



$$K = K_{s1}\beta_n = 10^{-2.5} = 3.2 \times 10^{-3}.$$

- **3.5** $n = 2$: the complex is **diamminesilver(I)**, $[\text{Ag}(\text{NH}_3)_2]^+$.

- **3.6**

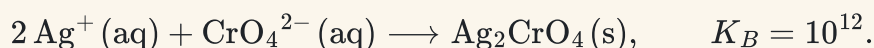
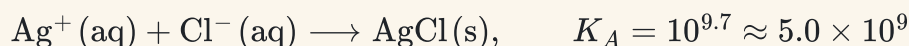


- **3.7**



Using the supplied apparent potential, $K \approx 2.6 \times 10^{35}$.

- **3.8**



- **3.9** A is **silver chloride**, AgCl , white; B is **silver chromate**, Ag_2CrO_4 , red.

- **3.10** The usual endpoint-as-equivalence calculation gives

$$c(\text{Cl}^-) \approx 0.01075 \text{ mol dm}^{-3} \approx 1.1 \times 10^{-2} \text{ mol dm}^{-3}.$$

Accounting for dissolved ions at the endpoint gives a nominal corrected value of $0.01065 \text{ mol dm}^{-3}$.

- **3.11** $V_{\text{Ag}(\text{min})} \approx 8 \times 10^{-6} \text{ cm}^3$, about 8 nL.

- **3.12** $[\text{Cl}^-]_{\text{res}} \approx 2.5 \times 10^{-6} \text{ mol dm}^{-3}$. This is approximately 2.9×10^{-4} of the chloride concentration that would remain at the same total volume without precipitation: about **99.97% of the chloride has precipitated**.

Solution

For the calculations, activities are approximated by concentrations divided by $c^\circ = 1 \text{ mol dm}^{-3}$. These normalization factors are suppressed in concentration quotients below. Pure solids and liquid water have unit activity, and equilibrium constants are dimensionless.

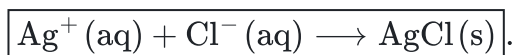
The names and SMILES of the species used in the answers are collected here. Dative-bond SMILES use $\rightarrow$ and $\leftarrow$ to indicate ligand donation. Both silver complexes are linear; chromate is tetrahedral. Those geometries are not specified by these strings. The salt representations list constituent ions and do not describe their crystal lattices.

Species	Name	SMILES
Ag^+	Silver(I) ion	[Ag+]
Cl^-	Chloride ion	[Cl-]
$[\text{AgCl}_2]^-$	Dichloridoargentate(I) ion	[Cl-] -> [Ag+] <- [Cl-]

Species	Name	SMILES
NH ₃	Ammonia	N
[Ag(NH ₃) ₂] ⁺	Diamminesilver(I) ion	[NH3]->[Ag+]<-[NH3]
H ⁺	Hydrogen ion, or proton	[H+]
NH ₄ ⁺	Ammonium ion	[NH4+]
H ₂ O	Water	O
HO ⁻	Hydroxide ion	[OH-]
O ₂	Dioxygen	O=O
CrO ₄ ²⁻	Chromate ion	[O-][Cr](=O)(=O)[O-]
AgCl	Silver chloride	[Ag+].[Cl-]
Ag ₂ CrO ₄	Silver chromate	[Ag+].[Ag+].[O-][Cr](=O)(=O)[O-]
Ag	Silver atom; the solid is metallic silver	[Ag]

3.1

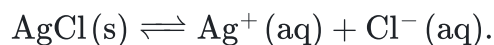
Silver nitrate supplies silver(I) ions, while hydrochloric acid supplies chloride ions. Their precipitation reaction is



The other ions remain in solution as spectators.

3.2

The dissolution equilibrium is



In pure water, dissolution gives equal concentrations of the two ions:

$$[\text{Ag}^+] = [\text{Cl}^-] = s.$$

Thus,

$$K_{\text{s1}} = 10^{-9.7}, \quad s = c^\circ \sqrt{K_{\text{s1}}} = 10^{-4.85} \text{ mol dm}^{-3}.$$

Therefore,

$$\boxed{s = 1.4 \times 10^{-5} \text{ mol dm}^{-3}}.$$

"Insoluble" here means sparingly soluble, rather than having exactly zero solubility.

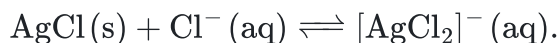
3.3

By definition,

$$\text{pCl} = -\log_{10} a_{\text{Cl}^-}.$$

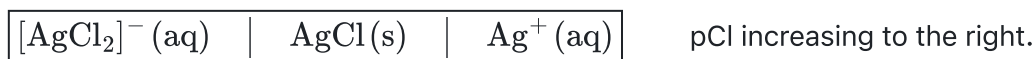
Consequently, the left side of the axis represents high chloride concentration, and the right side represents low chloride concentration.

At high chloride concentration, formation of the 1:2 complex promotes dissolution:



At intermediate chloride concentration, solid silver chloride exists. At sufficiently low chloride concentration, the solubility product permits silver to remain dissolved predominantly as Ag^+ .

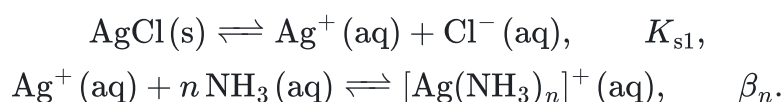
The three domains must therefore be labelled, from left to right,



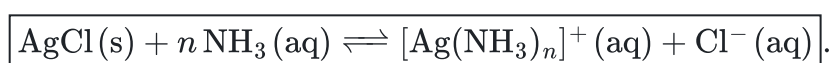
No numerical boundary values are required.

3.4

Add the dissolution and complex-formation equilibria:



Their sum is



Equilibrium constants multiply when reactions are added:

$$K = K_{\text{s1}} \beta_n = 10^{-9.7} 10^{7.2} = 10^{-2.5}.$$

Hence,

$K = 3.2 \times 10^{-3}$

Although this constant is less than one, a sufficiently high ammonia concentration shifts the equilibrium toward dissolution.

3.5

When the last grain disappears, the solution is just saturated with respect to silver chloride. Neglecting dilution, the dissolved silver and chloride analytical concentrations are both

$$\frac{0.1 \text{ mol}}{1 \text{ dm}^3} = 0.1 \text{ mol dm}^{-3}.$$

The free silver concentration is

$$[\text{Ag}^+] = \frac{10^{-9.7}}{0.1} \approx 2.0 \times 10^{-9} \text{ mol dm}^{-3},$$

so essentially all dissolved silver is complexed:

$$[\text{Ag}(\text{NH}_3)_n]^+ \approx 0.1 \text{ mol dm}^{-3}.$$

Using the equilibrium constant from 3.4,

$$10^{-2.5} = \frac{[\text{Ag}(\text{NH}_3)_n]^+ [\text{Cl}^-]}{[\text{NH}_3]^n} = \frac{(0.1)^2}{1.78^n}.$$

Therefore,

$$1.78^n = 10^{0.5}, \quad n = \frac{0.5}{\log_{10}(1.78)} = 1.997 \approx 2.$$

Thus,

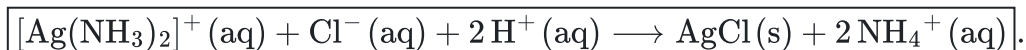
$n = 2, \quad [\text{Ag}(\text{NH}_3)_2]^+$

3.6

Acid protonates ammonia:

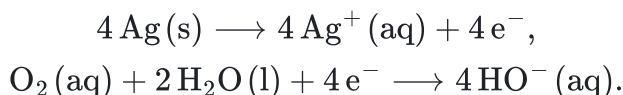


Removing free ammonia destabilizes the silver–ammonia complex. The released silver(I) precipitates with chloride. The overall balanced equation is

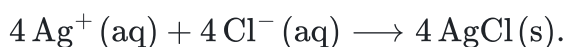


3.7

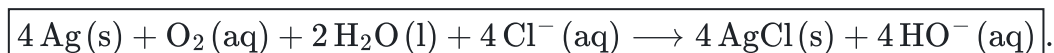
The oxidation and reduction half-reactions are



The silver(I) ions then precipitate:



Adding gives the required equation, with coefficient 1 for dioxygen:



Before coupling to precipitation, the potential difference calculated from the supplied potentials is

$$\Delta E' = 0.75 - 0.80 = -0.05 \text{ V}.$$

For four transferred electrons,

$$\log_{10} K_{\text{redox}} = \frac{4\Delta E'}{RT \ln(10)/F}.$$

At 298 K, $RT \ln(10)/F \approx 0.0592 \text{ V}$. Precipitation of four formula units contributes the factor K_{s1}^{-4} , so

$$\begin{aligned} \log_{10} K &= \frac{4(0.75 - 0.80)}{0.0592} - 4 \log_{10} K_{\text{s1}} \\ &= -3.38 + 4(9.7) \\ &= 35.42. \end{aligned}$$

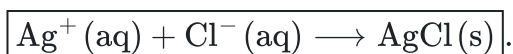
Therefore,

$$\boxed{K \approx 2.6 \times 10^{35}}.$$

Precipitation removes silver(I) ions and strongly favors the coupled oxidation. Because the oxygen potential is supplied as an apparent seawater potential, the calculated constant has the corresponding medium-dependent interpretation.

3.8

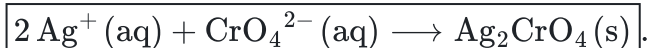
The first precipitation reaction is



It is the reverse of silver chloride dissolution, so

$$\boxed{K_A = \frac{1}{K_{\text{s1}}} = 10^{9.7} \approx 5.0 \times 10^9}.$$

The second precipitation reaction is



Similarly,

$$K_B = \frac{1}{K_{s2}} = 10^{12}.$$

3.9

Solid A is **silver chloride**, AgCl , the white precipitate formed when silver(I) ions encounter the initially abundant chloride ions.

Solid B is **silver chromate**, Ag_2CrO_4 , the red precipitate. As chloride is consumed, the free silver concentration rises until

$$[\text{Ag}^+]^2[\text{CrO}_4^{2-}] = K_{s2}.$$

Silver chromate then begins to precipitate, producing the endpoint color.

3.10

Taking the first appearance of the red precipitate as the equivalence point, the 1:1 silver-to-chloride stoichiometry gives

$$n_{\text{Cl}^-,0} \approx cV_{\text{Ag}}.$$

Thus,

$$n_{\text{Cl}^-,0} \approx (0.050 \text{ mol dm}^{-3})(4.30 \times 10^{-3} \text{ dm}^3) = 2.15 \times 10^{-4} \text{ mol}.$$

The original sample concentration is therefore

$$c_{\text{Cl}} \approx \frac{2.15 \times 10^{-4}}{20.00 \times 10^{-3}} = 0.01075 \text{ mol dm}^{-3}.$$

Hence, to the precision justified by the data,

$$c_{\text{Cl}} \approx 1.1 \times 10^{-2} \text{ mol dm}^{-3}.$$

The indicator solution changes the total volume but not the original chloride amount. A small correction for dissolved ions at the endpoint is evaluated in 3.12.

3.11

Including the indicator, the initial solution volume is approximately

$$V_i = 20.00 + 0.5 = 20.5 \text{ cm}^3.$$

Before precipitation, the chloride concentration is therefore approximately

$$[\text{Cl}^-]_i = \frac{2.15 \times 10^{-4} \text{ mol}}{20.5 \times 10^{-3} \text{ dm}^3} = 1.05 \times 10^{-2} \text{ mol dm}^{-3}.$$

Silver chloride starts precipitating when its ionic product reaches its solubility product:

$$[\text{Ag}^+]_{\min} = \frac{K_{s1}}{[\text{Cl}^-]_i} \approx 1.90 \times 10^{-8} \text{ mol dm}^{-3}.$$

The required titrant volume is so small that its dilution effect is negligible:

$$\begin{aligned}
 V_{\text{Ag}}(\text{min}) &\approx \frac{[\text{Ag}^+]_{\text{min}} V_i}{c} \\
 &= \frac{(1.90 \times 10^{-8})(20.5 \times 10^{-3})}{0.050} \text{ dm}^3 \\
 &= 7.8 \times 10^{-9} \text{ dm}^3 \\
 &= 7.8 \times 10^{-6} \text{ cm}^3.
 \end{aligned}$$

Thus,

$$V_{\text{Ag}}(\text{min}) \approx 8 \times 10^{-6} \text{ cm}^3 \approx 8 \text{ nL}.$$

This explains why precipitation is described as immediate.

3.12

At the instant silver chromate begins to precipitate, its precipitated amount is negligible, so essentially all added chromate remains dissolved.

The chromate amount is

$$n_{\text{CrO}_4^{2-}} = (7.76 \times 10^{-3})(0.5 \times 10^{-3}) = 3.88 \times 10^{-6} \text{ mol}.$$

The total volume is

$$V_{\text{tot}} = 20.00 + 0.5 + 4.30 = 24.8 \text{ cm}^3.$$

Hence,

$$[\text{CrO}_4^{2-}] = \frac{3.88 \times 10^{-6}}{24.8 \times 10^{-3}} = 1.56 \times 10^{-4} \text{ mol dm}^{-3}.$$

At the onset of silver chromate precipitation,

$$[\text{Ag}^+] = \sqrt{\frac{K_{s2}}{[\text{CrO}_4^{2-}]}} = \sqrt{\frac{10^{-12}}{1.56 \times 10^{-4}}} \approx 8.0 \times 10^{-5} \text{ mol dm}^{-3}.$$

Silver chloride is also present, so

$$[\text{Cl}^-]_{\text{res}} = \frac{K_{s1}}{[\text{Ag}^+]} = \frac{10^{-9.7}}{8.0 \times 10^{-5}}.$$

Therefore,

$$[\text{Cl}^-]_{\text{res}} \approx 2.5 \times 10^{-6} \text{ mol dm}^{-3}.$$

For a comparison that accounts for dilution, the chloride concentration at this total volume **without precipitation** would be

$$c_{\text{Cl,diluted}} = \frac{2.15 \times 10^{-4}}{24.8 \times 10^{-3}} = 8.67 \times 10^{-3} \text{ mol dm}^{-3}.$$

The fraction remaining dissolved is approximately

$$\frac{[\text{Cl}^-]_{\text{res}}}{c_{\text{Cl,diluted}}} = \frac{2.50 \times 10^{-6}}{8.67 \times 10^{-3}} = 2.9 \times 10^{-4}.$$

Thus, about **99.97% of the chloride has precipitated** when the red solid first appears. This makes chromate a suitable endpoint indicator.

The endpoint is nevertheless slightly beyond exact equivalence. At the onset of chromate precipitation, the silver and chloride balances give

$$cV_{\text{Ag}} - c_{\text{Cl}}V_0 = ([\text{Ag}^+] - [\text{Cl}^-]_{\text{res}})V_{\text{tot}}.$$

The excess silver amount is approximately

$$(8.0 \times 10^{-5} - 2.5 \times 10^{-6})(24.8 \times 10^{-3}) = 1.92 \times 10^{-6} \text{ mol}.$$

This corresponds to approximately 0.038 cm^3 of titrant, or an endpoint error of about 0.9%. Including this correction gives

$$c_{\text{Cl}} = \frac{2.15 \times 10^{-4} - 1.92 \times 10^{-6}}{20.00 \times 10^{-3}} \approx 0.01065 \text{ mol dm}^{-3},$$

which still rounds to $1.1 \times 10^{-2} \text{ mol dm}^{-3}$ at the precision of the stated titrant concentration.

The solution was checked against the official solution.

Problem 4: From gunpowder to the discovery of iodine

In the 19th century, the French entrepreneur B. Courtois specialized in the production of nitrate **A** ($\text{M}_\text{A}(\text{NO}_3)_m$), used for gunpowder. Initially imported from Asia, **A** was later produced from nitrate **B** ($\text{M}_\text{B}(\text{NO}_3)_n$) using exchange reaction with compound **C**, obtained from algae.

4.1 Find the formulas of nitrates **A** and **B** knowing that they are anhydrous salts of alkaline or alkaline-earth metal (M_A and M_B). One of the nitrates contains no more than 1 w% of non-metallic impurities while the other contains 9 ± 3 w% of impurities. The content of metals M_A and M_B in the samples is 38.4 w% and 22.4 w%, respectively. Support your answer with calculations.

To obtain **A**, 262.2 g of solid compound **C** were added to the solution containing 442.8 g of **B**. **B** is known to be in excess. As a result, 190.0 g of white precipitate **D** were formed and removed by filtration. The filtrate was evaporated, and the obtained solid mixture **E** was heated until the mass of the sample (containing only nitrites, NO_2^-) was constant. The only gaseous product was dioxygen: 60.48 dm^3 at 0°C and 1 atm (dioxygen can be considered as an ideal gas).

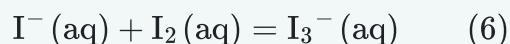
4.2 Calculate the composition (in w%) of mixture **E** considering that it contained only compounds **A** and **B** and no other impurities, and that **C** was taken in pure anhydrous state.

4.3 Determine the formulas of compounds **C** and **D** and write the balanced reaction equation between **B** and **C**.

In 1811, when working with algae ashes, Courtois observed that copper vessels were worn out faster than usual. While he was studying this phenomenon, his cat entered the laboratory and spilled the solution of concentrated sulfuric acid on the dry algae ashes: violet vapors instantly came out of the vessel (1, sulfuric acid is the oxidizing agent): iodine (I_2) had just been discovered! Iodine was the cause of the copper corrosion (2). However, because of the medicinal applications of iodine, Courtois opened a new manufacture to produce it by reaction of algae with chlorine (3). Nowadays, the iodine is prepared from the set of reactants (NO_3^- , I^- , H^+) (4) or (IO_3^- , I^- , H^+) (5).

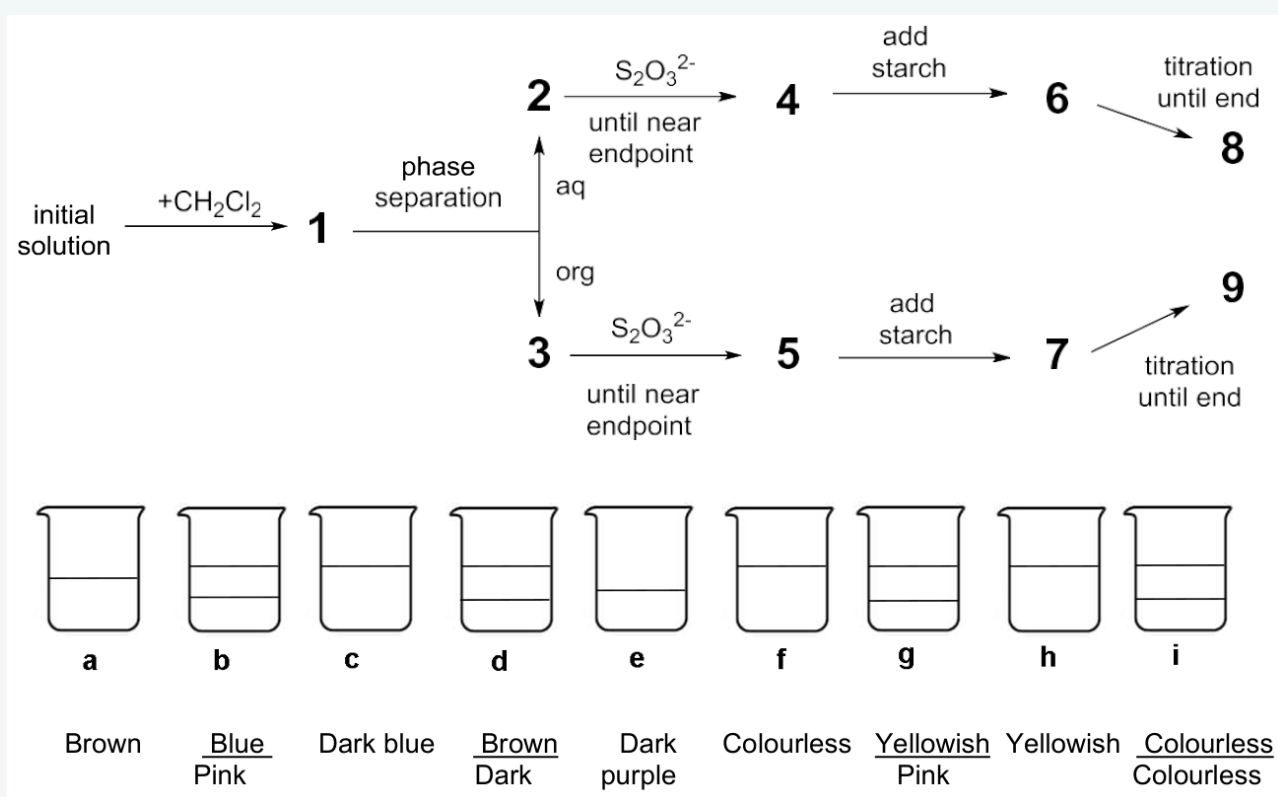
4.4 Write balanced equations for reactions 1 – 5.

The solubility of iodine is very low in water but significantly increases when iodide ions are added. Together they form ions such as triiodide, I_3^- :



Equilibrium (6) can be studied through the extraction of I_2 with dichloromethane. Indeed, I^- and I_3^- do not dissolve in organic solvents but I_2 does and, when extracted, it is 15 times more concentrated in dichloromethane than in water.

The following experiment was performed. To prepare the initial solution, a few crystals of solid iodine were dissolved in 50.0 cm³ of an aqueous solution of potassium iodide (0.1112 g). Then, 50.0 cm³ of dichloromethane were added, and the mixture was vigorously shaken until equilibration. After phase separation, each phase was titrated by 16.20 cm³ (organic phase) and by 8.00 cm³ (aqueous phase) of the standard aqueous solution of sodium thiosulphate pentahydrate (14.9080 g in 1.000 dm³ of solution) in the presence of starch. The process is schematically represented below:



4.5 Find the correspondence between the stages on the scheme (1–9) and the schematic pictures representing them (a–i).

Stages	Picture
1	
2	
3	
4	
5	
6	
7	

Stages	Picture
8	
9	

4.6 Write balanced equations for the two possible chemical reactions in the aqueous phase during the titration involving iodine species and sodium thiosulphate.

4.7 Calculate the mass of iodine used to prepare the initial solution.

4.8 Calculate the equilibrium constant K° for equilibrium of reaction (6).

Official English text of the problem.

Answers

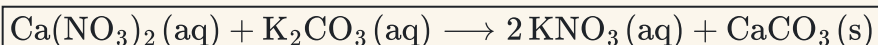
- 4.1** **A** is potassium nitrate, KNO_3 , SMILES $[\text{K}+] \cdot [\text{O}-] [\text{N}+] (= \text{O}) [\text{O}-]$. **B** is calcium nitrate, $\text{Ca}(\text{NO}_3)_2$, SMILES $[\text{Ca}+2] \cdot [\text{O}-] [\text{N}+] (= \text{O}) [\text{O}-] \cdot [\text{O}-] [\text{N}+] (= \text{O}) [\text{O}-]$. Their calculated impurity contents are approximately 0.70% and 8.29%, respectively.

- 4.2** Using standard atomic masses and the ideal-gas law,

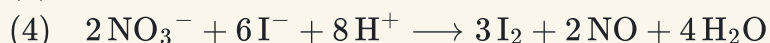
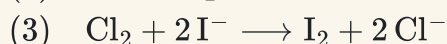
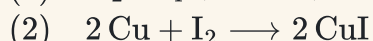
$$w(\mathbf{A}) = 74.4\%, \quad w(\mathbf{B}) = 25.6\%.$$

The integer molar-mass convention, with $V_m = 22.4 \text{ dm}^3 \text{ mol}^{-1}$, gives 74.5% and 25.5%; see the calculation below.

- 4.3** **C** is potassium carbonate, K_2CO_3 , SMILES $[\text{K}+] \cdot [\text{K}+] \cdot [\text{O}-] \text{C}(=\text{O}) [\text{O}-]$. **D** is calcium carbonate, CaCO_3 , SMILES $[\text{Ca}+2] \cdot [\text{O}-] \text{C}(=\text{O}) [\text{O}-]$.



- 4.4** One balanced set, taking sulfuric acid to be reduced to hydrogen sulfide in reaction (1), is

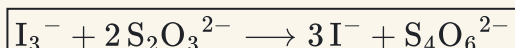
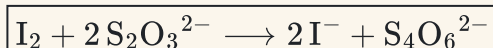


Alternative sulfur reduction products for (1), and the alternative nitrogen dioxide equation for (4), are given in the solution.

