

# IChO 2000

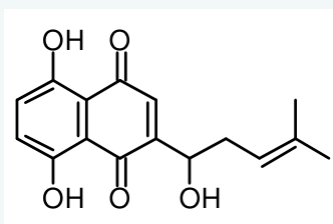
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## Problem 1: Synthesis of Compounds with Wound Healing Properties



Shikonin is a red compound found in the roots of the plant *Lithospermum erythrorhizon* which grows in Asia. Extracts of the root have been used for centuries in folk medicine and are used today in ointments for healing of wounds.



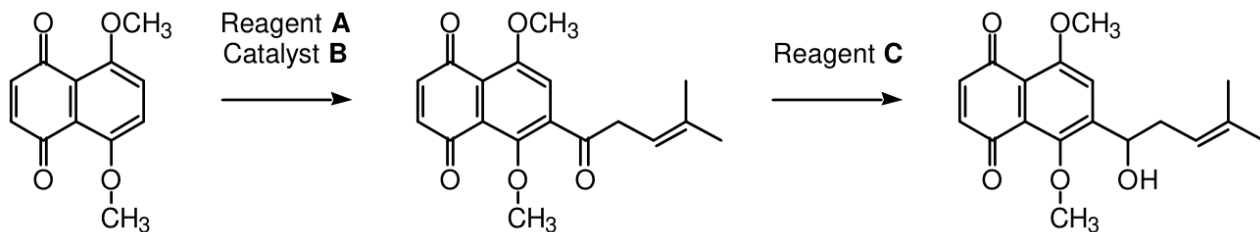
Shikonin

**1.1** How many stereoisomers of Shikonin are possible ?

**1.2** Do all stereoisomers of Shikonin have the same melting point? Mark with an X.

|     |    |
|-----|----|
| yes | no |
|-----|----|

The following sequence is part of a synthetic route to Shikonin:



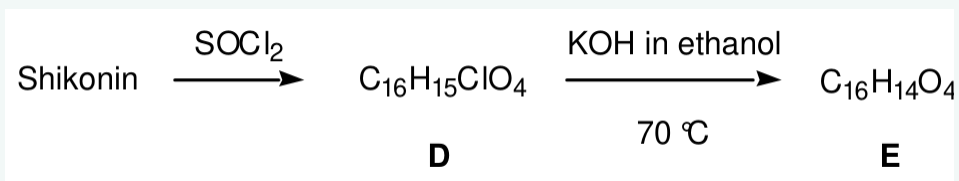
**1.3** Draw the structural formula of reagent **A**.

**1.4** Indicate (by means of an X in the appropriate check-box) the correct IUPAC name for reagent **A**.

|                                  |                          |
|----------------------------------|--------------------------|
| 2-Methyl-2-pentenoyl chloride    | <input type="checkbox"/> |
| 1-Chloro-4-methyl-3-pentene      | <input type="checkbox"/> |
| 4-Methyl-3-pentenoyl chloride    | <input type="checkbox"/> |
| 4-Methyl-3-pentene-1-ol          | <input type="checkbox"/> |
| 4,4-Dimethyl-3-butenoyl chloride | <input type="checkbox"/> |

**1.5** Write the molecular formula of reagent **C**.

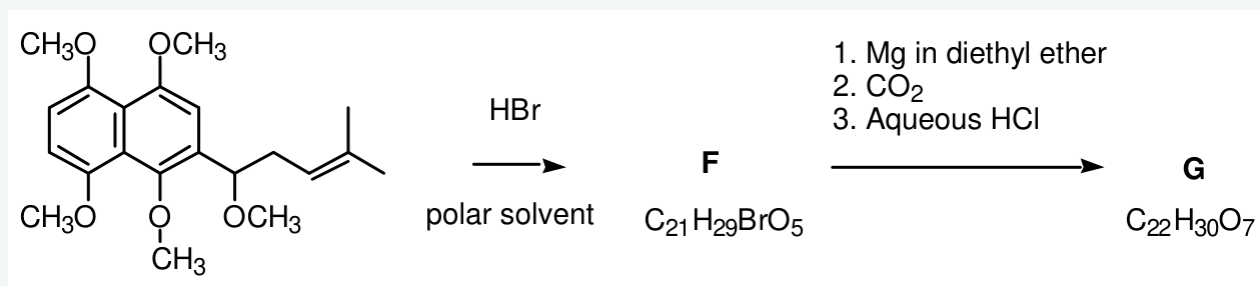
Numerous Shikonin analogues have been synthesized with a view to obtaining more potent compounds. One reaction sequence is shown below:



**1.6** Draw the structural formula of compound **E**.

**1.7** How many stereoisomers of compound **E**, if any, are possible

Another route to useful Shikonin analogues is the following:



**1.8** Draw the structural formula of compound **F**.

**1.9** Draw the structural formula of compound **G**.

Official English text of the problem.

## Answers

- **1.1: 2 stereoisomers**, forming an enantiomeric pair.
- **1.2: Yes.** Put an X under "yes."
- **1.3: A is 4-methylpent-3-enoyl chloride**,  $\text{ClC(=O)CH}_2\text{CH=C(CH}_3)_2$ . SMILES: CC(C)=CCC(=O)Cl.
- **1.4: Mark the third option: 4-Methyl-3-pentenoyl chloride.**
- **1.5: C:  $\text{NaBH}_4$ , sodium borohydride.** SMILES: [Na+].[BH4-].
- **1.6: E is 5,8-dihydroxy-2-(4-methylpenta-1,3-dien-1-yl)naphthalene-1,4-dione.** Its side chain is  $-\text{CH}=\text{CH}-\text{CH}=\text{C(CH}_3)_2$ . SMILES, with alkene configuration unspecified: O=C1C(C=CC=C(C)C)=CC(=O)c2c(O)ccc(O)c21.
- **1.7: 2 stereoisomers**, with (1*E*) and (1*Z*) configurations of the side-chain double bond nearest the ring.
- **1.8: F is 2-(4-bromo-1-methoxy-4-methylpentyl)-1,4,5,8-tetramethoxynaphthalene.** SMILES: COc1ccc(OC)c2c(OC)c(C(OC)CCC(Br)(C)C)cc(OC)c12.
- **1.9: G is 5-methoxy-2,2-dimethyl-5-(1,4,5,8-tetramethoxynaphthalen-2-yl)pentanoic acid.** SMILES: COc1ccc(OC)c2c(OC)c(C(OC)CCC(C)(C)C(=O)O)cc(OC)c12.

## Solution

### 1.1

The side-chain carbon carrying the alcoholic hydroxyl group has four different substituents:

- A hydroxyl group.
- A hydrogen atom.
- The substituted naphthoquinone ring.
- The remaining chain,  $-\text{CH}_2-\text{CH}=\text{C(CH}_3)_2$ .

It is therefore a stereogenic centre. There are no other stereogenic centres, and the side-chain alkene cannot have *E/Z* isomers because one of its carbons carries two identical methyl groups.

Thus,

$$N_{\text{stereoisomers}} = 2^1 = \boxed{2}.$$

The two configurations are:

| Stereoisomer                                | Isomeric SMILES                                             |
|---------------------------------------------|-------------------------------------------------------------|
| ( <i>R</i> )-Shikonin                       | <chem>O=C1C([C@H](O)CC=C(C)C)=CC(=O)c2c(O)ccc(O)c21</chem>  |
| ( <i>S</i> )-Shikonin, also called alkannin | <chem>O=C1C([C@@H](O)CC=C(C)C)=CC(=O)c2c(O)ccc(O)c21</chem> |

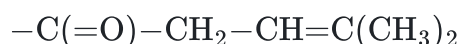
### 1.2

The two stereoisomers are enantiomers. Pure enantiomers have identical melting points under corresponding achiral conditions, so the answer is **yes**.

A racemic mixture can have a different melting point, but it is a mixture of these stereoisomers rather than an additional stereoisomer.

### 1.3

The first transformation introduces the group



onto the aromatic ring. This is a Friedel–Crafts acylation, so the required acid chloride is obtained by replacing the bond to the aromatic ring with chlorine:



This is **4-methylpent-3-enoyl chloride, A**, SMILES CC(C)=CCC(=O)Cl.

The starting material is **5,8-dimethoxynaphthalene-1,4-dione**, SMILES O=C1C=CC(=O)c2c(OC)ccc(OC)c21. The acylation product is **5,8-dimethoxy-6-(4-methylpent-3-enoyl)naphthalene-1,4-dione**, SMILES O=C1C=CC(=O)c2c(OC)c(C(=O)CC=C(C)C)cc(OC)c21.

The balanced equation is

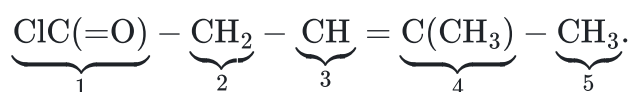


Catalyst **B** promotes electrophilic acylation. Replacement of an aromatic hydrogen by the acyl group releases hydrogen chloride, SMILES Cl.

For the requested drawing, show an acid chloride carbonyl bonded to  $\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)_2$ .

### 1.4

Number the chain from the acid chloride carbonyl carbon:



The parent chain has five carbons, the double bond begins at carbon 3, and the methyl substituent is at carbon 4.

Therefore, select **4-Methyl-3-pentenoyl chloride**, the third option. Its modern systematic form is **4-methylpent-3-enoyl chloride**.

### 1.5

The indicated net change is reduction of the side-chain ketone to a secondary alcohol:

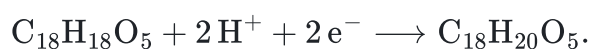


The conventional reagent assignment is **sodium borohydride**:



SMILES [Na+] . [BH4-].

Hydride addition to the carbonyl carbon gives an alkoxide; protonation gives the alcohol. The balanced organic reduction half-equation is



The product is **6-(1-hydroxy-4-methylpent-3-en-1-yl)-5,8-dimethoxynaphthalene-1,4-dione**, SMILES O=C1C=CC(=O)c2c(OC)c(C(O)CC=C(C)C)cc(OC)c21.

With achiral reagents and conditions, reduction creates a racemic pair at the new alcohol-bearing stereogenic centre.

## 1.6

Thionyl chloride,  $\text{SOCl}_2$ , SMILES O=S(Cl)Cl, replaces the side-chain alcoholic hydroxyl group with chlorine. This agrees with the formula given for **D**: replacing OH by Cl converts  $\text{C}_{16}\text{H}_{16}\text{O}_5$  into  $\text{C}_{16}\text{H}_{15}\text{ClO}_4$ .

Thus **D** is **2-(1-chloro-4-methylpent-3-en-1-yl)-5,8-dihydroxynaphthalene-1,4-dione**, SMILES O=C1C(C(Cl)CC=C(C)C)=CC(=O)c2c(O)ccc(O)c21.

The balanced substitution equation is



The gaseous by-products are sulfur dioxide,  $\text{O}=\text{S}=\text{O}$ , and hydrogen chloride,  $\text{HCl}$ .

Heating **D** with potassium hydroxide,  $[\text{K}^+] \cdot [\text{OH}^-]$ , in ethanol,  $\text{CCO}$ , eliminates hydrogen chloride across the first two side-chain carbons. Chlorine leaves the carbon adjacent to the ring, and hydrogen is removed from the neighbouring methylene carbon:



The balanced elimination equation is



The by-products are potassium chloride,  $[\text{K}^+] \cdot [\text{Cl}^-]$ , and water,  $\text{H}_2\text{O}$ .

Therefore, draw **E** by retaining the naphthoquinone ring and both phenolic hydroxyl groups, and replacing Shikonin's side chain with



The complete structure is **5,8-dihydroxy-2-(4-methylpenta-1,3-dien-1-yl)naphthalene-1,4-dione**, SMILES O=C1C(C=CC=C(C)C)=CC(=O)c2c(O)ccc(O)c21.

## 1.7

The newly formed double bond has two different substituents on each carbon:

- On its ring-side carbon: the naphthoquinone group and hydrogen.
- On its other carbon: the remaining unsaturated chain and hydrogen.

It therefore has *E/Z* stereoisomerism. The more distant double bond still has two identical methyl groups on one carbon, so it contributes no additional configurations. The original stereogenic centre has become planar.

Hence,

$$N_{\text{stereoisomers}} = 2.$$

| Stereoisomer of <b>E</b>                                                | Isomeric SMILES                                        |
|-------------------------------------------------------------------------|--------------------------------------------------------|
| 5,8-Dihydroxy-2-[(1E)-4-methylpenta-1,3-dien-1-yl]naphthalene-1,4-dione | <chem>O=C1C(/C=C/C=C(C)C)=CC(=O)c2c(O)ccc(O)c21</chem> |
| 5,8-Dihydroxy-2-[(1Z)-4-methylpenta-1,3-dien-1-yl]naphthalene-1,4-dione | <chem>O=C1C(/C=C\C=C(C)C)=CC(=O)c2c(O)ccc(O)c21</chem> |

In the *E* drawing, the ring and the remaining chain lie on opposite sides of the new double bond; in the *Z* drawing, they lie on the same side. Rotation about the intervening single bond gives conformers, which are not additional configurational stereoisomers.

