

IChO 1990

Theory problems and solutions · Paris, France · 7 theory problems with complete solutions

eulersolve.org/icho/1990/

Problem 1: Phosphoric acid

The elemental phosphorus is present in the nature as phosphate in a complex mineral apatite. This mineral contains, in addition to phosphate, silica and the following ions: Ca^{2+} , CO_3^{2-} , SO_4^{2-} , SiO_3^{2-} , and F^- .

Let us assume that this mineral is a mixture of tricalcium phosphate, $\text{Ca}_3(\text{PO}_4)_2$, calcium sulphate, calcium fluoride, calcium carbonate and silica.

For uses as fertilizer the calcium bis(dihydrogenphosphate), $\text{Ca}(\text{H}_2\text{PO}_4)_2$, which is soluble in water, has been prepared. For this purpose, apatite is treated with a mixture of phosphoric and sulphuric acid. At the same time this operation eliminates the majority of impurities.

The elemental analysis of an apatite gave the following results in which, except of fluorine, the elemental composition is expressed as if the elements were in the form of oxides:

	CaO	P ₂ O ₅	SiO ₂	F	SO ₃	CO ₂
% by mass	47.3	28.4	3.4	3.4	3.5	6.1

Operation 1 - A sample of m_0 of this mineral is treated with 50.0 cm^3 of a solution containing $0.500 \text{ mol dm}^{-3}$ phosphoric and $0.100 \text{ mol dm}^{-3}$ sulphuric acids. The mixture is completely dehydrated by heating up to about 70°C avoiding temperature rising above 90°C . This operation is carried out under the hood since toxic gaseous substances are emitted. The dry residue is ground and weighed; m_1 is the mass of the residue obtained.

In these conditions only dihydrogenphosphate, $\text{Ca}(\text{H}_2\text{PO}_4)_2$, is formed while silica and silicate do not react.

Operation 2 - 1.00 g of this residue is treated with 50.0 cm^3 of water at 40°C , then filtered, dried and weighed. The mass of the residue obtained is m_2 . This new residue is mainly containing gypsum, $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$, whose solubility can be considered as constant between 20°C and 50°C and is equal to 2.3 g dm^{-3} .

1.1 Write the balanced equations for the reactions that are involved.

1.2 From what mass of apatite should one start if all the reactions are stoichiometric?

Starting with m_0 of obtained apatite, $m_1 = 5.49 \text{ g}$ of residue are obtained.

1.3 What mass should theoretically be obtained?

1.4 This result is due to the presence of products that are not expected to be found in the residue. Give two of them that under these experimental conditions can plausibly account for the data.

Traditionally, in industry the analysis and the yield are expressed as percentage of oxide. The phosphorous content is expressed as if it were P_2O_5 .

If n_2 is the amount of a soluble product obtained, n_1 the amount of a substance added as acid, n_0 the amount of apatite added, the yield is:

$$r_{\text{exp}} = \frac{n_2}{n_1 + n_0} 100$$

$m_2 = 0.144$ g of residue is obtained on the filter.

1.5 Calculate r_{exp} .

1.6 The experimental yield is over 100%. Calculate a value of r nearer to the real yield.

Relative atomic masses of P: 31; Ca: 40; O: 16; H: 1; F: 19; C: 12; Si: 28; S: 32.

Values of pK :

$$\frac{HSO_4^-}{SO_4^{2-}} = 2 \quad \frac{HF}{F^-} = 3 \quad \frac{H_3PO_4}{H_2PO_4^-} = 2 \quad \frac{H_2PO_4^-}{HPO_4^{2-}} = 7 \quad \frac{HPO_4^{2-}}{PO_4^{3-}} = 12$$

Official English text of the problem.

Answers

- 1.1** Acid treatment produces calcium bis(dihydrogenphosphate), calcium sulphate, hydrogen fluoride and carbon dioxide. Washing dissolves the dihydrogenphosphate and partly dissolves the gypsum. Balanced equations and SMILES are given in Solution 1.1.
- 1.2** $m_0 = 2.79$ g, from the acid-equivalent balance.
- 1.3** $m_{1,\text{theor}} = 5.39$ g, from the gross mass balance, retaining unassigned mineral material as nonvolatile matter.
- 1.4** Two plausible products are **gypsum**, $CaSO_4 \cdot 2H_2O$, $[Ca+2] \cdot O=S(=O) ([O-]) [O-] \cdot O \cdot O$, and **calcium bis(dihydrogenphosphate) monohydrate**, $Ca(H_2PO_4)_2 \cdot H_2O$, $[Ca+2] \cdot O=P(O)(O) [O-] \cdot O=P(O)(O) [O-] \cdot O$.
- 1.5** $r_{\text{exp}} \approx 111.1\%$.
- 1.6** Direct subtraction of the dissolved gypsum mass gives the approximate correction $r \approx 96.2\%$. Explicitly accounting for hydrate water gives about 99% if the excess mass in operation 1 is entirely retained water. The distinction and the limitations of the printed data are explained below.

Solution

1.1 — Reactions

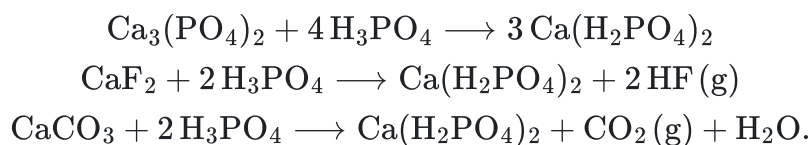
The following representations specify the molecular species and the ionic formula units used below. For crystalline salts, disconnected SMILES do not specify the crystal lattice or coordination geometry.

Substance	SMILES
Phosphoric acid, H_3PO_4	$O=P(O)(O)O$

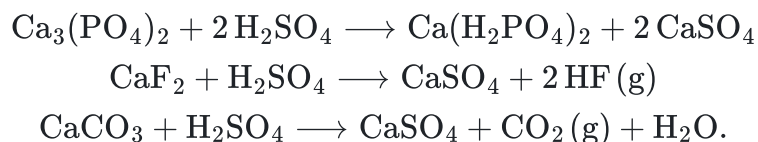
Substance	SMILES
Sulphuric acid, H_2SO_4	<chem>O=S(=O)(O)O</chem>
Tricalcium phosphate, $\text{Ca}_3(\text{PO}_4)_2$	<chem>[Ca+2].[Ca+2].[Ca+2].O=P([O-])([O-])[O-].O=P([O-])([O-])[O-]</chem>
Calcium bis(dihydrogenphosphate), $\text{Ca}(\text{H}_2\text{PO}_4)_2$	<chem>[Ca+2].O=P(O)(O)[O-].O=P(O)(O)[O-]</chem>
Calcium sulphate, CaSO_4	<chem>[Ca+2].O=S(=O)([O-])[O-]</chem>
Calcium fluoride, CaF_2	<chem>[Ca+2].[F-].[F-]</chem>
Calcium carbonate, CaCO_3	<chem>[Ca+2].O=C([O-])[O-]</chem>
Hydrogen fluoride, HF	<chem>[H]F</chem>
Carbon dioxide, CO_2	<chem>O=C=O</chem>
Water, H_2O	<chem>O</chem>
Calcium ion, Ca^{2+}	<chem>[Ca+2]</chem>
Dihydrogenphosphate ion, H_2PO_4^-	<chem>O=P(O)(O)[O-]</chem>
Sulphate ion, SO_4^{2-}	<chem>O=S(=O)([O-])[O-]</chem>

Silica is an extended network solid; a single molecular SMILES would not represent its structure. Here P_2O_5 is an analytical reporting equivalent, not a molecular product of the reactions.

With phosphoric acid, the balanced reactions are



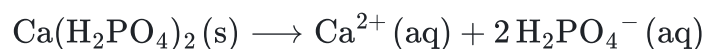
Corresponding reactions with sulphuric acid are



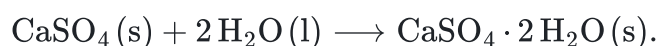
These equations give alternative balanced contributions to the reaction with the mixed acids; each constituent need not react exclusively with one acid.

The supplied pK values support counting one acidic proton per molecule of phosphoric acid and two per molecule of sulphuric acid for these transformations. The phosphate groups become dihydrogenphosphate groups, fluoride becomes hydrogen fluoride, and carbonate releases carbon dioxide and water. Escape of the volatile products assists conversion. Hydrogen fluoride is the hazardous gaseous product in the stated model.

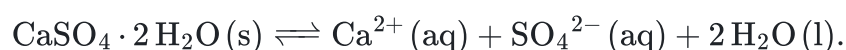
During operation 2,



and calcium sulphate hydrates:



Gypsum dissolves to a limited extent:



Silica and silicate remain unreacted, as stipulated.

1.2 — Required mass of apatite

The amounts of acid supplied are

$$n(\text{H}_3\text{PO}_4) = (0.0500 \text{ dm}^3)(0.500 \text{ mol dm}^{-3}) = 0.0250 \text{ mol},$$

$$n(\text{H}_2\text{SO}_4) = (0.0500 \text{ dm}^3)(0.100 \text{ mol dm}^{-3}) = 0.00500 \text{ mol}.$$

Thus the available amount of acid equivalents is

$$N_{\text{acid}} = 0.0250 + 2(0.00500) = 0.0350 \text{ mol}.$$

The acid demand follows directly from the phosphate, fluoride and carbonate analyses:

Constituent	Amount per gram of mineral	Acid equivalents required per mole
$\text{Ca}_3(\text{PO}_4)_2$	$\frac{0.284}{142} = 0.002000 \text{ mol g}^{-1}$	4
CaF_2	$\frac{0.034}{38} = 0.00089474 \text{ mol g}^{-1}$	2
CaCO_3	$\frac{0.061}{44} = 0.00138636 \text{ mol g}^{-1}$	2

One mole of tricalcium phosphate contains the phosphorus equivalent of one mole of P_2O_5 . Calcium sulphate and silica contribute no acid demand in this model.

Therefore,

$$m_0 \left[4 \frac{0.284}{142} + 2 \frac{0.034}{38} + 2 \frac{0.061}{44} \right] = 0.0350.$$

The expression in brackets is $0.0125622 \text{ mol g}^{-1}$, giving

$$m_0 = 2.78614 \text{ g} \approx 2.79 \text{ g}.$$

The printed analysis is not a completely consistent five-component composition. For the calculations that follow, unassigned mineral mass is treated as nonvolatile material.

1.3 — Theoretical residue mass

The total mass of acid solutes added is

$$m_{\text{acids}} = (0.0250)(98) + (0.00500)(98) = 2.940 \text{ g}.$$

Complete conversion releases hydrogen fluoride, carbon dioxide and the water produced from carbonate:

$$n(\text{HF}) = \frac{0.034m_0}{19} = 0.00498572 \text{ mol},$$

$$n(\text{CO}_2) = n(\text{H}_2\text{O})_{\text{reaction}} = \frac{0.061m_0}{44} = 0.00386260 \text{ mol}.$$

Their masses are

$$m(\text{HF}) = 0.0997143 \text{ g},$$

$$m(\text{CO}_2) = 0.169954 \text{ g},$$

$$m(\text{H}_2\text{O})_{\text{reaction}} = 0.0695268 \text{ g}.$$

The solvent water also evaporates and contributes nothing to the final dry mass. Consequently,

$$\begin{aligned}
 m_{1,\text{theor}} &= m_0 + m_{\text{acids}} - m(\text{HF}) - m(\text{CO}_2) - m(\text{H}_2\text{O})_{\text{reaction}} \\
 &= 2.78614 + 2.940 - 0.0997143 - 0.169954 - 0.0695268 \\
 &= \boxed{5.38694 \text{ g} \approx 5.39 \text{ g}}.
 \end{aligned}$$

The measured residue is heavier by

$$\Delta m = 5.49 - 5.38694 = 0.10306 \text{ g}.$$

1.4 — Two plausible unexpected products

Heating to about 70 °C can remove free water while leaving water of crystallization. Two plausible products are the hydrates identified in the Answers:



and



Their retained water increases the measured mass relative to an anhydrous calculation.

If the whole excess is water, its amount is only

$$n(\text{H}_2\text{O})_{\text{retained}} = \frac{0.10306}{18} = 5.73 \times 10^{-3} \text{ mol}.$$

There is sufficient calcium sulphate, or sufficient calcium bis(dihydrogenphosphate), for partial hydration of either to account for this excess. The weighing alone cannot identify which hydrate, or what mixture of hydrates, is present.

1.5 — Apparent experimental yield

On the initial gravimetric interpretation, all mass disappearing from the 1.00 g sample is assigned to calcium bis(dihydrogenphosphate):

$$m_{\text{soluble, sample}} = 1.00 - 0.144 = 0.856 \text{ g}.$$

For the entire 5.49 g batch,

$$m_{\text{soluble, batch}} = \frac{5.49}{1.00} (0.856) = 4.69944 \text{ g}.$$

The relevant molar masses are

$$M(\text{Ca}(\text{H}_2\text{PO}_4)_2) = 234 \text{ g mol}^{-1}, \quad M(\text{P}_2\text{O}_5) = 142 \text{ g mol}^{-1}.$$

Each mole of calcium bis(dihydrogenphosphate) contains one mole of P_2O_5 equivalent. The apparent recovered amount, expressed as oxide mass, is therefore

$$m_{\text{P}_2\text{O}_5, \text{apparent}} = 4.69944 \frac{142}{234} = 2.85180 \text{ g}.$$

The total phosphorus supplied comprises the mineral phosphorus and the added phosphoric acid:

$$\begin{aligned}
 m_{\text{P}_2\text{O}_5, \text{input}} &= 0.284m_0 + \frac{n(\text{H}_3\text{PO}_4)}{2} (142) \\
 &= (0.284)(2.78614) + \frac{0.0250}{2} (142) \\
 &= 2.56626 \text{ g}.
 \end{aligned}$$

Thus

$$r_{\text{exp}} = \frac{2.85180}{2.56626} 100 = 111.13\% \approx 111.1\%.$$

This is an apparent yield because the dissolved material is not exclusively calcium bis(dihydrogenphosphate).

