

IChO 1985

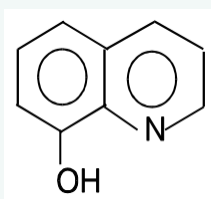
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Problem 1: Determination of aluminium with 8-hydroxyquinoline and bromate

A solution was formed from 0.5284 g of a sample of an alloy containing aluminium. The aluminium was then precipitated as aluminium 8-hydroxyquinolate. The precipitate was separated, dissolved in hydrochloric acid and the 8-hydroxyquinoline formed was titrated with a standard solution of potassium bromate containing potassium bromide. The concentration of the standard potassium bromate solution was 0.0200 M and 17.40 cm³ of it were required. The resultant product is a dibromo derivative of 8-hydroxyquinoline.

The structural formula of 8-hydroxyquinoline is:



The relative atomic mass of aluminium is 26.98.

Problems:

- 1.1 Write the balanced equation for the reaction of the aluminium (III) ion with 8-hydroxyquinoline, showing clearly the structure of the products.
- 1.2 Give the name of the type of compound which is formed during the precipitation.
- 1.3 Write the balanced equation for the reaction in which bromine is produced.
- 1.4 Write the balanced equation for the reaction of bromine with 8-hydroxyquinoline.
- 1.5 Calculate the molar ratio of aluminium ions to bromate ions.
- 1.6 Calculate the percentage by weight of aluminium in the alloy.

Official English text of the problem.

Answers

- 1.1



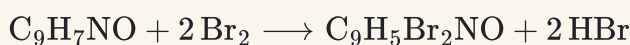
The precipitate is aluminium tris(quinolin-8-olate), with three bidentate ligands coordinated through oxygen and nitrogen; its structure and SMILES are specified below.

- 1.2 A **chelate complex**, specifically a neutral complex with three five-membered chelate rings.

- 1.3



- 1.4



The organic product is **5,7-dibromoquinolin-8-ol**, SMILES Oc1c(Br)cc(Br)c2cccnc12.

- 1.5

$$n(\text{Al}^{3+}) : n(\text{BrO}_3^-) = 1 : 2$$

- 1.6

$$\text{Aluminium content} = 0.888\% \text{ by mass}$$

Solution

1.1 — Precipitation and structure

8-Hydroxyquinoline, also called quinolin-8-ol or oxine, has formula $\text{C}_9\text{H}_7\text{NO}$ and SMILES Oc1cccc2cccnc12. Loss of its hydroxyl proton gives the quinolin-8-olate ion, $\text{C}_9\text{H}_6\text{NO}^-$, SMILES [O-]c1cccc2cccnc12.

Each ligand binds aluminium through two donor atoms:

- the negatively charged phenoxide oxygen;
- the quinoline nitrogen, using its lone pair.

Three singly charged ligands neutralize one aluminium(III) ion, Al^{3+} , SMILES [Al+3]. Therefore,



where the hydrogen ion, or proton, has SMILES [H+].

The product is **aluminium tris(quinolin-8-olate)**, also called aluminium 8-hydroxyquinolate. An extended SMILES explicitly representing all six donor-to-metal bonds is:

[Al+3]123(<-[O-]c4cccc5cccn->1c45)(<-[O-]c4cccc5cccn->2c45)<-[O-]c4cccc5cccn->3c45

Here the arrows denote coordinate bonds directed from the donor atom towards aluminium.

To draw the product, place aluminium at the centre and surround it with three quinolin-8-olate ligands. Join both the oxygen and nitrogen of **each** ligand to the same aluminium centre. Each ligand forms a five-membered ring following the sequence aluminium–oxygen–carbon-8–carbon-8a–nitrogen. The six donor atoms give a distorted octahedral coordination geometry. No particular geometric or optical isomer is specified.

1.2 — Type of compound

The product is a **chelate complex**. A chelating ligand binds the same metal ion through at least two donor atoms, forming a ring that includes the metal. Here each quinolin-8-olate ligand is bidentate, and three such ligands produce three chelate rings.

1.3 — Production of bromine

In acidic solution, bromate oxidizes bromide to bromine. The species are bromate, SMILES [O-][Br](=O)=O; bromide, [Br-]; bromine, BrBr; and water, O.

Bromine in bromate has oxidation state +5, so its reduction to oxidation state zero requires five electrons. Five bromide ions, each initially at oxidation state −1, supply these electrons. Balancing oxygen with water and hydrogen with protons gives



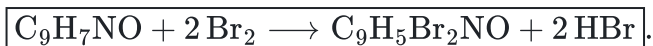
Thus, **one mole of bromate produces three moles of bromine**.

1.4 — Bromination of 8-hydroxyquinoline

The hydroxyl group activates the benzene portion of the quinoline system towards electrophilic substitution. Bromination occurs at positions **7 and 5**, respectively ortho and para to the hydroxyl group.

The product is **5,7-dibromo-8-hydroxyquinoline**, or 5,7-dibromoquinolin-8-ol, SMILES Oc1c(Br)cc(Br)c2ccncc12. Its structure retains the original quinoline skeleton and hydroxyl group at position 8, with bromine atoms replacing the hydrogens at positions 5 and 7.

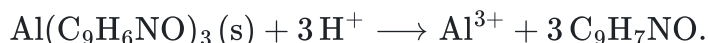
Each substitution consumes one bromine molecule and produces one hydrogen bromide molecule, SMILES [H]Br. Consequently,



One mole of 8-hydroxyquinoline therefore consumes **two moles of bromine**.

1.5 — Aluminium-to-bromate molar ratio

Acid dissolution of the precipitate releases three molecules of 8-hydroxyquinoline per aluminium ion. Representing the liberated ligand in its neutral form,



Each of these three ligand molecules consumes two bromine molecules. Hence,

$$n(\text{Br}_2) = 2 n(\text{C}_9\text{H}_7\text{NO}) = 6 n(\text{Al}^{3+}).$$

From part 1.3,

$$n(\text{Br}_2) = 3 n(\text{BrO}_3^-).$$

Equating these expressions gives

$$6 n(\text{Al}^{3+}) = 3 n(\text{BrO}_3^-),$$

so

$$n(\text{Al}^{3+}) : n(\text{BrO}_3^-) = 1 : 2.$$

1.6 — Aluminium mass percentage

The volume of bromate solution is

$$V = 17.40 \text{ cm}^3 = 0.01740 \text{ L}.$$

The amount of bromate used is

$$n(\text{BrO}_3^-) = cV = (0.0200 \text{ mol L}^{-1})(0.01740 \text{ L}) = 3.48 \times 10^{-4} \text{ mol}.$$

Using the 1 : 2 aluminium-to-bromate ratio,

$$n(\text{Al}) = \frac{3.48 \times 10^{-4}}{2} = 1.74 \times 10^{-4} \text{ mol}.$$

The given relative atomic mass corresponds to a molar mass of 26.98 g mol^{-1} . Retaining guard digits,

$$m(\text{Al}) = (1.74 \times 10^{-4} \text{ mol})(26.98 \text{ g mol}^{-1}) = 0.00469452 \text{ g}.$$

Therefore,

$$\text{Aluminium mass percentage} = \frac{0.00469452 \text{ g}}{0.5284 \text{ g}} \times 100\% = 0.8884406\%.$$

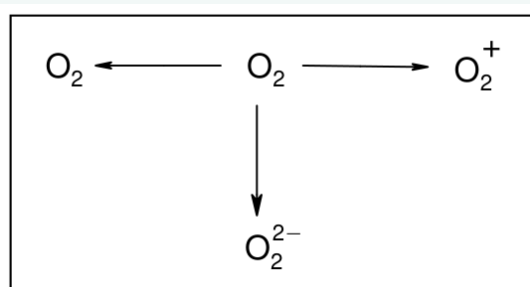
The bromate concentration has three significant figures, so the final result is

$$0.888\% \text{ aluminium by mass}.$$

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 2: Dioxygen species O_2^+ , O_2^- and O_2^{2-} : bond orders, distances and energies

It is possible to prepare compounds containing ions O_2^- , O_2^{2-} or even O_2^+ . These ions are usually formed from molecules of oxygen during various reactions, as indicated in the scheme below:



2.1 Indicate clearly which of the above reactions correspond to the oxidation and which to the reduction of the oxygen molecule.

2.2 For each of the ions in the scheme give the formula of a compound containing that particular ion.

2.3 It has been found that one of the species in the scheme is diamagnetic. Which one is it?

2.4 Copy out the following table:

Species	Bond order	Interatomic distance	Bonding energy
O ₂			
O ₂ ⁺			
O ₂ ⁻			
O ₂ ²⁻			

The interatomic distances, O—O, in the above species have the values 112, 121, 132 and about 149 pm. Write these values in the appropriate column in the table.

$$1 \text{ pm} = 10^{-12} \text{ m}.$$

2.5 Three of the bond energies, $E_{\text{O}-\text{O}}$, have the values approximately 200, 490 and 625 kJ mol⁻¹. The value for one of the species is uncertain and, therefore, not given. Write the values in the appropriate spaces in the table.

2.6 Determine the bond order for the individual species and write the answers in the table.

2.7 Is it possible to prepare compounds containing the F₂²⁻ ion? Give reasons for your answer.

Official English text of the problem.

