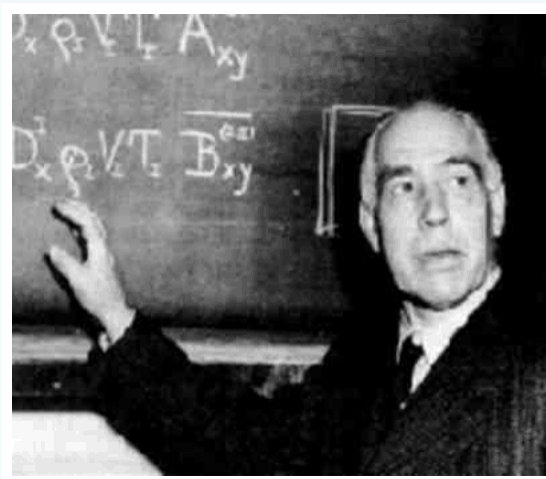


# IChO 2001

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## Problem 1: Hydrogen Atom and Hydrogen Molecule



Niels Bohr (1885–1962)

The observed wavelengths in the line spectrum of hydrogen atom were first expressed in terms of a series by Johann Jakob Balmer, a Swiss teacher. Balmer's empirical formula is

$$\frac{1}{\lambda} = R_H \left( \frac{1}{2^2} - \frac{1}{n^2} \right); \quad n = 3, 4, 5, \dots$$

Here,

$$R_H = \frac{m_e e^4}{8 \epsilon_0^2 h^3 c} = 109\,678 \text{ cm}^{-1}$$

is the Rydberg konstant,  $m_e$  is the mass of an electron. Niels Bohr derived this expression theoretically in 1913. The formula is easily generalized to any one electron atom/ion.

**1.1** Calculate the longest wavelength in Å ( $1 \text{ Å} = 10^{-10} \text{ m}$ ) in the 'Balmer series' of singly ionized helium ( $\text{He}^+$ ). Ignore nuclear motion in your calculation.

**1.2** A formula analogous to Balmer's formula applies to the series of spectral lines which arise from transitions from higher energy levels to the lowest energy level of hydrogen atom. Write this formula and use it to determine the ground state energy of a hydrogen atom in eV.

A 'muonic hydrogen atom' is like a hydrogen atom in which the electron is replaced by a heavier particle, the muon. The mass of a muon is about 207 times the mass of an electron, while its charge is the same as that of an electron. A muon has a very short lifetime, but we ignore its unstable nature here.

**1.3** Determine the lowest energy and the radius of the first Bohr orbit of the muonic hydrogen atom. Ignore the motion of the nucleus in your calculation. The radius of the first Bohr orbit of a hydrogen atom (called the Bohr radius,  $a_0 = \frac{\epsilon_0 \hbar^2}{m_e e^2 \pi}$ ) is 0.53 Å.

The classical picture of an "orbit" in Bohr's theory has now been replaced by the quantum mechanical notion of an 'orbital'. The orbital  $\psi_{1s}(r)$  for the ground state of a hydrogen atom is given by

$$\Psi_{1s}(r) = \frac{1}{\sqrt{\pi a_0^3}} e^{-r/a_0}$$

where  $r$  is the distance of the electron from the nucleus and  $a_0$  is the Bohr radius.

**1.4** Consider a spherical shell of radius  $a_0$  and thickness  $0.001a_0$ . Estimate the probability of finding the electron in this shell. Volume of a spherical shell of inner radius  $r$  and small thickness  $\Delta r$  equals  $4\pi r^2 \Delta r$ .

The  $\text{H}_2$  molecule can dissociate through two different channels:

- (i)  $\text{H}_2 \rightarrow \text{H} + \text{H}$  (two separate hydrogen atoms)
- (ii)  $\text{H}_2 \rightarrow \text{H}^+ + \text{H}^-$  (a proton and a hydride ion)

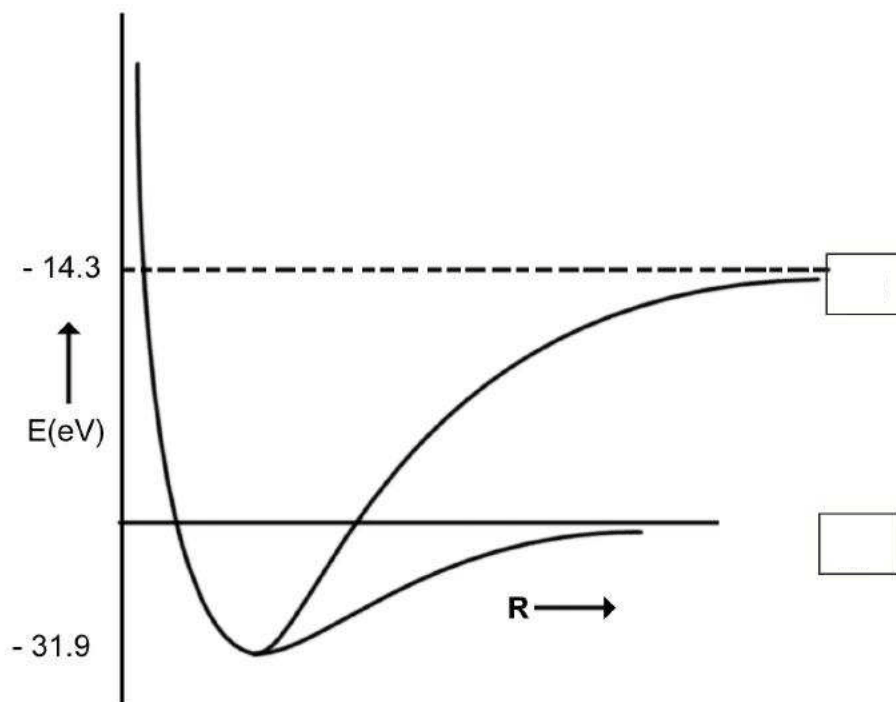
The graph of energy ( $E$ ) vs internuclear distance ( $R$ ) for  $\text{H}_2$  is shown schematically in the figure. The atomic and molecular energies are given in the same scale.

**1.5** Put appropriate channel labels (i) or (ii) in the boxes below.

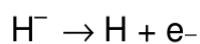
**1.6** Determine the values of the dissociation energies ( $D_e$  in eV) of the  $\text{H}_2$  molecule corresponding to

channel (i)

channel (ii)



1.7 From the given data, calculate the energy change for the process



1.8  $\text{H}^-$  is a two-electron atomic system. Assuming that the Bohr energy formula is valid for each electron with nuclear charge  $Z$  replaced by  $Z_{\text{eff}}$ , calculate  $Z_{\text{eff}}$  for  $\text{H}^-$ .

Official English text of the problem.

## Answers

- 1.1  $\lambda_{\text{max}} = 1.641 \times 10^3 \text{ \AA}$ , for the  $n = 3 \rightarrow 2$  transition.
- 1.2  $\lambda^{-1} = R_{\text{H}}(1 - n^{-2})$ ,  $n = 2, 3, \dots$ ;  $E_1 = -13.6 \text{ eV}$ .
- 1.3  $E_1^{(\mu)} \approx -2.81 \times 10^3 \text{ eV}$ ;  $r_1^{(\mu)} \approx 2.6 \times 10^{-3} \text{ \AA} = 2.6 \times 10^{-13} \text{ m}$ .
- 1.4  $P \approx 5.41 \times 10^{-4} = 0.0541\%$ .
- 1.5 Upper box: (ii). Lower box: (i).
- 1.6 Channel (i):  $D_e = 4.7 \text{ eV}$ . Channel (ii):  $D_e = 17.6 \text{ eV}$ .
- 1.7  $\Delta E = +0.7 \text{ eV}$ ; energy must be supplied.
- 1.8  $Z_{\text{eff}} = 0.725$ .

## Solution

The species used below are the hydrogen atom  $\text{H}$ ,  $[\text{H}]$ ; hydrogen molecule  $\text{H}_2$ ,  $[\text{H}][\text{H}]$ ; singly ionized helium  $\text{He}^+$ ,  $[\text{He}^+]$ ; proton  $\text{H}^+$ ,  $[\text{H}^+]$ ; and hydride ion  $\text{H}^-$ ,  $[\text{H}^-]$ . Ordinary SMILES cannot represent a free electron, replacement of an electron by a muon, or an orbital wavefunction.

Energies are measured relative to separated nuclei and free electrons at rest. For numerical conversion,  $hc = 1.23984198 \times 10^{-4} \text{ eV cm}$ .

### 1.1 — Longest wavelength in the helium-ion Balmer series

For a one-electron ion of nuclear charge  $Z$ , neglecting nuclear motion,

$$\frac{1}{\lambda} = R_{\text{H}} Z^2 \left( \frac{1}{n_f^2} - \frac{1}{n_i^2} \right).$$

The Balmer series has  $n_f = 2$ . Its longest wavelength corresponds to its smallest transition energy, hence  $n_i = 3$ . For singly ionized helium,  $Z = 2$ :

$$\frac{1}{\lambda_{\text{max}}} = 4R_{\text{H}} \left( \frac{1}{4} - \frac{1}{9} \right) = \frac{5}{9} R_{\text{H}}.$$

Therefore,

$$\lambda_{\text{max}} = \frac{9}{5(109\,678)} \text{ cm} = 1.64117 \times 10^{-5} \text{ cm}.$$

Using  $1 \text{ cm} = 10^8 \text{ \AA}$ ,

$$\boxed{\lambda_{\text{max}} \approx 1641 \text{ \AA}}.$$

### 1.2 — Transitions to the ground state and its energy

Transitions terminating at  $n_f = 1$  constitute the Lyman series:

$$\boxed{\frac{1}{\lambda} = R_{\text{H}} \left( 1 - \frac{1}{n^2} \right), \quad n = 2, 3, 4, \dots}$$

At the series limit,  $n \rightarrow \infty$ , the initial electron is at the zero-energy ionization threshold. Thus,

$$0 - E_1 = \frac{hc}{\lambda_{\text{limit}}} = hcR_{\text{H}}.$$

Consequently,

$$E_1 = -hcR_{\text{H}} = -(1.23984198 \times 10^{-4})(109\,678) \text{ eV} = -13.5983 \text{ eV}.$$

Hence,

$$\boxed{E_1 \approx -13.6 \text{ eV}}.$$

The negative sign indicates that the electron is bound.

### 1.3 — Muonic hydrogen

With a fixed nucleus and an orbiting particle of mass  $m$  and charge  $-e$ , the Bohr formulas give

$$E_n = -\frac{me^4}{8\varepsilon_0^2 h^2 n^2}, \quad r_n = \frac{\varepsilon_0 h^2 n^2}{\pi m e^2}.$$

Thus the binding-energy magnitude is proportional to  $m$ , while the radius is inversely proportional to  $m$ . Substituting  $m_\mu = 207m_e$ ,

$$E_1^{(\mu)} = 207E_1^{(\text{H})} = 207(-13.5983) \text{ eV} \approx -2814.9 \text{ eV}.$$

Therefore,

$$E_1^{(\mu)} \approx -2.81 \times 10^3 \text{ eV}.$$

The first-orbit radius is

$$r_1^{(\mu)} = \frac{a_0}{207} = \frac{0.53}{207} \text{ \AA} = 2.5604 \times 10^{-3} \text{ \AA}.$$

To the precision of the supplied Bohr radius,

$$r_1^{(\mu)} \approx 2.6 \times 10^{-3} \text{ \AA} = 2.6 \times 10^{-13} \text{ m}.$$

#### 1.4 — Probability within the spherical shell

The probability density is the squared magnitude of the wavefunction:

$$|\Psi_{1s}(r)|^2 = \frac{1}{\pi a_0^3} e^{-2r/a_0}.$$

For a sufficiently thin shell,

$$P \approx |\Psi_{1s}(r)|^2 4\pi r^2 \Delta r.$$

At  $r = a_0$ , with  $\Delta r = 0.001a_0$ ,

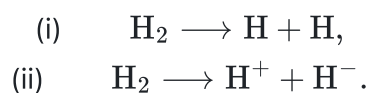
$$\begin{aligned} P &\approx \frac{e^{-2}}{\pi a_0^3} 4\pi a_0^2 (0.001a_0) \\ &= 0.004e^{-2} \\ &= 5.4134 \times 10^{-4}. \end{aligned}$$

Thus,

$$P \approx 5.41 \times 10^{-4} = 0.0541\%.$$

#### 1.5 — Identification of the dissociation channels

The two balanced dissociation equations are



For channel (i), the energy of the two infinitely separated ground-state hydrogen atoms is

$$E_\infty^{(i)} = 2E_1^{(\text{H})} \approx 2(-13.6) = -27.2 \text{ eV}.$$

This must be the lower asymptote. The upper asymptote, at  $-14.3 \text{ eV}$ , therefore corresponds to channel (ii).

Fill the **upper box with (ii)** and the **lower box with (i)**.

For the ionic channel, the bare proton has zero electronic energy, so the upper asymptote also establishes

$$E(\text{H}^-) = -14.3 \text{ eV}.$$

## 1.6 — Dissociation energies

The molecular potential-energy minimum is

$$E_{\min}(\text{H}_2) = -31.9 \text{ eV}.$$

Each dissociation energy is the product asymptote minus this minimum.

For channel (i),

$$\begin{aligned}\text{H}_2 &\longrightarrow \text{H} + \text{H}, \\ D_e^{(i)} &= -27.2 - (-31.9) = \boxed{4.7 \text{ eV}}.\end{aligned}$$

For channel (ii),

$$\begin{aligned}\text{H}_2 &\longrightarrow \text{H}^+ + \text{H}^-, \\ D_e^{(ii)} &= -14.3 - (-31.9) = \boxed{17.6 \text{ eV}}.\end{aligned}$$

Enter these values in the corresponding channel (i) and channel (ii) answer boxes.

## 1.7 — Electron detachment from hydride

The balanced process is



Using zero energy for the detached free electron,

$$\begin{aligned}\Delta E &= E(\text{H}) + E(\text{e}^-) - E(\text{H}^-) \\ &= -13.6 + 0 - (-14.3) \\ &= \boxed{+0.7 \text{ eV}}.\end{aligned}$$

The process requires 0.7 eV per hydride ion.

## 1.8 — Effective nuclear charge of hydride

In the stipulated model, both electrons occupy the  $n = 1$  level, and each has energy

$$E_{\text{electron}} = -13.6 Z_{\text{eff}}^2 \text{ eV}.$$

The total energy is therefore

$$E(\text{H}^-) = 2(-13.6 Z_{\text{eff}}^2) = -27.2 Z_{\text{eff}}^2 \text{ eV}.$$

Equating this to the energy obtained from the graph,

$$-27.2 Z_{\text{eff}}^2 = -14.3,$$

so

$$Z_{\text{eff}} = \sqrt{\frac{14.3}{27.2}} = 0.725.$$

Its value below 1 represents screening of the proton's attraction by the other electron within this model.

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

## Problem 2: Phosphoric Acid

Phosphoric acid is of a great importance in fertilizer industry. Besides, phosphoric acid and its various salts have a number of applications in metal treatment, food, detergent and toothpaste industries.

**2.1** The  $pK$  values of the three successive dissociations of phosphoric acid at 25 °C are:

$$pK_{1a} = 2.12$$

$$pK_{2a} = 7.21$$

$$pK_{3a} = 12.32$$

Write down the conjugate base of dihydrogen phosphate ion and determine its  $pK_b$  value.

Small quantities of phosphoric acid are extensively used to impart the sour or tart taste to many soft drinks such as colas and root beers. A cola having a density of  $1.00 \text{ g cm}^{-3}$  contains 0.05 % by weight of phosphoric acid.

**2.2** Determine the pH of the cola (ignoring the second and the third dissociation steps for phosphoric acid). Assume that the acidity of the cola arises only from phosphoric acid.

**2.3** Phosphoric acid is used as a fertiliser for agriculture.  $1.00 \times 10^{-3} \text{ M}$  phosphoric acid is added to an aqueous soil suspension and the pH is found to be 7.00.

Determine the fractional concentrations of all the different phosphate species present in the solution. Assume that no component of the soil interacts with any phosphate species.

**2.4** Zinc is an essential micronutrient for plant growth. Plant can absorb zinc in water soluble form only. In a given soil water with  $pH = 7.0$ , zinc phosphate was found to be the only source of zinc and phosphate. Calculate the concentration of  $[\text{Zn}^{2+}]$  and  $[\text{PO}_4^{3-}]$  ions in the solution.  $K_{sp}$  for zinc phosphate is  $9.1 \times 10^{-33}$ .

Official English text of the problem.