1.6 — Correction for dissolved gypsum

The mass of gypsum corresponding to its solubility in 50.0 cm^3 is

$$m_{\text{gypsum,dissolved}} = (2.3 \text{ g dm}^{-3})(0.0500 \text{ dm}^3) = 0.115 \text{ g}.$$

There is sufficient sulphate in the sample to reach this amount: the batch contains

$$n_{\text{sulphate,total}} = 0.00500 + \frac{0.035m_0}{80} = 0.00621893 \text{ mol},$$

equivalent to approximately 0.195 g of gypsum per 1.00 g sample.

A **simple direct mass correction** subtracts the dissolved gypsum from the apparent soluble material:

$$m_{\text{phosphate,sample}} \approx 0.856 - 0.115 = 0.741 \text{ g}.$$

It then gives

$$r \approx \frac{(5.49)(0.741)(142/234)}{2.56626} 100 = 96.20\% \approx 96.2\%.$$

This removes the principal source of the yield above 100%, but hydrate water makes it an approximate gravimetric correction.

For explicit accounting, 0.115 g of dissolved gypsum corresponds to only

$$0.115 \frac{136}{172} = 0.0909302 \text{ g}$$

of **anhydrous calcium sulphate**. Subtracting that mass alone gives 99.32%.

A more complete balance can also include the hydrate explanation from 1.4. Assume that:

- the excess 0.10306 g in operation 1 is entirely retained water;
- sulphate remaining on the filter is gypsum;
- other nonphosphate material is insoluble.

For the full batch, the dissolved sulphate amount is

$$n_{\text{sulphate,dissolved}} = \frac{5.49}{1.00} \frac{0.115}{172} = 0.00367064 \text{ mol}.$$

Hence the dissolved anhydrous calcium sulphate mass is

$$m_{\text{sulphate,dissolved}} = (136)(0.00367064) = 0.499207 \text{ g}.$$

The water retained in the final gypsum filter cakes is

$$\begin{aligned} m_{\text{water,filter}} &= 36 (0.00621893 - 0.00367064) \\ &= 0.0917386 \text{ g}. \end{aligned}$$

The mass loss therefore contains dissolved phosphate, dissolved anhydrous sulphate, and the net loss of hydrate water. Solving for the anhydrous phosphate mass gives

$$m_{\text{phosphate,dissolved}} = 4.69944 - 0.499207 - 0.103059 + 0.0917386 \\ = 4.18891 \text{ g.}$$

Thus, under these additional assumptions,

$$r = \frac{4.18891(142/234)}{2.56626} 100 = 99.05\% \approx 99.1\%.$$

The solution was checked against the official solution.

Problem 2: Ionic solutions - aqueous solutions of copper salts

This part is about the acidity of the hydrated Cu^{2+} ion and the precipitation of the hydroxide.

Consider a $1.00 \times 10^{-2} \text{ mol dm}^{-3}$ solution of copper(II) nitrate. The pH of this solution is 4.65.

2.1 Give the equation for the formation of the conjugate base of the hydrated Cu^{2+} ion.

2.2 Calculate the pK_a of the corresponding acid-base pair.

The solubility product of copper(II) hydroxide is $K_{sp} = 1 \times 10^{-20}$.

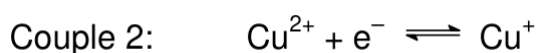
2.3 At what pH value hydroxide $\text{Cu}(\text{OH})_2$ precipitates from the solution under consideration? Justify your calculation showing that the conjugate base of this hydrated Cu^{2+} ion is present in negligible quantity.

Disproportionation of copper(I) ions

The Cu^+ ion is involved in two redox couples:



Standard electrode potential $E_1^0 = +0.52 \text{ V}$



Standard electrode potential $E_2^0 = +0.16 \text{ V}$

2.4 Write down the equation for the disproportionation of copper(I) ions and calculate the corresponding equilibrium constant.

2.5 Calculate the composition of the solution (in mol dm^{-3}) obtained on dissolving $1.00 \times 10^{-2} \text{ mol}$ of copper(I) in 1.0 dm^3 of water.

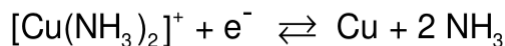
2.6 Apart from Cu^+ ions, name two chemical species which also disproportionate in aqueous solution; write down the equations and describe the experimental conditions under which disproportionation is observed.

Consider the stability of copper(I) oxide, Cu_2O , in contact with a $1.00 \times 10^{-2} \text{ mol dm}^{-3}$ solution of Cu^{2+} ions. The solubility product of copper(I) oxide is $K_{sp} = [\text{Cu}^+][\text{OH}^-] = 1 \times 10^{-15}$

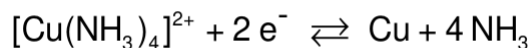
2.7 Calculate the pH value at which Cu_2O becomes stable. Quote a simple experiment allowing the observation of the precipitation of Cu_2O .

Complex formation involving Cu^+ and Cu^{2+} ions

2.8 The dissociation constant of the complex ion $[\text{Cu}(\text{NH}_3)_2]^+$ is $K_D = 1 \times 10^{-11}$. Calculate the standard electrode potential of the couple:



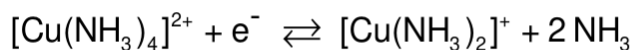
2.9 The standard electrode potential of the couple



$$E_3^0 = -0,02 \text{ V}.$$

Calculate the dissociation constant for the complex ion $[\text{Cu}(\text{NH}_3)_4]^{2+}$.

2.10 Deduce from it the standard electrode potential of the couple:



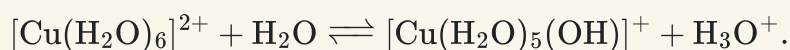
Does the disproportionation of the cation $[\text{Cu}(\text{NH}_3)_2]^+$ take place?

Official English text of the problem.

Answers

The main numerical answers use the customary room-temperature approximations $pK_w = 14.00$ and $2.303RT/F = 0.060 \text{ V}$. Results using 0.05916 V are also tabulated in the Solution. Names and SMILES are collected there.

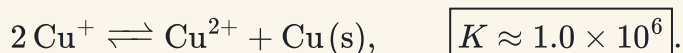
• **2.1**



• **2.2** $pK_a = 7.30$.

• **2.3** $\text{pH} = 5.00$. The conjugate base represents approximately 0.50% of dissolved copper(II).

• **2.4**

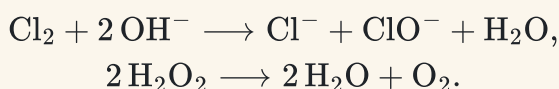


• **2.5** In the disproportionation-only model,

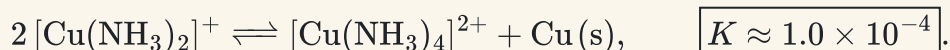
$$[\text{Cu}^+] \approx 7.0 \times 10^{-5} \text{ mol dm}^{-3}, \quad [\text{Cu}^{2+}] \approx 5.0 \times 10^{-3} \text{ mol dm}^{-3}.$$

Approximately $5.0 \times 10^{-3} \text{ mol}$ of copper metal is deposited.

• **2.6** Two examples are chlorine in cold, dilute aqueous alkali and hydrogen peroxide on warming:



- 2.7 $\boxed{\text{pH} = 3.00}$; copper(I) oxide becomes stable against disproportionation above this boundary. Warming freshly precipitated copper(II) hydroxide with ethanal in alkaline water gives brick-red copper(I) oxide.
- 2.8 $\boxed{E^\circ = -0.14 \text{ V}}$.
- 2.9 $\boxed{K_D = 1.0 \times 10^{-12}}$.
- 2.10 $\boxed{E^\circ = +0.10 \text{ V}}$. Disproportionation is strongly suppressed:

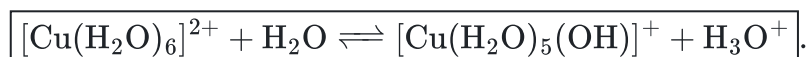


Solution

Activities are approximated by concentrations relative to $c^\circ = 1 \text{ mol dm}^{-3}$; pure solids and water have unit activity. Consequently, concentrations substituted into the equilibrium expressions below are their numerical values in mol dm^{-3} . Hydration is implicit when a simple copper-ion formula is used.

2.1 — Formation of the conjugate base

Writing the hydrated copper(II) ion conventionally as the hexaaqua complex,



A coordinated water molecule loses a proton. Its oxygen remains coordinated as a hydroxido ligand, so the complex charge decreases from +2 to +1. Copper remains in oxidation state +2.

The conjugate base is therefore the **pentaaquahydroxidocopper(II) ion**.

2.2 — Acid dissociation constant

Let $C = 1.00 \times 10^{-2} \text{ mol dm}^{-3}$. The measured pH gives

$$h = [\text{H}_3\text{O}^+] = 10^{-4.65} = 2.2387 \times 10^{-5} \text{ mol dm}^{-3}.$$

Each hydrolysis event produces one conjugate-base ion and one hydronium ion. Water autoionization contributes only

$$[\text{OH}^-] = \frac{10^{-14}}{h} = 4.47 \times 10^{-10} \text{ mol dm}^{-3},$$

so the conjugate-base concentration is effectively h , and the remaining acid concentration is $C - h$. Thus,

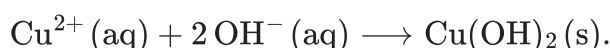
$$K_a \simeq \frac{h^2}{C - h} = \frac{(2.2387 \times 10^{-5})^2}{1.00 \times 10^{-2} - 2.2387 \times 10^{-5}} = 5.02 \times 10^{-8}.$$

Therefore,

$$\boxed{pK_a = -\log_{10} K_a = 7.30}.$$

2.3 — Precipitation of copper(II) hydroxide

The precipitation reaction is



At its onset,

$$[\text{Cu}^{2+}][\text{OH}^-]^2 = K_{sp}.$$

Initially taking the free copper(II) concentration as $1.00 \times 10^{-2} \text{ mol dm}^{-3}$,

$$[\text{OH}^-] = \sqrt{\frac{10^{-20}}{10^{-2}}} = 1.0 \times 10^{-9} \text{ mol dm}^{-3}.$$

Hence,

$$\text{pOH} = 9.00, \quad \boxed{\text{pH} = 5.00}.$$

To check the approximation, the acid–base equilibrium gives

$$\frac{[\text{Cu}(\text{H}_2\text{O})_5(\text{OH})^+]}{[\text{Cu}(\text{H}_2\text{O})_6^{2+}]} = \frac{K_a}{[\text{H}_3\text{O}^+]} = \frac{5.02 \times 10^{-8}}{10^{-5}} = 5.02 \times 10^{-3}.$$

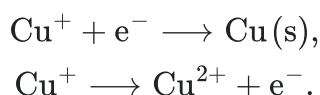
The conjugate-base fraction is therefore

$$\frac{5.02 \times 10^{-3}}{1 + 5.02 \times 10^{-3}} \approx 0.0050 = 0.50\%.$$

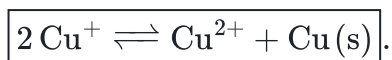
Its concentration is negligible for the precipitation calculation. Including it changes the calculated onset only to approximately pH 5.001.

2.4 — Disproportionation of copper(I)

The two relevant half-reactions, oriented for disproportionation, are



Their sum is



The standard cell potential is

$$E_{\text{disp}}^\circ = E_1^\circ - E_2^\circ = 0.52 - 0.16 = 0.36 \text{ V}.$$

One electron is transferred per reaction as written, so $n = 1$. Using

$$\log_{10} K = \frac{nE_{\text{disp}}^\circ}{0.060},$$

we obtain

$$\log_{10} K = 6.00, \quad \boxed{K = 1.0 \times 10^6}.$$

The equilibrium expression is

$$K = \frac{a_{\text{Cu}^{2+}}}{a_{\text{Cu}^+}^2}.$$

The large value explains why uncomplexed aqueous copper(I) disproportionates extensively.

2.5 — Composition after disproportionation

Use the disproportionation equilibrium introduced in this subsection, with initial copper(I) concentration

$$C_0 = 1.00 \times 10^{-2} \text{ mol dm}^{-3}.$$

If $x \text{ mol dm}^{-3}$ of copper(II) forms, the same amount of copper metal forms, while $2x$ of copper(I) is consumed:

$$[\text{Cu}^{2+}] = x, \quad [\text{Cu}^+] = C_0 - 2x.$$

Therefore,

$$10^6 = \frac{x}{(0.0100 - 2x)^2}.$$

Solving gives

$$\begin{aligned} [\text{Cu}^+] &= 7.046 \times 10^{-5} \text{ mol dm}^{-3}, \\ [\text{Cu}^{2+}] &= 4.965 \times 10^{-3} \text{ mol dm}^{-3}. \end{aligned}$$

Thus, to appropriate precision,

$$\begin{aligned} [\text{Cu}^+] &\approx 7.0 \times 10^{-5} \text{ mol dm}^{-3}, \\ [\text{Cu}^{2+}] &\approx 5.0 \times 10^{-3} \text{ mol dm}^{-3}. \end{aligned}$$

In 1.0 dm^3 , approximately $5.0 \times 10^{-3} \text{ mol}$ of copper metal is deposited.

Copper(II) hydrolysis alone would affect only about 0.3% of the dissolved copper(II), so it is neglected here. This calculation excludes oxide precipitation.

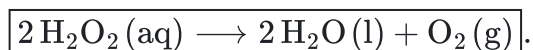
2.6 — Other disproportionation reactions

Chlorine. Pass chlorine into cold, dilute aqueous alkali:



Chlorine changes from oxidation state 0 to both -1 , in chloride, and $+1$, in hypochlorite. The cold, dilute conditions favor hypochlorite as the oxidized product.

Hydrogen peroxide. Warm an aqueous hydrogen peroxide solution:



Oxygen changes from oxidation state -1 in the peroxide to -2 in water and 0 in oxygen gas. Oxygen evolution provides the observable evidence of decomposition.