- 4.5**

$$1 \rightarrow d, \quad 2 \rightarrow a, \quad 3 \rightarrow e, \quad 4 \rightarrow h, \quad 5 \rightarrow g, \quad 6 \rightarrow c, \quad 7 \rightarrow b, \quad 8 \rightarrow f, \quad 9 \rightarrow i.$$

- 4.6**



• 4.7

$$m(\text{I}_2) = 0.1845 \text{ g.}$$

• 4.8 Under the dilute-solution activity approximation,

$$K^\circ \approx 6.9 \times 10^2$$

dimensionless; the unrounded calculation gives approximately 693.

Solution

SMILES for ionic salts below give their constituent ions, not their crystal structures. Ordinary SMILES also do not fully describe resonance delocalization, electronic spin, or coordination and molecular geometry.

4.1 — Identification of the nitrates

Let z be the metal charge, M its atomic molar mass, and p the mass fraction of pure nitrate in a sample. The nitrate ion, NO_3^- , has SMILES $[\text{O}-][\text{N}+](=\text{O})[\text{O}-]$ and molar mass 62.01 g mol^{-1} .

Because the impurities contribute no metal, the measured metal mass fraction is

$$w = p \frac{M}{M + 62.01z}.$$

Therefore,

$$\frac{M}{z} = \frac{62.01w}{p - w}.$$

The two permitted purity intervals are $0.99 \leq p \leq 1$ and $0.88 \leq p \leq 0.94$.

Sample and assumed purity	Required M/z , g mol^{-1}	Conclusion
B , $0.99 \leq p \leq 1$	17.90–18.13	No alkali or alkaline-earth metal fits
B , $0.88 \leq p \leq 0.94$	19.40–21.17	Calcium fits: $40.08/2 = 20.04$
A , consequently $0.99 \leq p \leq 1$	38.66–39.29	Potassium fits: $39.10/1 = 39.10$

Thus the cations are potassium, K^+ , SMILES $[\text{K}+]$, and calcium, Ca^{2+} , SMILES $[\text{Ca}+2]$, giving

$$\mathbf{A = KNO_3, \quad B = Ca(NO_3)_2.}$$

The impurity contents independently check this assignment:

$$100(1 - p_A) = 100 \left(1 - \frac{0.384}{39.10/101.11} \right) = 0.700\%,$$

$$100(1 - p_B) = 100 \left(1 - \frac{0.224}{40.08/164.10} \right) = 8.29\%.$$

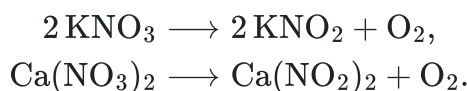
These satisfy the stated limits.

4.2 — Composition of mixture E

Under the stated purity assumptions, the mass of the dry nitrate mixture is

$$m_E = 442.8 + 262.2 - 190.0 = \boxed{515.0 \text{ g}}.$$

Using the stipulated nitrite-only decomposition,



The products are potassium nitrite, KNO_2 , SMILES $[\text{K}^+] \cdot [\text{O}-]\text{N}=\text{O}$; calcium nitrite, $\text{Ca}(\text{NO}_2)_2$, SMILES $[\text{Ca}^{+2}] \cdot [\text{O}-]\text{N}=\text{O} \cdot [\text{O}-]\text{N}=\text{O}$; and dioxygen, O_2 , SMILES $\text{O}=\text{O}$. The nitrite ion itself is $[\text{O}-]\text{N}=\text{O}$.

At 273.15 K and 101325 Pa,

$$n(\text{O}_2) = \frac{PV}{RT} = \frac{101325(60.48 \times 10^{-3})}{8.3144626(273.15)} = 2.69832 \text{ mol}.$$

Let $a = n(\text{KNO}_3)$ and $b = n(\text{Ca}(\text{NO}_3)_2)$ in **E**. The oxygen and mass balances give

$$\frac{a}{2} + b = 2.69832,$$

$$101.11a + 164.10b = 515.0.$$

Solving without rounding intermediate values,

$$a = 3.78836 \text{ mol}, \quad b = 0.804137 \text{ mol}.$$

Consequently,

$$m_A = 383.041 \text{ g}, \quad m_B = 131.959 \text{ g},$$

and

$w_A = 74.4\%, \quad w_B = 25.6\%.$

The numerical data also warrant stating the rounding convention explicitly. With rounded molar masses $M_A = 101$ and $M_B = 164 \text{ g mol}^{-1}$, and $V_m = 22.4 \text{ dm}^3 \text{ mol}^{-1}$, the equations instead become

$$a + 2b = 5.400, \quad 101a + 164b = 515.0.$$

They give exactly

$$a = 3.800, \quad b = 0.8000 \text{ mol},$$

hence

$$w_A = \frac{383.8}{515.0}(100) = 74.5\%, \quad w_B = \frac{131.2}{515.0}(100) = 25.5\%.$$

This rounded convention also reproduces the carbonate masses in 4.3 exactly.

4.3 — Identification of C and D

Initially,

$$n_{B,0} = \frac{442.8}{164.10} = 2.69835 \text{ mol}.$$

The amount of calcium removed into **D** is therefore

$$n_{\text{Ca, precipitated}} = 2.69835 - 0.804137 = 1.89422 \text{ mol}.$$

The precipitate mass per mole of calcium is

$$\frac{190.0}{1.89422} \approx 100.3 \text{ g mol}^{-1}.$$

Subtracting the calcium contribution leaves approximately

$$100.3 - 40.08 \approx 60.2 \text{ g}$$

of anion per mole of calcium. This identifies carbonate, CO_3^{2-} , SMILES [O-]C(=O)[O-], whose molar mass is approximately 60.01 g mol^{-1} . Calcium carbonate is a white, sparingly soluble precipitate.

The corresponding potassium salt is potassium carbonate. Its inferred molar mass is

$$M_C = \frac{262.2}{a/2} = \frac{262.2}{3.78836/2} \approx 138.4 \text{ g mol}^{-1},$$

consistent with K_2CO_3 , $M = 138.21 \text{ g mol}^{-1}$, within the numerical convention discussed above.

With integer molar masses, the identification is exact:

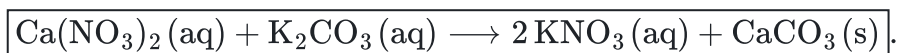
$$n_C = n_D = 1.900 \text{ mol},$$

$$M_C = \frac{262.2}{1.900} = 138.0 \text{ g mol}^{-1}, \quad M_D = \frac{190.0}{1.900} = 100.0 \text{ g mol}^{-1}.$$

Thus



and



4.4 — Reactions producing iodine and corroding copper

The additional species used in these equations are identified below.

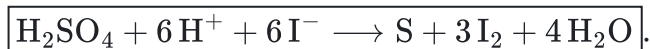
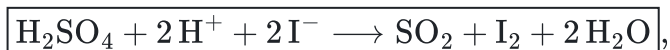
Name	Formula	SMILES
Sulfuric acid	H_2SO_4	<chem>OS(=O)(=O)O</chem>
Hydrogen ion	H^+	<chem>[H+]</chem>
Iodide ion	I^-	<chem>[I-]</chem>
Iodine	I_2	<chem>I I</chem>
Hydrogen sulfide	H_2S	<chem>S</chem>
Water	H_2O	<chem>O</chem>
Sulfur dioxide	SO_2	<chem>O=S=O</chem>
Elemental sulfur, cyclic molecular form	S_8	<chem>S1SSSSSS1</chem>
Copper	Cu	<chem>[Cu]</chem>
Copper(I) iodide	CuI	<chem>[Cu+] . [I-]</chem>
Chlorine	Cl_2	<chem>ClCl</chem>
Chloride ion	Cl^-	<chem>[Cl-]</chem>
Nitric oxide	NO	<chem>[N]=O</chem>
Nitrogen dioxide	NO_2	<chem>O=[N+][O-]</chem>
Iodate ion	IO_3^-	<chem>[O-]I(=O)=O</chem>

The copper SMILES represents an atom, not the metallic lattice. The sulfur-ring SMILES does not specify its crown conformation; elemental sulfur is written as S for stoichiometric bookkeeping below.

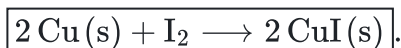
Reaction (1). Iodide is oxidized from -1 to 0 . If sulfur is reduced from $+6$ to -2 , eight iodide ions supply the eight electrons required:



The statement does not specify the sulfur reduction product. Concentrated sulfuric acid and iodide can also give sulfur dioxide or elemental sulfur; their balanced equations are



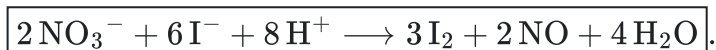
Reaction (2). Copper is oxidized to copper(I), while iodine is reduced to iodide:



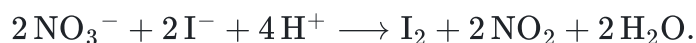
Reaction (3). Chlorine oxidizes iodide to iodine and is itself reduced to chloride:



Reaction (4). Taking the nitrate reduction product to be nitric oxide, nitrogen changes from +5 to +2, accepting three electrons per nitrogen atom:



If nitrogen dioxide is instead the reduction product, the corresponding balanced equation is



Reaction (5). Iodate iodine changes from +5 to 0; five iodide ions supply the five electrons. The six iodine atoms form three iodine molecules:



4.5 — Correspondence between stages and pictures

Dichloromethane, CH_2Cl_2 , SMILES `c1cc1`, is denser than water, so the organic phase is the lower layer. Adding aqueous thiosulfate to the separated organic phase creates a new upper aqueous layer.

Stage	Picture	Description
1	d	Two layers: brown aqueous phase above the dark organic phase
2	a	Separated aqueous phase, brown
3	e	Separated organic phase, dark purple
4	h	Aqueous phase near the endpoint, yellowish
5	g	Organic-phase titration near the endpoint: yellowish upper aqueous layer and pink lower organic layer
6	c	Starch added to the aqueous sample: dark blue
7	b	Starch added during organic-phase titration: blue upper aqueous layer and pink lower organic layer
8	f	Aqueous titration completed: colourless
9	i	Organic-phase titration completed: both layers colourless

The blue colour arises from iodine/polyiodide associated with helical starch chains. Starch and its indicator complex do not have a single, definite molecular composition and therefore have no unique molecular SMILES.

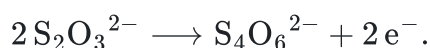
4.6 — Titration reactions

The relevant ions are:

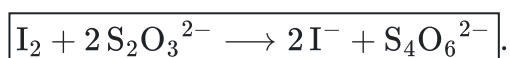
Name	Formula	SMILES
Triiodide	I_3^-	<chem>I[I-]I</chem>
Thiosulfate	$\text{S}_2\text{O}_3^{2-}$	<chem>[O-]S(=O)(=O)[S-]</chem>
Tetrathionate	$\text{S}_4\text{O}_6^{2-}$	<chem>[O-]S(=O)(=O)SSS(=O)(=O)[O-]</chem>

Triiodide is linear and has three-centre, four-electron bonding. Its SMILES is a formal connectivity representation and does not encode that bonding description or geometry.

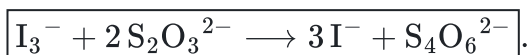
Thiosulfate is oxidized to tetrathionate:



Combining this with the reduction of dissolved iodine gives



For triiodide,



Thus one mole of either I_2 or I_3^- consumes two moles of thiosulfate. Each triiodide ion contains one titratable iodine-molecule equivalent.

4.7 — Mass of iodine initially added

Sodium thiosulfate pentahydrate, $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$, has SMILES [Na+] . [Na+] . [O-]S(=O)(=O)[S-] . O . O . O . O . O and molar mass approximately $248.18 \text{ g mol}^{-1}$.

The titrant concentration is

$$c_T = \frac{14.9080 \text{ g}}{(248.18 \text{ g mol}^{-1})(1.000 \text{ dm}^3)} = 0.0600693 \text{ mol dm}^{-3}.$$

Both phase titrations together measure all the initially added molecular iodine, including the portion converted into triiodide:

$$n_0(\text{I}_2) = \frac{c_T}{2}(V_{\text{org}} + V_{\text{aq}}).$$

Therefore,

$$n_0(\text{I}_2) = \frac{0.0600693}{2}(0.01620 + 0.00800) = 7.26839 \times 10^{-4} \text{ mol}.$$

Using $M(\text{I}_2) = 253.80 \text{ g mol}^{-1}$,

$$m_0(\text{I}_2) = (7.26839 \times 10^{-4})(253.80) = \boxed{0.1845 \text{ g}}.$$

The iodide originally supplied by potassium iodide is not counted as added molecular iodine and does not itself consume thiosulfate.

4.8 — Equilibrium constant

Potassium iodide, KI , has SMILES [K+] . [I-] and molar mass $166.00 \text{ g mol}^{-1}$.

First determine the species present **after extraction but before titration**.

The organic phase contains only molecular iodine among the iodine species. Hence

$$n_{\text{I}_2, \text{org}} = \frac{c_T V_{\text{org, titrant}}}{2} = \frac{(0.0600693)(0.01620)}{2} = 4.86561 \times 10^{-4} \text{ mol.}$$

Its concentration in the 0.0500 dm^3 organic phase is

$$[\text{I}_2]_{\text{org}} = \frac{4.86561 \times 10^{-4}}{0.0500} = 9.73123 \times 10^{-3} \text{ mol dm}^{-3}.$$

The partition ratio applies to **free molecular iodine**:

$$\frac{[\text{I}_2]_{\text{org}}}{[\text{I}_2]_{\text{aq}}} = 15.$$

Thus

$$[\text{I}_2]_{\text{aq}} = 6.48748 \times 10^{-4} \text{ mol dm}^{-3}.$$

The aqueous titration measures the sum of molecular iodine and triiodide:

$$n_{\text{I}_2, \text{aq}} + n_{\text{I}_3^-, \text{aq}} = \frac{(0.0600693)(0.00800)}{2} = 2.40277 \times 10^{-4} \text{ mol.}$$

Consequently,

$$[\text{I}_3^-] = \frac{2.40277 \times 10^{-4}}{0.0500} - 6.48748 \times 10^{-4} = 4.15680 \times 10^{-3} \text{ mol dm}^{-3}.$$

The initial amount of potassium iodide is

$$n_{\text{KI}} = \frac{0.1112}{166.00} = 6.69880 \times 10^{-4} \text{ mol.}$$

Formation of each triiodide ion consumes one iodide ion. Because neither ionic species enters the organic phase,

$$[\text{I}^-] + [\text{I}_3^-] = \frac{6.69880 \times 10^{-4}}{0.0500} = 0.0133976 \text{ mol dm}^{-3}.$$

Therefore,

$$[\text{I}^-] = 0.0133976 - 0.00415680 = 9.24079 \times 10^{-3} \text{ mol dm}^{-3}.$$

The thermodynamic equilibrium constant is

$$K^\circ = \frac{a_{\text{I}_3^-}}{a_{\text{I}^-} a_{\text{I}_2}}.$$

Taking $a_i \simeq [i]/c^\circ$, with $c^\circ = 1 \text{ mol dm}^{-3}$,

$$K^\circ \simeq \frac{[\text{I}_3^-]c^\circ}{[\text{I}^-][\text{I}_2]_{\text{aq}}}.$$

Substitution gives

$$K^\circ \simeq \frac{(4.15680 \times 10^{-3})(1)}{(9.24079 \times 10^{-3})(6.48748 \times 10^{-4})} = 693.4.$$

Hence

$$K^\circ \approx 6.9 \times 10^2$$

with no units.

The solution was checked against the official solution.

Problem 5: Azobenzene- β -cyclodextrin complexes for the formation of nanomachines

Nanomachines are molecular assemblies that enable the transformation of an energy source into a nano-movement for applications such as drug delivery. Numerous nanomachines make use of the isomerization of azo compounds ($R-N=N-R'$) upon irradiation.

5.1 Draw the stereoisomers of azobenzene ($H_5C_6-N=N-C_6H_5$) and draw a line between the two carbon atoms that are the furthest apart. Compare these two distances (d_{trans} and d_{cis}).

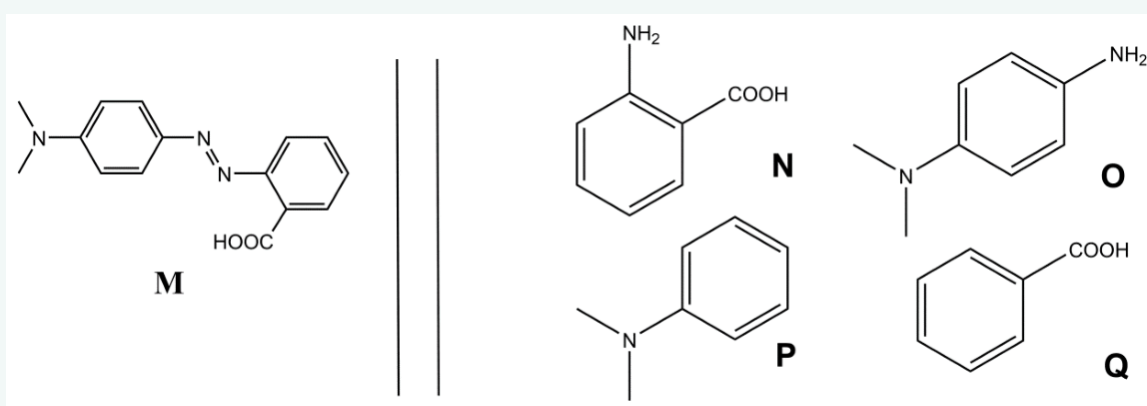


Fig. 1. Possible reactants for the synthesis of M.

5.2 M can be synthesized in two steps from simple reactants (Fig 1). Choose among the suggested reactants (N to Q) the ones that can provide M with very high regioselectivity. Sodium nitrite ($NaNO_2$) in cold aqueous hydrochloric acid is used as reagent for the first step of the synthesis.

Determination of the association constant K_t

β -cyclodextrin (C, Fig. 2) is a cyclic heptamer of glucose, which can form inclusion complexes with azo compounds. In tasks 3 to 6, we will determine by spectroscopy the association constant K_t , corresponding to the formation of the inclusion complex CM_{trans} as depicted in Fig. 2.

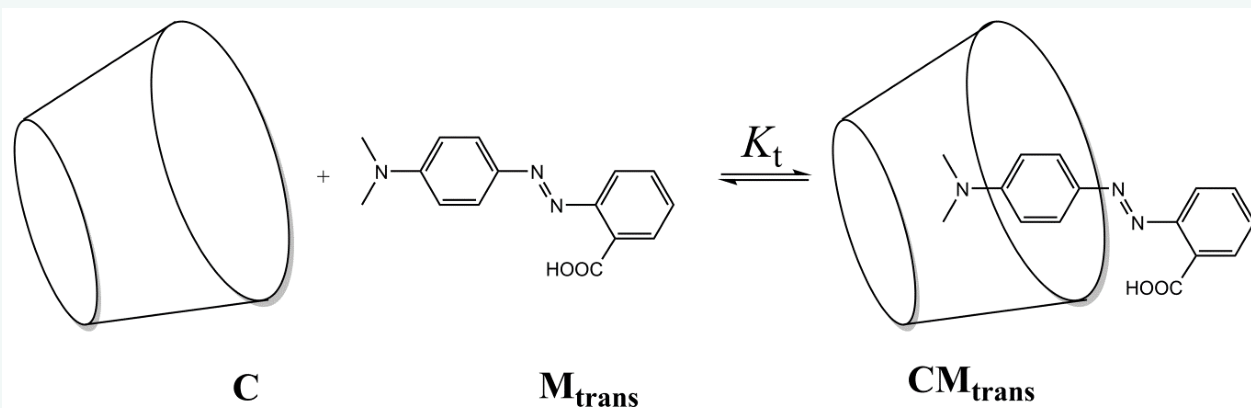


Fig. 2 – Formation of the $\mathbf{CM}_{\text{trans}}$ inclusion complex.

Several solutions are prepared by mixing $\mathbf{C}$ and $\mathbf{M}_{\text{trans}}$ in different proportions to reach initial concentrations $[\mathbf{C}]_0$ and $[\mathbf{M}_{\text{trans}}]_0$. While $[\mathbf{M}_{\text{trans}}]_0$ is identical for all solutions, $[\mathbf{C}]_0$ varies. We follow, at a fixed wavelength, the evolution of the difference in absorbance ΔA between the absorbance of each solution and the pure $\mathbf{M}_{\text{trans}}$ solution. We note the molar absorption coefficients of $\mathbf{CM}_{\text{trans}}$ and $\mathbf{M}_{\text{trans}}$, $\varepsilon_{\mathbf{CM}_{\text{trans}}}$ and $\varepsilon_{\mathbf{M}_{\text{trans}}}$, respectively. L is the path length of the beam through the sample. The absorbance of $\mathbf{C}$ ($\varepsilon_{\mathbf{C}}$) is negligible.

5.3 Demonstrate that $\Delta A = \alpha[\mathbf{CM}_{\text{trans}}]$ and express α in terms of known constant(s).

5.4 Demonstrate that in case when $\mathbf{C}$ is in large excess with respect to $\mathbf{M}_{\text{trans}}$ (i.e. $[\mathbf{C}]_0 \gg [\mathbf{M}_{\text{trans}}]_0$), the concentration of $\mathbf{C}$ may be considered as constant, $[\mathbf{C}] \simeq [\mathbf{C}]_0$.

5.5 Demonstrate that in case when $\mathbf{C}$ is in a large excess with respect to $\mathbf{M}_{\text{trans}}$, (i.e. $[\mathbf{C}]_0 \gg [\mathbf{M}_{\text{trans}}]_0$),

$$\Delta A = \alpha \frac{\beta[\mathbf{C}]_0}{1 + K_t[\mathbf{C}]_0}$$

and express β in terms of constant(s) and initial concentration(s).

5.6 Determine K_t using the following experimental curve (Fig. 3).

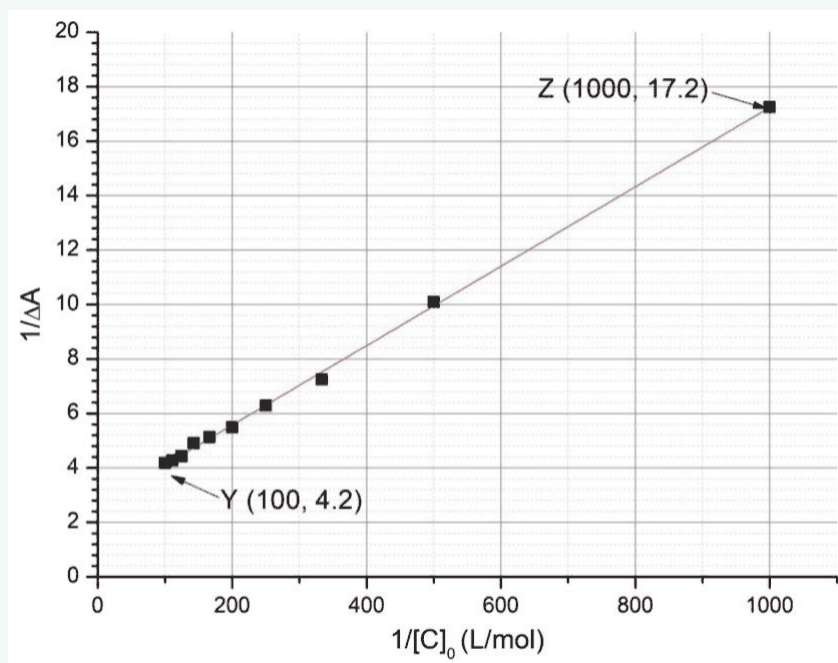


Fig. 3 – Evolution of $1/\Delta A$ as a function of $1/[\mathbf{C}]_0$.

Determination of the association constant K_c

In tasks 7 to 9, we will determine by kinetic studies the association constant K_c , corresponding to the formation of the inclusion complex with $\mathbf{M}_{\text{cis}}$, $\mathbf{CM}_{\text{cis}}$. A sample containing only $\mathbf{M}_{\text{trans}}$ is irradiated, thus producing a known amount of $\mathbf{M}_{\text{cis}}$, $[\mathbf{M}_{\text{cis}}]_0$. $\mathbf{M}_{\text{cis}}$ (free or within the inclusion complex) then thermally isomerizes into $\mathbf{M}_{\text{trans}}$. In the absence of $\mathbf{C}$, the isomerization follows a first order kinetics with a rate constant k_1 . All complexation equilibria are faster than the isomerization processes. The kinetic scheme corresponding to this experiment is provided in Fig. 4.