## 1.8

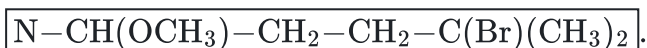
Let *N* denote the **1,4,5,8-tetramethoxynaphthalen-2-yl** group.

The starting compound is **1,4,5,8-tetramethoxy-2-(1-methoxy-4-methylpent-3-en-1-yl)naphthalene**, SMILES COc1ccc(OC)c2c(OC)c(C(OC)CC=C(C)C)cc(OC)c12. Its side chain is

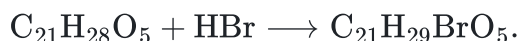


Hydrogen bromide,  $\text{HBr}$ , adds ionically to the alkene in the stated polar solvent. Protonation places the positive charge on the carbon bearing two methyl groups, giving the more stable tertiary carbocation. Bromide,  $[\text{Br}^-]$ , then bonds to that carbon.

The Markovnikov product therefore has the side chain



The balanced equation is



This matches the supplied formula for **F**. In particular, the unchanged carbon and oxygen counts support addition of hydrogen bromide with retention of all five methoxy groups.

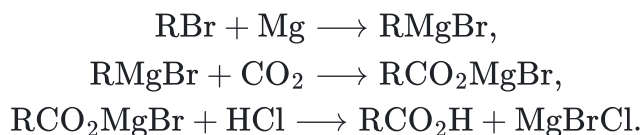
Thus **F** is **2-(4-bromo-1-methoxy-4-methylpentyl)-1,4,5,8-tetramethoxynaphthalene**, SMILES COc1ccc(OC)c2c(OC)c(C(OC)CCC(Br)(C)C)cc(OC)c12.

For the drawing, replace the original side-chain double bond by a single bond, place bromine on the carbon bearing the two methyl groups, and add hydrogen to the other alkene carbon.

## 1.9

Magnesium inserts into the carbon–bromine bond to form a Grignard reagent. Reaction with carbon dioxide creates a carbon–carbon bond to the carbon dioxide carbon; aqueous acid then gives the carboxylic acid.

Writing *R* for the organic group remaining when bromine is removed from **F**, the balanced steps are



The relevant intermediates can be represented formally as:

| Intermediate                                     | SMILES                                                                |
|--------------------------------------------------|-----------------------------------------------------------------------|
| The alkylmagnesium bromide derived from <b>F</b> | <chem>COc1ccc(OC)c2c(OC)c(C(OC)CCC(C)(C)[Mg]Br)cc(OC)c12</chem>       |
| Its magnesium bromide carboxylate                | <chem>COc1ccc(OC)c2c(OC)c(C(OC)CCC(C)(C)C(=O)O[Mg]Br)cc(OC)c12</chem> |

These SMILES show formal connectivity. They do not specify the ether coordination or aggregation present in a Grignard solution. Diethyl ether is CCOCC; carbon dioxide is O=C=O.

The overall balanced equation is



where the mixed magnesium halide can be represented ionically as  $[\text{Mg}^{+2}] \cdot [\text{Br}^-] \cdot [\text{Cl}^-]$ .

Consequently, the product side chain is



The extra carbon and two extra oxygen atoms come from carbon dioxide; protonation supplies the additional hydrogen. This gives precisely the stated formula,  $\text{C}_{22}\text{H}_{30}\text{O}_7$ .

Thus **G** is **5-methoxy-2,2-dimethyl-5-(1,4,5,8-tetramethoxynaphthalen-2-yl)pentanoic acid**,  
SMILES COC1CCC(OC)C2C(OC)C(C(OC)CCC(C)(C)C(=O)O)CC(OC)C12.

The starting methoxy-bearing stereogenic centre is unspecified in the supplied drawing, so it is also left unspecified in the SMILES for **F** and **G**. The carbon bearing two methyl groups is not stereogenic.

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The solution was checked against the official solution.

## Problem 2: Bridge between Denmark and Sweden



On July 1, 2000, the combined tunnel and bridge connecting Denmark and Sweden was officially opened. It consists of a tunnel from Copenhagen to an artificial island, and a bridge from the island to Malmö in Sweden. The major construction materials employed are concrete and steel. This problem deals with chemical reactions relating to production and degradation of such materials.

Concrete is produced from a mixture of cement, water, sand and small stones. Cement consists primarily of calcium silicates and calcium aluminates formed by heating and grinding of clay and limestone. In the later steps of cement production a small amount of gypsum,  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ , is added to improve subsequent hardening of the concrete. The use of elevated temperatures during the final production may lead to formation of unwanted hemihydrate,  $\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$ . Consider the following reaction:



The following thermodynamic data apply at 25 °C, standard pressure: 1.00 bar:

| Compound                                                      | $\Delta_f H^\circ$ (kJ mol <sup>-1</sup> ) | $S^\circ$ (J K <sup>-1</sup> mol <sup>-1</sup> ) |
|---------------------------------------------------------------|--------------------------------------------|--------------------------------------------------|
| $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}(\text{s})$           | -2021.0                                    | 194.0                                            |
| $\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}(\text{s})$ | -1575.0                                    | 130.5                                            |
| $\text{H}_2\text{O}(\text{g})$                                | -241.8                                     | 188.6                                            |

Gas constant:  $R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1} = 0.08314 \text{ L bar mol}^{-1} \text{ K}^{-1}$

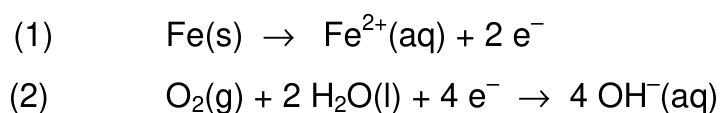
0 °C = 273.15 K.

**2.1** Calculate  $\Delta H^\circ$  (in kJ) for transformation of 1.00 kg of  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}(\text{s})$  to hemihydrate  $\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}(\text{s})$ . Is this reaction endothermic or is it exothermic?

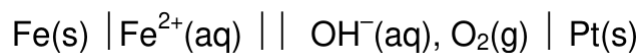
**2.2** Calculate the equilibrium pressure (in bar) of water vapour in a closed vessel containing  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}(\text{s})$ ,  $\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}(\text{s})$  and  $\text{H}_2\text{O}(\text{g})$  at 25 °C.

**2.3** Calculate the temperature at which the equilibrium water vapour pressure is 1.00 bar in the system described in problem 2-2. Assume that  $\Delta H^\circ$  and  $\Delta S^\circ$  are temperature independent.

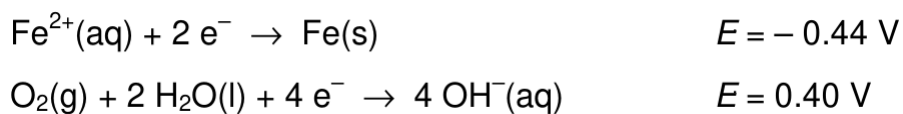
Corrosion of metals is associated with electrochemical reactions. This also applies for the formation of rust on iron surfaces, where the initial electrode reactions usually are:



An electrochemical cell in which these electrode reactions take place is constructed. The temperature is 25 °C. The cell is represented by the following cell diagram:



Standard electrode potentials (at 25 °C):



Nernst factor:  $RT \ln 10 / F = 0.05916 \text{ volt}$  (at 25 °C)

Faraday constant:  $F = 96485 \text{ C mol}^{-1}$

2.4 Calculate the standard electromotive force (the standard cell voltage),  $E^\circ$ , at 25 °C.

2.5 Write down the overall reaction which takes place during discharge of the cell under standard conditions.

2.6 Calculate the equilibrium constant at 25 °C for the overall cell reaction.

2.7 The overall reaction referred to above is allowed to proceed for 24 hours under standard conditions and at a constant current of 0.12 A. Calculate the mass of Fe converted to  $\text{Fe}^{2+}$  after 24 hours. Oxygen and water may be assumed to be present in excess.

2.8 Calculate  $E$  for the cell at 25 °C for the following conditions :

$$[\text{Fe}^{2+}] = 0.015 \text{ M}, \quad \text{pH}_{\text{right-hand half-cell}} = 9.00, \quad p(\text{O}_2) = 0.700 \text{ bar}.$$

Official English text of the problem.

## Answers

- 2.1:  $\Delta H^\circ = +484 \text{ kJ}$  for 1.00 kg of gypsum; the reaction is **endothermic**.
- 2.2:  $p(\text{H}_2\text{O}) = 8.15 \times 10^{-3} \text{ bar}$ .
- 2.3:  $T = 379.7 \text{ K} = 106.5 \text{ }^\circ\text{C}$ .
- 2.4:  $E^\circ = 0.84 \text{ V}$ .
- 2.5:  $2 \text{ Fe(s)} + \text{O}_2(\text{g}) + 2 \text{ H}_2\text{O(l)} \longrightarrow 2 \text{ Fe}^{2+}(\text{aq}) + 4 \text{ OH}^-(\text{aq})$ .
- 2.6:  $K = 6.2 \times 10^{56}$ , dimensionless, for the reaction written in 2.5.
- 2.7:  $m(\text{Fe}) = 3.0 \text{ g}$ .
- 2.8:  $E = 1.19 \text{ V}$ .

## Solution

The chemical identities used throughout are:

| Substance or species                                  | Name                               | SMILES                                              |
|-------------------------------------------------------|------------------------------------|-----------------------------------------------------|
| $\text{CaSO}_4 \cdot 2 \text{ H}_2\text{O}$           | Calcium sulfate dihydrate (gypsum) | [Ca+2].[O-]S(=O)(=O)[O-].O.O                        |
| $\text{CaSO}_4 \cdot \frac{1}{2} \text{ H}_2\text{O}$ | Calcium sulfate hemihydrate        | [Ca+2].[O-]S(=O)(=O)[O-].[Ca+2].[O-]S(=O)(=O)[O-].O |
| $\text{H}_2\text{O}$                                  | Water                              | O                                                   |
| $\text{O}_2$                                          | Dioxygen                           | O=O                                                 |
| $\text{Fe}^{2+}$                                      | Iron(II) ion                       | [Fe+2]                                              |
| $\text{OH}^-$                                         | Hydroxide ion                      | [OH-]                                               |
| Fe                                                    | Iron                               | [Fe]                                                |
| Pt                                                    | Platinum                           | [Pt]                                                |

The hydrate SMILES specify components, not crystal packing or coordination geometry. The hemihydrate entry represents **two formula units**, giving one water molecule. Atom SMILES do not describe metallic lattices, and SMILES do not specify physical phases.

## 2.1

The dehydration reaction is



Using formation enthalpies,

$$\begin{aligned} \Delta_r H^\circ &= \sum \nu \Delta_f H^\circ_{\text{products}} - \sum \nu \Delta_f H^\circ_{\text{reactants}} \\ &= (-1575.0) + \frac{3}{2}(-241.8) - (-2021.0) \\ &= +83.3 \text{ kJ mol}^{-1}. \end{aligned}$$

Using conventional atomic molar masses,

$$M(\text{CaSO}_4 \cdot 2 \text{H}_2\text{O}) = 40.08 + 32.06 + 4(16.00) + 2[2(1.008) + 16.00] = 172.172 \text{ g mol}^{-1}.$$

Therefore,

$$n = \frac{1000 \text{ g}}{172.172 \text{ g mol}^{-1}} = 5.808 \text{ mol},$$

and

$$\Delta H^\circ = (5.808 \text{ mol})(83.3 \text{ kJ mol}^{-1}) = \boxed{+484 \text{ kJ}}.$$

The positive enthalpy change means that heat is absorbed: the reaction is **endothermic**.