2.7 — Stability and precipitation of copper(I) oxide

At the boundary between disproportionation and stability, the copper(I) concentration satisfies

$$K = \frac{[\text{Cu}^{2+}]}{[\text{Cu}^+]^2}.$$

With $[\text{Cu}^{2+}] = 1.00 \times 10^{-2} \text{ mol dm}^{-3}$,

$$[\text{Cu}^+] = \sqrt{\frac{10^{-2}}{10^6}} = 1.0 \times 10^{-4} \text{ mol dm}^{-3}.$$

The problem explicitly defines the oxide solubility product as

$$[\text{Cu}^+][\text{OH}^-] = 10^{-15}.$$

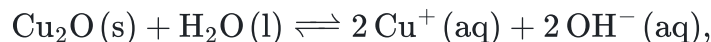
Consequently,

$$[\text{OH}^-] = \frac{10^{-15}}{10^{-4}} = 10^{-11} \text{ mol dm}^{-3},$$

and

$$\boxed{\text{pH} = 14.00 - 11.00 = 3.00}.$$

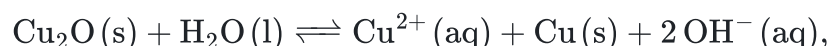
The direction of stability can also be established from the complete reactions. Oxide dissolution is



whose equilibrium constant is the square of the supplied product:

$$K_{\text{diss}} = (10^{-15})^2 = 10^{-30}.$$

Adding copper(I) disproportionation gives

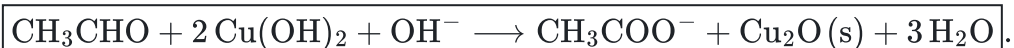


with

$$K_{\text{overall}} = 10^{-30} \times 10^6 = 10^{-24}.$$

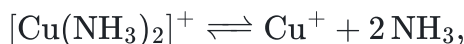
Above pH 3, the increased hydroxide concentration favors the left-hand side. Thus copper(I) oxide is stable against this decomposition.

For an experiment, warm freshly precipitated blue copper(II) hydroxide with **ethanal** in alkaline water. Ethanal supplies the electrons needed to reduce copper(II) to copper(I), producing brick-red copper(I) oxide:



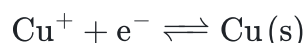
2.8 — Reduction potential of diamminecopper(I)

The complex dissociates according to

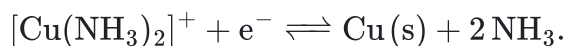


$$K_{D,I} = \frac{a_{\text{Cu}^+} a_{\text{NH}_3}^2}{a_{[\text{Cu}(\text{NH}_3)_2]^+}} = 10^{-11}.$$

Adding this dissociation to



gives the required half-reaction:



By addition of standard Gibbs energies,

$$-FE_8^\circ = -RT \ln K_{D,I} - FE_1^\circ.$$

Therefore,

$$E_8^\circ = E_1^\circ + \frac{RT}{F} \ln K_{D,I} = 0.52 + 0.060 \log_{10}(10^{-11}),$$

so

$$\boxed{E_8^\circ = -0.14 \text{ V}}.$$

Complexation stabilizes copper(I), making its reduction to the metal less favorable.

2.9 — Dissociation constant of tetraamminecopper(II)

First obtain the standard potential for



The two successive one-electron reductions have potentials 0.16 and 0.52 V. Adding their Gibbs energies gives

$$-2FE^{\circ} = -F(0.16) - F(0.52),$$

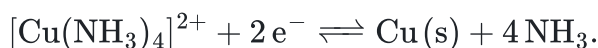
hence

$$E^{\circ} = \frac{0.16 + 0.52}{2} = 0.34 \text{ V}.$$

The complex dissociation is



Adding it to the two-electron reduction gives



Thus,

$$E_3^{\circ} = 0.34 + \frac{0.060}{2} \log_{10} K_{D,\text{II}}.$$

Substitution of $E_3^{\circ} = -0.02 \text{ V}$ yields

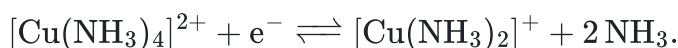
$$\log_{10} K_{D,\text{II}} = \frac{2(-0.02 - 0.34)}{0.060} = -12.$$

Therefore,

$$\boxed{K_{D,\text{II}} = 1.0 \times 10^{-12}}.$$

2.10 — Potential between the complexes and disproportionation

The desired half-reaction is



Adding it to the half-reaction in 2.8 gives the two-electron half-reaction in 2.9. Consequently,

$$-2FE_3^{\circ} = -FE_{10}^{\circ} - FE_8^{\circ},$$

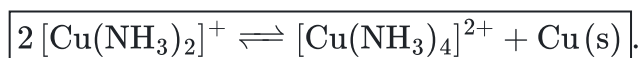
so

$$E_{10}^{\circ} = 2E_3^{\circ} - E_8^{\circ} = 2(-0.02) - (-0.14).$$

Therefore,

$$\boxed{E_{10}^{\circ} = +0.10 \text{ V}}.$$

Disproportionation of the copper(I) complex would be



Its standard cell potential is

$$E_{\text{disp,amm}}^{\circ} = E_8^{\circ} - E_{10}^{\circ} = -0.14 - 0.10 = -0.24 \text{ V},$$

giving

$$\log_{10} K_{\text{disp,amm}} = \frac{-0.24}{0.060} = -4,$$

$$K_{\text{disp,amm}} = 10^{-4}.$$

Thus **no appreciable disproportionation is expected under standard conditions**. This means that disproportionation is strongly suppressed; it does not require the equilibrium product concentration to be exactly zero.

As an independent check,

$$K_{\text{disp,amm}} = K_{\text{disp}} \frac{K_{D,\text{I}}^2}{K_{D,\text{II}}} = 10^6 \frac{(10^{-11})^2}{10^{-12}} = 10^{-4}.$$

Effect of using the more precise Nernst coefficient

Using $2.303RT/F = 0.05916 \text{ V}$ consistently at 25°C gives the following values. The chemical conclusions are unchanged.

Part	Result with 0.05916 V
2.4	$K = 1.2 \times 10^6$
2.5	$[\text{Cu}^+] = 6.4 \times 10^{-5} \text{ mol dm}^{-3}$, $[\text{Cu}^{2+}] \approx 5.0 \times 10^{-3} \text{ mol dm}^{-3}$
2.7	$\text{pH} = 3.04$
2.8	$E_8^\circ \approx -0.13 \text{ V}$
2.9	$K_{D,\text{II}} = 6.8 \times 10^{-13}$
2.10	$E_{10}^\circ \approx +0.09 \text{ V}$, $K_{\text{disp,amm}} = 1.8 \times 10^{-4}$

Chemical names and SMILES

Each species is identified once below. The arrows in the complex SMILES are dative-bond extensions to SMILES.

Formula	Name	SMILES
H_2O	Water	<chem>O</chem>
H_3O^+	Hydronium ion	<chem>[OH3+]</chem>
OH^-	Hydroxide ion	<chem>[OH-]</chem>
NO_3^-	Nitrate ion	<chem>[O-][N+](=O)[O-]</chem>
Cu^+	Copper(I) ion	<chem>[Cu+]</chem>
Cu^{2+}	Copper(II) ion	<chem>[Cu+2]</chem>
$[\text{Cu}(\text{H}_2\text{O})_6]^{2+}$	Hexaaquacopper(II) ion	<chem>[OH2]->[Cu+2](<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])</chem>
$[\text{Cu}(\text{H}_2\text{O})_5(\text{OH})]^+$	Pentaaquahydroxidocopper(II) ion	<chem>[OH-]->[Cu+2](<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])(<-[OH2])</chem>
Cl_2	Chlorine	<chem>ClCl</chem>
Cl^-	Chloride ion	<chem>[Cl-]</chem>
ClO^-	Hypochlorite ion	<chem>[O-]Cl</chem>
H_2O_2	Hydrogen peroxide	<chem>OO</chem>

Formula	Name	SMILES
O ₂	Dioxygen	O=O
CH ₃ CHO	Ethanal	CC=O
CH ₃ COO ⁻	Ethanoate, or acetate, ion	CC(=O)[O-]
NH ₃	Ammonia	N
[Cu(NH ₃) ₂] ⁺	Diamminecopper(I) ion	[NH3]->[Cu+]<-[NH3]
[Cu(NH ₃) ₄] ²⁺	Tetraamminecopper(II) ion	[NH3]->[Cu+2](<-[NH3])(<-[NH3])<-[NH3]
Cu(s)	Copper metal	[Cu]
Cu(OH) ₂ (s)	Copper(II) hydroxide	[Cu+2].[OH-].[OH-]
Cu ₂ O(s)	Copper(I) oxide	[Cu+].[Cu+].[O-2]

The solid representations give an atom or formal ionic formula unit; they do not describe the crystal lattice. Bare-ion SMILES omit hydration.

The explicit aqua complexes use a six-coordinate, distorted octahedral model. Diamminecopper(I) is approximately linear. In aqueous tetraamminecopper(II), the four ammonia donors typically occupy an approximately square equatorial arrangement, with additional axial water coordination. These geometries are not specified by the SMILES. Likewise, OO does not fix hydrogen peroxide's torsion angle, and O=O does not encode dioxygen's triplet spin state.

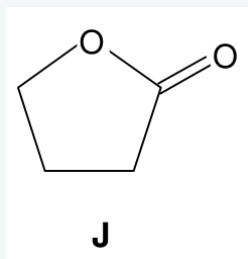
The solution was checked against the official solution. Where this solution differs from the official solution, the official solution contains an error or a misprint.

Problem 3: Organic synthesis - synthesis of haloperidol

Haloperidol is a powerful neuroleptic prescribed in cases of psychomotoric disorder and for the treatment of various psychoses. A synthesis of this compound is proposed.

3.1 Give a scheme for the preparation of methyl 4-chlorobenzoate starting from benzene and all necessary inorganic substances. Diazomethane (H₂CN₂) must be used in your synthesis.

γ-Butyrolactone (**J**) is a cyclic ester represented below.



3.2 How can γ-butyrolactone **J** be converted into 4-hydroxybutanoic acid (**K**)?

3.3 Convert **K** into 4-chlorobutanoyl chloride (**L**).

The reactions described below do not correspond to those used in the industrial synthesis of haloperidol for which the route is quite complex.

Methyl 4-chlorobenzoate is treated with an excess of vinylmagnesium bromide in anhydrous ether. **M** is obtained after hydrolysis. When **M** is treated with an excess of hydrogen bromide in anhydrous conditions in the presence of benzoyl peroxide, **N** is obtained. **N** reacts with ammonia to form 4-(4-chlorophenyl)-4-hydroxypiperidine (**O**).

3.4 Write down the structure of **M**, **N** and **O** and indicate the mechanism of the reaction leading to **M**.

In the presence of a moderate amount of aluminium chloride, **L** reacts with fluorobenzene to yield mainly a ketone **P** ($C_{10}H_{10}OFCl$).

3.5 Sketch the structure of **P** and indicate the mechanism.

3.6 Give a chemical and physical test method for the determination of the carbonyl group. How can you make sure that the carbonyl group does not belong to an aldehyde group?

P reacts with **O** in basic media in a 1 : 1 molar ratio to give **H** that contains only one chlorine atom on the aromatic ring.

3.7 Give the structure of **H** which is haloperidol.

3.8 State the multiplicity of each resonance in the ^1H NMR spectrum of **K**. Assume that all coupling constants between protons and adjacent carbons are identical.

Official English text of the problem.

Answers

- **3.1** Chlorinate benzene; nitrate and isolate the para isomer; reduce the nitro group; diazotize; replace the diazonium group with cyanide; hydrolyze the nitrile; methylate with diazomethane. The product is **methyl 4-chlorobenzoate**, COC(=O)c1ccc(Cl)cc1.
- **3.2** Hydrolyze **J** with aqueous sodium hydroxide, then acidify to obtain **K**, **4-hydroxybutanoic acid**, O=C(O)CCCO.
- **3.3** Treat **K** with excess phosphorus pentachloride to obtain **L**, **4-chlorobutanoyl chloride**, O=C(Cl)CCCCl.
- **3.4**
- **M**: **3-(4-chlorophenyl)penta-1,4-dien-3-ol**, C=CC(O)(c1ccc(Cl)cc1)C=C.
- **N**: **1,5-dibromo-3-(4-chlorophenyl)pentan-3-ol**, OC(c1ccc(Cl)cc1)(CCBr)CCBr.
- **O**: **4-(4-chlorophenyl)piperidin-4-ol**, OC1(c2ccc(Cl)cc2)CCNCC1.
- Formation of **M** involves two successive Grignard additions, with elimination of methoxide after the first addition, followed by protonation.
- **3.5** **P** is **4-chloro-1-(4-fluorophenyl)butan-1-one**, O=C(CCCCl)c1ccc(F)cc1, formed by para Friedel–Crafts acylation.
- **3.6** A positive **2,4-dinitrophenylhydrazine** test establishes an aldehyde or ketone carbonyl; IR shows a strong carbonyl absorption near 1700 cm^{-1} . A negative Tollens test, supported by the absence of an aldehydic proton in the ^1H NMR spectrum, identifies the carbonyl as a ketone.
- **3.7** **H**, **haloperidol**, is **4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)butan-1-one**, O=C(CCCN1CCC(O)(c2ccc(Cl)cc2)CC1)c1ccc(F)cc1.

- **3.8** For **K**, written as $\text{HOOC}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{OH}$, the three methylene resonances are respectively **triplet, quintet, triplet**. The alcoholic and carboxylic acid protons normally give **two broad singlets**, assuming rapid proton exchange.

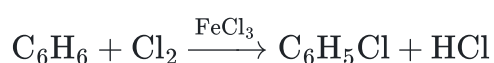
Solution

3.1 — Preparation of methyl 4-chlorobenzoate

A route through an aromatic nitrile supplies the carboxyl carbon from inorganic cyanide. The ester methyl group comes from the required diazomethane.

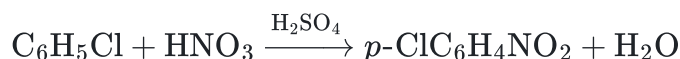
1. Chlorination of benzene.

Benzene, c1ccccc1, reacts with chlorine, ClCl, using iron(III) chloride as catalyst, to give chlorobenzene, Clc1ccccc1:



2. Nitration and isolation of the para isomer.

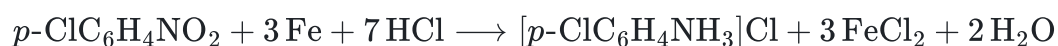
Chlorine deactivates the ring but directs electrophilic substitution to the ortho and para positions. Nitration therefore gives a mixture from which **1-chloro-4-nitrobenzene**, O=[N+]([O-])c1ccc(Cl)cc1, is isolated:



Separation is essential: the equation represents the desired para branch, not an exclusively para-selective reaction.

