

IChO 2009

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Problem 1: Estimating the Avogadro constant

Many different methods have been used to determine the Avogadro constant. Three different methods are given below.

Method A – from X-ray diffraction data (modern)

The unit cell is the smallest repeating unit in a crystal structure. The unit cell of a gold crystal is found by X-ray diffraction to have the face-centred cubic unit structure (i.e. where the centre of an atom is located at each corner of a cube and in the middle of each face). The side of the unit cell is found to be 0.408 nm.

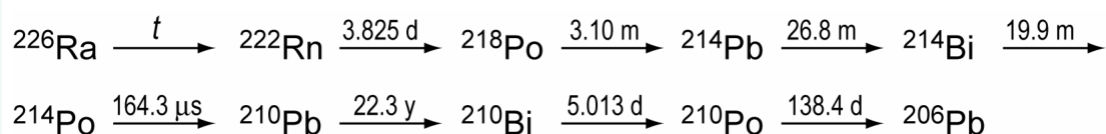
1.1 Sketch the unit cell and calculate how many Au atoms the cell contains.

1.2 The density of Au is $1.93 \cdot 10^4 \text{ kg m}^{-3}$. Calculate the volume and mass of the cubic unit cell.

1.3 Hence calculate the mass of a gold atom and the Avogadro constant, given that the relative atomic mass of Au is 196.97.

Method B – from radioactive decay (Rutherford, 1911)

The radioactive decay series of ^{226}Ra is as follows:



The times indicated are half-lives, the units are y = years, d = days, m = minutes. The first decay, marked t above, has a much longer half-life than the others.

1.4 In the table below, identify which transformations are α -decays and which are β -decays.

	α -decay	β -decay
$^{226}\text{Ra} \longrightarrow ^{222}\text{Rn}$		
$^{222}\text{Rn} \longrightarrow ^{218}\text{Po}$		
$^{218}\text{Po} \longrightarrow ^{214}\text{Pb}$		
$^{214}\text{Pb} \longrightarrow ^{214}\text{Bi}$		
$^{214}\text{Bi} \longrightarrow ^{214}\text{Po}$		
$^{214}\text{Po} \longrightarrow ^{210}\text{Pb}$		
$^{210}\text{Pb} \longrightarrow ^{210}\text{Bi}$		

	α -decay	β -decay
$^{210}\text{Bi} \longrightarrow ^{210}\text{Po}$		
$^{210}\text{Po} \longrightarrow ^{206}\text{Pb}$		

1.5 A sample containing 192 mg of ^{226}Ra was purified and allowed to stand for 40 days. Identify the first isotope in the series (excluding Ra) that has not reached a steady state.

1.6 The total rate of α -decay from the sample was then determined by scintillation to be 27.7 GBq (where $1 \text{ Bq} = 1 \text{ count s}^{-1}$). The sample was then sealed for 163 days. Calculate the number of α particles produced.

1.7 At the end of the 163 days the sample was found to contain 10.4 mm^3 of He, measured at 101325 Pa and 273 K. Calculate the Avogadro constant from these data.

1.8 Given that the relative isotopic mass of ^{226}Ra measured by mass spectrometry is 226.25, use the textbook value of the Avogadro constant ($6.022 \cdot 10^{23} \text{ mol}^{-1}$) to calculate the number of ^{226}Ra atoms in the original sample, n_{Ra} , the decay rate constant, λ , and the half-life, t , of ^{226}Ra (in years). You need only consider the decays up to but not including the isotope identified in 1.5.

Method C – dispersion of particles (Perrin, 1909)

One of the first accurate determinations of the Avogadro constant was carried out by studying the vertical distribution under gravity of colloidal particles suspended in water. In one such experiment, particles with radius $2.12 \cdot 10^{-7} \text{ m}$ and density $1.206 \cdot 10^3 \text{ kg m}^{-3}$ were suspended in a tube of water at 15°C . After allowing sufficient time to equilibrate, the mean numbers of particles per unit volume observed at four heights from the bottom of the tube were:

height / 10^{-6} m	5	35	65	95
mean number per unit volume	4.00	1.88	0.90	0.48

1.9 Assuming the particles to be spherical, calculate:

i) the mass, m , of a particle;

ii) the mass, $m_{\text{H}_2\text{O}}$, of the water it displaces;

iii) the effective mass, m^* , of the particle in water accounting for buoyancy (i.e. taking account of the upthrust due to the displaced volume of water).

Take the density of water to be 999 kg m^{-3} .

At equilibrium, the number of particles per unit volume at different heights may be modelled according to a Boltzmann distribution:

$$\frac{n_h}{n_{h_0}} = \exp \left[-\frac{E_h - E_{h_0}}{RT} \right]$$

where

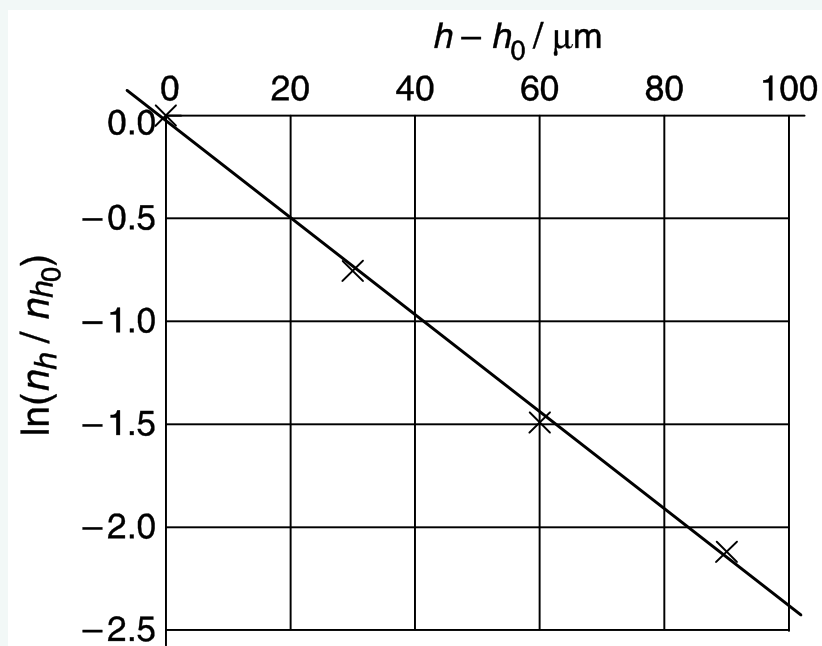
n_h is the number of particles per unit volume at height h ,

n_{h_0} is the number of particles per unit volume at the reference height h_0 ,

E_h is the gravitational potential energy per mole of particles at height h relative to the particles at the bottom of the tube,

R is the gas constant, $8.3145 \text{ J K}^{-1} \text{ mol}^{-1}$.

A graph of $\ln(n_h/n_{h_0})$ against $(h - h_0)$, based on the data in the table above, is shown below. The reference height is taken to be $5 \text{ }\mu\text{m}$ from the bottom of the tube.



1.10 Derive an expression for the gradient (slope) of the graph.

1.11 Determine the Avogadro constant from these data.

Official English text of the problem.

Answers

- **1.1:** A cube with atom centres at its eight corners and six face centres; **4 atoms per unit cell**.
- **1.2:** $V_{\text{cell}} = 6.79 \times 10^{-29} \text{ m}^3$; $m_{\text{cell}} = 1.31 \times 10^{-24} \text{ kg}$.
- **1.3:** $m_{\text{atom}} = 3.28 \times 10^{-25} \text{ kg}$; $N_{\text{A}} = 6.01 \times 10^{23} \text{ mol}^{-1}$.
- **1.4:** In table order: α , α , α , β^- , β^- , α , β^- , β^- , α .
- **1.5:** Lead-210, ^{210}Pb .
- **1.6:** 3.90×10^{17} α particles.
- **1.7:** $N_{\text{A}} = 8.40 \times 10^{23} \text{ mol}^{-1}$.
- **1.8:** $n_{\text{Ra}} = 5.11 \times 10^{20} \text{ atoms}$; $\lambda = 1.36 \times 10^{-11} \text{ s}^{-1}$; $t = 1.62 \times 10^3 \text{ years}$.
- **1.9:** i) $m = 4.81 \times 10^{-17} \text{ kg}$; ii) $m_{\text{H}_2\text{O}} = 3.99 \times 10^{-17} \text{ kg}$; iii) $m^* = 8.26 \times 10^{-18} \text{ kg}$.
- **1.10:** $s = -\frac{N_{\text{A}} m^* g}{RT}$, with s in m^{-1} when height is measured in metres.
- **1.11:** $N_{\text{A}} \approx 7.1 \times 10^{23} \text{ mol}^{-1}$.

Solution

1.1

Sketch a cube with an atom centre at each of its eight corners and at the centre of each of its six faces. There is no atom at the body centre. Hidden edges and hidden atom positions may be indicated with dashed lines.

Each corner atom is shared by eight unit cells, while each face-centred atom is shared by two. Thus the number of atoms belonging to one unit cell is

$$Z = 8 \left(\frac{1}{8} \right) + 6 \left(\frac{1}{2} \right) = \boxed{4}.$$

1.2

The cube edge is

$$a = 0.408 \text{ nm} = 4.08 \times 10^{-10} \text{ m}.$$

Therefore,

$$V_{\text{cell}} = a^3 = (4.08 \times 10^{-10})^3 = 6.7917312 \times 10^{-29} \text{ m}^3 \approx \boxed{6.79 \times 10^{-29} \text{ m}^3}.$$

Using the density,

$$m_{\text{cell}} = \rho V_{\text{cell}} = (1.93 \times 10^4)(6.7917312 \times 10^{-29}) \approx \boxed{1.31 \times 10^{-24} \text{ kg}}.$$

1.3

The unit cell contains four gold atoms, so

$$m_{\text{atom}} = \frac{m_{\text{cell}}}{4} = 3.277010304 \times 10^{-25} \text{ kg} \approx \boxed{3.28 \times 10^{-25} \text{ kg}}.$$

The molar mass of gold is $196.97 \text{ g mol}^{-1} = 0.19697 \text{ kg mol}^{-1}$. Consequently,

$$N_{\text{A}} = \frac{M_{\text{Au}}}{m_{\text{atom}}} = \frac{0.19697}{3.277010304 \times 10^{-25}} = \boxed{6.01 \times 10^{23} \text{ mol}^{-1}}.$$

1.4

An α particle is a helium-4 nucleus, ${}^4\text{He}^{2+}$, with SMILES [4He+2]. Its emission decreases the mass number by 4 and the atomic number by 2.

In β^- decay, the mass number is unchanged and the atomic number increases by 1. An electron and an electron antineutrino, $\bar{\nu}_e$, are emitted.

The balanced nuclear equations are:

Balanced nuclear equation	Decay
${}^{226}_{88}\text{Ra} \longrightarrow {}^{222}_{86}\text{Rn} + {}^4_2\text{He}$	α
${}^{222}_{86}\text{Rn} \longrightarrow {}^{218}_{84}\text{Po} + {}^4_2\text{He}$	α
${}^{218}_{84}\text{Po} \longrightarrow {}^{214}_{82}\text{Pb} + {}^4_2\text{He}$	α
${}^{214}_{82}\text{Pb} \longrightarrow {}^{214}_{83}\text{Bi} + {}^0_{-1}\text{e} + \bar{\nu}_e$	β^-
${}^{214}_{83}\text{Bi} \longrightarrow {}^{214}_{84}\text{Po} + {}^0_{-1}\text{e} + \bar{\nu}_e$	β^-
${}^{214}_{84}\text{Po} \longrightarrow {}^{210}_{82}\text{Pb} + {}^4_2\text{He}$	α

Balanced nuclear equation	Decay
${}^{210}_{82}\text{Pb} \longrightarrow {}^{210}_{83}\text{Bi} + {}^0_{-1}\text{e} + \bar{\nu}_e$	β^-
${}^{210}_{83}\text{Bi} \longrightarrow {}^{210}_{84}\text{Po} + {}^0_{-1}\text{e} + \bar{\nu}_e$	β^-
${}^{210}_{84}\text{Po} \longrightarrow {}^{206}_{82}\text{Pb} + {}^4_2\text{He}$	α

Thus every assignment follows directly from the changes in mass number and atomic number.

1.5

A daughter isotope reaches an approximate steady state when its rate of formation equals its rate of decay. With a nearly constant parent activity, this requires several daughter half-lives.

For ${}^{222}\text{Rn}$, 40 days corresponds to

$$\frac{40}{3.825} = 10.46$$

half-lives. Its activity has therefore reached approximately

$$1 - 2^{-10.46} = 0.99929$$

of its equilibrium value. The following isotopes through ${}^{214}\text{Po}$ have much shorter half-lives and also reach approximate steady state.

The next isotope, ${}^{210}\text{Pb}$, has a half-life of 22.3 years, much longer than 40 days. It is still accumulating. Therefore the first isotope that has not reached steady state is

$$\boxed{{}^{210}\text{Pb, lead-210}}.$$

1.6

Treat the measured total α activity as constant over the collection period. This uses the long half-life of radium and neglects the small changes associated with the slowly accumulating later daughters.

The elapsed time is

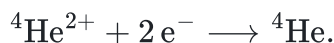
$$\Delta t = 163 \times 24 \times 60 \times 60 = 1.40832 \times 10^7 \text{ s}.$$

Hence,

$$N_\alpha = A_\alpha \Delta t = (27.7 \times 10^9 \text{ s}^{-1})(1.40832 \times 10^7 \text{ s}) = \boxed{3.90 \times 10^{17} \text{ particles}}.$$

1.7

Each α particle acquires two electrons to become one helium-4 atom, ${}^4\text{He}$, SMILES [${}^4\text{He}$]:



Thus the number of helium atoms collected equals the number of α particles produced.