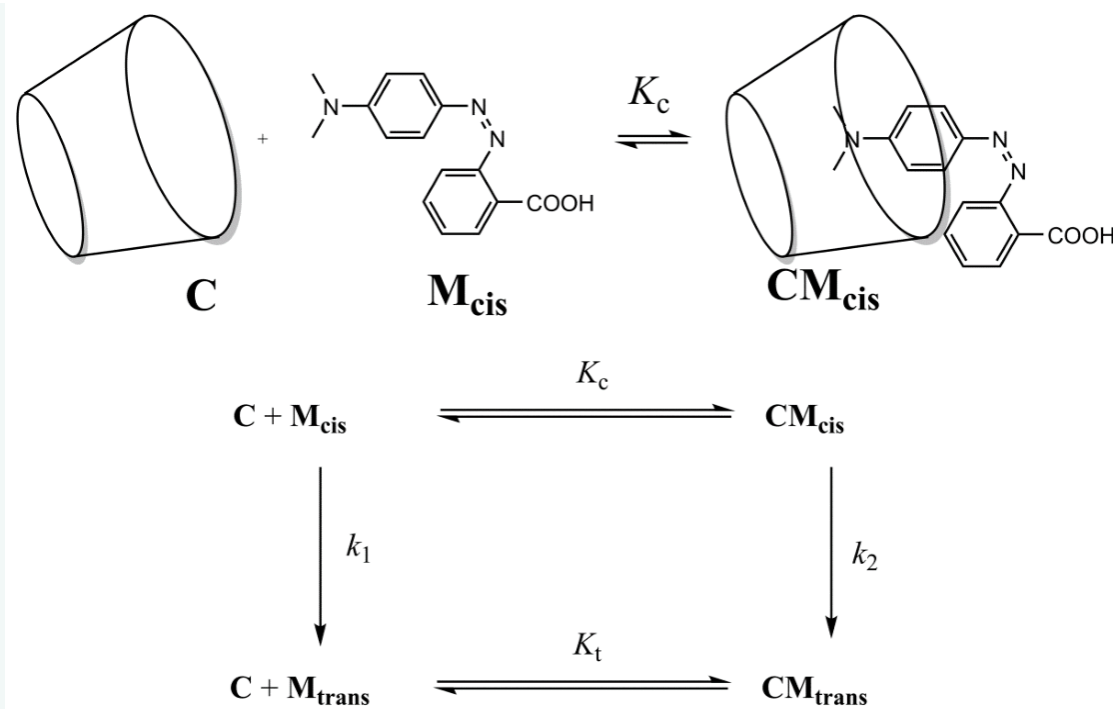


Fig. 4 – Kinetic scheme for the isomerization of $\mathbf{M}_{\text{cis}}$ in the presence of $\mathbf{C}$.

The rate of disappearance r for the total amount of $\mathbf{M}_{\text{cis}}$ (free and complexed) is defined as

$$r = k_1[\mathbf{M}_{\text{cis}}] + k_2[\mathbf{CM}_{\text{cis}}].$$

Experimentally, r follows an apparent first order kinetic law with an apparent rate constant k_{obs} :

$$r = k_{\text{obs}}([\mathbf{M}_{\text{cis}}] + [\mathbf{CM}_{\text{cis}}]).$$

5.7 Demonstrate that

$$k_{\text{obs}} = \frac{\gamma + \delta k_2[\mathbf{C}]}{1 + K_c[\mathbf{C}]}$$

and express γ and δ in terms of known constant(s).

5.8 Choose in which condition(s) the half-life $t_{1/2}$ corresponding to k_{obs} can be expressed as $t_{1/2} = \ln(2/\gamma)(1 + K_c[\mathbf{C}]_0)$ given that $[\mathbf{C}]_0 \gg [\mathbf{M}_{\text{cis}}]_0$. Mathematically justify your answer.

5.9 Assuming the condition(s) in task 8 satisfied, determine K_c by a linear regression using the data below. You may use a calculator or plot a graph.

$[\mathbf{C}]_0$ (mol dm ⁻³)	$t_{1/2}$ (s)	$[\mathbf{C}]_0$ (mol dm ⁻³)	$t_{1/2}$ (s)
0	3.0	$3.0 \cdot 10^{-3}$	5.9
$1.0 \cdot 10^{-4}$	3.2	$5.0 \cdot 10^{-3}$	7.7
$5.0 \cdot 10^{-4}$	3.6	$7.5 \cdot 10^{-3}$	9.9
$1.0 \cdot 10^{-3}$	4.1	$1.0 \cdot 10^{-2}$	12.6

Formation of nanomachines

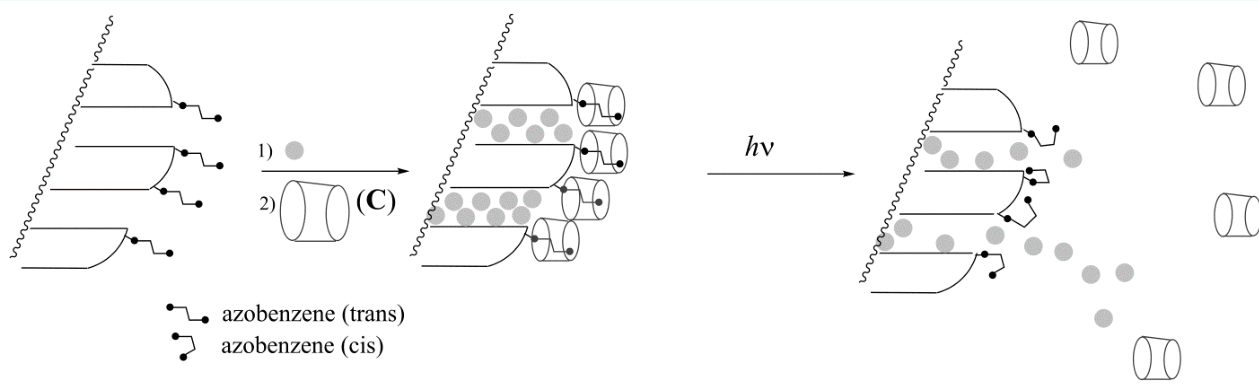


Fig. 5 – Cleavage of an azobenzene–cyclodextrin inclusion complex induced by a light-triggered isomerization, which allows delivery of a dye (grey circles).

Another azobenzene compound (for which $K_c \ll K_t$), initially in the *trans* form, is covalently grafted on silica (Fig. 5). The silica pores are filled with a dye (rhodamine B, grey circles in Fig. 5). Upon addition of **C**, an inclusion complex is formed, which blocks the pores and prevents the release of the dye.

5.10 Choose the most appropriate condition (one choice only) so that the pores are initially blocked in the presence of **C**, and the dye can be released upon irradiation.

This azobenzene-silica powder loaded with a dye is placed in the corner of a cuvette (Fig. 6) so that the powder cannot move into solution. The powder is irradiated at a wavelength λ_1 to trigger the release of the dye from the pores (Fig. 5). To monitor this release by absorbance spectroscopy we measure the absorbance of the solution at wavelength λ_2 .

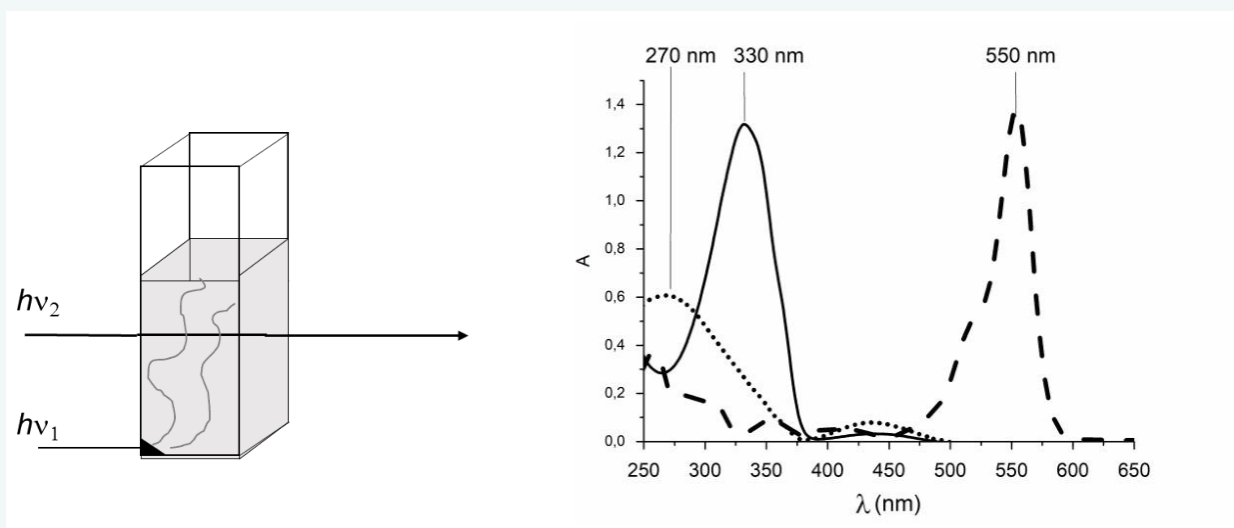


Fig. 6 – Left: experimental setup used to monitor the release of the dye; right: absorbance spectra of *trans*-azobenzene (full line), *cis*-azobenzene (dotted line) and rhodamine B (dashed line).

5.11 Determine λ_1 .

5.12 Determine λ_2 .

Official English text of the problem.

Answers

- **5.1:** *trans*-(*E*)-azobenzene, c1ccc(/N=N/c2ccccc2)cc1, and *cis*-(*Z*)-azobenzene, c1ccc(/N=N\c2ccccc2)cc1. Their maximum carbon-to-carbon distances satisfy $d_{\text{trans}} > d_{\text{cis}}$.
- **5.2:** Choose **N**, anthranilic acid, Nc1cccc1C(=O)O, and **P**, *N,N*-dimethylaniline, CN(C)c1ccccc1. Diazotize **N**, then couple with **P** at its para position.
- **5.3:** $\alpha = L(\varepsilon_{\text{CM}_{\text{trans}}} - \varepsilon_{\text{M}_{\text{trans}}})$.
- **5.4:** $0 \leq [\text{C}]_0 - [\text{C}] \leq [\text{M}_{\text{trans}}]_0 \ll [\text{C}]_0$, hence $[\text{C}] \simeq [\text{C}]_0$.
- **5.5:** $\beta = K_t[\text{M}_{\text{trans}}]_0$.
- **5.6:** $K_t \approx 1.9 \times 10^2 \text{ L mol}^{-1}$.
- **5.7:** $\gamma = k_1$, $\delta = K_c$.
- **5.8:** With constant free host concentration, require $k_2 K_c [\text{C}]_0 \ll k_1$, including the limiting case $k_2 = 0$. The corrected expression is $t_{1/2} \simeq \frac{\ln 2}{\gamma} (1 + K_c [\text{C}]_0)$.
- **5.9:** The regression gives $t_{1/2} = (3.0804 \text{ s}) + (935.675 \text{ s L mol}^{-1})[\text{C}]_0$, hence $K_c \approx 3.0 \times 10^2 \text{ L mol}^{-1}$.
- **5.10:** $K_c [\text{C}] \ll 1 \ll K_t [\text{C}]$, equivalently $1/K_t \ll [\text{C}] \ll 1/K_c$. Under host excess, use $[\text{C}] \simeq [\text{C}]_0$.
- **5.11:** $\lambda_1 = 330 \text{ nm}$.
- **5.12:** $\lambda_2 = 550 \text{ nm}$.

Solution

5.1 — Azobenzene stereoisomers and distances

Azobenzene has two geometrical isomers about its N=N double bond:

Isomer	Name	Isomeric SMILES
<i>trans</i>	(<i>E</i>)-Azobenzene, or (<i>E</i>)-diphenyldiazene	<chem>c1ccc(/N=N/c2ccccc2)cc1</chem>
<i>cis</i>	(<i>Z</i>)-Azobenzene, or (<i>Z</i>)-diphenyldiazene	<chem>c1ccc(/N=N\c2ccccc2)cc1</chem>

For the requested drawings, place the N=N bond horizontally:

- In the **trans** drawing, put one phenyl ring above-left and the other below-right. Join the two distal para carbon atoms, one on each ring, and label the segment d_{trans} .
- In the **cis** drawing, put both phenyl rings on the same side, above-left and above-right. For the usual planar schematic with approximately 120° bond angles at nitrogen, join the leftmost carbon of the left ring to the rightmost carbon of the right ring—the outward-facing meta positions—and label the segment d_{cis} .

The trans form is extended, whereas the cis form is folded:

$$d_{\text{trans}} > d_{\text{cis}}.$$

These are schematic drawings. Actual cis-azobenzene is nonplanar; the SMILES specifies the double-bond stereochemistry but does not specify phenyl-ring torsions or numerical interatomic distances.

5.2 — Synthesis of M

The proposed reactants are:

Label	Name	SMILES
N	Anthranilic acid, or 2-aminobenzoic acid	<chem>Nc1ccccc1C(=O)O</chem>
O	4-Amino- <i>N,N</i> -dimethylaniline	<chem>CN(C)c1ccc(N)cc1</chem>
P	<i>N,N</i> -Dimethylaniline	<chem>CN(C)c1ccccc1</chem>
Q	Benzoic acid	<chem>O=C(O)c1ccccc1</chem>

Choose **N and P**.

First, diazotize the primary aromatic amino group of N using cold sodium nitrite, $[\text{Na}^+] \cdot [\text{O}^-]\text{N}=\text{O}$, in aqueous hydrochloric acid. This gives the **2-carboxybenzenediazonium ion**, O=C(O)c1ccccc1[N+]#N.

The balanced net ionic equation is



The amino/diazonium group and carboxyl group occupy adjacent positions throughout. Here nitrite is $[\text{O}^-]\text{N}=\text{O}$, the hydrogen ion is $[\text{H}^+]$, and water is O ; sodium ion, $[\text{Na}^+]$, and chloride ion, $[\text{Cl}^-]$, are spectators.

Next, carry out azo coupling with P:



The resulting product is **M, methyl red**, shown as (*E*)-**2-[(4-(dimethylamino)phenyl)diazenyl]benzoic acid**:

CN(C)c1ccc(/N=N/c2ccccc2C(=O)O)cc1

The regioselectivity follows from two features:

1. N already fixes the carboxyl group **ortho to the future azo linkage**.
2. P's dimethylamino group strongly activates its aromatic ring toward electrophilic azo coupling. Its less hindered **para position** is preferred over its ortho positions.

Mechanistically, the activated aromatic ring of P attacks the terminal nitrogen of the diazonium group; loss of the proton from the attacked carbon restores aromaticity.

The alternative O/Q pairing is unsuitable: Q's carboxyl group deactivates its ring and directs electrophilic substitution meta, whereas M would require coupling ortho to that group.

5.3 — Absorbance change

Let

$$m_0 = [\mathbf{M}_{\text{trans}}]_0, \quad x = [\mathbf{CM}_{\text{trans}}].$$

Because complexation is 1:1,

$$[\mathbf{M}_{\text{trans}}] = m_0 - x.$$

By the Beer–Lambert law, neglecting the host's absorption,

$$A = L [\varepsilon_{M_{\text{trans}}} (m_0 - x) + \varepsilon_{CM_{\text{trans}}} x].$$

For the reference solution containing the same total concentration of uncomplexed guest,

$$A_0 = L \varepsilon_{M_{\text{trans}}} m_0.$$

Consequently,

$$\Delta A = A - A_0 = L (\varepsilon_{CM_{\text{trans}}} - \varepsilon_{M_{\text{trans}}}) x.$$

Thus

$$\boxed{\Delta A = \alpha [CM_{\text{trans}}], \quad \alpha = L (\varepsilon_{CM_{\text{trans}}} - \varepsilon_{M_{\text{trans}}})}.$$

With concentrations in mol L^{-1} , α has units L mol^{-1} .

5.4 — Host concentration in large excess

The host balance is

$$[C]_0 = [C] + [CM_{\text{trans}}].$$

At most all the guest can be complexed, so

$$0 \leq [CM_{\text{trans}}] \leq [M_{\text{trans}}]_0.$$

Therefore,

$$0 \leq \frac{[C]_0 - [C]}{[C]_0} \leq \frac{[M_{\text{trans}}]_0}{[C]_0} \ll 1.$$

The fractional depletion of free host is negligible:

$$\boxed{[C] \simeq [C]_0}.$$

5.5 — Dependence of absorbance on host concentration

The association constant is

$$K_t = \frac{[CM_{\text{trans}}]}{[C][M_{\text{trans}}]}.$$

Writing $c_0 = [C]_0$, and using the approximation established above,

$$K_t = \frac{x}{c_0(m_0 - x)}.$$

Rearranging,

$$\begin{aligned} x &= K_t c_0 (m_0 - x), \\ x(1 + K_t c_0) &= K_t c_0 m_0, \\ x &= \frac{K_t m_0 c_0}{1 + K_t c_0}. \end{aligned}$$

Substitution into $\Delta A = \alpha x$ gives

$$\boxed{\Delta A = \alpha \frac{K_t [M_{\text{trans}}]_0 [C]_0}{1 + K_t [C]_0}}.$$

Comparison with the requested expression yields

$$\boxed{\beta = K_t [M_{\text{trans}}]_0}.$$

Since K_t has units of inverse concentration, β is dimensionless.

5.6 — Determination of K_t

Taking the reciprocal of the expression in 5.5,

$$\frac{1}{\Delta A} = \frac{1}{\alpha\beta} \frac{1}{[\mathbf{C}]_0} + \frac{K_t}{\alpha\beta}.$$

Thus, for a plot of $y = 1/\Delta A$ against $X = 1/[\mathbf{C}]_0$,

$$\text{slope } s = \frac{1}{\alpha\beta}, \quad \text{intercept } b = \frac{K_t}{\alpha\beta},$$

and therefore

$$\boxed{K_t = \frac{b}{s}}.$$

Using the labelled points $Y = (100, 4.2)$ and $Z = (1000, 17.2)$,

$$s = \frac{17.2 - 4.2}{(1000 - 100) \text{ L mol}^{-1}} = 0.014444 \text{ mol L}^{-1}.$$

The intercept is

$$b = 4.2 - (0.014444 \text{ mol L}^{-1})(100 \text{ L mol}^{-1}) = 2.7556.$$

Hence

$$K_t = \frac{2.7556}{0.014444 \text{ mol L}^{-1}} = 190.77 \text{ L mol}^{-1},$$

or, to sensible precision,

$$\boxed{K_t \approx 1.9 \times 10^2 \text{ L mol}^{-1}}.$$

5.7 — Apparent isomerization rate constant

The cis guest is (*Z*)-methyl red, or (*Z*)-2-[(4-(dimethylamino)phenyl)diazenyl]benzoic acid:

CN(C)c1ccc(/N=N/c2ccccc2C(=O)O)cc1

Its inclusion complex contains this guest noncovalently inside β -cyclodextrin. The guest's SMILES does not encode its placement within the host cavity.

Fast complexation equilibrium gives

$$K_c = \frac{[\mathbf{CM}_{\text{cis}}]}{[\mathbf{C}][\mathbf{M}_{\text{cis}}]},$$

so

$$[\mathbf{CM}_{\text{cis}}] = K_c[\mathbf{C}][\mathbf{M}_{\text{cis}}].$$

The disappearance rate is therefore

$$r = (k_1 + k_2 K_c[\mathbf{C}])[\mathbf{M}_{\text{cis}}].$$

The total concentration of cis guest is

$$[\mathbf{M}_{\text{cis}}] + [\mathbf{CM}_{\text{cis}}] = (1 + K_c[\mathbf{C}])[\mathbf{M}_{\text{cis}}].$$

Dividing rate by total cis concentration,

$$k_{\text{obs}} = \frac{k_1 + k_2 K_c [\mathbf{C}]}{1 + K_c [\mathbf{C}]}.$$

Comparison with the stated expression gives

$$\gamma = k_1, \quad \delta = K_c.$$

The dimensions are consistent: γ is in s^{-1} , while δ is in L mol^{-1} .

5.8 — Conditions for the half-life expression

First, the printed factor $\ln(2/\gamma)$ must be corrected to $(\ln 2)/\gamma$. A logarithm cannot have a dimensional argument, and $\gamma = k_1$ has units s^{-1} .

Let the total cis concentration be

$$u = [\mathbf{M}_{\text{cis}}] + [\mathbf{CM}_{\text{cis}}].$$

When free host concentration remains constant,

$$-\frac{du}{dt} = k_{\text{obs}} u,$$

and integration gives

$$u(t) = u(0)e^{-k_{\text{obs}} t}.$$

Thus

$$t_{1/2} = \frac{\ln 2}{k_{\text{obs}}}.$$

With $[\mathbf{C}] \simeq [\mathbf{C}]_0$, the expression from 5.7 becomes

$$t_{1/2} = \frac{\ln 2 (1 + K_c [\mathbf{C}]_0)}{k_1 + k_2 K_c [\mathbf{C}]_0}.$$

To obtain the requested linear dependence on host concentration, the second term in the denominator must be negligible:

$$k_2 K_c [\mathbf{C}]_0 \ll k_1.$$

Equivalently, isomerization through the complexed population must contribute negligibly to the total rate:

$$k_2 [\mathbf{CM}_{\text{cis}}] \ll k_1 [\mathbf{M}_{\text{cis}}].$$

Then

$$t_{1/2} \simeq \frac{\ln 2}{k_1} (1 + K_c [\mathbf{C}]_0) = \frac{\ln 2}{\gamma} (1 + K_c [\mathbf{C}]_0).$$

The expression is exact within the constant-host model when $k_2 = 0$. Merely requiring $k_2 \ll k_1$ is insufficient if $K_c [\mathbf{C}]_0$ is very large.

The host-excess approximation must also cover binding by the trans product. If appreciable unconverted trans guest remains after irradiation, host excess must apply to the **total** binding guest, including that residual trans population.

5.9 — Linear regression and K_c

Under the conditions above,

$$t_{1/2} = \frac{\ln 2}{k_1} + \frac{\ln 2}{k_1} K_c [\mathbf{C}]_0.$$

Writing

$$t_{1/2} = a + b[\mathbf{C}]_0,$$

we identify

$$a = \frac{\ln 2}{k_1}, \quad b = aK_c,$$

so

$$\boxed{K_c = \frac{b}{a}}.$$

For the eight tabulated points, let $x_i = [\mathbf{C}]_{0,i}$ and $y_i = t_{1/2,i}$. Ordinary least squares gives

$$b = \frac{n \sum x_i y_i - (\sum x_i)(\sum y_i)}{n \sum x_i^2 - (\sum x_i)^2}, \quad a = \frac{\sum y_i - b \sum x_i}{n}.$$

Using the supplied data,

$$a = 3.0804004 \text{ s}, \quad b = 935.67515 \text{ s L mol}^{-1}.$$

Thus the required plot is an increasing straight line of $t_{1/2}$ against $[\mathbf{C}]_0$, with this intercept and slope. Its R^2 is approximately 0.9990.

The association constant is

$$K_c = \frac{935.67515 \text{ s L mol}^{-1}}{3.0804004 \text{ s}} = 303.75 \text{ L mol}^{-1}.$$

Therefore,

$$\boxed{K_c \approx 3.0 \times 10^2 \text{ L mol}^{-1}}.$$

Using the graph's rounded coefficients, $a = 3.1 \text{ s}$ and $b = 936 \text{ s L mol}^{-1}$, gives 302 L mol^{-1} , consistent with this result.

5.10 — Conditions for light-triggered pore opening

For a guest with association constant K , the fraction complexed at free host concentration $[\mathbf{C}]$ is

$$f_{\text{bound}} = \frac{K[\mathbf{C}]}{1 + K[\mathbf{C}]}.$$

To block the pores initially, the trans guest should be predominantly complexed:

$$f_{\text{trans}} \simeq 1 \implies K_t[\mathbf{C}] \gg 1.$$

After irradiation, the cis guest should be predominantly uncomplexed:

$$f_{\text{cis}} \simeq 0 \implies K_c[\mathbf{C}] \ll 1.$$

The appropriate condition is therefore

$$\boxed{K_c[\mathbf{C}] \ll 1 \ll K_t[\mathbf{C}]},$$

or equivalently,

$$\frac{1}{K_t} \ll [\text{C}] \ll \frac{1}{K_c}.$$

If host depletion is negligible, this can be expressed using $[\text{C}]_0$.

