

IChO 1999

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Problem 1: Combustion calorimetry and molecular state of compound Q

A compound **Q** (molar mass 122.0 g mol^{-1}) consists of carbon, hydrogen and oxygen.

PART A

The standard enthalpy of formation of $\text{CO}_2(\text{g})$ and $\text{H}_2\text{O}(\text{l})$ at 25.00°C are -393.51 and $-285.83 \text{ kJ mol}^{-1}$, respectively. The gas constant, $R = 8.314 \text{ J K}^{-1} \text{ mol}^{-1}$.

(Relative atomic masses : $\text{H} = 1.0$; $\text{C} = 12.0$; $\text{O} = 16.0$)

A sample of solid **Q** that weighs 0.6000 g , is combusted in an excess of oxygen in a bomb calorimeter, which initially contains 710.0 g of water at 25.000°C . After the reaction is completed, the temperature is observed to be 27.250°C , and 1.5144 g of $\text{CO}_2(\text{g})$ and 0.2656 g of $\text{H}_2\text{O}(\text{l})$ are produced.

1.1 Determine the molecular formula and write a balanced equation with correct state of matters for the combustion of **Q**.

If the specific heat of water is $4.184 \text{ J g}^{-1} \text{ K}^{-1}$ and the internal energy change of the reaction (ΔU^0) $-3079 \text{ kJ mol}^{-1}$.

1.2 Calculate the heat capacity of the calorimeter (excluding the water).

1.3 Calculate the standard enthalpy of formation (ΔH_f^0) of **Q**.

PART B

The following data refer to the distribution of **Q** between benzene and water at 6°C , C_B and C_W being equilibrium concentrations of the species of **Q** in the benzene and water layers, respectively:

Assume that there is only one species of **Q** in benzene independent of concentration and temperature.

Concentration (mol dm^{-3})

C_B	C_W
0.0118	0.00281
0.0478	0.00566
0.0981	0.00812
0.156	0.0102

1.4 Show by calculation whether **Q** is monomer or dimer in benzene. Assume that **Q** is a monomer in water.

The freezing point depression, for an ideal dilute solution, is given by

$$T_f^0 - T_f = \frac{R(T_f^0)^2 X_s}{\Delta H_f}$$

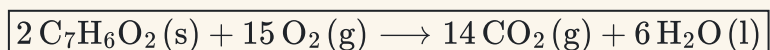
where T_f is the freezing point of the solution, T_f^0 the freezing point of solvent, ΔH_f the heat of fusion of the solvent, and X_s the mole fraction of solute. The molar mass of benzene is 78.0 g mol^{-1} . At 1 atm pure benzene freezes at 5.40°C . The heat of fusion of benzene is 9.89 kJ mol^{-1} .

1.5 Calculate the freezing point (T_f) of a solution containing 0.244 g of **Q** in 5.85 g of benzene at 1 atm.

Official English text of the problem.

Answers

- **1.1** Molecular formula: $\text{C}_7\text{H}_6\text{O}_2$.



- **1.2** Calorimeter heat capacity, excluding water: 3.759 kJ K^{-1} .
- **1.3** Standard enthalpy of formation: $\Delta H_f^0(\text{Q} (\text{s})) \approx -532 \text{ kJ mol}^{-1}$.
- **1.4** **Q is a dimer, Q_2 , in benzene**, since C_B/C_W^2 is approximately constant.
- **1.5** Freezing point: $T_f = 4.54^\circ \text{C}$.

Solution

The specified molecular species are carbon dioxide $\text{O}=\text{C}=\text{O}$, water O , dioxygen $\text{O}=\text{O}$, and benzene c1ccccc1 . The data determine **Q**'s molecular formula and association state. A unique chemical name or SMILES for **Q** or its dimer cannot be assigned without further structural information.

1.1 Molecular formula and combustion equation

The amount of **Q** burned is

$$n_Q = \frac{0.6000 \text{ g}}{122.0 \text{ g mol}^{-1}} = 4.91803 \times 10^{-3} \text{ mol.}$$

All carbon appears in carbon dioxide, and all hydrogen appears in water:

$$n(\text{C}) = n(\text{CO}_2) = \frac{1.5144 \text{ g}}{44.0 \text{ g mol}^{-1}} = 0.0344182 \text{ mol,}$$

$$n(\text{H}) = 2n(\text{H}_2\text{O}) = 2 \frac{0.2656 \text{ g}}{18.0 \text{ g mol}^{-1}} = 0.0295111 \text{ mol.}$$

Their masses in the sample are therefore

$$m(\text{C}) = 0.413018 \text{ g,} \quad m(\text{H}) = 0.0295111 \text{ g.}$$

Since Q contains only carbon, hydrogen, and oxygen, its oxygen content follows by difference:

$$m(\text{O}) = 0.6000 - 0.413018 - 0.0295111 = 0.157471 \text{ g},$$

$$n(\text{O}) = \frac{0.157471 \text{ g}}{16.0 \text{ g mol}^{-1}} = 0.00984192 \text{ mol}.$$

Dividing each atomic amount by the amount of Q gives the number of atoms per molecule:

$$\frac{n(\text{C})}{n_Q} = 6.9984 \approx 7, \quad \frac{n(\text{H})}{n_Q} = 6.0006 \approx 6, \quad \frac{n(\text{O})}{n_Q} = 2.0012 \approx 2.$$

Thus,

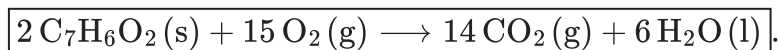


with molar mass

$$7(12.0) + 6(1.0) + 2(16.0) = 122.0 \text{ g mol}^{-1},$$

in agreement with the given value.

Balancing carbon, hydrogen, and then oxygen gives



1.2 Heat capacity of the calorimeter

A bomb calorimeter operates at constant volume, so the reaction heat is the internal-energy change:

$$q_{\text{rxn}} = n_Q \Delta U^0 = \frac{0.6000}{122.0} (-3079) = -15.1426 \text{ kJ}.$$

The water and calorimeter therefore absorb 15.1426 kJ. Their temperature increase is

$$\Delta T = 27.250 - 25.000 = 2.250 \text{ K}.$$

The water absorbs

$$q_{\text{water}} = m_{\text{water}} c_{\text{water}} \Delta T = (710.0)(4.184)(2.250) = 6683.94 \text{ J} = 6.68394 \text{ kJ}.$$

Energy conservation gives

$$-q_{\text{rxn}} = q_{\text{water}} + C_{\text{cal}} \Delta T.$$

Consequently,

$$C_{\text{cal}} = \frac{15.1426 - 6.68394}{2.250} = 3.7594 \text{ kJ K}^{-1},$$

or

$$\boxed{C_{\text{cal}} = 3.759 \text{ kJ K}^{-1}}.$$

1.3 Standard enthalpy of formation of Q

For the combustion of one mole of Q, the change in gaseous stoichiometric amount is

$$\Delta n_g = 7 - \frac{15}{2} = -\frac{1}{2}.$$

Water is liquid and therefore does not contribute to Δn_g . Using

$$\Delta H_c^0 = \Delta U^0 + \Delta n_g RT$$

at $T = 298.15 \text{ K}$,

$$\begin{aligned}\Delta H_c^0 &= -3079 - \frac{1}{2}(8.314 \times 10^{-3})(298.15) \\ &= -3080.239 \text{ kJ mol}^{-1}.\end{aligned}$$

By Hess's law, with $\Delta H_f^0(\text{O}_2(\text{g})) = 0$,

$$\Delta H_c^0 = 7\Delta H_f^0(\text{CO}_2(\text{g})) + 3\Delta H_f^0(\text{H}_2\text{O}(\text{l})) - \Delta H_f^0(\text{Q}(\text{s})).$$

Therefore,

$$\begin{aligned}\Delta H_f^0(\text{Q}(\text{s})) &= 7(-393.51) + 3(-285.83) - (-3080.239) \\ &= -531.821 \text{ kJ mol}^{-1}.\end{aligned}$$

To a precision appropriate to the given combustion energy,

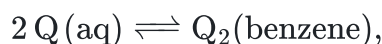
$$\boxed{\Delta H_f^0(\text{Q}(\text{s})) \approx -532 \text{ kJ mol}^{-1}}.$$

1.4 Molecular state of Q in benzene

For monomeric Q in both solvents, the distribution equilibrium would require

$$\frac{C_B}{C_W} = \text{constant}.$$

If Q forms a dimer in benzene, the overall equilibrium is



and the corresponding concentration expression requires

$$\frac{C_B}{C_W^2} = \text{constant}.$$

The two tests give:

C_B (mol dm ⁻³)	C_W (mol dm ⁻³)	C_B/C_W	C_B/C_W^2 (dm ³ mol ⁻¹)
0.0118	0.00281	4.20	1.494×10^3
0.0478	0.00566	8.45	1.492×10^3
0.0981	0.00812	12.1	1.488×10^3
0.156	0.0102	15.3	1.499×10^3

The monomer ratio varies substantially, whereas the dimer ratio is approximately constant:

$$\frac{C_B}{C_W^2} \approx 1.49 \times 10^3 \text{ dm}^3 \text{ mol}^{-1}.$$

Hence,

$$\boxed{\text{Q exists as a dimer in benzene.}}$$

1.5 Freezing point of the benzene solution

The stipulated independence of molecular state from concentration and temperature allows the dimer result to be used at the freezing point.

The solute particles are dimers, with molar mass

$$M(\text{Q}_2) = 2(122.0) = 244.0 \text{ g mol}^{-1}.$$

Thus,

$$n_s = \frac{0.244 \text{ g}}{244.0 \text{ g mol}^{-1}} = 0.00100 \text{ mol},$$

while the amount of benzene is

$$n_{\text{benzene}} = \frac{5.85 \text{ g}}{78.0 \text{ g mol}^{-1}} = 0.0750 \text{ mol}.$$

The mole fraction of solute particles is

$$X_s = \frac{n_s}{n_s + n_{\text{benzene}}} = \frac{0.00100}{0.00100 + 0.0750} = 0.0131579.$$

Convert the solvent freezing point and heat of fusion to the required units:

$$T_f^0 = 5.40 + 273.15 = 278.55 \text{ K}, \quad \Delta H_f = 9890 \text{ J mol}^{-1}.$$

Using the supplied equation,

$$\begin{aligned} \Delta T_f &= \frac{R(T_f^0)^2 X_s}{\Delta H_f} \\ &= \frac{(8.314)(278.55)^2(0.0131579)}{9890} \\ &= 0.8582 \text{ K}. \end{aligned}$$

Therefore,

$$T_f = 5.40 - 0.8582 = 4.5418 \text{ }^\circ\text{C},$$

giving

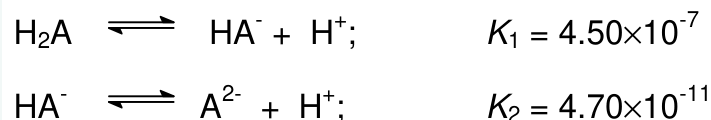
$$\boxed{T_f = 4.54 \text{ }^\circ\text{C}}.$$

The solution was checked against the official solution.