## 2.2

For the same reaction,

$$\begin{aligned} \Delta_r S^\circ &= 130.5 + \frac{3}{2}(188.6) - 194.0 \\ &= 219.4 \text{ J K}^{-1} \text{ mol}^{-1}. \end{aligned}$$

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

$$\begin{aligned} \Delta_r G^\circ &= \Delta_r H^\circ - T \Delta_r S^\circ \\ &= 83300 - (298.15)(219.4) \\ &= 17885.9 \text{ J mol}^{-1}. \end{aligned}$$

Hence the dimensionless equilibrium constant is

$$K_p = \exp\left(-\frac{\Delta_r G^\circ}{RT}\right) = \exp\left[-\frac{17885.9}{(8.314)(298.15)}\right] = 7.35 \times 10^{-4}.$$

Both pure solids have unit activity. Treating the vapour as an ideal gas,

$$K_p = \left(\frac{p(\text{H}_2\text{O})}{p^\circ}\right)^{3/2}, \quad p^\circ = 1.00 \text{ bar}.$$

Thus,

$$p(\text{H}_2\text{O}) = p^\circ K_p^{2/3} = (1.00 \text{ bar})(7.35 \times 10^{-4})^{2/3} = \boxed{8.15 \times 10^{-3} \text{ bar}}.$$

## 2.3

When the equilibrium water vapour pressure equals the standard pressure,

$$K_p = \left( \frac{1.00 \text{ bar}}{1.00 \text{ bar}} \right)^{3/2} = 1.$$

Consequently,  $\Delta_r G^\circ = -RT \ln K_p = 0$ . With temperature-independent enthalpy and entropy,

$$0 = \Delta_r H^\circ - T \Delta_r S^\circ,$$

so

$$T = \frac{\Delta_r H^\circ}{\Delta_r S^\circ} = \frac{83300 \text{ J mol}^{-1}}{219.4 \text{ J K}^{-1} \text{ mol}^{-1}} = 379.67 \text{ K}.$$

Therefore,

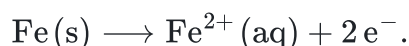
$$\boxed{T = 379.7 \text{ K} = 106.5^\circ \text{C}}.$$

## 2.4

The oxygen reduction couple has the more positive standard reduction potential, so oxygen is reduced at the cathode:



Iron is oxidized at the anode:



The tabulated **reduction** potential for the iron couple is  $-0.44 \text{ V}$ . Thus,

$$E_{\text{cell}}^\circ = E_{\text{cathode}}^\circ - E_{\text{anode, reduction}}^\circ = 0.40 - (-0.44) = \boxed{0.84 \text{ V}}.$$

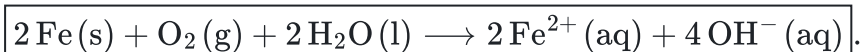
Electrode potentials are not multiplied when half-reactions are multiplied to balance electrons.

## 2.5

Multiplying the iron oxidation half-reaction by two gives



Adding the oxygen reduction half-reaction cancels four electrons:



Both atoms and total charge are balanced. The positive standard cell voltage establishes this as the spontaneous discharge direction under standard conditions.

## 2.6

For the overall reaction as written in **2.5**,  $n = 4$  mol of electrons are transferred per mole of reaction. Combining

$$\Delta_r G^\circ = -nFE^\circ \quad \text{and} \quad \Delta_r G^\circ = -RT \ln K$$

gives

$$\log_{10} K = \frac{nFE^\circ}{RT \ln 10} = \frac{nE^\circ}{0.05916 \text{ V}}.$$

Therefore,

$$\log_{10} K = \frac{4(0.84)}{0.05916} = 56.795,$$

and

$$K = 10^{56.795} \approx 6.2 \times 10^{56}.$$

This dimensionless value corresponds specifically to the equation with two iron atoms in **2.5**.

## 2.7

The charge passed is

$$q = It = (0.12 \text{ C s}^{-1})(24 \times 3600 \text{ s}) = 10368 \text{ C}.$$

Each mole of iron converted to iron(II) releases two moles of electrons, so

$$n(\text{Fe}) = \frac{q}{2F} = \frac{10368 \text{ C}}{2(96485 \text{ C mol}^{-1})} = 0.0537286 \text{ mol}.$$

Using  $M(\text{Fe}) = 55.85 \text{ g mol}^{-1}$ ,

$$m(\text{Fe}) = (0.0537286)(55.85) \text{ g} = 3.0007 \text{ g}.$$

To the precision of the current,

$$m(\text{Fe}) = 3.0 \text{ g}.$$

## 2.8

At 25 °C, using  $\text{p}K_{\text{w}} = 14.00$ ,

$$\text{pOH} = 14.00 - \text{pH} = 14.00 - 9.00 = 5.00,$$

so

$$[\text{OH}^{-}] = 10^{-5.00} \text{ mol L}^{-1}.$$

For the overall reaction in **2.5**, the reaction quotient is

$$Q = \frac{a(\text{Fe}^{2+})^2 a(\text{OH}^{-})^4}{p(\text{O}_2)/p^{\circ}}.$$

Pure iron and liquid water have unit activity. Approximating dissolved-ion activities by their concentrations divided by  $c^{\circ} = 1 \text{ mol L}^{-1}$ ,

$$Q = \frac{(0.015)^2 (10^{-5})^4}{0.700} = 3.2143 \times 10^{-24}.$$

The Nernst equation, with  $n = 4$ , gives

$$\begin{aligned} E &= E^{\circ} - \frac{0.05916 \text{ V}}{4} \log_{10} Q \\ &= 0.84 \text{ V} - \frac{0.05916 \text{ V}}{4} \log_{10}(3.2143 \times 10^{-24}) \\ &= 0.84 \text{ V} + 0.34746 \text{ V} \\ &= 1.18746 \text{ V}. \end{aligned}$$

Thus,

$$E = 1.19 \text{ V}.$$

The solution was checked against the official solution.

## Problem 3: Bioinorganic Chemistry

The square planar complex *cis*-diammine dichloroplatinum(II) is an important drug for the treatment of certain cancers.

**3.1** Draw the structures of *cis*- and *trans*-diammine dichloroplatinum(II) and label each structure as *cis* or *trans*.

A number of ionic compounds also have the empirical formula  $\text{Pt}(\text{NH}_3)_2\text{Cl}_2$ .

**3.2** Write molecular formulas for all possible ionic compounds which comply with the following conditions: each compound has

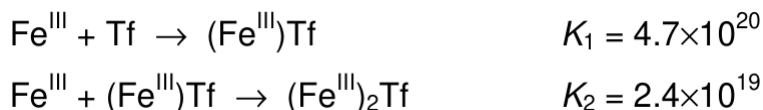
1) empirical formula  $\text{Pt}(\text{NH}_3)_2\text{Cl}_2$ , 2) an anion and a cation and is composed of discrete, monomeric square planar platinum(II) complex, 3) only one type of cation and one type of anion. The answer must clearly reveal the composition of each discrete platinum(II) complex entity in each compound

**3.3** How many *5d* electrons are there in the platinum(II) ion?

The valence d-orbital energy splitting diagram for a square planar complex can be regarded as being derived from that for an octahedral complex in which the metal-ligand interactions due to the two ligands coordinated along the *z* axis vanish, while the bonds to the four remaining ligands (coordinated along the *x* and *y* axes) become stronger.

**3.4** Which of the five *5d* orbitals attain the highest energy (*i. e.* is the least likely to be occupied by electrons) in the general case of a square-planar  $\text{Pt}(\text{II})$  complex?

Serum transferrin (abbreviated: Tf) is a monomeric protein whose main function in the human body is the transport of iron(III). Each transferrin molecule can bind up to two iron(III) ions with stepwise binding constants  $K_1$  and  $K_2$  at biological conditions except that the temperature is  $25^\circ\text{C}$  corresponding to the reactions:



In the diferric protein,  $(\text{Fe}^{\text{III}})_2\text{Tf}$ , the two iron(III) ions are bound at two similar, but non-identical sites, and the two possible monoferric protein products,  $(\text{Fe}^{\text{III}})\text{Tf}$ , can be denoted  $\{\text{Fe}^{\text{III}} \cdot \text{Tf}\}$  and  $\{\text{Tf} \cdot \text{Fe}^{\text{III}}\}$ . Their relative abundance at equilibrium is given by the constant

$$K = [\{\text{Tf} \cdot \text{Fe}^{\text{III}}\}] [\{\text{Fe}^{\text{III}} \cdot \text{Tf}\}]^{-1} = 5.9.$$

**3.5** Calculate the values of the two constants  $K'_1 = [\{\text{Fe}^{\text{III}} \cdot \text{Tf}\}] [\text{Fe}^{\text{III}}]^{-1} [\text{Tf}]^{-1}$  and  $K''_1 = [\{\text{Tf} \cdot \text{Fe}^{\text{III}}\}] [\text{Fe}^{\text{III}}]^{-1} [\text{Tf}]^{-1}$ , respectively, corresponding to the formation of each monoferric form of transferrin.

**3.6** Calculate the values of the two constants  $K'_2 = [(\text{Fe}^{\text{III}})_2\text{Tf}] [\text{Fe}^{\text{III}}]^{-1} [\{\text{Fe}^{\text{III}} \cdot \text{Tf}\}]^{-1}$  and  $K''_2 = [(\text{Fe}^{\text{III}})_2\text{Tf}] [\text{Fe}^{\text{III}}]^{-1} [\{\text{Tf} \cdot \text{Fe}^{\text{III}}\}]^{-1}$  respectively, corresponding to the formation of diferric transferrin from each of the monoferric forms.

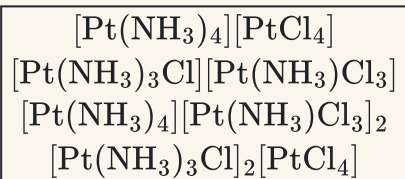
The bound iron(III) ion at each binding site is surrounded by six donor atoms from various ligands. Thus, two oxygen atoms of a carbonate anion coordinate to the metal, and the following amino acid side chains from the protein primary structure also coordinate to the iron(III) ion with one potential donor atom each: one aspartate, one histidine and two tyrosine residues.

**3.7** What is the total number of oxygen donor atoms that surround a 6-coordinate iron(III) ion in transferrin?

Official English text of the problem.

## Answers

- **3.1:** Both complexes are square planar. In **cisplatin**, the two ammine ligands are adjacent, at  $90^\circ$ ; in **transplatin**, they are opposite, at  $180^\circ$ . Their stereochemical SMILES are given in the solution.
- **3.2:** There are **four** ionic compounds:



- **3.3:**  $\boxed{8}$  electrons: platinum(II) is  $5d^8$ .
- **3.4:**  $\boxed{5d_{x^2-y^2}}$ .
- **3.5:**  $\boxed{K'_1 = 6.8 \times 10^{19} \text{ L mol}^{-1}}, \boxed{K''_1 = 4.0 \times 10^{20} \text{ L mol}^{-1}}$ .
- **3.6:**  $\boxed{K'_2 = 1.7 \times 10^{20} \text{ L mol}^{-1}}, \boxed{K''_2 = 2.8 \times 10^{19} \text{ L mol}^{-1}}$ .
- **3.7:**  $\boxed{5}$  oxygen donor atoms.

## Solution

### 3.1 — The two geometrical isomers

The ligands are ammonia,  $\text{NH}_3$ , SMILES  $\text{N}$ , and chloride,  $\text{Cl}^-$ , SMILES  $[\text{Cl-}]$ . Both complexes have four-coordinate, square-planar platinum(II).

- **cis-Diamminedichloridoplatinum(II), cisplatin:**

SMILES:  $[\text{NH}_3] \rightarrow [\text{Pt@SP1+2}] (<-[\text{NH}_3]) (<-[\text{Cl-}]) <-[\text{Cl-}]$

Draw platinum at the centre of a square, with ammonia ligands above and to the right, and chloride ligands below and to the left. The two ammonia ligands are adjacent; the two chloride ligands are also adjacent.

- **trans-Diamminedichloridoplatinum(II), transplatin:**

SMILES: [NH3]->[Pt@SP2+2](<-[NH3])(<-[Cl-])<-[Cl-]

Draw platinum at the centre, with ammonia ligands above and below, and chloride ligands to the left and right. Each pair of identical ligands is opposite.

All four platinum–donor bonds lie in one plane. In these coordination SMILES, arrows denote ligand-to-metal dative bonds, and the @SP descriptors specify square-planar stereochemistry for the written neighbour order.

### 3.2 — Enumeration of the ionic compounds

A monomeric square-planar complex has four donor ligands. With  $n$  neutral ammonia ligands and  $4 - n$  chloride ligands, its composition and charge are

$$[\text{Pt}(\text{NH}_3)_n\text{Cl}_{4-n}]^{n-2},$$

because platinum contributes +2 and each chloride contributes −1.

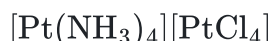
The charged possibilities are therefore:

| $n$ | Complex ion                             | Name                           | SMILES                                                          |
|-----|-----------------------------------------|--------------------------------|-----------------------------------------------------------------|
| 4   | $[\text{Pt}(\text{NH}_3)_4]^{2+}$       | Tetraammineplatinum(II)        | <chem>[NH3]-&gt;[Pt+2](&lt;-[NH3])(&lt;-[NH3])&lt;-[NH3]</chem> |
| 3   | $[\text{Pt}(\text{NH}_3)_3\text{Cl}]^+$ | Triamminechloridoplatinum(II)  | <chem>[NH3]-&gt;[Pt+2](&lt;-[NH3])(&lt;-[NH3])&lt;-[Cl-]</chem> |
| 1   | $[\text{Pt}(\text{NH}_3)\text{Cl}_3]^-$ | Amminetrichloridoplatinate(II) | <chem>[NH3]-&gt;[Pt+2](&lt;-[Cl-])(&lt;-[Cl-])&lt;-[Cl-]</chem> |
| 0   | $[\text{PtCl}_4]^{2-}$                  | Tetrachloridoplatinate(II)     | <chem>[Cl-]-&gt;[Pt+2](&lt;-[Cl-])(&lt;-[Cl-])&lt;-[Cl-]</chem> |

The  $n = 2$  complex is neutral and cannot itself supply either required ion.