## Answers

- 2.1:** The conjugate base is the **hydrogen phosphate ion**,  $\text{HPO}_4^{2-}$ , SMILES O=P([O-])[O-].

$$pK_b = 6.79$$

- 2.2:**

$$pH \approx 2.46$$

- 2.3:** With  $C_T$  the total concentration of dissolved phosphate, the dimensionless fractions are:

| Species                                             | SMILES                     | Fraction, $[\text{species}]/C_T$ |
|-----------------------------------------------------|----------------------------|----------------------------------|
| Phosphoric acid, $\text{H}_3\text{PO}_4$            | <chem>O=P(O)(O)O</chem>    | $8.15 \times 10^{-6}$            |
| Dihydrogen phosphate ion, $\text{H}_2\text{PO}_4^-$ | <chem>O=P([O-])(O)O</chem> | $0.618578 \approx 0.619$         |

| Species                                     | SMILES                           | Fraction, $[\text{species}]/C_T$ |
|---------------------------------------------|----------------------------------|----------------------------------|
| Hydrogen phosphate ion, $\text{HPO}_4^{2-}$ | <chem>O=P([O-])([O-])O</chem>    | $0.381412 \approx 0.381$         |
| Phosphate ion, $\text{PO}_4^{3-}$           | <chem>O=P([O-])([O-])[O-]</chem> | $1.83 \times 10^{-6}$            |

- **2.4:** For zinc(II) ion,  $\text{Zn}^{2+}$ , SMILES [zn+2], and phosphate ion:

$$[\text{Zn}^{2+}] = 9.1 \times 10^{-5} \text{ mol L}^{-1}$$

$$[\text{PO}_4^{3-}] = 1.1 \times 10^{-10} \text{ mol L}^{-1}$$

## Solution

Use concentrations in place of activities and  $pK_w = 14.00$  at  $25^\circ\text{C}$ . The additional species appearing in the equilibria are water,  $\text{H}_2\text{O}$ , SMILES O; hydronium ion,  $\text{H}_3\text{O}^+$ , SMILES [OH3+]; and hydroxide ion,  $\text{OH}^-$ , SMILES [OH-].

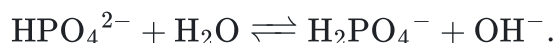
The phosphate SMILES above represent particular Lewis structures; they do not depict resonance delocalization.

### 2.1

A conjugate base is formed by removing one proton. Thus dihydrogen phosphate gives hydrogen phosphate:



This is the **second** dissociation of phosphoric acid, so its acid constant is  $K_{2a}$ . The corresponding base reaction is



For this conjugate acid–base pair,

$$K_{2a}K_b = K_w,$$

and therefore

$$pK_b = pK_w - pK_{2a} = 14.00 - 7.21 = 6.79.$$

### 2.2

One litre of cola has mass

$$m = (1000 \text{ cm}^3)(1.00 \text{ g cm}^{-3}) = 1000 \text{ g}.$$

Its phosphoric acid content is

$$m(\text{H}_3\text{PO}_4) = \frac{0.05}{100}(1000 \text{ g}) = 0.50 \text{ g}.$$

Using  $M(\text{H}_3\text{PO}_4) = 98.0 \text{ g mol}^{-1}$ , the analytical acid concentration is

$$C = \frac{0.50 \text{ g}}{(98.0 \text{ g mol}^{-1})(1.00 \text{ L})} = 5.102 \times 10^{-3} \text{ mol L}^{-1}.$$

Retaining only the first dissociation,



Let  $x = [\text{H}_3\text{O}^+]$ . Neglecting water's contribution to this acidic solution,

$$[\text{H}_2\text{PO}_4^-] = x, \quad [\text{H}_3\text{PO}_4] = C - x.$$

Hence

$$K_{1a} = \frac{x^2}{C - x},$$

so

$$x^2 + K_{1a}x - K_{1a}C = 0.$$

The positive root gives

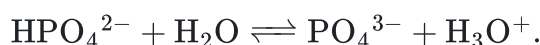
$$x = \frac{-K_{1a} + \sqrt{K_{1a}^2 + 4K_{1a}C}}{2} = 3.493 \times 10^{-3} \text{ mol L}^{-1}.$$

Here  $x/C \approx 0.685$ , so the approximation  $C - x \approx C$  would be unsuitable. Thus

$$\boxed{\text{pH} = -\log_{10}(3.493 \times 10^{-3}) = 2.46}.$$

## 2.3

The third dissociation, completing the equilibria already written above, is



For brevity, write  $K_1 = K_{1a}$ ,  $K_2 = K_{2a}$ , and  $K_3 = K_{3a}$ . Their values are

$$K_1 = 7.586 \times 10^{-3}, \quad K_2 = 6.166 \times 10^{-8}, \quad K_3 = 4.786 \times 10^{-13}.$$

At the specified pH,

$$h = [\text{H}_3\text{O}^+] = 1.00 \times 10^{-7} \text{ mol L}^{-1}.$$

The successive equilibria give

$$\frac{[\text{H}_2\text{PO}_4^-]}{[\text{H}_3\text{PO}_4]} = \frac{K_1}{h}, \quad \frac{[\text{HPO}_4^{2-}]}{[\text{H}_2\text{PO}_4^-]} = \frac{K_2}{h}, \quad \frac{[\text{PO}_4^{3-}]}{[\text{HPO}_4^{2-}]} = \frac{K_3}{h}.$$

The phosphate balance is

$$C_T = [\text{H}_3\text{PO}_4] + [\text{H}_2\text{PO}_4^-] + [\text{HPO}_4^{2-}] + [\text{PO}_4^{3-}].$$

Defining

$$D = h^3 + K_1h^2 + K_1K_2h + K_1K_2K_3,$$

the fractions follow directly:

$$\begin{aligned} \alpha_0 &= \frac{[\text{H}_3\text{PO}_4]}{C_T} = \frac{h^3}{D} = 8.15445 \times 10^{-6}, \\ \alpha_1 &= \frac{[\text{H}_2\text{PO}_4^-]}{C_T} = \frac{K_1h^2}{D} = 0.61857795, \\ \alpha_2 &= \frac{[\text{HPO}_4^{2-}]}{C_T} = \frac{K_1K_2h}{D} = 0.38141207, \\ \alpha_3 &= \frac{[\text{PO}_4^{3-}]}{C_T} = \frac{K_1K_2K_3}{D} = 1.82555 \times 10^{-6}. \end{aligned}$$

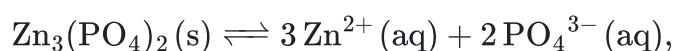
These fractions sum to unity. At fixed pH,  $C_T$  cancels from the fractional concentrations. For the stated  $C_T = 1.00 \times 10^{-3} \text{ mol L}^{-1}$ , the corresponding concentrations are:

| Species                   | Concentration / $\text{mol L}^{-1}$ |
|---------------------------|-------------------------------------|
| $\text{H}_3\text{PO}_4$   | $8.15 \times 10^{-9}$               |
| $\text{H}_2\text{PO}_4^-$ | $6.19 \times 10^{-4}$               |
| $\text{HPO}_4^{2-}$       | $3.81 \times 10^{-4}$               |
| $\text{PO}_4^{3-}$        | $1.83 \times 10^{-9}$               |

## 2.4

Charge neutrality requires zinc phosphate to have formula  $\text{Zn}_3(\text{PO}_4)_2$ : three zinc(II) ions balance two phosphate ions. Its constituent-ion SMILES is  $[\text{Zn}^{+2}] \cdot [\text{Zn}^{+2}] \cdot [\text{Zn}^{+2}] \cdot \text{O}=\text{P}([\text{O}^-])([\text{O}^-])$   
 $[\text{O}^-] \cdot \text{O}=\text{P}([\text{O}^-])([\text{O}^-])$ ; this does not specify its crystal lattice.

The dissolution equilibrium is



with

$$K_{\text{sp}} = [\text{Zn}^{2+}]^3 [\text{PO}_4^{3-}]^2.$$

Let  $s$  be the molar solubility of zinc phosphate. Within the supplied equilibrium model, dissolved zinc is treated as  $\text{Zn}^{2+}$ . Since the solid is the only source of both zinc and phosphate,

$$[\text{Zn}^{2+}] = 3s, \quad C_T = 2s.$$

The dissolved phosphate distributes among all four protonation states. At pH 7.0, part 2.3 gives

$$\alpha_3 = \frac{[\text{PO}_4^{3-}]}{C_T} = 1.82555 \times 10^{-6},$$

so

$$[\text{PO}_4^{3-}] = 2s\alpha_3.$$

Consequently,

$$K_{\text{sp}} = (3s)^3 (2s\alpha_3)^2 = 108\alpha_3^2 s^5.$$

Therefore,

$$s = \left[ \frac{9.1 \times 10^{-33}}{108(1.82555 \times 10^{-6})^2} \right]^{1/5} = 3.02389 \times 10^{-5} \text{ mol L}^{-1}.$$

The requested concentrations are

$$[\text{Zn}^{2+}] = 3s = 9.1 \times 10^{-5} \text{ mol L}^{-1}$$

and

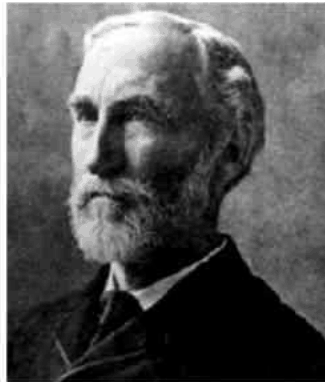
$$[\text{PO}_4^{3-}] = 2s\alpha_3 = 1.1 \times 10^{-10} \text{ mol L}^{-1}.$$

Using the unrounded concentrations reproduces  $[\text{Zn}^{2+}]^3 [\text{PO}_4^{3-}]^2 = 9.1 \times 10^{-33}$ .

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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: Second Law of Thermodynamics



J.W.Gibbs (1839 –1903)

J.W.Gibbs (1839 –1903)

The second law of thermodynamics is a fundamental law of science. In this problem we consider the thermodynamics of an ideal gas, phase transitions and chemical equilibrium.

3.00 mol of  $\text{CO}_2$  gas expands isothermally (in thermal contact with the surroundings; temperature = 15 °C) against a fixed external pressure of 1.00 bar. The initial and final volumes of the gas are 10.0 dm<sup>3</sup> and 30.0 dm<sup>3</sup>, respectively.

**3.1** Choose the correct option for change in the entropy of the system ( $\Delta S_{\text{sys}}$ ) and of the surroundings ( $\Delta S_{\text{sur}}$ ):

|     | $\Delta S_{\text{sys}}$ | $\Delta S_{\text{sur}}$ |                          |
|-----|-------------------------|-------------------------|--------------------------|
| (a) | $> 0$                   | $= 0$                   | <input type="checkbox"/> |
| (b) | $< 0$                   | $> 0$                   | <input type="checkbox"/> |
| (c) | $> 0$                   | $< 0$                   | <input type="checkbox"/> |
| (d) | $= 0$                   | $= 0$                   | <input type="checkbox"/> |

(Mark X in the correct box.)

**3.2** Calculate  $\Delta S_{\text{sys}}$  assuming  $\text{CO}_2$  to be an ideal gas.

**3.3** Calculate  $\Delta S_{\text{sur}}$ .

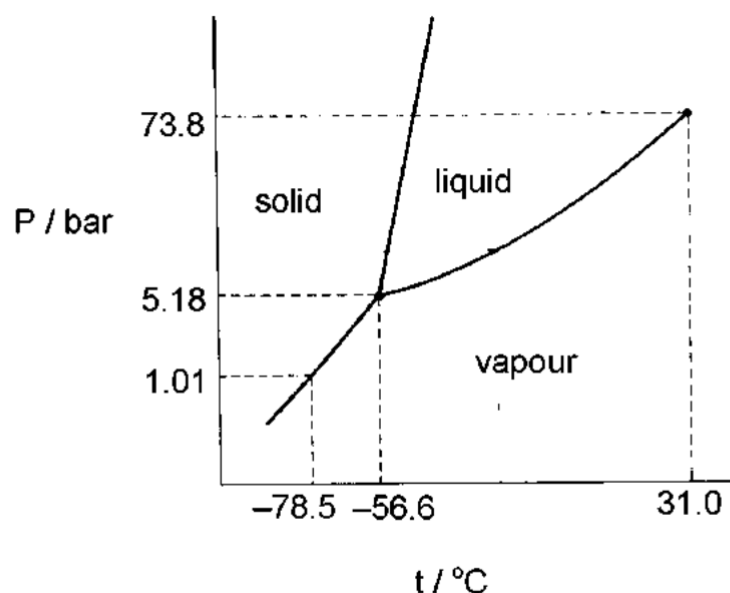
**3.4** Calculate the change in entropy of the universe.

Does your answer agree with the Second Law of Thermodynamics?

(Mark X in the correct box.)

☐ Yes   ☐ No

The pressure – temperature phase diagram of  $\text{CO}_2$  is given below schematically. The diagram is not to scale.



Phase diagram of CO<sub>2</sub>

Phase diagram of CO<sub>2</sub>

**3.5** CO<sub>2</sub> gas, initially at a pressure of 4.0 bar and temperature of 10.0 °C is cooled at constant pressure. In this process,

- (a) it goes first to the liquid phase and then to the solid phase. ☐
- (b) it goes to the solid phase without going through the liquid phase. ☐

**3.6** Starting with the same pressure and temperature as above (in 3.5), CO<sub>2</sub> is compressed isothermatically. In this process,

- (a) it goes first to the liquid phase and then to the solid phase. ☐
- (b) it goes to the solid phase without going through the liquid phase. ☐

**3.7** From the data given in the phase diagram, calculate the molar enthalpy change of sublimation of CO<sub>2</sub>. Write down the formula used.

**3.8** CO gas, used extensively in organic synthesis, can be obtained by reacting CO<sub>2</sub> gas with graphite. Use the data given below to show that the equilibrium constant at 298.15 K is less than unity.

At 298.15 K

|                     | $\Delta H_f^0 / \text{kJ mol}^{-1}$ | $S^0 / \text{J K}^{-1} \text{mol}^{-1}$ |
|---------------------|-------------------------------------|-----------------------------------------|
| CO <sub>2</sub> (g) | -393.51                             | 213.79                                  |
| CO (g)              | -110.53                             | 197.66                                  |
| C(graphite)         |                                     | 5.74                                    |

**3.9** Estimate the temperature at which the reaction would have an equilibrium constant equal to 1. Ignore slight variations in the thermodynamic data with temperature.

**3.10** The reaction above (in 3.8) is carried out between  $\text{CO}_2$  and excess hot graphite in a reactor maintained at about 800 °C and a total pressure of 5.0 bar. The equilibrium constant  $K_p$  under these conditions is 10.0. Calculate the partial pressure of CO at equilibrium.

Official English text of the problem.

## Answers

- **3.1: (c):**  $\Delta S_{\text{sys}} > 0$ ,  $\Delta S_{\text{sur}} < 0$ . Mark X in box (c).
- **3.2:**  $\Delta S_{\text{sys}} = +27.4 \text{ J K}^{-1}$ .
- **3.3:**  $\Delta S_{\text{sur}} = -6.94 \text{ J K}^{-1}$ .
- **3.4:**  $\Delta S_{\text{univ}} = +20.5 \text{ J K}^{-1}$ . Mark X in **Yes**.
- **3.5: (b):** carbon dioxide ( $\text{O}=\text{C}=\text{O}$ ) passes directly from gas to solid.
- **3.6: (a):** gas  $\rightarrow$  liquid  $\rightarrow$  solid, with sufficiently large compression.
- **3.7:**  $\Delta_{\text{sub}} H_m \approx +26.2 \text{ kJ mol}^{-1}$ , using
 
$$\ln\left(\frac{P_2}{P_1}\right) = \frac{\Delta_{\text{sub}} H_m}{R} \left(\frac{1}{T_1} - \frac{1}{T_2}\right).$$
- **3.8:**  $\Delta_r G^\circ = +120.04 \text{ kJ mol}^{-1}$ , giving  $K \approx 9.31 \times 10^{-22} < 1$ .
- **3.9:**  $T \approx 981 \text{ K} \approx 708^\circ\text{C}$ .
- **3.10:** Carbon monoxide ( $[\text{C}-]\#[\text{O}+]$ ):  $p_{\text{CO}} = 3.66 \text{ bar} \approx 3.7 \text{ bar}$ .

## Solution

The molecular species used throughout are **carbon dioxide**,  $\text{CO}_2$ , SMILES  $\text{O}=\text{C}=\text{O}$ , and **carbon monoxide**, CO, SMILES  $[\text{C}-]\#[\text{O}+]$ . Graphite is an extended carbon lattice and has no single finite molecular SMILES.

Use  $R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1}$  and  $1 \text{ bar dm}^3 = 100 \text{ J}$ .

### 3.1

An isothermal expansion increases the entropy of an ideal gas because its accessible volume increases.

The gas performs work against the external pressure. Its internal energy remains constant at constant temperature, so it absorbs heat from the surroundings. The surroundings therefore lose entropy.

Thus,

$$\Delta S_{\text{sys}} > 0, \quad \Delta S_{\text{sur}} < 0.$$

Mark X in **box (c)**.

### 3.2

Entropy is a state function, so the system's entropy change can be calculated along a reversible isothermal path between the specified initial and final states:

$$\Delta S_{\text{sys}} = \int_{V_i}^{V_f} \frac{\delta q_{\text{rev}}}{T} = \int_{V_i}^{V_f} \frac{nR}{V} dV = nR \ln\left(\frac{V_f}{V_i}\right).$$

Therefore,

$$\begin{aligned}\Delta S_{\text{sys}} &= (3.00 \text{ mol})(8.314 \text{ J mol}^{-1} \text{ K}^{-1}) \ln\left(\frac{30.0}{10.0}\right) \\ &= \boxed{+27.4 \text{ J K}^{-1}}.\end{aligned}$$

The actual expansion is irreversible; its actual heat divided by the temperature is not the system's entropy change.