The gas volume is

$$V = 10.4 \text{ mm}^3 = 1.04 \times 10^{-8} \text{ m}^3.$$

From the ideal-gas equation,

$$n_{\text{He}} = \frac{PV}{RT} = \frac{(101325)(1.04 \times 10^{-8})}{(8.3145)(273)} = 4.64249 \times 10^{-7} \text{ mol}.$$

Therefore,

$$N_A = \frac{N_\alpha}{n_{\text{He}}} = \frac{3.9010464 \times 10^{17}}{4.64249 \times 10^{-7}} = \boxed{8.40 \times 10^{23} \text{ mol}^{-1}}.$$

1.8

Using the stated isotopic mass and textbook Avogadro constant, the initial number of radium atoms is

$$n_{\text{Ra}} = \frac{0.192 \text{ g}}{226.25 \text{ g mol}^{-1}} (6.022 \times 10^{23} \text{ mol}^{-1}) = \boxed{5.11 \times 10^{20} \text{ atoms}}.$$

Before decay of ^{210}Pb , the four α -emitting nuclides are



At steady state, the activity of each of these daughters equals the radium activity. The total α activity is therefore four times the radium activity:

$$A_\alpha = 4A_{\text{Ra}} = 4\lambda n_{\text{Ra}}.$$

Thus,

$$A_{\text{Ra}} = \frac{27.7 \times 10^9}{4} = 6.925 \times 10^9 \text{ s}^{-1},$$

and

$$\lambda = \frac{6.925 \times 10^9}{5.1103823 \times 10^{20}} = \boxed{1.36 \times 10^{-11} \text{ s}^{-1}}.$$

For first-order radioactive decay,

$$t = \frac{\ln 2}{\lambda} = 5.115 \times 10^{10} \text{ s}.$$

Taking one year as 365 days,

$$t = \frac{5.115 \times 10^{10}}{365 \times 86400} = \boxed{1.62 \times 10^3 \text{ years}}.$$

1.9

The volume of a spherical particle is

$$V_p = \frac{4}{3}\pi r^3 = \frac{4}{3}\pi(2.12 \times 10^{-7})^3 = 3.99113 \times 10^{-20} \text{ m}^3.$$

i) The particle mass is

$$m = \rho_p V_p = (1.206 \times 10^3)(3.99113 \times 10^{-20}) = \boxed{4.81 \times 10^{-17} \text{ kg}}.$$

ii) The displaced water, H_2O (SMILES O), occupies the same volume as the particle:

$$m_{\text{H}_2\text{O}} = \rho_w V_p = (999)(3.99113 \times 10^{-20}) = \boxed{3.99 \times 10^{-17} \text{ kg}}.$$

iii) The upward buoyant force equals the weight of the displaced water. Therefore,

$$m^*g = mg - m_{\text{H}_2\text{O}}g,$$

so, retaining unrounded values,

$$m^* = (\rho_p - \rho_w)V_p = (1206 - 999)(3.99113 \times 10^{-20}) = \boxed{8.26 \times 10^{-18} \text{ kg}}.$$

1.10

Accounting for buoyancy, the potential-energy increase per particle between h_0 and h is $m^*g(h - h_0)$. The corresponding increase per mole is

$$E_h - E_{h_0} = N_A m^* g (h - h_0).$$

Substituting into the given Boltzmann distribution and taking natural logarithms gives

$$\ln \left(\frac{n_h}{n_{h_0}} \right) = -\frac{N_A m^* g}{RT} (h - h_0).$$

Hence the gradient with respect to height in metres is

$$s = -\frac{N_A m^* g}{RT} = -\frac{4\pi r^3 (\rho_p - \rho_w) g N_A}{3RT}.$$

Its units are m^{-1} . The negative sign expresses the decrease in particle concentration with increasing height.

For the displayed numerical horizontal coordinate $x = (h - h_0)/(1 \mu\text{m})$, the gradient is

$$\frac{d}{dx} \ln \left(\frac{n_h}{n_{h_0}} \right) = -\frac{N_A m^* g (10^{-6} \text{ m})}{RT}.$$

1.11

The drawn line passes approximately through $(0, 0)$ and $(100 \mu\text{m}, -2.4)$. Therefore,

$$s \approx \frac{-2.4}{100 \times 10^{-6} \text{ m}} = -2.4 \times 10^4 \text{ m}^{-1}.$$

Rearranging the expression from 1.10,

$$N_A = -\frac{sRT}{m^*g}.$$

Using $T = 15 + 273.15 = 288.15 \text{ K}$ and $g = 9.81 \text{ m s}^{-2}$,

$$N_A \approx \frac{(2.4 \times 10^4)(8.3145)(288.15)}{(8.26165 \times 10^{-18})(9.81)} = 7.09 \times 10^{23} \text{ mol}^{-1}.$$

To the precision justified by reading the graph,

$$N_A \approx 7.1 \times 10^{23} \text{ mol}^{-1}.$$

The solution was checked against the official solution.

Problem 2: Interstellar production of H₂

Interstellar production of H₂

If two atoms collide in interstellar space the energy of the resulting molecule is so great that it rapidly dissociates. Hydrogen atoms only react to give stable H₂ molecules on the surface of dust particles. The dust particles absorb most of the excess energy and the newly formed H₂ rapidly desorbs. This question examines two kinetic models for H₂ formation on the surface of a dust particle.

In both models, the rate constant for adsorption of H atoms onto the surface of dust particles is $k_a = 1.4 \cdot 10^{-5} \text{ cm}^3 \text{ s}^{-1}$. The typical number density of H atoms (number of H atoms per unit volume) in interstellar space is $[\text{H}] = 10 \text{ cm}^{-3}$.

[Note: In the following, you may treat numbers of surface-adsorbed atoms and number densities of gas-phase atoms in the same way as you would normally use concentrations in the rate equations. As a result, the units of the rate constants may be unfamiliar to you. Reaction rates have units of numbers of atoms or molecules per unit time.]

2.1 Calculate the rate at which H atoms adsorb onto a dust particle. You may assume that this rate is constant throughout.

Desorption of H atoms is first order with respect to the number of adsorbed atoms. The rate constant for the desorption step is $k_d = 1.9 \cdot 10^{-3} \text{ s}^{-1}$.

2.2 Assuming that only adsorption and desorption take place, calculate the steady-state number, N , of H atoms on the surface of a dust particle.

The H atoms are mobile on the surface. When they meet they react to form H_2 , which then desorbs. The two kinetic models under consideration differ in the way the reaction is modelled, but share the same rate constants k_a , k_d , and k_r , for adsorption, desorption, and bimolecular reaction, as given below.

$$k_a = 1.4 \cdot 10^{-5} \text{ cm}^3 \text{ s}^{-1}$$

$$k_d = 1.9 \cdot 10^{-3} \text{ s}^{-1}$$

$$k_r = 5.1 \cdot 10^4 \text{ s}^{-1}$$

Model A

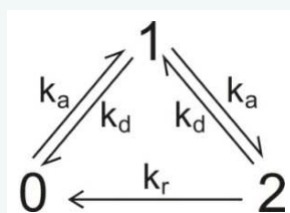
Reaction to form H_2 is assumed to be second order. On a dust particle the rate of removal of H atoms by reaction is $k_r N^2$.

2.3 Write down an equation for the rate of change of N , including adsorption, desorption and reaction. Assuming steady state conditions, determine the value of N .

2.4 Calculate the rate of production of H_2 per dust particle in this model.

Model B

Model B attempts to analyse the probability that the dust particles carry 0, 1 or 2 H atoms. The three states are linked by the following reaction scheme. The assumption is made that no more than 2 atoms may be adsorbed simultaneously.



x_0 , x_1 and x_2 are the fractions of dust particles existing in state 0, 1 or 2, respectively. These fractions may be treated in the same way as concentrations in the following kinetic analysis. For a system in state m with fraction x_m , the rates of the three possible processes are

Adsorption ($m \rightarrow m + 1$) : rate = $k_a [\text{H}] x_m$

Desorption ($m \rightarrow m - 1$) : rate = $k_d m x_m$

Reaction ($m \rightarrow m - 2$) : rate = $\frac{1}{2} k_r m(m - 1) x_m$

2.5 Write down equations for the rates of change, dx_m/dt , of the fractions x_0 , x_1 and x_2 .

2.6 Assuming steady-state conditions, use the above rate equations to find expressions for the ratios x_2/x_1 and x_1/x_0 , and evaluate these ratios.

2.7 Evaluate the steady state fractions x_0 , x_1 and x_2 .

[If you were unable to determine the ratios in 2.6, use $x_2/x_1 = a$ and $x_1/x_0 = b$ and give the result algebraically.]

2.8 Evaluate the rate of production of H_2 per dust particle in this model.

2.9 It is currently not possible to measure the rate of this reaction experimentally, but the most recent computer simulations of the rate give a value of $9.4 \cdot 10^{-6} s^{-1}$. Which of the following statements apply to each model under these conditions? Mark any box you consider to be appropriate.

Statement	Model A	Model B	Neither model
The rate determining step is adsorption of H atoms.			
The rate-determining step is desorption of H_2 molecules.			
The rate determining step is the bimolecular reaction of H atoms on the surface.			
The rate determining step is adsorption of the second H atom.			
The implicit assumption that reaction can take place regardless of the number of atoms adsorbed leads to substantial error (at least a factor of two).			
Limiting the number of atoms adsorbed on the particle to 2 leads to substantial error (at least a factor of two).			

Official English text of the problem.

Answers

Let $F = k_a [H]$. The molecular product is **dihydrogen**, H_2 , SMILES [H][H]. All production rates below are per dust particle.

- 2.1:** $F = 1.4 \times 10^{-4} \text{ atoms s}^{-1}$.
- 2.2:** $N = 7.4 \times 10^{-2}$ adsorbed atoms on average.
- 2.3:** $dN/dt = F - k_d N - k_r N^2$, giving $N = 5.2 \times 10^{-5}$ adsorbed atoms on average.
- 2.4:** $R_A = \frac{1}{2} k_r N^2 = 7.0 \times 10^{-5} \text{ molecules s}^{-1}$.

• 2.5:

$$\begin{aligned}\frac{dx_0}{dt} &= -Fx_0 + k_d x_1 + k_r x_2, \\ \frac{dx_1}{dt} &= Fx_0 - (F + k_d)x_1 + 2k_d x_2, \\ \frac{dx_2}{dt} &= Fx_1 - (2k_d + k_r)x_2.\end{aligned}$$

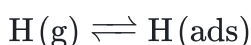
• 2.6:

$$\frac{x_2}{x_1} = \frac{F}{2k_d + k_r} = 2.7 \times 10^{-9}, \quad \frac{x_1}{x_0} = \frac{F(2k_d + k_r)}{k_d(2k_d + k_r) + k_r F} = 6.9 \times 10^{-2}.$$

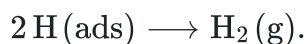
- 2.7: $x_0 \simeq 0.936, \quad x_1 \simeq 0.064, \quad x_2 \simeq 1.8 \times 10^{-10}.$
- 2.8: $R_B = k_r x_2 = 9.0 \times 10^{-6} \text{ molecules s}^{-1}.$
- 2.9: In the order printed: **A; neither; neither; B; A; neither**, distinguishing overall adsorption supply from second-atom adsorption. Under a broader reading of the first statement, **B can also be marked there**, since adsorption of the second atom is itself adsorption of an H atom.

Solution

Atomic hydrogen, H, has SMILES [H]. The balanced surface processes are



and, including the rapid release of the molecular product,



Here "ads" denotes adsorption on dust; surface binding is not represented by the SMILES.

2.1

The adsorption rate per particle is

$$F = k_a [\text{H}] = (1.4 \times 10^{-5} \text{ cm}^3 \text{ s}^{-1}) (10 \text{ cm}^{-3}).$$

Thus

$$F = 1.4 \times 10^{-4} \text{ H atoms per particle per second.}$$

2.2

With adsorption and desorption alone,

$$\frac{dN}{dt} = F - k_d N.$$

At steady state, adsorption balances desorption:

$$N = \frac{F}{k_d} = \frac{1.4 \times 10^{-4}}{1.9 \times 10^{-3}} = 0.073684 \dots$$

Therefore,

$$N = 7.4 \times 10^{-2} \text{ atoms per particle.}$$

This is an average over particles or time; individual particles carry integer numbers of atoms.

2.3

The problem defines $k_r N^2$ as the rate of **removal of atoms** by reaction. Hence

$$\frac{dN}{dt} = F - k_d N - k_r N^2.$$

The steady-state condition gives

$$k_r N^2 + k_d N - F = 0.$$

Only the nonnegative root is physically meaningful:

$$N = \frac{\sqrt{k_d^2 + 4k_r F} - k_d}{2k_r}.$$

Substitution gives

$$N = \frac{\sqrt{(1.9 \times 10^{-3})^2 + 4(5.1 \times 10^4)(1.4 \times 10^{-4})} - 1.9 \times 10^{-3}}{2(5.1 \times 10^4)} = 5.2375 \times 10^{-5}.$$

Thus

$$N = 5.2 \times 10^{-5} \text{ atoms per particle.}$$

2.4

Each molecule consumes two atoms, so the molecular production rate is half the atom-removal rate:

$$R_A = \frac{1}{2} k_r N^2.$$

Using the unrounded value of N ,

$$R_A = \frac{1}{2} (5.1 \times 10^4) (5.2375 \times 10^{-5})^2 = 6.9950 \times 10^{-5} \text{ s}^{-1}.$$

Therefore,

$$R_A = 7.0 \times 10^{-5} \text{ molecules per particle per second.}$$

The steady-state atom balance provides a check:

$$2R_A = F - k_d N.$$

2.5

The transition rates are

Transition	Rate
$0 \rightarrow 1$, adsorption	Fx_0
$1 \rightarrow 0$, desorption	$k_d x_1$
$1 \rightarrow 2$, adsorption	Fx_1
$2 \rightarrow 1$, desorption	$2k_d x_2$
$2 \rightarrow 0$, reaction	$k_r x_2$

The factor of two for desorption from state 2 arises because either atom can desorb. For reaction in state 2,

$$\frac{1}{2}k_r m(m-1)x_m = \frac{1}{2}k_r(2)(1)x_2 = k_r x_2.$$

Adsorption from state 2 is excluded by the imposed two-atom limit. Taking incoming minus outgoing flux for each state gives

$$\begin{aligned}\frac{dx_0}{dt} &= -Fx_0 + k_d x_1 + k_r x_2, \\ \frac{dx_1}{dt} &= Fx_0 - k_d x_1 - Fx_1 + 2k_d x_2, \\ \frac{dx_2}{dt} &= Fx_1 - 2k_d x_2 - k_r x_2.\end{aligned}$$

Their sum is zero, as required for conservation of the total fraction:

$$\frac{d}{dt}(x_0 + x_1 + x_2) = 0.$$

2.6

At steady state, the equation for x_2 gives

$$Fx_1 = (2k_d + k_r)x_2.$$

Consequently,

$$a \equiv \frac{x_2}{x_1} = \frac{F}{2k_d + k_r} = \frac{1.4 \times 10^{-4}}{2(1.9 \times 10^{-3}) + 5.1 \times 10^4} = 2.74510 \times 10^{-9}.$$

Thus

$$\frac{x_2}{x_1} = 2.7 \times 10^{-9}.$$

The steady-state equation for x_0 gives

$$Fx_0 = k_d x_1 + k_r x_2 = (k_d + k_r a)x_1.$$

Therefore,

$$b \equiv \frac{x_1}{x_0} = \frac{F}{k_d + k_r a} = \frac{F(2k_d + k_r)}{k_d(2k_d + k_r) + k_r F}.$$

Numerically,

$$b = 0.06862745 \dots,$$

so

$$\frac{x_1}{x_0} = 6.9 \times 10^{-2}.$$

2.7

The fractions satisfy

$$x_0 + x_1 + x_2 = 1, \quad x_1 = bx_0, \quad x_2 = abx_0.$$

It follows that

$$x_0 = \frac{1}{1+b+ab}, \quad x_1 = \frac{b}{1+b+ab}, \quad x_2 = \frac{ab}{1+b+ab}.$$

Using the unrounded ratios,

$$x_0 = 0.935779816\dots, \quad x_1 = 0.064220184\dots, \quad x_2 = 1.7629069 \times 10^{-10}.$$

Hence

$$x_0 \simeq 0.936, \quad x_1 \simeq 0.064, \quad x_2 \simeq 1.8 \times 10^{-10}.$$

The extremely small x_2 reflects the very short lifetime of a particle carrying two atoms.