Problem 2: A diprotic acid and an acid-base indicator

PART A

A diprotic acid, H_2A , undergoes the following dissociation reactions :



A 20.00 cm^3 aliquot of a solution containing a mixture of Na_2A and NaHA is titrated with 0.300 M hydrochloric acid. The progress of the titration is followed with a glass electrode pH meter. Two points on the titration curve are as follows :

$\text{cm}^3 \text{ HCl added}$	pH
1.00	10.33
10.00	8.34

2.1 On adding 1.00 cm^3 of HCl , which species reacts first and what would be the product?

- 2.2** What is the amount (mmol) of the product formed in (2.1)?
- 2.3** Write down the main equilibrium of the product from (2.1) reacting with the solvent?
- 2.4** What are the amounts (mmol) of Na_2A and NaHA initially present?
- 2.5** Calculate the total volume of HCl required to reach the second equivalence point.

PART B

Solutions I, II and III contain a pH indicator HIn ($K_{\text{In}} = 4.19 \times 10^{-4}$) and other reagents as indicated in the table. The absorbance values at 400 nm of the solutions measured in the same cell, are also given in the table. K_a of CH_3COOH is 1.75×10^{-5} .

Table:

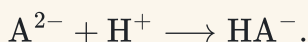
	Solution I	Solution II	Solution III
Total concentration of indicator HIn	$1.00 \times 10^{-5} \text{ M}$	$1.00 \times 10^{-5} \text{ M}$	$1.00 \times 10^{-5} \text{ M}$
Other reagents	1.00 M HCl	0.100 M NaOH	1.00 M CH_3COOH
Absorbance at 400	0.000	0.300	?

- 2.6** Calculate the absorbance at 400 nm of solution III.
- 2.7** Apart from H_2O , H^+ and OH^- , what are all the chemical species present in the solution resulting from mixing solution II and solution III at 1 : 1 volume ratio?
- 2.8** What is the absorbance at 400 nm of the solution in (2.7)?
- 2.9** What is the transmittance at 400 nm of the solution in (2.7)?

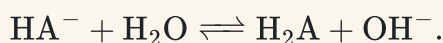
Official English text of the problem.

Answers

- 2.1:** The dianion A^{2-} reacts first, producing the hydrogen anion HA^- :



- 2.2:** 0.300 mmol of HA^- is formed stoichiometrically.
- 2.3:**



- 2.4:** Initially, 3.00 mmol of the disodium salt Na_2A and 2.40 mmol of the sodium hydrogen salt NaHA .
- 2.5:** 28.0 cm^3 of hydrochloric acid in total.
- 2.6:** Absorbance $\mathcal{A}_{400} \approx 0.027$.
- 2.7:** Sodium ion Na^+ , $[\text{Na}^+]$; acetic acid CH_3COOH , $\text{CC}(=\text{O})\text{O}$; acetate ion CH_3COO^- , $\text{CC}(=\text{O})[\text{O}^-]$; acidic indicator HIn ; and indicator anion In^- .
- 2.8:** Absorbance $\mathcal{A}_{400} = 0.218$.
- 2.9:** Transmittance $T = 0.605$, or 60.5%.

The structures represented by **A** and **In** are unspecified. Consequently, unique molecular SMILES cannot be assigned to their acid–base forms or the corresponding salts.

Solution

The other structurally specified participants used below are water, O ; hydrogen ion, $[\text{H}^+]$; hydroxide ion, $[\text{OH}^-]$; and chloride ion, $[\text{Cl}^-]$. Aqueous hydrochloric acid and sodium hydroxide are represented ionically as $[\text{H}^+] \cdot [\text{Cl}^-]$ and $[\text{Na}^+] \cdot [\text{OH}^-]$, respectively.

2.1

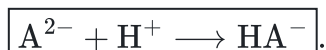
The given dissociation constants are

$$K_1 = 4.50 \times 10^{-7}, \quad K_2 = 4.70 \times 10^{-11}.$$

The protonation constants of A^{2-} and HA^- are, respectively,

$$\frac{1}{K_2} = 2.13 \times 10^{10}, \quad \frac{1}{K_1} = 2.22 \times 10^6.$$

Thus, A^{2-} is the stronger base and is protonated preferentially:



The product is the hydrogen anion HA^- , the singly deprotonated form of the diprotic acid.

2.2

The amount of hydrogen ion added is

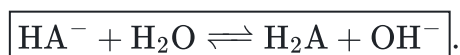
$$n(\text{H}^+) = 0.300 \text{ mol L}^{-1} \times 1.00 \times 10^{-3} \text{ L} = 3.00 \times 10^{-4} \text{ mol}.$$

The reaction has a 1:1 stoichiometry, so the amount of HA^- formed is

$$\boxed{n(\text{HA}^-)_{\text{formed}} = 0.300 \text{ mmol}}.$$

2.3

The ion HA^- is amphiprotic. Its principal reaction with water is basic hydrolysis:



Using the conventional aqueous value $K_w = 1.00 \times 10^{-14}$,

$$K_b(\text{HA}^-) = \frac{K_w}{K_1} = \frac{1.00 \times 10^{-14}}{4.50 \times 10^{-7}} = 2.22 \times 10^{-8}.$$

This exceeds its acid-dissociation constant, $K_2 = 4.70 \times 10^{-11}$, by a factor of about 473, explaining why the basic reaction predominates.

2.4

Let the initial amounts in the aliquot be

$$x = n_0(\text{Na}_2\text{A}), \quad y = n_0(\text{NaHA}),$$

both expressed in mmol.

At the first equivalence point, the initial dianion has been protonated to HA^- . For a solution dominated by this amphiprotic ion,

$$[\text{H}^+] \simeq \sqrt{K_1 K_2},$$

and therefore

$$pH \simeq \frac{pK_1 + pK_2}{2} = \frac{6.3468 + 10.3279}{2} = 8.3373.$$

This agrees with the measured $pH = 8.34$ after 10.00 cm^3 of acid. Thus, within the usual titration approximations, this is the first equivalence point:

$$x = 0.300 \text{ mmol cm}^{-3} \times 10.00 \text{ cm}^3 = 3.00 \text{ mmol}.$$

After adding 1.00 cm^3 , the stoichiometric amounts are

$$n(\text{A}^{2-}) = x - 0.300, \quad n(\text{HA}^-) = y + 0.300.$$

For this buffer,

$$pH = pK_2 + \log_{10} \frac{[\text{A}^{2-}]}{[\text{HA}^-]}.$$

Since $pH = 10.33 \simeq pK_2$, the two concentrations, and hence their amounts in the same solution, are approximately equal:

$$x - 0.300 = y + 0.300.$$

Consequently,

$$y = 3.00 - 0.600 = 2.40 \text{ mmol}.$$

Thus,

$$\boxed{n_0(\text{Na}_2\text{A}) = 3.00 \text{ mmol}}, \quad \boxed{n_0(\text{NaHA}) = 2.40 \text{ mmol}}.$$

2.5

At the second equivalence point, protonation to H_2A is stoichiometrically complete:



Each initial A^{2-} requires two hydrogen ions overall, whereas each initial HA^- requires one. Hence,

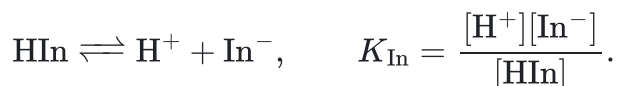
$$n(\text{HCl})_{\text{total}} = 2x + y = 2(3.00) + 2.40 = 8.40 \text{ mmol}.$$

Therefore,

$$\boxed{V_{\text{HCl}} = \frac{8.40 \text{ mmol}}{0.300 \text{ mmol cm}^{-3}} = 28.0 \text{ cm}^3}.$$

2.6

The indicator equilibrium is



Solution I is strongly acidic, so the indicator is almost entirely HIn . Its absorbance of 0.000 shows that the acidic form has negligible absorption at 400 nm.

Solution II is strongly basic, so the indicator is essentially entirely In^- . The Beer–Lambert law therefore gives

$$\varepsilon_{-\ell} = \frac{0.300}{1.00 \times 10^{-5} \text{ mol L}^{-1}} = 3.00 \times 10^4 \text{ L mol}^{-1},$$

where ℓ is the cell path length.

Writing $C_{\text{In}} = [\text{HIn}] + [\text{In}^-]$, the indicator equilibrium gives

$$[\text{In}^-] = C_{\text{In}} \frac{K_{\text{In}}}{K_{\text{In}} + [\text{H}^+]}$$

Thus, when $C_{\text{In}} = 1.00 \times 10^{-5} \text{ M}$,

$$\mathcal{A}_{400} = 0.300 \frac{K_{\text{In}}}{K_{\text{In}} + [\text{H}^+]}$$

In solution III, acetic acid dissociates according to



Its concentration is much greater than the indicator concentration, so the indicator's effect on the pH is negligible. Using the weak-acid approximation,

$$[\text{H}^+] \simeq \sqrt{K_a C} = \sqrt{(1.75 \times 10^{-5})(1.00)} = 4.18 \times 10^{-3} \text{ M}.$$

Therefore,

$$\mathcal{A}_{\text{III}} = 0.300 \frac{4.19 \times 10^{-4}}{4.19 \times 10^{-4} + 4.18 \times 10^{-3}} \simeq 0.0273.$$

At the absorbance precision used in the table,

$$\boxed{\mathcal{A}_{\text{III}} \approx 0.027}.$$

2.7

Hydroxide from solution II neutralizes part of the acetic acid from solution III:



For equal starting volumes V , the amounts of acetic acid and hydroxide are proportional to $1.00V$ and $0.100V$, respectively. Acetic acid remains in excess, and the mixture contains an acetic acid/acetate buffer.

Both indicator forms are present through the equilibrium



Equivalently, their proton exchange with the buffer can be written as



Excluding the three species specified in the question, the complete list is:

Species	Name	SMILES
Na^+	Sodium ion	[Na+]
CH_3COOH	Acetic acid	CC(=O)O
CH_3COO^-	Acetate ion	CC(=O)[O-]
HIn	Acidic indicator	Structure unspecified
In^-	Indicator conjugate-base anion	Structure unspecified

2.8

After neutralization and dilution to twice the original volume, the buffer concentrations are approximately

$$[\text{CH}_3\text{COOH}] = \frac{1.00 - 0.100}{2} = 0.450 \text{ M},$$
$$[\text{CH}_3\text{COO}^-] = \frac{0.100}{2} = 0.0500 \text{ M}.$$

Their subsequent equilibrium changes are small compared with these concentrations. Hence,

$$[\text{H}^+] = K_a \frac{[\text{CH}_3\text{COOH}]}{[\text{CH}_3\text{COO}^-]} \simeq 1.75 \times 10^{-5} \frac{0.450}{0.0500} = 1.575 \times 10^{-4} \text{ M}.$$

Both starting solutions have the same total indicator concentration, so mixing them leaves that concentration unchanged:

$$C_{\text{In,mix}} = \frac{C_{\text{In}}V + C_{\text{In}}V}{2V} = 1.00 \times 10^{-5} \text{ M}.$$

The absorbing fraction of the indicator is therefore

$$\frac{[\text{In}^-]}{C_{\text{In,mix}}} = \frac{4.19 \times 10^{-4}}{4.19 \times 10^{-4} + 1.575 \times 10^{-4}} = 0.7268.$$

Thus,

$$\boxed{\mathcal{A}_{\text{mix}} = 0.300(0.7268) = 0.218}.$$

2.9

Absorbance and transmittance are related by

$$\mathcal{A} = -\log_{10} T, \quad T = \frac{I}{I_0}.$$

Using the unrounded absorbance,

$$T = 10^{-0.2180399} = 0.605285.$$

Therefore,

$$\boxed{T = 0.605}, \quad \boxed{\%T = 60.5\%}.$$

The solution was checked against the official solution.