### 3.3

Using the convention that  $w$  is work done on the gas,

$$w = -P_{\text{ext}}(V_f - V_i).$$

Thus,

$$\begin{aligned}w &= -(1.00 \text{ bar})(30.0 - 10.0) \text{ dm}^3 \\ &= -20.0 \text{ bar dm}^3 \\ &= -2.00 \times 10^3 \text{ J}.\end{aligned}$$

For an ideal gas, internal energy depends only on temperature. Since the expansion is isothermal,

$$\Delta U = q_{\text{sys}} + w = 0,$$

and hence

$$q_{\text{sys}} = -w = +2.00 \times 10^3 \text{ J}.$$

The surroundings supply this heat at the constant temperature

$$T_{\text{sur}} = 15 + 273.15 = 288.15 \text{ K}.$$

Consequently,

$$\Delta S_{\text{sur}} = \frac{q_{\text{sur}}}{T_{\text{sur}}} = -\frac{q_{\text{sys}}}{T_{\text{sur}}} = \frac{-2.00 \times 10^3}{288.15} = \boxed{-6.94 \text{ J K}^{-1}}.$$

### 3.4

The entropy change of the universe is the sum of the system and surroundings contributions:

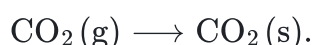
$$\begin{aligned}\Delta S_{\text{univ}} &= \Delta S_{\text{sys}} + \Delta S_{\text{sur}} \\ &= 27.4016 - 6.94083 \\ &= \boxed{+20.5 \text{ J K}^{-1}}.\end{aligned}$$

This positive value agrees with the second law and indicates entropy production in the irreversible expansion. Mark X in **Yes**.

### 3.5

The pressure 4.0 bar is below the triple-point pressure, 5.18 bar. There is therefore no stable liquid phase along this constant-pressure cooling path.

Moving leftward at 4.0 bar on the phase diagram crosses the gas–solid boundary. Carbon dioxide deposits directly as a solid:

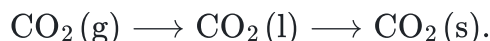


Mark X in **box (b)**.

### 3.6

The temperature  $10.0\text{ }^{\circ}\text{C}$  lies above the triple-point temperature,  $-56.6\text{ }^{\circ}\text{C}$ , and below the critical temperature,  $31.0\text{ }^{\circ}\text{C}$ .

Increasing pressure at this fixed temperature first crosses the vapour–liquid boundary, so the gas condenses. With sufficiently large further compression, the positively sloping solid–liquid boundary is crossed and the liquid solidifies:



Mark X in **box (a)**.

### 3.7

The sublimation process is



Approximate the vapour as an ideal gas, neglect the solid's molar volume compared with the vapour's, and take the sublimation enthalpy as constant over the temperature interval. The integrated Clausius–Clapeyron equation is then

$$\ln\left(\frac{P_2}{P_1}\right) = -\frac{\Delta_{\text{sub}}H_m}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right).$$

The two points on the solid–vapour equilibrium curve are

$$\begin{aligned} P_1 &= 1.01 \text{ bar}, & T_1 &= -78.5 + 273.15 = 194.65 \text{ K}, \\ P_2 &= 5.18 \text{ bar}, & T_2 &= -56.6 + 273.15 = 216.55 \text{ K}. \end{aligned}$$

Therefore,

$$\begin{aligned} \Delta_{\text{sub}}H_m &= \frac{R \ln(P_2/P_1)}{1/T_1 - 1/T_2} \\ &= \frac{(8.314 \text{ J mol}^{-1} \text{ K}^{-1}) \ln(5.18/1.01)}{(1/194.65 - 1/216.55) \text{ K}^{-1}} \\ &= 2.6161 \times 10^4 \text{ J mol}^{-1}. \end{aligned}$$

Thus,

$$\boxed{\Delta_{\text{sub}}H_m \approx +26.2 \text{ kJ mol}^{-1}}.$$

The positive sign corresponds to heat absorption during sublimation.

### 3.8

The balanced reaction is



Graphite is the standard state of elemental carbon, so its standard enthalpy of formation is zero. The standard reaction enthalpy is

$$\begin{aligned} \Delta_r H^\circ &= 2\Delta_f H^\circ(\text{CO}) - \Delta_f H^\circ(\text{CO}_2) - \Delta_f H^\circ(\text{C}(\text{graphite})) \\ &= 2(-110.53) - (-393.51) - 0 \\ &= \boxed{+172.45 \text{ kJ mol}^{-1}}. \end{aligned}$$

The standard reaction entropy is

$$\begin{aligned}\Delta_r S^\circ &= 2S^\circ(\text{CO}) - S^\circ(\text{CO}_2) - S^\circ(\text{C}(\text{graphite})) \\ &= 2(197.66) - 213.79 - 5.74 \\ &= \boxed{+175.79 \text{ J K}^{-1} \text{ mol}^{-1}}.\end{aligned}$$

At 298.15 K,

$$\begin{aligned}\Delta_r G^\circ &= \Delta_r H^\circ - T\Delta_r S^\circ \\ &= 172.45 - (298.15)(0.17579) \\ &= \boxed{+120.04 \text{ kJ mol}^{-1}}.\end{aligned}$$

Since

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

a positive standard reaction Gibbs energy implies  $K < 1$ . Numerically,

$$\ln K = -\frac{120038.2}{(8.314)(298.15)} = -48.4256,$$

so

$$\boxed{K \approx 9.31 \times 10^{-22} < 1}.$$

### 3.9

When  $K = 1$ ,

$$\Delta_r G^\circ = -RT \ln 1 = 0.$$

Ignoring the temperature dependence of the reaction enthalpy and entropy,

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

and therefore

$$\begin{aligned}T &= \frac{\Delta_r H^\circ}{\Delta_r S^\circ} \\ &= \frac{172450 \text{ J mol}^{-1}}{175.79 \text{ J K}^{-1} \text{ mol}^{-1}} \\ &= \boxed{981 \text{ K}}.\end{aligned}$$

In degrees Celsius,

$$\boxed{t \approx 708^\circ \text{C}}.$$

### 3.10

For



the activity of the pure graphite is unity. Using ideal-gas partial pressures and  $p^\circ = 1 \text{ bar}$ ,

$$K_p = \frac{(p_{\text{CO}}/p^\circ)^2}{p_{\text{CO}_2}/p^\circ} = \frac{p_{\text{CO}}^2}{p_{\text{CO}_2}p^\circ}.$$

The gas contains only carbon monoxide and carbon dioxide, so

$$p_{\text{CO}} + p_{\text{CO}_2} = 5.0 \text{ bar}.$$

Let  $x = p_{\text{CO}}/p^\circ$ . Then  $p_{\text{CO}_2}/p^\circ = 5.0 - x$ , and the supplied equilibrium constant gives

$$10.0 = \frac{x^2}{5.0 - x}.$$

Rearrangement yields

$$x^2 + 10.0x - 50.0 = 0.$$

The physically admissible root is

$$x = \frac{-10.0 + \sqrt{10.0^2 + 4(50.0)}}{2} = 3.66025.$$

Thus,

$$\boxed{p_{\text{CO}} = 3.66 \text{ bar} \approx 3.7 \text{ bar}}.$$

The corresponding carbon dioxide partial pressure is 1.34 bar, and these values satisfy both the total pressure and the equilibrium expression.

---

The solution was checked against the official solution.

## Problem 4: Thorium, uranium and lead in monazite



**Beach Sand Mineral in Kerala**

### Beach Sand Mineral in Kerala

Beach sand mineral, monazite, is a rich source of thorium, available in large quantities in the state of Kerala in India. A typical monazite sample contains about 9 %  $\text{ThO}_2$  and 0.35 %  $\text{U}_3\text{O}_8$ .  $^{208}\text{Pb}$  and  $^{206}\text{Pb}$  are the stable end-products in the radioactive decay series of  $^{232}\text{Th}$  and  $^{238}\text{U}$ , respectively. All the lead (Pb) found in monazite is of radiogenic origin.

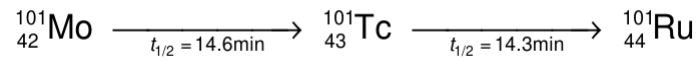
The isotopic atom ratio  $^{208}\text{Pb}/^{232}\text{Th}$ , measured mass spectrometrically, in a monazite sample was found to be 0.104. The half-lives of  $^{232}\text{Th}$  and  $^{238}\text{U}$   $1.41 \times 10^{10}$  years and  $4.47 \times 10^9$  years, respectively. Assume that  $^{208}\text{Pb}$ ,  $^{206}\text{Pb}$ ,  $^{232}\text{Th}$  and  $^{238}\text{U}$  remained entirely in the monazite sample since the formation of monazite mineral.

**4.1** Calculate the age (time elapsed since its formation) of the monazite sample.

**4.2** Estimate the isotopic atom ratio  $^{206}\text{Pb}/^{238}\text{U}$  in the monazite sample.

**4.3** Thorium-232 is a fertile material for nuclear energy. In thermal neutron irradiation, it absorbs a neutron and the resulting isotope forms  $^{233}\text{U}$  by successive  $\beta^-$  decays. Write the nuclear reactions for the formation of  $^{233}\text{U}$  from  $^{232}\text{Th}$ .

In nuclear fission of  $^{233}\text{U}$  a complex mixture of radioactive fission products is formed. The fission product  $^{101}\text{Mo}$  initially undergoes radioactive decay as shown below:



**4.4** A freshly prepared radiochemically pure sample of  $^{101}\text{Mo}$  contains 5000 atoms of  $^{101}\text{Mo}$  initially. How many atoms of

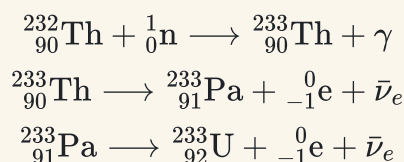
- i)  $^{101}\text{Mo}$
- ii)  $^{101}\text{Tc}$
- iii)  $^{101}\text{Ru}$

will be present in the sample after 14.6 min?

Official English text of the problem.

## Answers

- **4.1:**  $2.01 \times 10^9 \text{ years}$ .
- **4.2:**  $N(^{206}\text{Pb})/N(^{238}\text{U}) = 0.366$ .
- **4.3:** Neutron capture produces thorium-233, which undergoes two successive  $\beta^-$  decays through protactinium-233 to uranium-233:



- **4.4:** Expected populations, rounded to whole atoms: **(i)** 2500 atoms of  $^{101}\text{Mo}$ ; **(ii)** 1720 atoms of  $^{101}\text{Tc}$ ; **(iii)** 780 atoms of  $^{101}\text{Ru}$ .

## Solution

### 4.1 — Age of the monazite

Take the radiogenic lead to have accumulated since mineral formation, with no initial lead and negligible accumulation of intermediate decay-chain nuclides. Each parent nucleus that completes its decay chain produces one lead nucleus.

Let  $P_0$  be the initial number of parent atoms,  $P$  the present number, and  $D$  the number of radiogenic daughter atoms. Radioactive decay gives

$$P = P_0 e^{-\lambda t}, \quad D = P_0 - P, \quad \lambda = \frac{\ln 2}{t_{1/2}}.$$

Consequently,

$$\frac{D}{P} = \frac{P_0 - P}{P} = e^{\lambda t} - 1,$$

and hence

$$t = \frac{t_{1/2}}{\ln 2} \ln \left( 1 + \frac{D}{P} \right).$$

For the thorium-232–lead-208 system,

$$t = \frac{1.41 \times 10^{10} \text{ years}}{\ln 2} \ln(1 + 0.104) = 2.0126364 \times 10^9 \text{ years}.$$

Thus,

$$\boxed{t = 2.01 \times 10^9 \text{ years}}.$$

#### 4.2 — Lead-206/uranium-238 atom ratio

The uranium system has aged for the same time. Therefore,

$$\frac{N(^{206}\text{Pb})}{N(^{238}\text{U})} = e^{\lambda_U t} - 1, \quad \lambda_U = \frac{\ln 2}{4.47 \times 10^9 \text{ years}}.$$

Using the unrounded age from 4.1,

$$\frac{N(^{206}\text{Pb})}{N(^{238}\text{U})} = \exp \left( \frac{\ln 2 (2.0126364 \times 10^9 \text{ years})}{4.47 \times 10^9 \text{ years}} \right) - 1 = 0.366281.$$

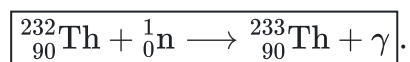
Hence,

$$\boxed{\frac{N(^{206}\text{Pb})}{N(^{238}\text{U})} = 0.366}.$$

The oxide mass percentages are unnecessary for these calculations because the required quantities are daughter/parent atom ratios.

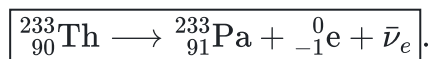
#### 4.3 — Formation of uranium-233

Neutron capture increases the mass number by one without changing the atomic number. Thorium-232 therefore forms thorium-233:

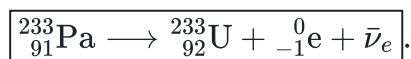


In each  $\beta^-$  decay, a neutron converts into a proton, emitting an electron and an electron antineutrino. The mass number remains unchanged, while the atomic number increases by one.

Thus, thorium-233 ( $Z = 90$ ) first forms protactinium-233 ( $Z = 91$ ):



Protactinium-233 then forms uranium-233 ( $Z = 92$ ):



Here  $\bar{\nu}_e$  denotes the electron antineutrino. Each equation conserves mass number and electric charge.

#### 4.4 — Successive decay of molybdenum-101 and technetium-101

Let  $N_1, N_2, N_3$  denote the numbers of  $^{101}\text{Mo}$ ,  $^{101}\text{Tc}$ , and  $^{101}\text{Ru}$  atoms, respectively. Initially,

$$N_1(0) = N_0 = 5000, \quad N_2(0) = N_3(0) = 0.$$

The decay constants are

$$\lambda_1 = \frac{\ln 2}{14.6 \text{ min}} = 0.0474758 \text{ min}^{-1},$$

$$\lambda_2 = \frac{\ln 2}{14.3 \text{ min}} = 0.0484718 \text{ min}^{-1}.$$

##### (i) Molybdenum-101

After one molybdenum half-life,

$$N_1(14.6 \text{ min}) = N_0 e^{-\lambda_1 t} = 5000 \left( \frac{1}{2} \right).$$

Thus,

$$\boxed{N_1 = 2500 \text{ atoms}}.$$

##### (ii) Technetium-101

Technetium is simultaneously produced by molybdenum decay and consumed by its own decay:

$$\frac{dN_2}{dt} = \lambda_1 N_1 - \lambda_2 N_2 = \lambda_1 N_0 e^{-\lambda_1 t} - \lambda_2 N_2.$$

With  $N_2(0) = 0$ , integration gives

$$N_2(t) = N_0 \frac{\lambda_1}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t}).$$

At  $t = 14.6 \text{ min}$ , this becomes

$$N_2 = 5000 \frac{14.3}{14.6 - 14.3} \left( \frac{1}{2} - 2^{-14.6/14.3} \right) = 1720.3295.$$

Therefore,

$$\boxed{N_2 \approx 1720 \text{ atoms}}.$$

##### (iii) Ruthenium-101

Each decay step preserves one heavy nucleus, and ruthenium is the terminal product in the given chain. Thus,

$$N_1 + N_2 + N_3 = N_0.$$

Therefore,

$$N_3 = 5000 - 2500 - 1720.3295 = 779.6705,$$

so

$$\boxed{N_3 \approx 780 \text{ atoms}}.$$

These are expected populations; individual radioactive decays are stochastic.

---

The solution was checked against the official solution.

## Problem 5: Halogen Chemistry

Halogens in their reactions among themselves and with a variety of other elements give rise to a large number of compounds with diverse structure, bonding and chemical behaviour. Metal halides, halogen derivatives and interhalogens represent major types of halogen compounds.

### (A) Photography

A "black and white" photographic film contains a coating of silver bromide on a support such as cellulose acetate.

**5.1** Write the photochemical reaction that occurs when light falls on  $\text{AgBr (s)}$  coated on a film.

**5.2** During the developing process, unexposed  $\text{AgBr}$  is washed away by complexation of  $\text{Ag(I)}$  by sodium thiosulphate solution. Write down this chemical reaction.

**5.3** These washings are often disposed of as waste. However, metallic silver can be recovered from them by adding cyanide, followed by zinc. Write down the reactions involved.

### (B) Shapes, spectra and reactivity

The most reactive halogen, fluorine, reacts with other halogens  $\text{Cl}_2$ ,  $\text{Br}_2$  and  $\text{I}_2$  under controlled conditions giving a tetra-atomic, hexa-atomic and an octa-atomic molecule, respectively.

**5.4** Write the formulae and 3-dimensional structures of these interhalogen molecules on the basis of VSEPR theory. Show the disposition of the lone pairs on the central atom, where appropriate.

A mixture of iodine vapour and chlorine gas when fed into a mass spectrometer gave two sets (A and B) of mass spectral peaks corresponding to molecular ions of two chemical species at  $m/z$ :

A: 162, 164

B: 464, 466, 468, 470, 472, 474, 476

**5.5** Identify the molecular species corresponding to  $m/z = 162$ , 164, 466 and 476. Draw the structure of the heaviest species ( $m/z = 476$ ) indicating clearly the lone pairs on atom(s) of I (iodine). Show the isotopic composition of each species.