Answers

- 2.1** Oxidation: $\text{O}_2 \longrightarrow \text{O}_2^+ + \text{e}^-$. Reduction: $\text{O}_2 + \text{e}^- \longrightarrow \text{O}_2^-$ and $\text{O}_2 + 2\text{e}^- \longrightarrow \text{O}_2^{2-}$.
- 2.2** Suitable compounds are potassium superoxide, KO₂; sodium peroxide, Na₂O₂; and dioxygenyl hexafluoroplatinate(V), O₂PtF₆. Their SMILES are given in the solution.
- 2.3** The **peroxide ion**, O₂²⁻, is diamagnetic.
- 2.4** Distances: O₂, 121 pm; O₂⁺, 112 pm; O₂⁻, 132 pm; O₂²⁻, approximately 149 pm.
- 2.5** Using the peroxide single-bond assignment discussed below: O₂, approximately 490 kJ mol⁻¹; O₂⁺, approximately 625 kJ mol⁻¹; O₂²⁻, approximately 200 kJ mol⁻¹. The superoxide value is left unspecified.
- 2.6** Bond orders: O₂, 2; O₂⁺, 2.5; O₂⁻, 1.5; O₂²⁻, 1.
- 2.7** **No stable, discrete bonded F₂²⁻ ion is predicted:** its bond order is zero. Reduction gives two separate fluoride ions.

Solution

2.1 — Oxidation and reduction

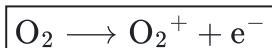
The oxygen species have the following names and formal SMILES representations:

Species	Name	SMILES
O ₂	Dioxygen	O=O
O ₂ ⁺	Dioxygenyl ion	[O+]=O

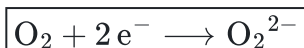
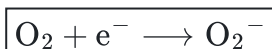
Species	Name	SMILES
O_2^-	Superoxide ion	<chem>[O-][O]</chem>
O_2^{2-}	Peroxide ion	<chem>[O-][O-]</chem>

These SMILES specify formal connectivity and charge. They do not express fractional molecular orbital bond orders or the distribution of electrons between molecular orbitals. In particular, O=O does not specify dioxygen's triplet ground state.

Oxidation is electron loss, so formation of the dioxygenyl ion is oxidation:



Reduction is electron gain. Formation of either negative ion is therefore reduction:



Each equation conserves both oxygen atoms and total charge.

2.2 — Compounds containing the ions

One example for each ion is:

Ion	Compound formula	Compound name	SMILES
O_2^-	<chem>KO2</chem>	Potassium superoxide	<chem>[K+] . [O-][O]</chem>
O_2^{2-}	<chem>Na2O2</chem>	Sodium peroxide	<chem>[Na+] . [Na+] . [O-][O-]</chem>
O_2^+	<chem>O2PtF6</chem>	Dioxygenyl hexafluoroplatinate(V)	<chem>[O+]=O . F[Pt-](F)(F)(F)(F)F</chem>

The charge balances are respectively $+1 - 1 = 0$, $2(+1) - 2 = 0$, and $+1 - 1 = 0$.

In the last compound, the counterion is hexafluoroplatinate(V), [PtF6]^-, represented by F[Pt-](F)(F)(F)(F)F. Its six fluorine ligands have octahedral coordination around platinum. The SMILES does not specify this geometry or the crystal lattice; the formal charge on platinum in this covalent SMILES representation is not its oxidation state.

2.3 — Diamagnetism

All four oxygen species have filled lower molecular orbitals. Their magnetic differences arise from the two degenerate antibonding π_{2p}^* orbitals.

Neutral dioxygen has two electrons in these orbitals. By Hund's rule, they occupy different orbitals with parallel spins. Removing one electron gives the dioxygenyl ion; adding one or two gives superoxide or peroxide:

Species	Occupation of the two π^* orbitals	Unpaired electrons	Magnetic character
O_2	$(\uparrow)(\uparrow)$	2	Paramagnetic
O_2^+	$(\uparrow)(\text{empty})$	1	Paramagnetic
O_2^-	$(\uparrow\downarrow)(\uparrow)$	1	Paramagnetic
O_2^{2-}	$(\uparrow\downarrow)(\uparrow\downarrow)$	0	Diamagnetic

Thus only the peroxide ion has every electron paired:

O_2^{2-} is diamagnetic.

2.4 — Interatomic distances

Removing an electron from an antibonding orbital strengthens and shortens the bond. Adding electrons to antibonding orbitals weakens and lengthens it. Consequently,

$$r(\text{O}_2^+) < r(\text{O}_2) < r(\text{O}_2^-) < r(\text{O}_2^{2-}).$$

Assigning the supplied distances in increasing order gives

$$\begin{aligned} r(\text{O}_2^+) &= 112 \text{ pm}, \\ r(\text{O}_2) &= 121 \text{ pm}, \\ r(\text{O}_2^-) &= 132 \text{ pm}, \\ r(\text{O}_2^{2-}) &\approx 149 \text{ pm}. \end{aligned}$$

2.5 — Bond energies

The expected bond-strength order is the reverse of the bond-length order:

$$E(\text{O}_2^+) > E(\text{O}_2) > E(\text{O}_2^-) > E(\text{O}_2^{2-}).$$

The conventional assignment associates approximately 490 kJ mol^{-1} with the dioxygen double bond and approximately 625 kJ mol^{-1} with the stronger dioxygenyl bond. Assigning approximately 200 kJ mol^{-1} to the peroxide single bond leaves the superoxide entry unspecified:

$$\begin{aligned} E(\text{O}_2^+) &\approx 625 \text{ kJ mol}^{-1}, \\ E(\text{O}_2) &\approx 490 \text{ kJ mol}^{-1}, \\ E(\text{O}_2^{2-}) &\approx 200 \text{ kJ mol}^{-1}. \end{aligned}$$

Bond order does not determine a numerical bond energy through an exact proportionality, so the missing value should not be calculated by interpolation.

2.6 — Bond orders

For these oxygen species, the valence molecular orbital configuration can be written as

$$(\sigma_{2s})^2(\sigma_{2s}^*)^2(\sigma_{2p_z})^2(\pi_{2p_x})^2(\pi_{2p_y})^2(\pi_{2p}^*)^n,$$

where the final factor denotes the total occupation of the two degenerate antibonding π^* orbitals.

There are eight bonding electrons and $2 + n$ antibonding electrons. Therefore,

$$\text{bond order} = \frac{N_{\text{bonding}} - N_{\text{antibonding}}}{2} = \frac{8 - (2 + n)}{2}.$$

The values of n are 2, 1, 3, 4 for O_2 , O_2^+ , O_2^- , and O_2^{2-} , respectively. Hence,

$$\begin{aligned} \text{O}_2 : \quad & \frac{8 - 4}{2} = 2, \\ \text{O}_2^+ : \quad & \frac{8 - 3}{2} = 2.5, \\ \text{O}_2^- : \quad & \frac{8 - 5}{2} = 1.5, \\ \text{O}_2^{2-} : \quad & \frac{8 - 6}{2} = 1. \end{aligned}$$

The completed table, using the energy assignment in 2.5, is:

Species	Bond order	Interatomic distance / pm	Bonding energy / kJ mol ⁻¹
O ₂	2	121	approximately 490
O ₂ ⁺	2.5	112	approximately 625
O ₂ ⁻	1.5	132	Unspecified
O ₂ ²⁻	1	approximately 149	approximately 200

2.7 — The proposed difluorine dianion

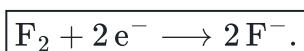
Difluorine, F₂, has SMILES FF and fourteen valence electrons. Its bonding orbitals contain eight electrons and its antibonding orbitals contain six, giving

$$\text{bond order of F}_2 = \frac{8 - 6}{2} = 1.$$

Adding two electrons fills the remaining antibonding $\sigma_{2p_z}^*$ orbital. The hypothetical difluorine dianion would then have

$$\text{bond order of F}_2^{2-} = \frac{8 - 8}{2} = 0.$$

There is no net covalent bonding stabilization, and separation also relieves repulsion between the negative ions. Thus compounds are expected to contain individual fluoride ions, F⁻, SMILES [F-], rather than a stable bonded difluorine dianion. The balanced overall reduction is



The appropriate product representation is [F-] · [F-]: two separate fluoride ions, with no bond between them.

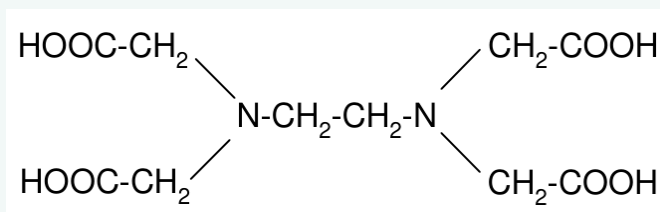
The solution was checked against the official solution.

Problem 3: Solubility of calcium sulphate and the calcium-EDTA complex

Calcium sulphate is a sparingly soluble compound. Its solubility product is given by:

$$K_s(\text{CaSO}_4) = [\text{Ca}^{2+}][\text{SO}_4^{2-}] = 6.1 \times 10^{-5}$$

Ethylenediaminetetraacetic acid (EDTA) has the formula C₁₀H₁₆N₂O₈ and the structure:



The anion of this acid, C₁₀H₁₂N₂O₈⁴⁻, forms a stable complex CaC₁₀H₁₂N₂O₈²⁻ with calcium ions. The stability constant of this complex ion is given by:

$$K = \frac{[\text{CaC}_{10}\text{H}_{12}\text{N}_2\text{O}_8^{2-}]}{[\text{Ca}^{2+}][\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_8^{4-}]} = 1.0 \times 10^{11}$$

EDTA is completely dissociated in strongly alkaline solution. The equation for this dissociation is:



Problems:

3.1 Calculate the concentration of calcium ions in a saturated solution of calcium sulphate.

3.2 Calculate the concentration of free Ca^{2+} cations in a solution of 0.1 M $\text{Na}_2(\text{CaC}_{10}\text{H}_{12}\text{N}_2\text{O}_8)$. You should ignore any protonation of the ligand.