There are two possible cations and two possible anions. Pairing each cation with each anion and imposing electrical neutrality gives exactly four salts:

#### 1. Tetraammineplatinum(II) tetrachloridoplatinate(II)



SMILES: [NH3]->[Pt+2](<-[NH3])(<-[NH3])<-[NH3].[Cl-]->[Pt+2](<-[Cl-])(<-[Cl-])<-[Cl-]

#### 2. Triamminechloridoplatinum(II) amminetrichloridoplatinate(II)



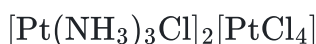
SMILES: [NH3]->[Pt+2](<-[NH3])(<-[NH3])<-[Cl-].[NH3]->[Pt+2](<-[Cl-])(<-[Cl-])<-[Cl-]

#### 3. Tetraammineplatinum(II) bis(amminetrichloridoplatinate(II))



SMILES: [NH3]->[Pt+2](<-[NH3])(<-[NH3])<-[NH3].[NH3]->[Pt+2](<-[Cl-])(<-[Cl-])<-[Cl-].[NH3]->[Pt+2](<-[Cl-])(<-[Cl-])<-[Cl-]

#### 4. Bis(triamminechloridoplatinum(II)) tetrachloridoplatinate(II)



SMILES: [NH3]->[Pt+2](<-[NH3])(<-[NH3])<-[Cl-].[NH3]->[Pt+2](<-[NH3])(<-[NH3])<-[Cl-].[Cl-]->[Pt+2](<-[Cl-])(<-[Cl-])<-[Cl-]

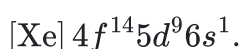
The first two contain platinum, ammonia and chloride in the ratio 2 : 4 : 4; the last two have the ratio 3 : 6 : 6. Both reduce to the required empirical ratio 1 : 2 : 2.

This enumeration is exhaustive within the stated ligand inventory: the empirical formula supplies exactly four monodentate ligands per platinum, so all must be coordinated to maintain four-coordinate, monomeric complexes. All platinum centres above are square planar; dots in the salt SMILES separate the ions.

### 3.3 — Number of 5d electrons

The platinum(II) ion,  $\text{Pt}^{2+}$ , has SMILES [Pt+2].

Neutral platinum has ground-state electron configuration



Removing the 6s electron and one 5d electron gives



Thus the ion has **eight 5d electrons**.

### 3.4 — Highest-energy orbital

The four ligands lie along the  $x$  and  $y$  axes. The lobes of  $d_{x^2-y^2}$  point directly towards them, producing the strongest ligand–metal  $\sigma$ -antibonding interaction.

Removing the axial ligands reduces the interactions involving the  $z$  direction, while strengthening the four in-plane bonds raises the  $d_{x^2-y^2}$ -derived level particularly strongly. Therefore,

|                                           |
|-------------------------------------------|
| highest-energy orbital = $5d_{x^2-y^2}$ . |
|-------------------------------------------|

For square-planar  $5d^8$  platinum(II), this orbital is normally unoccupied.

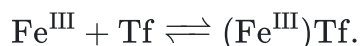
### 3.5 — Binding constants for the two monoferric forms

The iron(III) ion is  $\text{Fe}^{3+}$ , SMILES [Fe+3]. We retain the problem's  $\text{Fe}^{\text{III}}$  notation and its protein shorthand. Full SMILES for transferrin and its iron complexes cannot be reconstructed from the supplied text, which gives neither a protein sequence nor a complete molecular structure.

Define the concentrations

$$a = [\{\text{Fe}^{\text{III}} \cdot \text{Tf}\}], \quad b = [\{\text{Tf} \cdot \text{Fe}^{\text{III}}\}], \quad f = [\text{Fe}^{\text{III}}], \quad t = [\text{Tf}].$$

The first macroscopic binding step is



Its product concentration includes **both** monoferric forms. Consequently,

$$K_1 = \frac{a+b}{ft} = K'_1 + K''_1.$$

The given abundance ratio also gives

$$K = \frac{b}{a} = \frac{K''_1}{K'_1} = 5.9.$$

Combining these relationships,

$$K_1' = \frac{K_1}{1 + K}, \quad K_1'' = \frac{KK_1}{1 + K}.$$

Using  $K_1 = 4.7 \times 10^{20}$ ,

$$K_1' = \frac{4.7 \times 10^{20}}{6.9} = 6.8116 \times 10^{19} \simeq \boxed{6.8 \times 10^{19} \text{ L mol}^{-1}},$$

$$K_1'' = \frac{5.9(4.7 \times 10^{20})}{6.9} = 4.0188 \times 10^{20} \simeq \boxed{4.0 \times 10^{20} \text{ L mol}^{-1}}.$$

For the concentration-based definitions in the question, concentrations in  $\text{mol L}^{-1}$  give binding constants in  $\text{L mol}^{-1}$ . The abundance ratio  $K$  is dimensionless.

### 3.6 — Binding constants for formation of diferric transferrin

Let

$$d = [(\text{Fe}^{\text{III}})_2\text{Tf}].$$

The second macroscopic binding step is



so

$$K_2 = \frac{d}{f(a+b)}.$$

The two microscopic constants refer to the individual monoferric reactants:

$$K_2' = \frac{d}{fa}, \quad K_2'' = \frac{d}{fb}.$$

Since  $b/a = K$ ,

$$K_2' = K_2 \frac{a+b}{a} = K_2(1+K),$$

and

$$K_2'' = K_2 \frac{a+b}{b} = K_2 \frac{1+K}{K}.$$

Using  $K_2 = 2.4 \times 10^{19}$ ,

$$K_2' = (2.4 \times 10^{19})(6.9) = 1.656 \times 10^{20} \simeq \boxed{1.7 \times 10^{20} \text{ L mol}^{-1}},$$

$$K_2'' = (2.4 \times 10^{19}) \frac{6.9}{5.9} = 2.8068 \times 10^{19} \simeq \boxed{2.8 \times 10^{19} \text{ L mol}^{-1}}.$$

As a consistency check, either microscopic binding path must give the same overall equilibrium constant:

$$\boxed{K_1'K_2' = K_1''K_2'' = K_1K_2}.$$

This derivation does not require an assumption that the two binding sites are independent.

### 3.7 — Oxygen donor count

The donor contributions are:

| Ligand or residue                                    | SMILES                                 | Donor atoms at one iron centre |
|------------------------------------------------------|----------------------------------------|--------------------------------|
| Carbonate ion, $\text{CO}_3^{2-}$                    | <chem>O=C([O-])[O-]</chem>             | Two oxygen atoms               |
| Aspartate side chain                                 | <chem>*CC(=O)[O-]</chem>               | One carboxylate oxygen         |
| Histidine side chain                                 | <chem>*Cc1cnc[nH]1</chem>              | One imidazole nitrogen         |
| Two tyrosine side chains, coordinating as tyrosinate | <chem>*Cc1ccc([O-])cc1</chem> for each | One oxygen from each residue   |

Here \* marks attachment to the rest of the protein; these are side-chain fragment SMILES. The histidine fragment shows a neutral tautomer, whose unprotonated ring nitrogen supplies the donor lone pair.

Therefore,

$$N_{\text{O}} = \underbrace{2}_{\text{carbonate}} + \underbrace{1}_{\text{aspartate}} + \underbrace{2}_{\text{two tyrosines}} = \boxed{5}.$$

Together with the histidine nitrogen, these give the specified six donor atoms.

The solution was checked against the official solution.

## Problem 4: A Naturally Occurring Compound

A naturally occurring compound **A** containing only C, H and O has the following elemental composition, percentage mass,

C: 63.2 %, H: 5.3%, O: 31.5%.

**4.1** Derive the empirical formula of compound **A**.

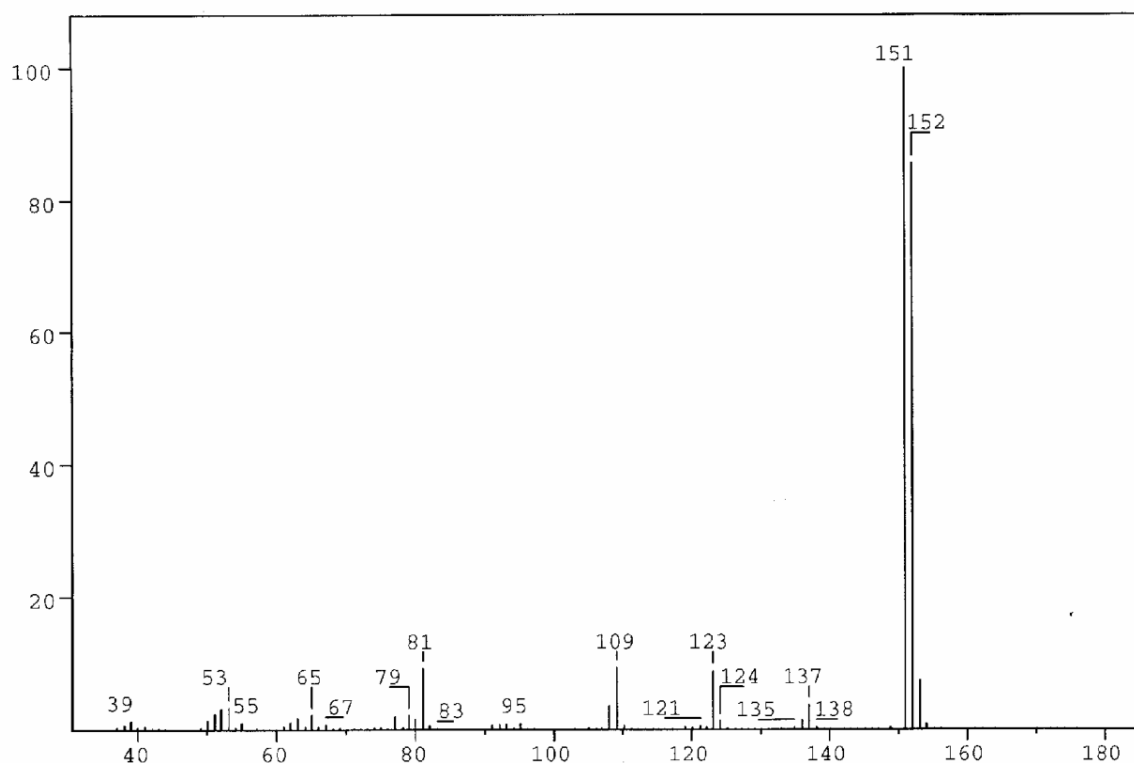


Figure 1

The mass spectrum of compound **A** is shown in Figure 1.

**4.2** What is the molecular formula for compound **A**?

A solution of **A** in ether is shaken with an aqueous solution of NaOH. After this, no **A** remains in the ether phase. Another solution of **A** in ether is shaken with an aqueous solution of NaHCO<sub>3</sub>. **A** remains in the ether phase.

**4.3** Which of the following classes of compounds does **A** belong to according to these experiments? Mark with an X.

|                                  |                                 |                                   |                                 |
|----------------------------------|---------------------------------|-----------------------------------|---------------------------------|
| alcohol <input type="checkbox"/> | phenol <input type="checkbox"/> | aldehyde <input type="checkbox"/> | ketone <input type="checkbox"/> |
| acid <input type="checkbox"/>    | ester <input type="checkbox"/>  | ether <input type="checkbox"/>    |                                 |

Compound **A** gave rise to formation of a silver mirror with Tollens' reagent ( $\text{Ag}(\text{NH}_3)_2^+$ ).