Problem 3: The thorium decay series

One of naturally occurring radioactive decay series begins with ${}^{232}_{90}\text{Th}$ and ends with a stable ${}^{208}_{82}\text{Pb}$.

3.1 How many beta (β^-) decays are there in this series? Show by calculation.

3.2 How much energy in MeV is released in the complete chain?

3.3 Calculate the rate of production of energy (power) in watts ($1 \text{ W} = \text{J s}^{-1}$) produced by 1.00 kilogram of ${}^{232}\text{Th}$ ($t_{1/2} = 1.40 \times 10^{10}$ years).

3.4 ^{228}Th is a member of the thorium series. What volume in cm^3 of helium at 0°C and 1 atm collected when 1.00 gram of ^{228}Th ($t_{1/2} = 1.91$ years) is stored in a container for 20.0 years. The half-lives of all intermediate nuclides are short compared to the half-life of ^{228}Th .

3.5 One member of thorium series, after isolation, is found to contain 1.50×10^{10} atoms of the nuclide and decays at the rate of 3440 disintegrations per minute. What is the half-life in years?

The necessary atomic masses are :

$$^4_2\text{He} = 4.00260 \text{ u}, \quad ^{208}_{82}\text{Pb} = 207.97664 \text{ u}, \quad ^{232}_{90}\text{Th} = 232.03805 \text{ u}; \quad \text{and } 1\text{u} = 931.5 \text{ MeV}$$

$$1 \text{ MeV} = 1.602 \times 10^{-13} \text{ J}$$

$$N_A = 6.022 \times 10^{23} \text{ mol}^{-1}$$

The molar volume of an ideal gas at 0°C and 1 atm is $22.4 \text{ dm}^3 \text{ mol}^{-1}$.

Official English text of the problem.

Answers

- **3.1:** 4 beta-minus decays.
- **3.2:** 42.67 MeV per complete decay chain.
- **3.3:** $2.79 \times 10^{-5} \text{ W}$, assuming secular equilibrium of the complete chain.
- **3.4:** $4.91 \times 10^2 \text{ cm}^3$ of helium.
- **3.5:** 5.75 years.

Solution

3.1

An alpha decay decreases the mass number by 4 and the atomic number by 2. A beta-minus decay leaves the mass number unchanged and increases the atomic number by 1.

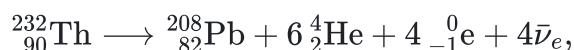
Let a and b be the numbers of alpha and beta-minus decays, respectively. Conservation of mass number gives

$$232 = 208 + 4a \implies a = 6.$$

The atomic-number change therefore satisfies

$$82 = 90 - 2(6) + b \implies \boxed{b = 4}.$$

The overall nuclear equation is



where $\bar{\nu}_e$ denotes an electron antineutrino.

3.2

Using the given neutral-atom masses, the mass defect is

$$\begin{aligned} \Delta m &= M(^{232}\text{Th}) - M(^{208}\text{Pb}) - 6M(^4\text{He}) \\ &= 232.03805 - 207.97664 - 6(4.00260) \\ &= 0.04581 \text{ u}. \end{aligned}$$

No separate beta-electron mass term is needed: the electron masses cancel when the nuclear mass balance is expressed using neutral-atom masses.

Consequently,

$$Q = \Delta mc^2 = (0.04581 \text{ u})(931.5 \text{ MeV u}^{-1}) = \boxed{42.67 \text{ MeV}}.$$

In joules, retaining guard digits,

$$Q = (42.672015)(1.602 \times 10^{-13}) = 6.83606 \times 10^{-12} \text{ J}.$$

3.3

Using the full-chain energy assumes that the daughter nuclides are in secular equilibrium: the number of completed chains per second then equals the activity of the thorium-232.

The number of thorium-232 atoms is

$$N = \frac{1000 \text{ g}}{232.03805 \text{ g mol}^{-1}} (6.022 \times 10^{23} \text{ mol}^{-1}) = 2.59526 \times 10^{24}.$$

Taking one year as 365 days,

$$t_{1/2} = (1.40 \times 10^{10})(365)(24)(3600) = 4.41504 \times 10^{17} \text{ s}.$$

The decay constant and activity are

$$\lambda = \frac{\ln 2}{t_{1/2}},$$

$$A = \lambda N = \frac{(\ln 2)(2.59526 \times 10^{24})}{4.41504 \times 10^{17} \text{ s}} = 4.07448 \times 10^6 \text{ s}^{-1}.$$

Thus the total rate of nuclear energy release is

$$\begin{aligned} P &= AQ \\ &= (4.07448 \times 10^6 \text{ s}^{-1})(6.83606 \times 10^{-12} \text{ J}) \\ &= \boxed{2.79 \times 10^{-5} \text{ W}}. \end{aligned}$$

3.4

The decrease in mass number from 228 to 208 requires

$$a = \frac{228 - 208}{4} = 5$$

alpha decays per completed chain. Atomic-number balance also gives two beta-minus decays, so the overall nuclear equation is



Each alpha particle ultimately becomes one helium-4 atom, ${}^4\text{He}$, SMILES [4He]. Thus each completed chain produces five helium atoms.

The fraction of thorium-228 that decays during 20.0 years is

$$f = 1 - \exp(-\lambda t) = 1 - 2^{-t/t_{1/2}} = 1 - 2^{-20.0/1.91} = 0.9992955.$$

Because the intermediate half-lives are short, we approximate each decayed thorium-228 atom as having completed its chain. Using $M({}^{228}\text{Th}) \approx 228 \text{ g mol}^{-1}$,

$$n_{\text{He}} = 5 \left(\frac{1.00 \text{ g}}{228 \text{ g mol}^{-1}} \right) (0.9992955) = 0.0219144 \text{ mol.}$$

At the specified temperature and pressure,

$$\begin{aligned} V_{\text{He}} &= (0.0219144 \text{ mol})(22.4 \times 10^3 \text{ cm}^3 \text{ mol}^{-1}) \\ &= 490.882 \text{ cm}^3 \\ &= \boxed{4.91 \times 10^2 \text{ cm}^3}. \end{aligned}$$

3.5

For an isolated radionuclide, the activity is $A = \lambda N$. Therefore,

$$t_{1/2} = \frac{\ln 2}{\lambda} = \frac{N \ln 2}{A}.$$

Substitution gives

$$t_{1/2} = \frac{(1.50 \times 10^{10})(\ln 2)}{3440 \text{ min}^{-1}} = 3.02244 \times 10^6 \text{ min.}$$

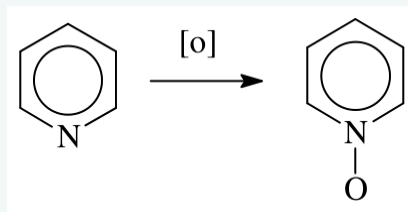
Converting to years,

$$t_{1/2} = \frac{3.02244 \times 10^6}{60 \times 24 \times 365} \text{ years} = \boxed{5.75 \text{ years}}.$$

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 4: Iron and chromium complexes of ligand L

Ligand **L** can form complexes with many transition metals. **L** is synthesized by heating a mixture of a bipyridine, glacial acetic acid and hydrogen peroxide to 70 – 80 °C for 3 hrs. The final product **L** crystallizes out as fine needles and its molecular mass is 188. An analogous reaction with pyridine is ;



Complexes of **L** with Fe and Cr have the formulae of $\text{FeL}_m(\text{ClO}_4)_n \cdot 3 \text{H}_2\text{O}$ (**A**) and $\text{CrL}_x\text{Cl}_y(\text{ClO}_4)_z \cdot \text{H}_2\text{O}$ (**B**), respectively. Their elemental analyses and physical properties are given in Tables 4a and 4b. The relationship of colour and wavelength is given in Table 4c.

Table 4a: Elemental analyses.

Complex	Elemental analyses , (wt. %)
A	Fe 5.740, C 37.030, H 3.090 , Cl 10.940, N 8.640
B	Cr 8.440, C 38.930, H 2.920, Cl 17.250, N 9.080

Use the following data:

Atomic number: Cr = 24, Fe = 26

Relative atomic mass: H = 1, C = 12, N = 14, O = 16, Cl = 35.45, Cr = 52, Fe = 55.8

Table 4b: Physical properties

Complex	Magnetic moment, μ B.M.	Colour
A	6.13	Yellow
B	Not measured	Purple

Table 4c Relationship of wavelength to colour.

Wavelength (nm) and colour absorbed	Complementary colour
400 (violet)	Yellow Green
450 (blue)	Yellow
490 (blue green)	Orange
500 (green)	Red
570 (yellow green)	Violet
580 (yellow)	Blue
600 (orange)	Blue green
650 (red)	Green

4.1 Write down the molecular formula of **L**.

4.2 If **L** is a bidentate chelating ligand, draw the structure of the bipyridine used. Also draw the structure of **L**.

4.3 Does the ligand **L** have any charge, i. e. net charge?

4.4 Draw the structure when one molecule of **L** binds to metal ion (M).

4.5 From the data in Table 4a, determine the empirical formula of **A**. What are the values of m and n in $\text{FeL}_m(\text{ClO}_4)_n \cdot 3\text{H}_2\text{O}$? Write the complete formula of **A** in the usual IUPAC notation. What is the ratio of cation to anion when **A** dissolves in water?

4.6 What is the oxidation number of Fe in **A**? How many d-electrons are present in Fe ion in the complex? Write the high spin and the low spin configurations that may exist for this complex. Which configuration, high or low spin, is the correct one? What is the best evidence to support your answer?

4.7 From Table 4c, estimate λ_{max} (nm) of **A**.

4.8 Detail analysis of **B** shows that it contains Cr^{3+} ion. Calculate the 'spin-only' magnetic moment of this compound.

4.9 Compound **B** is a 1 : 1 type electrolyte. Determine the empirical formula of **B** and the values of x, y, z in $\text{CrL}_x\text{Cl}_y(\text{ClO}_4)_z \cdot \text{H}_2\text{O}$.

Official English text of the problem.

Answers

Names and SMILES for the structures are supplied in the corresponding solution parts.

- **4.1** $L = C_{10}H_8N_2O_2$.
- **4.2** The precursor is **2,2'-bipyridine**; **L** is **2,2'-bipyridine N,N'-dioxide**.
- **4.3** **L** has **zero net charge**.
- **4.4** Both N-oxide oxygen atoms coordinate to the same metal ion, giving an *O, O'*-chelating ligand and a **seven-membered chelate ring**.
- **4.5** The empirical formula is $C_{30}H_{30}Cl_3FeN_6O_{21}$.

$$m = 3, \quad n = 3, \quad A = [Fe(C_{10}H_8N_2O_2)_3](ClO_4)_3 \cdot 3H_2O$$

The cation-to-anion ratio is $1 : 3$.

- **4.6** Iron has oxidation number $+3$ and configuration d^5 . The possible octahedral configurations are high-spin $t_{2g}^3e_g^2$ and low-spin $t_{2g}^5e_g^0$. **A is high-spin**, supported by its measured magnetic moment of 6.13 B.M.
- **4.7** $\lambda_{\max} \approx 450 \text{ nm}$.
- **4.8** $\mu_{\text{so}} = \sqrt{15} \mu_B = 3.87 \text{ B. M.}$.
- **4.9** The empirical formula is $C_{20}H_{18}Cl_3CrN_4O_9$.

$$x = 2, \quad y = 2, \quad z = 1, \quad B = [Cr(C_{10}H_8N_2O_2)_2Cl_2]ClO_4 \cdot H_2O$$

Solution

In the coordination SMILES below, $\rightarrow$ and $\leftarrow$ denote dative bonds directed from the donor atom to the metal. Coordination geometry is described separately.