2.8

Each $2 \rightarrow 0$ reaction produces one molecule. Its transition rate already counts molecular formation events, so

$$R_B = k_r x_2.$$

Therefore,

$$R_B = (5.1 \times 10^4)(1.7629069 \times 10^{-10}) = 8.990825 \times 10^{-6} \text{ s}^{-1},$$

or

$$R_B = 9.0 \times 10^{-6} \text{ molecules per particle per second.}$$

The corresponding atom balance is

$$F(x_0 + x_1) = k_d(x_1 + 2x_2) + 2R_B,$$

which the calculated fractions satisfy.

2.9

Distinguishing overall adsorption supply from the specific second-atom arrival gives the following markings.

Statement	Model A	Model B	Neither model
Adsorption of H atoms is rate determining.	✓		
Desorption of H ₂ molecules is rate determining.			✓
The bimolecular surface reaction is rate determining.			✓
Adsorption of the second H atom is rate determining.		✓	
Allowing reaction regardless of the number of adsorbed atoms causes an error of at least a factor of two.	✓		
Limiting adsorption to two atoms causes an error of at least a factor of two.			✓

For **Model A**, desorption removes atoms at only

$$k_d N = (1.9 \times 10^{-3})(5.2375 \times 10^{-5}) = 9.95 \times 10^{-8} \text{ s}^{-1},$$

which is negligible compared with $F = 1.4 \times 10^{-4} \text{ s}^{-1}$. Almost every arriving atom is therefore consumed in the model:

$$R_A \simeq \frac{F}{2}.$$

The adsorption supply controls production.

For **Model B**, a singly occupied particle usually loses its atom before another arrives. The relevant mean times are

$$\tau_{\text{arrival}} = \frac{1}{F} \simeq 7.1 \times 10^3 \text{ s}, \quad \tau_{\text{desorption}} = \frac{1}{k_d} \simeq 5.3 \times 10^2 \text{ s}.$$

The probability that the second atom arrives before the first desorbs is

$$\frac{F}{F + k_d} = 0.0686 \simeq 6.9\%.$$

Once two atoms are present, their reaction is extremely fast:

$$\tau_{\text{reaction}} = \frac{1}{k_r} \simeq 2.0 \times 10^{-5} \text{ s}.$$

Thus the crucial slow event is adsorption of a **second atom while the first remains on the particle**. Indeed, since k_r is very large,

$$R_B \simeq Fx_1 \simeq \frac{F^2}{k_d + 2F}.$$

The surface reaction is fast in both models, and the statement explicitly assumes rapid desorption of the newly formed molecule. Neither of those processes is rate determining.

Finally, comparison with the supplied simulation rate gives

$$\frac{R_A}{R_{\text{sim}}} = \frac{6.9950 \times 10^{-5}}{9.4 \times 10^{-6}} = 7.44,$$

whereas

$$\frac{R_B}{R_{\text{sim}}} = \frac{8.9908 \times 10^{-6}}{9.4 \times 10^{-6}} = 0.956.$$

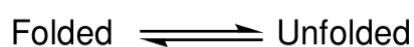
Model A overestimates production by about **7.4-fold**. A fractional mean occupancy is valid, but using N^2 fails to represent the requirement that two atoms coexist on the same particle. Model B explicitly enforces that requirement.

Model B is only about **4.4% below** the simulation value. Its two-atom limit therefore does not produce an error approaching a factor of two under these conditions.

The solution was checked against the official solution.

Problem 3: Protein Folding

The unfolding reaction for many small proteins can be represented by the equilibrium:



You may assume that the protein folding reaction takes place in a single step. The position of this equilibrium changes with temperature; the melting temperature T_m is defined as the temperature at which half of the molecules are unfolded and half are folded.

The intensity of the fluorescence signal at a wavelength of 356 nm of a $1.0 \mu\text{M}$ ($\text{M} = \text{mol dm}^{-3}$) sample of the protein Chymotrypsin Inhibitor 2 (CI2) was measured as a function of temperature over the range 58 to 66 °C:

Temperature / °C	58	60	62	64	66
Fluorescence intensity (arbitrary units)	27	30	34	37	40

A $1.0 \mu\text{M}$ sample in which all of the protein molecules are folded gives a fluorescence signal of 21 units at 356 nm. A $1.0 \mu\text{M}$ sample in which all of the protein molecules are unfolded gives a fluorescence signal of 43 units.

3.1 Assuming that the fluorescence intensity from each species is directly proportional to its concentration, calculate the fraction, x , of unfolded molecules present at each temperature.

3.2 Give an expression for the equilibrium constant, K , in terms of x , and hence calculate the value of K at each temperature.

3.3 Estimate the value of T_m for this protein (to the nearest 1 °C).

Assuming that the values of ΔH° and ΔS° for the protein unfolding reaction are constant with temperature then:

$$\ln K = -\frac{\Delta H^\circ}{RT} + C$$

where C is a constant.

3.4 Plot a suitable graph and hence determine the values of ΔH° and ΔS° for the protein unfolding reaction.

[If you have been unable to calculate values for ΔH° and ΔS° , you should use the following incorrect values for the subsequent parts of the problem:

$$\Delta H^\circ = 130 \text{ kJ mol}^{-1}; \Delta S^\circ = 250 \text{ J K}^{-1} \text{ mol}^{-1}.]$$

3.5 Calculate the equilibrium constant for the unfolding reaction at 25 °C.

[If you have been unable to calculate a value for K , you should use the following incorrect value for the subsequent parts of the problem: $K = 3.6 \cdot 10^{-6}$]

The first order rate constant for the CI2 protein folding reaction can be determined by following the fluorescence intensity when a sample of unfolded protein is allowed to refold (typically the pH of the solution is changed). The concentration of protein when a $1.0 \mu\text{M}$ sample of unfolded CI2 was allowed to refold was measured at a temperature of 25 °C:

time / ms	0	10	20	30	40
concentration / μM	1	0.64	0.36	0.23	0.14

3.6 Plot a suitable graph and hence determine the value of the rate constant for the protein folding reaction, k_f , at 25 °C.

[If you have been unable to calculate the value for k_f , you should use the following incorrect value for the subsequent parts of the question: $k_f = 60 \text{ s}^{-1}$.]

3.7 Determine the value of the rate constant for the protein *unfolding* reaction, k_u , at 25 °C.

3.8 At 20 °C the rate constant for the protein folding reaction is 33 s^{-1} . Calculate the activation energy for the protein folding reaction.

Official English text of the problem.

Answers

- **3.1** At 58, 60, 62, 64, 66 °C, respectively:

$$x = 0.273, 0.409, 0.591, 0.727, 0.864.$$

- **3.2**

$$K = \frac{x}{1 - x}$$

giving, in the same temperature order,

$$K = 0.375, 0.692, 1.44, 2.67, 6.33.$$

- **3.3** $T_m \approx 61 \text{ °C}$.

- **3.4** Plot $\ln K$ against $1/T$:

$$\Delta H^\circ \approx +327 \text{ kJ mol}^{-1}, \quad \Delta S^\circ \approx +978 \text{ J K}^{-1} \text{ mol}^{-1}.$$

- **3.5** $K(25 \text{ °C}) \approx 7.0 \times 10^{-7}$.

- **3.6** Plot $\ln([U]_t/[U]_0)$ against time:

$$k_f \approx 49.6 \text{ s}^{-1} \approx 50 \text{ s}^{-1}.$$

- **3.7** $k_u \approx 3.5 \times 10^{-5} \text{ s}^{-1}$.

- **3.8** $E_a \approx 59 \text{ kJ mol}^{-1}$, or approximately 60 kJ mol^{-1} using the graph-rounded $k_f = 50 \text{ s}^{-1}$.

Solution

Let F and U denote folded and unfolded chymotrypsin inhibitor 2 (CI2), respectively. These are conformational states of the same protein. Its amino-acid sequence is not supplied, so a molecular SMILES cannot be specified from the data; ordinary SMILES would not describe the distinction between its folded and unfolded conformations.

The numerical results below use least-squares straight-line fits to all five points, retaining unrounded fit parameters for subsequent calculations. We use $R = 8.314 \text{ J K}^{-1} \text{ mol}^{-1}$.

3.1 — Fraction of unfolded molecules

If the unfolded fraction is x , the folded fraction is $1 - x$. Since fluorescence contributions are proportional to concentration and additive, the measured intensity I is

$$I = 21(1 - x) + 43x = 21 + 22x.$$

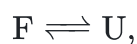
Thus,

$$x = \frac{I - 21}{22}.$$

Temperature / °C	I	x
58	27	$6/22 = 0.2727$
60	30	$9/22 = 0.4091$
62	34	$13/22 = 0.5909$
64	37	$16/22 = 0.7273$
66	40	$19/22 = 0.8636$

3.2 — Equilibrium constants

For the unfolding equilibrium, using the state labels defined above,



the equilibrium constant is

$$K = \frac{[U]}{[F]}.$$

Writing the total protein concentration as c_{tot} ,

$$[U] = xc_{\text{tot}}, \quad [F] = (1 - x)c_{\text{tot}},$$

so

$$K = \frac{x}{1 - x} = \frac{I - 21}{43 - I}.$$

Temperature / °C	K
58	$6/16 = 0.375$
60	$9/13 = 0.6923$
62	$13/9 = 1.4444$
64	$16/6 = 2.6667$
66	$19/3 = 6.3333$

These equilibrium constants are dimensionless.

3.3 — Melting temperature

At the melting temperature,

$$x = \frac{1}{2}, \quad K = 1.$$

The corresponding fluorescence intensity is

$$I_m = \frac{21 + 43}{2} = 32.$$

This lies between the intensities of 30 at 60 °C and 34 at 62 °C. Linear interpolation gives

$$T_m = 60 + \frac{32 - 30}{34 - 30}(62 - 60) = 61 \text{ °C}.$$

Therefore, to the nearest degree,

$$\boxed{T_m = 61\text{ }^{\circ}\text{C}}.$$

3.4 — Enthalpy and entropy of unfolding

The thermodynamic relations

$$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ}$$

and

$$\Delta G^{\circ} = -RT \ln K$$

give

$$\ln K = -\frac{\Delta H^{\circ}}{R} \frac{1}{T} + \frac{\Delta S^{\circ}}{R}.$$

Thus, plot $\ln K$ **on the vertical axis against** $1/T$, in K^{-1} , **on the horizontal axis**, using absolute temperatures.

T/K	$1/T/\text{K}^{-1}$	$\ln K$
331.15	0.00301978	-0.98083
333.15	0.00300165	-0.36772
335.15	0.00298374	0.36772
337.15	0.00296604	0.98083
339.15	0.00294855	1.84583

The points lie approximately on a descending straight line. A least-squares fit gives

$$\ln K = - (3.93049 \times 10^4 \text{ K}) \frac{1}{T} + 117.65318.$$

The slope is $-\Delta H^{\circ}/R$, so

$$\Delta H^{\circ} = -R(\text{slope}) \approx (8.314)(3.93049 \times 10^4) \text{ J mol}^{-1}.$$

Hence,

$$\boxed{\Delta H^{\circ} \approx +327 \text{ kJ mol}^{-1}}.$$

The intercept is $C = \Delta S^{\circ}/R$, giving

$$\Delta S^{\circ} = RC \approx (8.314)(117.65318) \text{ J K}^{-1} \text{ mol}^{-1},$$

and therefore

$$\boxed{\Delta S^{\circ} \approx +978 \text{ J K}^{-1} \text{ mol}^{-1}}.$$

Unfolding is endothermic and has a positive standard entropy change. As a consistency check, the fitted line gives

$$T_m = \frac{\Delta H^{\circ}}{\Delta S^{\circ}} \approx 334.07 \text{ K} = 60.92\text{ }^{\circ}\text{C},$$

consistent with part 3.3.

3.5 — Equilibrium constant at 25 °C

At 25 °C,

$$T = 298.15 \text{ K.}$$

Using the fitted equation directly avoids rounding errors in extrapolation:

$$\ln K = -\frac{39304.939}{298.15} + 117.65318 = -14.1762.$$

Therefore,

$$K = e^{-14.1762} = 6.97 \times 10^{-7},$$

so

$$\boxed{K(25^\circ \text{C}) \approx 7.0 \times 10^{-7}}.$$

The equilibrium strongly favours the folded protein.

3.6 — Folding rate constant

The decreasing concentrations in the kinetic table refer to unfolded protein. Since the equilibrium unfolded fraction at 25 °C is only

$$x_{\text{eq}} = \frac{K}{1 + K} \approx 7.0 \times 10^{-7},$$

reverse unfolding is negligible over these measurements. The first-order folding equation is therefore

$$-\frac{d[U]}{dt} = k_f[U].$$

Integration gives

$$[U]_t = [U]_0 e^{-k_f t},$$

or

$$\ln \left(\frac{[U]_t}{[U]_0} \right) = -k_f t.$$

Plot $\ln([U]_t/[U]_0)$ **vertically against t , in seconds, horizontally.**

t / s	$[U]_t/[U]_0$	$\ln([U]_t/[U]_0)$
0.000	1.00	0.00000
0.010	0.64	-0.44629
0.020	0.36	-1.02165
0.030	0.23	-1.46968
0.040	0.14	-1.96611

The graph is approximately a straight line through the origin with a negative slope. A least-squares fit gives

$$\ln \left(\frac{[U]_t}{[U]_0} \right) = 0.01038 - (49.556 \text{ s}^{-1})t.$$

Consequently,

$$\boxed{k_f = 49.6 \text{ s}^{-1} \approx 50 \text{ s}^{-1}}.$$

For an exact reversible treatment, the equilibrium concentration would be subtracted before taking logarithms, and the decay constant would be $k_f + k_u$. The correction is negligible at the precision of these data.

3.7 — Unfolding rate constant

At equilibrium, the unfolding and folding rates are equal:

$$k_u[F]_{\text{eq}} = k_f[U]_{\text{eq}}.$$

Therefore,

$$\frac{k_u}{k_f} = \frac{[U]_{\text{eq}}}{[F]_{\text{eq}}} = K,$$

so

$$k_u = Kk_f.$$

Using the unrounded results,

$$k_u = (6.9718 \times 10^{-7})(49.556 \text{ s}^{-1}) = 3.4549 \times 10^{-5} \text{ s}^{-1}.$$

Thus,

$$\boxed{k_u \approx 3.5 \times 10^{-5} \text{ s}^{-1}}.$$

3.8 — Activation energy for folding

The Arrhenius equation is

$$k_f = Ae^{-E_a/(RT)}.$$

Assuming a constant pre-exponential factor over this temperature interval,

$$\ln\left(\frac{k_2}{k_1}\right) = \frac{E_a}{R}\left(\frac{1}{T_1} - \frac{1}{T_2}\right).$$

Here,

$$\begin{aligned} T_1 &= 293.15 \text{ K}, & k_1 &= 33 \text{ s}^{-1}, \\ T_2 &= 298.15 \text{ K}, & k_2 &= 49.556 \text{ s}^{-1}. \end{aligned}$$

Hence,

$$E_a = \frac{R \ln(k_2/k_1)}{1/T_1 - 1/T_2} = \frac{(8.314 \text{ J K}^{-1} \text{ mol}^{-1}) \ln(49.556/33)}{(1/293.15 - 1/298.15) \text{ K}^{-1}}.$$

This gives

$$E_a \approx 5.91 \times 10^4 \text{ J mol}^{-1},$$

or

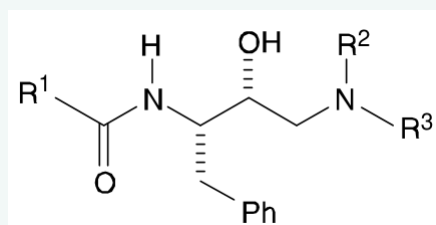
$$\boxed{E_a \approx 59 \text{ kJ mol}^{-1}}.$$

Using $k_f = 50 \text{ s}^{-1}$ rounded from the graph gives approximately 60 kJ mol^{-1} , consistent with graphical precision.