**4-1** Which of the following functional groups does this indicate the presence of in **A**? Mark with an X.

|                                                        |                                                     |
|--------------------------------------------------------|-----------------------------------------------------|
| hydroxy group of an alcohol <input type="checkbox"/>   | hydroxy group of a phenol <input type="checkbox"/>  |
| carbonyl group of an aldehyde <input type="checkbox"/> | carbonyl group of a ketone <input type="checkbox"/> |
| carboxylic group <input type="checkbox"/>              | ester group <input type="checkbox"/>                |
| alkoxy group of an ether <input type="checkbox"/>      |                                                     |

| Table of Integrals |          |       |
|--------------------|----------|-------|
| FROM               | TO       | VALUE |
| 10.00 PPM          | 9.69 PPM | 0.94  |
| 7.56 PPM           | 7.32 PPM | 1.91  |
| 7.15 PPM           | 6.92 PPM | 0.93  |
| 6.41 PPM           | 6.20 PPM | 0.94  |
| 4.02 PPM           | 3.89 PPM | 3.10  |

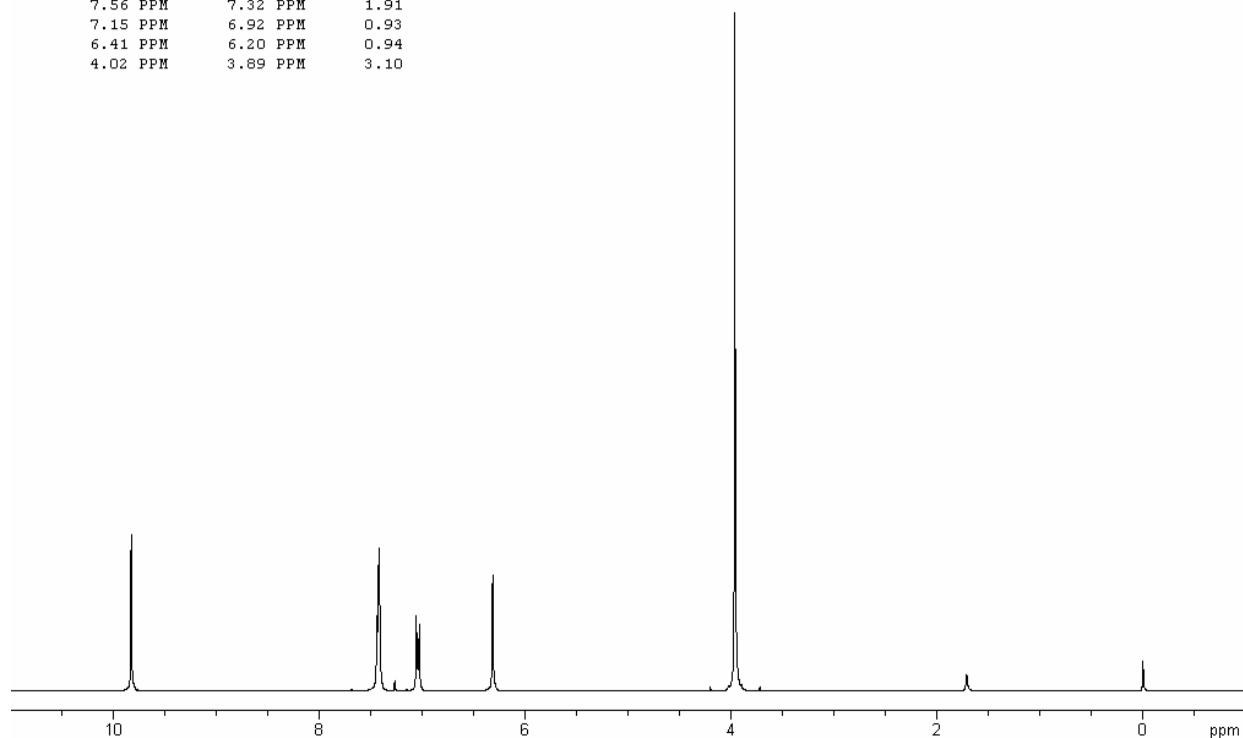


Figure 2a

The  $^1\text{H}$  NMR spectrum of compound **A** recorded at 300 MHz is shown in Figure 2a (solvent  $\text{CDCl}_3$  (7.27 ppm), reference tetramethylsilane). The signals at 3.9, 6.3 and 9.8 ppm are singlets. Figure 2b is an expansion of the region 6.9 – 7.6 ppm.

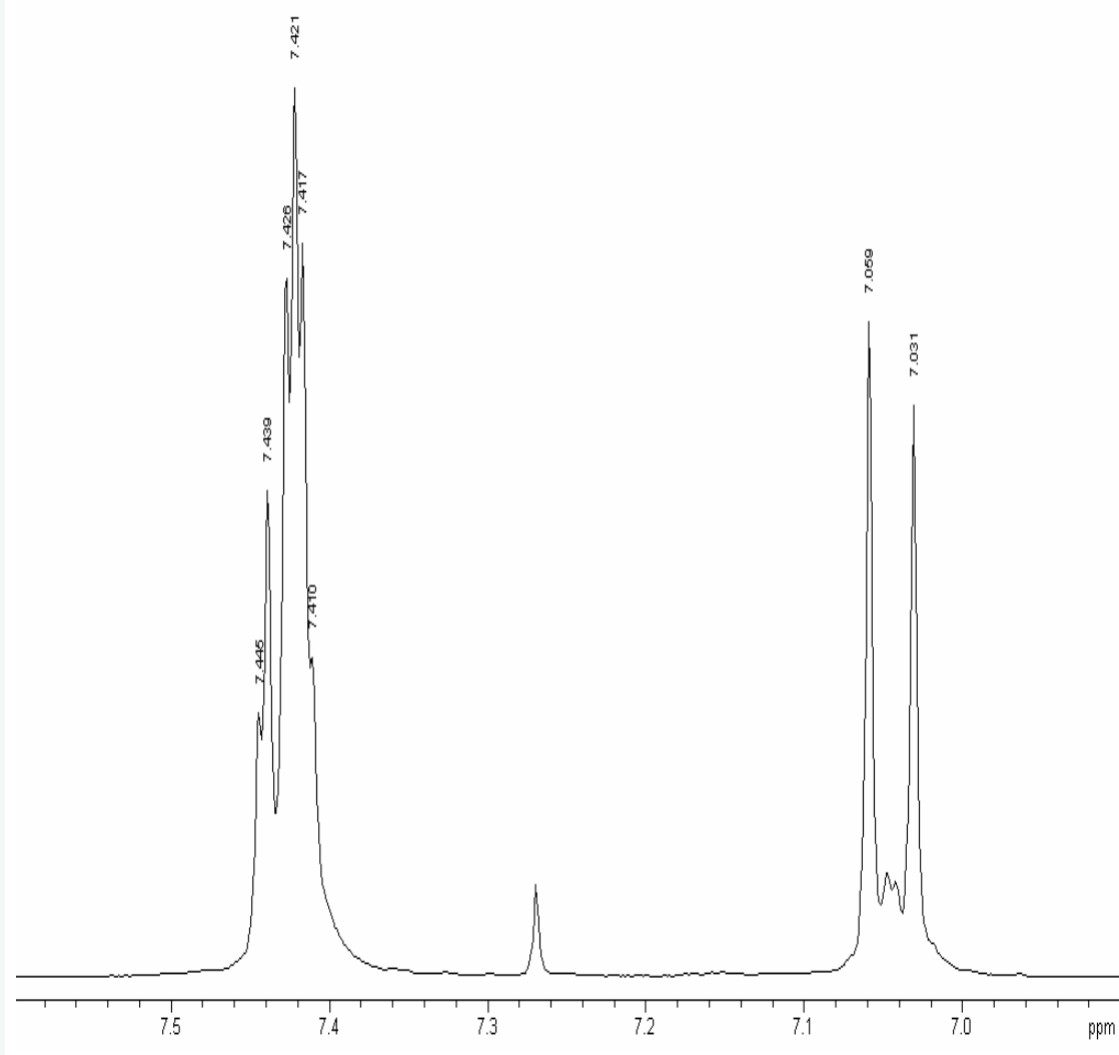


Figure 2b

Selected chemical shift and coupling constant values are given in Table 1.

The signal at 6.3 ppm disappears when a drop of  $D_2O$  is added.

**4.5** Which of the following does this indicate? Mark with an X.

- Exchange of carbon-bonded hydrogen ☐
- Exchange of oxygen-bonded hydrogen ☐
- Dilution effect ☐
- Hydrolysis ☐

The same signal moves to a lower ppm value upon dilution with  $CDCl_3$ .

**4.6** Which of the following does this indicate?

Indicate the true statements (more than one).

- Increased hydrogen bonding ☐
- Decrease in hydrogen bonding ☐
- Intermolecular hydrogen bonding ☐
- Intramolecular hydrogen bonding ☐

- No hydrogen bonding ☐

**4.7** Draw the four possible structural formulas for compound **A** based on the information given above

**4.8** Give structural formulas for the fragments lost corresponding to the peaks at 137 and 123 mass units in the mass spectrum.

**4.9** Two of the isomers have a lower  $pK_a$  value than the others. Write the formulas for those.

Table 1.  $^1\text{H}$  Chemical Shift  $\delta$

#### Hydrogens attached to carbon

|                  |                                   |                                                                                                |
|------------------|-----------------------------------|------------------------------------------------------------------------------------------------|
| <i>Methyl</i>    | $\text{CH}_3-\text{C}^-$          | 0.9 – 1.6 ppm                                                                                  |
|                  | $\text{CH}_3-\text{C}=\text{O}^-$ | 2.0 – 2.4 ppm                                                                                  |
|                  | $\text{CH}_3-\text{O}-\text{R}$   | 3.3 – 3.8 ppm                                                                                  |
|                  | $\text{CH}_3-\text{OCOR}$         | 3.7 – 4.0 ppm                                                                                  |
| <i>Methylene</i> | $\text{CH}_2-\text{C}^-$          | 1.4 – 2.7 ppm                                                                                  |
|                  | $\text{CH}_2-\text{C}=\text{O}^-$ | 2.2 – 2.9 ppm                                                                                  |
|                  | $\text{CH}_2-\text{OR}$           | 3.4 – 4.1 ppm                                                                                  |
|                  | $\text{CH}_2-\text{OCOR}$         | 4.3 – 4.4 ppm                                                                                  |
| <i>Methine</i>   | $\text{CH}^-$                     | 1.5 – 5.0 ppm<br>depending on the substituents. Generally higher than for methyl and methylene |
| <i>Alkene</i>    |                                   | 4.0 – 7.3 ppm<br>depending on the substituent                                                  |
| <i>Aldehyde</i>  | $\text{R}-\text{CHO}$             | 9.0 – 10.0 ppm                                                                                 |

Table 1 (continued)  $^1\text{H}$  Chemical Shift  $\delta$

#### Hydrogens attached to oxygen

|                         |                |                 |
|-------------------------|----------------|-----------------|
| <i>Alcohols</i>         | $\text{ROH}$   | 0.5 – 5.0 ppm   |
| <i>Phenols</i>          | $\text{ArOH}$  | 4.0 – 7.0 ppm   |
| <i>Carboxylic acids</i> | $\text{RCOOH}$ | 10.0 – 13.0 ppm |

#### Selected spin-spin coupling constants

|                                   |                                               |            |
|-----------------------------------|-----------------------------------------------|------------|
| <i>Alkanes</i><br>(free rotation) | $\text{H}-\text{C}-\text{C}-\text{H}$ vicinal | 6 – 8 Hz   |
| <i>Alkenes</i>                    | trans                                         | 11 – 18 Hz |
|                                   | cis                                           | 6 – 12 Hz  |
|                                   | geminal                                       | 0 – 3 Hz   |
| <i>Aromates</i>                   | ortho                                         | 6 – 10 Hz  |
|                                   | meta                                          | 1 – 4 Hz   |
|                                   | para                                          | 0 – 2 Hz   |

Official English text of the problem.

## Answers

- **4.1:** Empirical formula:  $\boxed{\text{C}_8\text{H}_8\text{O}_3}$ .
- **4.2:** Molecular formula:  $\boxed{\text{C}_8\text{H}_8\text{O}_3}$ , from the molecular-ion peak at  $m/z = 152$ .
- **4.3:** Mark **phenol**.
- **4-1 (fourth subquestion):** Mark **carbonyl group of an aldehyde**.
- **4.5:** Mark **Exchange of oxygen-bonded hydrogen**.
- **4.6:** Mark **Decrease in hydrogen bonding** and **Intermolecular hydrogen bonding**.
- **4.7:** The four candidate structures are: 1. **4-Hydroxy-3-methoxybenzaldehyde (vanillin):**  
O=Cc1cc(OC)c(O)cc1 2. **3-Hydroxy-4-methoxybenzaldehyde (isovanillin):**  
O=Cc1cc(O)c(OC)cc1 3. **4-Hydroxy-2-methoxybenzaldehyde:** O=Cc1c(OC)cc(O)cc1  
4. **5-Hydroxy-2-methoxybenzaldehyde:** O=Cc1c(OC)ccc(O)c1
- **4.8:** At  $m/z = 137$ , loss of a **methyl radical**,  $\text{CH}_3^\bullet$ ,  $[\text{CH}_3]$ ; at  $m/z = 123$ , loss of a **formyl radical**,  $\text{HCO}^\bullet$ ,  $[\text{CH}] = \text{O}$ .
- **4.9:** The two lower- $pK_a$  isomers are **4-hydroxy-3-methoxybenzaldehyde (vanillin)**,  
O=Cc1cc(OC)c(O)cc1, and **4-hydroxy-2-methoxybenzaldehyde**,  
O=Cc1c(OC)cc(O)cc1.