3.3 How many moles of calcium sulphate will dissolve in 1 litre of a strongly alkaline solution of 0.1 M $\text{Na}_4\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_8$?

What would be the concentrations of the calcium and sulphate ions in the resulting solution?

3.4 Suggest a structure for the complex ion $[\text{CaC}_{10}\text{H}_{12}\text{N}_2\text{O}_8]^{2-}$ assuming that it is approximately octahedral.

3.5 Is the structure you have suggested in 4) optically active?

If your answer is "yes" then draw the structure of the other optical isomer enantiomer).

3.6 Explain why the complexes formed by the anion $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_8^{4-}$ are exceptionally stable.

Official English text of the problem.

Answers

- **3.1:** $[\text{Ca}^{2+}] = 7.8 \times 10^{-3} \text{ mol L}^{-1}$.
- **3.2:** $[\text{Ca}^{2+}] = 1.0 \times 10^{-6} \text{ mol L}^{-1}$.
- **3.3:** Approximately 0.10 mol dissolves. The resulting free-ion concentrations are $[\text{Ca}^{2+}] \approx 6.1 \times 10^{-4} \text{ mol L}^{-1}$ and $[\text{SO}_4^{2-}] \approx 0.10 \text{ mol L}^{-1}$. Retaining the small additional dissolution gives 0.100606 ... mol and the same numerical sulphate concentration in mol L^{-1} .
- **3.4:** The calcium(II)–EDTA ion, $[\text{Ca}(\text{EDTA})]^{2-}$, has EDTA bound through **two cis nitrogen donors and four carboxylate oxygen donors**, forming an approximately octahedral, hexadentate complex. Its stereochemical SMILES and drawing instructions appear below.
- **3.5: Yes.** The proposed structure is chiral and has a non-superimposable mirror-image enantiomer, specified below. A racemic mixture has no net optical rotation.
- **3.6:** Its exceptional stability arises from the **chelate effect**, six donor–metal interactions, five five-membered chelate rings, and favorable attraction between calcium and the negatively charged oxygen donors.

Solution

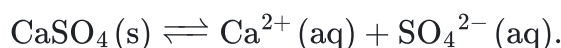
Write Y^{4-} for the ethylenediaminetetraacetate ion and $[\text{CaY}]^{2-}$ for its calcium complex.

The relevant species have the following names and SMILES. The calcium sulphate entry represents an ionic formula unit, not a discrete molecule or its crystal lattice.

Species	Name	SMILES
$C_{10}H_{16}N_2O_8$	Ethylenediaminetetraacetic acid	<chem>O=C(O)CN(CC(=O)O)CCN(CC(=O)O)CC(=O)O</chem>
Y^{4-}	Ethylenediaminetetraacetate ion	<chem>O=C([O-])CN(CC(=O)[O-])CCN(CC(=O)[O-])CC(=O)[O-]</chem>
Ca^{2+}	Calcium(II) ion	<chem>[Ca+2]</chem>
SO_4^{2-}	Sulphate ion	<chem>[O-]S(=O)(=O)[O-]</chem>
$CaSO_4$	Calcium sulphate	<chem>[Ca+2].[O-]S(=O)(=O)[O-]</chem>

3.1 — Saturated calcium sulphate solution

The dissolution equilibrium is



Let the molar solubility in water be s_0 . Each mole dissolved produces one mole of each ion, so

$$[Ca^{2+}] = [SO_4^{2-}] = s_0.$$

Thus

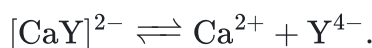
$$s_0^2 = K_s, \quad s_0 = \sqrt{6.1 \times 10^{-5}} = 7.810 \dots \times 10^{-3} \text{ mol L}^{-1}.$$

Therefore,

$$\boxed{[Ca^{2+}] = 7.8 \times 10^{-3} \text{ mol L}^{-1}}.$$

3.2 — Dissociation of the calcium–EDTA complex

The equilibrium is



Let $C = 0.1 \text{ mol L}^{-1}$ be the analytical complex concentration and x the concentration dissociated. Ignoring ligand protonation,

$$[Ca^{2+}] = [Y^{4-}] = x, \quad [[CaY]^{2-}] = C - x.$$

The given formation constant gives

$$K = \frac{C - x}{x^2}, \quad Kx^2 + x - C = 0.$$

Because the complex is very stable, $x \ll C$, giving

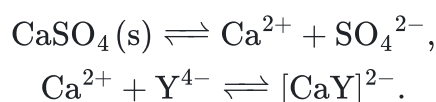
$$x \simeq \sqrt{\frac{C}{K}} = \sqrt{\frac{0.1}{1.0 \times 10^{11}}} = 1.0 \times 10^{-6} \text{ mol L}^{-1}.$$

Here $x/C = 10^{-5}$, so neglecting x relative to C is justified.

$$\boxed{[Ca^{2+}] = 1.0 \times 10^{-6} \text{ mol L}^{-1}}.$$

3.3 — Dissolution in strongly alkaline EDTA solution

Dissolution and complex formation occur together:



Adding these gives



whose equilibrium constant is

$$K_{\text{net}} = K_s K = (6.1 \times 10^{-5})(1.0 \times 10^{11}) = 6.1 \times 10^6.$$

Complex formation therefore greatly increases dissolution.

Assume excess solid is available and the solution volume remains 1 L. Define

$$c = [\text{Ca}^{2+}], \quad b = [[\text{CaY}]^{2-}], \quad \ell = [\text{Y}^{4-}], \quad s = [\text{SO}_4^{2-}],$$

and let $C_L = 0.1 \text{ mol L}^{-1}$ be the total ligand concentration.

The ligand and calcium balances are

$$b + \ell = C_L, \quad s = b + c.$$

The equilibrium equations are

$$cs = K_s, \quad b = Kc\ell.$$

Combining the ligand balance with complex formation gives

$$b = \frac{C_L Kc}{1 + Kc}.$$

Consequently, the exact equation for free calcium is

$$c \left(c + \frac{C_L Kc}{1 + Kc} \right) = K_s.$$

Almost all EDTA is complexed, so initially take $b \simeq C_L$. Then

$$c(c + C_L) \simeq K_s,$$

and therefore

$$c \simeq \frac{\sqrt{C_L^2 + 4K_s} - C_L}{2} = 6.0632 \times 10^{-4} \text{ mol L}^{-1}.$$

This approximation is consistent because

$$Kc \simeq 6.1 \times 10^7 \gg 1.$$

Indeed, the remaining free ligand concentration is only

$$\ell = \frac{C_L}{1 + Kc} \simeq 1.65 \times 10^{-9} \text{ mol L}^{-1}.$$

Using the full balances gives the following numerical values, with extra digits retained only to show the small correction:

$$\begin{aligned} c &= 0.000606323725 \dots \text{ mol L}^{-1}, \\ b &= 0.099999998351 \dots \text{ mol L}^{-1}, \\ s &= b + c = 0.100606322076 \dots \text{ mol L}^{-1}. \end{aligned}$$

Thus

$$n(\text{CaSO}_4) = sV = 0.100606322076 \dots \text{ mol} \approx 0.10 \text{ mol}.$$

The requested free-ion concentrations are

$$[\text{Ca}^{2+}] \approx 6.1 \times 10^{-4} \text{ mol L}^{-1},$$

$$[\text{SO}_4^{2-}] \approx 0.10 \text{ mol L}^{-1}.$$

The total dissolved calcium concentration is s , whereas the free calcium concentration is only c .

3.4 — Structure of the calcium–EDTA ion

EDTA supplies six donor atoms:

- The two tertiary amine nitrogen atoms, each donating a lone pair.
- One oxygen atom from each of the four carboxylate groups.

It therefore acts as a **hexadentate ligand**. Under the stipulated octahedral model, these six donors occupy the six vertices around calcium. The nitrogen donors are *cis*, allowing their ethylene bridge to form a five-membered chelate ring.

A precise drawing can be specified as follows. Put calcium at the origin, with the xy -plane as the page and $+z$ pointing toward the viewer. Label the nitrogen donors N_A, N_B ; label the two oxygen donors belonging to arms attached to each nitrogen O_{A1}, O_{A2} and O_{B1}, O_{B2} .

Donor	Position in enantiomer A
N_A	$+x$: right
N_B	$+y$: above
O_{A1}	$-y$: below
O_{A2}	$+z$: toward the viewer
O_{B1}	$-x$: left
O_{B2}	$-z$: behind the page

Draw bonds from calcium to all six donors, using a solid wedge for the forward oxygen and a hashed wedge for the rear oxygen. Connect the two nitrogen atoms through the $-\text{CH}_2-\text{CH}_2-$ bridge. Connect each nitrogen to its two designated oxygen donors through separate $\text{N}-\text{CH}_2-\text{C}(=\text{O})-\text{O}^-$ arms. The carbonyl oxygen of each arm is not coordinated in this model.

Calcium(II)–ethylenediaminetetraacetate ion, enantiomer A, has the coordination SMILES:

```
[Ca@OH1+2]12345<-N(CC(=O)[O-]->2)(CC(=O)[O-]->3)CCN->4(CC(=O)[O-]->1)CC(=O)[O-]->5
```

Here the arrows denote donor-to-metal coordinate bonds, and @OH1 is an extended SMILES octahedral stereochemical descriptor. This notation specifies connectivity and configuration, but not exact bond lengths, chelate-ring puckering, or departures from a regular octahedron.