4.1 — Molecular formula of L

Pyridine, SMILES n1cccc1, has molecular formula C_5H_5N . Joining two pyridine rings through a carbon-carbon bond replaces one hydrogen on each ring, giving a bipyridine formula of $C_{10}H_8N_2$.

Its relative molecular mass is

$$M_r(\text{bipyridine}) = 10(12) + 8(1) + 2(14) = 156.$$

The illustrated reaction converts pyridine into **pyridine N-oxide**, SMILES [O-][n+]1cccc1. The mass increase for the bipyridine is

$$188 - 156 = 32 = 2(16),$$

so both nitrogen atoms are oxidized, adding two oxygen atoms:

$$L = C_{10}H_8N_2O_2.$$

The ligand is **2,2'-bipyridine N,N'-dioxide**, SMILES [O-][n+]1cccc1-c1cccc[n+]1[O-].

The overall oxidation is balanced as



Here hydrogen peroxide, SMILES oo, is the oxidant; acetic acid, SMILES CC(=O)O, is the reaction medium; and water, SMILES o, is the coproduct.

4.2 — Structures of the precursor and L

The precursor is **2,2'-bipyridine**, SMILES n1cccc1-c1ccccn1.

To draw it:

- Draw two aromatic six-membered pyridine rings.
- Number the nitrogen in each ring as position 1.
- Connect carbon 2 of one ring directly to carbon 2' of the other.

To draw **L**, retain that framework and attach one oxygen atom to each ring nitrogen, showing each N-oxide group as $\text{N}^+ - \text{O}^-$. Its SMILES is [O-][n+]1cccc1-c1cccc[n+]1[O-].

The 2,2' linkage allows rotation about the inter-ring bond to bring the two oxygen donors into a conformation suitable for binding the same metal ion.

4.3 — Charge of L

Each N-oxide group contains one formally positive nitrogen and one formally negative oxygen. Thus

$$q(L) = 2(+1) + 2(-1) = \boxed{0}.$$

The ligand is electrically neutral overall.

4.4 — Coordination of one L molecule

Both oxygen atoms donate lone pairs to the same metal ion. Thus **L** is a $\kappa^2\text{O}, \text{O}'$ ligand.

A generic **metal-L chelate fragment** has the dative-bond SMILES:

[*]1<-[O-][n+]2cccc2-c2cccc[n+]2[O-]>-1

The wildcard * represents M; its identity, charge and remaining ligands are unspecified in this generic fragment.

For the drawing, orient the N-oxide groups toward the metal and draw one coordination bond from each oxygen to M. Tracing the closed chelate ring gives:

M → first oxygen → first nitrogen → carbon 2 → carbon 2' → second nitrogen → second oxygen → M.

There are therefore **seven atoms in the chelate ring**. The bonds to the metal are through oxygen.

4.5 — Composition and formula of A

Take a 100.000 g sample. The amount of iron is

$$n_{\text{Fe}} = \frac{5.740 \text{ g}}{55.8 \text{ g mol}^{-1}} = 0.10287 \text{ mol}.$$

Each ligand contains ten carbon atoms, so

$$n_L = \frac{37.030 \text{ g}}{10(12) \text{ g mol}^{-1}} = 0.30858 \text{ mol}.$$

Consequently,

$$m = \frac{n_L}{n_{\text{Fe}}} = \frac{0.30858}{0.10287} \approx \boxed{3}.$$

All chlorine in the stated formula of **A** belongs to perchlorate:

$$n = \frac{10.940/35.45}{5.740/55.8} = 3.0000 \approx \boxed{3}.$$

For completeness, the oxygen percentage by difference is

$$w_{\text{O}} = 100 - (5.740 + 37.030 + 3.090 + 10.940 + 8.640) = 34.560\%.$$

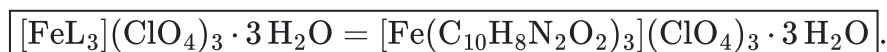
Dividing the elemental amounts by the amount of iron gives:

Element	Atomic ratio relative to Fe
Fe	1.000
C	29.998
H	30.039
Cl	3.000
N	5.999
O	20.998

Thus the empirical formula is



Three bidentate ligands provide six oxygen donors, giving an approximately octahedral complex cation. The complete coordination formula is



Its name is **tris(2,2'-bipyridine N,N'-dioxide)iron(III) perchlorate trihydrate**, with SMILES:

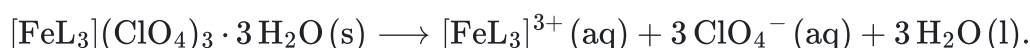
[Fe+3]123(<-[O-][n+]4cccc4-c4cccc[n+]4[O-]>1)<-[O-][n+]4cccc4-c4cccc[n+]4[O-]>2<-[O-][n+]4cccc4-c4cccc[n+]4[O-]>3.[O-]Cl(=O)(=O)=O.[O-]Cl(=O)(=O)=O.[O-]Cl(=O)(=O)=O.O.O.O

The **tris(L)iron(III) cation** is the first connected component:

[Fe+3]123(<-[O-][n+]4cccc4-c4cccc[n+]4[O-]>1)<-[O-][n+]4cccc4-c4cccc[n+]4[O-]>2<-[O-][n+]4cccc4-c4cccc[n+]4[O-]>3

The counterion is **perchlorate**, ClO_4^- , SMILES [O-]Cl(=O)(=O)=O.

Dissolution is represented by



Therefore,

$$\boxed{\text{cation} : \text{anion} = 1 : 3}.$$

4.6 — Iron oxidation state, electron configuration and spin

The three perchlorate ions have total charge -3 . Because each **L** is neutral, iron must have oxidation number

$$\boxed{+3}.$$

The metal is **iron(III)**, Fe^{3+} , SMILES [Fe+3]. Its *d*-electron count is

$$26 - 3 - 18 = 5,$$

so it is a d^5 ion.

For the approximately octahedral complex, the possibilities are:

State	Configuration	t_{2g} occupancy	e_g occupancy	Unpaired electrons
High spin	$t_{2g}^3 e_g^2$	$(\uparrow)(\uparrow)(\uparrow)$	$(\uparrow)(\uparrow)$	5
Low spin	$t_{2g}^5 e_g^0$	$(\uparrow\downarrow)(\uparrow\downarrow)(\uparrow)$	$(\uparrow)(\uparrow)$	1

For u unpaired electrons, the spin-only magnetic moment is

$$\mu_{\text{so}} = \sqrt{u(u+2)} \mu_{\text{B}}.$$

Hence

$$\mu_{\text{HS}} = \sqrt{5(7)} \mu_{\text{B}} = 5.92 \text{ B. M.},$$

whereas

$$\mu_{\text{LS}} = \sqrt{1(3)} \mu_{\text{B}} = 1.73 \text{ B. M.}.$$

The measured moment, 6.13 B. M., is close to the five-unpaired-electron prediction. Therefore,

$$\boxed{\text{A contains high-spin iron(III), } t_{2g}^3 e_g^2}.$$

The **measured magnetic moment** is the best evidence.

4.7 — Absorption maximum of A

The observed colour is yellow. Table 4c identifies yellow as the complementary colour to absorbed blue light at 450 nm. Therefore,

$$\boxed{\lambda_{\text{max}} \approx 450 \text{ nm}}.$$

This is the estimate obtained from the supplied colour table.

4.8 — Spin-only magnetic moment of B

Chromium(III), Cr^{3+} , SMILES [Cr+3], has

$$24 - 3 - 18 = 3$$

d -electrons.

In an octahedral field its configuration is $t_{2g}^3 e_g^0$, with one electron in each t_{2g} orbital. Thus there are three unpaired electrons:

$$\mu_{\text{so}} = \sqrt{3(3+2)} \mu_{\text{B}} = \sqrt{15} \mu_{\text{B}} = \boxed{3.87 \text{ B. M.}}.$$

4.9 — Composition and formula of B

Again using a 100.000 g sample,

$$n_{\text{Cr}} = \frac{8.440}{52} = 0.16231 \text{ mol}.$$

The ligand-to-chromium ratio from the carbon analysis is

$$x = \frac{38.930/(10 \times 12)}{8.440/52} = 1.9988 \approx \boxed{2}.$$

The total number of chlorine atoms per chromium atom is

$$y + z = \frac{17.250/35.45}{8.440/52} = 2.9980 \approx 3.$$

The oxygen percentage by difference is

$$w_O = 100 - (8.440 + 38.930 + 2.920 + 17.250 + 9.080) = 23.380\%.$$

The complete elemental ratios are:

Element	Atomic ratio relative to Cr
Cr	1.000
C	19.988
H	17.991
Cl	2.998
N	3.996
O	9.003

Thus

$$\text{empirical formula of B} = \text{C}_{20}\text{H}_{18}\text{Cl}_3\text{CrN}_4\text{O}_9.$$

Two ligands contribute four oxygen atoms and the water contributes one. The remaining four oxygen atoms belong to one perchlorate:

$$4 + 1 + 4z = 9 \implies z = 1.$$

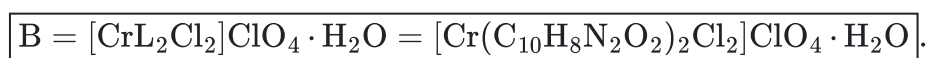
Since $y + z = 3$,

$$y = 2.$$

This agrees with the electrolyte information. Two neutral ligands and two coordinated **chloride ions**, SMILES [Cl-], give a complex cation of charge

$$+3 + 2(0) + 2(-1) = +1.$$

One perchlorate counterion then gives a 1 : 1 electrolyte:



The compound is **bis(2,2'-bipyridine N,N'-dioxide)dichloridochromium(III) perchlorate monohydrate**, with SMILES:

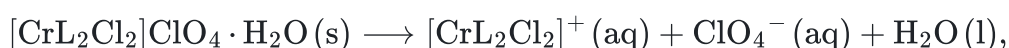
[Cr+3]12(<-[Cl-])(<-[Cl-])(<-[O-][n+]3ccccc3-c3cccc[n+]3[O-]->1)<-[O-][n+]3ccccc3-c3cccc[n+]3[O-]->2.[O-]Cl(=O)(=O)=O.O

Its **bis(L)dichloridochromium(III) cation** has SMILES:

[Cr+3]12(<-[Cl-])(<-[Cl-])(<-[O-][n+]3ccccc3-c3cccc[n+]3[O-]->1)<-[O-][n+]3ccccc3-c3cccc[n+]3[O-]->2

The four oxygen donors and two chlorido donors give approximately octahedral coordination. The information supplied does not select a cis or trans arrangement of the chlorido ligands.

The dissolution equation is



confirming the 1 : 1 cation-to-anion ratio.

The solution was checked against the official solution.

Problem 5: Glycoside A from Rosaceae seeds

Glycoside **A** ($C_{20}H_{27}NO_{11}$), found in seeds of *Rosaceae* gives a negative test with Benedict's or Fehling's solutions. Enzymatic hydrolysis of **A** yields (-) **B**, C_8H_7NO and **C**, $C_{12}H_{22}O_{11}$, but complete acid hydrolysis gives as organic products, (+) **D**, $C_6H_{12}O_6$ and (-) **E**, $C_8H_8O_3$.