## Solution

### 4.1 — Empirical formula

Take a 100.0 g sample. Using atomic molar masses 12.01, 1.008 and 16.00  $\text{g mol}^{-1}$ ,

$$\begin{aligned}n_{\text{C}} &= \frac{63.2}{12.01} = 5.262 \text{ mol}, \\n_{\text{H}} &= \frac{5.3}{1.008} = 5.258 \text{ mol}, \\n_{\text{O}} &= \frac{31.5}{16.00} = 1.969 \text{ mol}.\end{aligned}$$

Dividing by the oxygen amount gives

$$n_{\text{C}} : n_{\text{H}} : n_{\text{O}} = 2.673 : 2.671 : 1.$$

Multiplication by three gives approximately 8 : 8 : 3. Therefore,

$$\boxed{\text{Empirical formula} = \text{C}_8\text{H}_8\text{O}_3}.$$

Its empirical formula mass is

$$M_{\text{emp}} = 8(12.01) + 8(1.008) + 3(16.00) = 152.14 \text{ g mol}^{-1}.$$

### 4.2 — Molecular formula

The molecular-ion peak occurs at  $m/z = 152$ . For a singly charged molecular ion, this corresponds to a molecular mass of approximately 152 u, hence a molar mass of approximately 152  $\text{g mol}^{-1}$ .

Thus,

$$\frac{M}{M_{\text{emp}}} \approx \frac{152}{152.14} \approx 1,$$

so the molecular and empirical formulas coincide:



The formula alone does not specify connectivity; the possible molecular structures are established in 4.7.

### 4.3 — Interpretation of the extraction experiments

Hydroxide deprotonates the phenolic group, producing an ionic phenoxide that transfers into the aqueous phase:



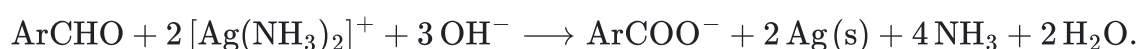
Here Ar denotes the substituted aromatic residue. In generic SMILES, with \* denoting that residue, the phenol is \*O and its phenoxide is \*[O-]. Hydroxide is [OH-], and water is O.

Bicarbonate,  $\text{O}=\text{C}(\text{[O-]})\text{O}$ , is too weak a base to produce substantial extraction under the stated conditions. This distinguishes the observed behavior from that expected for an ordinary carboxylic acid, which would react with aqueous bicarbonate.

Therefore, mark **phenol**. These extraction experiments establish the phenolic group; the other functional groups require the subsequent evidence.

### 4-1 — Interpretation of Tollens' test

The silver mirror indicates reduction of silver(I) to metallic silver while the aldehyde is oxidized to a carboxylate:



This equation is balanced in atoms and charge. The aldehyde carbon undergoes a two-electron oxidation, reducing two silver(I) ions.

The generic aldehyde and carboxylate structures are \*C=O and \*C(=O)[O-], respectively.

Diamminesilver(I) has dative-bond SMILES [NH3]->[Ag+]<-[NH3] and approximately linear nitrogen-silver-nitrogen coordination. Ammonia is N.

Thus, mark **carbonyl group of an aldehyde**. The one-proton singlet at 9.8 ppm independently supports this assignment.

### 4.5 — Disappearance of the 6.3 ppm signal

The phenolic hydrogen exchanges with deuterium:



Heavy water is [2H]O[2H], the generic oxygen-deuterated phenol is \*O[2H], and monodeuterated water is [2H]O.

The resulting oxygen-bound deuterium does not give the original signal in a  $^1\text{H}$  NMR spectrum. Therefore, mark **Exchange of oxygen-bonded hydrogen**.

### 4.6 — Effect of dilution

Hydrogen bonding deshields the phenolic proton, moving its resonance to a higher chemical shift. Dilution reduces association between separate molecules. The resulting decrease in hydrogen bonding increases shielding, moving the signal to a lower ppm value.

Therefore, mark:

- **Decrease in hydrogen bonding**
- **Intermolecular hydrogen bonding**

A purely intramolecular hydrogen bond would ordinarily be much less sensitive to concentration.

#### 4.7 — Four possible structures

The degree of unsaturation is

$$\text{DBE} = \frac{2(8) + 2 - 8}{2} = 5.$$

A benzene ring accounts for four degrees of unsaturation, and an aldehyde carbonyl accounts for the fifth.

The NMR integrals give the following assignments:

| Signal or integration region | Integral                   | Assignment             |
|------------------------------|----------------------------|------------------------|
| 9.8 ppm                      | $0.94 \approx 1 \text{ H}$ | Aldehyde hydrogen      |
| 7.56–7.32 ppm                | $1.91 \approx 2 \text{ H}$ | Two aromatic hydrogens |
| 7.15–6.92 ppm                | $0.93 \approx 1 \text{ H}$ | One aromatic hydrogen  |
| 6.3 ppm                      | $0.94 \approx 1 \text{ H}$ | Phenolic hydrogen      |
| 3.9 ppm                      | $3.10 \approx 3 \text{ H}$ | Methoxy hydrogens      |

The phenol and aldehyde account for two oxygen atoms. The remaining oxygen belongs to a methoxy group,  $-\text{OCH}_3$ , generic SMILES `*OC`, which accounts for the three-proton singlet at 3.9 ppm.

Thus, **A** is a benzene bearing one hydroxy, one methoxy and one formyl substituent:



The aromatic splitting constrains their relative positions. For the well-resolved doublet near 7.04 ppm,

$$J = (7.059 - 7.031) \text{ ppm} \times 300 \text{ Hz ppm}^{-1} = 8.4 \text{ Hz}.$$

This is an **ortho** coupling according to Table 1. The overlapping resonances near 7.42 ppm also show smaller splittings consistent with **meta** coupling.

The pattern corresponds to three aromatic hydrogens with one ortho relationship, one meta relationship and one para relationship: a **1,2,4-type trisubstituted benzene**. In comparison, three consecutive aromatic hydrogens would have two ortho couplings, while the hydrogens of a 1,3,5-trisubstituted ring would have only meta relationships.

The intended additional restriction from the hydrogen-bonding observations is that the hydroxy and formyl groups are **not ortho**. An ortho arrangement would favor a six-membered intramolecular hydrogen-bonded arrangement between the phenolic hydrogen and aldehyde oxygen.

Applying these restrictions gives four candidates. To draw them, place the formyl group at carbon 1 of a benzene ring and add the other substituents at the positions below. Every remaining ring carbon bears hydrogen.

| Candidate | Hydroxy position | Methoxy position | Name and SMILES                                                                           |
|-----------|------------------|------------------|-------------------------------------------------------------------------------------------|
| I         | 4                | 3                | <b>4-Hydroxy-3-methoxybenzaldehyde (vanillin)</b> —<br><chem>O=Cc1cc(OC)c(O)cc1</chem>    |
| II        | 3                | 4                | <b>3-Hydroxy-4-methoxybenzaldehyde (isovanillin)</b> —<br><chem>O=Cc1cc(O)c(OC)cc1</chem> |
| III       | 4                | 2                | <b>4-Hydroxy-2-methoxybenzaldehyde</b> —<br><chem>O=Cc1c(OC)cc(O)cc1</chem>               |
| IV        | 5                | 2                | <b>5-Hydroxy-2-methoxybenzaldehyde</b> —<br><chem>O=Cc1c(OC)ccc(O)c1</chem>               |

These structures require no stereochemical specification.

#### 4.8 — Fragments lost in the mass spectrum

Calculate each loss relative to the molecular ion at  $m/z = 152$ :

| Product peak | Nominal mass lost  | Lost fragment and structure                                        |
|--------------|--------------------|--------------------------------------------------------------------|
| $m/z = 137$  | $152 - 137 = 15$ u | <b>Methyl radical</b> , $\text{CH}_3^\bullet$ , <chem>[CH3]</chem> |
| $m/z = 123$  | $152 - 123 = 29$ u | <b>Formyl radical</b> , $\text{HCO}^\bullet$ , <chem>[CH]=O</chem> |

The methyl loss corresponds to cleavage of the oxygen–methyl bond of the methoxy group. The formyl loss corresponds to removal of the aldehyde substituent from the aromatic ring; its unpaired electron is on carbon.

These are the assigned net losses from the molecular ion; the mass differences alone do not establish a unique fragmentation sequence.

#### 4.9 — Isomers with lower $pK_a$

The lower- $pK_a$  isomers have the aldehyde group **para to the phenolic hydroxy group**:

- **I: 4-Hydroxy-3-methoxybenzaldehyde (vanillin)** — O=Cc1cc(OC)c(O)cc1
- **III: 4-Hydroxy-2-methoxybenzaldehyde** — O=Cc1c(OC)cc(O)cc1

Their conjugate bases are:

- **4-Formyl-2-methoxyphenolate** — O=Cc1cc(OC)c([O-])cc1
- **4-Formyl-3-methoxyphenolate** — O=Cc1c(OC)cc([O-])cc1

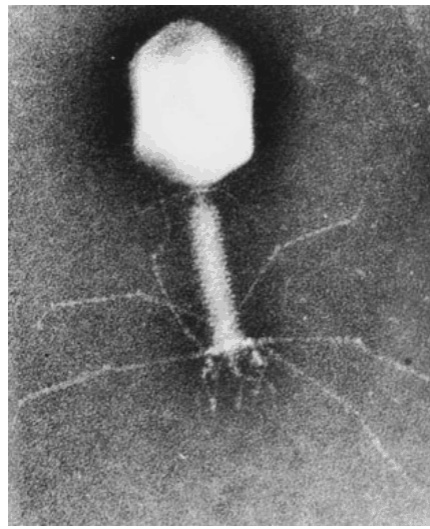
In these phenoxide ions, resonance can distribute negative charge through the ring to the para position and onward onto the aldehyde oxygen. This additional stabilization favors deprotonation and lowers  $pK_a$ .

For candidates II and IV, the aldehyde is meta to the phenolic group, so this direct resonance stabilization of the conjugate base is unavailable.

---

The solution was checked against the official solution.

## Problem 5: Protein and DNA



DNA is composed of 2'-deoxy-nucleotides carrying the bases adenine (A), guanine (G), cytosine (C) and thymine (T). The molar mass of the 2'-deoxy-nucleotide-5'-triphosphates is given in table 2:

Table 2

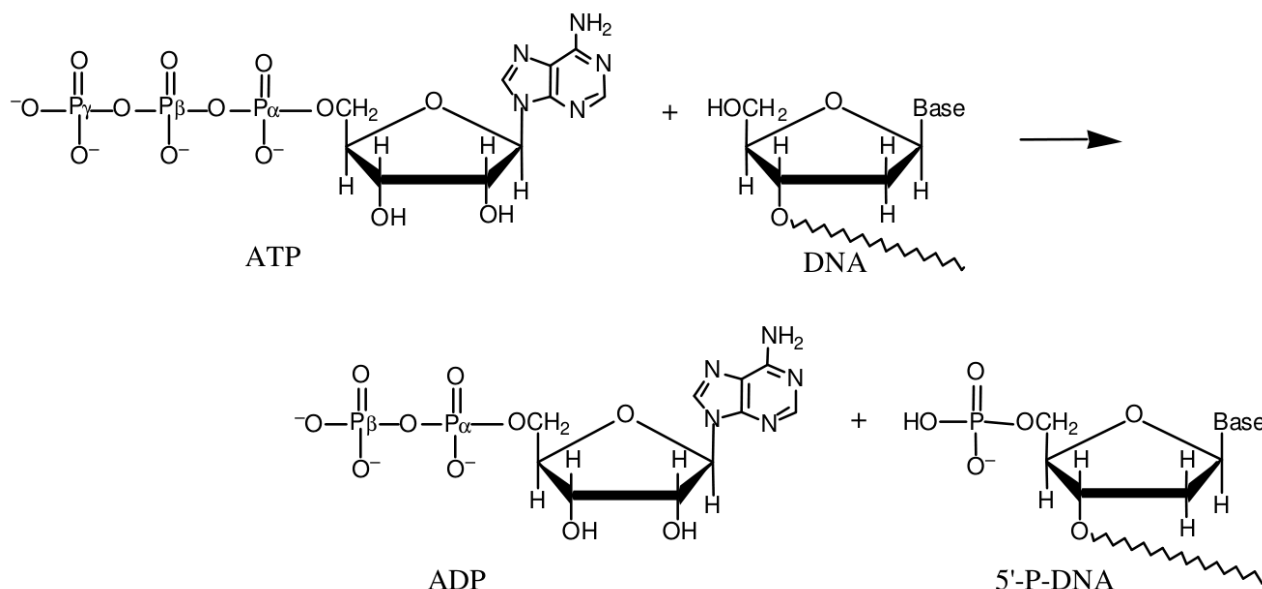
| dNTP | Molar mass /g mol <sup>-1</sup> |
|------|---------------------------------|
| dATP | 487                             |
| dGTP | 503                             |
| dCTP | 464                             |
| dTTP | 478                             |

**5.1** Calculate the molar mass of a double stranded DNA fragment consisting of 1000 base pairs with a uniform distribution of the four bases.