This part explicitly concerns **another azobenzene compound**, with $K_c \ll K_t$. The numerical constants determined for M in 5.6 and 5.9 do not apply to this grafted compound.

5.11 — Irradiation wavelength

The solid absorption curve for trans-azobenzene has its strong maximum at 330 nm. At that wavelength, cis-azobenzene absorbs less strongly.

Therefore, preferential excitation of the initially trans guest is achieved with

$$\lambda_1 = 330 \text{ nm}.$$

The resulting trans-to-cis isomerization weakens host binding, removes the cyclodextrin caps, and allows dye release.

5.12 — Monitoring wavelength

Rhodamine B has its strong absorption maximum at 550 nm, where both azobenzene isomers have negligible absorption.

Thus

$$\lambda_2 = 550 \text{ nm}.$$

At this wavelength, the solution absorbance tracks the concentration of released dye through the Beer–Lambert law:

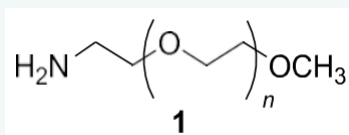
$$A_{550} = \varepsilon_{\text{RhB},550} L [\text{RhB}]_{\text{solution}}.$$

The solution was checked against the official solution.

Problem 6: Characterization of a block-copolymer

Block-copolymers, obtained by linking different polymers (blocks), have unique properties, such as the ability to self-assemble. In this problem, the synthesis and characterization of such macromolecules are studied.

Study of the first block

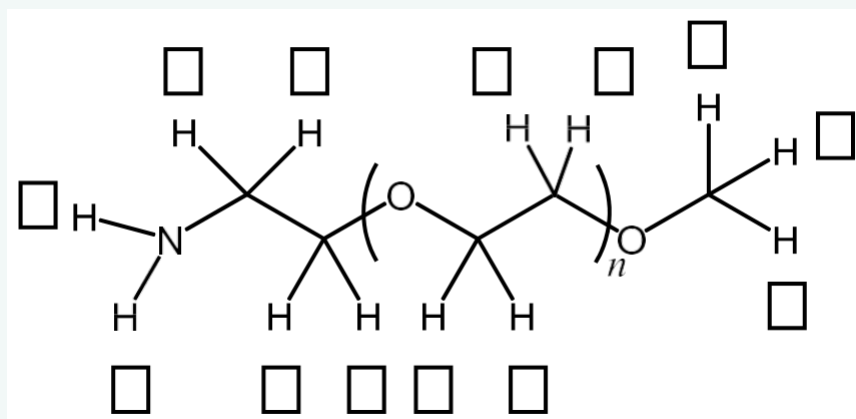


In this first part, we will study the water soluble homopolymer 1 (α -methoxy- ω -aminopolyethyleneglycol). The ^1H NMR spectrum of 1 (DMSO- d_6 , 60 °C, 500 MHz) includes the following signals:

Index	δ (ppm)	Peak Area
a	2.7*	0.6
b	3.3	0.9
c	3.4	0.6
d	~ 3.5	133.7

Table 1, *in the presence of D₂O, the signal at 2.7 ppm disappears.

6.1 Match the ^1H NMR signals (a, b, c, d) from Table 1 with each of the corresponding protons.

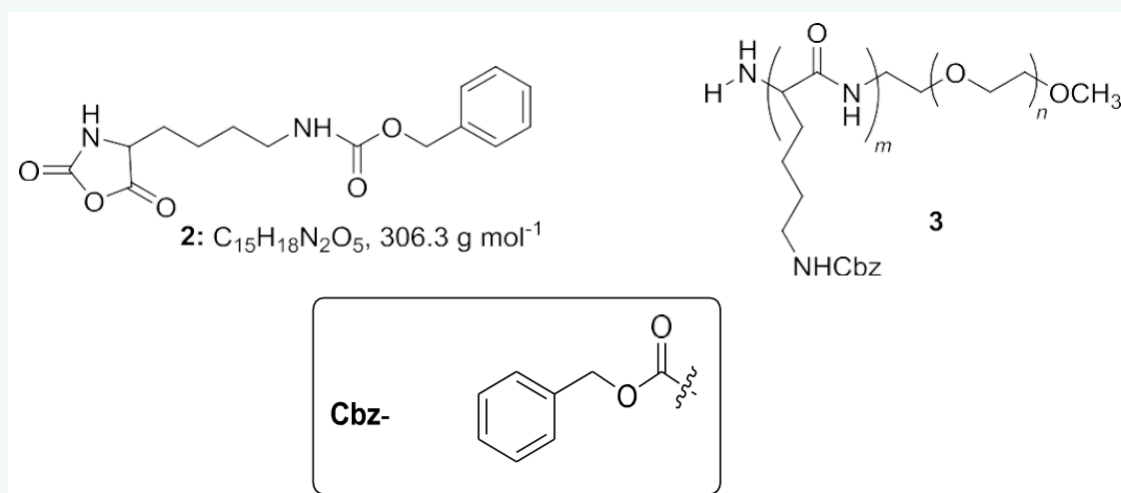


6.2 Express the average degree of polymerization n as a function of the area $A_{\text{OC}_2\text{H}_4}$ of the NMR peak of the repeating unit and the area A_{OCH_3} of the NMR peak of the methyl end group. Calculate n .

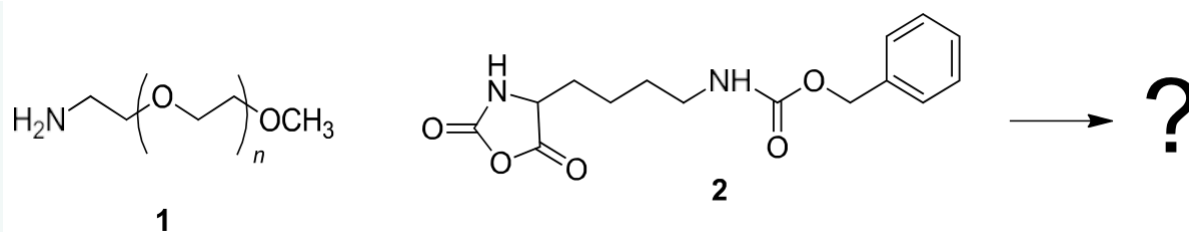
Study of a diblock-copolymer

The synthesis of the second block of the copolymer is performed through the reaction of 1 with 2 (ϵ - (benzyloxycarbonyl)-lysine *N*-carboxyanhydride).

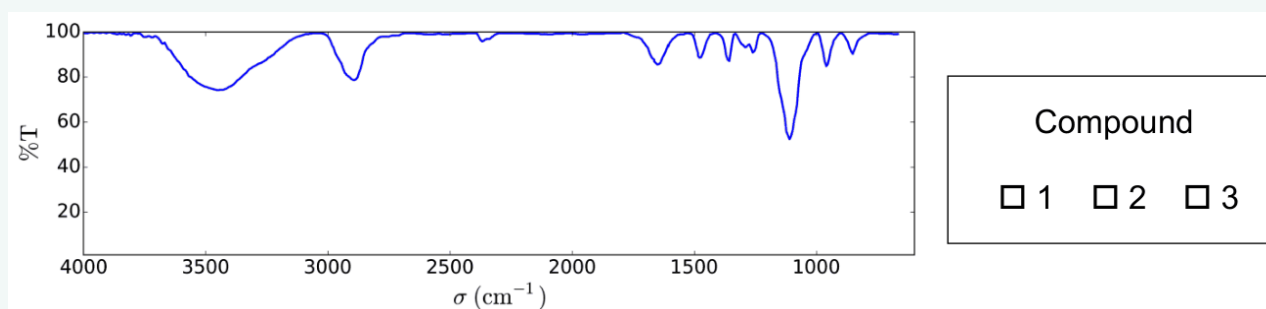
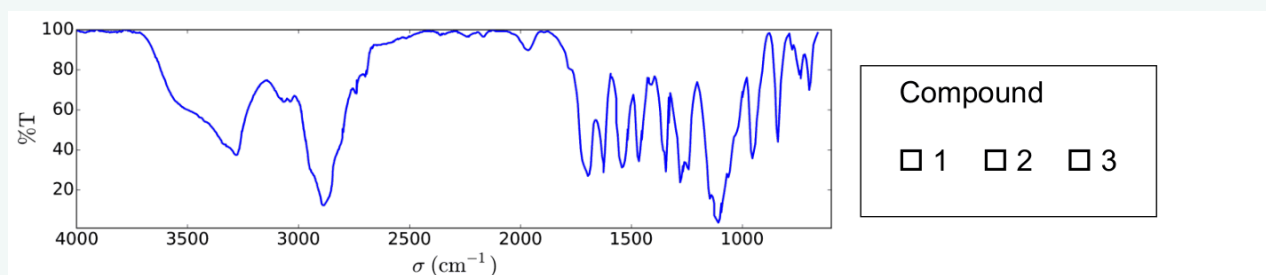
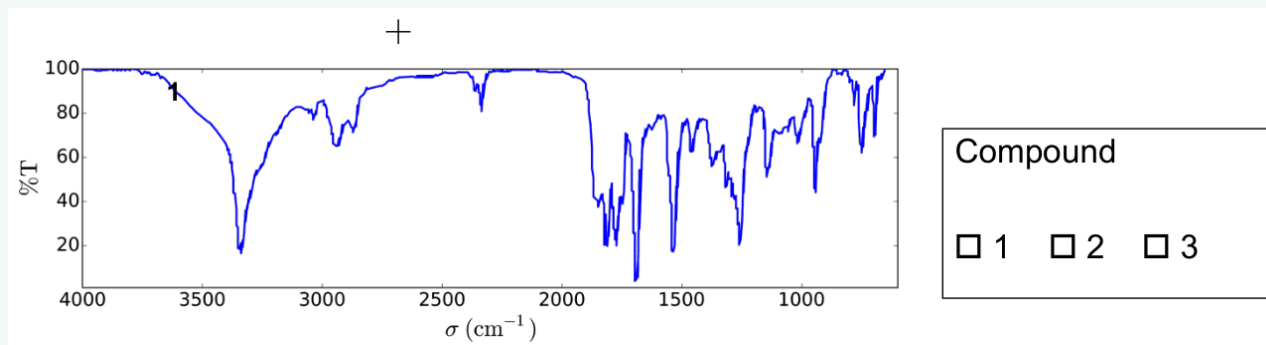
This yields the block-copolymer 3.



6.3 Draw the reaction intermediate that is formed in the first step of the addition of 1 to 2. The second step of the mechanism leads to the formation of a gas molecule, **6**. Draw its structure.



6.4 Infrared (IR) measurements are performed to characterize the compounds. Match the three IR spectra with compounds 1, 2 and 3.



6.5 The ^1H NMR spectrum of copolymer 3 (in $\text{DMSO}-d_6$, at 60 °C, 500 MHz) is reported in Fig. 1. Using some or all of the NMR signals, the areas of which are reported in Table 2, calculate its number average molar mass M_n , considering n from question 2. For your calculations, draw a circle around the group(s) of atoms you used and give their corresponding symbol(s) (α , β ...).

Table 2

Peak	Area
α	22.4
β	119
γ	23.8
δ	47.6
ϵ	622

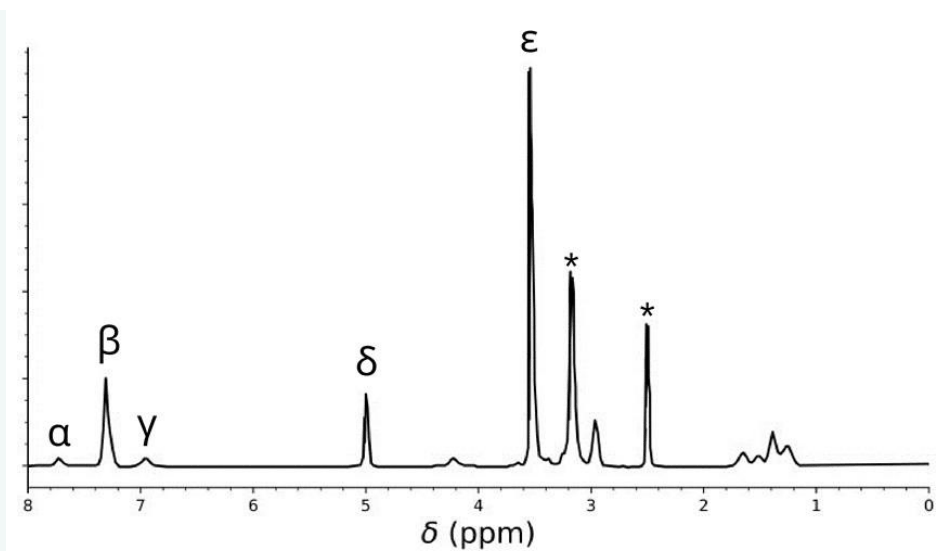


Fig. 1 – signals marked with * correspond to the solvent and water.

This reaction of 1 with 2 yielded the copolymers 3a after 20 h, 3b after 25 h and 3c after 30 h of reaction at 40 °C. Results of size-exclusion chromatography (SEC) experiments are presented in Fig. 2.

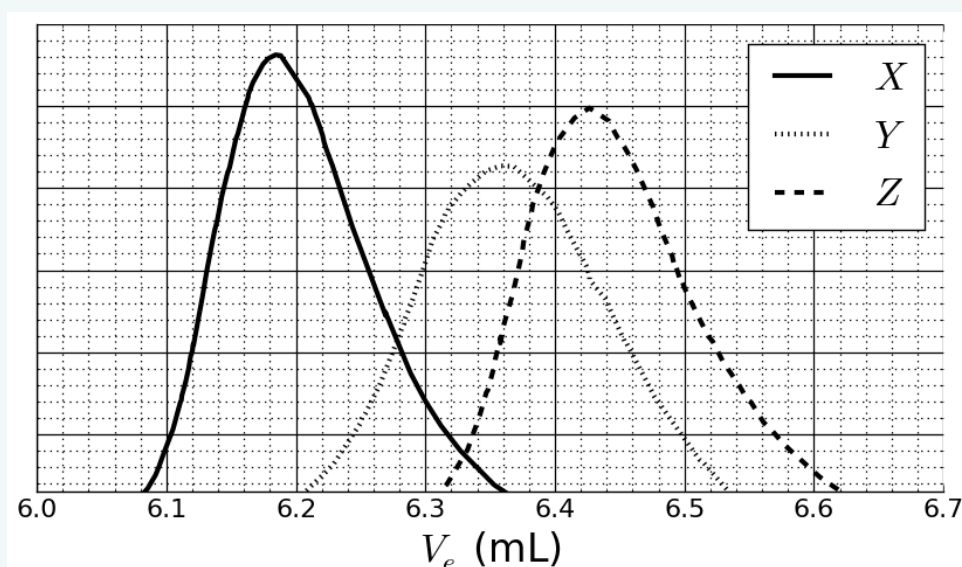


Fig. 2 – SEC chromatograms of 3a, 3b and 3c as a function of the elution volume, V_e .

6.6 Match the signals in Fig. 2 with the copolymers 3a, 3b and 3c.

3a: ☐ X ☐ Y ☐ Z

3b: ☐ X ☐ Y ☐ Z

3c: ☐ X ☐ Y ☐ Z

In order to calibrate the chromatogram, a mixture of standard polymers of known masses (3, 30, 130, 700 and 7000 kg mol⁻¹) has been studied (Fig. 3).

The log value of the molar mass is a linear function of the elution volume, V_e .

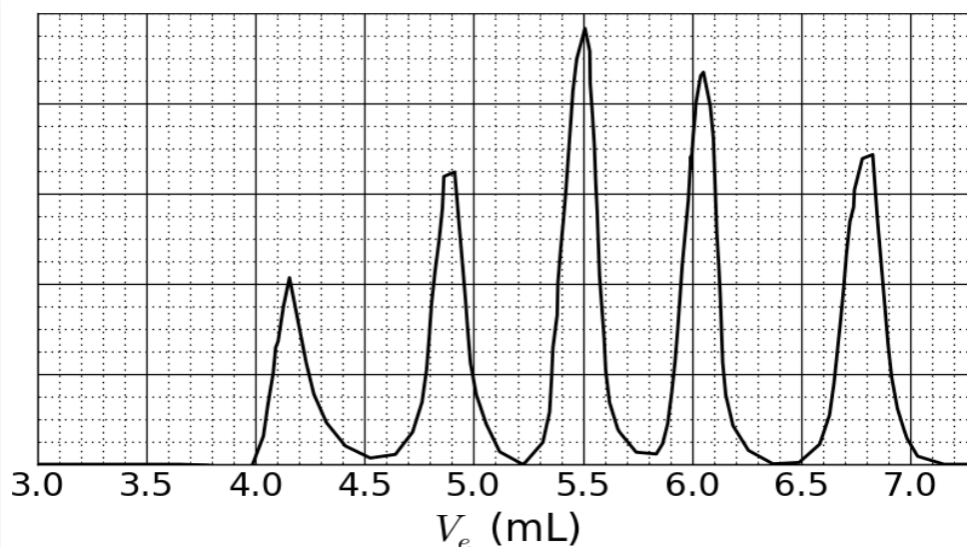
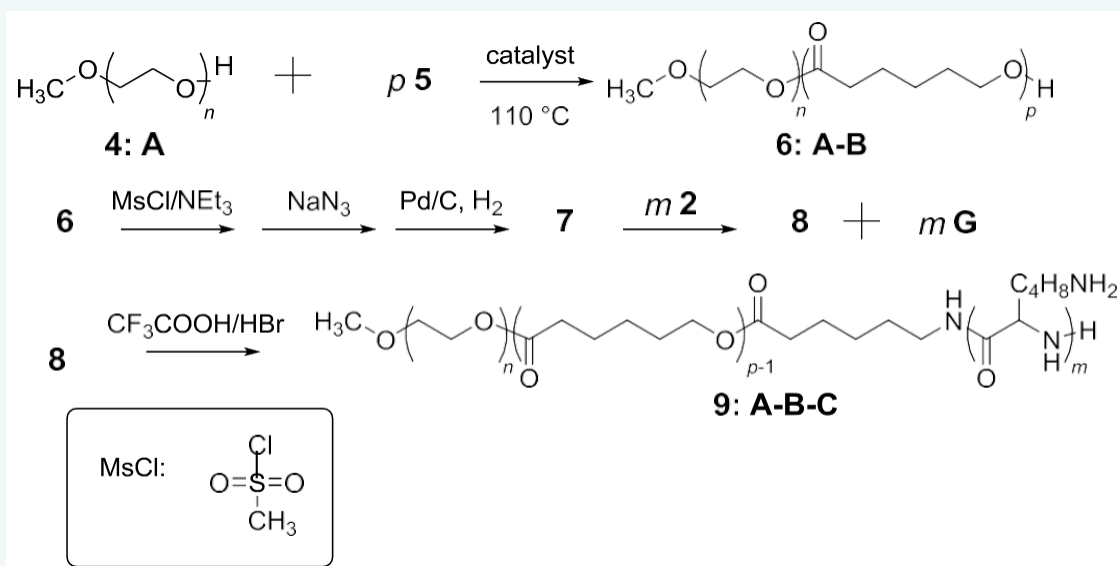


Fig. 3 – SEC chromatogram of the mixture of standards.

6.7 Based on the SEC curves in Fig. 2 and 3, determine V_e of the polymer that corresponds to curve X and use it to estimate the degree of polymerization m of its second block. Detail your calculation; you may use a calculator or plot a graph.

Triblock copolymer synthesis

For biological applications, involving the formation of micelles, a triblock copolymer 9 can be synthesized through the introduction of a middle block, B, using monomer 5.



6.8 Draw the structures of 5, 7 and 8.

6.9 Amphiphilic block copolymers, such as 9: A-B-C, can be used for medical applications, as they self-assemble into micelles in water (pH = 7), which can be used as drug carriers. Assign each block of the copolymer to a property. Draw a scheme of the micelle with only 4 polymer chains.

Official English text of the problem.

Answers

In the structural fragments below, [*] denotes the remainder of the chain, defined explicitly in the solution.

- **6.1:** **a:** both amino protons; **b:** the three methoxy protons; **c:** the two protons on the carbon directly bonded to the amino nitrogen; **d:** all remaining methylene protons.
- **6.2:** Using the entire observed peak d,

$$n = \frac{3A_{\text{OC}_2\text{H}_4}}{4A_{\text{OCH}_3}} - \frac{1}{2} = 110.9 \approx 111.$$

- **6.3:** The ring-opened intermediate is the N^α -**carbamic acid adduct**, $\text{O}=\text{C}(\text{O})\text{NC}(\text{CCCCNC}(=\text{O})\text{OCc1ccccc1})\text{C}(=\text{O})\text{N}[*]$. It loses **carbon dioxide**, $G = \text{CO}_2$, $\text{O}=\text{C}=\text{O}$.
- **6.4:** The three spectra, in reading order, correspond to

$$2, \quad 3, \quad 1.$$

- **6.5:** The protected lysine block contains approximately 17 residues:

$$M_n(3) \approx 9.4 \times 10^3 \text{ g mol}^{-1}.$$

Use β , the Cbz phenyl protons, and ϵ , the PEG methylene protons; δ , the Cbz benzylic methylene, gives the same result.

- **6.6:** $3\mathbf{a} = Z$, $3\mathbf{b} = Y$, $3\mathbf{c} = X$.
- **6.7:** $V_e(X) \approx 6.18 \text{ mL}$, giving $M_X \approx 1.9 \times 10^4 \text{ g mol}^{-1}$ and $m \approx 52$, approximately.
- **6.8:** **5:** ϵ -caprolactone, $\text{O}=\text{C}1\text{OCCCCC1}$. **7:** amino-terminated PEG–poly(ϵ -caprolactone), ending in $[*]\text{C}(=\text{O})\text{CCCCCN}$. **8:** PEG–poly(ϵ -caprolactone)–poly(N^ϵ -Cbz-lysine), formed by adding m protected lysine residues to the terminal nitrogen of 7; its peptide repeat is $[*]\text{C}(=\text{O})\text{C}(\text{CCCCNC}(=\text{O})\text{OCc1ccccc1})\text{N}[*]$.
- **6.9:** **A:** neutral hydrophilic PEG. **B:** hydrophobic poly(ϵ -caprolactone). **C:** hydrophilic, positively charged polylysine. Draw four B segments gathered into the micelle core, with four A arms and four C arms extending into water.

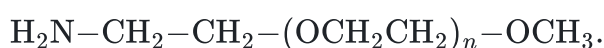
Solution

For variable-length polymers, a single ordinary SMILES cannot specify the whole distribution. Below, a **SMILES construction** means concatenating the stated strings, repeating a fragment the specified integer number of times. The accompanying formulas define the connectivity and average repeat counts.

The supplied structures do not specify absolute stereochemistry at the lysine α -carbons. Accordingly, the SMILES leave these stereocentres unspecified; the reactions shown retain their configuration.

6.1 — Assignment of the proton signals

Compound **1**, α -methoxy- ω -aminopolyethyleneglycol, has the connectivity



Its SMILES construction is $\text{CO} + n$ copies of $\text{CCO} + \text{CCN}$, reading from the methoxy end.

Signal	Assignment	Number of protons per chain	Reason
a, 2.7 ppm	Terminal NH_2	2	These exchangeable protons disappear after addition of deuterium oxide.
b, 3.3 ppm	Terminal OCH_3	3	Its integral is $3/2$ times either two-proton end-group integral.
c, 3.4 ppm	$\text{NH}_2\text{—CH}_2$	2	This is the remaining distinct two-proton terminal methylene.
d, approximately 3.5 ppm	All other methylenes	$4n + 2$	These are the oxygen-adjacent methylene protons of the PEG chain.

For the requested drawing, put **a** in both boxes beside nitrogen-bound hydrogens, **b** in all three boxes beside the terminal methyl hydrogens, **c** in both boxes on the methylene directly bonded to nitrogen, and **d** in every other methylene-proton box.

Deuterium oxide is heavy water, SMILES $[\text{2H}]\text{O}[\text{2H}]$; replacement of amino hydrogen by deuterium removes those nuclei from the proton NMR spectrum.