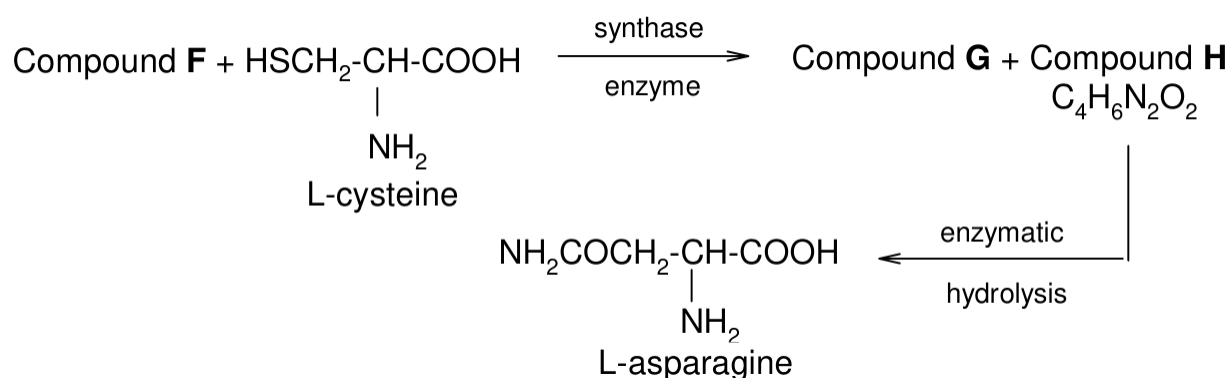
C has a β -glycosidic linkage and gives positive test with Benedict's or Fehling's solution.

Methylation of **C** with MeI/Ag_2O gives $C_{20}H_{38}O_{11}$, which upon acidic hydrolysis gives 2,3,4-tri-O-methyl-D-glucopyranose and 2,3,4,6-tetra-O-methyl-D-glucopyranose.

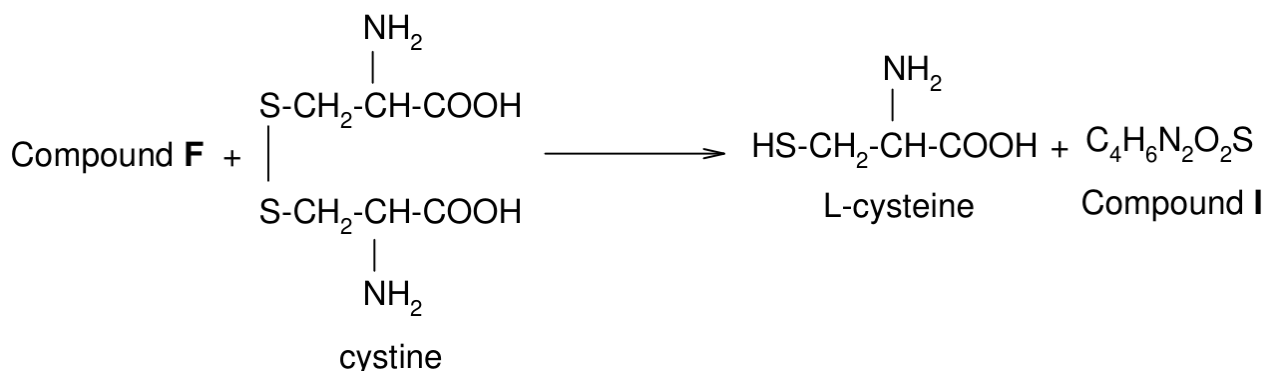
($\pm$)**B** can be prepared from benzaldehyde and $NaHSO_3$ followed by $NaCN$. Acidic hydrolysis of ($\pm$)**B** gives ($\pm$)**E**, $C_8H_8O_3$.

5.1 Write structures of **A – D** with appropriate stereochemistry in Haworth projection, except for **B**.

Glycoside **A** is found to be toxic and believed to be due to extremely toxic compound **F**, liberated under the hydrolytic conditions. Detoxification of compound **F** in plant may be accompanied by the reactions (stereochemistry not shown).



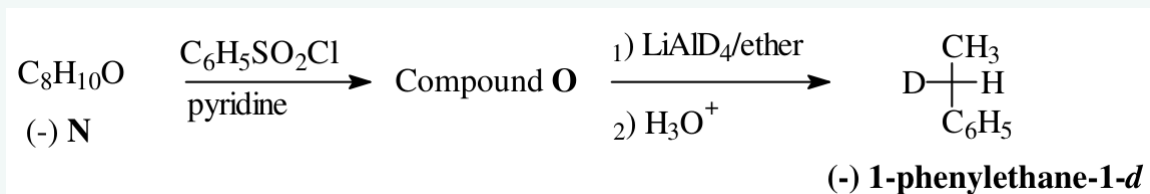
A small amount of compound **F** in human being is believed to be detoxified by a direct reaction with cystine giving L-cysteine and compound **I**, $C_4H_6N_2O_2S$ which is excreted in urine (stereochemistry not shown).



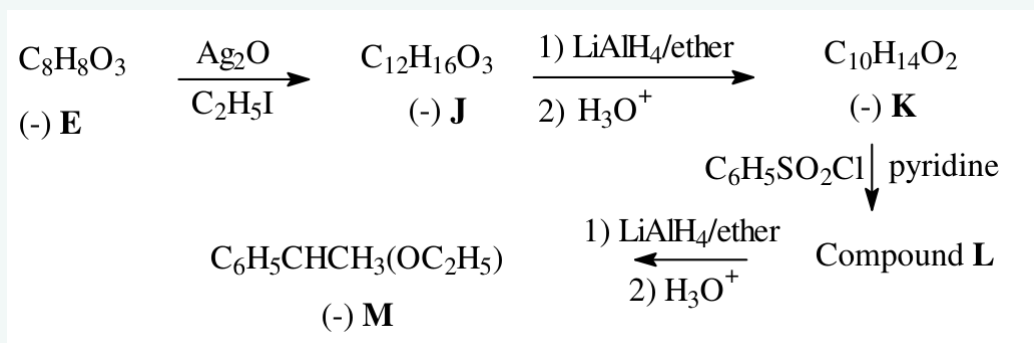
Compound **I** shows no absorption at 2150–2250 cm^{-1} in its IR spectrum but a band at 1640 cm^{-1} and the bands of carboxyl group are observed.

5.2 Write molecular formula for compounds **F** and **G**, and structural formula for compounds **H** and **I** and indicate stereochemistry of **H**. (Table 5.1 may be useful for structure identification.)

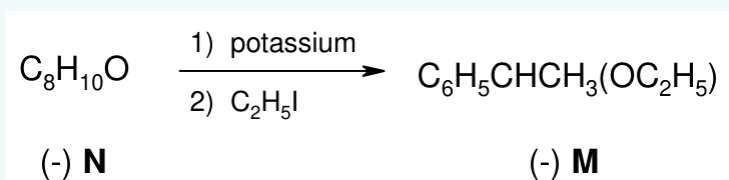
(-)-1-Phenylethane-1-*d*, $\text{C}_6\text{H}_5\text{CHDCH}_3$ can be prepared in optically active form and the magnitude of its rotation has the relatively high value, $[\alpha]_{\text{D}}$ is equal to -0.6.



The absolute configuration of (-)-1-phenylethane-1-*d* is related to (-) **E** according to the following reactions.



Compound (-) **M** can also be obtained from compound **N** as follows.



5.3 Deduce the absolute configuration of (-) **E** and the structure with configuration of each intermediate (**J** – **O**) in the sequence with the proper *R*, *S*-assignment as indicated in the answer sheet.

5.4 Choose the mechanism involved in the conversion of compound **O** to 1-phenylethane-1-*d*.

Table 5.1 Characteristic Infrared Absorption

Stretching Vibration	Region (cm^{-1})	Stretching Vibration	Region (cm^{-1})
C–H (alkane)	2850–2960	O–H (free alcohol)	3400–3600
C–H (alkene)	3020–3100	O–H (H-bonded alcohol)	3300–3500
C=C	1650–1670	O–H (acid)	2500–3100
C–H (alkyne)	3300	C–O	1030–1150
$\text{C}\equiv\text{C}$	2100–2260	NH, NH_2	3310–3550
C–H (aromatics)	3030	C–N	1030, 1230

Stretching Vibration	Region (cm ⁻¹)	Stretching Vibration	Region (cm ⁻¹)
C=C (aromatics)	1500-1600	C=N	1600-1700
C-H (aldehyde)	2700-2775, 2820-2900	C≡N	2210-2260
C=O	1670-1780		

Official English text of the problem.

Answers

- **5.1:** **A** is conventionally identified as **amygdalin**, the β-D-gentiobioside of (*R*)-mandelonitrile. **B** is (*R*)-mandelonitrile. **C** is **gentiobiose**, β-D-glucopyranosyl-(1 → 6)-D-glucopyranose. **D** is **D-glucose**.
- **5.2:** **F** is hydrogen cyanide, HCN; **G** is hydrogen sulfide, H₂S. **H** is **β-cyano-L-alanine**, configuration *S*. **I** is **2-amino-4,5-dihydro-1,3-thiazole-4-carboxylic acid**, equivalently its 2-iminothiazolidine tautomer.
- **5.3:** The configurations are $E : R, J : R, K : R, L : R, M : S, N : S, O : S$. Their structures are specified below.
- **5.4:** *S_N2 displacement by deuteride*, with inversion at the benzylic carbon, gives (*R*)-1-phenylethane-1-*d*.

The following SMILES specify the structures. For the reducing sugars **C** and **D**, a β reducing-end anomer is shown; their free anomeric centres can mutarotate.

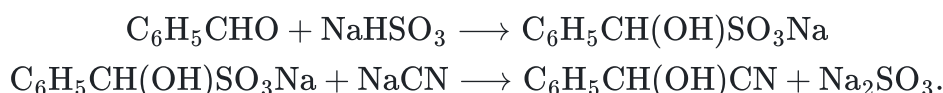
Compound	Name and stereochemical SMILES
A	Amygdalin, (<i>R</i>)-mandelonitrile β-D-gentiobioside: <chem>N#C[C@H](O[C@@H]1O[C@H](CO[C@@H]2O[C@H](CO)[C@@H](O)[C@H](O)[C@H]2O)[C@@H](O)[C@H](O)[C@H]1O)c1ccccc1</chem>
B	(<i>R</i>)-Mandelonitrile: <chem>N#C[C@H](O)c1ccccc1</chem>
C	Gentiobiose: <chem>O[C@@H]1O[C@H](CO[C@@H]2O[C@H](CO)[C@@H](O)[C@H](O)[C@H]2O)[C@@H](O)[C@H](O)[C@H]1O</chem>
D	D-Glucose, β-D-glucopyranose shown: <chem>O[C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O</chem>
E	(<i>R</i>)-Mandelic acid: <chem>O=C(O)[C@H](O)c1ccccc1</chem>
F	Hydrogen cyanide: <chem>C#N</chem>
G	Hydrogen sulfide: <chem>S</chem>
H	β-Cyano-L-alanine, (<i>S</i>)-2-amino-3-cyanopropanoic acid: <chem>N[C@@H](CC#N)C(=O)O</chem>
I	(4 <i>R</i>)-2-Amino-4,5-dihydro-1,3-thiazole-4-carboxylic acid: <chem>NC1=N[C@@H](CS1)C(=O)O</chem>
J	Ethyl (<i>R</i>)-2-ethoxy-2-phenylacetate: <chem>CCOC(=O)[C@H](OCC)c1ccccc1</chem>
K	(<i>R</i>)-2-Ethoxy-2-phenylethan-1-ol: <chem>OC[C@H](OCC)c1ccccc1</chem>
L	(<i>R</i>)-2-Ethoxy-2-phenylethyl benzenesulfonate: <chem>CCO[C@@H](COS(=O)(=O)c1ccccc1)c1ccccc1</chem>
M	(<i>S</i>)-1-Ethoxy-1-phenylethane: <chem>C[C@H](OCC)c1ccccc1</chem>