This DNA fragment can be isolated and cloned by using the PCR method (polymerase chain reaction), in which a heat stable DNA polymerase enzyme multiplies the number of molecules of a specific piece of DNA in a cyclic process. Under optimal conditions the number of double-stranded DNA copies doubles in each cycle. Using the PCR method you perform 30 cycles starting from a single double stranded DNA molecule.

**5.2** Calculate the approximate mass of the DNA you obtain from this experiment.

The bacteria-virus T4 enzyme - polynucleotide kinase (PNK) catalyzes the transfer of the terminal phosphate of ATP ( $\gamma$ -orthophosphate) to the 5'-hydroxyl termini of ribo- and deoxyribonucleotides:



PNK is commonly used to label DNA at the 5'-end with the radioactive phosphorus isotope  $^{32}\text{P}$  using ATP in which the  $\gamma\text{-P}$  (the outermost of the phosphorus atoms) is replaced with  $^{32}\text{P}$ . The amount of  $^{32}\text{P}$  and thus the amount of labeled DNA can be measured.

A 10  $\mu\text{L}$  solution containing double stranded DNA is labelled 100 % with  $[\gamma\text{-}^{32}\text{P}]\text{ATP}$  by PNK. 37 days ago, the specific activity of  $[\gamma\text{-}^{32}\text{P}]\text{ATP}$  was 10 Ci/mmol or  $370 \cdot 10^9$  Bq/mmol.  $^{32}\text{P}$  has a half-life of 14.2 days, and during the decay a  $\beta$ -particle is emitted. Now the labelled DNA emits 40000  $\beta$ -particles/s.

**5-3** Calculate the concentration of the DNA solution.

In an experiment in which PNK is incubated with  $[\gamma\text{-}^{32}\text{P}]\text{ATP}$  and single stranded DNA, the reaction can be monitored by isolating labeled DNA and measuring the  $\beta$ -particle emission. Using this kind of measurements in a 1  $\text{cm}^3$  experimental mixture, a labeling of 9 nmol DNA/min was calculated. PNK has a catalytic rate constant (turnover number) of  $0.05 \text{ s}^{-1}$  and molar mass of  $34620 \text{ g mol}^{-1}$ .

**5.4** Calculate the concentration (in  $\text{mg/cm}^3$ ) of PNK in the experimental mixture.

Aromatic amino acids, tryptophan, tyrosine and phenylalanine absorb UV light of a wavelength between 240 nm and 300 nm. In a protein containing several aromatic amino acids, the sum of the molar absorptivity per amino acid  $\sum \epsilon_{\text{amino acid}}$ , is approximately equal to the molar absorptivity,  $\epsilon_{\text{protein}}$ , for the protein. The molar absorptivity,  $\epsilon_{\text{amino acid}}$ , at 280 nm for tyrosine, tryptophan and phenylalanine is  $1400 \text{ M}^{-1} \text{ cm}^{-1}$ ,  $5600 \text{ M}^{-1} \text{ cm}^{-1}$  and  $5 \text{ M}^{-1} \text{ cm}^{-1}$ , respectively. The absorbance of a 10  $\mu\text{M}$  solution of PNK is 0.644 at 280 nm and with 1.00 cm light path. The amino acid sequence of PNK contains 14 tyrosines and 9 phenylalanines.

( $\text{M} = \text{mol dm}^{-3}$ )

**5.5** Calculate the number of tryptophan residues in a PNK molecule.

Official English text of the problem.

## Answers

- **5.1:**  $M_{\text{DNA}} \approx 6.18 \times 10^5 \text{ g mol}^{-1}$ .
- **5.2:**  $m_{\text{DNA}} \approx 1.10 \times 10^{-9} \text{ g} = 1.10 \text{ ng}$ .
- **5.3:**  $c_{\text{DNA}} \approx 6.58 \times 10^{-5} \text{ mol dm}^{-3} = 65.8 \text{ } \mu\text{M}$ , counting each labelled 5' end as one DNA molecule (amount of labelled DNA = amount of  $^{32}\text{P}$ , as the statement says).
- **5.4:**  $c_m(\text{PNK}) \approx 0.104 \text{ mg cm}^{-3}$ , or about  $0.10 \text{ mg cm}^{-3}$ .
- **5.5:** 8 tryptophan residues per PNK molecule.

## Solution

### 5.1 — Molar mass of the DNA fragment

There are two nucleotides per base pair, so the fragment contains

$$N_{\text{nt}} = 2(1000) = 2000$$

nucleotide residues. A uniform distribution means 500 residues of each base.

During incorporation into DNA, the two terminal phosphate groups of a nucleotide triphosphate leave as pyrophosphate. Using the ionic mass convention of the table, the removed pyrophosphate group is  $\text{P}_2\text{O}_7^{4-}$ , with

$$M_{\text{PP}_i} = 2(31) + 7(16) = 174 \text{ g mol}^{-1}.$$

Pyrophosphate ion has SMILES [O-]P(=O)([O-])OP(=O)([O-])[O-].

The average molar mass of an incorporated nucleotide residue is therefore

$$\overline{M}_{\text{residue}} = \frac{487 + 503 + 464 + 478}{4} - 174 = 309 \text{ g mol}^{-1}.$$

Neglecting the small contribution from terminal groups,

$$M_{\text{DNA}} \approx 2000(309) = 6.18 \times 10^5 \text{ g mol}^{-1}.$$

### 5.2 — Mass after 30 PCR cycles

Each cycle doubles the number of double-stranded DNA molecules. Starting from one molecule,

$$N = 2^{30} = 1\,073\,741\,824.$$

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

$$n_{\text{DNA}} = \frac{2^{30}}{N_A} = 1.783 \times 10^{-15} \text{ mol}.$$

Thus,

$$m_{\text{DNA}} = n_{\text{DNA}} M_{\text{DNA}} = (1.783 \times 10^{-15})(6.18 \times 10^5) \text{ g},$$

$$m_{\text{DNA}} \approx 1.10 \times 10^{-9} \text{ g} = 1.10 \text{ ng}.$$

### 5.3 — DNA concentration from radioactive labelling

The specific activity decreases according to

$$a(t) = a_0 2^{-t/t_{1/2}}.$$

After 37 days,

$$a(37) = (370 \times 10^9) 2^{-37/14.2} = 6.079 \times 10^{10} \text{ Bq mmol}^{-1}.$$

One emitted  $\beta$ -particle corresponds to one decay, so the measured activity is

$$A = 40000 \text{ Bq}.$$

Since the amount of labelled DNA equals the amount of  $^{32}\text{P}$  (each labelled 5' end counts as one DNA molecule),

$$n_{\text{DNA}} = \frac{A}{a(37)} = \frac{40000}{6.079 \times 10^{10}} = 6.580 \times 10^{-7} \text{ mmol} = 6.580 \times 10^{-10} \text{ mol}.$$

The sample volume is

$$V = 10 \mu\text{L} = 1.0 \times 10^{-5} \text{ dm}^3.$$

Consequently,

$$c_{\text{DNA}} = \frac{6.580 \times 10^{-10}}{1.0 \times 10^{-5}} = 6.58 \times 10^{-5} \text{ mol dm}^{-3} = 65.8 \mu\text{M}.$$

No factor of two is applied, because each labelled 5' end counts as one DNA molecule.

#### 5.4 — PNK mass concentration

The observed labelling rate is

$$\dot{n}_{\text{DNA}} = \frac{9 \text{ nmol}}{60 \text{ s}} = 0.15 \text{ nmol s}^{-1}.$$

Using the stated turnover number as the reaction rate per enzyme molecule,

$$\dot{n}_{\text{DNA}} = k_{\text{cat}} n_{\text{PNK}}.$$

Therefore,

$$n_{\text{PNK}} = \frac{0.15 \text{ nmol s}^{-1}}{0.05 \text{ s}^{-1}} = 3.0 \text{ nmol}.$$

The corresponding enzyme mass is

$$m_{\text{PNK}} = (3.0 \times 10^{-9} \text{ mol})(34620 \text{ g mol}^{-1}) = 1.0386 \times 10^{-4} \text{ g} = 0.10386 \text{ mg}.$$

Since the experimental volume is  $1 \text{ cm}^3$ ,

$$c_m(\text{PNK}) = 0.10386 \text{ mg cm}^{-3} \approx 0.10 \text{ mg cm}^{-3}.$$

#### 5.5 — Number of tryptophan residues

The Beer–Lambert law gives

$$A = \varepsilon_{\text{PNK}} c l.$$

Hence,

$$\varepsilon_{\text{PNK}} = \frac{0.644}{(10 \times 10^{-6} \text{ mol dm}^{-3})(1.00 \text{ cm})} = 64400 \text{ M}^{-1} \text{ cm}^{-1}.$$

Let  $x$  be the number of tryptophan residues. Adding the contributions from the three aromatic amino acids,

$$64400 = 14(1400) + x(5600) + 9(5).$$

Thus,

$$x = \frac{64400 - 19600 - 45}{5600} = 7.99196.$$

The residue count must be an integer, and the absorptivity relation is approximate:

$$x = 8.$$

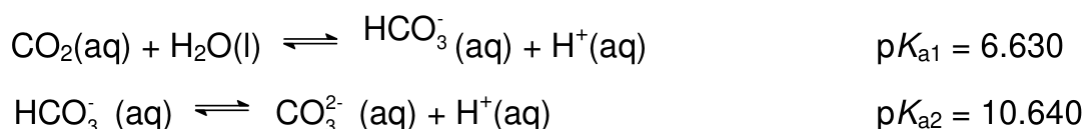
The residue is L-tryptophan; its neutral free-amino-acid SMILES is N[C@@H](Cc1c[nH]c2ccccc12)C(=O)O. Within PNK, its amino and carboxyl groups participate in the peptide backbone.

The solution was checked against the official solution.

## Problem 6: Hard Water

In Denmark the subsoil consists mainly of limestone. In contact with ground water containing carbon dioxide some of the calcium carbonate dissolves as calcium hydrogen carbonate. As a result, such ground water is hard, and when used as tap water the high content of calcium hydrogen carbonate causes problems due to precipitation of calcium carbonate in, for example, kitchen and bathroom environments.

Carbon dioxide,  $\text{CO}_2$ , is a diprotic acid in aqueous solution. The  $pK_a$ -values at  $0^\circ\text{C}$  are:



The liquid volume change associated with dissolution of  $\text{CO}_2$  may be neglected for all of the following problems. The temperature is to be taken as being  $0^\circ\text{C}$ .

**6.1** The total concentration of carbon dioxide in water which is saturated with carbon dioxide at a carbon dioxide partial pressure of 1.00 bar is  $0.0752 \text{ mol dm}^{-3}$ . Calculate the volume of carbon dioxide gas which can be dissolved in one litre of water under these conditions.

The gas constant

$$R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1} = 0.08314 \text{ L bar mol}^{-1} \text{ K}^{-1}$$

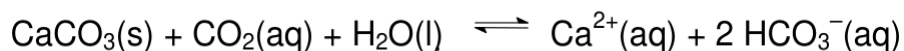
**6.2** Calculate the equilibrium concentration of hydrogen ions and the equilibrium concentration of  $\text{CO}_2$  in water saturated with carbon dioxide at a carbon dioxide partial pressure of 1.00 bar.

**6.3** Calculate the equilibrium concentration of hydrogen ions in a 0.0100 M aqueous solution of sodium hydrogen carbonate saturated with carbon dioxide at a carbon dioxide partial pressure of 1.00 bar.

**6.4** Calculate the equilibrium concentration of hydrogen ions in a 0.0100 M aqueous solution of sodium carbonate saturated with carbon dioxide at a carbon dioxide partial pressure of 1.00 bar. Ignore water dissociation effects.

**6.5** The solubility of calcium carbonate in water at  $0^\circ\text{C}$  is 0.0012 g per  $100 \text{ cm}^3$  of water. Calculate the concentration of calcium ions in a saturated solution of calcium carbonate in water.

The hard groundwater in Denmark is formed via contact of water with limestone in the subsoil which reacts with carbon dioxide dissolved in the groundwater according to the equilibrium equation:



The equilibrium constant,  $K$ , for this reaction is  $10^{-4.25}$  at  $0^\circ\text{C}$ .

**6.6** Calculate the concentration of calcium ions in water in equilibrium with calcium carbonate in an atmosphere with a partial pressure of carbon dioxide of 1.00 bar.

**6.7** A 0.0150 M solution of calcium hydroxide is saturated with carbon dioxide gas at a partial pressure of 1.00 bar. Calculate the concentration of calcium ions in the solution by considering the equilibrium equation given above in connection with problem 6.6.

**6.8** The calcium hydroxide solution referred to in problem 6.7 is diluted to twice the volume with water before saturation with carbon dioxide gas at a partial pressure of 1.00 bar. Calculate the concentration of calcium ions in the resulting solution saturated with  $\text{CO}_2$ .

**6.9** Calculate the solubility product constant for calcium carbonate from the data given above.

Official English text of the problem.

## Answers

Here,  $\text{M} = \text{mol dm}^{-3}$ .