In aqueous medium chlorine gas oxidises sodium thiosulphate to an ion containing the highest oxidation state of sulphur.

**5.6** Write down the chemical equation for this reaction.

**5.7** Write down the Lewis dot structure of the thiosulphate ion. Circle the sulphur atom that has the lower oxidation state.

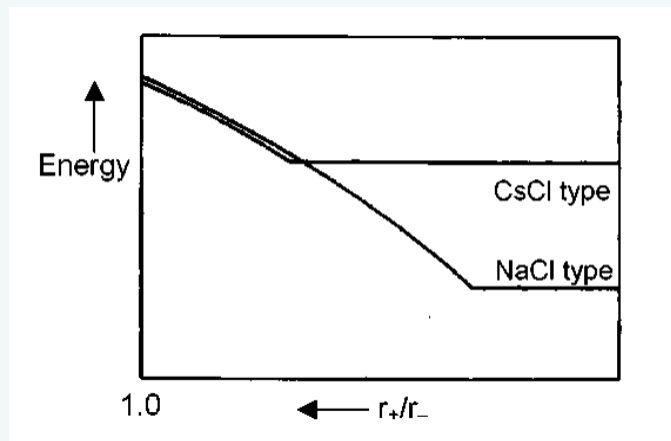
**5.8** Chlorine dioxide reacts with sodium hydroxide as shown below. Identify the products X and Y (both containing chlorine) and balance the equation.

**5.9** Reaction of chlorine an alkali is used by manufacturing bleach. Write the chemical reaction for its formation.

**5.10** Write the oxidation state(s) of chlorine in bleach.

### (C) Alkali metal halides and X-ray crystallography

X-ray crystallography reveals many aspects of the structure of metal halides. The radius ratio ( $r_+/r_-$ ) is a useful parameter to rationalise their structure and stability. A table of radius ratio ( $r_+/r_-$ ) for some alkali halides with radius ratio ( $r_-$  kept constant) is shown schematically for NaCl-type and CsCl-type crystal structures.



|                 | Li <sup>+</sup> | Na <sup>+</sup> | K <sup>+</sup> | Rb <sup>+</sup> | Cs <sup>+</sup> |
|-----------------|-----------------|-----------------|----------------|-----------------|-----------------|
| Cl <sup>-</sup> | 0.33            | 0.52            | 0.74           | 0.82            | 0.93            |
| Br <sup>-</sup> | 0.31            | 0.49            | 0.68           | 0.76            | 0.87            |
| I <sup>-</sup>  | 0.28            | 0.44            | 0.62           | 0.69            | 0.78            |

**5.11** For a given anion, the graph for NaCl-type structure levels off at low  $r_+/r_-$  values because of

- (a) cation-cation contact along the face diagonal. ☐
- (b) anion-anion contact along the face diagonal. ☐
- (c) cation-anion contact along the cell edge. ☐

(Mark X in the correct box.)

**5.12** Which among the halides LiBr, NaBr and RbBr is likely to undergo phase transition from NaCl-type to CsCl-type structure with change of temperature and / or pressure?

**5.13** Show by calculation the radius ratio ( $r_+/r_-$ ) at which the energy of CsCl-type structure levels off.

**5.14** Using CuK $\alpha$  X-rays ( $\lambda = 154 \text{ nm}$ ), diffraction by a KCl crystal (fcc structure) is observed at an angle ( $\theta$ ) of  $14.2^\circ$ . Given that (i) diffraction takes place from the planes with  $h^2 + k^2 + l^2 = 4$ , (ii) in a cubic crystal  $d_{hkl} = a/(h^2 + k^2 + l^2)^{1/2}$ , where "d" is the distance between adjacent hkl planes and "a" is a lattice parameter, and (iii) reflections in an fcc structure can occur only from planes with "all odd" or "all even" hkl (Miller) indices, calculate the lattice parameter "a" for KCl.

**5.15** Indicate in the table given below the required information for the 2<sup>nd</sup> and 3<sup>rd</sup> nearest neighbours of a K<sup>+</sup> ion in the KCl lattice.

| 2 <sup>nd</sup> nearest neighbours |                    |               | 3 <sup>rd</sup> nearest neighbours |                    |               |
|------------------------------------|--------------------|---------------|------------------------------------|--------------------|---------------|
| number                             | sign of the charge | distance (pm) | number                             | sign of the charge | distance (pm) |
|                                    |                    |               |                                    |                    |               |

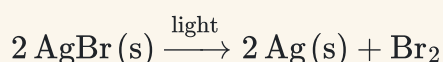
**5.16** Determine the lowest value of diffraction angle  $\theta$  possible for the KCl structure.

Official English text of the problem.

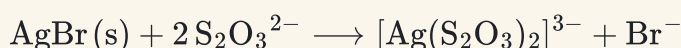
## Answers

Names, SMILES, structural descriptions and derivations are supplied in the corresponding solution parts below.

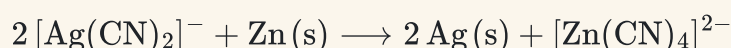
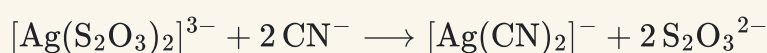
- 5.1



- 5.2



- 5.3

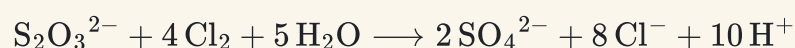


- 5.4  $\text{ClF}_3$ : T-shaped, two equatorial lone pairs;  $\text{BrF}_5$ : square pyramidal, one lone pair opposite the apical fluorine;  $\text{IF}_7$ : pentagonal bipyramidal, no iodine lone pairs.
- 5.5 The molecular-ion isotopic compositions are

| $m/z$ | Composition                                                                          |
|-------|--------------------------------------------------------------------------------------|
| 162   | $[\text{}^{127}\text{I } ^{35}\text{Cl}]^{+\bullet}$                                 |
| 164   | $[\text{}^{127}\text{I } ^{37}\text{Cl}]^{+\bullet}$                                 |
| 466   | $[\text{}^{127}\text{I}_2 \text{}^{35}\text{Cl}_5 \text{}^{37}\text{Cl}]^{+\bullet}$ |
| 476   | $[\text{}^{127}\text{I}_2 \text{}^{37}\text{Cl}_6]^{+\bullet}$                       |

The heavier species derives from the planar iodine trichloride dimer,  $\text{I}_2\text{Cl}_6$ , with two bridging chlorines. Each iodine in the neutral parent has two lone pairs perpendicular to the molecular plane.

- 5.6



- 5.7 A Lewis contributor is  $[\text{O}-]\text{S}(=\text{O})(=\text{O})[\text{S}-]$ . Circle the terminal sulphur: its oxidation state is  $-1$ ; the central sulphur has oxidation state  $+5$ .
- 5.8 The products are sodium chlorite and sodium chlorate:



- **5.9**



using cold, dilute alkali.

- **5.10** Chlorine is +1 in hypochlorite and −1 in the accompanying chloride. In the active bleaching compound NaClO itself, chlorine is +1.
- **5.11 (b)** Anion-anion contact along the face diagonal.
- **5.12** RbBr.
- **5.13**

$$\frac{r_+}{r_-} = \sqrt{3} - 1 = 0.732$$

- **5.14** Literally using the printed  $\lambda = 154 \text{ nm}$ :

$$a = 628 \text{ nm}.$$

With the apparent intended wavelength,  $\lambda = 154 \text{ pm}$ :

$$a = 628 \text{ pm}.$$

- **5.15** Second neighbours: **12**  $\text{K}^+$  ions, at  $a/\sqrt{2}$ . Third neighbours: **8**  $\text{Cl}^-$  ions, at  $\sqrt{3}a/2$ . The distances are respectively **444 pm** and **544 pm** if  $\lambda = 154 \text{ pm}$ , or  $4.44 \times 10^5 \text{ pm}$  and  $5.44 \times 10^5 \text{ pm}$  using the printed wavelength.
- **5.16**

$$\theta_{\min} = 12.3^\circ$$

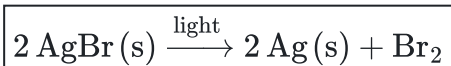
from the (111) reflection, using the supplied fcc selection rule.

## Solution

SMILES specify connectivity, not the spatial arrangements or lone pairs described below. For ionic solids, a dot-disconnected SMILES represents an ionic formula unit rather than the crystal lattice. Coordination complexes use the dative-bond SMILES extension  $\rightarrow$ .

### 5.1

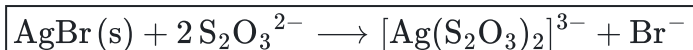
Light causes photochemical decomposition of silver bromide, AgBr, ionic formula-unit SMILES  $[\text{Ag}^+] \cdot [\text{Br}^-]$ :



Silver(I) ions ( $[\text{Ag}^+]$ ) are reduced to silver atoms, while bromide ions ( $[\text{Br}^-]$ ) are oxidised to bromine,  $\text{Br}_2$ , BrBr. The resulting metallic silver produces the dark regions of the image.

### 5.2

Sodium thiosulphate,  $[\text{Na}^+] \cdot [\text{Na}^+] \cdot [\text{O}-]\text{S}(=\text{O})(=\text{O})[\text{S}-]$ , supplies thiosulphate ions,  $\text{S}_2\text{O}_3^{2-}$ ,  $[\text{O}-]\text{S}(=\text{O})(=\text{O})[\text{S}-]$ . Their complexation of silver(I) allows unexposed silver bromide to dissolve:



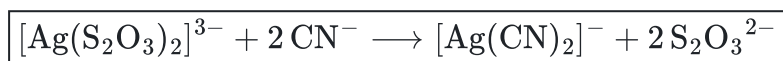
The soluble product is **bis(thiosulphato)argentate(I)**:



The ligands bind through their terminal sulphur atoms; the idealised two-coordinate arrangement around silver is linear. The equation conserves charge: both sides have total charge  $-4$ .

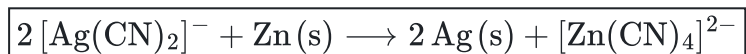
### 5.3

Cyanide,  $\text{CN}^-$ ,  $[\text{C}-]\# \text{N}$ , replaces thiosulphate to form the very stable **dicyanoargentate(I)** ion:



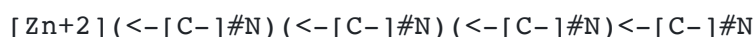
Dicyanoargentate(I) has SMILES  $[\text{C}-](\# \text{N}) \rightarrow [\text{Ag}^+] < - [\text{C}-]\# \text{N}$  and approximately linear carbon–silver–carbon coordination.

Zinc then reduces silver(I) to metallic silver:



Zinc changes from oxidation state 0 to  $+2$ , supplying the two electrons required to reduce two silver(I) centres.

The zinc product is **tetracyanozincate(II)**:



Its four carbon donors have approximately tetrahedral coordination around zinc.

### 5.4

The stated total numbers of atoms give three, five and seven fluorine atoms around chlorine, bromine and iodine, respectively.

| Molecule and name                      | SMILES                                                                | VSEPR description                                                          | Required three-dimensional structure                                                                                                                       |
|----------------------------------------|-----------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\text{ClF}_3$ , chlorine trifluoride  | $\text{FCl}(\text{F})\text{F}$                                        | $\text{AX}_3\text{E}_2$ ; trigonal-bipyramidal electron-domain arrangement | <b>T-shaped.</b> Two fluorines occupy axial positions and one occupies an equatorial position. Both lone pairs occupy the other two equatorial positions.  |
| $\text{BrF}_5$ , bromine pentafluoride | $\text{FBr}(\text{F})(\text{F})(\text{F})\text{F}$                    | $\text{AX}_5\text{E}$ ; octahedral electron-domain arrangement             | <b>Square pyramidal.</b> Four fluorines form a square base, the fifth is the apex, and the lone pair occupies the position opposite the apex.              |
| $\text{IF}_7$ , iodine heptafluoride   | $\text{FI}(\text{F})(\text{F})(\text{F})(\text{F})(\text{F})\text{F}$ | $\text{AX}_7$                                                              | <b>Pentagonal bipyramidal.</b> Five fluorines form an equatorial pentagon; two lie on the perpendicular axis, on opposite sides. Iodine has no lone pairs. |

For  $\text{ClF}_3$ , equatorial lone pairs minimise the number of  $90^\circ$  interactions. In idealised  $\text{IF}_7$ , adjacent equatorial bonds make  $72^\circ$ , and each axial bond is perpendicular to the equatorial plane.

## 5.5

The relevant isotopes are  $^{127}\text{I}$ ,  $^{35}\text{Cl}$  and  $^{37}\text{Cl}$ . For singly charged molecular ions, replacing one chlorine-35 by chlorine-37 increases  $m/z$  by 2.

For set A:

$$127 + 35 = 162, \quad 127 + 37 = 164.$$

Thus species A is **iodine monochloride**,  $\text{ICl}$ ,  $\text{ICl}$ .

Set B has seven members, consistent with six chlorine atoms containing 0, 1, ..., 6 chlorine-37 atoms. Its lowest mass satisfies

$$464 - 6(35) = 254 = 2(127),$$

so species B is **diiodine hexachloride**,  $\text{I}_2\text{Cl}_6$ , the iodine trichloride dimer. In general,

$$m/z = 2(127) + (6 - k)(35) + k(37) = 464 + 2k.$$

The requested assignments are:

| $m/z$ | Isotopic composition of molecular ion                               | One formal, localised radical-cation SMILES                                 |
|-------|---------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 162   | $[^{127}\text{I} \ ^{35}\text{Cl}]^{+\bullet}$                      | <chem>[127I+][35Cl]</chem>                                                  |
| 164   | $[^{127}\text{I} \ ^{37}\text{Cl}]^{+\bullet}$                      | <chem>[127I+][37Cl]</chem>                                                  |
| 466   | $[^{127}\text{I}_2 \ ^{35}\text{Cl}_5 \ ^{37}\text{Cl}]^{+\bullet}$ | <chem>[127I]1([35Cl])([35Cl])[35Cl+][127I-]([35Cl])([37Cl])[35Cl+]</chem> 1 |
| 476   | $[^{127}\text{I}_2 \ ^{37}\text{Cl}_6]^{+\bullet}$                  | <chem>[127I]1([37Cl])([37Cl])[37Cl+][127I-]([37Cl])([37Cl])[37Cl+]</chem> 1 |

The 466 peak does not establish which chlorine position contains chlorine-37; the SMILES selects one representative placement.

For the requested structural drawing, describe the neutral parent dimer as follows:

- Draw a planar four-membered ring with alternating iodine and bridging chlorine atoms: iodine–chlorine–iodine–chlorine.
- Attach two additional terminal chlorines to each iodine, outside the ring.
- Each iodine therefore has four chlorine neighbours in an approximately square-planar arrangement.
- Place **two lone pairs on each iodine**, one above and one below the molecular plane. This is an  $\text{AX}_4\text{E}_2$  arrangement.
- Label both iodines  $^{127}\text{I}$  and all six chlorines  $^{37}\text{Cl}$ .

A charge-separated Lewis SMILES for this neutral heaviest parent is:

[127I-]1([37Cl])([37Cl])[37Cl+][127I-]([37Cl])([37Cl])[37Cl+]1

The formal charges in this representation account for the bridging bonds; they are not oxidation states. Iodine has oxidation state +3.

The observed molecular ion has one fewer electron than its neutral parent. In the localised ion representation above, one iodine retains two lone pairs, while the other has one lone pair and an unpaired electron. The mass data do not determine the actual distribution of the ion's charge or spin.

## 5.6

Sulphur's highest oxidation state is +6, so the product is **sulphate**,  $\text{SO}_4^{2-}$ ,  $[\text{O}-]\text{S}(=\text{O})(=\text{O})[\text{O}-]$ .

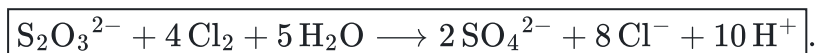
The oxidation half-reaction is



Chlorine is reduced according to



Adding gives



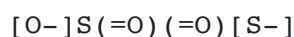
Here chlorine is  $\text{ClCl}$ , water is  $\text{O}$ , chloride is  $[\text{Cl}-]$ , and the hydrogen ion is  $[\text{H}^+]$ . Sodium ions are spectators.

## 5.7

The thiosulphate ion contains

$$2(6) + 3(6) + 2 = 32$$

valence electrons. One suitable Lewis contributor has SMILES:



Describe the drawing precisely as follows:

- Place one sulphur at the centre, bonded to three oxygens and one terminal sulphur.
- Draw two sulphur–oxygen double bonds, one sulphur–oxygen single bond and one sulphur–sulphur single bond.
- Put two lone pairs on each doubly bonded oxygen.
- Put three lone pairs and formal charge  $-1$  on the singly bonded oxygen.
- Put three lone pairs and formal charge  $-1$  on the terminal sulphur.
- The central sulphur has no lone pairs. Enclose the structure in brackets with overall charge  $2-$ .

There are three equivalent contributors differing in which oxygen bears the single bond and negative charge. The four bond directions around the central sulphur are approximately tetrahedral.