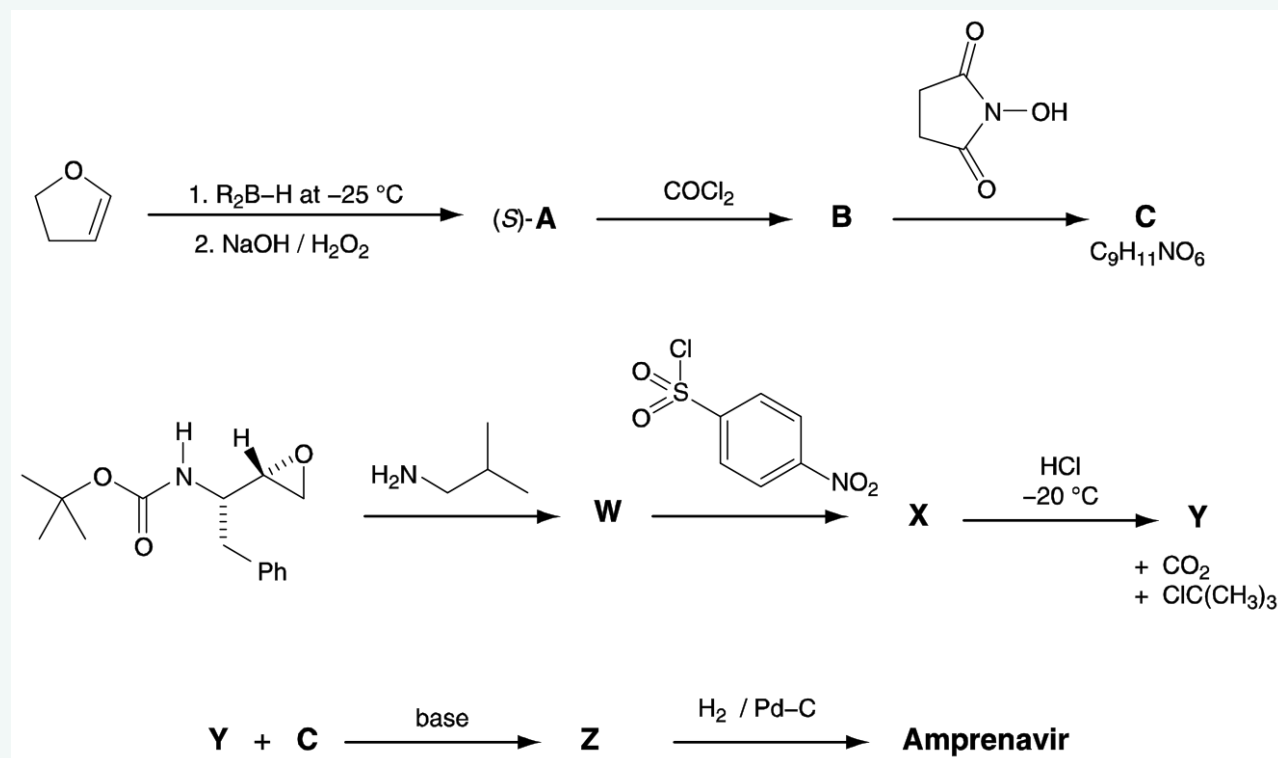
The solution was checked against the official solution.

Problem 4: Synthesis of Amprenavir

One class of anti-HIV drugs, known as *protease inhibitors*, works by blocking the active site of one of the enzymes used in assembly of the viruses within the host cell. Two successful drugs, *saquinavir* and *amprenavir*, contain the structural unit shown below which mimics the transition state within the enzyme. In the structure, R^1 , R^2 and R^3 may represent any atom or group other than hydrogen.



Amprenavir may be synthesised as shown in the convergent scheme below.



The reagent R_2B-H used in the first step is chiral.

Product **A** is formed as the (*S*)-enantiomer.

Three of the signals in the ^1H NMR spectrum of Amprenavir disappear on shaking with D_2O : δ 4.2 (2H), δ 4.9 (1H) and δ 5.1 (1H).

4.1 Suggest structures for:

- the intermediates **A**, **B**, **C**, **W**, **X**, **Y** and **Z**,
- Amprenavir*.

Your answers should clearly show the stereochemistry at each centre.

Answers

- **4.1(a), A — (3*S*)-Tetrahydrofuran-3-ol.**
O[C@@H]1COCC1
- **4.1(a), B — (3*S*)-Tetrahydrofuran-3-yl chloroformate.**
O=C(Cl)O[C@@H]1COCC1
- **4.1(a), C — N-Succinimidyl (3*S*)-tetrahydrofuran-3-yl carbonate**, the activated carbonate of **A**.
O=C(ON1C(=O)CCC1=O)O[C@@H]1COCC1
- **4.1(a), W — tert-Butyl [(2*S*,3*R*)-3-hydroxy-4-[(2-methylpropyl)amino]-1-phenylbutan-2-yl]carbamate.**
CC(C)(C)OC(=O)N[C@@H](Cc1ccccc1)[C@H](O)CNCC(C)C
- **4.1(a), X — tert-Butyl [(2*S*,3*R*)-3-hydroxy-4-[(2-methylpropyl)(4-nitrobenzenesulfonyl)amino]-1-phenylbutan-2-yl]carbamate.**
CC(C)(C)OC(=O)N[C@@H](Cc1ccccc1)[C@H](O)CN(CC(C)C)S(=O)(=O)c1ccc([N+](=O)[O-])cc1
- **4.1(a), Y — N-[(2*R*,3*S*)-3-amino-2-hydroxy-4-phenylbutyl]-N-(2-methylpropyl)-4-nitrobenzenesulfonamide**, shown as the free base.
N[C@@H](Cc1ccccc1)[C@H](O)CN(CC(C)C)S(=O)(=O)c1ccc([N+](=O)[O-])cc1
- **4.1(a), Z — (3*S*)-Tetrahydrofuran-3-yl [(2*S*,3*R*)-3-hydroxy-4-[(2-methylpropyl)(4-nitrobenzenesulfonyl)amino]-1-phenylbutan-2-yl]carbamate.**
O=C(O[C@@H]1COCC1)N[C@@H](Cc1ccccc1)[C@H](O)CN(CC(C)C)S(=O)(=O)c1ccc([N+](=O)[O-])cc1
- **4.1(b), Amprenavir — the 4-amino analogue of Z.** Its tetrahydrofuran centre is (3*S*), and its amino-alcohol chain has configuration (2*S*,3*R*), numbering from the phenyl-bearing methylene.
O=C(O[C@@H]1COCC1)N[C@@H](Cc1ccccc1)[C@H](O)CN(CC(C)C)S(=O)(=O)c1ccc(N)cc1

Solution

4.1(a): Identification of the intermediates

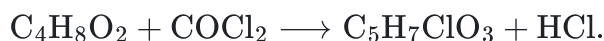
A: asymmetric hydroboration–oxidation.

The starting alkene is **2,3-dihydrofuran**, C1COC=C1. Hydroboration places boron on the alkene carbon farther from the ring oxygen and hydrogen on the carbon adjacent to that oxygen. Oxidation replaces the carbon–boron bond by a carbon–oxygen bond with retention of configuration.

The product is therefore tetrahydrofuran-3-ol. The problem specifies formation of the (*S*)-enantiomer, establishing **A** as (3*S*)-tetrahydrofuran-3-ol.

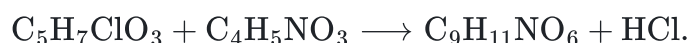
B and C: formation of an activated carbonate.

The alcohol oxygen of **A** attacks **phosgene**, $\text{O}=\text{C}(\text{Cl})\text{Cl}$, displacing chloride and giving chloroformate **B**:

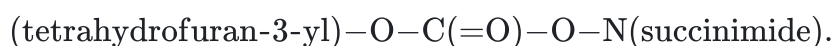


Here hydrogen chloride has SMILES Cl . The stereogenic carbon is unaffected, so **B** retains the (3*S*) configuration.

The next reagent is **N-hydroxysuccinimide**, $\text{ON}1\text{C}(=\text{O})\text{CCC1}=\text{O}$. Its hydroxyl oxygen replaces the remaining chloride of **B**, giving activated carbonate **C**:



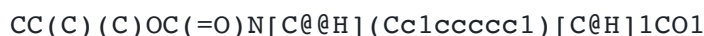
Thus **C** contains the linkage



Its molecular formula is exactly the supplied $\text{C}_9\text{H}_{11}\text{NO}_6$. Again, reaction occurs at the carbonyl carbon, so the tetrahydrofuran stereocentre remains (3*S*).

W: regioselective epoxide opening.

The starting epoxide is **tert-butyl [(1*S*)-1-[(2*S*)-oxiran-2-yl]-2-phenylethyl]carbamate**:



The nucleophile is **2-methylpropan-1-amine (isobutylamine)**, $\text{CC}(\text{C})\text{CN}$. Its nitrogen attacks the less hindered, terminal epoxide carbon. The carbon–oxygen bond at that carbon breaks; subsequent proton transfer gives the alcohol and secondary amine in **W**:



For the common four-carbon chain, number from the phenyl-bearing methylene: C2 bears the protected amino group, and C3 bears the newly formed hydroxyl group.

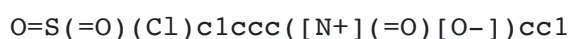
Neither existing stereocentre undergoes geometric inversion. Nevertheless, the substituted epoxide carbon changes its descriptor from *S* to *R*, because its CIP priorities change:

At the substituted epoxide carbon	After opening, at the alcohol carbon
1 : oxygen	1 : hydroxyl oxygen
2 : terminal epoxide carbon, whose next atoms are O, H, H	2 : adjacent amino-bearing carbon, whose next atoms are N, C, H
3 : adjacent amino-bearing carbon, whose next atoms are N, C, H	3 : terminal aminomethyl carbon, whose next atoms are N, H, H
4 : hydrogen	4 : hydrogen

The interchange of priorities 2 and 3 changes the descriptor without changing the geometry. Consequently, **W** has the required (2*S*, 3*R*) configuration.

X: sulfonamide formation.

The reagent is **4-nitrobenzenesulfonyl chloride**:



The secondary aliphatic amine of **W** attacks sulfur and displaces chloride. This nitrogen is more nucleophilic than the carbamate nitrogen or alcohol oxygen. Its N–H hydrogen is replaced by the 4-nitrobenzenesulfonyl group, producing tertiary sulfonamide **X**:



The hydroxyl group and both carbon configurations are retained.

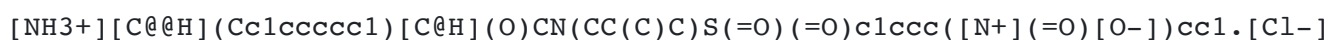
Y: removal of the Boc protecting group.

Hydrogen chloride removes the tert-butoxycarbonyl (Boc) group, exposing the primary amine. The specified coproducts are **carbon dioxide**, $\text{O}=\text{C}=\text{O}$, and **2-chloro-2-methylpropane (tert-butyl chloride)**, CC(C)(C)Cl.

Writing **Y** as its neutral free base gives the balanced equation:



With excess hydrogen chloride, the primary amino group is protonated. The corresponding **Y hydrochloride** is:



The base in the following step makes the amine available for coupling. Neither stereocentre changes. The (2*R*, 3*S*) descriptors in **Y**'s sulfonamide name arise solely from numbering its side chain from the opposite end.

Z: coupling the two synthetic fragments.

The primary amine of **Y** attacks the carbonate carbonyl of **C**. Collapse of the tetrahedral intermediate expels the N-hydroxysuccinimide-derived leaving group, forming the carbamate **Z**:

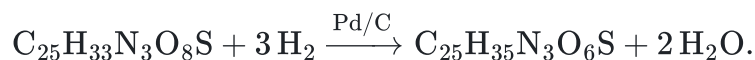


The amino group is acylated preferentially to the alcohol. The product therefore retains a free hydroxyl group and gains the linkage connecting the amino-alcohol chain to the (3*S*)-tetrahydrofuran fragment.

All three stereocentres retain their configurations: (2*S*, 3*R*) in the amino-alcohol chain and (3*S*) in the tetrahydrofuran ring.

4.1(b): Formation and identification of Amprenavir

Catalytic hydrogenation reduces the para-nitro group of **Z** to an amino group:



Hydrogen has SMILES [H][H], and water has SMILES O. No stereogenic carbon is altered, giving the Amprenavir structure listed above.

The product contains exactly four exchangeable hydrogens:

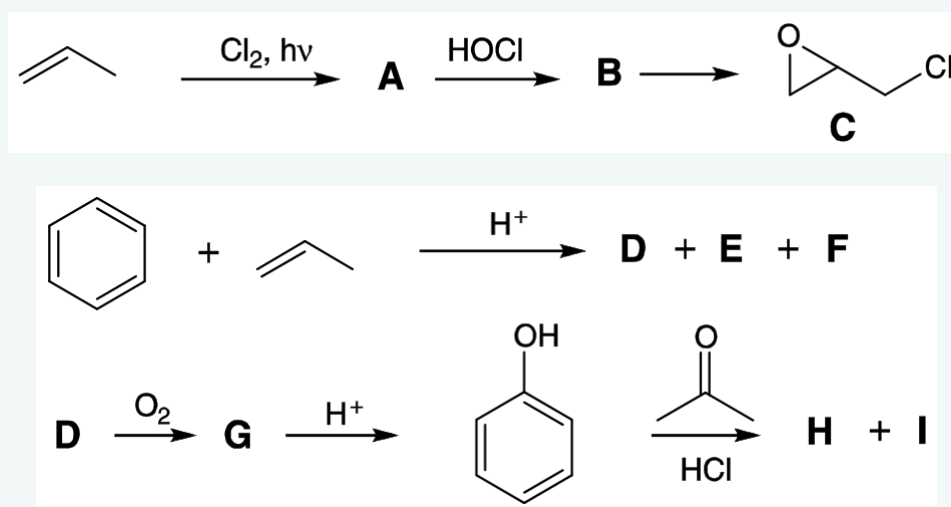
- The aromatic NH_2 group accounts for the **2H signal at $\delta 4.2$** .
- The alcohol OH and carbamate NH account for the **two 1H signals at $\delta 4.9$ and $\delta 5.1$** .
- The sulfonamide nitrogen has no hydrogen.