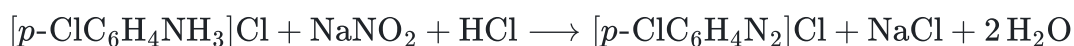
3. Reduction of the nitro group.

Iron and hydrochloric acid reduce the nitro group. In the acidic medium, the product is **4-chloroanilinium chloride**, [NH3+][Cl-]c1ccc(Cl)cc1:



4. Diazotization.

Sodium nitrite and hydrochloric acid at approximately 0–5 °C give **4-chlorobenzenediazonium chloride**, N#[N+][Cl-]c1ccc(Cl)cc1:



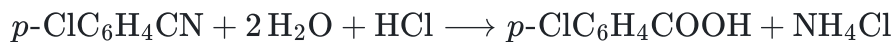
5. Sandmeyer cyanation.

Copper(I) cyanide, [Cu+].[Cl-]#N, replaces the diazonium group with a nitrile group, giving **4-chlorobenzonitrile**, N#Cc1ccc(Cl)cc1:



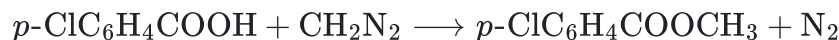
6. Hydrolysis of the nitrile.

Heating with aqueous acid gives **4-chlorobenzoic acid**, O=C(O)c1ccc(Cl)cc1:



7. Esterification with diazomethane.

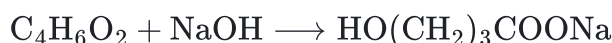
Diazomethane, $\text{C}=[\text{N}^+]=[\text{N}^-]$, converts the acid into **methyl 4-chlorobenzoate**, $\text{COC}(=\text{O})\text{c1ccc}(\text{Cl})\text{cc1}$, with evolution of nitrogen:



All added reagents in this route are inorganic except the explicitly required diazomethane.

3.2 — Opening the lactone ring

J, γ -butyrolactone or oxolan-2-one, $\text{O}=\text{C1CCCCO1}$, is a cyclic ester. Aqueous sodium hydroxide, $[\text{Na}^+][\text{OH}^-]$, opens its ring by ester saponification:



The product is **sodium 4-hydroxybutanoate**, $[\text{Na}^+]\text{O}=\text{C}([\text{O}^-])\text{CCCO}$. Acidification gives **K**, **4-hydroxybutanoic acid**, $\text{O}=\text{C}(\text{O})\text{CCCO}$:



Mechanistically, hydroxide attacks the ester carbonyl carbon. Collapse of the tetrahedral intermediate breaks the bond between the acyl carbon and the ring oxygen; proton transfer produces the hydroxycarboxylate.

Basic hydrolysis drives ring opening through formation of the carboxylate. Acidification should be mild, because the free hydroxy acid can cyclize back to the lactone, particularly on heating.

3.3 — Preparation of the bifunctional chloride

Use excess **phosphorus pentachloride**, $\text{ClP}(\text{Cl})(\text{Cl})(\text{Cl})\text{Cl}$. It replaces both the alcoholic hydroxyl group and the carboxylic hydroxyl group with chlorine:

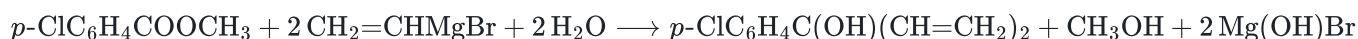


Thus **L** is **4-chlorobutanoyl chloride**, $\text{O}=\text{C}(\text{Cl})\text{CCCCl}$. The phosphorus-containing product is **phosphoryl chloride**, $\text{O}=\text{P}(\text{Cl})(\text{Cl})\text{Cl}$.

The two chlorine atoms have different roles: one belongs to an acyl chloride, while the other is attached to a terminal primary carbon.

3.4 — Structures of M, N and O, and the mechanism leading to M

Formation of M. Vinylmagnesium bromide, $\text{C}=\text{C}[\text{Mg}]\text{Br}$, supplies a vinyl group with nucleophilic carbon character. Two equivalents add per ester molecule:



This equation represents the addition and subsequent aqueous work-up. The other products are **methanol**, CO , and magnesium hydroxybromide, represented ionically as $[\text{Mg}+2][\text{OH}^-][\text{Br}^-]$.

The mechanism is as follows; magnesium counterions are omitted from the intermediate SMILES.

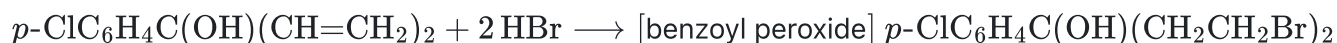
1. The carbon bonded to magnesium attacks the ester carbonyl carbon, while the carbonyl π electrons move onto oxygen. The resulting **tetrahedral alkoxide intermediate** is $\text{C}=\text{CC}([\text{O}^-])(\text{OC})\text{c1ccc}(\text{Cl})\text{cc1}$.

- The oxygen lone pair reforms the carbonyl bond, and the bond to the methoxy oxygen breaks, expelling **methoxide**, C[O-]. The intermediate ketone is **1-(4-chlorophenyl)prop-2-en-1-one**, C=CC(=O)c1ccc(Cl)cc1.
- A second vinylmagnesium bromide molecule attacks this ketone at its carbonyl carbon. This gives **3-(4-chlorophenyl)penta-1,4-dien-3-olate**, C=CC([O-])(c1ccc(Cl)cc1)C=C.
- Aqueous work-up protonates the alkoxide, yielding **M**, **3-(4-chlorophenyl)penta-1,4-dien-3-ol**, C=CC(O)(c1ccc(Cl)cc1)C=C.

Thus the central carbon of **M** bears a hydroxyl group, a para-chlorophenyl group and two vinyl groups.

Formation of N. Hydrogen bromide, HBr, in the presence of **benzoyl peroxide**,

O=C(c1ccccc1)OOC(=O)c1ccccc1, undergoes radical, anti-Markovnikov addition to each vinyl group:



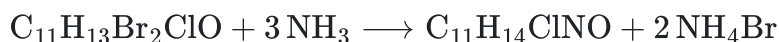
A bromine radical adds to the terminal carbon of each double bond, leaving the more substituted carbon radical. Hydrogen abstraction from another hydrogen bromide molecule completes the addition and regenerates a bromine radical.

The intended product **N** is therefore **1,5-dibromo-3-(4-chlorophenyl)pentan-3-ol**,



Formation of O. Ammonia, NH3, substitutes one terminal bromide. The resulting amino group then attacks the other terminal carbon intramolecularly, closing a six-membered ring. Deprotonation gives the secondary amine.

With excess ammonia also neutralizing the acid formed, the balanced equation is:



The salt is **ammonium bromide**, [NH4+].[Br-].

O is **4-(4-chlorophenyl)piperidin-4-ol**, OC1(c2ccc(Cl)cc2)CCNCC1. To sketch it, draw a six-membered saturated ring with one nitrogen bearing hydrogen; the carbon opposite nitrogen bears both the hydroxyl group and the para-chlorophenyl group.

3.5 — Friedel–Crafts acylation

L acylates **fluorobenzene**, Fc1ccccc1, in the presence of **aluminium chloride**, Cl[Al](Cl)Cl:



Fluorine deactivates the aromatic ring inductively but directs electrophilic substitution to the ortho and para positions through lone-pair donation. The less hindered para product predominates.

Therefore **P** is **4-chloro-1-(4-fluorophenyl)butan-1-one**, O=C(CCCCl)c1ccc(F)cc1.

To sketch **P**, draw a benzene ring bearing fluorine and -COCH2CH2CH2Cl in para positions. Its formula is:

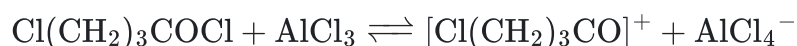


consistent with the formula supplied.

The mechanism has three principal steps.

1. Generation of the acyl electrophile.

Aluminium chloride accepts the acyl chloride's chloride ion:



The **4-chlorobutanoyl acylium ion** has resonance representations $\text{O}=[\text{C}^+]\text{CCCCl}$ and $\text{ClCCCC}=[\text{O}^+]$.

The counterion is **tetrachloroaluminate**, $[\text{Al}^-](\text{Cl})(\text{Cl})(\text{Cl})\text{Cl}$.

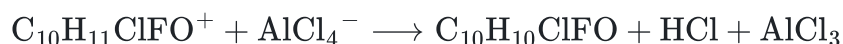
2. Aromatic attack.

Aromatic π electrons attack the acylium carbon at the position para to fluorine. This forms a nonaromatic **arenium ion**; one resonance contributor is $\text{O}=\text{C}(\text{CCCCl})\text{C1C}=\text{C}[\text{C}^+](\text{F})\text{C}=\text{C1}$.



3. Restoration of aromaticity.

Tetrachloroaluminate removes the proton from the carbon where substitution occurred. The carbon-hydrogen bond electrons restore the aromatic π system:



The ketone oxygen can coordinate to aluminium chloride; aqueous work-up releases **P** from that complex.

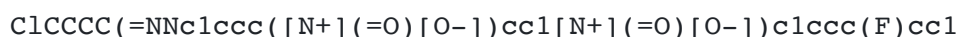
3.6 — Identification of the carbonyl group

Chemical test: 2,4-dinitrophenylhydrazine.

2,4-Dinitrophenylhydrazine, $\text{NNc1ccc}([\text{N}^+](=\text{O})[\text{O}^-])\text{cc1}[\text{N}^+](=\text{O})[\text{O}^-]$, reacts with an aldehyde or ketone to give a typically yellow or orange hydrazone precipitate:



The product is **the 2,4-dinitrophenylhydrazone of P**:



No particular hydrazone *E/Z* configuration is required for this qualitative test.

Physical test: infrared spectroscopy.

A strong carbonyl stretching absorption is expected near 1700 cm^{-1} , approximately $1685\text{--}1710\text{ cm}^{-1}$ for this aromatic-conjugated ketone.

Exclusion of an aldehyde: Tollens test.

An aldehyde reduces Tollens reagent to metallic silver; **P** should give a negative test. The reactive complex is the **diamminesilver(I) ion**, $[\text{NH}_3]_2\text{Ag}^+ \rightleftharpoons [\text{Ag}^+]\text{NH}_3$; the arrows in this SMILES denote nitrogen-to-silver coordination.

For example, **benzaldehyde**, $\text{O}=\text{Cc1ccccc1}$, gives **benzoate**, $\text{O}=\text{C}([\text{O}^-])\text{c1ccccc1}$, and silver:



A working aldehyde control should give the silver deposit, whereas **P** should not. The absence of an aldehydic proton resonance, normally around $\delta 9\text{--}10\text{ ppm}$, provides an additional spectroscopic check.

3.7 — Formation of haloperidol

The secondary amine nitrogen of **O** attacks the terminal primary carbon bearing chlorine in **P**, by an S_N2 reaction. Base removes the nitrogen-bound proton, giving a tertiary amine.

With sodium hydroxide representing the base, the overall balance is:



The product **H**, **haloperidol**, is:

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)butan-1-one

O=C(CCCN1CCC(O)(c2ccc(Cl)cc2)CC1)c1ccc(F)cc1

To sketch it, start from the piperidine structure **O** and replace its nitrogen-bound hydrogen with $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}-\text{C}_6\text{H}_4-\text{F}$, with fluorine para to the carbonyl attachment on that ring. The hydroxyl group and para-chlorophenyl substituent at piperidine carbon 4 remain present.

The chlorine originally on the terminal carbon of **P** is displaced. The only chlorine remaining in **H** is the chlorine on the aromatic ring, as required.

3.8 — Proton NMR multiplicities of K

Write **K** as:



Under the usual first-order treatment and rapid exchange of hydroxyl protons:

Proton set	Integral	Coupled neighboring carbon-bound protons	Multiplicity
<i>a</i> : methylene next to the carboxyl group	2	Two protons of <i>b</i>	Triplet, 1 : 2 : 1
<i>b</i> : middle methylene	2	Two protons of <i>a</i> and two of <i>c</i>	Quintet, 1 : 4 : 6 : 4 : 1
<i>c</i> : methylene next to the hydroxyl group	2	Two protons of <i>b</i>	Triplet, 1 : 2 : 1
Alcoholic hydroxyl proton	1	Coupling normally averaged out by exchange	Broad singlet
Carboxylic acid proton	1	No normally resolved coupling	Broad singlet

The middle methylene would generally be split separately by its two neighboring methylene groups. Here their coupling constants are stipulated to be identical, so the lines coincide to produce a quintet:

$$(1+x)^2(1+x)^2 = (1+x)^4 = 1 + 4x + 6x^2 + 4x^3 + x^4.$$

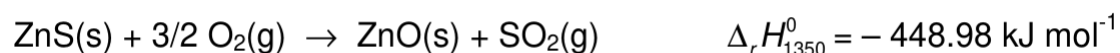
The total integration is $2 + 2 + 2 + 1 + 1 = 8$ protons, consistent with $\text{C}_4\text{H}_8\text{O}_3$.

The solution was checked against the official solution.

Problem 4: Chemical thermodynamics

The production of zinc from zinc sulphide proceeds in two stages: the roasting of zinc sulphide in the air and the reduction of the zinc oxide formed by carbon monoxide. In this problem we will consider the roasting of zinc sulphide.

This operation consists in burning zinc sulphide in the air. The equation of the reaction taking place is as follows:



Industrially this reaction is carried out at 1350 K.

4.1 Show that the reaction can be self-sustaining, i.e. that the heat produced is sufficient to bring the reactants from ambient temperature to the reaction temperature.

Suppose that the zinc containing mineral contains only zinc sulphide, ZnS .

4.2 Starting with a stoichiometric mixture of one mole zinc blend only and a necessary quantity of the air at 298 K, calculate the temperature to which the mixture will raise by the heat evolved during the roasting of the mineral at 1350 K under standard pressure. Is the reaction self-sustaining? Air is considered to be a mixture of oxygen and nitrogen in a volume ratio equal to 1 : 4.

In fact, zinc blend is never pure and is always mixed with a gangue that can be assumed to be entirely silica SiO_2 .