6.2 — Degree of polymerization of the first block

Let q be the integral corresponding to one proton per chain. The methoxy group gives

$$A_{\text{OCH}_3} = 3q.$$

The drawn structure contains one oxygen-adjacent terminal methylene outside the brackets, in addition to the n oxyethylene units. Therefore, the complete peak d has

$$A_d = (4n + 2)q.$$

Consequently,

$$\frac{A_d}{A_{\text{OCH}_3}} = \frac{4n + 2}{3},$$

and

$$n = \frac{1}{4} \left(\frac{3A_d}{A_{\text{OCH}_3}} - 2 \right).$$

Numerically,

$$n = \frac{1}{4} \left(\frac{3(133.7)}{0.9} - 2 \right) = 110.9167 \approx 111.$$

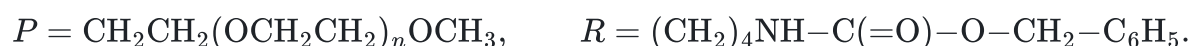
If $A_{\text{OC}_2\text{H}_4}$ means an integral already corrected to contain **only** the bracketed repeats, then

$$A_{\text{OC}_2\text{H}_4}^{\text{repeat}} = A_d - \frac{2}{3}A_{\text{OCH}_3}, \quad n = \frac{3A_{\text{OC}_2\text{H}_4}^{\text{repeat}}}{4A_{\text{OCH}_3}}.$$

Thus the familiar repeat-to-end-group ratio and the end-corrected expression are consistent.

6.3 — Ring opening and release of gas

Define



The initiating amine is therefore $P-NH_2$. The benzyloxycarbonyl, or **Cbz**, protecting group has attachment-fragment SMILES [*]C(=O)OCc1ccccc1.

Compound **2**, N^ϵ -Cbz-lysine N -carboxyanhydride, has SMILES:

O=C1OC(=O)C(CCCCNC(=O)OCc2ccccc2)N1

The amine attacks the carbonyl derived from the amino acid's carboxyl group—the ring carbonyl adjacent to the α -carbon. The carbonyl π electrons move to oxygen.

At elementary-step resolution, the immediate **zwitterionic tetrahedral addition intermediate** is:

O=C1OC([O-])([NH2+][*])C(CCCCNC(=O)OCc2ccccc2)N1

Here [*] is P . To draw it, retain the five-membered ring, replace the attacked carbonyl by a tetrahedral carbon bearing O^- , and attach the attacking NH_2^+-P group to that carbon.

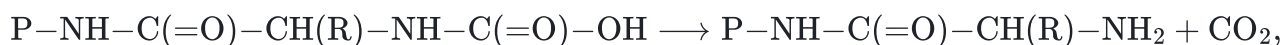
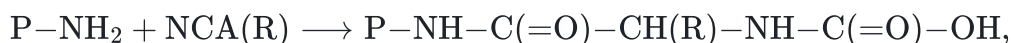
Collapse of this intermediate breaks the ring's acyl-oxygen bond. Proton transfer gives the **ring-opened N^α -carbamic acid adduct**:



Its SMILES is:

O=C(O)NC(CCCCNC(=O)OCc1ccccc1)C(=O)N[*]

This is the intermediate immediately preceding the gas-producing step. Its formation and decomposition can be written as



where $NCA(R)$ denotes monomer 2.

The first insertion product, the **PEG amide of N^ϵ -Cbz-lysine**, has SMILES:

NC(CCCCNC(=O)OCc1ccccc1)C(=O)N[*]

Its newly formed amino group can attack another monomer, propagating the peptide block. One molecule of gas is released per incorporated monomer.

Thus **G is carbon dioxide**, CO_2 , SMILES O=C=O. Draw it as a linear molecule with an $O-C-O$ angle of 180° .

The overall polymerization is



6.4 — Identification of the IR spectra

Spectrum in reading order	Compound	Diagnostic features
First spectrum	2	Strong high-frequency carbonyl bands of the cyclic anhydride, approximately in the $1850-1780\text{ cm}^{-1}$ region, together with the Cbz carbamate carbonyl.
Second spectrum	3	Peptide/carbamate carbonyl and amide bands, together with strong PEG ether absorption near 1100 cm^{-1} .

Spectrum in reading order	Compound	Diagnostic features
Third spectrum	1	Strong ether absorption and amino-group absorption, but no strong carbonyl band.

Ring opening consumes the cyclic anhydride functionality of 2 and creates peptide amide linkages in 3. Compound 1 contains no carbonyl groups.

6.5 — Number-average molar mass from NMR

Compound 3 is PEG–block–poly(*N*^ε-Cbz-lysine). Its SMILES is obtained by appending *m* copies of C(=O)C(CCCCNC(=O)OCc1ccccc1)N

to the SMILES construction for compound 1.

The following nonexchangeable signals are sufficient:

Signal	Group	Proton count per chain
β, approximately 7.3 ppm	Cbz phenyl groups	5 <i>m</i>
δ, approximately 5.0 ppm	Cbz benzylic OCH ₂ C ₆ H ₅ groups	2 <i>m</i>
ε, approximately 3.5 ppm	PEG oxygen-adjacent methylenes	4 <i>n</i> + 2

The two Cbz signals agree exactly after normalization:

$$\frac{A_{\beta}}{5} = \frac{119}{5} = 23.8, \quad \frac{A_{\delta}}{2} = \frac{47.6}{2} = 23.8.$$

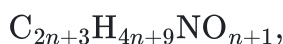
Using $n \approx 111$,

$$m = \frac{A_{\beta}/5}{A_{\epsilon}/(4n+2)} = \frac{119/5}{622/446} = 17.07 \approx 17.$$

Using only the bracketed PEG repeats and neglecting the two terminal methylene protons would give $m = 16.99$, with the same reported result.

For the requested circles, mark the **Cbz phenyl rings and their five aromatic hydrogens** as β and the **PEG methylene groups contributing to the 3.5 ppm signal** as ε. The Cbz benzylic methylene groups may additionally be circled and labelled δ.

The molecular formula of initiator 1 is



so its molar mass is

$$M(1) = nM(\text{C}_2\text{H}_4\text{O}) + M(\text{C}_3\text{H}_9\text{NO}) \approx 44.05n + 75.11.$$

At $n = 111$,

$$M(1) \approx 4965 \text{ g mol}^{-1}.$$

Each incorporated monomer loses one carbon dioxide molecule. The protected lysine residue therefore has formula $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_3$ and molar mass

$$M_{\text{residue}} = M(2) - M(\text{CO}_2) = 306.3 - 44.0 = 262.3 \text{ g mol}^{-1}.$$

Hence

$$M_n(3) = M(1) + mM_{\text{residue}},$$

$$M_n(3) \approx 4965 + 17.07(262.3) \approx 9.44 \times 10^3 \text{ g mol}^{-1}.$$

To an appropriate precision,

$$M_n(3) \approx 9.4 \text{ kg mol}^{-1}.$$

6.6 — Assignment of the SEC curves

In size-exclusion chromatography, larger polymer coils enter fewer pores and elute at smaller volumes.

As polymerization proceeds, the second block grows. Thus, under the stated comparison,

$$M(\mathbf{3c}) > M(\mathbf{3b}) > M(\mathbf{3a}),$$

and the elution volumes have the reverse order.

Since X elutes first, Y next and Z last,

$$\mathbf{3a} = Z, \quad \mathbf{3b} = Y, \quad \mathbf{3c} = X.$$

6.7 — SEC estimate of the second-block length

The maximum of curve X is approximately

$$V_e(X) \approx 6.18 \text{ mL}.$$

Assign the standards from largest mass at the smallest elution volume to smallest mass at the largest volume. Approximate readings from Fig. 3 are:

V_e / mL	$M / \text{kg mol}^{-1}$
4.15	7000
4.90	700
5.50	130
6.05	30
6.80	3

A linear fit to these five points gives

$$\log_{10} \left(\frac{M}{\text{kg mol}^{-1}} \right) \approx 9.046 - 1.258 \frac{V_e}{\text{mL}}.$$

At $V_e = 6.18 \text{ mL}$,

$$M_X \approx 10^{9.046 - 1.258(6.18)} \approx 18.7 \text{ kg mol}^{-1}.$$

Subtracting the PEG initiator contribution and dividing by the protected lysine residue mass gives

$$m_X = \frac{M_X - M(1)}{M_{\text{residue}}},$$

$$m_X \approx \frac{18\,700 - 4965}{262.3} \approx 52.$$

Thus

$$m_X \approx 5.2 \times 10^1.$$

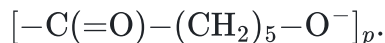
This is a graph-based estimate associated with the SEC peak. Its precision is lower than the displayed intermediate calculation digits suggest.

6.8 — Structures of 5, 7 and 8

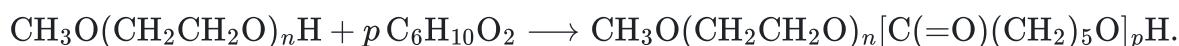
Compound 5 is ϵ -caprolactone, also called oxepan-2-one:



Draw a seven-membered cyclic ester containing one carbonyl carbon, one ring oxygen and five methylene carbons. Its ring-opening polymerization gives the polyester block

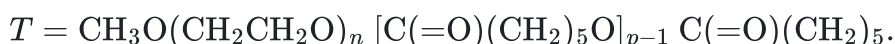


The lactone is incorporated without loss of a small molecule:



This is the reaction of 4 with p molecules of 5 to form 6.

For concise structural formulas, define



Then compound 6 is $T-\text{OH}$.

Compound 7 is the corresponding amino-terminated PEG–poly(ϵ -caprolactone):

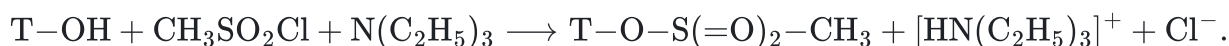


Its SMILES construction is:

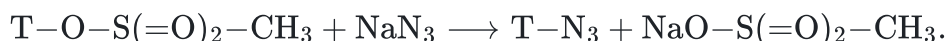
- CO;
- followed by n copies of CCO;
- followed by $p - 1$ copies of C(=O)CCCCO;
- followed by C(=O)CCCCN.

The three transformations replace the terminal hydroxyl group by an amino group.

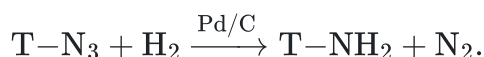
First, mesylation activates the alcohol:



Then azide displaces methanesulfonate:



Finally, catalytic hydrogenation reduces the organic azide:



The relevant species and their SMILES are:

Species	SMILES
Methanesulfonyl chloride	CS(=O)(=O)Cl
Triethylamine	CCN(CC)CC
Triethylammonium chloride	CC[NH+](CC)CC.[Cl-]
Polymer methanesulfonate, with $[*] = T$	[*]OS(=O)(=O)C
Sodium azide	[Na+].[N-]=[N+]=[N-]
Polymer azide, with $[*] = T$	[*]N=[N+]=[N-]
Sodium methanesulfonate	[Na+].CS(=O)(=O)[O-]

Species	SMILES
Hydrogen	[H][H]
Nitrogen	N#N

Compound 8 is PEG–poly(ε-caprolactone)–poly(*N*^ε-Cbz-lysine):



Its SMILES construction is the complete construction for 7 followed by m copies of

C(=O)C(CCCCNC(=O)OCc1ccccc1)N

Thus the terminal nitrogen of 7 becomes the amide nitrogen joining blocks B and C. The far end of the peptide block remains an amino group.

The balanced propagation reaction is



To draw 8, take structure 9 from the question and replace **every lysine side-chain** NH_2 by



The final acid treatment removes these Cbz groups. Written for the neutral amine groups shown in structure 9, the protecting-group cleavage balance is



Hydrogen bromide has SMILES Br; the acidic solvent, trifluoroacetic acid, is O=C(O)C(F)(F)F; the benzyl bromide by-product is BrCc1ccccc1. In the acidic reaction mixture, the liberated amines are protonated by additional acid.

The neutral connectivity of **9**, PEG–poly(ε-caprolactone)–polylysine, is obtained by appending m copies of

C(=O)C(CCCCN)N

to the construction for 7.

6.9 — Block properties and the four-chain micelle

Block	Chemical identity	Representative repeat SMILES	Property at pH 7
A	Polyethylene glycol	[*]CCO[*]	Hydrophilic and electrically neutral
B	Poly(ε-caprolactone)	[*]C(=O)CCCCO[*]	Hydrophobic and electrically neutral
C	Polylysine	[*]C(=O)C(CCCC[NH3+])N[*]	Hydrophilic and positively charged

PEG is hydrated through its ether oxygens. The caprolactone block contains long methylene sequences and favors the hydrophobic micelle core. The lysine side-chain amino groups are predominantly protonated at pH 7, giving $-\text{NH}_3^+$ groups and a hydrated, cationic block. The free terminal amino group can also be protonated.

For the requested **four-chain micelle**, draw the following arrangement:

1. Draw a circle representing the hydrophobic core.
2. Place exactly four folded B segments inside it, labelled B_1 through B_4 .
3. For each chain i , place both its A–B and B–C junctions near the core surface.

4. Extend one hydrated A_i arm and one positively charged C_i arm outward into water.

Each continuous chain therefore runs from an external A arm, through a buried B segment, and back out through an external C arm. The drawing contains **four B segments in the core and eight hydrophilic exterior arms: four A and four C**. Mark positive charges along the C arms.

SMILES describes each chain's covalent connectivity; it does not represent this folded conformation or the noncovalent micelle assembly.

The solution was checked against the official solution. Where this solution differs from the official solution, the official solution contains an error or a misprint.

Problem 7: Ring motion in a [2]catenane

In 2016, the Nobel Prize in Chemistry was awarded to J.-P. Sauvage, Sir J. F. Stoddart and B. L. Feringa "for the design and synthesis of molecular machines". An example of these is [2]catenane, a molecule consisting of two interlocked rings. In this system, one macrocycle contains a single phenanthroline (bidentate) ligand and the second contains two ligands: a phenanthroline and a terpyridine (tridentate) ligand. A copper ion is coordinated by one ligand from each macrocycle. Depending on the oxidation state of the copper (+I or +II), two configurations are obtained (Fig. 1).

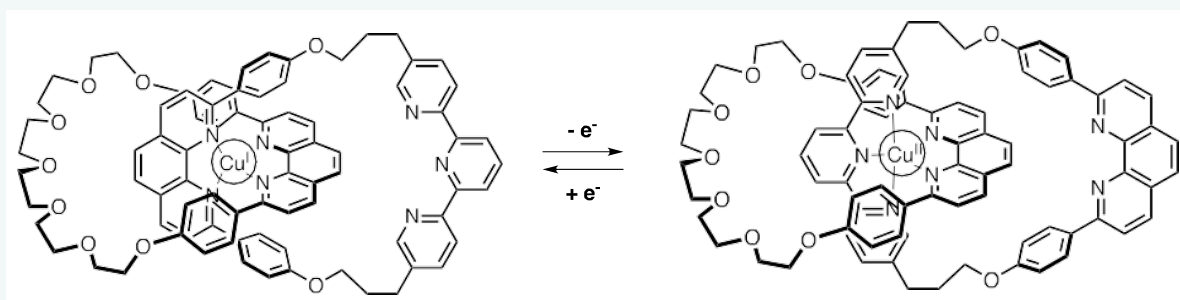
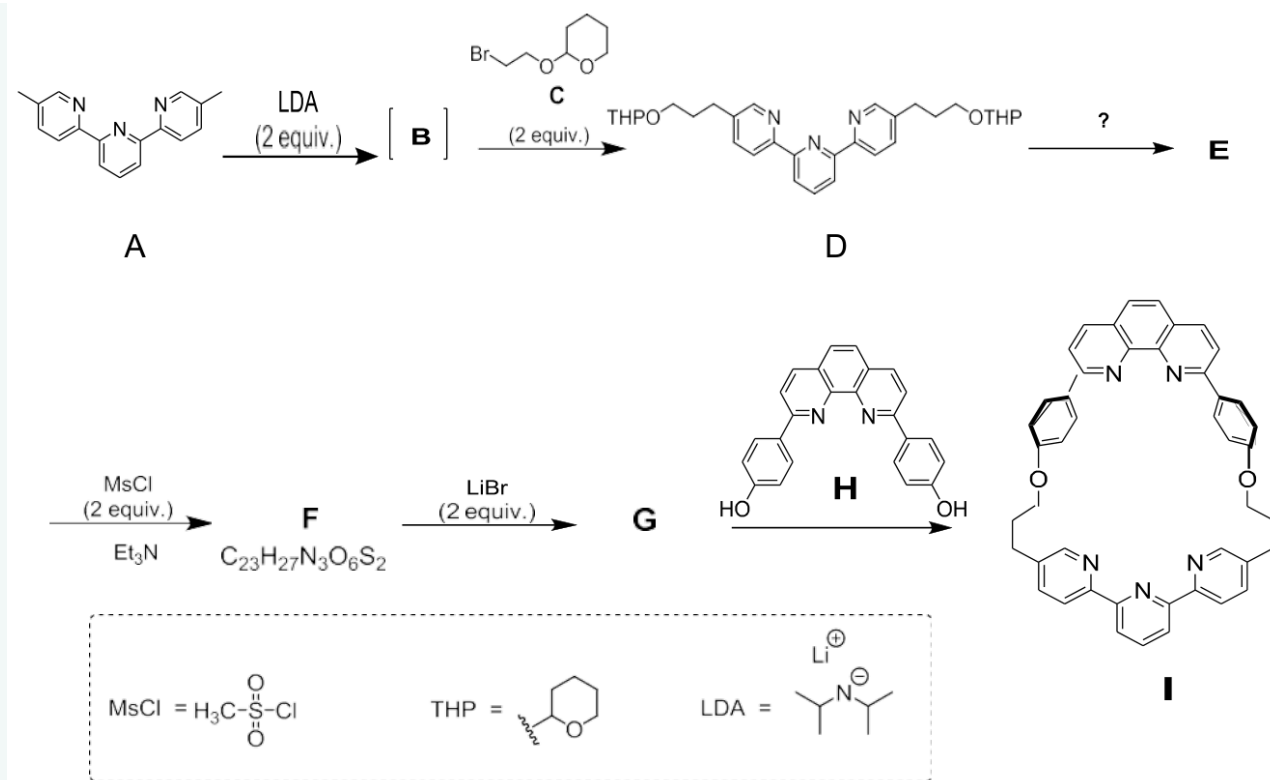


Fig. 1 – Multi-stability of a ring in a [2]catenane.

The synthesis of the macrocycle is the following:



7.1 Draw the structure of **B**.

7.2 Draw the structures of **E**, **F** and **G**.

7.3 Out of the following reaction conditions, choose which one(s) can produce **E** from **D**.

- ☐ H^+ , H_2O
- ☐ OH^- , H_2O
- ☐ NaBH_4 , CH_3OH
- ☐ H_2 , Pd/C, THF

Tick the relevant box.

7.4 In the synthetic strategy, MsCl is used to obtain:

- ☐ a leaving group
- ☐ a protecting group
- ☐ a deactivated group
- ☐ a directing group

Tick the relevant box.

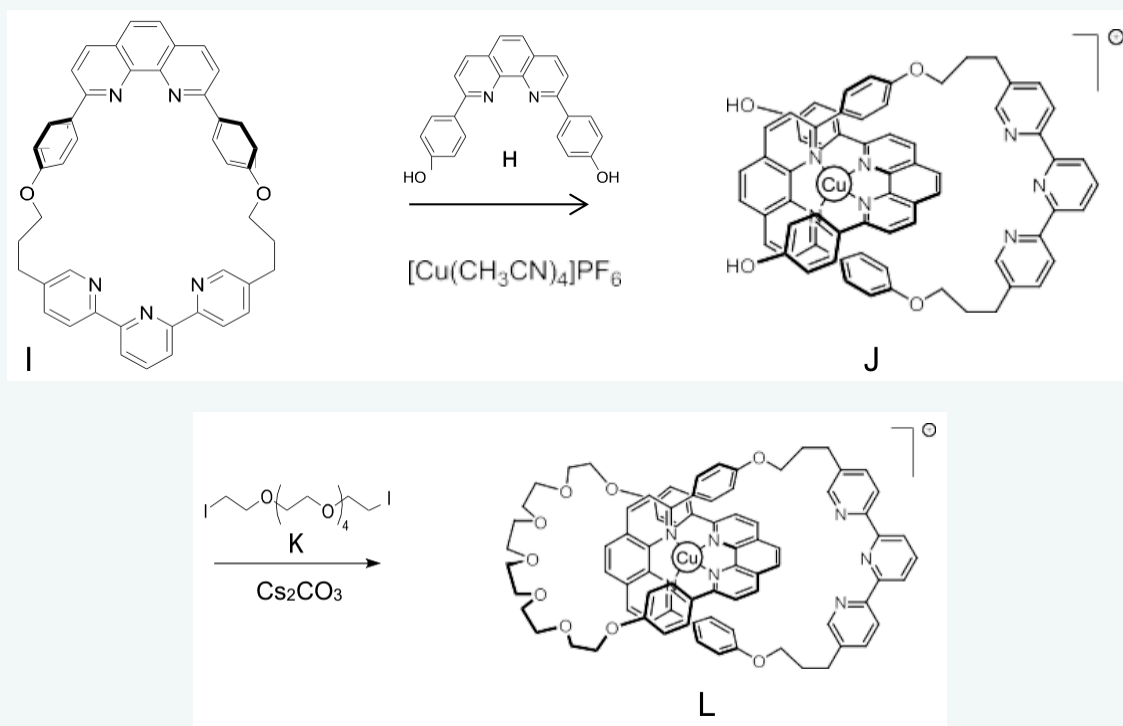
7.5 **G** is obtained by the reaction between **F** and LiBr in acetone. This reaction is:

- ☐ electrophilic aromatic substitution,
- ☐ nucleophilic aromatic substitution,
- ☐ $\text{S}_{\text{N}}1$
- ☐ $\text{S}_{\text{N}}2$

Tick the relevant boxes.

7.6 Draw the transition state of the rate-determining step of the reaction **F** $\rightarrow$ **G**, showing the 3D geometry. Depict only one reaction center. The main carbon chain can be represented as an R group.

The synthesis of [2]catenane **L** uses the template effect of a copper complex:



7.7 Write the full electronic configuration of Cu(0) in its ground state. Give the oxidation state of Cu in complex **J** and write the electronic configuration of Cu in the free ion corresponding to **J**.

7.8 Select the geometry of the copper ion in **L**. Assuming an ideal geometry of the ligands around the copper center, draw the electronic levels of the d-orbitals in accord with the crystal field theory. Fill the orbital diagram. Give the maximum value of the spin (S) for this complex. The geometry of the Cu in **L** is:

- ☐ octahedral,
- ☐ tetrahedral,
- ☐ square planar,
- ☐ trigonal bipyramidal.

7.9 Out of the following compounds, choose the one(s) that can remove the copper ion in **L** to obtain the free [2]catenane (tick relevant boxes):

- ☐ CH_3CN
- ☐ NH_4PF_6
- ☐ KCN
- ☐ tren

In [2]catenane **L**, the copper ion can exist in two oxidation states (+I) or (+II), and each of them exhibits a different coordination sphere (tetra- or penta-coordinated, respectively).