3.5 — Optical activity and the other enantiomer

Yes. The arrangement described above is chiral: its mirror image cannot be superimposed on it by rotating the complete complex while preserving the ligand connections. These opposite coordination configurations form a Δ/Λ enantiomeric pair.

To draw the other enantiomer, reflect the entire structure through the plane of the page:

- Keep N_A, N_B, O_{A1} , and O_{B1} at their stated positions.

- Put O_{A2} behind the page, at $-z$.
- Put O_{B2} toward the viewer, at $+z$.
- Preserve all nitrogen–arm connections and reflect the associated ligand backbone.

Thus the forward and rear oxygen donors exchange positions, with their attached arms reflected accordingly.

Calcium(II)–ethylenediaminetetraacetate ion, enantiomer B, has the coordination SMILES:

```
[Ca@OH2+2]12345<-N(CC(=O)[O-]->2)(CC(=O)[O-]->3)CCN->4(CC(=O)[O-]->1)CC(=O)[O-]->5
```

For this same SMILES atom order, changing @OH1 to @OH2 specifies the opposite octahedral configuration. A racemic mixture of the two enantiomers is optically inactive.

3.6 — Origin of the exceptional stability

The principal explanation is the **chelate effect**.

One EDTA ion makes six donor–metal interactions and forms **five five-membered chelate rings**: four involving the carboxylate arms and one involving the ethylene bridge between the nitrogen atoms. These ring sizes permit favorable binding without excessive ring strain.

After the first donor attaches, the remaining donors are held close to calcium. Their attachment is therefore intramolecular and avoids the repeated translational entropy cost associated with bringing separate ligands to the metal. Binding also releases coordinated solvent molecules into the surrounding solution, which can provide a favorable entropy contribution.

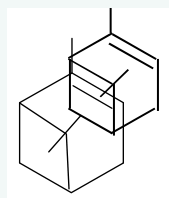
Finally, calcium is a hard Lewis acid and binds favorably to the negatively charged oxygen donors. Together, these interactions and the chelate effect account for the large formation constant.

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

Problem 4: Kinetics of the racemisation of alpha-pinene

At a temperature around 200 °C the racemisation of pinene can be followed in the gaseous phase by measuring the optical rotation.

If, for example, you take the (+)-enantiomer of α -pinene



an equilibrium is gradually established between the two enantiomers (optical isomers). The two opposing reactions are both of the first order.

In 1927 D. F. Smith obtained the following data in his study of racemisation of α -pinene:

T/K	α_1	α_2	t/min
490.9	32.75	18.01	579

T/K	α_1	α_2	t/min
490.9	29.51	15.59	587
503.9	30.64	8.74	371
505.4	12.95	8.05	120
510.1	23.22	6.15	216

α_1 and α_2 are the values for optical rotation in terms of the dimensions of the polarimeter scale; t is the time which has elapsed between the two measurements.

Problems:

4.1 What is the value for the equilibrium constant for the racemisation?

What is the corresponding value of $\Delta_r G^\circ$ (racemisation)?

What is the relationship between the forward and backward rate constants, k_1 and k_{-1} , in a state of dynamic equilibrium?

4.2 State the rate equation for the racemisation of pinene.

Derive a relationship which could be used to calculate the rate constant for the conversion of the (+)-enantiomer into the (-)-enantiomer using the data given in the table.

4.3 Calculate the rate constant for this reaction at the four temperatures given in the table.

4.4 Calculate the average value of the activation energy for this reaction. You should take the average of the values at a minimum of three temperatures or use a graphical method.

HINT:

If the loss of concentration of a substance obeys the rate equation:

$$-\frac{dc}{dt} = k(2c - \text{constant})$$

Then the dependence of concentration on time is given by:

$$\ln \frac{2c_0 - \text{constant}}{2c - \text{constant}} = 2kt$$

where c_0 is the initial concentration at time $t = 0$.

Official English text of the problem.

Answers

- 4.1:** $K = 1$, $\Delta_r G^\circ = 0$, and $k_1 = k_{-1} \equiv k$.
- 4.2:** With c_+ and c_- the enantiomer concentrations and $C = c_+ + c_-$,

$$-\frac{dc_+}{dt} = k(c_+ - c_-) = k(2c_+ - C), \quad \boxed{k = \frac{1}{2t} \ln \frac{\alpha_1}{\alpha_2}}$$

- 4.3:** The one-way conversion constants are:

T/K	k/min^{-1}	k/s^{-1}
490.9	5.30×10^{-4}	8.83×10^{-6}
503.9	1.69×10^{-3}	2.82×10^{-5}
505.4	1.98×10^{-3}	3.30×10^{-5}
510.1	3.08×10^{-3}	5.13×10^{-5}

The value at 490.9 K is the mean of the two determinations.

- **4.4:** An Arrhenius straight-line fit using all four temperatures gives

$$E_a \approx 189 \text{ kJ mol}^{-1}.$$

Solution

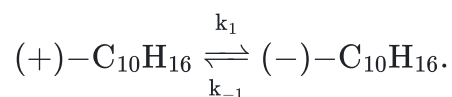
4.1

The two species are:

- **(+)-(1R,5R)- α -pinene**, denoted P_+ : CC1=CC[C@H]2C[C@@H]1C2(C)C.
- **(-)-(1S,5S)- α -pinene**, denoted P_- : CC1=CC[C@@H]2C[C@H]1C2(C)C.

The SMILES specify absolute configuration; the + and – signs specify measured optical rotation, whose sign is not encoded in SMILES.

Their balanced interconversion is



Enantiomers have equal standard molar Gibbs energies in an achiral environment. Consequently,

$$\Delta_r G^\circ = \mu_-^\circ - \mu_+^\circ = 0.$$

Using

$$\Delta_r G^\circ = -RT \ln K$$

gives

$$K = 1.$$

Thus the equilibrium mixture contains equal amounts of the two enantiomers:

$$c_{+,eq} = c_{-,eq}.$$

At dynamic equilibrium the opposing reaction rates are equal:

$$k_1 c_{+,eq} = k_{-1} c_{-,eq}.$$

Therefore,

$$k_1 = k_{-1} \equiv k.$$

4.2

The net rate of disappearance of the (+)-enantiomer is

$$-\frac{dc_+}{dt} = k_1 c_+ - k_{-1} c_-.$$

Since both rate constants equal k ,

$$-\frac{dc_+}{dt} = k(c_+ - c_-).$$

The total concentration is conserved:

$$C = c_+ + c_-, \quad c_- = C - c_+.$$

Hence the required concentration rate equation is

$$\boxed{-\frac{dc_+}{dt} = k(2c_+ - C)}.$$

At a fixed temperature and optical path length, the two enantiomers contribute equal and opposite rotations. Therefore, for a proportionality constant β ,

$$\alpha = \beta(c_+ - c_-) = \beta(2c_+ - C).$$

Differentiating and substituting the rate equation,

$$\frac{d\alpha}{dt} = 2\beta \frac{dc_+}{dt} = -2k\beta(2c_+ - C) = -2k\alpha.$$

Integration between two measurements separated by time t gives

$$\ln \frac{\alpha_2}{\alpha_1} = -2kt,$$

or

$$\boxed{\alpha_2 = \alpha_1 e^{-2kt}}, \quad \boxed{k = \frac{1}{2t} \ln \frac{\alpha_1}{\alpha_2}}.$$

The factor of two is essential: the optical rotation decays with constant $k_1 + k_{-1} = 2k$, whereas the requested one-way conversion constant is k . Neither measurement needs to correspond to an initially pure enantiomer.

4.3

For example, the first experiment gives

$$k = \frac{\ln(32.75/18.01)}{2(579 \text{ min})} = 5.16387 \times 10^{-4} \text{ min}^{-1}.$$

Applying the same expression to every row gives the following intermediate values:

T/K	t/min	$\ln(\alpha_1/\alpha_2)$	k/min^{-1}
490.9	579	0.597976	5.16387×10^{-4}
490.9	587	0.638100	5.43526×10^{-4}
503.9	371	1.254396	1.69056×10^{-3}
505.4	120	0.475424	1.98093×10^{-3}
510.1	216	1.328562	3.07537×10^{-3}

The arithmetic mean of the two measurements at 490.9 K is

$$\begin{aligned}\bar{k} &= \frac{5.16387 \times 10^{-4} + 5.43526 \times 10^{-4}}{2} \text{ min}^{-1} \\ &= 5.29956 \times 10^{-4} \text{ min}^{-1} \\ &\approx \boxed{5.30 \times 10^{-4} \text{ min}^{-1}}.\end{aligned}$$

The other three values, rounded to three significant figures, are

$$\begin{aligned}k(503.9 \text{ K}) &= 1.69 \times 10^{-3} \text{ min}^{-1}, \\ k(505.4 \text{ K}) &= 1.98 \times 10^{-3} \text{ min}^{-1}, \\ k(510.1 \text{ K}) &= 3.08 \times 10^{-3} \text{ min}^{-1}.\end{aligned}$$

Division by 60 converts these values to s^{-1} .