Compound	Name and stereochemical SMILES
N	(<i>S</i>)-1-Phenylethanol: <chem>C[C@H](O)c1ccccc1</chem>
O	(<i>S</i>)-1-Phenylethyl benzenesulfonate: <chem>C[C@H](OS(=O)(=O)c1ccccc1)c1ccccc1</chem>
Isotopic product	(<i>R</i>)-1-Phenylethane-1- <i>d</i> : <chem>[2H][C@H](C)c1ccccc1</chem>

Solution

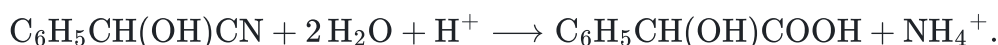
5.1 — Identification of the aglycone and sugars

Benzaldehyde, O=Cc1ccccc1, forms a bisulfite addition compound, which is converted into its cyanohydrin:



The species used here are sodium hydrogen sulfite [Na+].[O-]S(=O)O, sodium cyanide [Na+].[C-]#N, sodium hydroxy(phenyl)methanesulfonate [Na+].[O-]S(=O)(=O)C(O)c1ccccc1, and sodium sulfite [Na+].[Na+].[O-]S(=O)[O-].

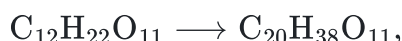
Attack on either face of the initially planar carbonyl gives racemic mandelonitrile, N#CC(O)c1ccccc1. Thus **B** is mandelonitrile. Hydrolysis of its nitrile group gives mandelic acid:



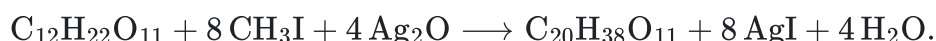
This converts racemic **B** into racemic mandelic acid, O=C(O)C(O)c1ccccc1. The absolute configuration of the naturally derived **B** and **E** is established in 5.3.

Both products of the methylation analysis are derivatives of D-glucopyranose. Therefore **C** contains two D-glucose units, and **D** is D-glucose.

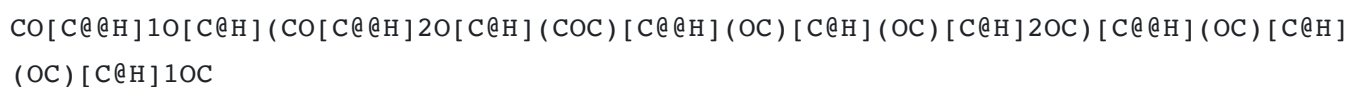
During methylation, each free hydroxyl becomes a methyl ether. The formula change is



corresponding to eight substitutions of OH by OCH₃, each adding CH₂. The balanced methylation is



The methylated product, **octa-O-methylgentiobiose**, represented with a β methyl-glycoside terminus, is:



Acid hydrolysis gives:

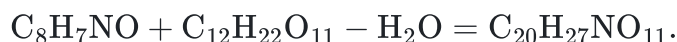
- **2,3,4-Tri-O-methyl-D-glucopyranose**, β anomer shown: O[C@H]1O[C@H](CO)[C@H](OC)[C@H](OC)[C@H]1OC.
- **2,3,4,6-Tetra-O-methyl-D-glucopyranose**, β anomer shown: O[C@H]1O[C@H](COC)[C@H](OC)[C@H](OC)[C@H]1OC.

The first product lacks methylation at position 6 because that oxygen originally participated in the intersugar linkage. The second glucose had free hydroxyls at positions 2, 3, 4 and 6. Therefore the linkage is 1 → 6; its stated β configuration identifies **C** as **gentiobiose**.

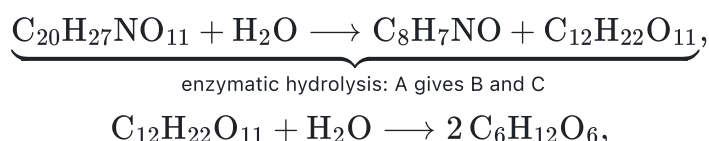
Hydrolysis also removes the methyl group installed at the originally free anomeric hydroxyl, releasing methanol:



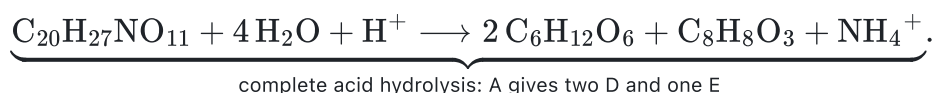
The reducing behaviour of **C** shows that one anomeric centre remains a hemiacetal. In **A**, this centre is converted into an acetal by attachment to the hydroxyl oxygen of mandelonitrile. Consequently **A** is nonreducing. Its formula agrees with condensation of **B** and **C**:



The hydrolyses balance as follows:



and, including nitrile hydrolysis,

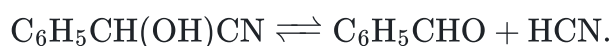


Haworth descriptions. Draw each glucopyranose ring with its ring oxygen at the upper right and C1 at the right. For each D-glucose unit, the C5 hydroxymethyl substituent points **up**, while the substituents at C2, C3 and C4 point **down, up and down**, respectively.

- In **C**, the nonreducing glucose's C1–O bond points **up** and connects to O6 of the reducing glucose. The reducing glucose's C1–OH can point down, α, or up, β.
- In the conventional structure of **A**, the reducing unit's C1–O bond also points **up**, and this oxygen connects to the (*R*)-mandelonitrile carbon.
- In **D**, C1–OH can point down or up. The α-D-glucopyranose alternative is $\text{O}[\text{C}@\text{H}]1\text{O}[\text{C}@\text{H}](\text{CO})[\text{C}@@\text{H}](\text{O})[\text{C}@\text{H}](\text{O})[\text{C}@\text{H}]1\text{O}$.
- For **B**, use a Fischer projection with CN at the top, phenyl at the bottom, H on the left and OH on the right. This is the *R* configuration.

5.2 — Toxic compound and detoxification products

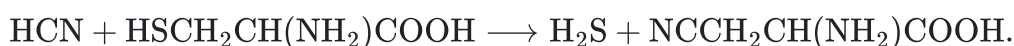
Mandelonitrile can dissociate into benzaldehyde and hydrogen cyanide:



Hence **F** = HCN]. Combining glycoside hydrolysis with this dissociation gives



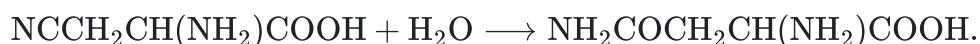
The plant reaction replaces the sulfhydryl group of L-cysteine with a cyano group:



Here NCCH₂ denotes N≡C–CH₂. Thus **G** = H₂S], and **H** is β-cyano-L-alanine.

L-Cysteine is $\text{N}[\text{C}@\text{H}] (\text{CS})\text{C}(=\text{O})\text{O}$. Its α -carbon retains its spatial arrangement during the side-chain substitution. **H** is consequently the **L**, or *S*, amino acid. Its Fischer projection has COOH at the top, CH_2CN at the bottom, NH_2 on the left and H on the right.

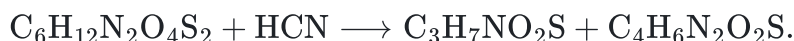
Hydration of the nitrile gives L-asparagine, $\text{N}[\text{C}@\text{H}] (\text{CC}(\text{N})=\text{O})\text{C}(=\text{O})\text{O}$:



For the human detoxification reaction, L-cystine is



The overall balance is



Cyanide attacks a disulfide sulfur, producing cysteine and **S-cyano-L-cysteine**, $\text{N}[\text{C}@\text{H}] (\text{CSC}\# \text{N})\text{C}(=\text{O})\text{O}$. The amino group can then attack the cyano carbon intramolecularly, forming a five-membered ring.

For **I**,

$$\text{DBE} = \frac{2(4) + 2 + 2 - 6}{2} = 3.$$

These three degrees of unsaturation are accounted for by one carboxyl carbonyl, one ring and one $\text{C}=\text{N}$ bond. The absence of a nitrile absorption and the band at 1640 cm^{-1} , within the given $1600\text{--}1700\text{ cm}^{-1}$ imine range, support this cyclic amidine.

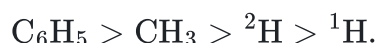
The ring sequence is sulfur–amidine carbon–nitrogen–carboxyl-bearing carbon–methylene. **I** can be written as either:

- **2-Amino-4,5-dihydro-1,3-thiazole-4-carboxylic acid:** $\text{NC1}=\text{N}[\text{C}@\text{H}] (\text{CS1})\text{C}(=\text{O})\text{O}$.
- Its tautomer, **2-iminothiazolidine-4-carboxylic acid:** $\text{N}=\text{C1N}[\text{C}@\text{H}] (\text{CS1})\text{C}(=\text{O})\text{O}$.

The retained cysteine stereocentre is *R*, although the question explicitly requires stereochemistry only for **H**.

5.3 — Absolute configurations and intermediates

First assign the configuration of the displayed deuterated product. Its CIP priorities are

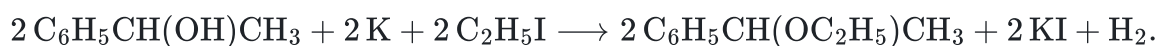


Phenyl outranks methyl because its attached carbon is compared with carbon neighbours, whereas methyl has hydrogen neighbours. Deuterium outranks protium by isotope mass.

In the supplied Fischer projection, methyl is at the top, phenyl at the bottom, D on the left and H on the right. Since the lowest-priority H points toward the observer, reversing the apparent sense gives *R*.

Deuteride displaces the sulfonate group of **O** with inversion. Therefore **O** is *S*. Sulfonylation of **N** modifies oxygen without breaking the stereogenic carbon–oxygen bond, so **N** is also *S*.

The route from **N** to **M** is oxygen alkylation. It likewise preserves the stereocentre:

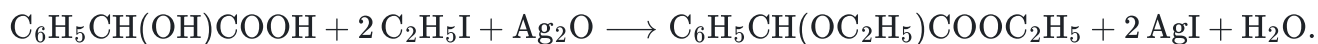


Thus **M** is *S*.

Now follow the other route.

1. E → J: ethylation of both acidic O–H groups

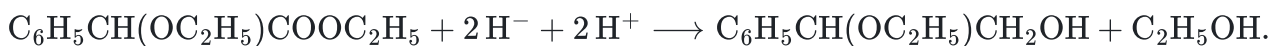
The alcohol becomes an ethyl ether and the carboxylic acid becomes an ethyl ester:



No bond at the stereogenic carbon is displaced.