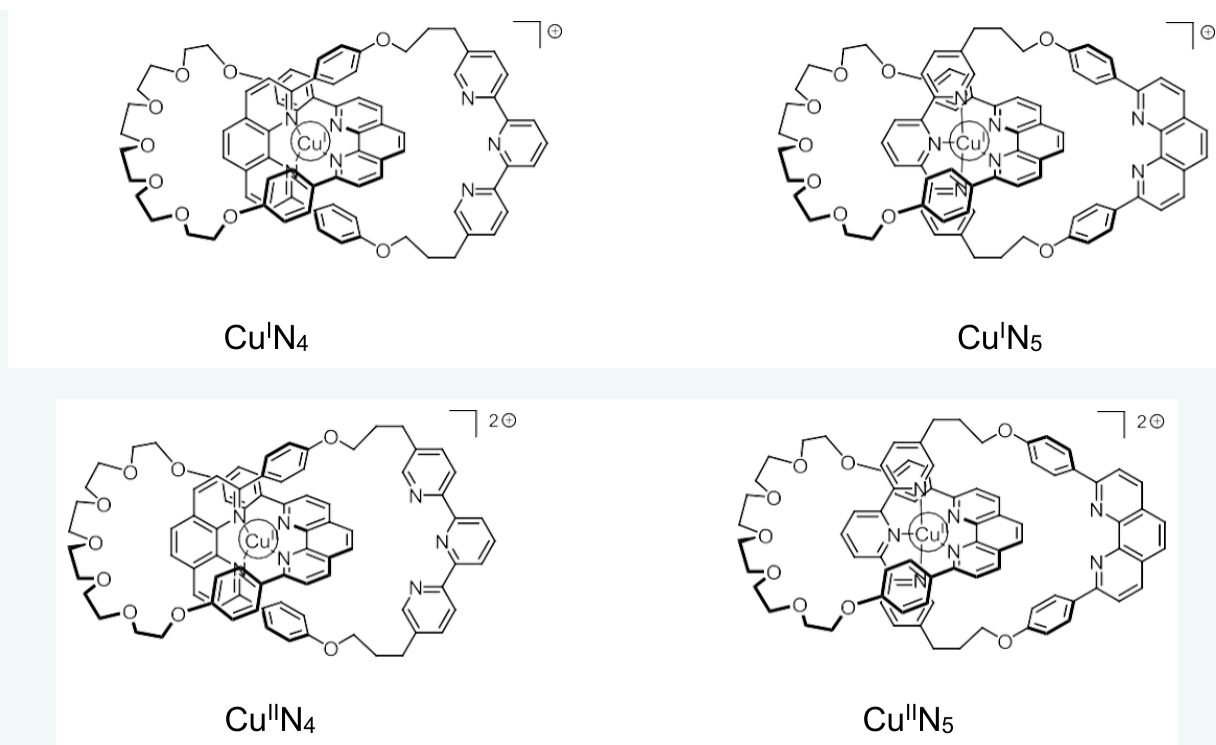


Fig. 2 – [2] catenate L states

The stability of Cu(I) complexes can be inferred by comparing their electronic structures to that of a noble gas.

7.10 Fill in the blanks with a number or a tick:

- The $\text{Cu}^{\text{I}}\text{N}_4$ complex has (number) electrons in the coordination sphere of the metal.
- The $\text{Cu}^{\text{I}}\text{N}_5$ complex has (number) electrons in the coordination sphere of the metal.
- The $\text{Cu}^{\text{I}}\text{N}_4$ complex is (tick):

- ☐ more stable than the $\text{Cu}^{\text{I}}\text{N}_5$ complex or
- ☐ less stable than the $\text{Cu}^{\text{I}}\text{N}_5$ complex.

7.11 Fill in the solid boxes with the designation of the involved complexes in Fig. 2 and complete the sequence to achieve electrochemical control of the system using the following notation for the dashed boxes:



(rotation) ; $+e^-$; $-e^-$.

Official English text of the problem.

Answers

Here, **terpyridine** means the 2, 2' : 6', 2''-terpyridine framework. SMILES are given at the first identification of each requested structure; subsequent letter labels refer to those structures.

- **7.1 — B:** The dilithium derivative of **A**, with both methyl substituents converted into $-\text{CH}_2-$ carbanions: **5,5''-bis(lithiomethyl)-2,2':6',2''-terpyridine**.

SMILES: [Li+].[Li+].[CH2-]c1ccc(-c2cccc(-c3ccc([CH2-])cn3)n2)nc1

- **7.2 — E, F and G:**

- **E:** 5,5''-Bis(3-hydroxypropyl)-2,2':6',2''-terpyridine.

SMILES: OCCCC1CCC(-C2CCCC(-C3CCC(CCCO)CN3)N2)NC1

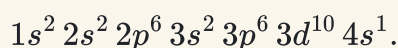
- **F:** 5,5''-Bis[3-(methanesulfonyloxy)propyl]-2,2':6',2''-terpyridine.

SMILES: CS(=O)(=O)OCCCC1CCC(-C2CCCC(-C3CCC(CCCOS(=O)(=O)C)CN3)N2)NC1

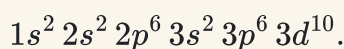
- **G:** 5,5''-Bis(3-bromopropyl)-2,2':6',2''-terpyridine.

SMILES: BrCCCC1CCC(-C2CCCC(-C3CCC(CCCBr)CN3)N2)NC1

- **7.3:** Select H^+ , H_2O only: aqueous acid removes the THP protecting groups.
- **7.4:** Select **a leaving group**.
- **7.5:** Select $\text{S}_{\text{N}}2$ only.
- **7.6:** Draw an $\text{S}_{\text{N}}2$ transition state with **$\text{Br}\cdots\text{C}\cdots\text{O}$ collinear**, partially formed $\text{C}-\text{Br}$ and partially broken $\text{C}-\text{O}$ bonds. The carbon's R, H, and H substituents lie in a plane perpendicular to that axis.
- **7.7:** Copper atom, [Cu]:



Copper in **J** is **+I**. The free copper(I) ion, [Cu+], has:



- **7.8: Tetrahedral;** lower e orbitals and upper t_2 orbitals, occupied as $e^4 t_2^6$. Every d orbital is doubly occupied; $S_{\text{max}} = 0$.
- **7.9:** Select **KCN and tren**:
- Potassium cyanide: [K+].[C-]#N
- Tris(2-aminoethyl)amine, tren: NCCN(CCN)CCN
- **7.10: 18 electrons, 20 electrons, and $\text{Cu}^{\text{I}}\text{N}_4$ is more stable.** The corresponding effective atomic numbers, including the metal's core electrons, are 36 and 38.
- **7.11:** The cycle is



Solution

7.1 — Formation and structure of B

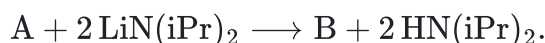
Compound **A** is **5,5''-dimethyl-2,2':6',2''-terpyridine**, SMILES

Cc1ccc(-c2cccc(-c3ccc(C)cn3)n2)nc1.

Lithium diisopropylamide, **LDA**, is a strong, sterically hindered base:

[Li+].CC(C)[N-]C(C)C.

Each equivalent removes one proton from one of the methyl substituents. With two equivalents, both methyl groups become pyridylmethyl carbanions:



The conjugate acid is **diisopropylamine**, CC(C)NC(C)C.

To draw **B**, retain all three pyridine rings and their connections exactly as in **A**, and replace each $-\text{CH}_3$ group by $-\text{CH}_2^-$. Include two Li^+ counterions. The ionic SMILES in the Answers does not specify lithium coordination or aggregation.

The electrophile **C** is **2-(2-bromoethoxy)tetrahydro-2H-pyran**, BrCCOC1CCCCO1.

Each carbanion attacks its primary brominated carbon:



Consequently, each arm in **D** is



The original methyl carbon supplies the first methylene; **C** supplies the next two.

7.2 — Structures of E, F and G

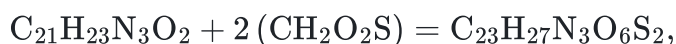
The terpyridine skeleton and the two three-carbon side chains remain unchanged throughout these transformations. Only the terminal functional groups change:

Compound	Each substituent at positions 5 and 5''	Molecular formula
E	$-\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	$\text{C}_{21}\text{H}_{23}\text{N}_3\text{O}_2$
F	$-\text{CH}_2\text{CH}_2\text{CH}_2\text{OS}(=\text{O})_2\text{CH}_3$	$\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}_6\text{S}_2$
G	$-\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}$	$\text{C}_{21}\text{H}_{21}\text{Br}_2\text{N}_3$

Thus:

1. Removing the THP groups gives the diol **E**.
2. Mesylating both alcohol groups gives the dimesylate **F**.
3. Replacing both mesylate groups with bromide gives the dibromide **G**.

As a consistency check, converting each alcohol to a mesylate adds a net $\text{CH}_2\text{O}_2\text{S}$. Therefore,



which matches the formula printed for **F**.

7.3 — Conditions for D → E

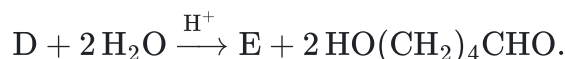
Compound **D** is **5,5''-bis[3-(tetrahydro-2H-pyran-2-yloxy)propyl]-2,2':6',2''-terpyridine**, SMILES c1cc(-c2ccc(CCCOC3CCCCO3)cn2)nc(-c2ccc(CCCOC3CCCCO3)cn2)c1.

Its THP ethers are acetals. Acetals undergo acid-catalysed hydrolysis, regenerating the protected alcohols. Select:



Here the proton is $[\text{H}^+]$ and water is O .

A balanced equation, writing the THP-derived product in its open-chain form, is



The coproduct is **5-hydroxypentanal**, $\text{O}=\text{CCCCCO}$, which can equilibrate with its cyclic hemiacetal.

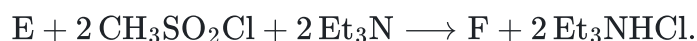
The other listed conditions do not perform the required deprotection:

- Aqueous hydroxide does not normally hydrolyse an acetal.
- Sodium borohydride in methanol does not cleave these THP acetals.
- Hydrogen with Pd/C is not the appropriate hydrogenolysis method for THP ethers.

No absolute configuration is specified at the THP acetal carbons in the problem, so the corresponding SMILES leave that stereochemistry unspecified.

7.4 — Role of MsCl

Methanesulfonyl chloride, or mesyl chloride, is $\text{CS}(=\text{O})(=\text{O})\text{Cl}$. It converts each alcohol into a methanesulfonate ester:



Triethylamine, $\text{CCN}(\text{CC})\text{CC}$, accepts the protons and gives **triethylammonium chloride**, $\text{CC}[\text{NH}^+](\text{CC})\text{CC} \cdot [\text{Cl}^-]$.

The conversion replaces a poor leaving group, hydroxide, with a good leaving group, **methanesulfonate**, also called **mesylate**, $\text{CS}(=\text{O})(=\text{O})[\text{O}^-]$.

The correct choice is therefore **a leaving group**.

7.5 — Mechanism of F → G

Lithium bromide, $[\text{Li}^+] \cdot [\text{Br}^-]$, supplies **bromide ions**, $[\text{Br}^-]$. Bromide attacks the primary carbon bearing the mesylate group and displaces mesylate:



The salt byproduct is **lithium methanesulfonate**, $[\text{Li}^+] \cdot \text{CS}(=\text{O})(=\text{O})[\text{O}^-]$.

This is an $\text{S}_{\text{N}}2$ reaction because:

- substitution occurs at a primary, saturated carbon;
- bromide is a nucleophile;
- mesylate is a good leaving group;
- **acetone**, $\text{CC}(=\text{O})\text{C}$, is a polar aprotic solvent favourable for this substitution.

The reacting carbon is not aromatic, and formation of a primary carbocation is unnecessary.

7.6 — Transition state and its three-dimensional geometry

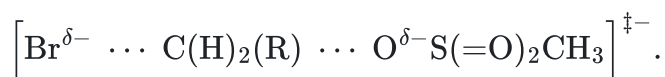
For one reaction centre, write the substrate as RCH_2OMs , a **primary alkyl methanesulfonate**, with generic SMILES $*\text{COS}(=\text{O})(=\text{O})\text{C}$. The asterisk represents the remainder of the molecule.

The single concerted substitution step is



The corresponding **primary alkyl bromide** has generic SMILES *CBr.

A schematic transition state is



The required drawing should show:

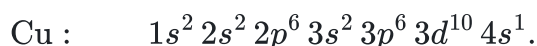
- The incoming bromide and departing oxygen on opposite sides of carbon, with $\angle \text{Br}-\text{C}-\text{O} = 180^\circ$.
- Dashed or dotted axial bonds for the forming C–Br bond and breaking C–O bond.
- The three remaining substituents, R, H, and H, approximately 120° apart in a plane perpendicular to the attack axis.
- An overall charge of -1 and a transition-state double dagger.

For a perspective drawing, place the attack axis horizontally, use an ordinary bond to R, and use a solid wedge and a hashed wedge for the two hydrogen bonds.

Electron flow is from a bromide lone pair to carbon, while the C–O bonding pair moves onto the departing oxygen. Ordinary SMILES cannot encode the fractional bonds of this transition state. Backside attack produces inversion of the local tetrahedral arrangement, although this particular carbon is not stereogenic because it bears two hydrogens.

7.7 — Copper configurations and oxidation state in J

Copper has atomic number 29. Its ground-state configuration is



Thus the ground state is $[\text{Ar}] 3d^{10} 4s^1$, rather than $[\text{Ar}] 3d^9 4s^2$.

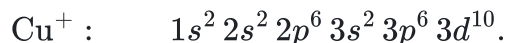
The nitrogen donors in **J** are neutral, and the complex is singly positively charged. Therefore,

$$\boxed{\text{oxidation state of copper in J} = +\text{I}}.$$

Ionisation removes the 4s electron:



The free copper(I) ion consequently has



7.8 — Geometry, crystal-field splitting and spin

In **L**, copper(I) binds two bidentate phenanthroline sites, giving four nitrogen donors. Its approximately **tetrahedral** coordination is idealised as T_d for the requested orbital diagram.

In a tetrahedral field, the *e* pair lies below the t_2 triplet:

Level	Orbitals	Energy relative to the barycentre	Occupation
Higher t_2	d_{xy}, d_{xz}, d_{yz}	$+\frac{2}{5}\Delta_t$	$\uparrow\downarrow \uparrow\downarrow \uparrow\downarrow$
Lower <i>e</i>	$d_{z^2}, d_{x^2-y^2}$	$-\frac{3}{5}\Delta_t$	$\uparrow\downarrow \uparrow\downarrow$

To draw the diagram, put two degenerate horizontal lines below three degenerate horizontal lines, and place two opposite-spin electrons on every line:

$$d^{10} = e^4 t_2^6.$$

All electrons are paired, so

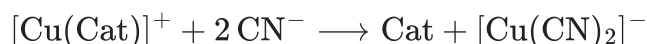
$$S_{\max} = 0.$$

7.9 — Removal of copper

Select **potassium cyanide** and **tren**.

Cyanide forms very stable copper(I) complexes and competes effectively with the catenane's nitrogen donors. Tren—**tris(2-aminoethyl)amine**—is a tetradentate ligand that can sequester copper through chelation.

Let Cat denote the neutral, mechanically interlocked catenane. Representative ligand-displacement equations are



and



The exact cyanide coordination number can depend on cyanide concentration; the first equation illustrates formation of **dicyanidocuprate(I)**. Its component SMILES is [Cu+].[C-]#N.[C-]#N, with two carbon-bound cyanide ligands.

The **copper(I)–tren complex** has component SMILES [Cu+].NCCN(CCN)CCN, with nitrogen coordination supplied by tren.

Acetonitrile, CC#N, is insufficiently competitive against the chelating catenane under the intended conditions. **Ammonium hexafluorophosphate**, [NH4+].[F-](F)(F)(F)(F)F, does not provide a suitable copper-sequestering ligand.

Removing copper does not separate the two closed rings: their mechanical interlocking remains.

7.10 — Electron counts and relative stability

Copper(I) supplies ten d electrons. Each neutral nitrogen donor contributes one lone pair, or two electrons.

For the four-coordinate state,

$$N_e(\text{Cu}^{\text{I}}\text{N}_4) = 10 + 4(2) = \boxed{18}.$$

For the five-coordinate state,

$$N_e(\text{Cu}^{\text{I}}\text{N}_5) = 10 + 5(2) = \boxed{20}.$$

Including the metal's 18 core electrons gives effective atomic numbers

$$18 + 18 = 36$$

and

$$18 + 20 = 38,$$

respectively. The first corresponds to krypton.

Within the electron-counting argument requested in the problem, the four-coordinate copper(I) state attains the favourable 18-electron count. Hence,

$$\boxed{\text{Cu}^{\text{I}}\text{N}_4 \text{ is more stable than } \text{Cu}^{\text{I}}\text{N}_5}.$$

7.11 — Electrochemically controlled cycle

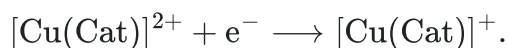
Electron transfer changes the oxidation state first. Subsequent relative rotation of the rings changes which binding site coordinates copper.

Step	Starting state	Operation	Result
1	$\text{Cu}^{\text{I}}\text{N}_4$	Remove one electron	$\text{Cu}^{\text{II}}\text{N}_4$
2	$\text{Cu}^{\text{II}}\text{N}_4$	Ring rotation	$\text{Cu}^{\text{II}}\text{N}_5$
3	$\text{Cu}^{\text{II}}\text{N}_5$	Add one electron	$\text{Cu}^{\text{I}}\text{N}_5$
4	$\text{Cu}^{\text{I}}\text{N}_5$	Ring rotation	$\text{Cu}^{\text{I}}\text{N}_4$

The balanced electron-transfer steps, with Cat denoting the unchanged catenane framework, are



and



The donor sets are:

- **N4:** one phenanthroline from each macrocycle, giving $2 + 2 = 4$ nitrogen donors.
- **N5:** the phenanthroline of the smaller macrocycle and the terpyridine of the larger macrocycle, giving $2 + 3 = 5$ nitrogen donors.

The N4 and N5 labels count coordinated nitrogen atoms; the molecular framework does not gain or lose nitrogen during rotation.

For the requested complex identifications, the following **component SMILES** specify the complete covalent ring structures and copper charge. Cu–N coordination is specified by the donor descriptions above. Mechanical interlocking and relative ring conformations are not encoded by these strings.

Copper(I) [2]catenane, encompassing the $\text{Cu}^{\text{I}}\text{N}_4$ and $\text{Cu}^{\text{I}}\text{N}_5$ coordination states:

```
[Cu+] .01CCCc2ccc(-c3cccc(-c4ccc(CCCOc5ccc(-c6ccc7ccc8ccc(-c9ccc1cc9)nc8c7n6)cc5)cn4)n3)nc2.01CCOCCOCCOCCOCCOCCOc2ccc(-c3ccc4ccc5ccc(-c6ccc1cc6)nc5c4n3)cc2
```

Copper(II) [2]catenane, encompassing the $\text{Cu}^{\text{II}}\text{N}_4$ and $\text{Cu}^{\text{II}}\text{N}_5$ coordination states:

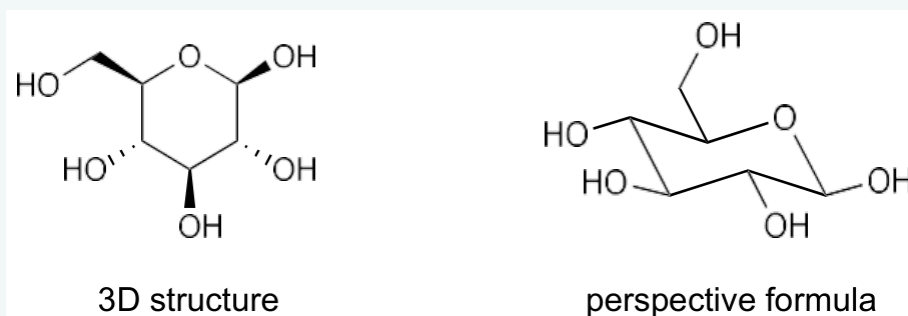
```
[Cu+2] .01CCCc2ccc(-c3cccc(-c4ccc(CCCOc5ccc(-c6ccc7ccc8ccc(-c9ccc1cc9)nc8c7n6)cc5)cn4)n3)nc2.01CCOCCOCCOCCOCCOCCOc2ccc(-c3ccc4ccc5ccc(-c6ccc1cc6)nc5c4n3)cc2
```

In each case the two organic components must be understood as **mechanically interlocked**, not as separate, freely separable molecules.

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

Problem 8: Identification and synthesis of inositols

In this problem, we define "3D structure" and "perspective formula" as indicated for β -glucose in the following figure.



Inositols are cyclohexane-1,2,3,4,5,6-hexols. Some of these 6-membered carbocycles, in particular *myo*-inositol, are involved in a number of biological processes.

Structure of *myo*-inositol

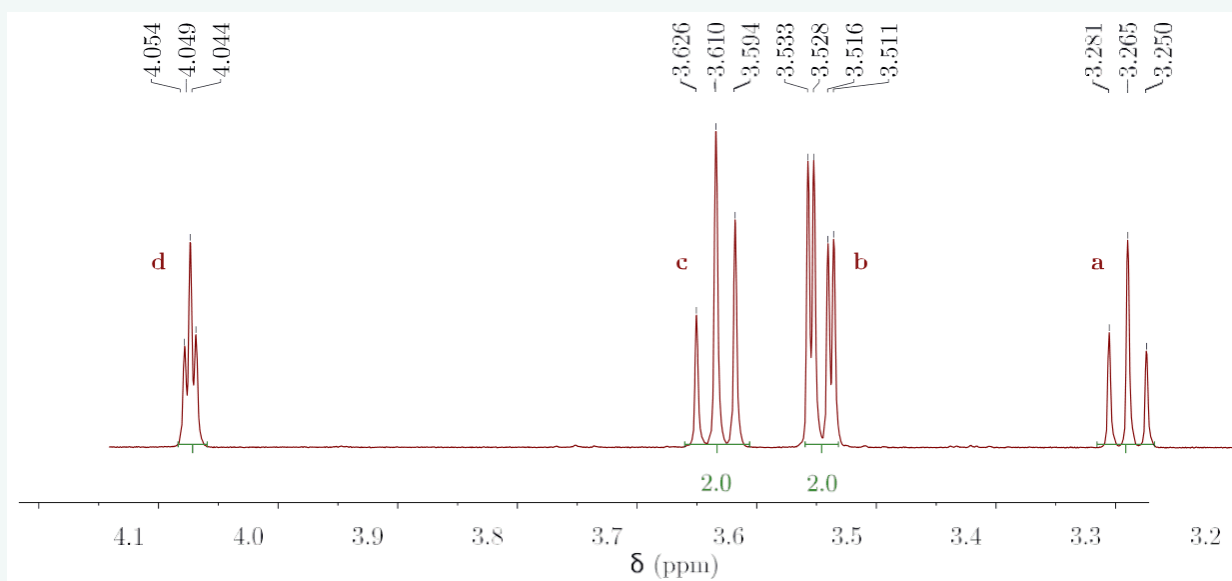
8.1 Draw the structural formula of inositols, without stereochemical details.

This family of molecules contains 9 different stereoisomers, including enantiomers.

8.2 Draw all 3D structures of the stereoisomers that are optically active.

The structure of a specific inositol, called *myo*-inositol, is studied here. Only one of its chair conformers is predominant and its structure can be deduced from its ^1H NMR spectrum. The spectrum below (next page) was obtained at 600 MHz in D_2O . No other signal from that compound was observed in the spectrum. The integration is indicated on the spectrum below each signal.

8.3 Give the molecular formula of the predominant compound derived from *myo*-inositol in this sample that is consistent with the number of protons observed in the ^1H NMR spectrum.

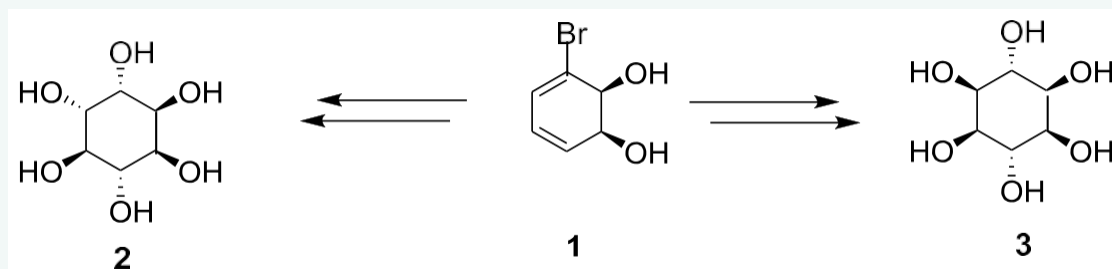


8.4 Based on the number and integrations of the proton signals, give the number of symmetry plane(s) that exist(s) in this molecule.

8.5 Complete the following perspective drawing of the most stable conformation of *myo*-inositol. Then label each hydrogen with the corresponding letter (a, b, c or d) according to the NMR spectrum above. Proton a must be on carbon a on the following representation. Draw its 3D structure.