4.4

The Arrhenius equation is

$$k = A \exp\left(-\frac{E_a}{RT}\right).$$

Thus a plot of

$$y = \ln\left(\frac{k}{1 \text{ min}^{-1}}\right) \quad \text{against} \quad x = \frac{1}{T}$$

should be a straight line with slope

$$m = -\frac{E_a}{R}.$$

Using the mean rate constant at 490.9 K, the four plotting points are:

$1/T \text{ (K}^{-1}\text{)}$	$\ln[k/(1 \text{ min}^{-1})]$
0.002037075	-7.542716
0.001984521	-6.382695
0.001978631	-6.224188
0.001960400	-5.784329

The points lie close to a descending straight line. An unweighted least-squares fit, implementing the graphical method numerically, gives

$$y = 38.8473 - (2.27775 \times 10^4 \text{ K})x.$$

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

$$\begin{aligned}E_a &= -Rm \\ &= (8.314 \text{ J mol}^{-1} \text{ K}^{-1})(2.27775 \times 10^4 \text{ K}) \\ &= 1.89372 \times 10^5 \text{ J mol}^{-1}.\end{aligned}$$

Therefore,

$$\boxed{E_a \approx 189 \text{ kJ mol}^{-1}}.$$

The solution was checked against the official solution.

Problem 5: Thermodynamics of a zinc - silver sulphate galvanic cell

The equilibrium voltage of the cell,



was measured at several temperatures and the results of the measurements are given in the following table:

$t / ^\circ\text{C}$	10	20	30
E / V	1.5784	1.5675	1.5566

Problems:

5.1 Give the equation for the reaction occurring in this galvanic cell.

5.2 Determine the value of the cell voltage at the temperature $T = 298 \text{ K}$.

5.3 Determine $\Delta_r G_{298}$ of the cell reaction.

5.4 Determine $\Delta_r H_{298}$ of the cell reaction.

Official English text of the problem.

Answers

- 5.1** $\text{Zn}(\text{s}) + 2 \text{Ag}^+(\text{aq}) \longrightarrow \text{Zn}^{2+}(\text{aq}) + 2 \text{Ag}(\text{s})$, equivalently $\text{Zn}(\text{s}) + \text{Ag}_2\text{SO}_4(\text{aq}) \longrightarrow \text{ZnSO}_4(\text{aq}) + 2 \text{Ag}(\text{s})$.
- 5.2** $E_{298} = 1.5622 \text{ V}$, or approximately 1.562 V .
- 5.3** $\Delta_r G_{298} = -301.5 \text{ kJ mol}^{-1}$.
- 5.4** $\Delta_r H_{298} \approx -364.1 \text{ kJ mol}^{-1}$.

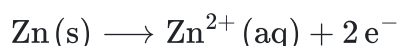
The molar quantities refer to the reaction as written, consuming one mole of zinc.

Solution

5.1

For the cell written, the positive voltage corresponds to oxidation at the left-hand zinc electrode and reduction at the right-hand silver electrode.

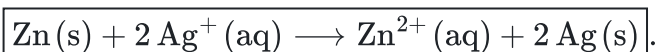
Anode:



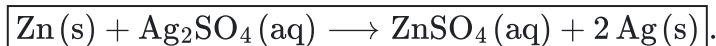
Cathode:



Adding the half-reactions gives



Thus, the number of electrons transferred per reaction as written is $n = 2$. Sulfate is a spectator ion, so the equivalent salt equation is



The ionic species are zinc(II) ion [Zn+2], silver(I) ion [Ag+], and sulfate ion [O-]S(=O)(=O)[O-]. The salts are zinc sulfate [Zn+2].[O-]S(=O)(=O)[O-] and silver(I) sulfate [Ag+].[Ag+].[O-]S(=O)(=O)[O-]. These disconnected ionic SMILES specify composition; they do not represent hydration or ion association in solution.

5.2

The voltage decreases by 0.0109 V in each 10°C interval. We therefore interpolate linearly over the measured range:

$$\left(\frac{\partial E}{\partial T}\right)_p = \frac{1.5566 - 1.5784}{303.15 - 283.15} = -1.090 \times 10^{-3} \text{ V K}^{-1}.$$

At $T = 298 \text{ K}$, $t = 24.85^\circ\text{C}$. Hence

$$\begin{aligned} E_{298} &= 1.5675 + (-1.090 \times 10^{-3})(298 - 293.15) \\ &= 1.5622135 \text{ V.} \end{aligned}$$

Therefore,

$$\boxed{E_{298} = 1.5622 \text{ V}}.$$

Using the usual approximation $298 \text{ K} \approx 25^\circ\text{C}$ instead gives 1.56205 V; both results are approximately 1.562 V.

5.3

For a reversible galvanic cell,

$$\Delta_r G = -nFE.$$

Using the standard Faraday constant $F = 96485 \text{ C mol}^{-1}$,

$$\begin{aligned} \Delta_r G_{298} &= -2(96485)(1.5622135) \text{ J mol}^{-1} \\ &= -301460 \text{ J mol}^{-1}. \end{aligned}$$

Thus,

$$\boxed{\Delta_r G_{298} = -301.5 \text{ kJ mol}^{-1}}.$$

This is the reaction Gibbs energy at the specified solution concentrations.

5.4

At constant pressure and fixed composition,

$$\left(\frac{\partial \Delta_r G}{\partial T}\right)_p = -\Delta_r S.$$

Differentiating $\Delta_r G = -nFE$ therefore gives

$$\Delta_r S = nF \left(\frac{\partial E}{\partial T}\right)_p.$$

Consequently,

$$\Delta_r S_{298} = 2(96485)(-1.090 \times 10^{-3}) = -210.3373 \text{ J mol}^{-1} \text{ K}^{-1}.$$

Using $\Delta_r H = \Delta_r G + T\Delta_r S$,

$$\begin{aligned}\Delta_{\text{r}}H_{298} &= -301.4603 + 298(-0.2103373) \text{ kJ mol}^{-1} \\ &= -364.1409 \text{ kJ mol}^{-1}.\end{aligned}$$

Hence,

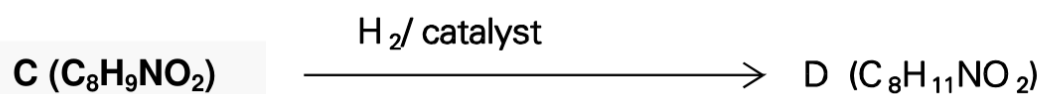
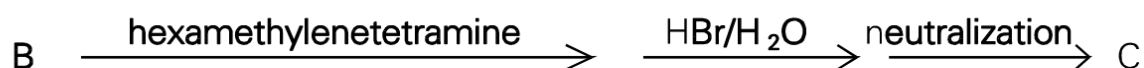
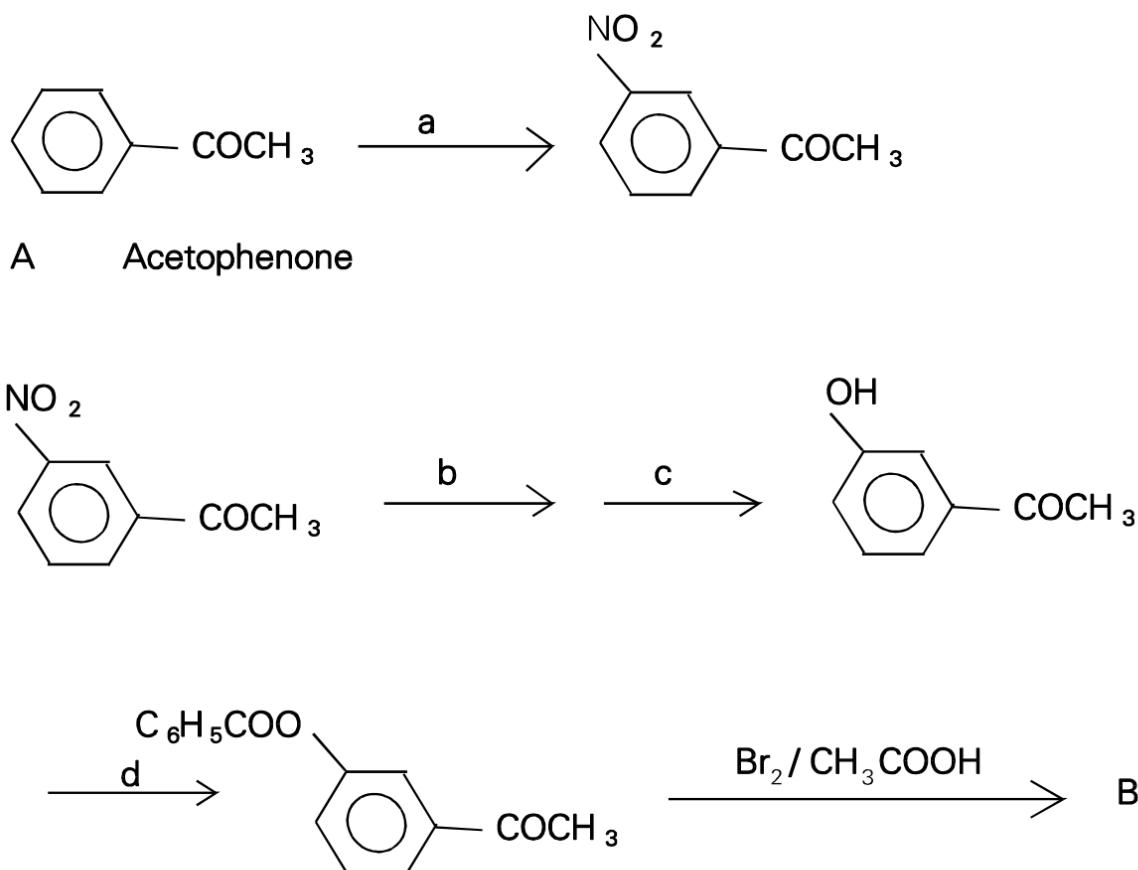
$$\boxed{\Delta_{\text{r}}H_{298} \approx -364.1 \text{ kJ mol}^{-1}}.$$

The negative sign shows that the cell reaction is exothermic.