The two one-proton signals need not be assigned individually to establish the structure; the stated exchange experiment identifies them collectively as OH and NH. Their disappearance on treatment with D₂O agrees with the proposed product.

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

Problem 5: Epoxy resins

The synthesis of epoxy resins is a multi-billion dollar industry worldwide. Epoxy resins are high performance adhesives synthesised from the reaction of a bis-epoxide with a diamine. The bis-epoxide is made from **H** and epichlorohydrin, **C**. Compounds **C** and **H** can be synthesised according to the schemes below.



The synthesis of epichlorohydrin **C** begins with the reaction of propene with chlorine in the presence of light.

5.1 Draw the structures of **A** and **B**.

5.2 Give the formula of a suitable reagent for the conversion of **B** into epichlorohydrin **C**.

The synthesis of **H** commences with the reaction of benzene with propene in the presence of an acid catalyst which gives **D** as the major product and **E** and **F** as minor products.

5.3 Draw the structures of **D**, **E**, and **F** from the following data:

D: Elemental composition: C 89.94 %, H 10.06 %; 6 signals in the ¹³C NMR spectrum.

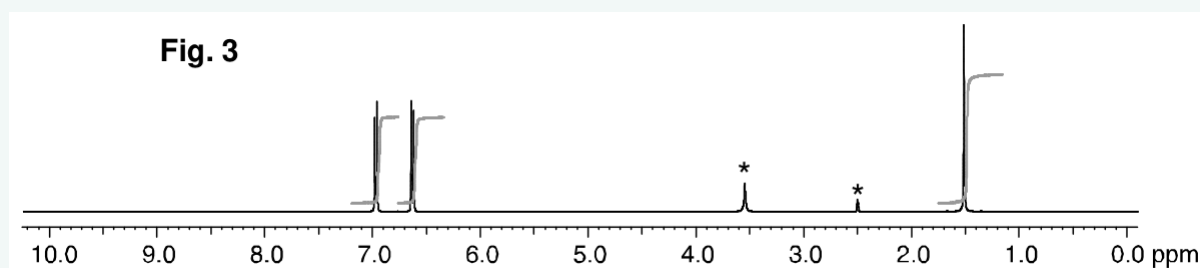
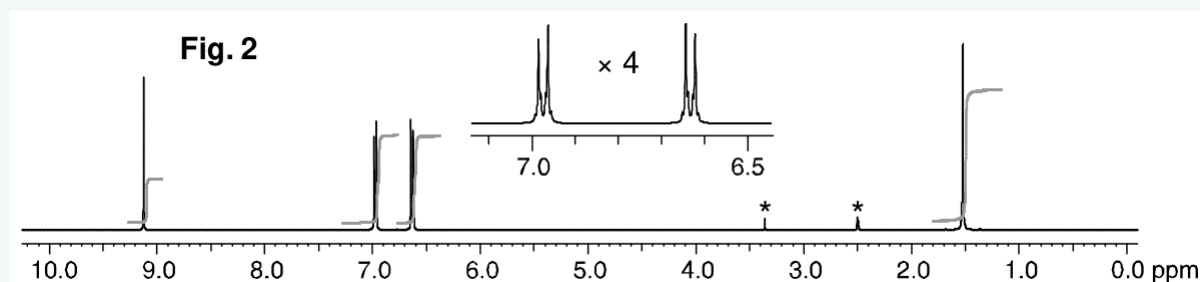
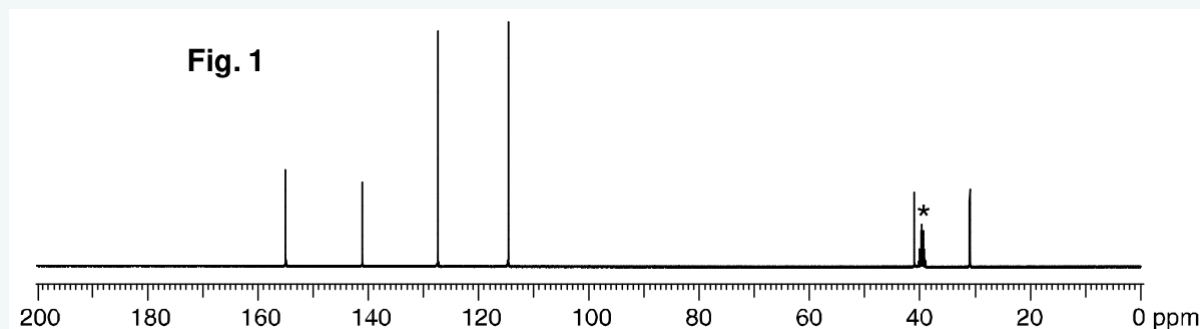
E: Elemental composition: C 88.82 %, H 11.18 %; 4 signals in the ¹³C NMR spectrum.

F: Elemental composition: C 88.82 %, H 11.18 %; 5 signals in the ¹³C NMR spectrum.

Bubbling oxygen through a hot solution of **D** gives **G** which on exposure to acid gives phenol (hydroxybenzene) and acetone (propanone). **G** turns starch iodide paper from white to dark blue. **G** has 6 signals in the ¹³C NMR spectrum and the following signals in the ¹H NMR spectrum: δ 7.78 (1H, s), 7.45 – 7.22 (5H, m), 1.56 (6H, s); addition of D₂O results in the disappearance of the signal at $\delta = 7.78$.

5.4 Draw the structure of **G**.

Exposure of phenol and acetone to hydrochloric acid gives compound **H**. The ^{13}C NMR spectrum for **H** is shown in Fig. 1. The ^1H NMR spectrum is shown in Fig. 2 together with a four-fold expansion of the region 6.5 – 7.1 ppm. The ^1H NMR spectrum after the addition of a drop of D_2O , is shown in Fig. 3. Peaks due to the solvent are marked with an asterisk (*).



5.5 Draw the structure of **H**.

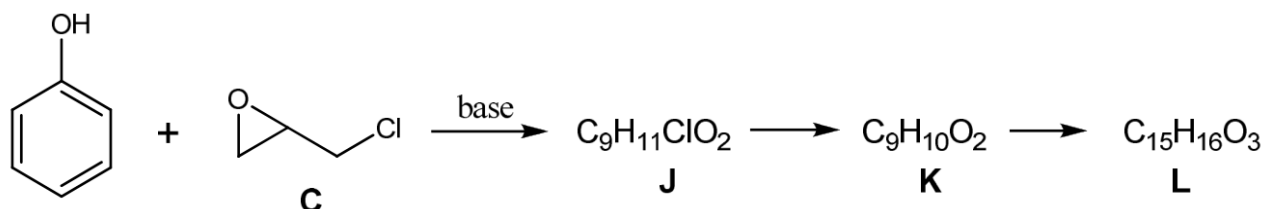
5.6 Draw one resonance structure of phenol which explains the regioselective formation of **H**.

A second compound, **I**, is also formed in the reaction of phenol with acetone. The ^{13}C NMR spectrum of **I** has 12 signals. The ^1H NMR spectrum has the following signals:

δ 7.50 – 6.51 (8H, m), 5.19 (1H, s), 4.45 (1H, s), 1.67 (6H, s); addition of D_2O results in the disappearance of the signals at $\delta = 5.19$ and 4.45

5.7 Draw a structure for **I**.

Excess phenol reacts with epichlorohydrin **C** in the presence of base to give compound **L** which has 6 signals in its ^{13}C NMR spectrum. If the reaction is stopped before completion compounds **J** and **K** can also be isolated. Compound **L** is formed from compound **K** and compound **K** is formed from compound **J**.



5.8 Draw the structures of **J**, **K** and **L**.

Treatment of **H** with a large excess of epichlorohydrin **C** and base gives a monomeric bis-epoxide **M**. **M** contains no chlorine atoms or OH groups.

5.9 Draw the structure of **M**.

Treatment of **H** with a small excess of epichlorohydrin and base gives **N**. **N** has the form: endgroup 1-[repeat unit]_n-endgroup 2 where *n* is approximately 10 – 15. **N** does not contain chlorine atoms and contains one OH group per repeat unit.

5.10 Draw the structure of **N** in the form indicated above:

(endgroup 1-[repeat unit]_n-endgroup 2).

5.11 Draw the repeat unit of the polymeric epoxy resin **O** formed from the reaction of the bis-epoxide **M** with ethane-1,2-diamine.

Official English text of the problem.

Answers

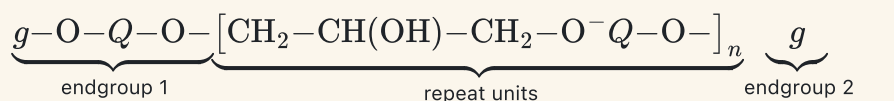
In the polymer structures below, [*] denotes an attachment point, not an actual atom. Define:

- **Q**: the **4,4'-isopropylidenediphenylene group**, [*]c1ccc(C(C)(C)c2ccc([*])cc2)cc1. Each external attachment is para to the central C(CH₃)₂ group.
- **g**: the **glycidyl (oxiran-2-ylmethyl) group**, [*]CC1CO1, attached through its exocyclic methylene carbon.

The conditions do not specify absolute stereochemistry. SMILES for chiral products therefore leave configuration unspecified; racemic products or stereoisomeric mixtures are intended.

- **5.1 — A**: allyl chloride, **3-chloroprop-1-ene**, C=CCC1. **B**: **1,3-dichloropropan-2-ol**, OC(CC1)CC1.
- **5.2 — A** suitable reagent is **sodium hydroxide**, NaOH, [Na+].[OH-].
- **5.3 — D**: **cumene (propan-2-ylbenzene)**, CC(C)c1ccccc1. **E**: **1,4-diisopropylbenzene**, CC(C)c1ccc(C(C)C)cc1. **F**: **1,2-diisopropylbenzene**, CC(C)c1ccccc1C(C)C.
- **5.4 — G**: **cumene hydroperoxide**, CC(C)(OO)c1ccccc1.
- **5.5 — H**: **bisphenol A, 2,2-bis(4-hydroxyphenyl)propane**, CC(C)(c1ccc(O)cc1)c1ccc(O)cc1.

- **5.6** — The **para-carbanionic, oxonium resonance contributor of phenol**, $[\text{OH}^+]=\text{C}1\text{C}=\text{C}[\text{CH}^-]\text{C}=\text{C}1$: oxygen bears a positive charge, and the carbon para to oxygen bears a negative charge.
- **5.7 — I: 2-(2-hydroxyphenyl)-2-(4-hydroxyphenyl)propane**, the ortho/para isomer of bisphenol A, CC(C)(c1ccccc1O)c1ccc(O)cc1.
- **5.8 — J: 1-chloro-3-phenoxypropan-2-ol**, OC(CC1)COc1ccccc1. **K: phenyl glycidyl ether, 2-(phenoxymethyl)oxirane**, c1ccc(OCC2CO2)cc1. **L: 1,3-diphenoxypropan-2-ol**, OC(COc1ccccc1)COc1ccccc1.
- **5.9 — M: bisphenol A diglycidyl ether (DGEBA)**, CC(C)(c1ccc(OCC2CO2)cc1)c1ccc(OCC2CO2)cc1.
- **5.10 — N: the glycidyl-terminated bisphenol A-epichlorohydrin oligomer**,



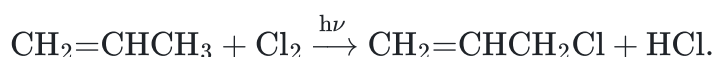
Its repeat-fragment SMILES is [*]CC(O)COc1ccc(C(C)(C)c2ccc(O[*])cc2)cc1.

- **5.11 — O: the ethane-1,2-diamine-cured DGEBA resin**. Its opened-DGEBA bridge is [*]CC(O)COc1ccc(C(C)(C)c2ccc(OCC(O)C[*])cc2)cc1. Fully reacted diamine junctions are [*]N([*])CCN([*])[*], with each nitrogen attached to two such bridges. The initial linear repeat, before further reaction of the remaining N–H bonds, is [*]NCCNCC(O)COc1ccc(C(C)(C)c2ccc(OCC(O)C[*])cc2)cc1.

Solution

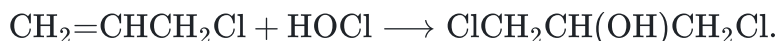
5.1 — Allylic chlorination and chlorohydrin formation

Propene, C=CC, undergoes allylic substitution with chlorine, ClCl, under the photochemical conditions intended in the scheme. Replacing an allylic hydrogen gives **A**, allyl chloride:



The coproduct is hydrogen chloride, Cl.

Hypochlorous acid, OC1, then adds across the double bond. The expected major chlorohydrin has its hydroxyl group on the more substituted alkene carbon:



Thus **B** has a central hydroxyl-bearing carbon and two identical chloromethyl groups.

5.2 — Formation of epichlorohydrin

Sodium hydroxide converts **B** into its alkoxide, **1,3-dichloropropan-2-olate**, [O-]C(CC1)CC1. The oxygen attacks one adjacent chloromethyl carbon intramolecularly, displacing chloride, [Cl-], and forming the three-membered epoxide ring.

The product **C** is **epichlorohydrin, 2-(chloromethyl)oxirane**, ClCC1CO1. The balanced overall equation is



The other products are sodium chloride, $[\text{Na}^+] \cdot [\text{Cl}^-]$, and water, O . The two equivalent chloromethyl groups of **B** lead to racemic **C**.

5.3 — Identification of the alkylbenzenes

Using standard atomic molar masses 12.01 g mol^{-1} for carbon and 1.008 g mol^{-1} for hydrogen, a 100.00 g sample gives:

Compound	Amount of carbon atoms	Amount of hydrogen atoms	H:C atomic ratio
D	$89.94/12.01 = 7.489 \text{ mol}$	$10.06/1.008 = 9.980 \text{ mol}$	1.333
E, F	$88.82/12.01 = 7.396 \text{ mol}$	$11.18/1.008 = 11.09 \text{ mol}$	1.500

Alkylating benzene, c1ccccc1 , with k molecules of propene gives the molecular formula

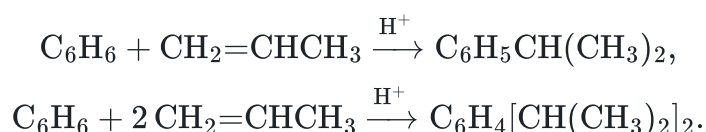
$$\text{C}_{6+3k}\text{H}_{6+6k}.$$

Consequently,

$$\frac{6+6k}{6+3k} = \begin{cases} 4/3 & \Rightarrow k = 1, \\ 3/2 & \Rightarrow k = 2. \end{cases}$$

Thus **D** is C_9H_{12} , whereas **E** and **F** are $\text{C}_{12}\text{H}_{18}$.

The acid catalyst is represented by a hydrogen ion, $[\text{H}^+]$. Protonation of propene produces a secondary isopropyl electrophile, represented as the **propan-2-yl cation**, $\text{C}[\text{CH}^+]\text{C}$. Electrophilic aromatic substitution therefore introduces isopropyl groups:



The second equation applies separately to the ortho and para products.