For oxidation states, assign sulphur–oxygen bonding electrons to oxygen and divide the sulphur–sulphur bonding pair equally. This gives

$$\boxed{\text{central S: } +5, \quad \text{terminal S: } -1}.$$

As a check,

$$(+5) + (-1) + 3(-2) = -2.$$

**Circle the terminal sulphur atom**, which is bonded only to the central sulphur.

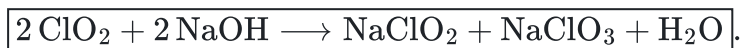
## 5.8

Chlorine dioxide,  $\text{ClO}_2$ ,  $\text{O}=[\text{Cl}]=\text{O}$ , is a radical with chlorine in oxidation state +4. In alkali it disproportionates to chlorine in oxidation states +3 and +5:

| Product                           | Chlorine oxidation state | SMILES                                                        |
|-----------------------------------|--------------------------|---------------------------------------------------------------|
| Sodium chlorite, $\text{NaClO}_2$ | +3                       | $[\text{Na}+] \cdot [\text{O}-]\text{Cl}=\text{O}$            |
| Sodium chlorate, $\text{NaClO}_3$ | +5                       | $[\text{Na}+] \cdot [\text{O}-]\text{Cl}(=\text{O})=\text{O}$ |

Sodium hydroxide has ionic formula-unit SMILES  $[\text{Na}+] \cdot [\text{OH}-]$ .

One chlorine gains one electron while another loses one electron, giving equal amounts of the two products:



Thus X and Y are sodium chlorite and sodium chlorate. Their label order cannot be recovered, because the scheme the problem refers to is not printed.

## 5.9

With cold, dilute sodium hydroxide, chlorine disproportionates to chloride and hypochlorite:



The products are **sodium chloride**,  $[\text{Na}+] \cdot [\text{Cl}-]$ , and **sodium hypochlorite**,  $[\text{Na}+] \cdot [\text{O}-]\text{Cl}$ .

Hypochlorite provides the bleaching action.

## 5.10

In chloride,  $\text{Cl}^-$ , chlorine has oxidation state  $-1$ .

For the hypochlorite ion,  $\text{ClO}^-$ ,  $[\text{O}-]\text{Cl}$ , let chlorine's oxidation state be  $x$ :

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

Therefore the mixture prepared in 5.9 contains chlorine in oxidation states

$$\boxed{-1 \text{ and } +1}.$$

The active hypochlorite component itself contains chlorine only in oxidation state  $+1$ .

## 5.11

In the sodium chloride structure, the anions form an fcc array. Their nearest separation is along a face diagonal and equals  $a/\sqrt{2}$ .

When neighbouring anions touch,

$$\frac{a}{\sqrt{2}} = 2r_-, \quad a = 2\sqrt{2}r_-.$$

Further reduction of the cation radius cannot reduce the lattice parameter in this hard-sphere model because the anions already touch. With  $r_-$  fixed, the lattice dimensions—and hence the schematic energy—level off.

Thus mark X in **box (b): anion-anion contact along the face diagonal**.

For reference, simultaneous cation–anion contact requires

$$r_+ + r_- = \frac{a}{2} = \sqrt{2}r_-,$$

giving the familiar limiting ratio  $\sqrt{2} - 1 \approx 0.414$ .

## 5.12

The three candidates are lithium bromide ( $[\text{Li}^+] \cdot [\text{Br}^-]$ ), sodium bromide ( $[\text{Na}^+] \cdot [\text{Br}^-]$ ) and rubidium bromide ( $[\text{Rb}^+] \cdot [\text{Br}^-]$ ).

Their supplied radius ratios are

$$0.31, \quad 0.49, \quad 0.76,$$

respectively. The geometrical limiting ratio for eight-coordinate caesium chloride,  $[\text{Cs}^+] \cdot [\text{Cl}^-]$ , is approximately 0.732, as derived next.

Rubidium bromide lies near this value, where the two arrangements can compete. It is therefore the most likely candidate in the supplied model:



This is a comparative prediction; the radius-ratio model alone does not determine every possible high-pressure phase transition.

## 5.13

In the caesium chloride structure, take the anions at the cube corners and the cation at its centre.

Cation–anion contact along the body diagonal gives

$$\sqrt{3}a = 2(r_+ + r_-).$$

The lattice stops shrinking when adjacent corner anions touch along an edge:

$$a = 2r_-.$$

Combining,

$$\sqrt{3}(2r_-) = 2(r_+ + r_-),$$

so

$$\boxed{\frac{r_+}{r_-} = \sqrt{3} - 1 = 0.732}.$$

Below this ratio, fixed-size anions prevent further contraction of the idealised structure.

## 5.14

Potassium chloride has ionic formula-unit SMILES  $[\text{K}^+] \cdot [\text{Cl}^-]$ .

Since  $h^2 + k^2 + l^2 = 4$ , the reflection belongs to the  $\{200\}$  family and

$$d_{200} = \frac{a}{2}.$$

First-order Bragg diffraction satisfies

$$\lambda = 2d_{200} \sin \theta = a \sin \theta.$$

Hence

$$a = \frac{\lambda}{\sin 14.2^\circ}.$$

Using the printed wavelength literally:

$$a = \frac{154 \text{ nm}}{\sin 14.2^\circ} = 627.784 \text{ nm} \approx \boxed{628 \text{ nm}}.$$

The stated wavelength appears to contain a unit error: CuK $\alpha$  radiation corresponds to approximately 154 pm = 0.154 nm, which gives an atomic-scale lattice parameter:

$$a = \frac{154 \text{ pm}}{\sin 14.2^\circ} = 627.784 \text{ pm} \approx \boxed{628 \text{ pm}}.$$

Both interpretations are retained below.

### 5.15

Place a potassium ion, K<sup>+</sup>, [K<sup>+</sup>], at the origin. In the rock-salt structure:

- Its first neighbours are six chloride ions at distance  $a/2$ .
- Its second neighbours lie at permutations of  $(\pm a/2, \pm a/2, 0)$ . There are  $3 \times 4 = 12$ , all potassium ions.
- Its third neighbours lie at  $(\pm a/2, \pm a/2, \pm a/2)$ . There are  $2^3 = 8$ , all chloride ions.

Thus

$$r_2 = \sqrt{\left(\frac{a}{2}\right)^2 + \left(\frac{a}{2}\right)^2} = \frac{a}{\sqrt{2}},$$

and

$$r_3 = \sqrt{3\left(\frac{a}{2}\right)^2} = \frac{\sqrt{3}a}{2}.$$

Using the apparent intended wavelength, the answer-sheet entries are:

| 2 <sup>nd</sup> : number | Sign of charge | Distance (pm) | 3 <sup>rd</sup> : number | Sign of charge | Distance (pm) |
|--------------------------|----------------|---------------|--------------------------|----------------|---------------|
| 12                       | +              | 444           | 8                        | −              | 544           |

The unrounded distances are 443.910 pm and 543.677 pm.

If the printed wavelength 154 nm is used literally, the corresponding distances are instead

$$\boxed{r_2 = 4.44 \times 10^5 \text{ pm}, \quad r_3 = 5.44 \times 10^5 \text{ pm}}.$$

The neighbour counts and charge signs are unchanged.

### 5.16

The lowest diffraction angle corresponds to the largest allowed plane spacing, hence the smallest nonzero allowed value of  $h^2 + k^2 + l^2$ .

The (100) and (110) indices have mixed parity and are forbidden by the supplied fcc rule. The first allowed family is {111}, for which

$$h^2 + k^2 + l^2 = 3, \quad d_{111} = \frac{a}{\sqrt{3}}.$$

Therefore

$$\sin \theta_{\min} = \frac{\lambda}{2d_{111}} = \frac{\sqrt{3}\lambda}{2a}.$$

Using  $\lambda/a = \sin 14.2^\circ$  from 5.14,

$$\theta_{\min} = \sin^{-1} \left( \frac{\sqrt{3}}{2} \sin 14.2^\circ \right) = 12.2655^\circ.$$

Thus

$$\theta_{\min} = 12.3^\circ.$$

The wavelength-unit issue does not affect this angle because it depends on the ratio  $\lambda/a$ .

The solution was checked against the official solution.

## Problem 6: Organic Chemistry of Indian Spices



The rhizomes of ginger (*Zingiber officinale*) are well known for their medicinal and flavouring properties. In Ayurveda (the traditional system of medicine in India) different formulations of ginger are used for the treatment of gastrointestinal problems, common cold and other ailments. Several compounds are responsible for the pungency of ginger. Many are simple substituted aromatic compounds with different side chains. Three of them, Zingerone, (+)[6] Gingerol (to be referred hereafter as Gingerol only), and Shogaol are particularly important.

Zingerone:  $\text{C}_{11}\text{H}_{14}\text{O}_3$

Gingerol:  $\text{C}_{17}\text{H}_{24}\text{O}_4$

Shogaol:  $\text{C}_{17}\text{H}_{22}\text{O}_3$

**6.1** Zingerone gives positive  $\text{FeCl}_3$  and 2,4-DNP (2,4-dinitrophenylhydrazine) tests. It does not react with Tollen's reagent. Therefore, Zingerone contains the following functional groups: (Mark X in the correct boxes.)

|                        |                          |                  |                          |
|------------------------|--------------------------|------------------|--------------------------|
| (a) alcoholic hydroxyl | <input type="checkbox"/> | (e) ester        | <input type="checkbox"/> |
| (b) aldehydic carbonyl | <input type="checkbox"/> | (f) alkoxyl      | <input type="checkbox"/> |
| (c) ketonic carbonyl   | <input type="checkbox"/> | (g) unsaturation | <input type="checkbox"/> |
| (d) phenolic hydroxyl  | <input type="checkbox"/> |                  |                          |

The data obtained from the  $^1\text{H}$  NMR spectrum of Zingerone are shown in Table 1. Some other relevant information is given in Table 2.

**Table 1:  $^1\text{H}$  NMR spectral data on Zingerone**

| Chemical shifts ( $\delta$ ) | Multiplicity                                              | Relative intensity |
|------------------------------|-----------------------------------------------------------|--------------------|
| 2.04                         | singlet                                                   | 3                  |
| 2.69, 2.71                   | two (closely spaced) triplets of equal intensity          | 4                  |
| 3.81                         | singlet                                                   | 3                  |
| 5.90                         | broad singlet ( $\text{D}_2\text{O}$ exchangeable)        | 1                  |
| 6.4 – 6.8                    | two doublets with similar chemical shifts and one singlet | 3                  |

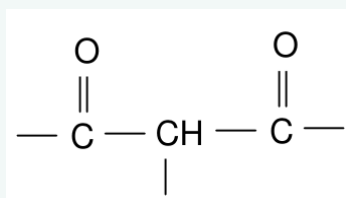
\*) For clarity, some of the data have been altered slightly.)

**Table 2: Approximate  $^1\text{H}$  chemical shifts ( $\delta$ ) and spin-spin coupling constants ( $J$ ) of some protons**

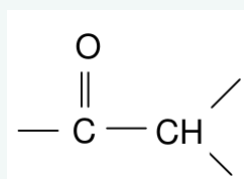
**$^1\text{H}$  Chemical shifts**

|           |           |      |            |
|-----------|-----------|------|------------|
| alkyl - H | 0.9 - 1.5 | [S1] | 3.4 - 3.6  |
| [S2]      | 2.0 - 2.7 | [S3] | 4.0 - 7.0  |
| [S4]      | 2.3 - 2.9 | [S5] | 6.0 - 8.0  |
| [S6]      | 3.3 - 3.9 | [S7] | 4.0 - 11.0 |

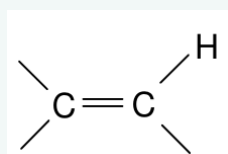
[S1]



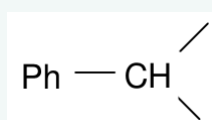
[S2]



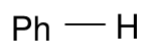
[S3]



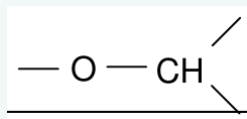
[S4]



[S5]



[S6]



[S7]

Spin-spin coupling constants ( $J$ )

|         |              |                                         |
|---------|--------------|-----------------------------------------|
| Alkenes | <i>cis</i>   | 5 – 14 Hz (commonly around 6 – 8 Hz)    |
|         | <i>trans</i> | 11 – 19 Hz (commonly around 14 – 16 Hz) |

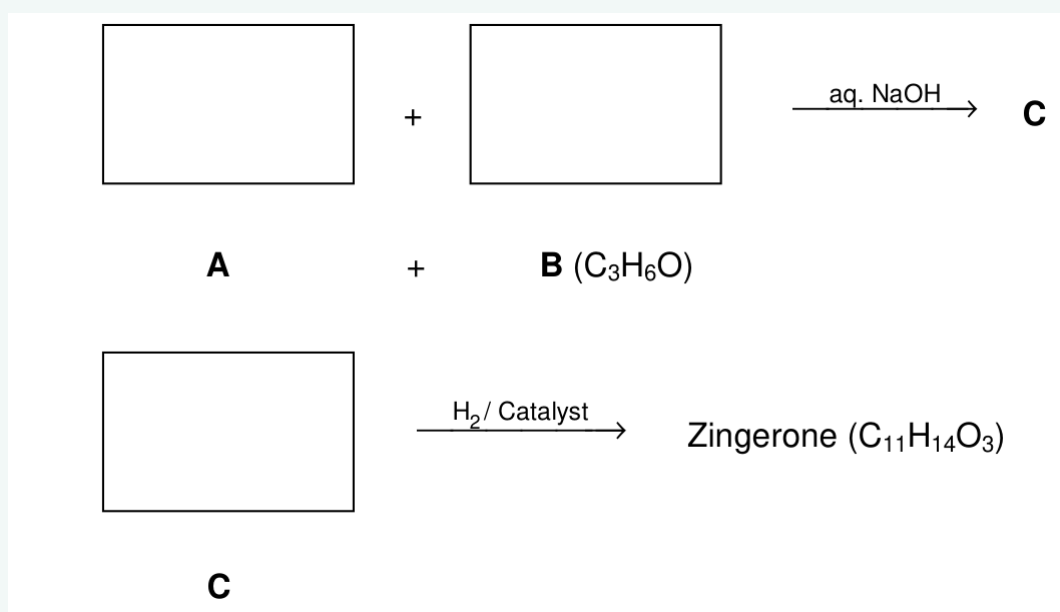
Zingerone on bromination with bromine water gives only one nuclear mono brominated product. The IR spectrum of Zingerone indicates the presence of a weak *intramolecular* hydrogen bond. The same is present even after Clemmensen reduction ( $\text{Zn} - \text{Hg}/\text{HCl}$ ) of Zingerone.

**6.2** From the information above deduce the following:

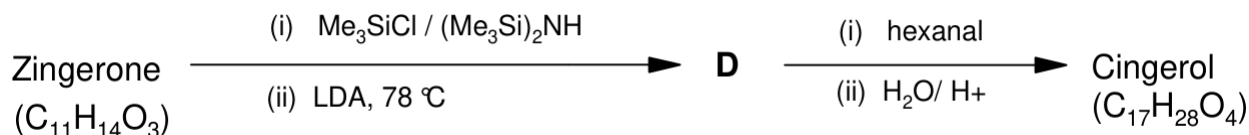
- side chain in Zingerone
- substituent on the aromatic ring
- relative positions of the substituents on the ring

**6.3** Draw a possible structure of Zingerone based on the above inferences.

**6.4** Complete the following reaction sequence for the synthesis of Zingerone.



**6.5** Zingerone can be easily converted into Gingerol by the following reaction sequence:



Notes: (1)  $\text{Me}_3\text{SiCl} / (\text{Me}_3\text{Si})_2\text{NH}$  is used to convert OH into  $-\text{OSiMe}_3$ ; the group  $-\text{SiMe}_3$  can be removed by acid hydrolysis.

(2) LDA is lithium diisopropylamine, a strong, very hindered, non-nucleophilic base.

i) Draw the structure of **D**.

ii) Draw the structure of Cingerol.

iii) Complete the Fischer projection of the *R*-enantiomer of Cingerol.

iv) In the above reaction sequence (6.5), about 2 – 3 % another constitutional isomer (**E**) of Cingerol is obtained. Draw the likely structure of **E**.

v) Will the compound **E** be formed as

(a) a pair of enantiomers? ☐

(b) a mixture of diastereomers? ☐

(c) a mixture of an enantiomeric pair and a meso isomer? ☐

(Mark X in the correct box.)

vi) Cingerol ( $\text{C}_{17}\text{H}_{26}\text{O}_4$ ) when heated with a mild acid (such as  $\text{KHSO}_4$ ) gives Shogaol ( $\text{C}_{17}\text{H}_{24}\text{O}_3$ ). Draw the structure of Shogaol.

**6.6** Turmeric (*Curcuma longa*) is a commonly used spice in Indian food. It is also used in Ayurvedic medicinal formulations. Curcumin ( $\text{C}_{21}\text{H}_{20}\text{O}_6$ ), an active ingredient of turmeric, is structurally related to Cingerol. It exhibits keto-enol tautomerism. Curcumin is responsible for the yellow colour of turmeric and probably also for the pungent taste.