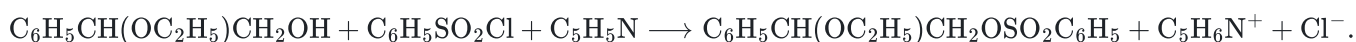
2. J → K: ester reduction

The ester group becomes CH_2OH , while the ethyl ether remains intact. A balanced net equation for reduction and work-up is

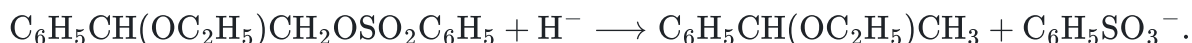


Hydride and acid are supplied in separate stages.

3. K → L: sulfonylation of the primary alcohol



4. L → M: replacement of the primary sulfonate by hydrogen



Substitution occurs at the neighbouring primary carbon, so the spatial arrangement at the original stereocentre remains unchanged.

The configuration labels nevertheless change between **L** and **M**, because the priorities change:

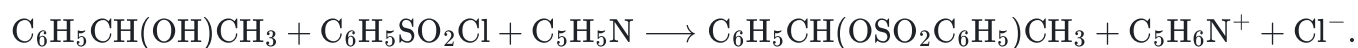
Compounds	CIP order at the stereogenic carbon
E	$\text{OH} > \text{COOH} > \text{C}_6\text{H}_5 > \text{H}$
J	$\text{OC}_2\text{H}_5 > \text{COOC}_2\text{H}_5 > \text{C}_6\text{H}_5 > \text{H}$
K	$\text{OC}_2\text{H}_5 > \text{CH}_2\text{OH} > \text{C}_6\text{H}_5 > \text{H}$
L	$\text{OC}_2\text{H}_5 > \text{CH}_2\text{OSO}_2\text{C}_6\text{H}_5 > \text{C}_6\text{H}_5 > \text{H}$
M	$\text{OC}_2\text{H}_5 > \text{C}_6\text{H}_5 > \text{CH}_3 > \text{H}$

The second and third priorities exchange when the substituted hydroxymethyl group becomes methyl. Consequently **E**, **J**, **K** and **L** are *R*, although **M** is *S*. This label change does **not** represent inversion of the stereocentre.

For precise Fischer drawings, put **phenyl at the bottom and H on the left** in every structure below. Place the listed groups at the top and right; horizontal bonds project toward the observer.

Compound	Top group	Right group	Configuration
E	COOH	OH	<i>R</i>
J	COOC ₂ H ₅	OC ₂ H ₅	<i>R</i>
K	CH ₂ OH	OC ₂ H ₅	<i>R</i>
L	CH ₂ OSO ₂ C ₆ H ₅	OC ₂ H ₅	<i>R</i>
M	CH ₃	OC ₂ H ₅	<i>S</i>
N	CH ₃	OH	<i>S</i>
O	CH ₃	OSO ₂ C ₆ H ₅	<i>S</i>

Formation of **O** balances as

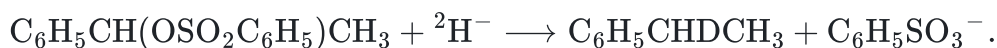


Finally, nitrile hydrolysis of **B** does not alter its stereogenic carbon. Its priority sequence is $\text{OH} > \text{CN} > \text{C}_6\text{H}_5 > \text{H}$, corresponding to the same ordering as in **E**. Therefore **B**, and the mandelonitrile centre of **A**, are also *R*.

The signs of optical rotation alone do not determine any of these *R/S* assignments.

5.4 — Mechanism of **O** → 1-phenylethane-1-d

The mechanism is a concerted S_N2 substitution:



Deuteride attacks the benzylic carbon from the side opposite the carbon–oxygen bond. Simultaneously, that bond's electron pair moves onto oxygen, releasing benzenesulfonate. The tetrahedral centre undergoes **Walden inversion**, giving the displayed *R* product from *S*-**O**.

The replacement changes the priority order from oxygen–phenyl–methyl to phenyl–methyl–deuterium. This is an even cyclic permutation, so the physical inversion also changes the descriptor from *S* to *R*.

For completeness, the remaining reagents and small products appearing in the equations are:

Species	SMILES
Water; methanol; ethanol	O; CO; CCO
Proton; ammonium; hydrogen	[H+]; [NH4+]; [H][H]
Hydride; deuteride	[H-]; [2H-]
Methyl iodide; ethyl iodide	CI; CCI
Silver(I) oxide; silver iodide	[Ag+] . [Ag+] . [O-2]; [Ag+] . [I-]
Potassium; potassium iodide	[K]; [K+] . [I-]
Pyridine; pyridinium; chloride	n1ccccc1; [nH+]1ccccc1; [Cl-]
Benzenesulfonyl chloride; benzenesulfonate	O=S(=O)(Cl)c1ccccc1; O=S(=O)([O-])c1ccccc1
Lithium aluminium hydride	[Li+] . [AlH4-]
Lithium aluminium deuteride	[Li+] . [2H][Al-]([2H])([2H])[2H]
Diethyl ether; hydronium	CCOCC; [OH3+]

The solution was checked against the official solution.

Problem 6: Sequence of peptide A

Peptide **A** has a molecular weight of 1007. Complete acid hydrolysis gives the following amino acids in equimolar amounts: Asp, Cystine, Glu, Gly, Ile, Leu, Pro, and Tyr (see Table 1). Oxidation of **A** with HCO_2OH gives only **B** which carries two residues of cysteic acid (**Cya** which is a cysteine derivative with its thiol group oxidized to sulfonic acid).

6.1 How many sulphonic acid groups are formed from oxidation of a disulfide bond ?

Partial hydrolysis of **B** gives a number of di and tri-peptides (B1-B6). The sequence of each hydrolysis product is determined in the following ways.

The N-terminal amino acid is identified by treating the peptide with 2,4-dinitrofluorobenzene (DNFB) to give DNP-peptide. After complete acid hydrolysis of the DNP-peptide, a DNP-amino acid is obtained which can be identified readily by comparison with standard DNP-amino acids.

6.2 B1, on treatment with DNFB followed by acid hydrolysis gives a product, DNP-Asp. This suggests that B1 has aspartic acid at the N-terminus. Write down the complete structure of DNP-Asp at its isoelectric point (no stereochemistry required).

Next, the C-terminal amino acid is identified by heating the peptide at 100 °C with hydrazine, which cleave all the peptide bonds and convert all except C-terminal amino acids into amino acid hydrazides, leaving the C-terminal carboxyl group intact.

In this way N- and C-terminal amino acids are identified and the complete sequences of B1-B6 are as shown :

B1	Asp-Cya	B4	Ile-Glu
B2	Cya-Tyr	B5	Cya-Pro-Leu
B3	Leu-Gly	B6	Tyr-Ile-Glu

Hydrolysis of **B** with an enzyme from *Bacillus subtilis* gives B7-B9 with the following compositions:

B7	Gly-NH ₂ (Glycinamide)
B8	Cya, Glu, Ile, Tyr
B9	Asp, Cya, Leu, Pro

6.3 Write down the sequence of B8, if DNP-Cya is obtained on treatment of B8 with DNFB followed by complete acid hydrolysis.

6.4 If the N- and C-terminal amino acids of B9 are identified as Asp and Leu respectively, write down the sequence of B9.

6.5 Write down the complete structure of **A** using abbreviation in Table 1, indicating the position of the disulfide bond.

However, the calculated molecular weight of **A** based on the above sequence is 2 mass units higher than the experimental value. On careful observation of the mixture from complete acid hydrolysis of **A**, 3 molar equivalents of ammonia are also produced in addition to the amino acids detected initially.

6.6 Suggest the revised structure of **A** and circle the site(s) of the structure to indicate all the possible source of ammonia.

6.7 Using the information in Table 2, calculate the isoelectric point of **A**.

Table 1: Formulae and symbols of common amino acids at isoelectric point

Name	Formula	Three-letter symbol
Alanine	CH ₃ CH(NH ₃ ⁺)CO ₂ ⁻	Ala
Arginine	H ₂ NC(=NH)NH(CH ₂) ₃ CH(NH ₃ ⁺)CO ₂ ⁻	Arg

Name	Formula	Three-letter symbol
Asparagine	$\text{H}_2\text{NCOCH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Asn
Aspartic Acid	$\text{HO}_2\text{CCH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Asp
Cysteine	$\text{HSCH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Cys
Cystine	$[\text{SCH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-]_2$	–
Glutamic Acid	$\text{HO}_2\text{CCH}_2\text{CH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Glu
Glutamine	$\text{H}_2\text{NCOCH}_2\text{CH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Gln
Glycine	$^+\text{H}_3\text{NCH}_2\text{CO}_2^-$	Gly
Histidine	(figure below)	His
Isoleucine	$\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Ile
Leucine	$(\text{CH}_3)_2\text{CHCH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Leu
Lysine	$\text{H}_2\text{N}(\text{CH}_2)_4\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Lys

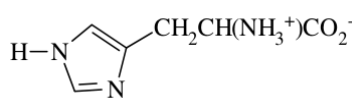


Table 1 (continued)

Name	Formula	Three-letter symbol
Methionine	$\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Met
Phenylalanine	$\text{PhCH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Phe
Proline	(first figure below)	Pro
Serine	$\text{HOCH}_2\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Ser
Threonine	$\text{CH}_3\text{CH}(\text{OH})\text{CH}(\text{NH}_3^+)\text{CO}_2^-$	Thr
Tryptophan	(second figure below)	Trp
Tyrosine	(third figure below)	Tyr
Valine	$(\text{CH}_3)_2\text{CHCH}(\text{NH}_3^+)\text{CO}_2^-$	Val

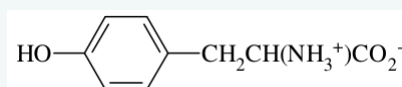
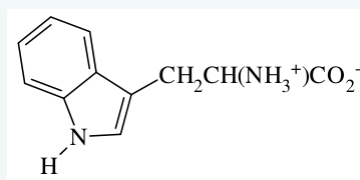
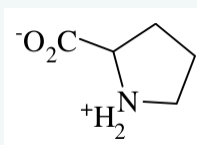


Table 2: $\text{p}K_a$ of some important groups in amino acids

Groups	Equilibrium	p <i>K</i> _a
Terminal carboxyl	(first figure below)	3.1
Asp /or Glu side-chain carboxyl	(second figure below)	4.4
His side-chain	(third figure below)	6.5
Terminal amino	(fourth figure below)	8.0
Cys side-chain	(fifth figure below)	8.5

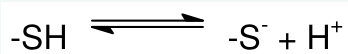
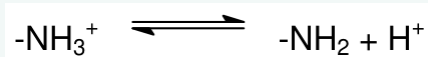
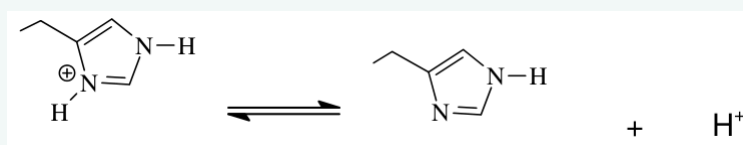
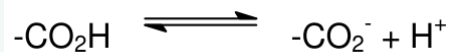
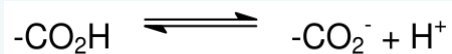
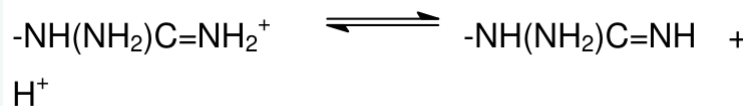
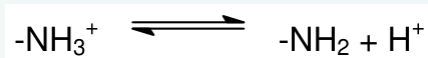
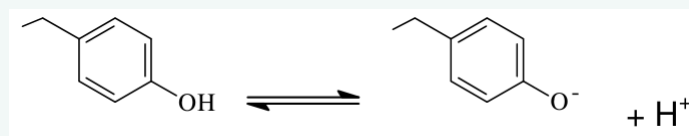


Table 2 (continued)

Groups	Equilibrium	p <i>K</i> _a
Tyr side-chain	(first figure below)	10.0
Lys side-chain amino	(second figure below)	10.0
Arg side-chain	(third figure below)	12.0



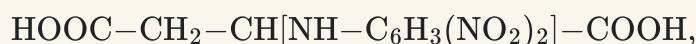
Official English text of the problem.