Their carbon equivalences identify the structures:

Compound	Aromatic carbon environments	Side-chain carbon environments	Total
D: cumene	4: ipso, ortho, meta, para	2: methine and equivalent methyls	6
E: para-diisopropylbenzene	2: substituted and proton-bearing carbons	2	4
F: ortho-diisopropylbenzene	3: three equivalent pairs	2	5

The meta isomer would have four aromatic environments and six carbon signals overall, so it does not match **E** or **F**. The formulas also reproduce the reported elemental percentages to their stated precision.

5.4 — Cumene hydroperoxide

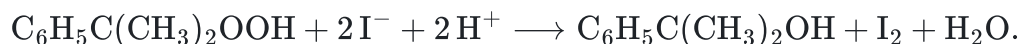
Oxidation of the benzylic position of cumene by dioxygen, $\text{O}=\text{O}$, gives **G**:



The data support a hydroperoxide:

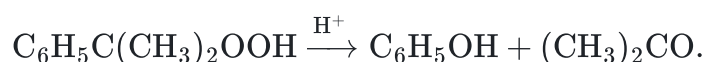
- The five aromatic protons identify a monosubstituted phenyl group.
- The 6H singlet at $\delta = 1.56$ corresponds to two equivalent methyl groups attached to a carbon without a hydrogen.
- The exchangeable 1H singlet at $\delta = 7.78$ is the hydroperoxide proton.
- Four aromatic carbon environments, one central carbon and one methyl environment give six ^{13}C signals.

A hydroperoxide oxidizes iodide to iodine, producing the dark-blue starch–iodine response. A balanced equation is



Here iodide is $[\text{I}^-]$, iodine is I_2 , and the organic reduction product is **cumyl alcohol, 2-phenylpropan-2-ol**, CC(C)(O)c1ccccc1.

Acid-catalysed Hock rearrangement of **G** gives **phenol**, Oc1ccccc1, and **acetone**, CC(=O)C:



5.5 — Bisphenol A

Two phenol molecules condense with one acetone molecule, eliminating one water molecule:



For **H**, each hydroxyl group is **para** to the central isopropylidene group.

The spectra establish the symmetry and substitution pattern:

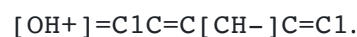
Approximate ^1H shift	Integral	Assignment
9.1 ppm	2H	Two equivalent phenolic OH groups
7.0 ppm	4H	One set of aromatic protons
6.65 ppm	4H	The other set of aromatic protons
1.55 ppm	6H	Two equivalent methyl groups

The two aromatic sets give the characteristic pattern of equivalent para-disubstituted rings. Addition of **deuterium oxide**, $[\text{2H}]\text{O}[\text{2H}]$, removes the OH resonance through hydrogen–deuterium exchange.

Excluding the starred solvent peaks, the ^{13}C spectrum contains six signals: four aromatic environments, the central quaternary carbon, and the equivalent methyl carbons. This identifies **bisphenol A**.

5.6 — Resonance and regioselectivity

Use the contributor



To draw it precisely, number the hydroxyl-bearing ring carbon 1:

- Draw a double bond from carbon 1 to oxygen; oxygen retains its hydrogen and bears a positive charge.
- Draw ring double bonds between carbons 2–3 and 5–6.
- Place a negative charge on carbon 4, para to oxygen; that carbon retains its hydrogen.

The electron flow is donation of an oxygen lone pair into the oxygen–carbon bond, accompanied by movement of ring π electrons toward the para carbon. This is a resonance contributor of phenol, not a separate reaction product.

It shows enhanced electron density at the para position. Related contributors enhance the ortho positions. Phenol therefore directs electrophilic substitution ortho and para; the less crowded para positions favour formation of **H**.

5.7 — The ortho/para bisphenol isomer

Compound **I** has two nonequivalent phenolic OH groups: their separate 1H singlets disappear after deuterium oxide addition. Its eight aromatic protons and equivalent six methyl protons are consistent with another bisphenol A isomer.

The carbon-signal count distinguishes the ortho/para structure:

$$\underbrace{6}_{\text{ortho-disubstituted ring}} + \underbrace{4}_{\text{para-disubstituted ring}} + \underbrace{1}_{\text{central carbon}} + \underbrace{1}_{\text{equivalent methyls}} = 12.$$

Thus draw one hydroxyl group **ortho** to the central carbon substituent and the other **para** to it.

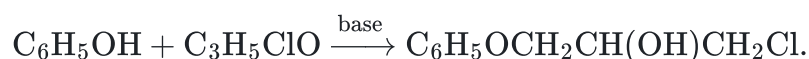
The balanced condensation is



where the $\text{C}_{15}\text{H}_{16}\text{O}_2$ product has the connectivity specified for **I**.

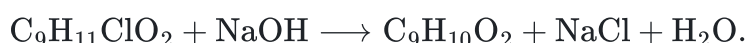
5.8 — Chlorohydrin, glycidyl ether and diether

Base produces the **phenoxide ion**, $[\text{O}-]\text{c}1\text{cccc}1$, which attacks the less substituted carbon of the epoxide ring of **C**. Ring opening and proton transfer give **J**:

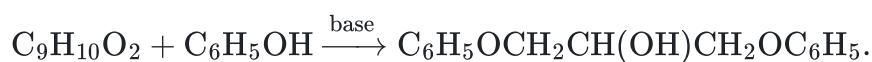


This product has formula $\text{C}_9\text{H}_{11}\text{ClO}_2$, as required.

Base then promotes intramolecular displacement of chloride, forming the epoxide **K**:



Further phenoxide attack opens **K** at its terminal epoxide carbon:



The resulting **L** has formula $\text{C}_{15}\text{H}_{16}\text{O}_3$. Its two ends are identical, so its six carbon signals comprise: 4 phenyl environments + 1 equivalent methylene environment + 1 central hydroxymethine environment.

5.9 — The monomeric bis-epoxide

Each phenolic group of **H** undergoes the chlorohydrin-formation/ring-closure sequence established in 5.8. With a large excess of epichlorohydrin, both ends become glycidyl ethers, giving **M**.

Draw a bisphenol A framework bearing an $-\text{O}-\text{CH}_2^-$ linkage to an oxirane ring at each para position. The oxirane oxygen bridges its adjacent methine and terminal methylene carbons.

The balanced overall reaction is



The four oxygen atoms in **M** are two aryl ether oxygens and two epoxide oxygens. There are no OH groups or chlorine atoms.

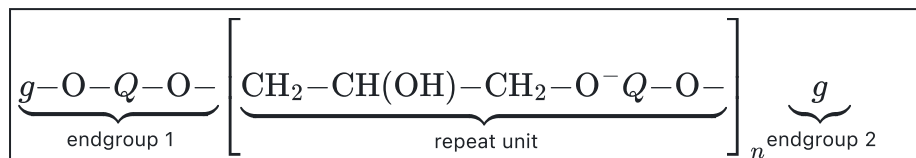
5.10 — The oligomer and its end groups

With a smaller excess of epichlorohydrin, phenolic groups also open glycidyl epoxide groups on other molecules. Each such chain-extension step creates the linkage



which contains exactly one secondary alcohol group.

The required structure is



The fragment SMILES, with attachment points, are:

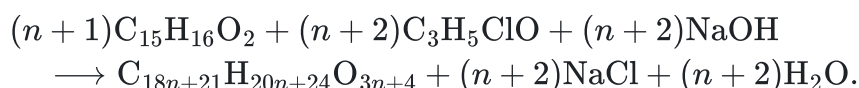
Fragment	SMILES
Endgroup 1: glycidylated bisphenol A ether end	<chem>CC(C)(c1ccc(OCC2COC2)cc1)c1ccc(O[*])cc1</chem>
Repeat unit	<chem>[*]CC(O)COc1ccc(C(C)(C)c2ccc(O[*])cc2)cc1</chem>
Endgroup 2: glycidyl group	<chem>[*]CC1CO1</chem>

Join the atoms adjacent to matching attachment points, removing the dummy atoms. Both termini are epoxides. Each repeat contributes one OH group, and no chlorine remains. Setting $n = 0$ recovers **M**, which checks the end-group assignment.

The repeat formula is $\text{C}_{18}\text{H}_{20}\text{O}_3$, and the complete oligomer formula is



Its balanced preparation can be written



For $n = 10$ – 15 , the ideal incorporated epichlorohydrin:bisphenol A ratio is

$$\frac{n+2}{n+1} = 1.063\text{--}1.091 \text{ mol mol}^{-1},$$

consistent with a small molar excess of epichlorohydrin.

5.11 — Amine opening and crosslinking

Ethane-1,2-diamine, NCCN , attacks the less substituted carbon of each epoxide. The epoxide oxygen becomes an OH group, while the attacked terminal carbon forms a carbon–nitrogen bond. No small molecule is eliminated.

Define the doubly opened **M** bridge P as



with fragment SMILES

[*]CC(O)COc1ccc(C(C)(C)c2ccc(OCC(O)C[*])cc2)cc1.

If each amino nitrogen reacts once, the linear addition repeat is



Its fragment SMILES is

```
[*]NCCNCC(O)COc1ccc(C(C)(C)c2ccc(OCC(O)C[*])cc2)cc1.
```

The corresponding repeat composition is obtained by direct addition:



Each nitrogen still has one N–H bond. These secondary amines can open further epoxide rings, producing crosslinks. In the fully reacted resin, each nitrogen has three carbon bonds: one to the ethylene bridge and two to opened-epoxide methylene groups.

To draw that network motif precisely:

1. Draw two nitrogen atoms joined by $-\text{CH}_2-\text{CH}_2^-$.
2. Give each nitrogen two additional bonds to $-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}_2-\text{O}^-$ arms.
3. Continue each arm through Q , then through another $-\text{O}-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}_2^-$ arm to a nitrogen elsewhere in the resin.

A representative four-attachment structural cell is

```
[*:1]N(CCN([*:2])CC(O)COc1ccc(C(C)(C)c2ccc(OCC(O)C[*:3])cc2)cc1)CC(O)COc3ccc(C(C)(C)c4ccc(OCC(O)C[*:4])cc4)cc3.
```

Attachments 1 and 2 terminate at nitrogens; attachments 3 and 4 terminate at methylene carbons. Connect nitrogen ends to methylene ends of other cells. This specifies the local covalent connectivity; the long-range crosslink arrangement need not be periodic.

A fully reacted cell contains two **M** molecules per diamine, because one diamine supplies four reactive N–H bonds:

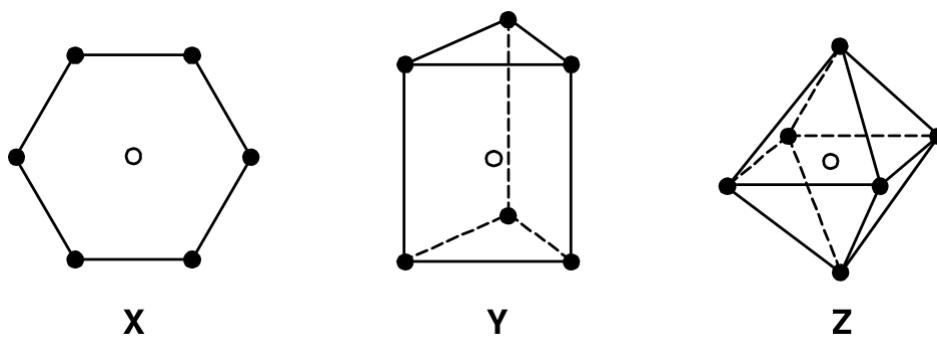


It contains four newly formed OH groups and no residual N–H bonds.

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

Problem 6: Transition metal complexes

Alfred Werner used the technique of 'isomer counting' to deduce the structure of metal complexes with coordination number six. Three of the shapes he considered are shown below.



In each structure, the empty circle shows the location of the central metal atom and the filled circles show the location of the ligands. Structure **X** is hexagonal planar, structure **Y** is trigonal prismatic and structure **Z** is octahedral.

For each of the three shapes, there is just one structure when all of the ligands are the same, i.e. when the complex has the general formula MA_6 where A is the ligand. However, when achiral ligands A are substituted by one or more achiral ligands, it may be possible for each structure to form geometrical isomers. It might also be possible for one or more of the geometrical isomers to be optically active and exist as pairs of enantiomers.

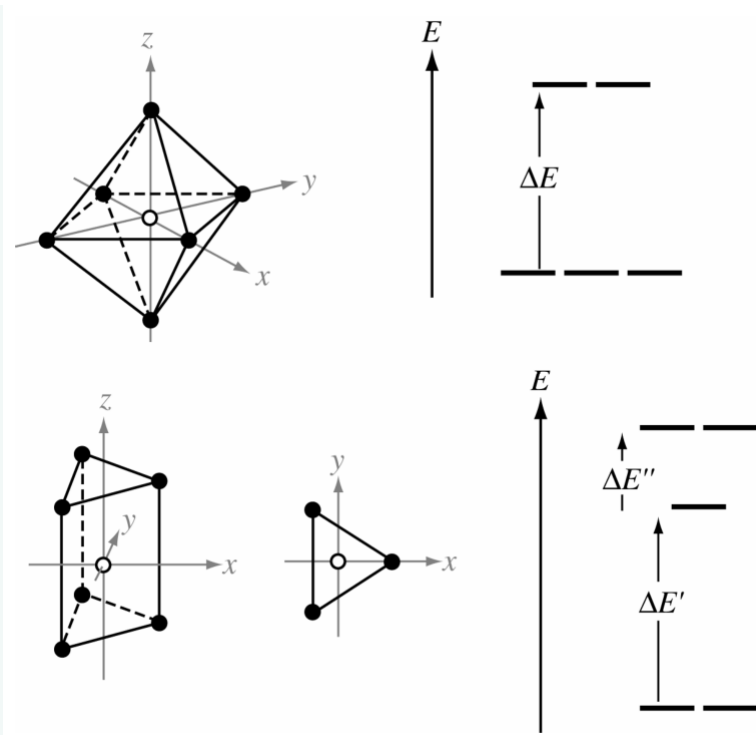
6.1 Fill in the table below to indicate how many geometrical isomers may be formed for each structure **X**, **Y**, and **Z** as the monodentate ligands A are substituted by monodentate ligands B or by symmetrical bidentate ligands, denoted C–C. Bidentate ligand C–C can only link between two atoms on adjacent positions, i.e. those positions connected by a line in the structures **X**, **Y**, and **Z**.