4.3 Assuming that the gangue does not react during the roasting, calculate the minimum ZnS content of the mineral for which the reaction would be self-sustaining at 1350 K despite the presence of silica. Give the answer in grams of ZnS per hundred grams of zinc blend.

Data:

Standard molar heat capacities averaged over the temperature range considered (in $\text{J K}^{-1} \text{mol}^{-1}$):

ZnS (solid):	58.05	ZnO (solid):	51.64
SO_2 (gas):	51.10	O_2 (gas):	34.24
N_2 (gas):	30.65	SiO_2 (solid):	72.50

Molar masses (in g mol^{-1}):

ZnS	SiO_2
97.5	60.1

Official English text of the problem.

Answers

- **4.1:** Yes. Heating the stoichiometric feed from 298 to 1350 K requires **308.56 kJ per mole of ZnS**, whereas roasting releases **448.98 kJ**.
- **4.2:** Assigning the stated reaction heat to heating the initial reactant mixture gives **1829 K**, so the reaction is self-sustaining. If the requested temperature means the **adiabatic final temperature of the reacted products**, it is **1840 K**.
- **4.3:** The minimum content is **46.8 g of ZnS per 100 g of mineral**, under the ideal heat balance.

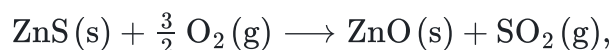
Solution

Use the supplied mean heat capacities as constants, take ambient temperature as 298 K, and neglect heat losses and phase changes.

The molecular gases involved are oxygen, O_2 , $O=O$; nitrogen, N_2 , $N\equiv N$; and sulphur dioxide, SO_2 , $O=S=O$. Zinc sulphide, zinc oxide and silica are extended solids, so individual molecular SMILES do not describe their bulk structures.

4.1

The balanced roasting reaction is



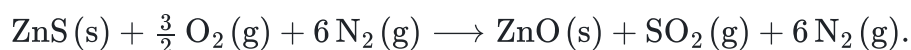
with

$$\Delta_r H_{1350}^\circ = -448.98 \text{ kJ mol}^{-1}.$$

For one mole of ZnS, the stoichiometric oxygen requirement is 1.5 mol. Since the oxygen-to-nitrogen volume ratio is 1 : 4, the accompanying nitrogen is

$$n(N_2) = 4(1.5) = 6.0 \text{ mol}.$$

Thus, including the inert nitrogen,



The total heat capacity of this feed is

$$\begin{aligned} C_R &= (1)(58.05) + (1.5)(34.24) + (6)(30.65) \\ &= 293.31 \text{ J K}^{-1}. \end{aligned}$$

Heating it from 298 to 1350 K requires

$$\begin{aligned} Q_{\text{preheat}} &= C_R(1350 - 298) \\ &= (293.31)(1052) \\ &= 308\,562.12 \text{ J} \\ &= 308.56 \text{ kJ}. \end{aligned}$$

Therefore,

$$Q_{\text{released}} - Q_{\text{preheat}} = 448.98 - 308.56212 = 140.42 \text{ kJ} > 0.$$

The reaction releases sufficient heat to bring fresh reactants, including the nitrogen in the air, to 1350 K. **Once initiated, the ideal roasting process can be self-sustaining.**

4.2

For the feed-heating interpretation of the question, the heat released by roasting one mole at 1350 K heats the initial stoichiometric mixture from 298 K to T_{heat} :

$$C_R(T_{\text{heat}} - 298) = 448\,980 \text{ J}.$$

Hence,

$$T_{\text{heat}} = 298 + \frac{448\,980}{293.31} = \boxed{1828.74 \text{ K} \approx 1829 \text{ K}}.$$

Since this exceeds 1350 K, the reaction is self-sustaining.

There is a distinction if the question instead asks for the final temperature after **complete adiabatic reaction**. The final material consists of one mole each of ZnO and SO₂, together with six moles of N₂. Its heat capacity is

$$\begin{aligned} C_P &= 51.64 + 51.10 + 6(30.65) \\ &= 286.64 \text{ J K}^{-1}. \end{aligned}$$

Use an enthalpy path consisting of heating the reactants to 1350 K, reacting at 1350 K, and then heating the products to T_{ad} . For an adiabatic constant-pressure process,

$$308\,562.12 - 448\,980 + 286.64(T_{\text{ad}} - 1350) = 0.$$

Thus,

$$\begin{aligned} T_{\text{ad}} &= 1350 + \frac{448\,980 - 308\,562.12}{286.64} \\ &= \boxed{1839.88 \text{ K} \approx 1840 \text{ K}}. \end{aligned}$$

The two calculations describe different quantities: **1829 K is the feed-heating equivalent of the stated reaction heat; 1840 K is the adiabatic final-product temperature.**

4.3

Take a basis of one mole of ZnS, accompanied by its stoichiometric air and n moles of inert silica.

At the minimum ZnS content, all the available reaction heat is just sufficient to heat the feed and gangue from 298 to 1350 K. The heat available for silica is therefore

$$Q_{\text{silica,max}} = 448\,980 - 308\,562.12 = 140\,417.88 \text{ J}.$$

Consequently,

$$n_{\text{max}} = \frac{140\,417.88 \text{ J}}{(72.50 \text{ J K}^{-1} \text{ mol}^{-1})(1052 \text{ K})} = 1.84106 \text{ mol}.$$

The corresponding silica mass is

$$m(\text{SiO}_2) = (1.84106)(60.1) = 110.648 \text{ g}.$$

One mole of ZnS has mass 97.5 g, so the limiting mineral contains

$$97.5 + 110.648 = 208.148 \text{ g}$$

in total. Its minimum ZnS mass percentage is

$$100 \frac{97.5}{208.148} = 46.8417.$$

Therefore,

46.8 g of ZnS per 100 g of mineral.

A lower ZnS content would provide insufficient heat to bring the stoichiometric feed and its silica gangue to 1350 K.

The solution was checked against the official solution.

Problem 5: Chemical kinetics

Nitramide NO_2NH_2 decomposes slowly in aqueous solution according to the reaction:



The experimental kinetic law is as follows:

$$\frac{d[\text{N}_2\text{O}]}{dt} = k \frac{[\text{NO}_2\text{NH}_2]}{[\text{H}_3\text{O}^+]}$$

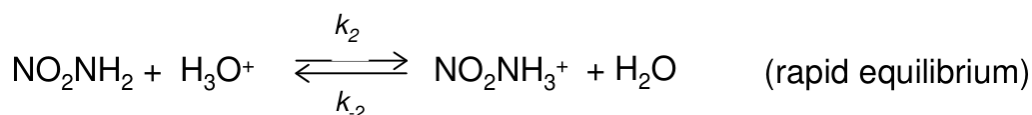
5.1 What is the apparent order of this reaction in a buffered solution?

5.2 Which of the following mechanisms is the most appropriate for the interpretation of this kinetic law? Justify your answer.

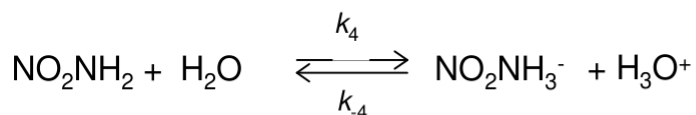
Mechanism 1:



Mechanism 2:



Mechanism 3:



5.3 Show the relationship between the experimentally observed rate constant and the rate constants of the selected mechanism.

5.4 Show that hydroxyl ions catalyze the decomposition of nitramide.

The decomposition is studied in a buffered solution of a constant volume V at a constant temperature by measuring the partial pressure of the gas N_2O , considered to be insoluble in water, in a constant volume of the same value V above the solution. The following results are obtained:

$t(\text{min})$	0	5	10	15	20	25
$p(\text{Pa})$	0	6800	12400	17200	20800	24000

After a sufficiently long time, the pressure stabilises at 40000 Pa.

5.5 Express the pressure p as a function of time and the constant k' such that

$$k' = \frac{k}{[H_3O^+]}$$

5.6 Verify graphically that the kinetic law is confirmed by these experimental results.

5.7 Calculate k' giving its units.

Official English text of the problem.

Answers

- **5.1:** First order, with the constant apparent rate coefficient $k' = k/[H_3O^+]$.
- **5.2: Mechanism 3**, involving the nitramidate ion $[NH-][N+](=O)[O-]$.
- **5.3:** With elementary mass-action constants for the reactions as written,

$$k = \frac{k_4 k_5}{k_{-4}} [H_2O]$$

If water concentration is absorbed into $\tilde{k}_4 = k_4[H_2O]$, then $k = \tilde{k}_4 k_5 / k_{-4}$.

- **5.4:** Hydroxide ions $[OH-]$ accelerate the reaction and are regenerated:

$$v = \frac{k}{K_w} [NO_2NH_2][OH^-]$$

- **5.5:**

$$p(t) = (40000 \text{ Pa}) (1 - e^{-k't})$$

- **5.6:** Plotting $\ln[p_\infty/(p_\infty - p)]$ against time gives an approximately straight line through the origin, as predicted.
- **5.7:**

$$k' \approx 3.7 \times 10^{-2} \text{ min}^{-1} \approx 6.1 \times 10^{-4} \text{ s}^{-1}$$

Solution

The species used below have the following names and SMILES. No stereochemistry is involved.

Formula	Name	SMILES
NO_2NH_2	Nitramide	<chem>N[N+](=O)[O-]</chem>

Formula	Name	SMILES
NO_2NH^-	Nitramidate ion, the conjugate base of nitramide	<chem>[NH-][N+](=O)[O-]</chem>
NO_2NH_3^+	N-protonated nitramide	<chem>[NH3+][N+](=O)[O-]</chem>
N_2O	Nitrous oxide, or dinitrogen monoxide	<chem>N#[N+][O-]</chem>
H_2O	Water	<chem>O</chem>
H_3O^+	Hydronium ion	<chem>[OH3+]</chem>
OH^-	Hydroxide ion	<chem>[OH-]</chem>

5.1 — Apparent reaction order

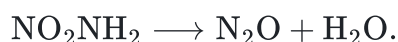
A buffer maintains approximately constant $[\text{H}_3\text{O}^+]$. Consequently,

$$v = \frac{d[\text{N}_2\text{O}]}{dt} = \frac{k}{\underbrace{[\text{H}_3\text{O}^+]}_{k'}} [\text{NO}_2\text{NH}_2].$$

The rate is proportional to the first power of the nitramide concentration. Thus the reaction is **apparently first order**, or pseudo-first-order, with rate coefficient k' .

5.2 — Selection of the mechanism

For **Mechanism 1**, the single elementary step is

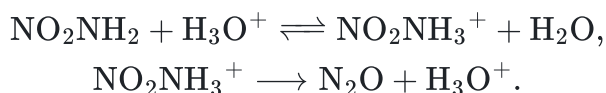


It predicts

$$v = k_1[\text{NO}_2\text{NH}_2],$$

which does not account for the experimentally observed inverse dependence on $[\text{H}_3\text{O}^+]$.

For **Mechanism 2**, the steps are



The first step is a rapid equilibrium. At constant water concentration,

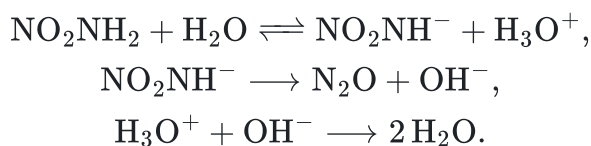
$$[\text{NO}_2\text{NH}_3^+] \propto [\text{NO}_2\text{NH}_2][\text{H}_3\text{O}^+].$$

The slow second step therefore gives

$$v = k_3[\text{NO}_2\text{NH}_3^+] \propto [\text{NO}_2\text{NH}_2][\text{H}_3\text{O}^+],$$

predicting a positive first-order dependence on hydronium concentration. This contradicts the observed inverse dependence.

For **Mechanism 3**, the balanced steps are



Here the first equilibrium has been corrected to contain NO_2NH^- .

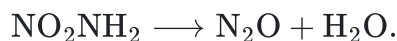
The rapid acid–base equilibrium gives, at constant water concentration,

$$[\text{NO}_2\text{NH}^-] \propto \frac{[\text{NO}_2\text{NH}_2]}{[\text{H}_3\text{O}^+]}.$$

Since decomposition of this anion is the rate-limiting step,

$$v = k_5[\text{NO}_2\text{NH}^-] \propto \frac{[\text{NO}_2\text{NH}_2]}{[\text{H}_3\text{O}^+]}$$

Thus **Mechanism 3 reproduces the experimental rate law**. Adding its three steps and cancelling intermediates also gives the correct overall reaction:



5.3 — Relationship between the rate constants

Applying the rapid-pre-equilibrium approximation to the first step of Mechanism 3,

$$k_4[\text{NO}_2\text{NH}_2][\text{H}_2\text{O}] = k_{-4}[\text{NO}_2\text{NH}^-][\text{H}_3\text{O}^+].$$

Therefore,

$$[\text{NO}_2\text{NH}^-] = \frac{k_4[\text{H}_2\text{O}]}{k_{-4}} \frac{[\text{NO}_2\text{NH}_2]}{[\text{H}_3\text{O}^]}.$$

Substitution into the rate expression for the slow step gives

$$v = k_5[\text{NO}_2\text{NH}^-] = \frac{k_4k_5[\text{H}_2\text{O}]}{k_{-4}} \frac{[\text{NO}_2\text{NH}_2]}{[\text{H}_3\text{O}^]}.$$

Comparison with the experimental law yields

$$k = \frac{k_4k_5[\text{H}_2\text{O}]}{k_{-4}}.$$

Water is the solvent, so its concentration is effectively constant. If it is already included in the forward coefficient, defined by

$$\tilde{k}_4 = k_4[\text{H}_2\text{O}],$$

the same result is written

$$k = \frac{\tilde{k}_4k_5}{k_{-4}}.$$

The rapid neutralization constant k_6 does not enter the rate law.

5.4 — Catalysis by hydroxide ions

At constant temperature, using the concentration form of the water ion product,

$$K_w = [\text{H}_3\text{O}^+][\text{OH}^-].$$

Hence

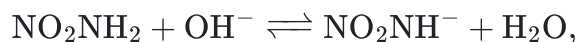
$$\frac{1}{[\text{H}_3\text{O}^+]} = \frac{[\text{OH}^-]}{K_w},$$

and the experimental law becomes

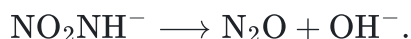
$$v = \frac{k}{K_w} [\text{NO}_2\text{NH}_2][\text{OH}^-].$$

Increasing hydroxide concentration therefore increases the rate.