Answers

Peptide SMILES below use conventional natural L-residue stereochemistry and neutral functional-group representations.

- **6.1: Two** sulfonic acid groups, $-\text{SO}_3\text{H}$, per disulfide bond.

- **6.2: N-(2,4-dinitrophenyl)aspartic acid**, shown as the neutral, nonzwitterionic form:



with the nitro groups at positions 2 and 4 relative to the nitrogen attachment.

SMILES: O=C(O)CC(Nc1ccc([N+](=O)[O-])cc1[N+](=O)[O-])C(=O)O

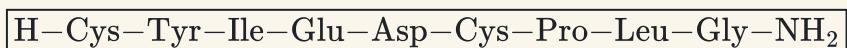
- **6.3: Peptide B8:** Cya-Tyr-Ile-Glu, written from N- to C-terminus.

SMILES: N[C@@H](CS(=O)(=O)O)C(=O)N[C@@H](Cc1ccc(O)cc1)C(=O)N[C@@H]([C@@H](C)CC)C(=O)N[C@@H](CCC(=O)O)C(=O)O

- **6.4: Peptide B9:** Asp-Cya-Pro-Leu.

SMILES: N[C@@H](CC(=O)O)C(=O)N[C@@H](CS(=O)(=O)O)C(=O)N1CCC[C@H]1C(=O)N[C@@H](CC(C)C)C(=O)O

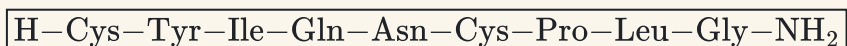
- **6.5: Provisional peptide A:**



with a disulfide between **Cys¹** and **Cys⁶**, a free N-terminal amino group, and a C-terminal carboxamide.

SMILES: N[C@@H](CS1)C(=O)N[C@@H](Cc2ccc(O)cc2)C(=O)N[C@@H]([C@@H](C)CC)C(=O)N[C@@H](CCC(=O)O)C(=O)N[C@@H](CC(=O)O)C(=O)N[C@@H](CS1)C(=O)N2CCC[C@H]2C(=O)N[C@@H](CC(C)C)C(=O)NCC(N)=O

- **6.6: Revised peptide A:**



retaining the **Cys¹-Cys⁶ disulfide**. Circle the three $-\text{C}(=\text{O})\text{NH}_2$ groups: the **Gln⁴ side-chain amide**, **Asn⁵ side-chain amide**, and **Gly⁹ terminal amide**.

SMILES: N[C@@H](CS1)C(=O)N[C@@H](Cc2ccc(O)cc2)C(=O)N[C@@H]([C@@H](C)CC)C(=O)N[C@@H](CCC(N)=O)C(=O)N[C@@H](CC(N)=O)C(=O)N[C@@H](CS1)C(=O)N2CCC[C@H]2C(=O)N[C@@H](CC(C)C)C(=O)NCC(N)=O

- **6.7:** $\text{pI} = 9.0$.

Solution

6.1

Oxidation converts each sulfur atom of a disulfide into a sulfonic acid group. Therefore one disulfide produces **two** such groups.

A balanced equation using the specified oxidant is



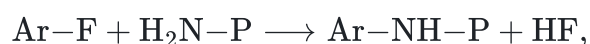
Here performic acid is $\text{O}=\text{COOH}$, formic acid is $\text{O}=\text{COH}$, and water is O .

Each cysteine-derived sulfur in the peptide consequently becomes a cysteic acid residue. Free L-cysteic acid, **Cya**, has SMILES N[C@@H](CS(=O)(=O)O)C(=O)O.

One molecule of cystine contains two amino-acid units. L-cystine has SMILES N[C@@H](CSSC[C@@H](N)C(=O)O)C(=O)O. Thus the stated equimolar hydrolysis products correspond to **nine residues**: two cysteine residues and one of each of the other seven amino acids.

6.2

DNFB labels the free N-terminal amino group by nucleophilic aromatic substitution. For an N-terminal group represented by $\text{H}_2\text{N}-\text{P}$, the formal balanced substitution is



where **Ar** is the 2,4-dinitrophenyl group. DNFB is **1-fluoro-2,4-dinitrobenzene**, Fc1ccc([N+](=O)[O-])cc1[N+](=O)[O-]; hydrogen fluoride is **F**. In the labeling medium, base takes up the acid produced.

Subsequent peptide-bond hydrolysis leaves the aryl–nitrogen bond intact. Obtaining DNP-Asp therefore identifies **Asp as the N-terminal residue of B1**.

The product is **N-(2,4-dinitrophenyl)aspartic acid**, whose SMILES is given in the answers. To draw it completely:

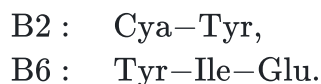
- Draw a benzene ring bearing the amino-acid nitrogen at position 1.
- Attach a nitro group at each of positions 2 and 4.
- Connect the nitrogen, bearing one hydrogen, to the aspartic-acid α -carbon.
- Attach $-\text{COOH}$, $-\text{CH}_2\text{COOH}$, and hydrogen to that α -carbon.

The two nitro groups strongly reduce the basicity of the aryl-substituted nitrogen. The displayed net-neutral form therefore has an uncharged $-\text{NH}-$ group and two protonated carboxyl groups. No stereochemistry is assigned in this structure, as requested.

6.3

The composition of B8 is Cya, Tyr, Ile, and Glu. Its DNP derivative identifies **Cya as its N-terminal residue**.

The overlapping fragments are



Their common Tyr residue joins them uniquely:



B4, Ile–Glu, independently confirms the final two residues.

6.4

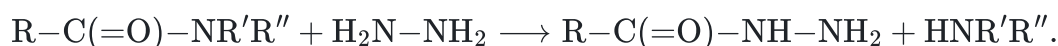
B9 contains Asp, Cya, Pro, and Leu, with Asp at its N-terminus and Leu at its C-terminus.

B1 supplies Asp–Cya, while B5 supplies Cya–Pro–Leu. Joining at their common Cya gives



This sequence satisfies both terminal identifications.

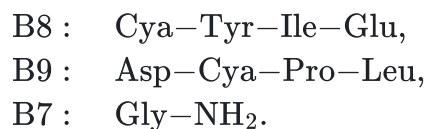
The hydrazinolysis used for C-terminal identification is an acyl substitution. Its general balanced form is



Hydrazine has SMILES NN. Under the identification procedure described in the problem, the C-terminal amino acid retains its carboxyl group and is distinguished from the amino-acid hydrazides.

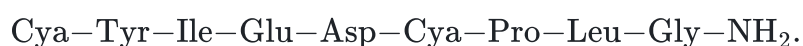
6.5

The three enzymatic fragments account for all nine residues:

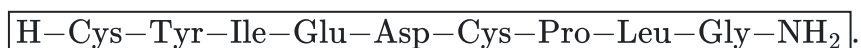


B7 is **glycinamide**, NCC(N)=O, so it establishes an amidated C-terminus.

The fragment B3, Leu-Gly, joins the end of B9 to B7. Consequently B9-B7 forms the C-terminal five-residue segment. B8 supplies the remaining N-terminal four residues, giving the provisional oxidized sequence



Reversing the structural consequence of oxidation replaces the Cya residues at positions 1 and 6 with disulfide-linked cysteine residues. Therefore



To indicate the disulfide precisely, connect the sulfur atoms of the two cysteine side chains, giving a side-chain linkage



between residues **1 and 6**. The N-terminal amino group remains free. The SMILES in answer 6.5 explicitly encodes this intramolecular bond.

6.6

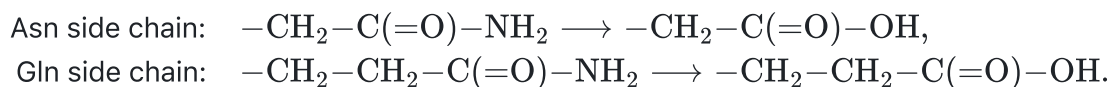
Acid hydrolysis converts a primary carboxamide into a carboxylic acid and ammonia. The formal balanced equation is



The primary-amide fragment is *C(N)=O, the carboxylic-acid fragment is *C(=O)O, and ammonia is N; the asterisk denotes the remainder of the structure. In the acidic hydrolysate, the released ammonia is protonated to **ammonium**, [NH4+].

The known terminal glycinamide accounts for **one equivalent** of ammonia. The remaining two equivalents require **two additional primary amides**.

Asp and Glu in an acid hydrolysate can arise from hydrolysis of the corresponding side-chain amides:



These transformations follow the balanced hydrolysis equation above. Thus the original residues were **Gln⁴ and Asn⁵**.

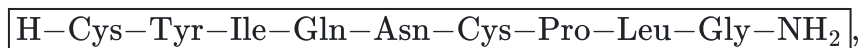
The mass difference supports exactly these two replacements. Replacing -COOH by -CONH2 replaces OH by NH₂, decreasing the molar mass by approximately

$$(14 + 2) - (16 + 1) = -1 \text{ g mol}^{-1}.$$

Two replacements decrease the molar mass by approximately 2 g mol^{-1} , matching the stated difference:

$$M_r(\text{revised A}) \simeq 1009 - 2 = 1007.$$

Hence the revised structure is



with the same Cys¹–Cys⁶ disulfide.

The three sites to circle are:

1. **Gln⁴**: the side-chain $-\text{CH}_2\text{CH}_2\text{C}(=\text{O})\text{NH}_2$.
2. **Asn⁵**: the side-chain $-\text{CH}_2\text{C}(=\text{O})\text{NH}_2$.
3. **Gly⁹**: the terminal $-\text{C}(=\text{O})\text{NH}_2$.

Each yields one equivalent of ammonia. The backbone peptide nitrogens remain attached to their respective amino-acid products during hydrolysis.

6.7

In the revised structure, the relevant ionizable groups from Table 2 are:

Group in A	$\text{p}K_a$	Charge change on deprotonation
Free N-terminal amino group	8.0	$+1 \rightarrow 0$
Tyr phenolic group	10.0	$0 \rightarrow -1$

The C-terminus is amidated, and the Gln and Asn side chains are amides. The two cysteine sulfur atoms form a disulfide, so there are no free thiol groups.

The electrically neutral form lies between loss of the N-terminal ammonium proton and loss of the Tyr phenolic proton. Therefore

$$\boxed{\text{pI} = \frac{8.0 + 10.0}{2} = 9.0}.$$

More explicitly, the mean charge under the supplied ionization model is

$$\bar{z} = \frac{1}{1 + 10^{\text{pH}-8.0}} - \frac{1}{1 + 10^{10.0-\text{pH}}}.$$

At $\text{pH} = 9.0$, the positive and negative contributions both have magnitude $1/11$, so $\bar{z} = 0$.

The solution was checked against the official solution.