In each case write the number of geometrical isomers in the space provided. If one of the isomers exists as a pair of enantiomers, include an asterisk, *, in the box. If two exist as two pairs of enantiomers, include two asterisks and so on. For example, if you think there are five geometrical isomers of a particular structure, three of which exist as pairs of enantiomers, write 5 ***

Number of predicted geometrical isomers

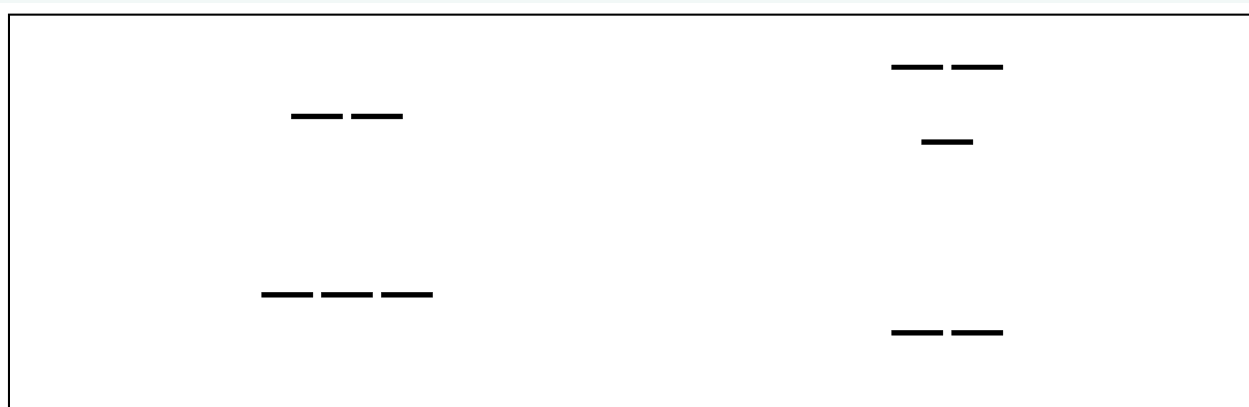
	Hexagonal planar X	Trigonal Prismatic Y	Octahedral Z
MA_6	1	1	1
MA_5B			
MA_4B_2			
MA_3B_3			
$MA_4(C-C)$			
$MA_2(C-C)_2$			
$M(C-C)_3$			

There are no known complexes that adopt the hexagonal planar geometry **X**, but structures are known for both the trigonal prismatic geometry **Y** and for the octahedral geometry **Z**. In these complexes, the orbitals derived from the metal d orbitals have different energies depending on the geometry of the complex. The splitting patterns for the trigonal prismatic geometry and for the octahedral geometry are shown below.



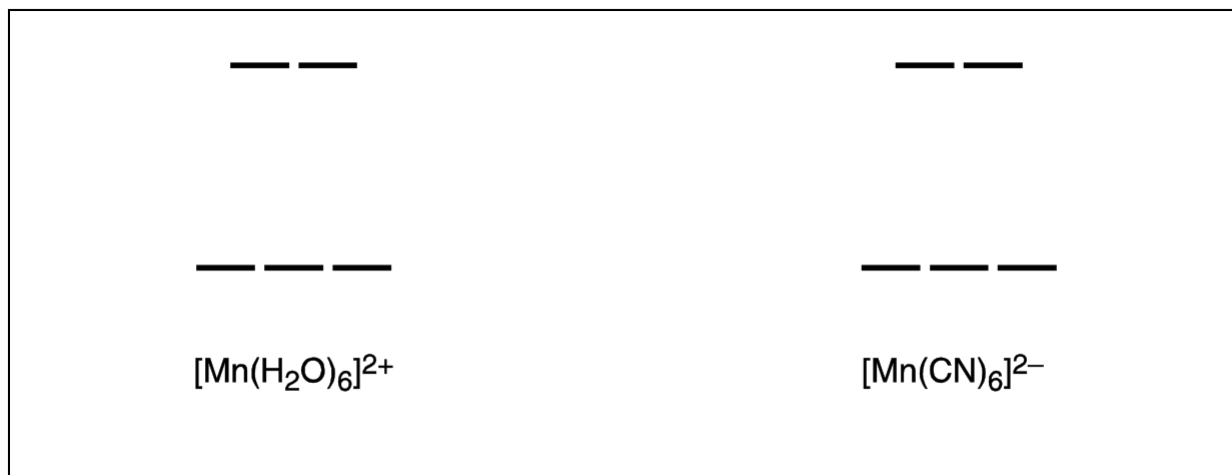
The separations in energy, ΔE , $\Delta E'$ and $\Delta E''$ depend on the particular complex.

6.2 For each of the splitting patterns shown below label which d orbitals are which.

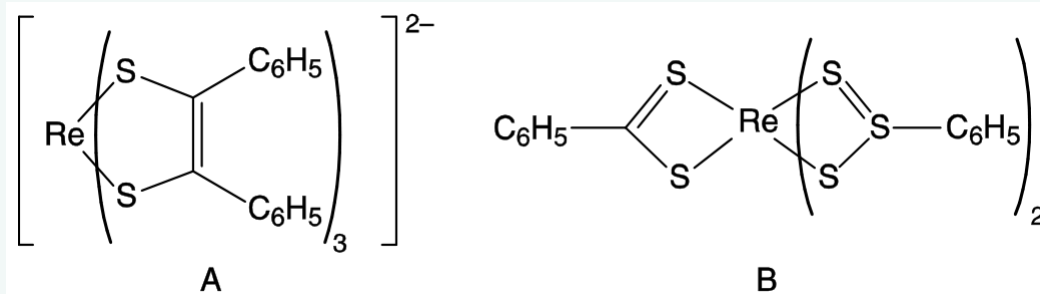


The two complexes $[\text{Mn}(\text{H}_2\text{O})_6]^{2+}$ and $[\text{Mn}(\text{CN})_6]^{2-}$ are both octahedral. One has a magnetic moment of 5.9 BM, the other has a magnetic moment of 3.8 BM but you must decide which is which.

6.3 On the diagram below, draw the electronic arrangements for each of the complexes.



The magnetic moments of complexes **A** and **B** shown below have been measured and found to be 1.9 and 2.7 BM but you must decide which is which.



6.4 Draw the orbital splitting diagrams for the two complexes, including the arrangements of the electrons.

Octahedral complexes are far more common than trigonal prismatic. Werner isolated five compounds **C – G** containing Co(III), Cl, and NH_3 only, each of which contained one octahedral complex. (There is actually a sixth compound but Werner could not isolate it.) Werner's five compounds had the molar conductivities shown below. The conductivities are extrapolated to infinite dilution and are expressed in arbitrary units. Compound **G** does not react with aqueous AgNO_3 ; compounds **C**, **D**, and **E** react with different stoichiometric ratios of aqueous AgNO_3 ; **E** and **F** react with the same stoichiometric ratio of aqueous AgNO_3 .

	C	D	E	F	G
molar conductivity	510	372	249	249	~ 0

6.5 As far as you are able, suggest a structure for each of the compounds **C – G**.

Werner was also the first person to separate the enantiomers of an octahedral compound, **H**, which contained no carbon atoms. The compound, **H**, is composed of only cobalt, ammonia, chloride and an oxygen species which could be either H_2O , or HO^- or O^{2-} . The compound contains octahedrally coordinated cobalt ions. All of the chloride is easily removed from the compound by titration with aqueous silver nitrate. A 0.2872 g sample of **H** (containing no water of crystallization) required 22.8 cm^3 of a silver nitrate solution ($c = 0.100 \text{ mol dm}^{-3}$) to exchange all the chloride.

6.6 Calculate the percentage, by mass, of chloride in **H**.

H is stable to acids, but is hydrolysed in alkali. A 0.7934 g sample of **H** (containing no water of crystallization) was heated with excess aqueous sodium hydroxide. Cobalt(III) oxide was formed and ammonia gas given off. The ammonia produced was distilled off and absorbed into 50.0 cm³ of aqueous HCl ($c_{\text{HCl}} = 0.500 \text{ mol dm}^{-3}$). The residual HCl required 24.8 cm³ of aqueous KOH solution ($c_{\text{KOH}} = 0.500 \text{ mol dm}^{-3}$) to be neutralized.

The remaining suspension of cobalt(III) oxide was allowed to cool, approximately 1 g of potassium iodide was added, and then the mixture was acidified with aqueous HCl. The liberated iodine was then titrated with aqueous solution of sodium thiosulfate ($c = 0.200 \text{ mol dm}^{-3}$) and required 21.0 cm³ for complete reaction.

6.7 Calculate the percentage, by mass, of ammonia in **H**.

6.8 Give the equation for the reaction of cobalt(III) oxide with potassium iodide in aqueous acid.

6.9 Calculate the percentage, by mass, of cobalt in **H**.

6.10 Calculate the identity of the oxygen species contained in **H**. Show your working.

6.11 Give the empirical formula of **H**.

6.12 Suggest a structure for the chiral compound **H**.

Official English text of the problem.

Answers

Molecular names and coordination SMILES are supplied in the corresponding solution parts.

- 6.1.** Each asterisk denotes one geometrical isomer that exists as an enantiomeric pair.

Formula	Hexagonal planar X	Trigonal prismatic Y	Octahedral Z
MA ₆	1	1	1
MA ₅ B	1	1	1
MA ₄ B ₂	3	3*	2
MA ₃ B ₃	3	3*	2
MA ₄ (C–C)	1	2	1
MA ₂ (C–C) ₂	2	4*	2*
M(C–C) ₃	1	2	1*

- 6.2.** From lowest to highest energy:
 - Octahedral: $(d_{xy}, d_{xz}, d_{yz}) < (d_{z^2}, d_{x^2-y^2})$.
 - Trigonal prismatic, for the pattern supplied: $(d_{xy}, d_{x^2-y^2}) < d_{z^2} < (d_{xz}, d_{yz})$.
- 6.3.**
 - [Mn(H₂O)₆]²⁺: high-spin d^5 , $t_{2g}^3 e_g^2$, five unpaired electrons, **5.9 BM**.
 - [Mn(CN)₆]²⁻: d^3 , t_{2g}^3 , three unpaired electrons, **3.8 BM**.

- **6.4.**
- **A:** Re(IV), d^3 , trigonal prismatic; three electrons in the lowest doublet, one unpaired; **1.9 BM.**
- **B:** Re(III), d^4 , low-spin octahedral in the intended strong-field treatment; t_{2g}^4 , two unpaired; **2.7 BM.**
- **6.5.**
- **C:** $[\text{Co}(\text{NH}_3)_6]\text{Cl}_3$.
- **D:** $[\text{Co}(\text{NH}_3)_5\text{Cl}]\text{Cl}_2$.
- **E, F:** cis- and trans- $[\text{Co}(\text{NH}_3)_4\text{Cl}_2]\text{Cl}$, in an undetermined order.
- **G:** $[\text{Co}(\text{NH}_3)_3\text{Cl}_3]$, either fac or mer; the data do not distinguish them.
- **6.6.** Chloride: **28.1% by mass.**
- **6.7.** Ammonia: **27.0% by mass.**
- **6.8.** $\text{Co}_2\text{O}_3 + 2\text{I}^- + 6\text{H}^+ \longrightarrow 2\text{Co}^{2+} + \text{I}_2 + 3\text{H}_2\text{O}$.
- **6.9.** Cobalt: **31.2% by mass.**
- **6.10.** The oxygen species is hydroxide, OH^- , SMILES $[\text{OH}-]$.
- **6.11.** Empirical formula: $\text{Co}_2(\text{NH}_3)_6(\text{OH})_3\text{Cl}_3$, equivalently $\text{Co}_2\text{Cl}_3\text{H}_{21}\text{N}_6\text{O}_3$.
- **6.12.** A suitable structure is **hexol chloride**, $[\text{Co}_4(\text{NH}_3)_{12}(\text{OH})_6]\text{Cl}_6$: a central octahedral cobalt ion joined through three pairs of hydroxide bridges to three peripheral tetraamminecobalt centres. Its central tris-chelate arrangement gives Δ and Λ enantiomers.

Solution

The coordination SMILES below use dative bonds, $\rightarrow$, and octahedral stereodescriptors, @OH, where appropriate. An @OH descriptor can specify geometrical configuration even when the complex is achiral. Trigonal-prismatic geometry is described in words because these octahedral descriptors do not encode it.

6.1 — Geometrical and optical isomers

A pair of enantiomers counts as **one geometrical isomer**, with an asterisk. Ligands A, B and C–C are unspecified placeholders, so they do not have unique molecular names or molecular SMILES.

For **X**, number the six sites consecutively around the hexagon.

- With one B ligand, every site is equivalent.
- With two B ligands, their separation can be one, two or three edges: three isomers.
- With three B ligands, representative occupied sets are 123, 124 and 135: three isomers.
- One chelate can occupy any edge: one isomer.
- Two chelates have representatives (12)(34) and (12)(45): two isomers.
- Three chelates have the single arrangement (12)(34)(56), up to symmetry.

All are achiral in the problem's idealized planar site-and-link model: reflection in the molecular plane leaves each arrangement unchanged.

For **Y**, label the upper triangle u_1, u_2, u_3 and the lower triangle l_1, l_2, l_3 , with vertical edges $u_i l_i$. The following representatives exhaust the possibilities:

Substitution	Representatives	Chirality
One B	u_1	Achiral
Two B	$u_1 u_2, u_1 l_1, u_1 l_2$	Only $u_1 l_2$ is chiral
Three B	$u_1 u_2 u_3, u_1 u_2 l_1, u_1 u_2 l_3$	Only $u_1 u_2 l_1$ is chiral
One chelate	$(u_1 u_2), (u_1 l_1)$	Both achiral
Two chelates	$(u_1 l_1)(u_2 l_2); (u_1 u_2)(u_3 l_3); (u_1 u_2)(l_1 l_2); (u_1 u_2)(l_1 l_3)$	Only the last is chiral
Three chelates	$(u_1 l_1)(u_2 l_2)(u_3 l_3); (u_1 u_2)(l_1 l_2)(u_3 l_3)$	Both achiral

For example, the two B ligands in $u_1 l_2$ occupy opposite ends of a diagonal of a rectangular face. Its mirror image cannot be superimposed by a proper rotation. The same test gives the other two starred prism arrangements.

For **Z**:

- MA_5B has one arrangement.
- MA_4B_2 has cis and trans arrangements.
- MA_3B_3 has fac and mer arrangements.
- One chelate can occupy any octahedral edge: one arrangement.
- Two chelates leave the two A ligands either cis or trans. The cis arrangement has Δ/Λ enantiomers; the trans arrangement is achiral.
- Three chelates give one geometrical arrangement with Δ/Λ enantiomers.

These results give the completed table in **Answers**.

6.2 — Identification of the d orbitals

In an octahedral complex, the ligands lie along the coordinate axes. The orbitals directed along these axes experience greater ligand repulsion:

$$\underbrace{d_{xy}, d_{xz}, d_{yz}}_{\text{lower } t_{2g}} < \underbrace{d_{z^2}, d_{x^2-y^2}}_{\text{upper } e_g}.$$

Thus write d_{xy}, d_{xz}, d_{yz} on the lower three lines and $d_{z^2}, d_{x^2-y^2}$ on the upper two lines, in any order within each degenerate set.

For the supplied trigonal-prismatic pattern, with z along the prism axis:

$$\underbrace{d_{xy}, d_{x^2-y^2}}_{\text{lowest doublet}} < \underbrace{d_{z^2}}_{\text{middle singlet}} < \underbrace{d_{xz}, d_{yz}}_{\text{highest doublet}}.$$

The unique singlet is d_{z^2} . The other four orbitals form the two indicated symmetry-related pairs.