The catalytic cycle can be expressed as

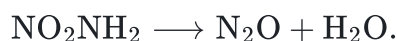


followed by



In the first step, hydroxide accepts a proton from the amino nitrogen of nitramide; the electron pair of the broken N–H bond remains on nitrogen. The resulting nitramidate ion decomposes in the slow step, regenerating hydroxide. These proton-transfer and regeneration events are not encoded by the SMILES alone.

Cancelling hydroxide and nitramidate gives



Hydroxide accelerates the reaction while being regenerated, establishing its catalytic role.

5.5 — Pressure as a function of time

Let $a(t)$ be the concentration of undecomposed nitramide and a_0 its initial value. In the buffered solution,

$$-\frac{da}{dt} = k'a,$$

so

$$a(t) = a_0 e^{-k't}.$$

One mole of nitramide produces one mole of nitrous oxide. Using the ideal-gas relation, with equal liquid and gas volumes V ,

$$\frac{p(t)V}{RT} = V(a_0 - a(t)).$$

At complete decomposition,

$$\frac{p_\infty V}{RT} = Va_0.$$

Dividing gives

$$\frac{p(t)}{p_\infty} = 1 - \frac{a(t)}{a_0} = 1 - e^{-k't}.$$

Therefore,

$$p(t) = p_\infty (1 - e^{-k't}) = (40000 \text{ Pa}) (1 - e^{-k't}).$$

The units of t must correspond to those used for k' .

5.6 — Graphical verification

Rearranging the pressure equation gives

$$\frac{p_\infty - p}{p_\infty} = e^{-k't},$$

and hence

$$y = \ln\left(\frac{p_\infty}{p_\infty - p}\right) = k't.$$

The logarithm has a dimensionless argument. From the measurements:

t / min	$p_{\infty} - p / \text{Pa}$	$y = \ln[p_{\infty}/(p_{\infty} - p)]$
0	40000	0.00000
5	33200	0.18633
10	27600	0.37106
15	22800	0.56212
20	19200	0.73397
25	16000	0.91629

On the graph, put **time in minutes on the horizontal axis** and **y on the vertical axis**. The six points lie very close to a straight line rising from the origin to approximately (25, 0.916).

An unconstrained least-squares fit gives

$$y = 0.00338 + (0.03666 \text{ min}^{-1})t, \quad R^2 = 0.9998.$$

The small intercept and nearly linear data support the predicted first-order law to the precision of the measurements.

5.7 — Numerical value of k'

The slope of the graph is k' . Using the initial and final measurements,

$$k' = \frac{\ln\left(\frac{40000}{40000 - 24000}\right)}{25 \text{ min}} = \frac{\ln(2.5)}{25 \text{ min}} = 0.03665 \text{ min}^{-1}.$$

This agrees with the slope obtained from all six measurements. Converting to seconds,

$$k' = \frac{0.03665}{60} \text{ s}^{-1} = 6.109 \times 10^{-4} \text{ s}^{-1}.$$

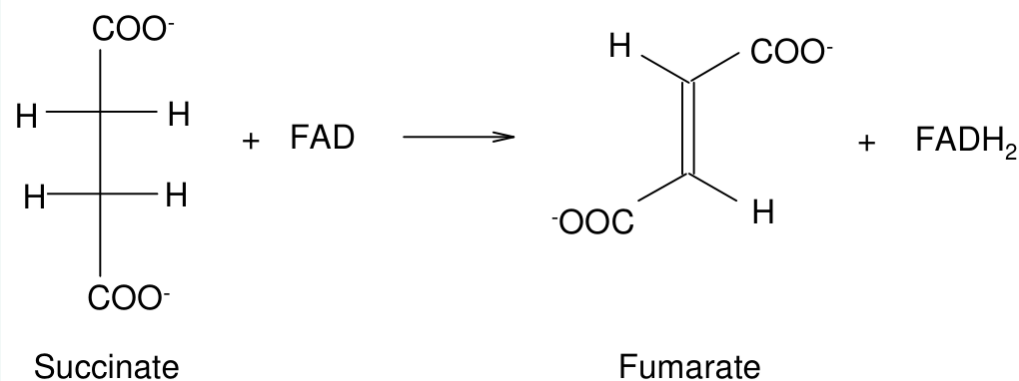
To sensible significant figures,

$$k' \approx 3.7 \times 10^{-2} \text{ min}^{-1} \approx 6.1 \times 10^{-4} \text{ s}^{-1}.$$

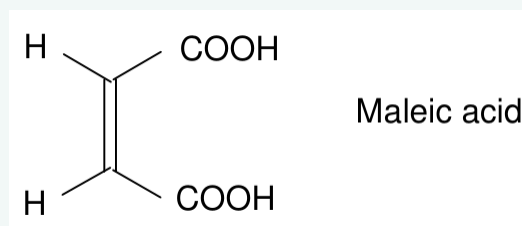
The solution was checked against the official solution.

Problem 6: Bio-organic chemistry

The reaction of dehydrogenation of succinate to fumarate is a one step in the tricarboxylic Krebs cycle, catalysed by the enzyme succinic dehydrogenase. Flavine-adenine-dinucleotide, FAD, acts as a coenzyme. The equation of the process:



The stereochemistry of the dehydrogenation of succinate to fumarate has been studied. Consider the enzymatic reaction with the 2,3-dideuteriosuccinates related to the acids or obtained by catalytic deuteration (in the presence of palladium on coal) of fumaric and maleic acids.



6.1 Using Fischer formulae, write down structures for all the possible stereoisomers obtained by catalytic deuteration of maleic and fumaric acids. How many isomers are there? Indicate those that are optically active. Establish a stereochemical relationship between them (compare the isomers two by two). Using Newman projections show the most stable conformation of each isomer.

The proportion of dideuterated fumarate (obtained when each of the above 2-3 dideuterated succinates is submitted to the enzymatic reaction) is 4 % when using fumaric acid as starting molecule, but 48.5 % when using maleic acid.

It is assumed that at the active site, the enzymatic dehydrogenation occurs on the succinate, in the most stable conformation as proposed in 6.1. The dehydrogenation stereochemistry can be *syn* or *anti*.

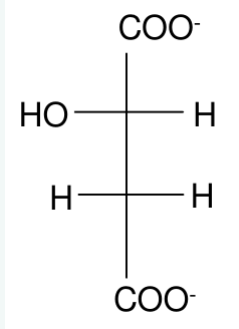
6.2 On the basis of the Newman projections of the most stable conformations of each isomer and the above facts, determine the percentage of dideuterated fumarate formed by *syn* and *anti* dehydrogenation.

(Assume that the percentages of dideuterated fumarate are 0 or 50 %, respectively.)

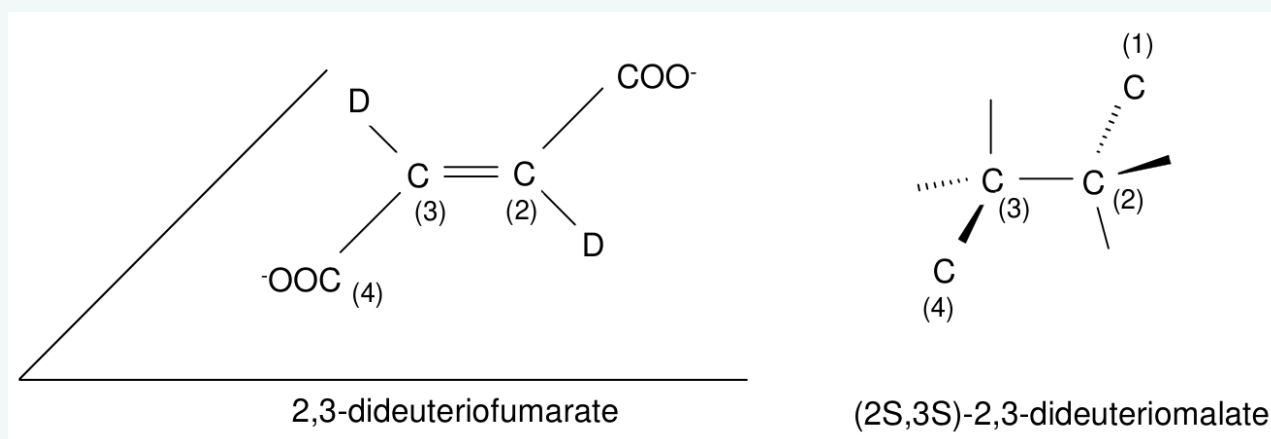
6.3 Show the stereochemistry of the enzymatic dehydrogenation.

In the following step of the Krebs cycle and in the presence of fumarase enzyme, fumarate adds on a water molecule to yield (*S*)-malate (also called as L-malate).

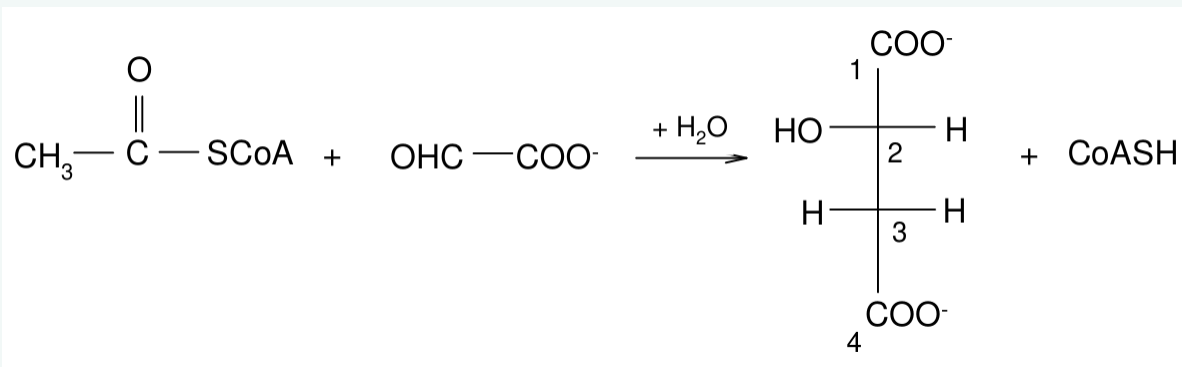
Fischer projection of (*S*)-malate:



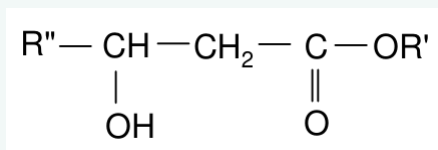
6.4 The 2,3-dideuteriofumarate reacts with fumarase to (2*S*, 3*S*)-2,3-dideuteriomalate (through addition of water). Show the stereochemical pathway of the reaction. Use the schematic drawing below to answer this question.



The acetylcoenzyme A, CH_3COSCoA reacts with glyoxylate, $\text{OHC}-\text{CO}_2^-$, in the presence of malate synthetase enzyme to (*S*)-malate.



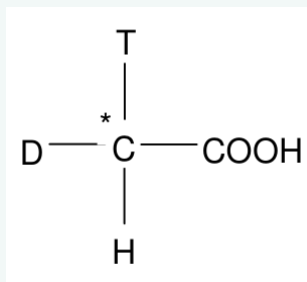
A similar reaction can proceed between an ester $\text{CH}_3\text{COOR}'$ (similar to the thioester CH_3COSCoA) and an aldehyde $\text{R}''\text{CHO}$ (similar to the glyoxylate) in the presence of $\text{R}'-\text{O}^-$ ions. It leads to a β -hydroxyester.



($\text{R}'-\text{O}^-$ enter the reaction as a base to produce an intermediate carbanion from the ester)

6.5 Write the steps of the mechanism.

The enzymatic reaction is carried out using acetylcoenzyme A which is obtained from acetic acid CHDTCOOH having *R*-configuration.



(tritium $\text{T} = {}^3_1\text{H}$, deuterium $\text{D} = {}^2_1\text{H}$)

The formed (*S*)-malate is dehydrated (the reverse reaction of question 6.4) by an enzymatic reaction.

6.6 What enzyme can be used?

The major product is monotritiated fumarate (79%) with 21 % untritiated fumarate.

6.7 Write down the Fischer projections of the two possible structures of the major product (*S*)-malate arising from the acetylcoenzyme A which has a labelled acetyl group with *R*-configuration.

6.8 What would be the products if the starting material has a labelled acetyl group with *S*-configuration?

Official English text of the problem.

Answers

- **6.1:** There are **three stereoisomers**: meso-(*2R, 3S*), (*2R, 3R*), and (*2S, 3S*). Maleic acid gives the meso compound; fumaric acid gives a racemic mixture of the other two. The latter are individually optically active enantiomers; each is a diastereomer of the meso compound. The most stable conformations are staggered, with the carboxyl groups anti.
- **6.2:** From maleic acid: **0% dideuterofumarate for syn, 50% for anti** dehydrogenation. From fumaric acid: **50% for syn, 0% for anti**.
- **6.3:** Succinic dehydrogenase effects **anti dehydrogenation**.
- **6.4:** Fumarase adds the hydroxyl group and hydrogen **anti**, giving (*2S, 3S*)-2,3-dideuteriomalate. In its vertical Fischer projection, the upper centre has hydroxyl left/deuterium right, and the lower centre has hydrogen left/deuterium right.
- **6.5:** The mechanism is **ester enolate formation → attack on the aldehyde → protonation of the resulting alkoxide**.
- **6.6:** **Fumarase**, also called fumarate hydratase.
- **6.7:** The two tritium-retaining possibilities are (*2S, 3S*)-3-tritiomalate and (*2S, 3S*)-3-deuterio-3-tritiomalate. In the Fischer projection with hydroxyl on the left at C2, **tritium is on the right at C3**, opposite hydrogen or deuterium.

- **6.8:** The corresponding major malates have (*2S*, *3R*) configuration: tritium is on the left at C3 and is removed by fumarase. Under the intended stereospecific comparison, the fumarate proportions reverse to **79% untritiated and 21% monotritiated**.

Solution

Throughout, [2H] denotes deuterium and [3H] denotes tritium in SMILES. In a Fischer projection, horizontal bonds point towards the observer and vertical bonds point away. Explicit cofactor SMILES below use protonated phosphate groups.