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 6: Synthesis of a sympathomimetic 2-phenylethylamine derivative from acetophenone

The following scheme describes the synthesis of a compound **D** (with sympathomimetic effects) whose skeleton consists of 2-phenylethylamine.



Problems:

6.1 What reagents were used in steps **a**, **b**, **c**, and **d**?

6.2 Give the structural formulae of compounds **B**, **C** and **D**.

6.3 Is it possible to prepare 3-hydroxyacetophenone from the reaction between phenol, acetylchloride and AlCl₃? Give reasons for your answer.

6.4 Give the formulae of the compounds that are formed by the reaction of compound **C** with a) 10% HCl and b) 10% NaOH.

6.5 By the asterisk denote the chirality centre in the formula of compound **D**.

6.6 Give the spatial formula of enantiomer (R) of compound **D**.

Answers

- **6.1 a:** Concentrated nitric acid $O=[N^+]([O^-])O$ and concentrated sulfuric acid $OS(=O)(=O)O$. **b:** Iron $[Fe]$ and hydrochloric acid Cl . **c:** Sodium nitrite $[Na^+].[O^-]N=O$ and hydrochloric acid at $0-5\text{ }^{\circ}C$, followed by warming with water O . **d:** Benzoyl chloride $O=C(Cl)c1ccccc1$ and sodium hydroxide $[Na^+].[OH^-]$.
- **6.2 B:** 3-(2-Bromoacetyl)phenyl benzoate, $O=C(CBr)c1cccc(OC(=O)c2ccccc2)c1$, molecular formula $C_{15}H_{11}BrO_3$. **C:** 2-Amino-1-(3-hydroxyphenyl)ethan-1-one, $NCC(=O)c1cccc(O)c1$, molecular formula $C_8H_9NO_2$. **D:** 2-Amino-1-(3-hydroxyphenyl)ethan-1-ol (norphenylephrine), $NCC(O)c1cccc(O)c1$, molecular formula $C_8H_{11}NO_2$.
- **6.3** No. The phenolic hydroxyl group directs ring acetylation to the **ortho and para** positions; this route does not prepare the required meta isomer.
- **6.4 a:** C hydrochloride, $[NH_3^+]CC(=O)c1cccc(O)c1.[Cl^-]$, formula $C_8H_{10}ClNO_2$. **b:** Sodium 3-(2-aminoacetyl)phenolate, $NCC(=O)c1cccc([O^-])c1.[Na^+]$, formula $C_8H_8NNaO_2$.
- **6.5** The sole chirality centre is the benzylic alcohol carbon:

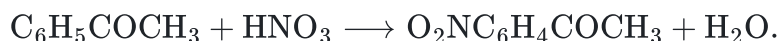
$$HO-C_6H_4-C^*H(OH)-CH_2NH_2$$
 with meta substitution on the ring.
- **6.6** (1R)-2-Amino-1-(3-hydroxyphenyl)ethan-1-ol: $NC[C@H](O)c1cccc(O)c1$. A Fischer projection has **3-hydroxyphenyl at the top, aminomethyl at the bottom, hydroxyl on the left, and hydrogen on the right**.

Solution

In the condensed equations below, the two substituents on each C_6H_4 ring are **meta**, except where ortho or para is explicitly specified.

6.1 — Reagents and transformations

Step a: nitration. Acetophenone, $CC(=O)c1ccccc1$, is nitrated with concentrated nitric and sulfuric acids:



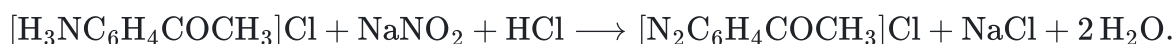
The acetyl group withdraws electron density and is a deactivating, meta-directing substituent. The principal product is therefore **3-nitroacetophenone**, $CC(=O)c1cccc([N^+](=O)[O^-])c1$.

Step b: reduction of the nitro group. Iron and hydrochloric acid reduce the nitro group to an amino group while preserving the ketone. In the acidic medium, the product is **3-aminoacetophenone hydrochloride**, $CC(=O)c1cccc([NH_3^+])c1.[Cl^-]$:



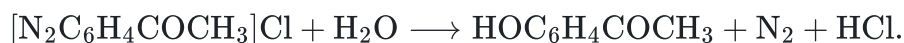
The inorganic reduction product is **iron(II) chloride**, $[\text{Fe}^{+2}] \cdot [\text{Cl}^-] \cdot [\text{Cl}^-]$.

Step c: diazotization followed by hydrolysis. Sodium nitrite and hydrochloric acid at 0–5 °C convert the aromatic amino group into a diazonium group:



The intermediate is **3-acetylbenzenediazonium chloride**, $\text{CC}(=\text{O})\text{c1cccc}([\text{N}^+\#\text{N})\text{c1} \cdot [\text{Cl}^-]$.

Warming its aqueous solution replaces the diazonium group with hydroxyl:



This gives **3-hydroxyacetophenone**, $\text{CC}(=\text{O})\text{c1cccc}(\text{O})\text{c1}$. The other products include **sodium chloride**, $[\text{Na}^+] \cdot [\text{Cl}^-]$, and **nitrogen**, $\text{N}\#\text{N}$.

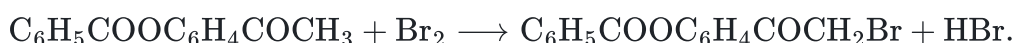
Step d: protection by benzylation. Benzoyl chloride and aqueous sodium hydroxide convert the phenolic hydroxyl group into a benzoate ester:



The product is **3-acetylphenyl benzoate**, $\text{CC}(=\text{O})\text{c1cccc}(\text{OC}(=\text{O})\text{c2ccccc2})\text{c1}$. Benzylation protects the phenolic group and reduces its strong activation of the aromatic ring toward bromination.

6.2 — Identification of B, C and D

Formation of B. Bromine, BrBr , in acetic acid, $\text{CC}(=\text{O})\text{O}$, brominates the ketone at its alpha carbon through the enol:

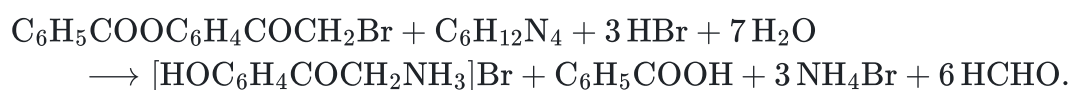


Thus **B** is the alpha-bromoketone **3-(2-bromoacetyl)phenyl benzoate**. The coproduct is hydrogen bromide, present as **hydrobromic acid**, HBr , in aqueous solution.

Formation of C. Hexamethylenetetramine, $\text{C1N2CN3CN1CN}(\text{C2})\text{C3}$, effects a **Delépine synthesis**: a cage nitrogen displaces bromide from the bromomethyl group, and subsequent acidic hydrolysis releases a primary amine.

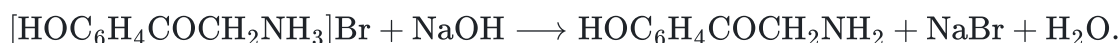
The aqueous acid treatment also hydrolyses the phenolic benzoate protecting group. This deprotection is required by the stated formula of C: the seven carbons of the benzoyl group are absent.

A balanced overall equation for the reaction with hexamethylenetetramine and the acidic hydrolysis is



The organic salt is **C hydrobromide**, $[\text{NH}_3^+]\text{CC}(=\text{O})\text{c1cccc}(\text{O})\text{c1} \cdot [\text{Br}^-]$. The other hydrolysis products are **benzoic acid**, $\text{O}=\text{C}(\text{O})\text{c1ccccc1}$, **ammonium bromide**, $[\text{NH}_4^+] \cdot [\text{Br}^-]$, and **formaldehyde**, $\text{C}=\text{O}$.

Neutralization releases C; using sodium hydroxide, the relevant equation is



Here **sodium bromide** is $[\text{Na}^+] \cdot [\text{Br}^-]$. Consequently,



with molecular formula $\text{C}_8\text{H}_9\text{NO}_2$, as given.

Formation of D. Catalytic hydrogenation with **hydrogen**, $[\text{H}][\text{H}]$, reduces the ketone to a secondary alcohol:



Therefore,



The addition of two hydrogen atoms changes $\text{C}_8\text{H}_9\text{NO}_2$ into $\text{C}_8\text{H}_{11}\text{NO}_2$, matching the supplied formula. With an achiral catalyst, reduction of the planar carbonyl group gives a racemic mixture.

6.3 — Why direct acetylation of phenol does not give the required isomer

The proposed reagents are **phenol**, Oc1ccccc1, **acetyl chloride**, CC(=O)Cl, and **aluminium chloride**, Cl[Al](Cl)Cl.

The phenolic hydroxyl group directs electrophilic aromatic substitution to the ortho and para positions. Consequently, this reaction does not establish the meta relationship required for 3-hydroxyacetophenone.