The  $^1\text{H}$  NMR spectrum of the keto form of Curcumin shows aromatic signal similar to that of Cingerol. It also shows a singlet around  $\delta$  3.5 (2H) and two doublets (2H each) in the region  $\delta$  6 – 7 with  $J = 16$  Hz. It can be synthesized by condensing TWO moles of **A** (refer to 6.4) with one mole of pentan-2,4-dione.

i) Draw the stereochemical structure of Curcumin.

ii) Draw the structure of the enol form of Curcumin.

iii) Curcumin is yellow in colour because it has

(a) a phenyl ring ☐

(b) a carbonyl group ☐

(c) an extended conjugation ☐

(d) a hydroxyl group ☐

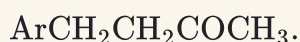
(Mark X in the correct box.)

## Answers

Hereafter, Ar denotes the **4-hydroxy-3-methoxyphenyl group**, fragment SMILES [\*]c1cc(OC)c(O)cc1. The wildcard marks the bond to the side chain.

- **6.1:** Mark **(c) ketonic carbonyl** and **(d) phenolic hydroxyl**.
- **6.2(i):** A **3-oxobutyl side chain**,  $-\text{CH}_2\text{CH}_2\text{COCH}_3$ ; fragment SMILES [\*]CCC(=O)C.
- **6.2(ii):** A **methoxy group**, fragment SMILES [\*]OC, in addition to the established **phenolic hydroxyl**, fragment SMILES [\*]O.
- **6.2(iii):** Taking the side-chain attachment as ring C1, put methoxy at C3 and hydroxyl at C4. Thus hydroxyl and methoxy are **ortho**, hydroxyl and side chain **para**, and methoxy and side chain **meta**.

- **6.3: Zingerone**, 4-(4-hydroxy-3-methoxyphenyl)butan-2-one:

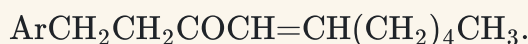


SMILES: CC(=O)CCc1cc(OC)c(O)cc1.

- **6.4 — A: Vanillin**, 4-hydroxy-3-methoxybenzaldehyde.  
SMILES: O=Cc1cc(OC)c(O)cc1.
- **6.4 — B: Acetone**, propan-2-one.  
SMILES: CC(=O)C.
- **6.4 — C: Dehydrozingerone**, shown as the usual *E* condensation product, (3*E*)-4-(4-hydroxy-3-methoxyphenyl)but-3-en-2-one.  
SMILES: CC(=O)/C=C/c1cc(OC)c(O)cc1.
- **6.5(i): D is the methyl-side lithium enolate of O-trimethylsilylzingerone.** The phenolic oxygen is protected, and the terminal methyl group has become the terminal enolate methylene.  
SMILES: C=C([O-])CCc1cc(OC)c(O[Si](C)(C)C)cc1.[Li+].
- **6.5(ii): [6]-Gingerol**, 5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decan-3-one:  
$$\text{ArCH}_2\text{CH}_2\text{COCH}_2\text{CH(OH)(CH}_2)_4\text{CH}_3.$$
  
SMILES, configuration unspecified: CCCCC(O)CC(=O)CCc1cc(OC)c(O)cc1.  
Its correct formula is  $\text{C}_{17}\text{H}_{26}\text{O}_4$ . The stated achiral synthesis gives a racemate.
- **6.5(iii): (5*R*)-[6]-Gingerol.**  
SMILES: CCCC[C@@H](O)CC(=O)CCc1cc(OC)c(O)cc1.  
In a Fischer projection with  $\text{CH}_2\text{COCH}_2\text{CH}_2\text{Ar}$  above and  $(\text{CH}_2)_4\text{CH}_3$  below the stereocentre, place **H on the left and OH on the right**.
- **6.5(iv): E**, 3-(4-hydroxy-3-methoxybenzyl)-4-hydroxynonan-2-one:  
$$\text{ArCH}_2\text{CH(COCH}_3\text{)CH(OH)(CH}_2)_4\text{CH}_3.$$
  
SMILES, configurations unspecified: CC(=O)C(Cc1cc(OC)c(O)cc1)C(O)CCCCC.

- **6.5(v): Mark (b), a mixture of diastereomers.** There are two enantiomeric pairs and no meso form.

- **6.5(vi): [6]-Shogaol**, 1-(4-hydroxy-3-methoxyphenyl)dec-4-en-3-one:



The expected major *4E* form has SMILES CCCCC/C=C/C(=O)CCc1cc(OC)c(O)cc1.

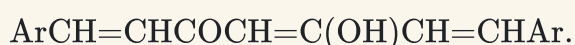
- **6.6(i): Diketo curcumin**, (1*E*,6*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione:



with both outer double bonds *E*.

SMILES: COc1cc(/C=C/C(=O)CC(=O)/C=C/c2cc(OC)c(O)cc2)ccc1O.

- **6.6(ii): The hydrogen-bonded enol tautomer of curcumin**, (1*E*,4*Z*,6*E*)-5-hydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,4,6-trien-3-one:



SMILES: COc1cc(/C=C/C(=O)/C=C(O)/C=C/c2cc(OC)c(O)cc2)ccc1O.

Orient the enolic OH toward the remaining carbonyl oxygen to form an intramolecular hydrogen bond.

- **6.6(iii): Mark (c), an extended conjugation.**

## Solution

### 6.1 — Functional-group tests

Iron(III) chloride,  $[\text{Fe}^{+3}] \cdot [\text{Cl}^-] \cdot [\text{Cl}^-] \cdot [\text{Cl}^-]$ , gives the characteristic positive test for a phenolic hydroxyl group.

2,4-Dinitrophenylhydrazine,  $\text{NNc1ccc}([\text{N}^+](=\text{O})[\text{O}^-])\text{cc1}[\text{N}^+](=\text{O})[\text{O}^-]$ , detects an aldehyde or ketone carbonyl. The negative Tollens test excludes the aldehyde alternative in the intended interpretation. The carbonyl is therefore ketonic.

The active Tollens ion is **diamminesilver(I)**,  $[\text{NH}_3] \rightarrow [\text{Ag}^+] \leftarrow [\text{NH}_3]$ ; its coordination geometry is linear.

Consequently, the boxes justified by these tests are **(c)** and **(d)**. The methoxy group is established by the subsequent NMR evidence.

### 6.2 — Side chain, substituents, and their relative positions

For zingerone,  $\text{C}_{11}\text{H}_{14}\text{O}_3$ , the degree of unsaturation is

$$\text{DBE} = \frac{2(11) + 2 - 14}{2} = 5.$$

A benzene ring accounts for four degrees of unsaturation, and the ketone accounts for the fifth. Thus the side chain requires no additional carbon–carbon double bond or ring.

The NMR assignments are:

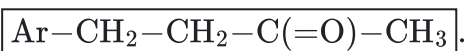
| $\delta$ , ppm | Integral | Assignment and deduction                                                                                                                                        |
|----------------|----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2.04           | 3        | A methyl directly attached to a carbonyl, $-\text{COCH}_3$ . It is a singlet because there is no proton on the adjacent carbonyl carbon.                        |
| 2.69,<br>2.71  | 4        | Two adjacent methylene groups, $-\text{CH}_2\text{CH}_2-$ , each appearing approximately as a triplet. One is benzylic and the other is adjacent to the ketone. |
| 3.81           | 3        | A methoxy group, $-\text{OCH}_3$ .                                                                                                                              |
| 5.90           | 1        | The exchangeable phenolic OH proton.                                                                                                                            |
| 6.4–6.8        | 3        | Three aromatic protons: two adjacent protons and one effectively isolated proton in the simplified spectrum.                                                    |

The integrated proton count is

$$3 + 4 + 3 + 1 + 3 = 14,$$

matching the molecular formula.

**6.2(i).** The acetyl methyl and the two coupled methylene groups require

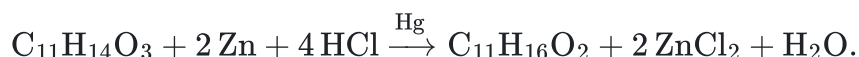


The two closely spaced methylene resonances cannot individually be assigned to the benzylic and carbonyl-adjacent positions from the supplied shifts alone.

**6.2(ii).** The 3H singlet at  $\delta$ 3.81 identifies methoxy. Together with the phenolic OH and the side chain, this gives three substituents on the aromatic ring.

**6.2(iii).** The intramolecular hydrogen bond survives removal of the ketone oxygen by Clemmensen reduction. Its acceptor must therefore be the methoxy oxygen. The hydroxyl and methoxy groups must be adjacent, allowing the phenolic OH to point toward the ether oxygen.

For completeness, the reduced compound is **4-butyl-2-methoxyphenol**, CCCCc1cc(OC)c(O)cc1. A balanced representation of the Clemmensen reduction is

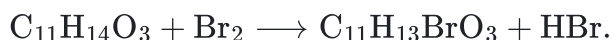


The aromatic NMR pattern and the bromination result complete the assignment. The phenolic OH strongly directs bromination to its ortho and para positions. To leave only one such position available:

- one ortho position is occupied by methoxy;
- the para position is occupied by the side chain;
- the other ortho position remains available for bromination.

With the side chain numbered C1, methoxy is therefore at C3, hydroxyl at C4, and bromination occurs at C5.

The product, **4-(3-bromo-4-hydroxy-5-methoxyphenyl)butan-2-one**, has SMILES CC(=O)CCc1cc(OC)c(O)c(Br)c1. Its formation is balanced as



In the original ring numbering, H5 and H6 give the two principal aromatic doublets, while H2 gives the approximate singlet. Small longer-range couplings are omitted in the simplified data.

### 6.3 — Zingerone

All the evidence is satisfied by



where Ar is 4-hydroxy-3-methoxyphenyl.

To draw it, attach a four-carbon chain to ring C1 in the order methylene–methylene–carbonyl carbon–methyl, place methoxy at ring C3, and place hydroxyl at ring C4. This is zingerone, with the name and SMILES given in the Answers.

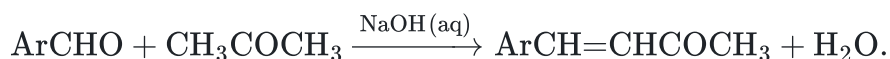
### 6.4 — Synthesis of zingerone

The final hydrogenation suggests that **C** is the corresponding conjugated enone:



Disconnecting its newly formed carbon–carbon double bond gives the aldehyde **vanillin, A**, and the ketone **acetone, B**.

The balanced aldol-condensation equation is

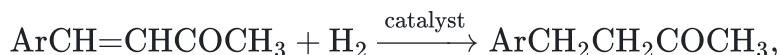


In molecular formulas,

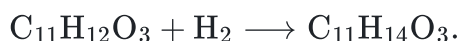


Hydroxide generates a small equilibrium concentration of acetone enolate. Its carbon attacks the aldehyde carbonyl carbon, while the aldehyde  $\pi$  electrons move onto oxygen. Proton transfer gives a  $\beta$ -hydroxy ketone, and elimination of water produces the conjugated enone **C**, dehydrozingerone.

Selective hydrogenation of the carbon–carbon double bond then gives zingerone:



or



The *E* enone is the usual favored condensation product; either alkene geometry would give the same saturated product on hydrogenation.

#### 6.5(i) — Formation and structure of D

The phenolic OH must first be protected so that it does not consume the strong base.

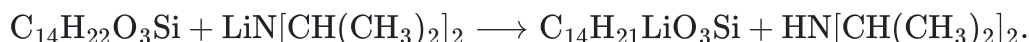
The relevant reagents and protected intermediate are:

| Name                          | SMILES                                          |
|-------------------------------|-------------------------------------------------|
| Chlorotrimethylsilane         | <chem>C[Si](C)(C)Cl</chem>                      |
| Hexamethyldisilazane          | <chem>C[Si](C)(C)N[Si](C)(C)C</chem>            |
| O-Trimethylsilylzingerone     | <chem>CC(=O)CCc1cc(OC)c(O[Si](C)(C)C)cc1</chem> |
| Lithium diisopropylamide, LDA | <chem>CC(C)[N-]C(C)C.[Li+]</chem>               |
| Diisopropylamine              | <chem>CC(C)NC(C)C</chem>                        |

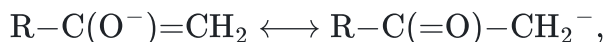
A balanced net representation of protection by hexamethyldisilazane is



The bulky base preferentially removes a proton from the less hindered terminal methyl group under the intended kinetic-enolate conditions. The deprotonation is



Thus **D** is represented by the resonance forms



with a lithium counterion, where **R** is the protected aromatic-ethyl residue.

To draw **D**, retain the aromatic methoxy group, replace phenolic OH by  $-\text{OSiMe}_3$ , and replace the terminal  $-\text{COCH}_3$  unit by  $-\text{C}(\text{O}^-)=\text{CH}_2$ , accompanied by  $\text{Li}^+$ .

Its SMILES in the Answers specifies the formal ion pair. Lithium coordination and aggregation are not specified by the problem.

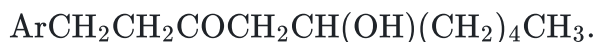
The usual temperature for this kinetic enolization is  $-78^\circ\text{C}$ ; the supplied scheme prints  $78^\circ\text{C}$ .

### 6.5(ii) — Formation and structure of gingerol

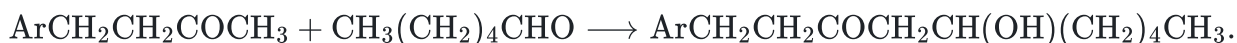
**Hexanal**,  $\text{CCCCCC=O}$ , provides an aldehyde carbon bearing a pentyl substituent.

The terminal carbon of **D** attacks the carbonyl carbon of hexanal. The aldehyde carbonyl becomes an alkoxide; acid workup protonates it and removes the phenolic trimethylsilyl protecting group.

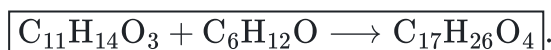
The resulting carbon skeleton is



The net carbon-skeleton reaction is an aldol addition:

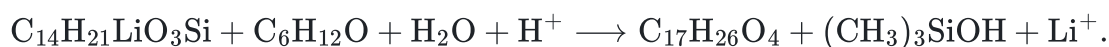


Therefore,



This establishes the correct gingerol formula independently of the conflicting printed formulas.

Including the lithium counterion and hydrolysis of the silyl group, a balanced net workup equation is



The silicon-containing product is **trimethylsilanol**,  $\text{C}[\text{Si}](\text{C})(\text{C})\text{O}$ .

Only one stereocentre is formed in this major product. Because the starting materials and reagents are achiral, the synthesis gives equal amounts of the two enantiomers unless a resolution or asymmetric step is added. The sign (+) in the introduction alone does not establish an *R* or *S* configuration.

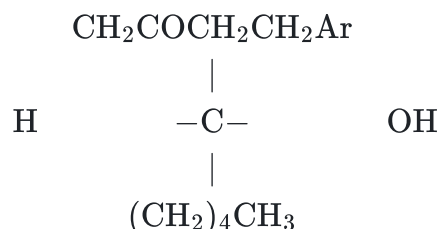
### 6.5(iii) — Fischer projection of the *R* enantiomer

At gingerol C5, the CIP priorities are



The two carbon chains initially tie: each begins with a methylene carbon. At the next comparison, the carbonyl carbon has the effective attached-atom list (O, O, C), which outranks the alkyl-chain list (C, H, H).

A suitable Fischer projection is

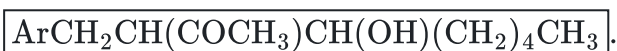


The horizontal bonds point toward the observer; the vertical bonds point away. Here the lowest-priority group, H, points toward the observer, so the apparent sense of the  $1 \rightarrow 2 \rightarrow 3$  sequence is reversed, giving *R*.

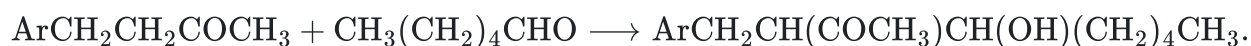
The corresponding stereochemical SMILES is CCCC[C@@H](O)CC(=O)CCc1cc(OC)c(O)cc1.

#### 6.5(iv) — Constitution of the minor product E

Zingerone also has an enolizable methylene on the other side of its carbonyl. Minor deprotonation there, followed by addition to hexanal, gives



The balanced net addition is



This is **3-(4-hydroxy-3-methoxybenzyl)-4-hydroxynonan-2-one**, E. It has the same molecular formula,  $\text{C}_{17}\text{H}_{26}\text{O}_4$ , as gingerol, but different connectivity.

#### 6.5(v) — Stereoisomers of E

E has two stereogenic centres, C3 and C4 in its nonan-2-one parent chain. There is no internal symmetry that could produce a meso form.

The four configurations and their explicit SMILES are:

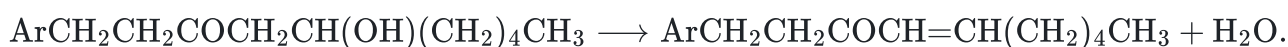
| Stereoisomer of E            | SMILES                                                   |
|------------------------------|----------------------------------------------------------|
| (3 <i>R</i> , 4 <i>R</i> )-E | <chem>CC(=O)[C@H](Cc1cc(OC)c(O)cc1)[C@H](O)CCCC</chem>   |
| (3 <i>S</i> , 4 <i>S</i> )-E | <chem>CC(=O)[C@@H](Cc1cc(OC)c(O)cc1)[C@@H](O)CCCC</chem> |
| (3 <i>R</i> , 4 <i>S</i> )-E | <chem>CC(=O)[C@H](Cc1cc(OC)c(O)cc1)[C@@H](O)CCCC</chem>  |
| (3 <i>S</i> , 4 <i>R</i> )-E | <chem>CC(=O)[C@@H](Cc1cc(OC)c(O)cc1)[C@H](O)CCCC</chem>  |

The first two form one enantiomeric pair, and the last two form another. Members belonging to different pairs are diastereomers. The relative amounts of the two pairs need not be equal.