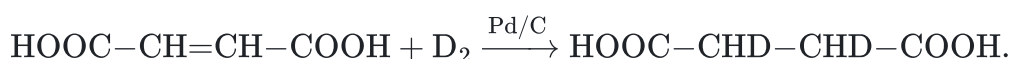
6.1 — Products of catalytic deuteration

The starting compounds are:

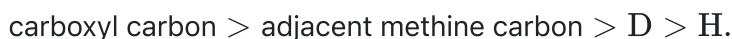
- Maleic acid, the *Z* isomer: O=C(O)/C=C\C(=O)O.
- Fumaric acid, the *E* isomer: O=C(O)/C=C/C(=O)O.
- Molecular deuterium: [2H][2H].

Catalytic addition on palladium is **syn**: both deuterium atoms are delivered to the same face of the double bond.

The balanced addition is



Each product has stereogenic centres at C2 and C3 because D and H are distinguishable. Their CIP priorities are



Of the four formal configurations, (*2R*, *3S*) and (*2S*, *3R*) describe the same meso compound. Thus there are **three stereoisomers**.

For the requested Fischer projections, put C1 at the top and C4 at the bottom, with a terminal COOH group at each end:

Product	Isomeric SMILES	C2: left, right	C3: left, right
meso-(<i>2R</i> , <i>3S</i>)-2,3-dideuteriosuccinic acid	<chem>O=C(O)[C@H]([2H])[C@H]([2H])C(=O)O</chem>	H, D	H, D
(<i>2R</i> , <i>3R</i>)-2,3-dideuteriosuccinic acid	<chem>O=C(O)[C@H]([2H])[C@@H]([2H])C(=O)O</chem>	H, D	D, H
(<i>2S</i> , <i>3S</i>)-2,3-dideuteriosuccinic acid	<chem>O=C(O)[C@@H]([2H])[C@H]([2H])C(=O)O</chem>	D, H	H, D

Consequently:

- **Maleic acid + syn addition** gives the **meso** compound.
- **Fumaric acid + syn addition** gives equal amounts of the *RR* and *SS* compounds, because its two faces are equivalent on an achiral catalyst.

The *RR* and *SS* compounds are enantiomers and are individually optically active. Their racemic mixture is optically inactive. The meso compound is achiral and optically inactive; it is a diastereomer of each member of the enantiomeric pair.

For the Newman projections, look **from C2 towards C3**. Put the front carboxyl group at **12 o'clock** and the rear carboxyl group at **6 o'clock**. The following clock positions specify all three projections:

Isomer	Front C2 substituents	Rear C3 substituents
meso-(2 <i>R</i> , 3 <i>S</i>)	D at 4; H at 8	D at 10; H at 2
(2 <i>R</i> , 3 <i>R</i>)	D at 4; H at 8	D at 2; H at 10
(2 <i>S</i> , 3 <i>S</i>)	D at 8; H at 4	D at 10; H at 2

These conformations are staggered, with a 180° carboxyl–carboxyl dihedral angle. They minimize the interaction between the two large carboxyl groups; in the dianions, they also separate the negative charges.

The corresponding enzymatic substrates are:

- meso-(2*R*, 3*S*)-2,3-dideuteriosuccinate: $\text{O}=\text{C}([\text{O}^-])[\text{C}@\text{H}](\text{[2H]})[\text{C}@\text{H}](\text{[2H]})\text{C}(=\text{O})[\text{O}^-]$.
- (2*R*, 3*R*)-2,3-dideuteriosuccinate: $\text{O}=\text{C}([\text{O}^-])[\text{C}@\text{H}](\text{[2H]})[\text{C}@@\text{H}](\text{[2H]})\text{C}(=\text{O})[\text{O}^-]$.
- (2*S*, 3*S*)-2,3-dideuteriosuccinate: $\text{O}=\text{C}([\text{O}^-])[\text{C}@@\text{H}](\text{[2H]})[\text{C}@\text{H}](\text{[2H]})\text{C}(=\text{O})[\text{O}^-]$.

6.2 — Predicted dideuterofumarate percentages

The possible fumarate products are:

- Unlabelled fumarate: $\text{O}=\text{C}([\text{O}^-])/\text{C}=\text{C}/\text{C}(=\text{O})[\text{O}^-]$.
- Monodeuterofumarate: $\text{O}=\text{C}([\text{O}^-])/\text{C}(\text{[2H]})=\text{C}/\text{C}(=\text{O})[\text{O}^-]$.
- 2,3-Dideuterofumarate: $\text{O}=\text{C}([\text{O}^-])/\text{C}(\text{[2H]})=\text{C}(\text{[2H]})/\text{C}(=\text{O})[\text{O}^-]$.

Dideuterofumarate is obtained only when **both ordinary hydrogen atoms are removed**, leaving both deuterium atoms in the alkene.

For the meso substrate, the Newman projection shows an anti H/H pair and an anti D/D pair. Thus anti elimination can retain either both deuteriums or neither. Under the stipulated idealization, these give 50% dideuterated product. Syn elimination removes one hydrogen and one deuterium, giving monodeuterofumarate.

For the *RR/SS* substrates, the anti pairs contain one hydrogen and one deuterium. Anti elimination therefore gives no dideuterofumarate. The formal syn alternative gives the complementary 50% result.

Starting acid	Deuterated succinate obtained	Dideuterofumarate from syn elimination	Dideuterofumarate from anti elimination
Maleic acid	meso	0%	50%
Fumaric acid	racemic <i>RR</i> + <i>SS</i>	50%	0%

These percentages use the problem's prescribed 0/50% approximation.

6.3 — Stereochemistry of succinic dehydrogenase

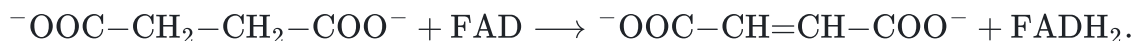
Experimentally,

maleic-acid-derived substrate: 48.5% $\approx$ 50%,
 fumaric-acid-derived substrate: 4% $\approx$ 0%.

This matches the **anti** column.

In the meso Newman projection specified above, show removal of the front hydrogen at **8 o'clock** and the rear hydrogen at **2 o'clock**. Their dihedral angle is 180°; both deuteriums remain in the resulting fumarate.

For unlabelled succinate, $\text{O}=\text{C}([\text{O}^-])\text{CCC}(=\text{O})[\text{O}^-]$, the balanced overall reaction is



The cofactor structures are:

- Flavin adenine dinucleotide, FAD: CC1=CC2=C(C=C1C)N(C3=NC(=O)NC(=O)C3=N2)C[C@H](O)[C@H](O)[C@H](O)COP(=O)(O)OP(=O)(O)OC[C@H]4O[C@@H](n5cnc6c(N)ncnc65)[C@H](O)[C@@H]4O.
- Reduced flavin adenine dinucleotide, FADH₂:
CC1=CC2=C(C=C1C)N(C3=NC(=O)NC(=O)C3=N2)C[C@H](O)[C@H](O)[C@H](O)COP(=O)(O)OP(=O)(O)OC[C@H]4O[C@@H](n5cnc6c(N)ncnc65)[C@H](O)[C@@H]4O.

6.4 — Stereochemistry of fumarase hydration

Water, O, adds to 2,3-dideuterofumarate according to



The specified product is (2*S*, 3*S*)-**2,3-dideuteriomalate**:



For comparison, ordinary (*S*)-malate is:



The product's Fischer projection has a vertical C1–C2–C3–C4 chain:

Centre	Left substituent	Right substituent
C2	OH	D
C3	H	D

The terminal groups are both COO[−].

To fill the **particular wedge-and-dash drawing supplied in the question**:

- At **C3**, put **D** on the ordinary bond pointing upward and **H** on the hashed bond pointing left.
- At **C2**, put **OH** on the solid wedge pointing right and **D** on the ordinary bond pointing downward.
- Keep the already indicated C1 and C4 bonds unchanged.

The newly introduced hydrogen is behind the drawing plane, while the newly introduced hydroxyl group is in front. Therefore hydration is **anti**.

The configuration assignments follow from:

C2: OH > C1 carboxyl > C3 chain > D,
 C3: C4 carboxyl > C2 chain > D > H.

Both centres are S , as required.

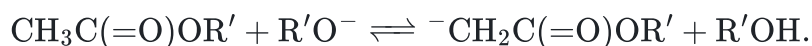
6.5 — Mechanism of the ester–aldehyde reaction

This is an **aldol-type addition of an ester enolate to an aldehyde**.

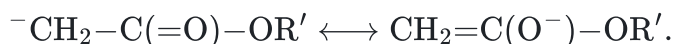
For the generic SMILES below, $[*:1]$ denotes R' , and $[*:2]$ denotes R'' .

Species	Name or description	SMILES
$\text{CH}_3\text{COOR}'$	Acetate ester	<chem>CC(=O)O[*:1]</chem>
$\text{R}'\text{O}^-$	Alkoxide base	<chem>[O-][*:1]</chem>
$\text{R}'\text{OH}$	Corresponding alcohol	<chem>O[*:1]</chem>
$\text{R}''\text{CHO}$	Aldehyde	<chem>O=C[*:2]</chem>
$^-\text{CH}_2\text{COOR}'$	Carbon-centred enolate contributor	<chem>[CH2-]C(=O)O[*:1]</chem>
$\text{CH}_2=\text{C}(\text{O}^-)\text{OR}'$	Oxygen-centred enolate contributor	<chem>C=C([O-])O[*:1]</chem>
$\text{R}''\text{CH}(\text{O}^-)\text{CH}_2\text{COOR}'$	Addition-product alkoxide	<chem>[*:2]C([O-])CC(=O)O[*:1]</chem>
$\text{R}''\text{CH}(\text{OH})\text{CH}_2\text{COOR}'$	β -Hydroxyester	<chem>[*:2]C(O)CC(=O)O[*:1]</chem>

Step 1: Removal of an α -hydrogen.

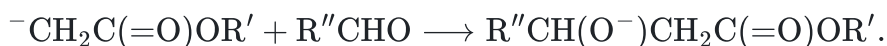


The base's oxygen lone pair attacks an α -hydrogen, and the C–H bond electrons remain in the ester enolate system:



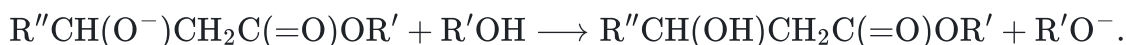
These are resonance contributors of one intermediate.

Step 2: Carbon–carbon bond formation.



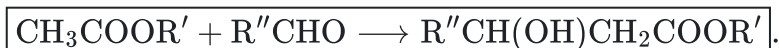
The enolate carbon attacks the aldehyde carbonyl carbon. The aldehyde's carbonyl π electrons move onto oxygen.

Step 3: Protonation.



The product alkoxide takes a proton from the alcohol, regenerating the base.

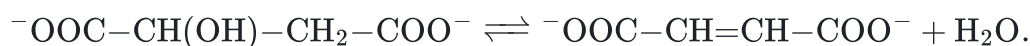
The balanced net reaction is



No unique product configuration is specified for this generic reaction. In the enzymatic analogue, malate synthase controls the newly formed hydroxyl-bearing centre to give the S configuration.

6.6 — Enzyme for dehydration

Use **fumarase**, the same enzyme that catalyses hydration in 6.4. Its reaction is reversible:

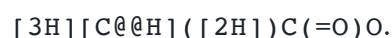


Microscopic reversibility requires dehydration to follow the reverse stereochemical pathway.

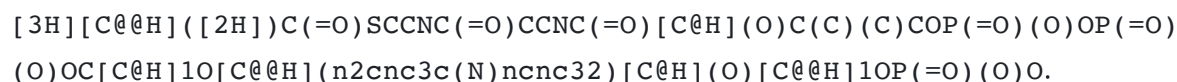
In the Fischer orientation with the C2 hydroxyl group on the **left**, fumarase removes that hydroxyl group together with the hydrogen isotope on the **left at C3**. This is the crucial identification for 6.7 and 6.8.

6.7 — Malates derived from the *R*-labelled acetyl group

The explicitly specified starting acid is (*R*)-[2-deuterio,2-tritio]acetic acid:



Its corresponding *R*-labelled acetyl-CoA is:



The other carbon substrate is **glyoxylate**, $O=CC(=O)[O^-]$. Its carboxyl and aldehyde carbons become malate C1 and C2, respectively. The acetyl methyl carbon becomes C3, and the acetyl carbonyl carbon becomes C4.

Formation of the C–C bond requires abstraction of one isotope from the labelled methyl group:

- Abstraction of **H** leaves **D** and **T** at malate C3.
- Abstraction of **D** leaves **H** and **T** at malate C3.

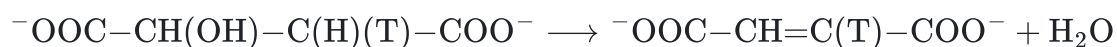
The major fumarate product retains tritium. Since fumarase removes the **left-hand C3 isotope**, the malate producing this fumarate must have **tritium on the right**.

The two requested Fischer projections therefore have terminal COO^- groups, C2 hydroxyl left/hydrogen right, and the following C3 substituents:

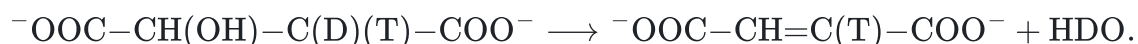
Tritium-retaining malate	C3 left	C3 right	Isomeric SMILES
(2 <i>S</i> , 3 <i>S</i>)-3-tritiomalate	H	T	<chem>O=C([O-])[C@@H](O)[C@H]([3H])C(=O)[O-]</chem>
(2 <i>S</i> , 3 <i>S</i>)-3-deuterio-3-tritiomalate	D	T	<chem>O=C([O-])[C@@H](O)[C@]([2H])([3H])C(=O)[O-]</chem>

At C3, the priority sequence is carboxyl carbon > C2 carbon > **T** > **H** or **D**, giving 3*S* in both cases.

The formal isotope-balanced dehydration equations are



and



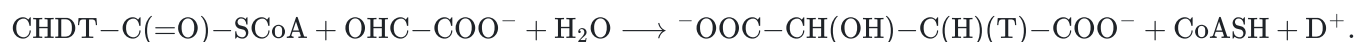
Here:

- Monotritiated fumarate is $O=C([O^-])/C([3H])=C/C(=O)[O^-]$.
- Monodeuterated water, **HDO**, is $[2H]O$.