6.3 — Manganese electron arrangements

The spin-only magnetic moment is approximately

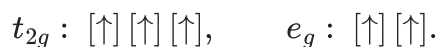
$$\mu_{\text{so}} = \sqrt{n(n+2)} \text{ BM},$$

where n is the number of unpaired electrons.

The **hexaaquamanganese(II) ion**, $[\text{Mn}(\text{H}_2\text{O})_6]^{2+}$, has coordination SMILES:

[Mn+2](<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])<-[OH2]

Water is neutral, so manganese is in oxidation state +2. Manganese is a group-7 element; therefore Mn(II) is d^5 . With weak-field water ligands, it is high spin:



There are five unpaired electrons:

$$\mu_{\text{so}} = \sqrt{5(5+2)} = \sqrt{35} = 5.92 \text{ BM.}$$

It therefore has the measured moment **5.9 BM**.

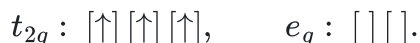
The **hexacyanidomanganate(IV) ion**, $[\text{Mn}(\text{CN})_6]^{2-}$, has coordination SMILES:

[Mn+4](<-[C-]#N)(<-[C-]#N)(<-[C-]#N)(<-[C-]#N)(<-[C-]#N)<-[C-]#N

Each cyanido ligand has charge -1 , so

$$x + 6(-1) = -2 \implies x = +4.$$

Mn(IV) is d^3 , giving



Thus

$$\mu_{\text{so}} = \sqrt{3(3+2)} = \sqrt{15} = 3.87 \text{ BM,}$$

corresponding to the measured **3.8 BM**. Both complexes are octahedral; the difference in electron count is essential.

6.4 — Rhenium electron arrangements

In **A**, each ene-dithiolate ligand is dianionic. Consequently,

$$x + 3(-2) = -2 \implies x = +4.$$

Rhenium is a group-7 element, so Re(IV) is d^3 .

A is the **tris[(Z)-1,2-diphenylethene-1,2-dithiolato]rhenate(IV) ion**, represented by the connectivity SMILES:

[Re+4]123(<-[S-]/C(c4ccccc4)=C(\[S-]->1)c4ccccc4)(<-[S-]/C(c4ccccc4)=C(\[S-]->2)c4ccccc4)<-[S-]/C(c4ccccc4)=C(\[S-]->3)c4ccccc4

An octahedral d^3 ion would have three unpaired electrons. The smaller magnetic moment instead corresponds to one unpaired electron, obtained in the supplied trigonal-prismatic splitting:

Level in A, highest first	Occupation
d_{xz}, d_{yz}	$[] []$
d_{z^2}	$[]$
$d_{xy}, d_{x^2-y^2}$	$[\uparrow\downarrow] [\uparrow]$

The choice of which member of the lowest doublet contains the pair is arbitrary. With one unpaired electron,

$$\mu_{\text{so}} = \sqrt{3} = 1.73 \text{ BM,}$$

consistent with assigning the observed **1.9 BM** to A. Its coordination geometry is **trigonal prismatic**, which the connectivity SMILES does not itself specify.

In **B**, each sulfur chelate is monoanionic. Since the complex is neutral,

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

so Re(III) is d^4 .

Reading the central **S** in the right-hand repeated ligand literally, B is **bis(benzenedithiosulfinato)(dithiobenzoato)rhenium(III)**, with connectivity SMILES:

[Re+3]123(<-S=C(c4ccccc4)[S-]->1)(<-S=S(c4ccccc4)[S-]->2)<-S=S(c4ccccc4)[S-]->3

Under the strong-field treatment intended for these 5d complexes, B has the low-spin octahedral arrangement:

Level in B, highest first	Occupation
$e_g : d_{z^2}, d_{x^2-y^2}$	[] []
$t_{2g} : d_{xy}, d_{xz}, d_{yz}$	[↑↓] [↑] [↑]

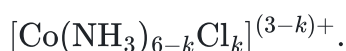
There are two unpaired electrons:

$$\mu_{\text{so}} = \sqrt{8} = 2.83 \text{ BM},$$

corresponding to **2.7 BM**. The displayed connectivity leaves its handedness unspecified, as does the problem's drawing.

6.5 — Werner's cobalt compounds

Co(III) has coordination number six. Ammonia is neutral, whereas each coordinated chlorido ligand lowers the complex charge by one:



The remaining chloride ions are counterions. These precipitate with silver ions, whereas coordinated chloride is not immediately removed in the stated test.

The conductivity sequence is consistent with four, three, two, two and zero ions per formula unit:

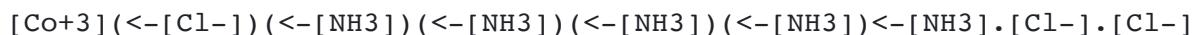
Compound	Structure	Counterion chlorides	Dissolved ions per formula unit
C	$[\text{Co}(\text{NH}_3)_6]\text{Cl}_3$	3	4
D	$[\text{Co}(\text{NH}_3)_5\text{Cl}]\text{Cl}_2$	2	3
E	One isomer of $[\text{Co}(\text{NH}_3)_4\text{Cl}_2]\text{Cl}$	1	2
F	The other isomer of $[\text{Co}(\text{NH}_3)_4\text{Cl}_2]\text{Cl}$	1	2
G	$[\text{Co}(\text{NH}_3)_3\text{Cl}_3]$	0	0

The structures, names and SMILES are:

- **C: hexaamminecobalt(III) chloride**

[Co+3](<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])<-[NH3].[Cl-].[Cl-].[Cl-]

- **D: pentaamminechloridocobalt(III) chloride**



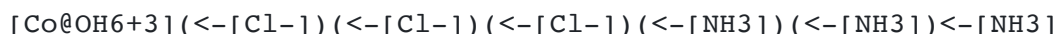
- **One of E/F: cis-tetraamminedichloridocobalt(III) chloride**, with adjacent chlorido ligands, at 90° :



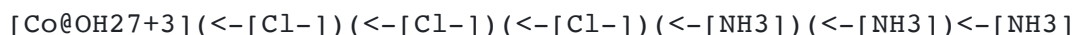
- **The other of E/F: trans-tetraamminedichloridocobalt(III) chloride**, with opposite chlorido ligands, at 180° :



- **G may be fac-triamminetrichloridocobalt(III)**, with all three chlorido ligands mutually cis on one triangular face:



- **Alternatively, G may be mer-triamminetrichloridocobalt(III)**, with two chlorido ligands trans and the third cis to both:



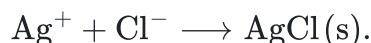
Neither conductivity nor the chloride-precipitation result distinguishes E from F, or fac-G from mer-G. The other geometrical isomer of G is the sixth compound mentioned in the question.

6.6 — Mass percentage of chloride

For the numerical calculations, use standard molar masses

$$M(\text{Cl}) = 35.45, \quad M(\text{NH}_3) = 17.03, \quad M(\text{Co}) = 58.93 \quad \text{g mol}^{-1}.$$

Chloride ion, $[\text{Cl}-]$, precipitates with silver(I) ion, $[\text{Ag}+]$, in a 1:1 ratio:



Silver chloride has the stoichiometric ionic SMILES $[\text{Ag}+] \cdot [\text{Cl}-]$; this does not describe its crystal lattice.

$$n(\text{Cl}^-) = (0.100 \text{ mol dm}^{-3})(22.8 \times 10^{-3} \text{ dm}^3) = 2.28 \times 10^{-3} \text{ mol}.$$

Therefore,

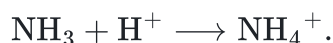
$$m(\text{Cl}^-) = (2.28 \times 10^{-3})(35.45) = 0.080826 \text{ g},$$

and

$$w(\text{Cl}^-) = \frac{0.080826}{0.2872} \times 100 = 28.1\%.$$

6.7 — Mass percentage of ammonia

Ammonia, N , consumes one equivalent of acid to form ammonium ion, $[\text{NH}_4+]$:



The remaining acid is measured by



Here the hydron, hydroxide ion and water have SMILES [H+], [OH-] and O, respectively.

Initially,

$$n_0(\text{H}^+) = (0.500)(50.0 \times 10^{-3}) = 0.0250 \text{ mol}.$$

The residual acid is

$$n_{\text{res}}(\text{H}^+) = (0.500)(24.8 \times 10^{-3}) = 0.0124 \text{ mol}.$$

Hence,

$$n(\text{NH}_3) = 0.0250 - 0.0124 = 0.0126 \text{ mol},$$

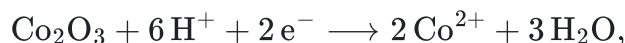
$$m(\text{NH}_3) = (0.0126)(17.03) = 0.2146 \text{ g},$$

and

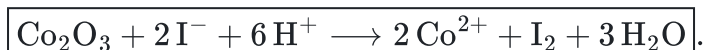
$$w(\text{NH}_3) = \frac{0.2146}{0.7934} \times 100 = 27.0\%.$$

6.8 — Reaction of cobalt(III) oxide with iodide

Cobalt(III) is reduced to cobalt(II), while iodide is oxidized to iodine:



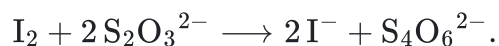
Adding gives



The relevant species are cobalt(III) oxide, stoichiometric ionic SMILES [Co+3].[Co+3].[O-2].[O-2].[O-2]; iodide ion, [I-]; cobalt(II) ion, [Co+2]; and iodine, I₂. Cobalt(III) oxide is an extended solid, so its ionic SMILES specifies composition rather than lattice structure.

6.9 — Mass percentage of cobalt

Iodine reacts with thiosulfate according to



The ions are **thiosulfate**, [O-]S(=O)(=O)[S-], and **tetrathionate**, [O-]S(=O)(=O)SSS(=O)(=O)[O-].

Thus,

$$n(\text{S}_2\text{O}_3^{2-}) = (0.200)(21.0 \times 10^{-3}) = 4.20 \times 10^{-3} \text{ mol},$$

$$n(\text{I}_2) = \frac{4.20 \times 10^{-3}}{2} = 2.10 \times 10^{-3} \text{ mol}.$$

From the equation in 6.8, two cobalt atoms correspond to one iodine molecule:

$$n(\text{Co}) = 2n(\text{I}_2) = 4.20 \times 10^{-3} \text{ mol}.$$

Consequently,

$$m(\text{Co}) = (4.20 \times 10^{-3})(58.93) = 0.2475 \text{ g},$$

$$w(\text{Co}) = \frac{0.2475}{0.7934} \times 100 = 31.2\%.$$

6.10 — Identification of the oxygen species

The unassigned mass percentage is approximately

$$100 - 28.14 - 27.05 - 31.20 = 13.61\%.$$

This includes both oxygen and any hydrogen belonging to its species.

For the 0.7934 g sample, the chloride content inferred from 6.6 is

$$n(\text{Cl}^-) = (2.280 \times 10^{-3}) \frac{0.7934}{0.2872} \approx 6.30 \times 10^{-3} \text{ mol}.$$

The cobalt and ammonia amounts therefore give

$$\text{Co} : \text{NH}_3 : \text{Cl}^- = 0.00420 : 0.0126 : 0.00630 = 1 : 3 : 1.5.$$

With cobalt in oxidation state +3 and ammonia neutral, the oxygen species must supply

$$3 - 1.5 = 1.5$$

negative charge units per cobalt atom.

The remaining mass per mole of cobalt is approximately

$$\frac{0.1361(0.7934 \text{ g})}{0.00420 \text{ mol}} = 25.7 \text{ g mol}^{-1}$$

per mole of cobalt. Compare the candidates:

Candidate	Amount required per cobalt by charge balance	Predicted remaining mass per mole of cobalt
Water, H_2O , 0	Cannot supply negative charge	Inconsistent
Hydroxide, OH^- , [OH-]	1.5 mol	$1.5(17.01) = 25.5 \text{ g}$
Oxide, O^{2-} , [O-2]	0.75 mol	$0.75(16.00) = 12.0 \text{ g}$

The measured residual mass agrees with hydroxide:

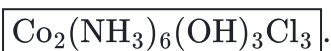
The oxygen species is OH^- .

6.11 — Empirical formula

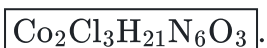
The component ratio is

$$\text{Co} : \text{NH}_3 : \text{OH}^- : \text{Cl}^- = 1 : 3 : 1.5 : 1.5.$$

Multiplying by two gives the smallest integral ratio:



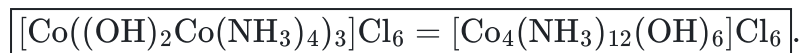
On an elemental basis this is



An empirical formula specifies a ratio, not a unique molecular graph. The molecular structure and SMILES proposed for H follow in 6.12.

6.12 — Structure and chirality of H

A suitable structure is **hexol chloride**, also described as **dodecaamminehexa-μ-hydroxidotetracobalt(III) chloride**:



Describe the drawing as follows:

1. Place one cobalt(III) ion at the centre of an octahedron.
2. Put six hydroxide oxygen donors at its six vertices.
3. Divide those donors into three adjacent pairs.
4. Connect each pair to one peripheral cobalt(III) ion, so each hydroxide bridges the central and a peripheral cobalt.
5. Complete each peripheral cobalt's octahedron with four ammonia ligands. Its two bridging oxygen donors are *cis*.
6. Place six chloride counterions outside the coordination sphere.

Every cobalt is six-coordinate:

- The central cobalt binds six hydroxide donors.
- Each peripheral cobalt binds two hydroxide donors and four ammonia ligands.

The complex-ion charge is

$$4(+3) + 6(-1) = +6,$$

requiring six chloride counterions. Its composition is twice the empirical formula obtained in 6.11.

For a precise stereochemical sketch, put the central donors on the $\pm x$, $\pm y$, $\pm z$ axes and pair them as

$$(+x, +y), \quad (-x, +z), \quad (-y, -z).$$

Each pair connects to a different peripheral cobalt. Reflecting this arrangement gives the opposite hand. The three paired bridges act as three bidentate ligands around the central cobalt, producing the familiar Δ/Λ **tris-chelate enantiomers**.

The two enantiomers of hexol chloride can be represented by the following coordination SMILES:

```
[Co@OH8+3]123(<-[OH-]->[Co+3](<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])<-[OH-]->1)(<-[OH-]->[Co+3](<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])<-[OH-]->2)<-[OH-]->[Co+3](<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])<-[OH-]->3.[Cl-].[Cl-].[Cl-].[Cl-].[Cl-].[Cl-])
[Co@OH10+3]123(<-[OH-]->[Co+3](<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])<-[OH-]->1)(<-[OH-]->[Co+3](<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])<-[OH-]->2)<-[OH-]->[Co+3](<-[NH3])(<-[NH3])(<-[NH3])(<-[NH3])<-[OH-]->3.[Cl-].[Cl-].[Cl-].[Cl-].[Cl-].[Cl-])
```

The @OH8 and @OH10 indices specify opposite configurations for this particular SMILES atom order; they are not signs of optical rotation. The peripheral *cis* coordination and the octahedral geometries are as described above.

The solution was checked against the official solution.