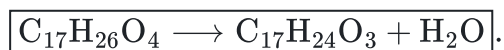
Thus the correct answer is **(b), a mixture of diastereomers**.

#### 6.5(vi) — Dehydration to shogaol

Gingerol is a  $\beta$ -hydroxy ketone. Acid-catalysed dehydration removes the hydroxyl at C5 and a hydrogen from C4, producing a carbon–carbon double bond conjugated with the ketone:



The molecular equation is



The product is **[6]-shogaol**. Draw the double bond between side-chain C4 and C5, immediately next to the C3 carbonyl.

The less crowded *E* enone is the expected favored product. The supplied data establish the conjugated alkene position but do not independently measure its geometry.

### 6.6(i) — Structure and stereochemistry of diketo curcumin

**Pentan-2,4-dione**, also called acetylacetone, has SMILES CC(=O)CC(=O)C.

Condensation of its two terminal methyl groups with two molecules of vanillin gives



The molecular balance is



The structure explains the NMR data:

- The two identical substituted aromatic rings give equivalent sets of aromatic signals resembling those of gingerol.
- The central  $\text{—COCH}_2\text{CO—}$  group gives a 2H singlet around  $\delta 3.5$ , consistent with the supplied 3.4–3.6 range for a carbon between two carbonyl groups.
- Molecular symmetry makes the four vinylic protons occur as two sets of two, giving two 2H doublets.
- $J = 16 \text{ Hz}$  lies in the supplied trans range and exceeds the supplied cis range. Both outer double bonds are therefore *E*.

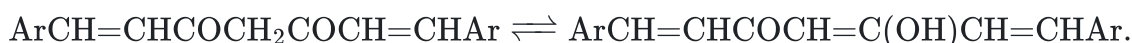
Its degree of unsaturation also agrees:

$$\text{DBE} = \frac{2(21) + 2 - 20}{2} = 12.$$

These comprise eight from the two benzene rings, two from the carbonyls, and two from the additional carbon–carbon double bonds.

### 6.6(ii) — Enol form

Enolization of one carbonyl using a hydrogen from the central methylene gives



The molecular formula remains  $\text{C}_{21}\text{H}_{20}\text{O}_6$ . Acid- or base-catalysed proton transfer changes one carbonyl into an enolic OH while forming the central carbon–carbon double bond.

Draw the enolic OH and the remaining carbonyl oxygen on the same side of the central framework. The favorable central *Z* arrangement permits an  $\text{O—H}\cdots\text{O}$  hydrogen bond closing a six-membered pseudoring. The two outer double bonds retain their *E* configurations.

The SMILES given in the Answers encodes 1*E*, 4*Z*, 6*E*. It does not itself encode the hydrogen bond or the approximately planar conformation that supports conjugation.

### 6.6(iii) — Origin of the yellow colour

The correct choice is **(c), extended conjugation**.

The aromatic rings, alkene bonds, and carbonyl/enol groups form extended conjugated systems. In the enol tautomer, conjugation extends continuously through the central chain. This lowers the energy of electronic excitation enough for absorption to reach the visible region; absorption toward the violet–blue part of the spectrum gives the observed yellow colour.

For completeness, the small species used in the equations above have the following names and SMILES:

| Species                    | SMILES              |
|----------------------------|---------------------|
| Water                      | O                   |
| Dihydrogen                 | [H][H]              |
| Sodium hydroxide           | [Na+].[OH-]         |
| Bromine                    | BrBr                |
| Hydrogen bromide           | Br                  |
| Zinc                       | [Zn]                |
| Mercury                    | [Hg]                |
| Hydrogen chloride          | Cl                  |
| Zinc chloride              | [Zn+2].[Cl-].[Cl-]  |
| Ammonia                    | N                   |
| Hydrogen ion               | [H+]                |
| Lithium ion                | [Li+]               |
| Potassium hydrogen sulfate | [K+].[O-]S(=O)(=O)O |

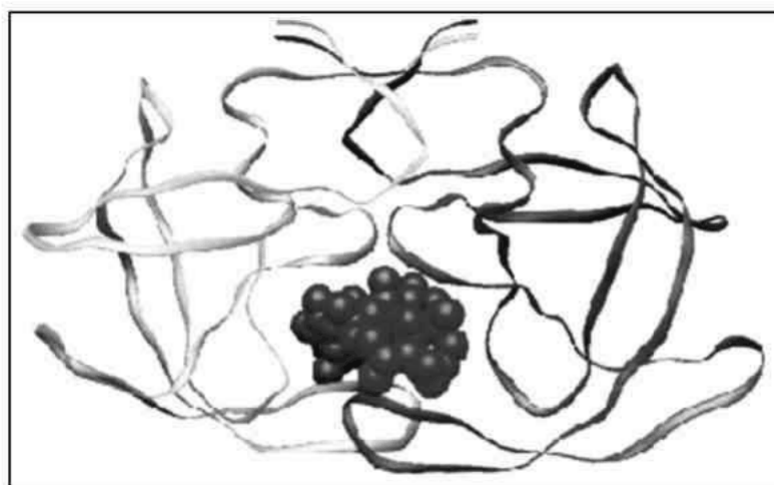
The solution was checked against the official solution.

## Problem 7: Peptides and Proteins

[In the amino-acid tables, S1–S8 refer to the structure figures reproduced immediately below each table.]

### PROBLEM 7

#### Peptides and Proteins



*Protein folding*

Proteins (polypeptides) are known to assume a variety of backbone conformations. In one conformation, the backbone is almost fully extended arrangement (as in a parallel or anti-parallel  $\beta$ -sheet), and in another conformation it is in a fully folded arrangement (as in an  $\alpha$ -helix).

**7.1** The end-to-end distance in a hexapeptide when it is in a fully extended conformation is approximately:

- (a) 10 Å ☐
- (b) 15 Å ☐
- (c) 20 Å ☐
- (d) 25 Å ☐

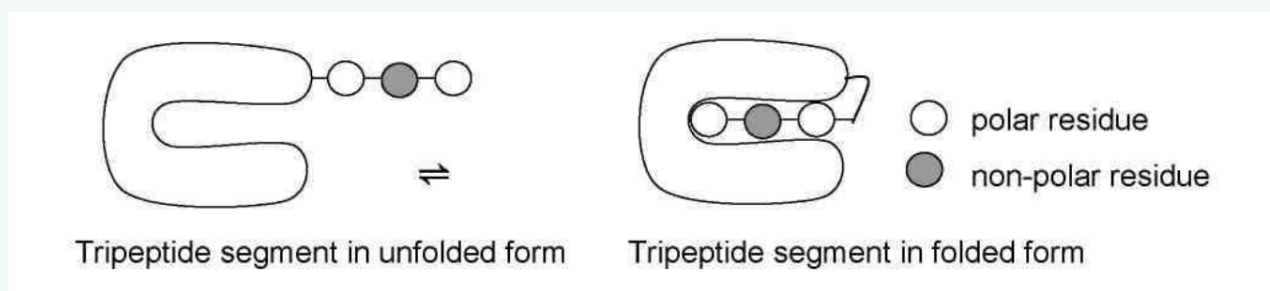
(Mark X in the correct box.)

**7.2** Assuming that the following hexapeptide is a  $\alpha$ -helix conformation, draw a connecting arrow between an oxygen atom and an amide NH with which it is hydrogen bonded.

**7.3** The following hexapeptides (**A** and **B**) display contrasting conformations in water at  $pH$  7.0, especially when their serine hydroxyls are phosphorylated. **A** is moderately helical and it becomes a stronger helix on serine phosphorylation. **B** is weakly helical and it is completely disordered on serine phosphorylation. Draw connecting arrows to indicate the interactions between the residues that are responsible for this differing behaviour.

Consider the following process of folding/unfolding of a tripeptide segment in a large protein. The free energy change ( $\Delta G$ ) will depend on the interaction of the unfolded tripeptide with the solvent (water) and with the rest of the protein in the folded state (see below). Assume that the tripeptide is made up of one non-polar (hydrophobic; shaded) and two polar (hydrophilic; unshaded) residues. Assume the following approximate changes in the interaction free energies :

- (a) a non-polar residue and the solvent (water):  $\Delta G = +8 \text{ kJ mol}^{-1}$
- (b) a non-polar residue and the rest of the protein:  $\Delta G = -4 \text{ kJ mol}^{-1}$
- (c) a polar residue and the solvent (water):  $\Delta G = -16 \text{ kJ mol}^{-1}$
- (d) a polar residue and the rest of the protein:  $\Delta G = -14 \text{ kJ mol}^{-1}$



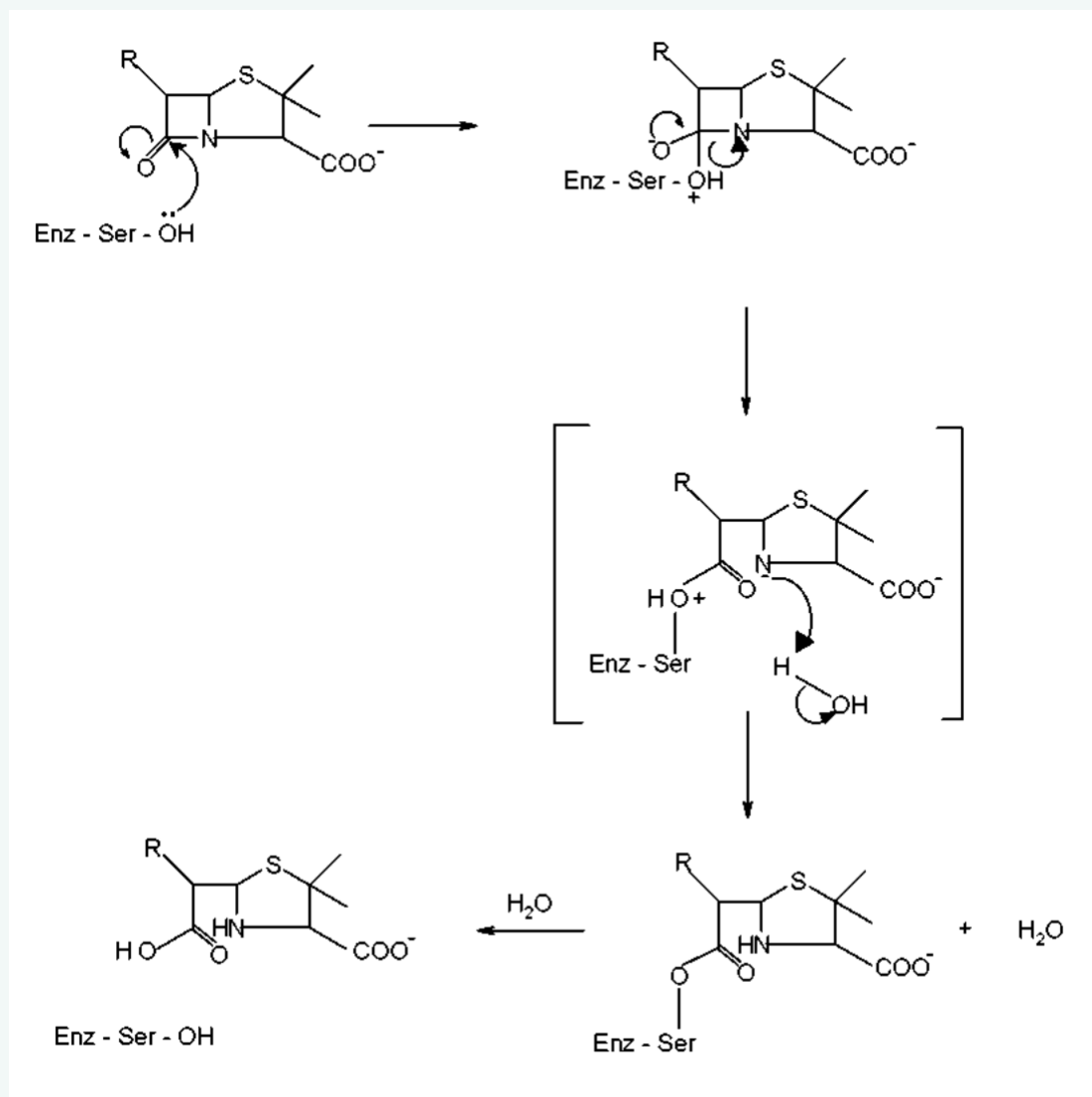
**7.4** Calculate  $\Delta G$  for the folding of the tripeptide segment.

**7.5** Calculate  $\Delta G$  for the folding of the tripeptide segment if all the three residues are polar.

#### *$\beta$ - lactamase and drug resistance*

Penicillins are effective drugs in combating bacterial infections. An alarming development over the years has, however, been the emergence of drug resistant bacteria. Penicillin resistance arises due to the secretion of an enzyme called ( $\beta$ -lactamase (also known as penicillinase), which

inactivates penicillin by opening its (3-lactam ring. The mechanism for this (3-lactam ring opening involves the nucleophilic attack by serine-OH at the active site of the enzyme as shown below.



An attempt was made to characterize the  $\beta$ -lactamase from *Staphylococcus aureus*. When the pure enzyme was treated with a radiolabelled [ $^{32}P$ ] phosphorylating agent, only the active site serine got labelled. On analysis, this serine {molecular mass = 105 mass units (Da)} constituted 0.35% by weight of the  $\beta$ -lactamase.

**7.6** Estimate the minimal molecular mass of this  $\beta$ -lactamase.

**7.7** The approximate number of amino acid residues present in a protein of this size is :

- (a) 100 ☐
- (b) 150 ☐
- (c) 275 ☐
- (d) 375 ☐

[Mark X in the correct box.]

To map its active site, the  $\beta$ -lactamase was hydrolysed using trypsin, a specific enzyme. This resulted in a hexapeptide P1 containing the active site serine. Amino acid analysis revealed the following in equimolar proportion : Glu, Leu, Lys, Met, Phe and Ser. Treatment of P1 with Edman's

reagent (phenyl isothiocyanate) yielded phenyl thiohydantoin (PTH) derivative of phenylalanine and a peptide P2.

Treatment of P1 with cyanogen bromide (CNBr) gave an acidic tetrapeptide P3 and a dipeptide P4.

Treatment of P2 with 1-fluoro-2,4-dinitrobenzene, followed by complete hydrolysis, yielded N-2,4-dinitrophenyl-Glu. P1, P2, and P3 contain the active site serine.

**7.8** From the above information, deduce the amino acid sequence of P1, P2, P3 and P4.

**7.9** Calculate the molecular mass of P3 in mass units (Da) from the information given in the attached Table.

The  $\beta$ -lactamase active site provides a unique microenvironment that makes the catalytic serine-OH an unusually reactive nucleophile. The first order rate constant for  $\beta$ -lactamase catalysed reaction is  $350 \text{ s}^{-1}$ . For penicillin hydrolysis by free serine-OH (at 1 M) in solution, the pseudo first order rate constant is  $0.5 \text{ s}^{-1}$ .

**7.10** From the information above, calculate the effective concentration of this nucleophile at the enzyme active site?

A molecule competing with penicillin for binding to the  $\beta$ -lactamase active site can inhibit the enzyme. Dissociation constants ( $K_D$ ) for the inhibitor-lactamase complex for three different inhibitors are given below :

| Inhibitor | Dissociation constant ( $K_D$ ) |
|-----------|---------------------------------|
| A         | $2.0 \times 10^{-3}$            |
| B         | $1.0 \times 10^{-6}$            |
| C         | $5.0 \times 10^{-9}$            |

**7.11** Indicate which of these inhibitors is most effective in protecting penicillin against  $\beta$ -lactamase. [Mark X in the correct box]

- A ☐  
B ☐  
C ☐

A  $\beta$ -lactamase inhibitor was designed rationally. On binding to the enzyme active site, a nucleophilic attack by the OH group of serine resulted in the opening of the  $\beta$ -lactam moiety of the inhibitor and elimination of  $\text{Br}^-$ . A reactive electrophile is generated as a result and it captures an active site residue X, inactivating the enzyme.

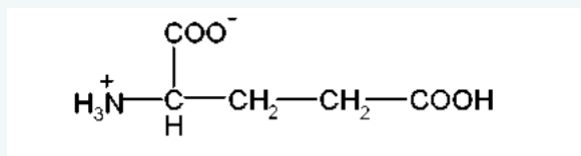
**7.12** Based on the above information, identify the electrophile (**A**) generated and the final product (**B**) formed in the enzyme inactivation by the inhibitor shown.