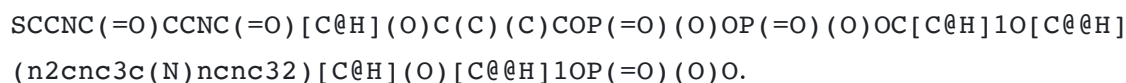
Both malates therefore give the same tritium-containing fumarate. The reported 79% retention locates the retained tritium but does **not** determine the separate amounts of these two malate isotopologues.

For completeness, with the carboxylate states used above, the synthesis balances can be written as $CHDT-C(=O)-SCoA + OHC-COO^- + H_2O \longrightarrow ^-OOC-CH(OH)-C(D)(T)-COO^- + CoASH + H^+$

or

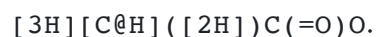


The proton and deuteron are $[\text{H}^+]$ and $[\text{2H}^+]$. Coenzyme A, CoASH, is:

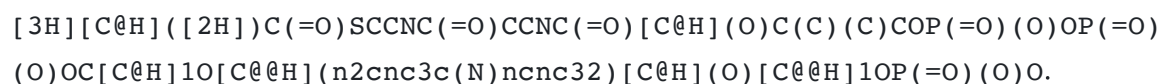


6.8 — Products from the *S*-labelled acetyl group

The opposite starting acid, (*S*)-[2-deuterio,2-tritio]acetic acid, is:



The corresponding *S*-labelled acetyl-CoA is:



In the intended stereospecific comparison, reversing the acetyl-group configuration reverses the isotope placement at C3. The enzyme still produces the *S* hydroxyl-bearing centre at C2.

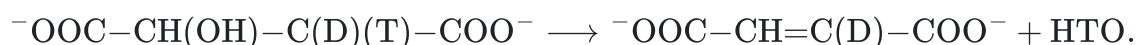
Thus the corresponding major malates are **C3 epimers**, with C2 hydroxyl left/hydrogen right and:

Malate	C3 left	C3 right	Isomeric SMILES
(2 <i>S</i> , 3 <i>R</i>)-3-tritiomalate	T	H	<chem>O=C([O-])[C@@H](O)[C@@H]([3H])C(=O)[O-]</chem>
(2 <i>S</i> , 3 <i>R</i>)-3-deuterio-3-tritiomalate	T	D	<chem>O=C([O-])[C@@H](O)[C@@]([2H])([3H])C(=O)[O-]</chem>

Fumarase now removes tritium:



or



Monotritiated water, HTO, is $[\text{3H}]\text{O}$. The fumarate products are therefore unlabelled fumarate or monodeuterofumarate, respectively; both are **untritiated**.

With unchanged branching fractions, the tritium-retaining and tritium-losing channels exchange:

$$f_{\text{T retained}}(S) = 1 - f_{\text{T retained}}(R) = 1 - 0.79 = 0.21.$$

Hence the expected fumarate distribution is

79% untritiated fumarate,	21% monotritiated fumarate.
---------------------------	-----------------------------

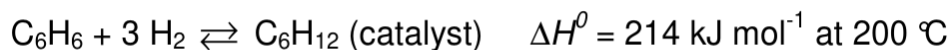
The problem does not specify how the untritiated fraction is divided between unlabelled and monodeuterated fumarate.

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

Problem 7: Hydrogenation of benzene in continuous reactors

In this problem tick the appropriate box in the tables of the answer sheet.

Hydrogenation of benzene to cyclohexane is performed in continuous reactors. The reaction is as follows:



Two basic types of continuous reactors are examined: a continuous plug flow reactor and a continuous stirred reactor.

The continuous plug flow reactor (Fig. 1)

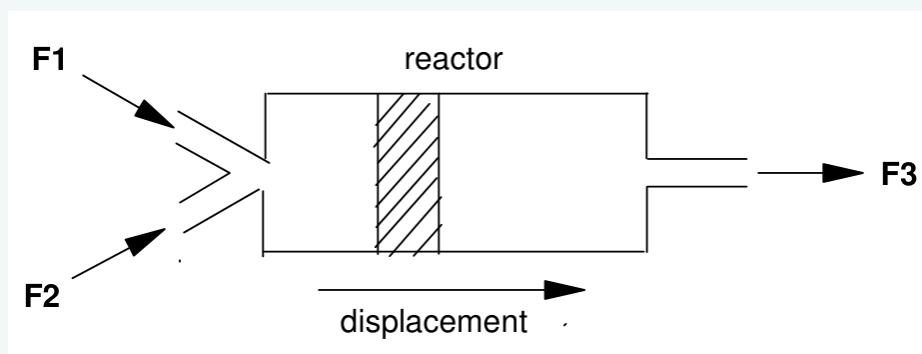


Fig. 1

The reagents are introduced and mixed at the inlet of the reactor (flow F1 and F2). Each slice of the reaction medium (marked zone in the diagram) moves along inside the plug flow reactor without mixing with the others and exits from the reactor (flow F3). When the flow has stabilized, concentrations and conditions are time-independent but dependent on the location in the reactor.

The continuous stirred reactor (Fig. 2)

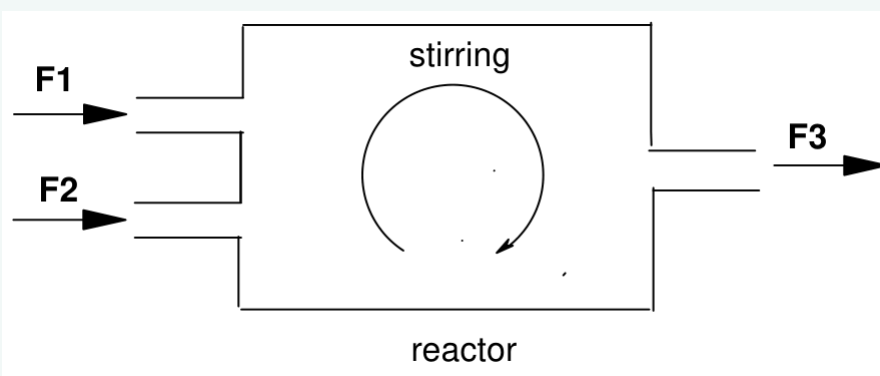


Fig. 2

The reagents are introduced into the reactor (flows F1 and F2). Inside the reactor they are stirred perfectly and instantaneously. When the flow is stabilized, concentrations and conditions are time-independent and identical at every point of the reactor.

The differential yield of hydrogenation ($\bar{Y}$) is given by

$$Y = -\frac{d([C_6H_{12}])}{d([C_6H_6])}.$$

The proportion of benzene already hydrogenated is given by

$$p = \frac{[C_6H_{12}]}{[C_6H_{12}] + [C_6H_6]}.$$

The relationship between p and Y is shown in Fig. 3.

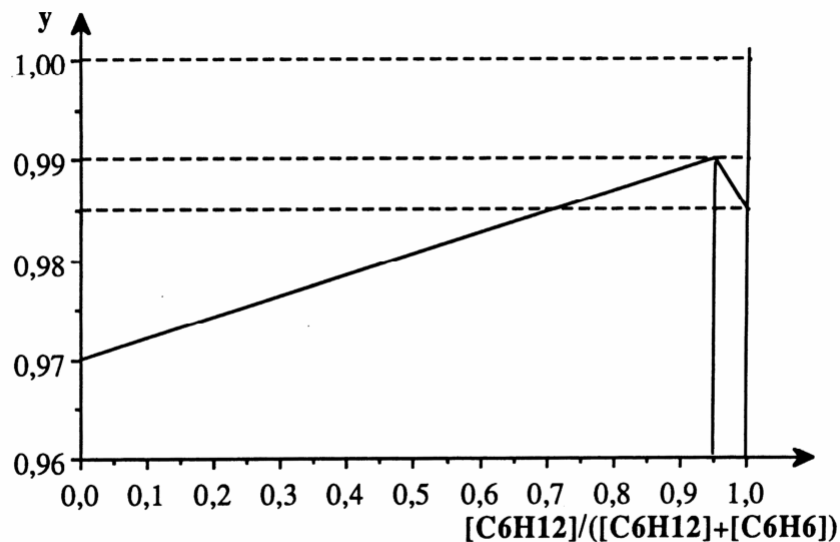


Fig. 3

The aim is to hydrogenate almost all the benzene, i.e. $0.9 \leq p \leq 1$ with the best mean yield

$$Y = -\frac{\Delta[C_6H_{12}]}{\Delta[C_6H_6]}.$$

7.1 What is the value of p in a continuous stirred reactor leading to the maximal mean yield of hydrogenation? What is the maximal value of Y ?

7.2 For a continuous plug flow reactor, give a rough value of Y for $0.9 \leq p \leq 1$:

$Y = 0.97, 0.98, 0.99$ or 1.00 ?

7.3 Represent by grey shading in the graph (Fig. 3) the quantities of benzene lost in installation P (plug flow reactor) and installation MP (stirred reactor + plug flow reactor).

7.4 Give the amount of annual benzene lost in installation P and MP assuming an annual consumption of 100 000 tons of benzene.

Official English text of the problem.

Answers

- 7.1:** $p \approx 0.95$; maximal mean yield $Y_{\max} \approx 0.99$, or **99%**.

- **7.2:** $Y \approx 0.98$, or **98%**.
- **7.3:** For **P**, shade between $Y = 1$ and the plotted curve over $0 \leq p \leq 1$. For **MP**, shade between $Y = 1$ and $Y = 0.99$ over $0 \leq p \leq 0.95$, then between $Y = 1$ and the descending plotted curve over $0.95 \leq p \leq 1$.
- **7.4:** Annual benzene losses are approximately 2.0×10^3 **tons for P** and 1.0×10^3 **tons for MP**.

Solution

The desired reaction is



The species are benzene `c1ccccc1`, hydrogen `[H][H]`, and cyclohexane `C1CCCCC1`. One mole of benzene gives one mole of cyclohexane in the desired reaction. Thus a differential yield below unity means that some consumed benzene does not appear as cyclohexane.

We write $\bar{Y}$ for the **mean yield**, distinguishing it from the differential yield $Y(p)$.

7.1

In a perfectly stirred reactor, the composition is uniform. All reaction therefore occurs at the same p , with the same differential yield. Consequently,

$$\bar{Y}_{\text{stirred}} = Y(p).$$

The maximum of the plotted curve occurs at approximately

$$p = 0.95, \quad \bar{Y}_{\text{max}} = 0.99.$$

7.2

In a plug flow reactor, each slice of material passes successively through compositions ranging from the inlet value $p = 0$ to the outlet value. Its mean yield therefore averages the differential yields encountered along that path.

More precisely, if X is the fraction of inlet benzene consumed,

$$\bar{Y}_P = \frac{1}{X_f} \int_0^{X_f} Y(p(X)) \, dX.$$

Because the yields are close to unity, $p \approx X$ is adequate for the graphical estimate requested. Over the principal rising section, the average yield is approximately

$$\bar{Y}_P \approx \frac{0.97 + 0.99}{2} = 0.98.$$

Moving the outlet within $0.9 \leq p \leq 1$ changes this only slightly. Hence the appropriate choice is

$$\bar{Y}_P \approx 0.98.$$

7.3

The quantity $1 - Y$ represents the fraction of an increment of consumed benzene that fails to give cyclohexane. Using $p \approx X$, its integral is the graphical estimate of the benzene loss.

For the comparison, take both installations to finish at $p = 1$, with the stirred stage of MP operated at its optimum $p = 0.95$.

- **Installation P:** Shade the entire region below the horizontal line $Y = 1$ and above the original yield curve, from $p = 0$ to $p = 1$. Its lower boundary rises from $(0, 0.97)$ to $(0.95, 0.99)$, then falls to $(1, 0.985)$.
- **Installation MP:** The stirred stage performs its reaction at $Y = 0.99$, so shade the rectangle bounded by $p = 0$, $p = 0.95$, $Y = 0.99$, and $Y = 1$. For the subsequent plug flow stage, add the region between $Y = 1$ and the descending curve from $p = 0.95$ to $p = 1$.

Equivalently, the MP shading is a strip of height 0.01 across the full interval $0 \leq p \leq 1$, together with a small triangle beneath it over $0.95 \leq p \leq 1$.

7.4

Reading the graph gives

$$Y(0) \approx 0.970, \quad Y(0.95) \approx 0.990, \quad Y(1) \approx 0.985.$$

For **P**, the shaded area consists of two trapezoids:

$$\begin{aligned} A_P &= \frac{(1 - 0.970) + (1 - 0.990)}{2} (0.95) \\ &\quad + \frac{(1 - 0.990) + (1 - 0.985)}{2} (0.05) \\ &= 0.019 + 0.000625 \\ &= 0.019625. \end{aligned}$$

The graphical estimate of the annual loss is therefore

$$m_{\text{loss,P}} \approx 100\,000 \text{ t yr}^{-1} \times 0.019625 = 1962.5 \text{ t yr}^{-1}.$$

At the accuracy warranted by the graph,

$$m_{\text{loss,P}} \approx 2.0 \times 10^3 \text{ t yr}^{-1}.$$

For **MP**, the shaded area is a rectangle followed by the same final trapezoid:

$$\begin{aligned} A_{\text{MP}} &= (1 - 0.990)(0.95) + \frac{(1 - 0.990) + (1 - 0.985)}{2} (0.05) \\ &= 0.0095 + 0.000625 \\ &= 0.010125. \end{aligned}$$

Thus

$$m_{\text{loss,MP}} \approx 100\,000 \text{ t yr}^{-1} \times 0.010125 = 1012.5 \text{ t yr}^{-1},$$

or appropriately rounded,

$$m_{\text{loss,MP}} \approx 1.0 \times 10^3 \text{ t yr}^{-1}.$$

These are masses of **benzene lost**, so no benzene-to-cyclohexane molar-mass conversion is required.

The shaded-area method is a small-loss approximation: strictly, p excludes material lost to other products and therefore differs slightly from the actual benzene conversion X . This distinction does not change the quoted rounded answers.

The solution was checked against the official solution.