- **6.1:**  $V = 1.71 \text{ L}$  of carbon dioxide gas at  $0^\circ\text{C}$  and 1.00 bar.
- **6.2:**  $[\text{H}^+] = 1.33 \times 10^{-4} \text{ M}$ ;  $[\text{CO}_2(\text{aq})] = 0.0751 \text{ M}$ .
- **6.3:**  $[\text{H}^+] = 1.76 \times 10^{-6} \text{ M}$ .
- **6.4:**  $[\text{H}^+] = 8.80 \times 10^{-7} \text{ M}$ .
- **6.5:**  $[\text{Ca}^{2+}] = 1.2 \times 10^{-4} \text{ M}$ .
- **6.6:**  $[\text{Ca}^{2+}] = 1.02 \times 10^{-2} \text{ M}$ .
- **6.7:**  $[\text{Ca}^{2+}] = 1.02 \times 10^{-2} \text{ M}$ ; some calcium carbonate precipitates.
- **6.8:**  $[\text{Ca}^{2+}] = 7.50 \times 10^{-3} \text{ M}$ ; all the calcium remains dissolved at final equilibrium.
- **6.9:**  $K_{\text{sp}} = 10^{-8.26} \approx 5.5 \times 10^{-9}$ , using the 1 M standard state.

## Solution

The species and their SMILES are listed below. Dot-separated salt SMILES describe ionic composition; they do not encode crystal lattices or aqueous solvation.

| Species                                  | SMILES                  |
|------------------------------------------|-------------------------|
| Carbon dioxide, $\text{CO}_2$            | <chem>O=C=O</chem>      |
| Water, $\text{H}_2\text{O}$              | <chem>O</chem>          |
| Hydrogen ion, $\text{H}^+$               | <chem>[H+]</chem>       |
| Hydrogen carbonate ion, $\text{HCO}_3^-$ | <chem>O=C([O-])O</chem> |

| Species                                                 | SMILES                                    |
|---------------------------------------------------------|-------------------------------------------|
| Carbonate ion, $\text{CO}_3^{2-}$                       | <chem>O=C([O-])[O-]</chem>                |
| Hydroxide ion, $\text{OH}^-$                            | <chem>[OH-]</chem>                        |
| Sodium ion, $\text{Na}^+$                               | <chem>[Na+]</chem>                        |
| Calcium ion, $\text{Ca}^{2+}$                           | <chem>[Ca+2]</chem>                       |
| Sodium hydrogen carbonate, $\text{NaHCO}_3$             | <chem>[Na+].O=C([O-])O</chem>             |
| Sodium carbonate, $\text{Na}_2\text{CO}_3$              | <chem>[Na+].[Na+].O=C([O-])[O-]</chem>    |
| Calcium carbonate, $\text{CaCO}_3$                      | <chem>[Ca+2].O=C([O-])[O-]</chem>         |
| Calcium hydroxide, $\text{Ca}(\text{OH})_2$             | <chem>[Ca+2].[OH-].[OH-]</chem>           |
| Calcium hydrogen carbonate, $\text{Ca}(\text{HCO}_3)_2$ | <chem>[Ca+2].O=C([O-])O.O=C([O-])O</chem> |

We use the concentration approximation for dissolved species and unit activities for pure liquid water and solid calcium carbonate. Standard-state concentration factors are suppressed in the equilibrium expressions.

## 6.1

The amount of carbon dioxide absorbed by one litre of water is

$$n = (0.0752 \text{ mol L}^{-1})(1.00 \text{ L}) = 0.0752 \text{ mol}.$$

Using the ideal-gas equation at  $T = 273.15 \text{ K}$ ,

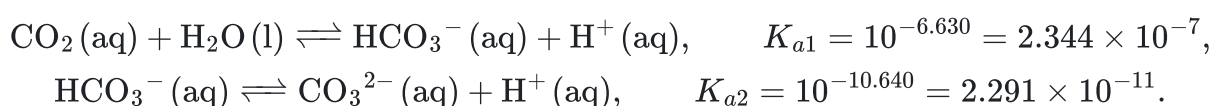
$$V = \frac{nRT}{p} = \frac{(0.0752)(0.08314)(273.15)}{1.00} \text{ L} = 1.70777 \text{ L}.$$

Thus,

$$\boxed{V = 1.71 \text{ L}}.$$

## 6.2

The two acid equilibria are



Define

$$h = [\text{H}^+], \quad c = [\text{CO}_2(\text{aq})], \quad b = [\text{HCO}_3^-], \quad d = [\text{CO}_3^{2-}].$$

Then

$$K_{a1} = \frac{hb}{c}, \quad K_{a2} = \frac{hd}{b}.$$

The total dissolved carbon concentration is

$$C_T = c + b + d = 0.0752 \text{ M}.$$

Water ionization and the second dissociation are negligible in this acidic solution. Consequently, charge balance gives  $b \simeq h$ , while carbon balance gives  $c \simeq C_T - h$ . Therefore,

$$K_{a1} = \frac{h^2}{C_T - h},$$

and

$$h = \frac{-K_{a1} + \sqrt{K_{a1}^2 + 4K_{a1}C_T}}{2} = 1.32656 \times 10^{-4} \text{ M.}$$

Hence

$$c = 0.0752 - 0.000132656 = 0.0750673 \text{ M.}$$

The neglected carbonate fraction is indeed tiny:

$$\frac{d}{b} = \frac{K_{a2}}{h} = 1.73 \times 10^{-7}.$$

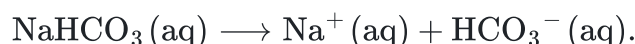
Thus,

$$\boxed{[\text{H}^+] = 1.33 \times 10^{-4} \text{ M}}, \quad \boxed{[\text{CO}_2(\text{aq})] = 0.0751 \text{ M}}.$$

At fixed temperature and carbon dioxide partial pressure, Henry's law fixes the concentration of molecular  $\text{CO}_2(\text{aq})$ . We therefore use  $c = 0.0750673 \text{ M}$  in the subsequent solutions saturated with carbon dioxide at 1.00 bar. Their **total** dissolved carbon concentrations can differ.

### 6.3

Sodium hydrogen carbonate dissociates:



Thus  $[\text{Na}^+] = 0.0100 \text{ M}$ . Neglecting water ionization, charge balance is

$$0.0100 + h = b + 2d.$$

Since  $h$  and  $d$  are small compared with 0.0100 M,

$$b \simeq 0.0100 \text{ M.}$$

The first acid equilibrium gives

$$h = \frac{K_{a1}c}{b} \simeq \frac{(2.34423 \times 10^{-7})(0.0750673)}{0.0100}.$$

Therefore,

$$\boxed{[\text{H}^+] = 1.76 \times 10^{-6} \text{ M}}.$$

This gives  $d = K_{a2}b/h \simeq 1.30 \times 10^{-7} \text{ M}$ , confirming that both correction terms in the charge balance are small.

### 6.4

Sodium carbonate supplies two sodium ions per formula unit:



Carbonate reacts with dissolved carbon dioxide:



The equilibrium constant for this conversion is

$$\frac{K_{a1}}{K_{a2}} = 10^{4.010},$$

so hydrogen carbonate predominates under the specified conditions.

Here  $[\text{Na}^+] = 0.0200 \text{ M}$ . Ignoring water dissociation as instructed,

$$0.0200 + h = b + 2d,$$

giving  $b \simeq 0.0200$  M.

Thus,

$$h \simeq \frac{K_{a1}c}{0.0200} = \frac{(2.34423 \times 10^{-7})(0.0750673)}{0.0200},$$

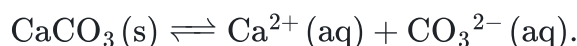
and

$$\boxed{[\text{H}^+] = 8.80 \times 10^{-7} \text{ M}}.$$

The resulting carbonate concentration is approximately  $5.21 \times 10^{-7}$  M, sufficiently small to validate the approximation.

## 6.5

Calcium carbonate dissolves according to



Each mole dissolved supplies one mole of calcium ions. Using  $M(\text{CaCO}_3) \simeq 100.1 \text{ g mol}^{-1}$  and  $100 \text{ cm}^3 = 0.100 \text{ dm}^3$ ,

$$[\text{Ca}^{2+}] = \frac{0.0012 \text{ g}}{(100.1 \text{ g mol}^{-1})(0.100 \text{ dm}^3)}.$$

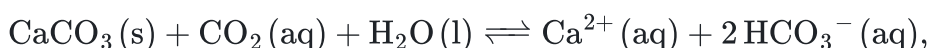
Therefore,

$$\boxed{[\text{Ca}^{2+}] = 1.2 \times 10^{-4} \text{ mol dm}^{-3}}.$$

Acid–base redistribution of dissolved carbonate does not change this calcium balance.

## 6.6

The given equilibrium is



with

$$K = \frac{[\text{Ca}^{2+}]b^2}{c} = 10^{-4.25}.$$

Let  $s = [\text{Ca}^{2+}]$ . Charge balance gives

$$2s + h = b + 2d.$$

Hydrogen carbonate is the predominant anion, so  $b \simeq 2s$ . Consequently,

$$K \simeq \frac{s(2s)^2}{c} = \frac{4s^3}{c},$$

and

$$s = \left( \frac{Kc}{4} \right)^{1/3} = \left( \frac{10^{-4.25}(0.0750673)}{4} \right)^{1/3} = 0.0101812 \text{ M}.$$

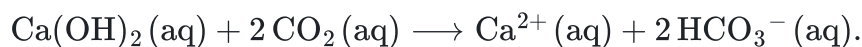
Thus,

$$\boxed{[\text{Ca}^{2+}] = 1.02 \times 10^{-2} \text{ M}}.$$

The corresponding hydrogen-ion concentration is about  $8.64 \times 10^{-7}$  M, and carbonate is also negligible compared with  $b \simeq 0.0204$  M.

## 6.7

Absorbed carbon dioxide neutralizes hydroxide, giving the overall conversion



If all the initial calcium remained dissolved, then approximately

$$[\text{Ca}^{2+}] = 0.0150 \text{ M}, \quad b = 0.0300 \text{ M}.$$

The reaction quotient for the equilibrium in 6.6 would be

$$Q = \frac{(0.0150)(0.0300)^2}{0.0750673} = 1.80 \times 10^{-4}.$$

Since

$$Q > K = 5.62 \times 10^{-5},$$

the equilibrium shifts toward solid calcium carbonate. Some calcium precipitates, and the remaining solution reaches the saturation concentration calculated in 6.6:

$$[\text{Ca}^{2+}] = 1.02 \times 10^{-2} \text{ M}.$$

Approximately  $0.0150 - 0.01018 = 0.0048$  mol of calcium carbonate precipitates per litre, confirming that a solid phase remains.

## 6.8

Dilution to twice the volume reduces the total calcium concentration to

$$C_{\text{Ca,tot}} = \frac{0.0150}{2} = 0.00750 \text{ M}.$$

If all this calcium is dissolved,  $b \simeq 0.0150$  M, and

$$Q = \frac{(0.00750)(0.0150)^2}{0.0750673} = 2.25 \times 10^{-5} < K.$$

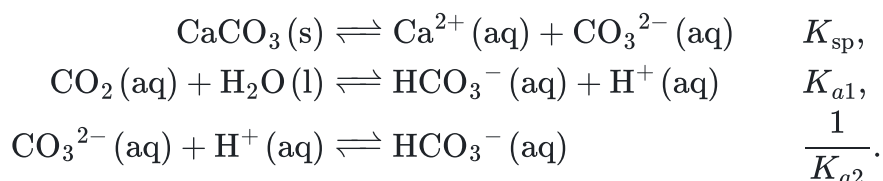
The final solution is therefore undersaturated with respect to calcium carbonate. Any calcium carbonate formed during addition of the gas can dissolve completely before the final equilibrium is reached.

All available calcium remains in solution:

$$[\text{Ca}^{2+}] = 7.50 \times 10^{-3} \text{ M}.$$

## 6.9

Combine the following equilibria:



Their sum is the reaction given before 6.6. Therefore,

$$K = K_{\text{sp}} \frac{K_{a1}}{K_{a2}},$$

so

$$K_{\text{sp}} = K \frac{K_{a2}}{K_{a1}} = 10^{-4.25} \frac{10^{-10.640}}{10^{-6.630}} = 10^{-8.260}.$$

Thus,

$$\boxed{K_{\text{sp}} \approx 5.5 \times 10^{-9}}.$$

Under the concentration approximation, the corresponding saturation product is

$$[\text{Ca}^{2+}][\text{CO}_3^{2-}] = 5.5 \times 10^{-9} \text{ mol}^2 \text{ dm}^{-6}.$$

Carbonate hydrolysis,



makes the free carbonate concentration smaller than the total molar solubility in 6.5. Consequently, that solubility cannot simply be squared to obtain  $K_{\text{sp}}$ .

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The solution was checked against the official solution.