Table

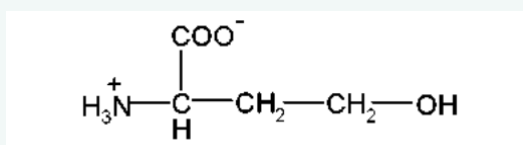
| Amino Acid          | Structure | Molecular mass (Da) |
|---------------------|-----------|---------------------|
| Glu – Glutamic acid | S1        | 147                 |
| Hms – Homoserine    | S2        | 119                 |
| Leu – Leucine       | S3        | 131                 |

| Amino Acid          | Structure | Molecular mass (Da) |
|---------------------|-----------|---------------------|
| Met – Methionine    | S4        | 149                 |
| Lys – Lysine        | S5        | 146                 |
| Phe – Phenylalanine | S6        | 165                 |

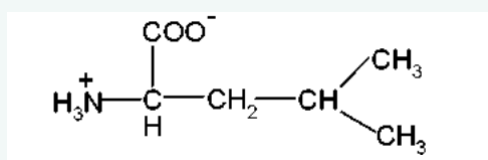
S1:



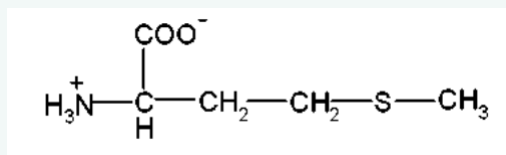
S2:



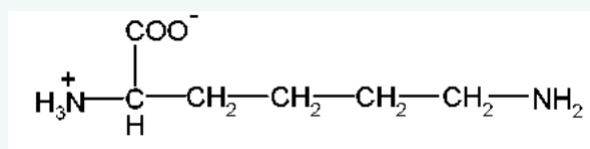
S3:



S4:



S5:



S6:

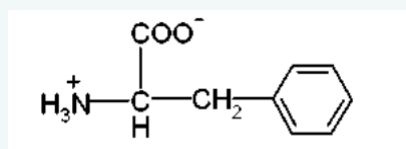
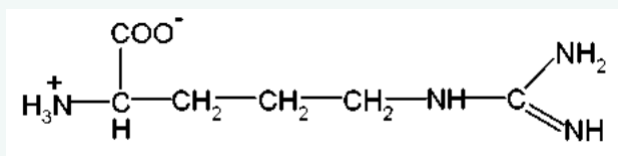


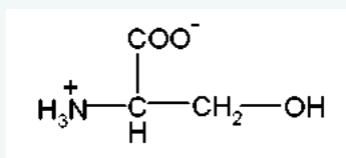
Table (continued)

| Amino Acid     | Structure | Molecular mass (Da) |
|----------------|-----------|---------------------|
| Arg – Arginine | S7        | 174                 |
| Ser – Serine   | S8        | 105                 |

S7:



S8:



Official English text of the problem.

## Answers

- **7.1: (c), approximately 20 Å.**
- **7.2:** Connect the carbonyl oxygen of residue  $i$  to the amide hydrogen of residue  $i + 4$ . For the hexapeptide:  $1 \rightarrow 5$  and  $2 \rightarrow 6$ .
- **7.3:** Phosphorylation introduces negative charge. Favorable phosphate–cation interactions can strengthen A's helix; unfavorable electrostatic interactions can destabilize B's helix. **The exact interacting residues cannot be identified without the missing sequences.**
- **7.4:**  $\Delta G_{\text{fold}} = -8 \text{ kJ mol}^{-1}$ .
- **7.5:**  $\Delta G_{\text{fold}} = +6 \text{ kJ mol}^{-1}$ .
- **7.6:**  $M_{\text{min}} = 3.0 \times 10^4 \text{ Da} = 30 \text{ kDa}$ .
- **7.7: (c), approximately 275 residues.**
- **7.8:** Sequences, written from N-terminus to C-terminus:
  - **P1:** Phe–Glu–Ser–Met–Leu–Lys.
  - **P2:** Glu–Ser–Met–Leu–Lys.
  - **P3:** Phe–Glu–Ser–Hms, using the homoserine form.
  - **P4:** Leu–Lys.
- **7.9:**  $M(\text{P3}) = 482 \text{ Da}$  for the homoserine form indicated by the table.
- **7.10:**  $c_{\text{eff}} = 7 \times 10^2 \text{ mol L}^{-1}$ .
- **7.11: C**, which has the smallest  $K_D$ .
- **7.12: A** is the inhibitor-derived electrophilic intermediate generated after  $\beta$ -lactam opening and bromide elimination; **B** is its covalent capture product with residue X. **Their specific structures cannot be determined without the missing inhibitor drawing.**

## Solution

### 7.1 — Length of the extended hexapeptide

An extended peptide backbone contributes approximately 3.3–3.5 Å along the chain per residue. Thus the approximate length of six residues is

$$L \approx 6(3.3\text{--}3.5) \text{ Å} \approx 20\text{--}21 \text{ Å}.$$

The appropriate choice is therefore **(c)**, 20 Å. This is an approximate chain length, rather than a distance between precisely specified terminal atoms.

### 7.2 — Hydrogen bonds in an α-helix

Number the residues from the N-terminus to the C-terminus. The characteristic α-helical hydrogen bond connects



For six residues, the two possible internal pairs are:

- Carbonyl oxygen of residue **1** with the amide hydrogen of residue **5**.
- Carbonyl oxygen of residue **2** with the amide hydrogen of residue **6**.

On the answer-sheet structure, draw the connecting arrows between those atoms. The carbonyl oxygen is the hydrogen-bond acceptor, and the amide group is the donor. These connections describe the helix's spatial arrangement; ordinary SMILES does not encode that conformation or its hydrogen bonds.

### 7.3 — Effect of serine phosphorylation

At pH 7, an unmodified serine side chain is neutral. Its phosphate ester is negatively charged, predominantly as the dianionic phosphate group. Phosphorylation therefore changes both hydrogen bonding and electrostatic interactions.

The relevant amino-acid structures are given below as free amino-acid ions. In an actual peptide, their α-amino and α-carboxyl groups instead participate in the backbone.

| Name                                                 | SMILES                                                |
|------------------------------------------------------|-------------------------------------------------------|
| L-Serine, zwitterion                                 | <chem>[NH3+][C@@H](CO)C(=O)[O-]</chem>                |
| O-Phospho-L-serine, with a dianionic phosphate group | <chem>[NH3+][C@@H](COP(=O)([O-])[O-])C(=O)[O-]</chem> |
| L-Arginine, protonated guanidinium form              | <chem>[NH3+][C@@H](CCCNC(=[NH2+])N)C(=O)[O-]</chem>   |
| L-Lysine, protonated side-chain amino group          | <chem>[NH3+][C@@H](CCCC[NH3+])C(=O)[O-]</chem>        |
| L-Glutamate                                          | <chem>[NH3+][C@@H](CCC(=O)[O-])C(=O)[O-]</chem>       |

An electrostatic explanation consistent with the observations is:

- **A:** The phosphate group approaches a positively charged side chain, such as arginine's guanidinium or lysine's ammonium group. An attractive ion pair, reinforced by hydrogen bonding, stabilizes the helical arrangement.
- **B:** The phosphate group approaches another negatively charged group, such as a glutamate carboxylate. Repulsion destabilizes that arrangement.

Residues separated by three or four positions can approach one another on an  $\alpha$ -helix, making their positions in the sequence important.

For such an arrangement, draw an attractive connection from a phosphate oxygen to the nearby cationic side chain in A, and indicate repulsion between the phosphate and nearby anionic group in B. Before phosphorylation, corresponding contacts involving serine's hydroxyl would be hydrogen bonds rather than phosphate salt bridges.

**These are conditional drawing instructions.** The missing A and B sequences prevent assigning particular residue numbers or establishing that these particular side chains are present. Interactions with charged termini or the helix dipole could also contribute; the reported conformational changes alone do not uniquely identify the contacts.

#### 7.4 — Folding with one non-polar and two polar residues

Use

$$\Delta G_{\text{fold}} = G_{\text{folded}} - G_{\text{unfolded}}.$$

For the unfolded segment, all three residues interact with water:

$$G_{\text{unfolded}} = 8 + 2(-16) = -24 \text{ kJ mol}^{-1}.$$

For the folded segment, they interact with the rest of the protein:

$$G_{\text{folded}} = -4 + 2(-14) = -32 \text{ kJ mol}^{-1}.$$

Therefore,

$$\Delta G_{\text{fold}} = -32 - (-24) = -8 \text{ kJ mol}^{-1}.$$

Equivalently, burying the non-polar residue contributes  $-12 \text{ kJ mol}^{-1}$ , whereas burying each polar residue costs  $+2 \text{ kJ mol}^{-1}$ .

#### 7.5 — Folding with three polar residues

Each polar residue changes its interaction free energy by

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

Consequently,

$$\Delta G_{\text{fold}} = 3(+2) = +6 \text{ kJ mol}^{-1}.$$

Folding is unfavorable under the simplified interaction-energy model supplied in the question.

#### 7.6 — Minimal molecular mass of $\beta$ -lactamase

The smallest possible enzyme molecule contains one labelled active-site serine. Using the stated serine mass of 105 Da,

$$\frac{105 \text{ Da}}{M_{\text{min}}} = \frac{0.35}{100} = 0.0035.$$

Thus

$$M_{\text{min}} = \frac{105}{0.0035} = 3.0 \times 10^4 \text{ Da}.$$

If there were  $n$  labelled serines per enzyme molecule, the inferred mass would be  $n$  times this value. Hence one labelled serine gives the minimum.

### 7.7 — Approximate number of residues

The standard approximate mean mass of an amino-acid **residue in a protein** is 110 Da. Therefore,

$$N \approx \frac{30\,000 \text{ Da}}{110 \text{ Da residue}^{-1}} \approx 273 \text{ residues.}$$

The nearest option is **(c), 275**.

### 7.8 — Sequences of P1–P4

The sequence follows from four cleavage and labelling observations.

**1. Trypsin identifies the C-terminal residue.**

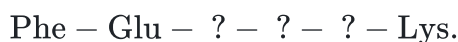
Trypsin cleaves peptide bonds on the C-terminal side of lysine or arginine. P1 contains lysine and no arginine, so its C-terminal residue is Lys.

**2. Edman degradation identifies the first residue.**

Release of the phenylalanine derivative establishes that P1 begins with Phe. P2 is the remaining pentapeptide.

**3. N-terminal labelling of P2 identifies the second residue of P1.**

The dinitrophenyl-Glu product establishes that P2 begins with Glu. Thus P1 has the partial sequence



**4. Cyanogen bromide locates methionine.**

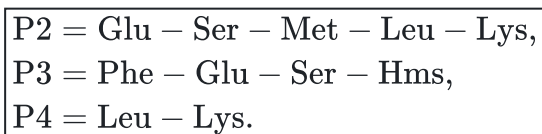
Cyanogen bromide,  $\text{BrC}\equiv\text{N}$ , cleaves on the C-terminal side of methionine. A hexapeptide yielding fragments of lengths four and two would have Met at position 4 or position 2. Position 2 is already Glu, so Met must occupy position 4.

P3 is the four-residue N-terminal fragment and contains the active-site Ser. Its only remaining position is position 3. Leu consequently occupies position 5.

Hence



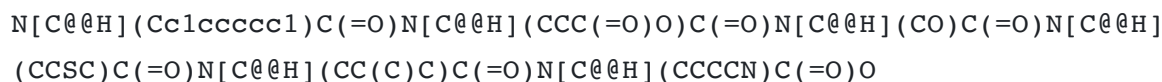
Cyanogen-bromide cleavage changes the methionine at the end of the N-terminal fragment into a homoserine derivative. Taking the open-chain homoserine form indicated by the table gives



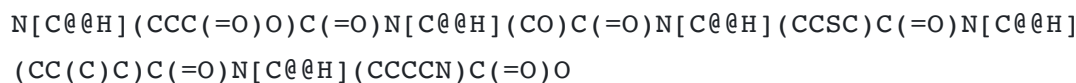
The glutamate side chain accounts for P3's acidic character.

The following SMILES show neutral peptide forms, with natural L stereochemistry and ordinary  $\alpha$ -peptide linkages:

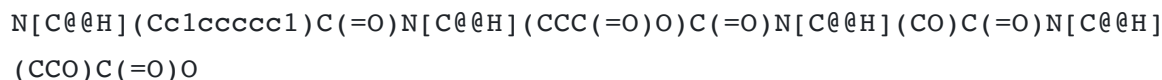
- **P1 — L-phenylalanyl-L-glutamyl-L-seryl-L-methionyl-L-leucyl-L-lysine:**



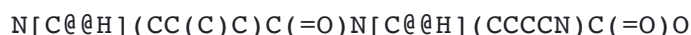
- **P2 — L-glutamyl-L-seryl-L-methionyl-L-leucyl-L-lysine:**



- **P3 — L-phenylalanyl-L-glutamyl-L-seryl-L-homoserine:**



- **P4 — L-leucyl-L-lysine:**



For conversion through to open-chain homoserine, the balanced overall cleavage, written using these neutral peptide forms, is



The additional species are water, O; methyl thiocyanate,  $\text{CSC}\#N$ ; and hydrogen bromide,  $[\text{H}]\text{Br}$ . The initially formed homoserine lactone accounts for the distinction discussed next.

## 7.9 — Molecular mass of P3

P3 contains Phe, Glu, Ser and Hms. L-Homoserine is  $\text{N}[\text{C}@\text{H}] (\text{CCO}) \text{C}(=\text{O}) \text{O}$ .

A linear tetrapeptide has three peptide bonds, so its mass equals the sum of the four free amino-acid masses minus three water molecules:

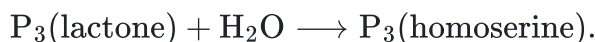
$$\begin{aligned} M(\text{P}_3) &= 165 + 147 + 105 + 119 - 3(18) \\ &= \boxed{482 \text{ Da}}. \end{aligned}$$

Methionine's mass must **not** be used for the terminal residue after cyanogen-bromide cleavage.

Chemically, cyanogen-bromide cleavage initially produces a terminal **homoserine  $\gamma$ -lactone**, which can hydrolyse to homoserine. The corresponding P3 lactone is L-phenylalanyl-L-glutamyl-L-seryl-L-homoserine  $\gamma$ -lactone:



Its hydrolysis is



Therefore the lactone would have mass  $482 - 18 = 464 \text{ Da}$ . The supplied homoserine table entry supports **482 Da** as the intended answer.

## 7.10 — Effective concentration of the nucleophile

For the reaction with free serine, the pseudo-first-order rate constant is

$$k_{\text{obs}} = k_2[\text{serine}].$$

At  $1 \text{ mol L}^{-1}$ ,

$$k_2 = \frac{0.5 \text{ s}^{-1}}{1 \text{ mol L}^{-1}} = 0.5 \text{ L mol}^{-1} \text{ s}^{-1}.$$

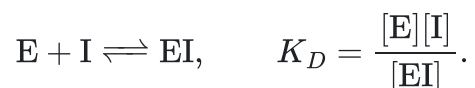
Define the effective concentration by equating the enzymatic rate constant to  $k_2 c_{\text{eff}}$ :

$$c_{\text{eff}} = \frac{350 \text{ s}^{-1}}{0.5 \text{ L mol}^{-1} \text{ s}^{-1}} = \boxed{7 \times 10^2 \text{ mol L}^{-1}}.$$

This is a **kinetic effective molarity**: the solution concentration that would give the same rate under this comparison. It is not a literal bulk concentration inside the enzyme.

### 7.11 — Most effective inhibitor

For reversible binding,



A smaller  $K_D$  means stronger binding. At the same free inhibitor concentration, it also means a greater fraction of enzyme is inhibitor-bound:

$$f_{\text{bound}} = \frac{[\text{I}]}{K_D + [\text{I}]}.$$

Since

$$5.0 \times 10^{-9} < 1.0 \times 10^{-6} < 2.0 \times 10^{-3},$$

**inhibitor C** is the most effective under comparable concentration conditions. Its molecular structure is not supplied, so no molecular name or SMILES can be inferred from its  $K_D$ .

### 7.12 — Electrophile formation and enzyme inactivation

The missing inhibitor drawing is essential for assigning the structures of A and B. The information supplied establishes the following mechanistic framework:

1. **Serine attacks the  $\beta$ -lactam carbonyl.** Draw a curved arrow from the serine oxygen lone pair to the carbonyl carbon, and another from the carbonyl  $\pi$  bond to oxygen.
2. **The  $\beta$ -lactam ring opens.** Collapse of the tetrahedral intermediate breaks the lactam's acyl carbon–nitrogen bond, with the necessary proton transfers. The initial product is a serine acyl-enzyme ester. Its ester linkage can be represented generically as  $[\ast]\text{C}(=\text{O})\text{O}[\ast]$ , with the wildcards representing the inhibitor-derived and enzyme-derived portions.
3. **Bromide is eliminated.** Bromide ion is  $[\text{Br}-]$ . Its departure generates electrophile **A**. The omitted inhibitor connectivity determines which bond breaks, which new bond or  $\pi$  system forms, and where the electrophilic center lies.
4. **Residue X traps A.** Draw an arrow from the nucleophilic lone pair on X to the electrophilic atom of A, with the corresponding electron redistribution. The resulting covalent adduct is **B**, which inactivates the enzyme.

The prose does not identify the bromine-bearing carbon, the inhibitor substituents, or the chemical identity of X. Consequently, **a unique chemical name, complete SMILES, detailed product drawing, or atom-balanced overall equation for A and B cannot be supplied without inventing missing structural information.**

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The solution was checked against the official solution.