O-Acetylation may occur first, giving **phenyl acetate**, CC(=O)Oc1ccccc1:



Aluminium chloride can promote a Fries rearrangement of this ester:

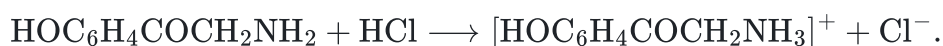


The resulting ring-acetylated products are **2-hydroxyacetophenone**, CC(=O)c1ccccc1O, and/or **4-hydroxyacetophenone**, CC(=O)c1ccc(O)cc1.

The supplied synthesis instead establishes the meta relationship by nitrating acetophenone, then converts the nitro substituent into hydroxyl.

6.4 — Reactions of C with acid and base

a) With 10% hydrochloric acid: the amino group is protonated, giving **C hydrochloride**:



Its structure is [NH3+]CC(=O)c1cccc(O)c1.[Cl-]; the phenolic group remains neutral.

b) With 10% sodium hydroxide: the phenolic hydroxyl group is deprotonated, giving **sodium 3-(2-aminoacetyl)phenolate**:



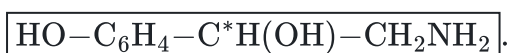
Its structure is NCC(=O)c1cccc([O-])c1.[Na+]; the amino group remains neutral.

6.5 — Chirality centre

The carbon formed by reduction of the carbonyl group bears four different substituents:

- hydroxyl;
- hydrogen;
- aminomethyl;
- 3-hydroxyphenyl.

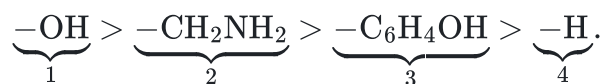
It is therefore the only chirality centre:



Place the asterisk on the **side-chain carbon directly bonded to the benzene ring and to the alcoholic hydroxyl group**.

6.6 — Spatial formula of the *R* enantiomer

The Cahn–Ingold–Prelog priorities at the stereocentre are



The two carbon-attached groups are distinguished at the next comparison: the aminomethyl carbon has the list (N, H, H), whereas the aromatic carbon has (C, C, C), including the aromatic multiple-bond duplication. Nitrogen outranks carbon, so aminomethyl has priority 2.

For a **Fischer projection**, place:

- the **3-hydroxyphenyl group at the top**;
- the **aminomethyl group at the bottom**;
- **hydroxyl on the left**;
- **hydrogen on the right**.

The horizontal bonds point toward the observer, and the vertical bonds point away. The sequence $1 \rightarrow 2 \rightarrow 3$ is counterclockwise on the page; because hydrogen points toward the observer, reversing that sense gives *R*.

The corresponding stereochemical SMILES is **NC[C@H](O)c1cccc(O)c1**, representing **(1*R*)-2-amino-1-(3-hydroxyphenyl)ethan-1-ol**.

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

Problem 7: Aldol reaction of propanal: intermediate and rate equation

Propanal, **A**, reacts in an aqueous-ethanolic solution of sodium hydroxide to yield compound **B** that is readily dehydrated to give compound **C** ($\text{C}_6\text{H}_{10}\text{O}$).

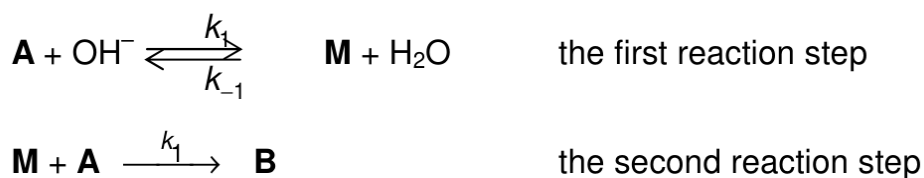
Problems:

7.1 Give the structural formulae of substances **B** and **C**.

7.2 Give the formula of intermediate **M** that is formed from propanal **A** by the action of hydroxide ions.

7.3 Give the formulae of the two most important mesomeric structures of intermediate **M** and denote the nonbonding electron pairs and the charge distribution.

7.4 The reaction of propanal **A** with sodium hydroxide, producing substance **B**, can be described by the scheme:



The rate of the formation of substance **B** is given by the equation:

$$v = k_2[\mathbf{M}][\mathbf{A}] \quad (1)$$

The above values of k are the rate constants for the individual reaction steps.

Assume that the concentration of intermediate **M** is small and constant during the reaction and express this fact by an equation involving terms with constants k_1 , k_{-1} and k_2 .

$$\frac{d[\mathbf{M}]}{dt} = 0 \quad (2)$$

Derive an expression for the concentration of **M** from equation 2 and then substitute for $[\mathbf{M}]$ in equation 1. This gives equation 3 which is the complete rate equation for the formation of substance **B**.

If it is assumed that the second reaction step is rate determining, then the rearrangement of equation 3 gives equation 4, the rate equation.

Give equations 2, 3, and 4.

7.5 Determine the overall order of the reaction described by equation 4.

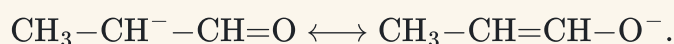
Official English text of the problem.

Answers

- **7.1 B** is **3-hydroxy-2-methylpentanal**, $\text{CH}_3\text{CH}_2\text{CH}(\text{OH})\text{CH}(\text{CH}_3)\text{CHO}$, SMILES CCC(O)C(C)C=O. **C** is **2-methylpent-2-enal**, $\text{CH}_3\text{CH}_2\text{CH}=\text{C}(\text{CH}_3)\text{CHO}$, SMILES CCC=C(C)C=O. The problem does not specify their stereochemistry.

- **7.2 M** is the **propanal enolate ion**, $\text{C}_3\text{H}_5\text{O}^-$, represented by $\text{CH}_3-\text{CH}^--\text{CH}=\text{O}$, SMILES C[CH-]C=O.

- **7.3** Its two principal resonance contributors are



Their SMILES are C[CH-]C=O and CC=C[O-], respectively. The carbon-centred contributor has one lone pair and charge -1 on the α carbon, and two lone pairs on oxygen. The oxygen-centred contributor has three lone pairs and charge -1 on oxygen.

- **7.4** Writing solvent water explicitly:

$$\frac{d[\mathbf{M}]}{dt} = k_1[\mathbf{A}][\text{OH}^-] - k_{-1}[\mathbf{M}][\text{H}_2\text{O}] - k_2[\mathbf{M}][\mathbf{A}] = 0. \quad (2)$$

Hence

$$[\mathbf{M}] = \frac{k_1[\mathbf{A}][\text{OH}^-]}{k_{-1}[\text{H}_2\text{O}] + k_2[\mathbf{A}]},$$

and

$$v = \frac{k_1 k_2 [\mathbf{A}]^2 [\text{OH}^-]}{k_{-1} [\text{H}_2\text{O}] + k_2 [\mathbf{A}]} \quad (3)$$

When $k_2[\mathbf{A}] \ll k_{-1}[\text{H}_2\text{O}]$,

$$v \simeq \frac{k_1 k_2}{k_{-1} [\text{H}_2\text{O}]} [\mathbf{A}]^2 [\text{OH}^-] = k_{\text{obs}} [\mathbf{A}]^2 [\text{OH}^-]. \quad (4)$$

The constant water concentration may instead be absorbed into the reverse rate constant.

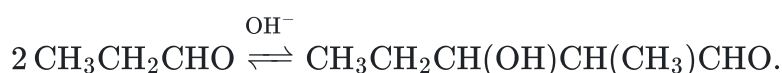
- **7.5** The overall reaction order is **three**: second order in propanal and first order in hydroxide, at fixed solvent composition.

Solution

7.1 — Identification of B and C

Propanal, **A**, is CH3CH2CHO, SMILES CCC=O. It contains α hydrogens, allowing base-catalysed self-aldol addition. Sodium hydroxide, SMILES [Na+].[OH-], supplies the hydroxide ion, SMILES [OH-].

The α carbon of one propanal molecule forms a bond to the carbonyl carbon of a second molecule. The first molecule retains its aldehyde group; the second molecule's carbonyl group becomes an alcohol group. The balanced overall addition is

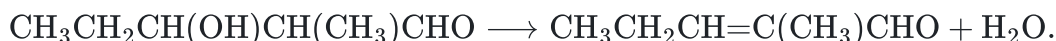


Numbering the product from its aldehyde carbon gives



Thus **B** is **3-hydroxy-2-methylpentanal**, SMILES CCC(O)C(C)C=O, with molecular formula $\text{C}_6\text{H}_{12}\text{O}_2$.

Dehydration removes the hydroxyl group at carbon 3 and a hydrogen from carbon 2, forming a double bond conjugated with the aldehyde group:



Water has SMILES O. The organic product **C** is **2-methylpent-2-enal**, SMILES CCC=C(C)C=O. Its molecular formula is $\text{C}_6\text{H}_{10}\text{O}$, agreeing with the stated formula.

The problem fixes connectivity but does not select configurations at the two stereogenic centres of **B**, or an *E/Z* configuration for **C**. These features are therefore left unspecified in the SMILES.

7.2 — Formation of intermediate M

Hydroxide removes a proton from the carbon adjacent to the aldehyde group:



The resulting **propanal enolate ion, M**, has molecular formula $\text{C}_3\text{H}_5\text{O}^-$, with carbon-centred representation $\text{C}[\text{CH}^-]\text{C}=\text{O}$.

In electron-flow terms, a hydroxide lone pair forms a bond to the α hydrogen, and the electrons of the broken carbon–hydrogen bond remain in the conjugated enolate system.