Synthesis of inositols

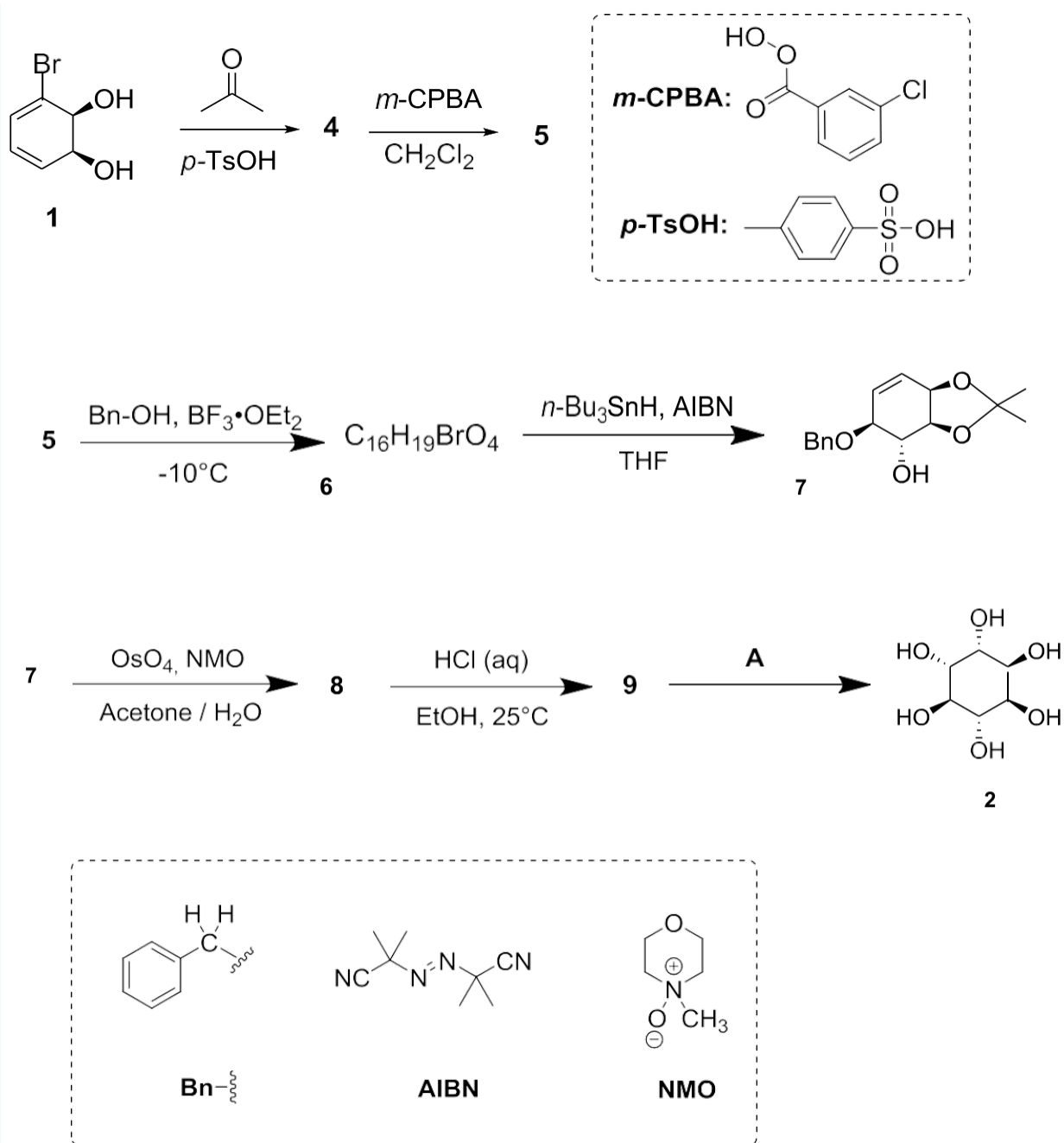
For medicinal applications, it is useful to synthesize some inositol phosphates on a large scale. We will study the synthesis of inositol **2** from bromodiol **1**.



8.6 Choose the correct structural relationship(s) between **2** and **3**. Tick relevant boxes.

- ☐ enantiomers
- ☐ epimers
- ☐ diastereomers
- ☐ atropoisomers

Inositol **2** can be obtained from compound **1** in 7 steps.



8.7 Draw the 3D structure of **4**.

8.8 The reaction leading to **5** occurs on the double bond with the highest electron density. Consider the structure of 1-bromo-1,3-cyclohexadiene below which is a substructure of **4**. Circle the double bond with the highest electron density. Represent all the electronic effects due to the bromine.

8.9 Draw the 3D structure of the major diastereoisomer **5**.

8.10 Give the total number of stereoisomers of **5** possibly obtained by this synthesis starting from enantiopure compound **1**.

8.11 For the step **5** → **6**, another product with the same molecular formula, denoted **6'**, can be produced. Draw the 3D structures of **6** and **6'**.

8.12 Draw the 3D structures of major diastereomers **8** and **9**.

8.13 Select the right set(s) of conditions **A** to obtain **2**. Tick relevant boxes.

- ☐ H_2 , Pd/C
- ☐ K_2CO_3 , HF
- ☐ HCOOH , H_2O
- ☐ $\text{BF}_3 \cdot \text{OEt}_2$

8.14 If the bromine is not present in compound **1**, in addition to **2**, another stereoisomer would be obtained. Considering that stereoselectivity of the reactions that take place in the synthesis remains unchanged and that the following steps involve the same number of equivalents as for **2**, draw the 3D structure of this stereoisomer and give its relationship with **2** (tick relevant boxes).

- ☐ enantiomers
- ☐ epimers
- ☐ diastereoisomers
- ☐ atropoisomers

8.15 During the synthesis of **2** from **1** choose the removal step(s) of protecting or directing groups.

☐ 1 → 4	☐ 7 → 8
☐ 4 → 5	☐ 8 → 9
☐ 5 → 6	☐ 9 → 2
☐ 6 → 7	

Official English text of the problem.

Answers

For precise drawing descriptions, number a hexagon **clockwise from its top vertex**: C1 at the top, C2 upper right, C3 lower right, C4 bottom, C5 lower left, and C6 upper left. This is working numbering, used consistently below.

A + denotes a solid wedge towards the reader; a – denotes a hatched wedge away. A six-sign sequence gives the directions of the carbon–oxygen bonds at C1–C6. At each saturated ring carbon, its hydrogen is on the opposite face.

- **8.1** Inositol, **cyclohexane-1,2,3,4,5,6-hexol**: a six-membered carbon ring bearing one hydroxy group on every carbon.
SMILES without stereochemistry: OC1C(O)C(O)C(O)C(O)C1O.
- **8.2** Only the **two chiro-inositol enantiomers**, the D/L pair, are optically active. Two mirror-image drawings are:

Chiro-inositol enantiomer I, also compound **2**: (–, +, +, –, +, –).

O[C@@H]1[C@H](O)[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

Chiro-inositol enantiomer II, its mirror image: (+, –, –, +, –, +).

O[C@H]1[C@H](O)[C@H](O)[C@@H](O)[C@H](O)[C@H]1O

- **8.3 Hydroxy-deuterated myo-inositol**, with molecular formula

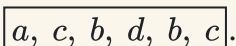


Its six hydroxy groups are predominantly OD.

SMILES: [2H]O[C@@H]1[C@@H](O[2H])[C@H](O[2H])[C@H](O[2H])[C@H](O[2H])[C@H]1O[2H].

- **8.4 One symmetry plane.**

- **8.5 Myo-inositol** has **five equatorial hydroxy groups and one axial hydroxy group** in its predominant chair. Hydrogen **d** is equatorial; the other five ring hydrogens are axial. Starting at the specified carbon a, the hydrogen labels around the ring are



A corresponding hexagonal drawing has hydroxy directions (−, +, −, −, −, +).

SMILES: O[C@@H]1[C@@H](O)[C@H](O)[C@H](O)[C@H](O)[C@H]1O.

- **8.6** Tick **epimers** and **diastereomers**.
- **8.7 Bromodiols acetone 4**: connect the two original oxygen atoms at C2 and C3 through a common $\text{C}(\text{CH}_3)_2$ group. Both ring carbon–oxygen bonds remain solid wedges. Retain bromine at C1 and double bonds $\text{C1}=\text{C6}$ and $\text{C4}=\text{C5}$.
SMILES: BrC1[C@@H](O2)[C@@H](OC2(C)C)C=CC=1.
- **8.8** Circle **$\text{C4}=\text{C5}$** , the double bond that does **not** bear bromine. Bromine exerts a **negative inductive effect**, $-I$, and a **positive mesomeric effect**, $+M$.
- **8.9 Epoxide 5**: epoxidize $\text{C4}=\text{C5}$, placing **both epoxide carbon–oxygen bonds on the hatched face**, opposite the acetone.
SMILES: BrC1[C@@H](O2)[C@@H](OC2(C)C)[C@H]3[C@H](O3)C=1.
- **8.10** $\boxed{2}$ stereoisomers: **two diastereomers**.
- **8.11** The two **regioisomeric benzyl-alcohol opening products** are:

6: C4 bears hatched OH; C5 bears solid-wedge OBn.

BrC1[C@@H](O2)[C@@H](OC2(C)C)[C@H](O)[C@@H](OCc2ccccc2)C=1

6': C4 bears solid-wedge OBn; C5 bears hatched OH.

BrC1[C@@H](O2)[C@@H](OC2(C)C)[C@@H](OCc2ccccc2)[C@H](O)C=1

Both retain the original acetonide and the brominated $\text{C1}=\text{C6}$ double bond.

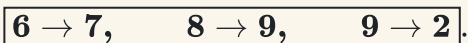
- **8.12 Protected chiro-inositol 8**: add hatched hydroxy groups at **both C1 and C6** of **7**, retaining its acetonide and benzyl ether.
O[C@@H]1[C@@H](O2)[C@@H](OC2(C)C)[C@H](O)[C@@H](OCc2ccccc2)[C@@H]1O

Monobenzyl-protected chiro-inositol 9: hydrolyse the acetonide of **8**, exposing solid-wedge hydroxy groups at C2 and C3. Retain the C5 benzyl ether.

O[C@@H]1[C@@H](O)[C@@H](O)[C@H](O)[C@@H](OCc2ccccc2)[C@@H]1O

- **8.13** Tick H_2 , Pd/C only.

- **8.14** The additional product is **the enantiomer of 2**, or **ent-2**. In the original ring orientation, its hydroxy directions are $(-, +, +, -, -, +)$.
SMILES: O[C@@H]1[C@H](O)[C@@H](O)[C@H](O)[C@H](O)[C@H]1O.
Tick **enantiomers** only.
- **8.15** Tick



Solution

8.1 — Inositol connectivity

Cyclohexane-1,2,3,4,5,6-hexol consists of six $\text{CH}(\text{OH})$ units joined into a ring. Thus, draw a hexagon with a hydroxy group attached by an ordinary single bond at every vertex, without wedges or hatches.

The molecular formula is $\text{C}_6\text{H}_{12}\text{O}_6$. Its constitution is represented by the non-stereochemical SMILES given in 8.1.

8.2 — Optically active stereoisomers

The nine configurational stereoisomers comprise seven achiral forms and one enantiomeric pair: **D- and L-chiro-inositol**.

This can be checked directly by assigning each hydroxy group one of the two ring faces. Rotating the hexagon cyclically preserves the sequence of face signs. Turning the hexagon over reverses their order and changes every sign. A mirror image changes every sign without reversing their order.

Classifying the face patterns under the proper rotations gives nine distinct configurations. Seven are equivalent to their own mirror images; the two chiro configurations are not.

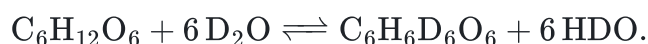
The pair specified in the Answers,



therefore gives the required two drawings. Every wedge becomes a hatch in the mirror image. Their configurations are encoded in the two stereochemical SMILES; a particular chair conformation is not encoded by SMILES.

8.3 — Exchange of hydroxy hydrogens

Each inositol molecule contains six carbon-bound hydrogens and six hydroxy hydrogens. In heavy water, the hydroxy hydrogens exchange with deuterium:



Heavy water is deuterium oxide, $[\text{2H}]\text{O}[\text{2H}]$; monodeuterated water is $[\text{2H}]\text{O}$.

The six carbon-bound hydrogens remain observable by ^1H NMR. The six deuteriums of the OD groups do not contribute to that spectrum. Consequently, the predominant isotopologue is



8.4 — Molecular symmetry

The four resonances represent proton populations



Thus, two ring hydrogens are individually unique, while the other four form two equivalent pairs.

A mirror plane passing through the carbons bearing **a** and **d** leaves those two hydrogens individually unchanged and exchanges the two **b** hydrogens and the two **c** hydrogens. The predominant chair therefore has **one mirror plane**.

In the working numbering, this plane passes through C1 and C4 and interchanges C2 with C6 and C3 with C5.

8.5 — NMR assignment and predominant chair

At a spectrometer frequency of 600 MHz,

$$J \text{ (Hz)} = 600 \text{ (Hz ppm}^{-1}) \times \Delta\delta \text{ (ppm)}.$$

For example, the separation between adjacent lines of signal **d** gives

$$J_d = 600(4.054 - 4.049) = 3.0 \text{ Hz}.$$

For signal **c**,

$$J_c \approx 600(3.626 - 3.610) = 9.6 \text{ Hz}.$$

For the doublet of doublets **b**, the two apparent couplings are

$$J_{\text{small}} = 600(3.533 - 3.528) = 3.0 \text{ Hz},$$

$$J_{\text{large}} = 600(3.533 - 3.516) = 10.2 \text{ Hz}.$$

The spectrum can therefore be summarized as follows. The values are apparent splittings read from the rounded peak labels.

Signal	Approximate δ / ppm	Number of hydrogens	Appearance	Coupling information
a	3.265	1	Triplet	Two large couplings, approximately 9–10 Hz
b	3.522	2	Doublet of doublets	One large coupling, approximately 10.2 Hz, and one small coupling, 3.0 Hz
c	3.610	2	Apparent triplet	Two similar large couplings, approximately 9.6 Hz
d	4.049	1	Triplet	Two small couplings, 3.0 Hz

In a cyclohexane chair, neighbouring axial hydrogens have approximately antiperiplanar geometry and a large vicinal coupling. An axial–equatorial pair gives a much smaller coupling.

Therefore:

- **a** is axial and has two axial **c** neighbours.
- Each **c** is axial, between axial **a** and axial **b**.
- Each **b** is axial, between axial **c** and equatorial **d**.
- **d** is equatorial and has two equivalent axial **b** neighbours.

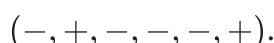
The ring sequence is consequently

$$\boxed{a - c - b - d - b - c}.$$

To fill the missing chair template, designate its required carbon a as C1 and follow this sequence around the ring. One precise chair description is:

Carbon	Hydrogen label	Hydrogen orientation	Hydroxy orientation
C1	a	Axial, up	Equatorial, down
C2	c	Axial, down	Equatorial, up
C3	b	Axial, up	Equatorial, down
C4	d	Equatorial, up	Axial, down
C5	b	Axial, up	Equatorial, down
C6	c	Axial, down	Equatorial, up

The corresponding hexagonal wedge-and-hatch drawing has hydroxy directions



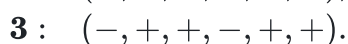
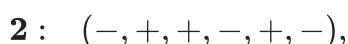
This chair has only **one axial hydroxy group**. Ring inversion would produce five axial hydroxy groups, increasing unfavourable axial interactions, so the depicted chair predominates.

8.6 — Relationship between 2 and 3

Compound **2** is the chiro-inositol enantiomer specified in 8.2.

Compound **3**, its C6 epimer, is a stereoisomer of cyclohexane-1,2,3,4,5,6-hexol with SMILES O[C@@H]1[C@@H](O)[C@@H](O)[C@H](O)[C@@H](O)[C@H]1O.

Their hydroxy configurations are



Only C6 changes configuration. They are therefore **epimers**, and hence also **diastereomers**. They are neither mirror images nor atropisomers.

8.7 — Formation of acetonide 4

Starting material **1** is the depicted enantiomer of **cis-3-bromocyclohexa-3,5-diene-1,2-diol**:



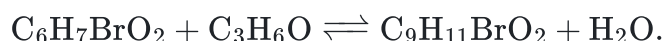
Acetone, or propan-2-one, CC(=O)C, reacts with the cis diol under catalysis by **p-toluenesulfonic acid**, Cc1ccc(S(=O)(=O)O)cc1.

The two diol oxygen atoms become connected through the carbon originally belonging to the acetone carbonyl group. The resulting bridge is



This forms a five-membered cyclic acetal, commonly called an **acetonide**. The original ring carbon-oxygen bonds are retained, so both remain solid wedges.

The balanced net reaction is



Water has SMILES o. Compound **4** has formula C9H11BrO2, and its complete stereochemical SMILES is given in the Answers.

8.8 — Bromine's electronic effects

The model substructure is **1-bromocyclohexa-1,3-diene**, BrC1=CC=CCC1. In the working numbering, its conjugated chain runs

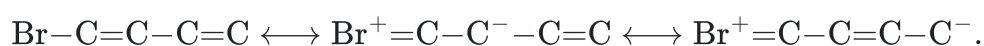


Bromine has two relevant electronic effects:

1. **Negative inductive effect**, $-I$. It withdraws electron density through the carbon–bromine sigma bond. Draw the bond-polarization arrow towards bromine. This withdrawal is strongest near the brominated double bond.
2. **Positive mesomeric effect**, $+M$. A bromine lone pair can donate into the conjugated system.

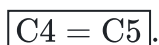
For the resonance arrows, draw a curved arrow from a bromine lone pair into the Br–C1 bond and move the C1=C6 π electrons onto C6. The resulting negative charge can then be delocalized: move the C6 lone pair into the C6–C5 bond and move the C5=C4 π electrons onto C4.

Omitting the rest of the ring, these contributors are



The corresponding charge-separated contributors of the model molecule can be encoded as [Br+]=C1[CH-]C=CCC1 and [Br+]=C1C=C[CH-]CC1. These are resonance contributors, not separate reaction products.

The double bond directly bearing bromine is more strongly depleted by its inductive effect. The more electron-rich double bond, and hence the one to circle, is



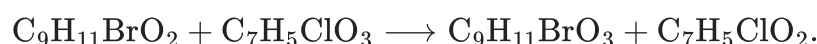
8.9 — Formation and configuration of epoxide 5

The reagent is **m-chloroperoxybenzoic acid**, or m-CPBA, OOC(=O)c1cccc(Cl)c1.

Peracid epoxidation transfers one oxygen atom to both carbons of an alkene in a concerted reaction. Thus, the two new carbon–oxygen bonds form on the same face.

The acetone occupies the solid-wedge face. Attack at C4=C5 from the less hindered opposite face gives the major epoxide **5**, with both epoxide carbon–oxygen bonds hatched. The original configurations at C2 and C3 are unchanged.

The balanced reaction is



The byproduct is **m-chlorobenzoic acid**, O=C(O)c1cccc(Cl)c1. The solvent, **dichloromethane**, is ClCCl.

8.10 — Number of possible stereoisomers of 5

Epoxidation can occur from either face of the selected double bond.

The original stereocentres of enantiopure **1** remain fixed, so the two products differ only in the face occupied by the epoxide. They are **diastereomers**.

The epoxide's two new centres are formed together with a fixed relative configuration; their configurations cannot be selected independently. Thus,

$$N = 2.$$

The minor epoxide, with both epoxide bonds on the solid-wedge face, has SMILES BrC1[C@@H](O2)[C@H](OC2(C)C)[C@H]3[C@@H](O3)C=1.

8.11 — Epoxide opening to **6** and **6'**

Benzyl alcohol, OCc1ccccc1, opens the Lewis-acid-activated epoxide.

Boron trifluoride diethyl etherate can be represented by its components as FB(F)F.CCOCC; in the actual adduct, the ether oxygen coordinates to boron. The disconnected SMILES does not encode that coordination bond.

Backside attack breaks the epoxide carbon–oxygen bond at the attacked carbon. The incoming benzyloxy group and the retained hydroxy group are consequently **anti**.

For **6**:

- Benzyl alcohol attacks C5.
- C5 changes from a hatched epoxide bond to a solid-wedge benzyloxy bond.
- The oxygen at C4 remains on the hatched face and becomes a hydroxy group.

For **6'**:

- Benzyl alcohol attacks C4.
- C4 acquires a solid-wedge benzyloxy group.
- C5 retains the hatched oxygen, which becomes a hydroxy group.

Both products satisfy the given molecular formula:



The displayed structure of **7** identifies **6** as the product having benzyloxy at C5 and hydroxy at C4.

The subsequent radical reaction replaces bromine by hydrogen without changing these stereocentres.

Protected cyclohexenetetrol 7 has SMILES

C1[C@@H](O2)[C@H](OC2(C)C)[C@H](O)[C@@H](OCc2ccccc2)C=1.

The balanced debromination is



Here the butyl groups are normal butyl groups. **Tri-*n*-butyltin hydride** is [SnH](CCCC)(CCCC)CCCC; **tri-*n*-butyltin bromide** is Br[Sn](CCCC)(CCCC)CCCC.

The radical initiator **AIBN**, 2,2'-azobis(2-methylpropanenitrile), is CC(C)(C#N)N=NC(C)(C)C#N. The solvent **tetrahydrofuran** is C1CCOC1.

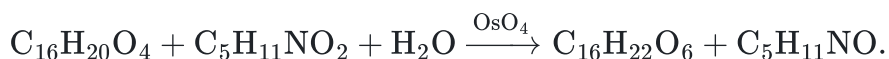
8.12 — Dihydroxylation and acetonide removal

Formation of 8. Osmium tetroxide, O=[Os](=O)(=O)=O, adds to the remaining C1=C6 double bond by **syn dihydroxylation**.

The less hindered face is opposite the solid-wedge acetonide and benzyloxy substituents. Both new hydroxy groups therefore occupy the hatched face, at C1 and C6. The pre-existing configurations remain unchanged.

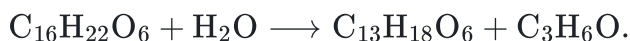
The reoxidant is **N-methylmorpholine N-oxide**, or NMO, C[N+](O-)(C)C(=O)OCC1. Its reduced product is **N-methylmorpholine**, CN1CCOCC1.

A balanced net equation for the catalytic oxidation is



Thus **8** is the benzyl/acetone-protected chiro-inositol specified in the Answers.

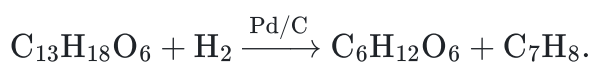
Formation of 9. Aqueous acid hydrolyses the acetone, regenerating the C2 and C3 hydroxy groups and releasing acetone. The original ring carbon–oxygen bonds are retained, so those hydroxy groups remain solid wedges.



The benzyl ether survives this treatment. Therefore, **9** is the C5 monobenzyl ether of **2**, with all six ring configurations already those required in the final product.

8.13 — Conditions for benzyl-ether removal

Hydrogen, [H][H], with palladium on carbon cleaves the benzyl ether by hydrogenolysis:



The organic byproduct is **toluene**, Cc1ccccc1.

Cleavage occurs at the benzyl–oxygen bond; the bond between the inositol carbon and oxygen remains intact. Consequently, the configuration at C5 is retained.

The correct choice is therefore



The other listed conditions do not provide the required benzyl-ether hydrogenolysis.

8.14 — Product obtained without bromine

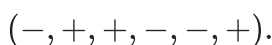
Without bromine, the starting cis diol becomes an achiral, symmetry-related diene, represented by C1[C@@H](O)[C@@H](O)C=CC=1.

The two double bonds are enantiotopic. The same face preference in epoxidation can therefore lead through either of two mirror-related reaction sequences.

One sequence epoxidizes C4=C5 and gives **2**. In the other:

1. C1=C6 is epoxidized on the hatched face.
2. Corresponding epoxide opening gives hatched hydroxy at C1 and solid-wedge benzyloxy at C6.
3. Syn dihydroxylation gives hatched hydroxy groups at C4 and C5.
4. Deprotection exposes all six hydroxy groups.

The final face sequence in the original orientation is



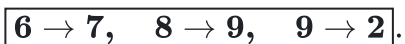
This is the mirror image of **2** after a rotation of the drawing. Its stereochemical SMILES is given in 8.14.

Although two positions appear different when the original atom labels are kept fixed, the correct whole-molecule relationship is **enantiomerism**, not epimerism. Tick **enantiomers** only.

8.15 — Removal of protecting or directing groups

Step	Group removed	Function in the synthesis
6 → 7	Bromine	Temporarily differentiates the two double bonds electronically
8 → 9	Acetonide	Protects the original cis diol
9 → 2	Benzyl group	Protects the hydroxy group introduced through epoxide opening

Thus the required removal steps are

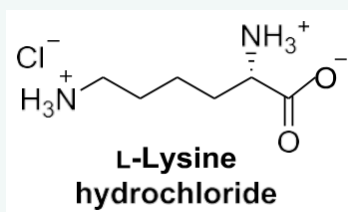


The answers were checked against the official answers published by the organisers.