7.3 — Mesomeric structures, lone pairs and charge

The two principal contributors to the propanal enolate are



The precise lone-pair and formal-charge assignments are:

Contributor	SMILES	Lone pairs on α carbon	Lone pairs on oxygen	Formal negative charge
Carbon-centred propanal enolate	<chem>C[CH-]C=O</chem>	1	2	−1 on the α carbon
Oxygen-centred propanal enolate	<chem>CC=C[O-]</chem>	0	3	−1 on oxygen

All other atoms have zero formal charge in these contributors.

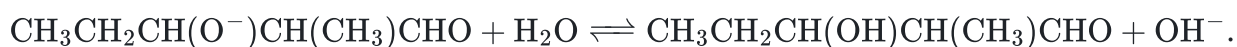
To obtain the oxygen-centred contributor from the carbon-centred one, the α -carbon lone pair forms a π bond to the aldehyde carbon, while the carbonyl π electrons move onto oxygen. The resonance arrow describes one delocalized ion, rather than an equilibrium between separate species. The oxygen-centred contributor is especially important because oxygen stabilizes negative charge.

7.4 — Steady-state and limiting rate equations

The reaction scheme abbreviates the product-forming sequence. Carbon–carbon bond formation initially produces the **aldolate ion**, the alkoxide of 3-hydroxy-2-methylpentanal, SMILES CCC([O-])C(C)C=O:



Rapid protonation by water then produces **B** and regenerates hydroxide:



Thus the stated rate $v = k_2[\text{M}][\text{A}]$ represents the carbon–carbon bond-forming step followed by rapid protonation.

Intermediate **M** is formed by deprotonation of **A** and consumed in two ways: reverse protonation by water and attack on another molecule of **A**. Under the stated steady-state approximation,

$$\frac{d[\text{M}]}{dt} = k_1[\text{A}][\text{OH}^-] - k_{-1}[\text{M}][\text{H}_2\text{O}] - k_2[\text{M}][\text{A}] = 0. \quad (2)$$

Rearranging,

$$[\text{M}](k_{-1}[\text{H}_2\text{O}] + k_2[\text{A}]) = k_1[\text{A}][\text{OH}^-],$$

so

$$[\text{M}] = \frac{k_1[\text{A}][\text{OH}^-]}{k_{-1}[\text{H}_2\text{O}] + k_2[\text{A}]}.$$

Substitution into equation (1) gives the complete steady-state rate equation:

$$v = \frac{k_1 k_2 [\mathbf{A}]^2 [\text{OH}^-]}{k_{-1} [\text{H}_2\text{O}] + k_2 [\mathbf{A}]} \quad (3)$$

When carbon–carbon bond formation is slow relative to the return of **M** to **A**,

$$k_2 [\mathbf{A}] \ll k_{-1} [\text{H}_2\text{O}].$$

The first step is then approximately a pre-equilibrium, and equation (3) reduces to

$$v \simeq \frac{k_1 k_2}{k_{-1} [\text{H}_2\text{O}]} [\mathbf{A}]^2 [\text{OH}^-] = k_{\text{obs}} [\mathbf{A}]^2 [\text{OH}^-] \quad (4)$$

At fixed solvent composition, $[\text{H}_2\text{O}]$ is constant. Equivalently, define the apparent reverse rate constant

$$k_{-1}^* = k_{-1} [\text{H}_2\text{O}].$$

Using this convention, the same equations become

$$(2) \quad 0 = k_1 [\mathbf{A}] [\text{OH}^-] - k_{-1}^* [\mathbf{M}] - k_2 [\mathbf{M}] [\mathbf{A}],$$

$$(3) \quad v = \frac{k_1 k_2 [\mathbf{A}]^2 [\text{OH}^-]}{k_{-1}^* + k_2 [\mathbf{A}]},$$

$$(4) \quad v \simeq \frac{k_1 k_2}{k_{-1}^*} [\mathbf{A}]^2 [\text{OH}^-].$$

For concentrations in mol L^{-1} and time in seconds, k_{obs} has units $\text{L}^2 \text{mol}^{-2} \text{s}^{-1}$, giving v in $\text{mol L}^{-1} \text{s}^{-1}$.

7.5 — Overall order

Equation (4), with solvent composition fixed, contains the concentration factors

$$[\mathbf{A}]^2 [\text{OH}^-]^1.$$

Consequently,

$$n = 2 + 1 = 3.$$

Water is part of the fixed solvent medium, so its concentration is included in the effective rate constant when assigning this order.

The solution was checked against the official solution.

Problem 8: Glycolysis equilibria of glucose-1-phosphate, glucose-6-phosphate and fructose-6-phosphate

The following reaction scheme represents part of anaerobic degradation of saccharides, i.e. the glycolysis, involving equilibrium constants K_1 and K_2 :



Problems:

8.1 Give the structural formulae for all the three reactants (compounds) that are mutually interconverted, i.e. α -D-glucose-1-phosphate, α -D-glucose-6-phosphate and α -D-fructose-6-phosphate.

8.2 In the beginning of the reaction the reaction mixture contained 1 mmol of glucose-6-phosphate. Calculate the amounts of glucose-6-phosphate, glucose-1-phosphate and fructose-6-phosphate in the mixture at equilibrium. (As the reaction take place in a constant volume, the ratio of the amounts of substances equals that of their concentrations.)

Official English text of the problem.

Answers

- **8.1** The structures, written with fully protonated phosphate groups, are:
- **α -D-glucose-1-phosphate**, in its glucopyranose form:
OC[C@H]1O[C@H](OP(=O)(O)O)[C@H](O)[C@@H](O)[C@@H]1O
- **α -D-glucose-6-phosphate**, in its glucopyranose form:
O=P(O)(O)OC[C@H]1O[C@H](O)[C@H](O)[C@@H](O)[C@@H]1O
- **α -D-fructose-6-phosphate**, in its fructofuranose form:
O=P(O)(O)OC[C@H]1O[C@@](O)(CO)[C@@H](O)[C@@H]1O
- **8.2** The equilibrium amounts, rounded to two significant figures, are:
- **Glucose-6-phosphate:** 0.64 mmol.
- **Glucose-1-phosphate:** 0.034 mmol.
- **Fructose-6-phosphate:** 0.32 mmol.

Solution

8.1 — Structures and stereochemistry

The phosphate ester group is represented as $\text{O}-\text{P}(=\text{O})(\text{OH})_2$. This specifies the acid form; the problem does not prescribe a pH or phosphate protonation state.

For the two glucose derivatives, draw a six-membered **pyranose ring**. Place the ring oxygen, O5, at the upper right, followed clockwise by C1, C2, C3, C4 and C5.

For the fructose derivative, draw a five-membered **furanose ring**. Place O5 at the top, followed clockwise by C2, C3, C4 and C5. Here C2 is the anomeric carbon. The ring results from addition of the C5 hydroxyl group to the C2 carbonyl group; C6 carries the phosphate ester.

The complete Haworth substituent orientations are:

Compound	Substituents below the ring	Substituents above the ring
α -D-glucose-1-phosphate	$\text{O}-\text{P}(=\text{O})(\text{OH})_2$ at C1; hydroxyl groups at C2 and C4	Hydroxyl group at C3; CH_2OH at C5
α -D-glucose-6-phosphate	Hydroxyl groups at C1, C2 and C4	Hydroxyl group at C3; $\text{CH}_2-\text{O}-\text{P}(=\text{O})(\text{OH})_2$ at C5

Compound	Substituents below the ring	Substituents above the ring
α -D-fructose-6-phosphate	Hydroxyl groups at C2 and C4	CH ₂ OH at C2; hydroxyl group at C3; CH ₂ –O–P(=O)(OH) ₂ at C5

In each structure, the side chain containing C6 points above the ring. The **α configuration** places the anomeric oxygen substituent on the opposite side: the phosphate ester at C1 for glucose-1-phosphate, the hydroxyl group at C1 for glucose-6-phosphate, and the hydroxyl group at C2 for fructose-6-phosphate.

Hydrogens on the remaining ring stereocentres point opposite the listed substituents. These Haworth descriptions specify configuration; they do not imply that the actual rings are planar.

8.2 — Equilibrium composition

Let the equilibrium amounts of glucose-1-phosphate, glucose-6-phosphate and fructose-6-phosphate be a , b and c , respectively.

The equilibrium constants refer to the forward directions shown in the scheme. Since the volume is constant,

$$K_1 = \frac{b}{a} = 19, \quad K_2 = \frac{c}{b} = 0.50.$$

Thus,

$$a = \frac{b}{19}, \quad c = 0.50b.$$

Each interconversion replaces one molecule with one molecule, so the total amount of the three compounds is conserved:

$$a + b + c = 1 \text{ mmol}.$$

Substituting gives

$$\frac{b}{19} + b + 0.50b = 1 \text{ mmol},$$

and hence

$$b = \frac{1}{1 + \frac{1}{19} + 0.50} \text{ mmol} = \frac{38}{59} \text{ mmol}.$$

The individual amounts are therefore

$$n(\text{glucose-6-phosphate}) = \frac{38}{59} \text{ mmol} = 0.6440678 \dots \text{ mmol} \approx \boxed{0.64 \text{ mmol}},$$

$$n(\text{glucose-1-phosphate}) = \frac{2}{59} \text{ mmol} = 0.0338983 \dots \text{ mmol} \approx \boxed{0.034 \text{ mmol}},$$

$$n(\text{fructose-6-phosphate}) = \frac{19}{59} \text{ mmol} = 0.3220339 \dots \text{ mmol} \approx \boxed{0.32 \text{ mmol}}.$$

Before rounding, these amounts sum to 1 mmol and reproduce both equilibrium constants exactly.

The solution was checked against the official solution.