Problem 9: Synthesis of levobupivacaine

Part I.

The local anesthetic bupivacaine (marketed as Marcaine) is on the World Health Organization List of Essential Medicines. Although the drug is currently used as a racemic mixture, it was demonstrated that one enantiomer of bupivacaine, levobupivacaine, is less cardiotoxic and, therefore, safer than the racemate. Levobupivacaine can be synthesized from the natural amino acid L-lysine.

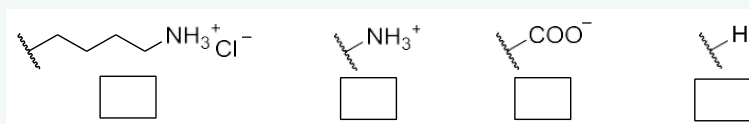


L-Lysine hydrochloride

9.1 Assign the absolute configuration of the stereogenic center in L-lysine hydrochloride and justify your answer by classifying the substituents in order of their priority.

Configuration: ☐ *R* ☐ *S*

Priority $1 > 2 > 3 > 4$:



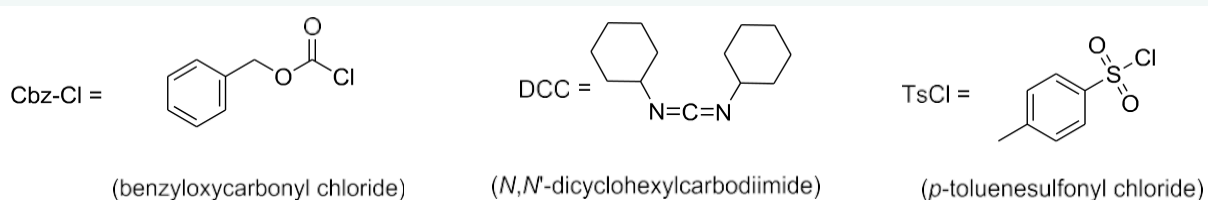
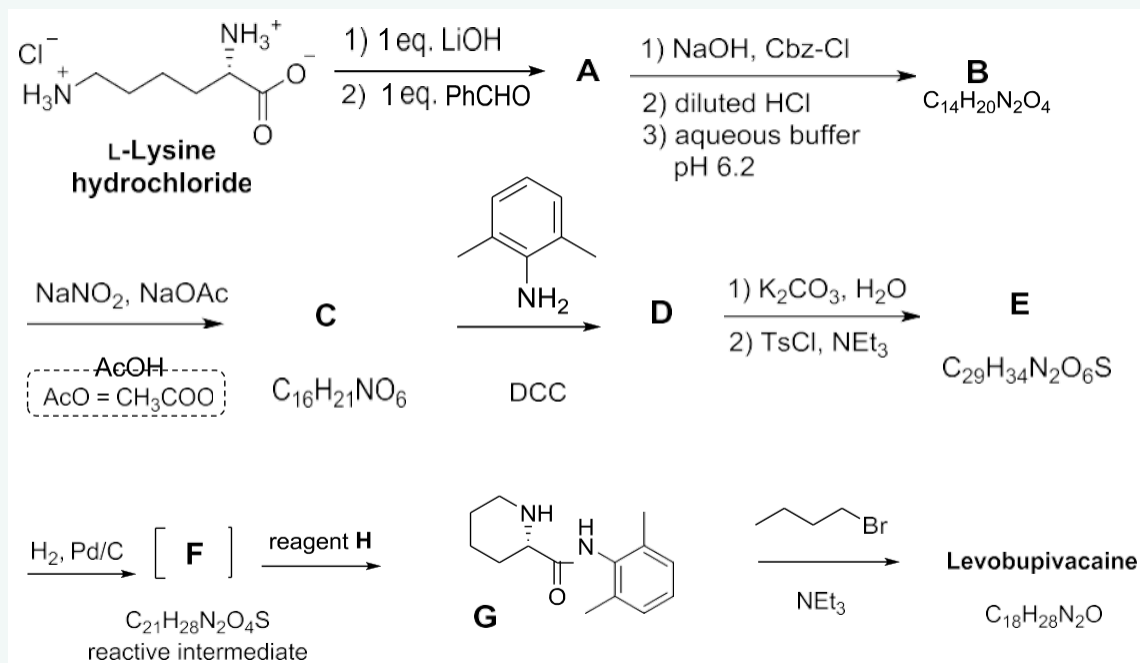
9.2 The prefix L in L-lysine refers to relative configuration. Choose all correct statements:

- ☐ Natural L-amino acids are levorotatory.
- ☐ Natural L-amino acids can be levorotatory or dextrorotatory.
- ☐ All natural L-amino acids are (*S*).
- ☐ All natural L-amino acids are (*R*).

Often, we want only one of the amino groups in L-lysine to react. A Cu^{2+} salt with excess aqueous hydroxide can selectively mask the reactivity of one of the amino groups. After the complex is formed, only the non-complexed NH_2 group is available to react.

9.3 Considering that L-lysine acts as a bidentate ligand and that two L-lysines coordinate to one Cu^{2+} ion in the presence of aqueous hydroxide, draw the structure of the intermediate complex.

Fortunately, in the synthesis of levobupivacaine shown below, the same amino group reacts even without Cu^{2+} salt.



From this point on, you can use the abbreviations proposed in the scheme above.

9.4 Draw the structure of compound **A**, including the appropriate stereochemistry.

9.5 Transformation of L-lysine into **A** is (choose proper answer(s)):

- ☐ an enantioselective reaction
- ☐ an enantiospecific reaction
- ☐ a regioselective reaction

9.6 Draw the structures of compounds **B – F**, including the appropriate stereochemistry.

9.7 What is the role of DCC in the transformation **C** $\rightarrow$ **D**? Tick relevant boxes.

- ☐ Protecting group for the amino group.
- ☐ Protecting group for the hydroxy group.
- ☐ Activating agent for the amide bond formation.

9.8 TsCl is used in the synthesis to enable (tick relevant boxes):

- ☐ Nucleophilic substitution of an amino group.
- ☐ Electrophilic substitution of an amino group.
- ☐ Nucleophilic substitution of a hydroxy group.
- ☐ Electrophilic substitution of a hydroxy group.

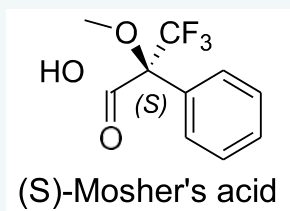
9.9 Mark all possible reagents which could be used as reagent **H**:

☐ diluted HCl	☐ Zn/HCl
☐ K ₂ CO ₃	☐ H ₂ SO ₄
☐ diluted KMnO ₄	☐ diluted NaOH
☐ SOCl ₂	☐ PCl ₅

9.10 Draw the structure of levobupivacaine, including the appropriate stereochemistry.

Part II.

The synthesis of levobupivacaine requires the use of enantiomerically pure L-lysine. A common method to confirm the enantiomeric purity of aminoacids is their transformation into amide using Mosher's acid (see the structure of the (*S*) isomer below).



(*S*)-Mosher's acid

9.11 Draw the structure of the amide formed when the α -amino group of L-lysine is derivatized with (*S*)-Mosher's acid. Clearly show the stereochemistry of each chiral center.

9.12 How many products will be formed from racemic lysine and (*S*)-Mosher's acid (consider that only the α -amino group of lysine is derivatized)? Tick relevant boxes.

- ☐ Two diastereoisomers.
- ☐ Four diastereoisomers.
- ☐ A racemic mixture of two enantiomers.
- ☐ Four compounds: two enantiomers and two diastereoisomers.

9.13 Choose the method(s) which can be used to quantitatively determine the enantiomeric purity of lysine after its derivatization with (*S*)-Mosher's acid. Tick the relevant boxes:

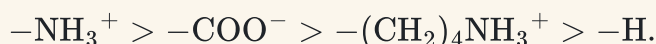
- ☐ NMR spectroscopy
- ☐ Liquid chromatography
- ☐ NMR spectroscopy
- ☐ Liquid chromatography

Official English text of the problem.

Answers

Cbz denotes benzyloxycarbonyl; Ts denotes *p*-toluenesulfonyl. The stereochemical SMILES below specify the configurations independently of any drawing orientation.

- **9.1:** *S*. Priorities:



Fill the four boxes, from left to right, with **3, 1, 2, 4**.

- **9.2:** Tick only **"Natural L-amino acids can be levorotatory or dextrorotatory."**
- **9.3:** **Bis(L-lysinato)copper(II)**, with each ligand coordinated through its α -amino nitrogen and one carboxylate oxygen. Both terminal amino groups remain free.

Dative-bond SMILES: [Cu+2]12(<-N[C@@H](CCCCN)C(=O)[O-]->1)<-N[C@@H](CCCCN)C(=O)[O-]->2

Draw a square-planar CuN_2O_2 core with two five-membered chelate rings; an arrangement with the two nitrogen donors opposite each other is suitable. The SMILES encodes the coordination connectivity, not this geometry.

- **9.4:** **A: N^ϵ -benzylidene-L-lysine**, shown as its zwitterion; the original stereocenter remains *S*.

[NH3+][C@@H](CCCCN=Cc1ccccc1)C(=O)[O-]

- **9.5:** Tick **"a regioselective reaction."**
- **9.6:** All five compounds retain the $2S$ configuration.

Compound	Name	Stereochemical SMILES
B	N^α -Cbz-L-lysine, zwitterionic form	<chem>O=C(OCc1ccccc1)N[C@@H](CCCC[NH3+])C(=O)[O-]</chem>
C	(2 <i>S</i>)-6-Acetoxy-2-(Cbz-amino)hexanoic acid	<chem>O=C(OCc1ccccc1)N[C@@H](CCCCOC(C)=O)C(=O)O</chem>
D	(2 <i>S</i>)-6-Acetoxy-2-(Cbz-amino)-N-(2,6-dimethylphenyl)hexanamide	<chem>O=C(OCc1ccccc1)N[C@@H](CCCCOC(C)=O)C(=O)Nc1c(C)cccc1C</chem>
E	(2 <i>S</i>)-2-(Cbz-amino)-N-(2,6-dimethylphenyl)-6-(tosyloxy)hexanamide	<chem>O=C(OCc1ccccc1)N[C@@H](CCCCOS(=O)(=O)c1ccc(C)cc1)C(=O)Nc1c(C)cccc1C</chem>
F	(2 <i>S</i>)-2-Amino-N-(2,6-dimethylphenyl)-6-(tosyloxy)hexanamide	<chem>N[C@@H](CCCCOS(=O)(=O)c1ccc(C)cc1)C(=O)Nc1c(C)cccc1C</chem>

- **9.7:** Tick **"Activating agent for the amide bond formation."**

DCC is **N,N'-dicyclohexylcarbodiimide**, C1CCCCC1N=C=NC1CCCCC1.

- **9.8:** Tick **"Nucleophilic substitution of a hydroxy group."**

TsCl is *p*-toluenesulfonyl chloride, Cc1ccc(S(=O)(=O)Cl)cc1.

- **9.9:** Tick **potassium carbonate**, K_2CO_3 , $[K^+].[K^+].[O^-]C(=O)[O^-]$, and **diluted sodium hydroxide**, $NaOH$, $[Na^+].[OH^-]$.
- **9.10:** **Levobupivacaine: (2S)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide.**

CCCCN1[C@@H](CCCC1)C(=O)Nc1c(C)cccc1C

- **9.11:** The α -N-[(S)-Mosher acyl] derivative of L-lysine. Both the Mosher center and the lysine center are *S*.

CO[C@@](C(F)(F)F)(c1ccccc1)C(=O)N[C@@H](CCCCN)C(=O)O

- **9.12:** Tick "Two diastereoisomers." Their configurations, ordered as (**Mosher center, lysine center**), are (*S*, *S*) and (*S*, *R*).
- **9.13:** **Both NMR spectroscopy and liquid chromatography.** Since the printed problem repeats both choices without qualification, all four printed entries describe applicable methods.

Solution

9.1 — Absolute configuration of L-lysine

The depicted L-lysine hydrochloride is **(S)-2,6-diaminohexanoic acid hydrochloride:**

[NH3+][C@@H](CCCC[NH3+])C(=O)[O-].[Cl-]

For the stereogenic carbon, compare the directly attached atoms. Nitrogen has higher atomic number than carbon, while hydrogen has the lowest:



To distinguish the two carbon substituents, compare the atoms attached to those carbons, counting a double bond according to the CIP duplicate-atom convention:

carboxylate carbon: (O, O, O),
side-chain carbon: (C, H, H).

Therefore,



In the supplied drawing, the amino group points away and the implicit hydrogen points toward the observer. The apparent clockwise $1 \rightarrow 2 \rightarrow 3$ sequence must therefore be reversed, giving *S*. The chloride counterion does not enter the priority comparison.

9.2 — Relative configuration and optical rotation

The designation **L** describes a relative stereochemical relationship; it does not specify the sign of optical rotation. Consequently, an L-amino acid can be levorotatory or dextrorotatory.

Nor does L always mean *S*. For example, **L-cysteine**, N[C@@H](CS)C(=O)O, has the *R* configuration: its sulfur-containing side chain outranks its carboxyl group in the CIP comparison.

Thus only the second statement is correct.

9.3 — Copper complex

In excess hydroxide, the carboxyl group is deprotonated and both amino groups can be present as neutral amines. Each lysinate ligand binds through:

1. the lone pair of the α -amino nitrogen;
2. one carboxylate oxygen.

This gives a favorable five-membered chelate ring with the sequence



Two such ligands give **bis(L-lysinato)copper(II)**, whose coordination SMILES is given in the Answers. Each ligand has charge -1 , so the complex with Cu^{2+} is neutral.

A balanced equation starting with the hydrochloride shown in the question is



The drawing should show two five-membered chelate rings around copper. Both stereocenters remain *S*, and both terminal ε -amino groups project outward without coordinating. Those terminal amino groups remain available for reaction.

9.4 — Identification of A

Benzaldehyde, O=Cc1ccccc1, condenses selectively with the terminal ε -amino group to form a **Schiff base**, or imine.

The sequence is:

- lithium hydroxide neutralizes one acid equivalent;
- the terminal amino group reacts with benzaldehyde;
- loss of water produces the terminal benzylidene imine.

The overall balanced equation is



Thus **A** is *N* $^\varepsilon$ -benzylidene-L-lysine. Its terminal group is $-\text{N}=\text{CHPh}$, while the α -amino group remains available for subsequent protection.

No bond at the stereogenic carbon is broken. Draw its substituents in the same spatial arrangement as in the starting lysine: *S*. The SMILES leaves the imine's *E/Z* geometry unspecified because the scheme does not establish it.

9.5 — Classification of the transformation

The reaction distinguishes between two amino groups at different positions and forms the imine at the terminal ε -amino group. It is therefore **regioselective**.

No new stereogenic center is generated, and the reaction does not select between enantiomers. The existing *S* center is simply preserved. Accordingly, "enantioselective" is not appropriate.

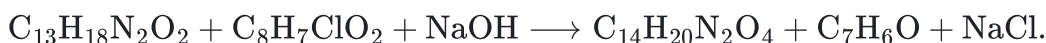
9.6 — Identification of B–F

The sequence uses the terminal imine as a temporary protecting group, allowing the α -amino group to be protected independently.

A → B: protect the α -amino group, then remove the imine.

Benzyl chloroformate, or Cbz–Cl, O=C(Cl)OCc1ccccc1, converts the free α -amino group into a Cbz carbamate. Diluted hydrochloric acid then hydrolyzes the terminal imine, releasing benzaldehyde and restoring the terminal amino group.

A balanced net equation for protection followed by imine hydrolysis is



The acid/base work-up establishes the final protonation state. At pH 6.2, **B**, N^α -Cbz-L-lysine, is predominantly represented with a carboxylate and a terminal ammonium group, as shown in its SMILES.

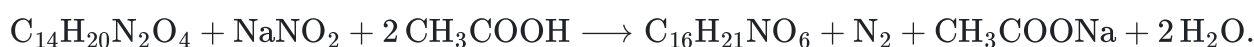
Its molecular formula is the supplied $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_4$.

B → C: replace the terminal amino group with acetate.

Acidified nitrite generates nitrous acid, $\text{ON}=\text{O}$. The unprotected terminal primary amine undergoes nitrosation and deamination, releasing nitrogen. In the acetic acid/acetate medium, the terminal carbon acquires an acetoxy group.

Acetic acid is CC(=O)O; an acetoxy substituent has connectivity $-\text{O}-\text{C}(=\text{O})-\text{CH}_3$.

A balanced net equation consistent with the reagents is



The protected α -nitrogen remains intact. Thus **C** is the terminal acetate, with formula $\text{C}_{16}\text{H}_{21}\text{NO}_6$. This formula distinguishes it from the corresponding terminal alcohol.

C → D: form the aromatic amide.

The carboxylic acid reacts with **2,6-dimethylaniline**, Nc1c(C)cccc1C, using DCC as the coupling reagent. The terminal acetate and the Cbz group remain intact.

DCC becomes **N,N'-dicyclohexylurea**, O=C(NC1CCCCC1)NC1CCCCC1.

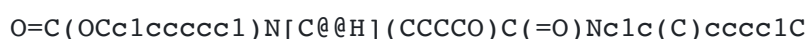
The balanced coupling equation is



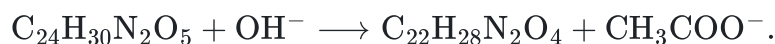
Therefore **D** is the N -(2,6-dimethylphenyl) carboxamide, with formula $\text{C}_{24}\text{H}_{30}\text{N}_2\text{O}_5$.

D → E: hydrolyze the acetate, then form the tosylate.

Aqueous potassium carbonate removes the terminal acetyl protecting group. The intermediate is **(2S)-2-(Cbz-amino)-N-(2,6-dimethylphenyl)-6-hydroxyhexanamide**:



Its formula is $\text{C}_{22}\text{H}_{28}\text{N}_2\text{O}_4$. The hydrolysis can be balanced in ionic form:



The resulting alcohol reacts with TsCl and **triethylamine**, CCN(CC)CC, to give the terminal tosylate **E**:



The product formula agrees with the supplied $C_{29}H_{34}N_2O_6S$.

E → F: remove the Cbz group by hydrogenolysis.

Hydrogen over palladium on carbon removes the Cbz protecting group. The products accompanying the free amine are **toluene**, Cc1ccccc1, and **carbon dioxide**, $O=C=O$:



Thus **F** contains a free α -amino group and a terminal tosylate. Its formula is the supplied $C_{21}H_{28}N_2O_4S$.

Throughout **B–F**, the bonds at the original stereogenic carbon retain their spatial arrangement. Nitrogen remains its highest-priority substituent, the carboxyl-derived group remains second, and the side chain remains third. Every compound therefore remains *2S*.

9.7 — Role of DCC

DCC activates the carboxyl group of **C** for amide formation.

The carboxyl group reacts with the carbodiimide to form an activated acyl intermediate, conventionally described as an **O-acylisourea**. The aniline nitrogen attacks the acyl carbon, and collapse of the intermediate gives the amide **D** and dicyclohexylurea.

DCC is therefore an **activating agent for amide bond formation**, not an amino- or hydroxy-protecting group.

9.8 — Role of TsCl

An unmodified hydroxy group is a poor leaving group. Tosylation converts it into a sulfonate ester, $-OTs$.

During the subsequent ring closure, the amino nitrogen attacks the carbon bearing that group and expels the ***p*-toluenesulfonate anion**, Cc1ccc(S(=O)(=O)[O-])cc1.

Consequently, TsCl enables **nucleophilic substitution of the hydroxy group**, after its conversion into a tosylate.

9.9 — Reagent H and ring closure

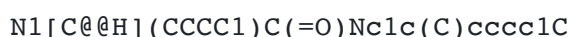
The free α -amino group in **F** attacks the terminal carbon bearing the tosylate through an intramolecular S_N2 reaction. The resulting ring contains:

- the amino nitrogen;
- the original stereogenic carbon;
- the four intervening methylene carbons.

It is therefore a **six-membered piperidine ring**.

The immediate cyclization product is an ammonium species; base removes a proton to give the neutral secondary amine. A base also keeps the starting amine available in its unprotonated, nucleophilic form. Suitable choices are **potassium carbonate** and **diluted sodium hydroxide**.

The product **G** is **(2S)-N-(2,6-dimethylphenyl)piperidine-2-carboxamide**:



Balanced equations for the two acceptable bases are



and



Acids protonate the amino group and suppress its nucleophilicity. The oxidizing, reducing, and chlorinating alternatives listed do not provide the required basic cyclization conditions.

The substitution occurs at a terminal methylene carbon, not at the original stereocenter. Its *S* configuration is retained.

9.10 — Levobupivacaine

The secondary ring nitrogen of **G** reacts with **1-bromobutane**, CCCCBr, by nucleophilic substitution, installing an *n*-butyl group. Triethylamine accepts the proton released in forming the neutral tertiary amine.

The balanced equation is

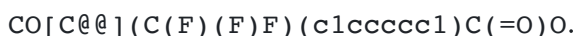


The resulting **levobupivacaine** is **(2*S*)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide**, with the SMILES given in the Answers.

For the requested drawing, use a piperidine ring bearing an *n*-butyl group on nitrogen and a -C(=O)-NH-(2,6-dimethylphenyl) substituent at C2. Show C2 as *S*. No particular chair conformation is required.

9.11 — Mosher amide of L-lysine

(S)-Mosher's acid, or **(S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid**, is

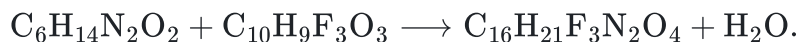


The neutral connectivity representation of **L-lysine** is



The Mosher carboxyl group forms an amide with the **α -amino nitrogen** of lysine. The lysine carboxyl group and terminal amino group remain unchanged.

The formal condensation balance is



This represents the net amidation; experimental formation of the amide requires suitable carboxyl activation.

Neither stereogenic carbon undergoes substitution. Both remain *S*. At the Mosher center, the priority order in the amide is

methoxy oxygen > trifluoromethyl carbon > amide carbonyl carbon > phenyl carbon.

Thus amidation also preserves the Mosher center's *S* descriptor.

For the drawing, connect the Mosher carbonyl carbon to lysine's α -nitrogen, and label both stereogenic centers *S*. The complete product SMILES is given in Answer 9.11; it uses the neutral acid/amine representation.

9.12 — Products from racemic lysine

Racemic lysine contains both configurations at its α -carbon. Reaction with a single enantiomer of Mosher's acid gives:

Product	Configuration: (Mosher, lysine)
(S)-Mosher amide of L-lysine	(S, S)
(S)-Mosher amide of D-lysine	(S, R)

The second product, **the α -N-[(S)-Mosher acyl] derivative of D-lysine**, has SMILES

CO[C@@](C(F)(F)F)(c1ccccc1)C(=O)N[C@H](CCCCN)C(=O)O.

These products differ at only one of their two stereogenic centers, so they are **diastereoisomers**. They are not mirror images: the Mosher center has the same configuration in both.

Therefore, **two diastereoisomers** are formed.

9.13 — Quantitative determination of enantiomeric purity

Derivatization converts the original enantiomers into diastereoisomers. These can have different properties even in an achiral analytical environment.

NMR spectroscopy: The two derivatives can give distinct chemical shifts. Integrating suitable resolved signals under quantitative conditions gives their molar ratio. The ^{19}F resonances of the trifluoromethyl groups are particularly useful because each derivative contributes three equivalent fluorine nuclei.

For integrals I_L, I_D representing p_L, p_D nuclei per molecule,

$$\frac{n_L}{n_D} = \frac{I_L/p_L}{I_D/p_D}.$$

Liquid chromatography: The diastereoisomers can have different retention times, including on a suitable achiral stationary phase. Resolved peak areas give their molar ratio after allowing for detector response factors:

$$\frac{n_L}{n_D} = \frac{A_L/r_L}{A_D/r_D},$$

where A_i is peak area and r_i is response per amount of substance.

The original lysine composition follows from

$$\%L = 100 \frac{n_L}{n_L + n_D},$$

and the magnitude of the enantiomeric excess is

$$ee(\%) = 100 \frac{|n_L - n_D|}{n_L + n_D}.$$

This requires derivatization without racemization and without unequal, uncorrected conversion of the two lysine enantiomers. Both listed analytical methods are therefore suitable.

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