

IChO 2014

Theory problems and solutions · Hanoi, Vietnam · 9 theory problems with complete solutions

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Problem 1: Particles in a box: polyenes

In quantum mechanics, the movement of π electrons along a neutral chain of conjugated carbon atoms may be modeled using the 'particle in a box' method. The energy of the π electrons is given by the following equation:

$$E_n = \frac{n^2 h^2}{8mL^2}$$

where n is the quantum number ($n = 1, 2, 3, \dots$), h is Planck's constant, m is the mass of electron, and L is the length of the box which may be approximated by $L = (k + 2) \times 1.40 \text{ \AA}$ (k being the number of conjugated double bonds along the carbon chain in the molecule). A photon with the appropriate wavelength λ may promote a π electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO). An approximate semi-empirical formula based on this model which relates the wavelength λ , to the number of double bonds k and constant B is as follows:

$$\lambda(\text{nm}) = B \times \frac{(k + 2)^2}{(2k + 1)} \quad \text{Equation 1}$$

1.1 Using this semi-empirical formula with $B = 65.01 \text{ nm}$ calculate the value of the wavelength λ (nm) for octatetraene ($\text{CH}_2=\text{CH}-\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$).

1.2 Derive equation 1 (an expression for the wavelength λ (nm) corresponding to the transfer of an electron from the HOMO to the LUMO) in terms of k and the fundamental constants, and hence calculate theoretical value of the constant $B_{\text{calc.}}$.

1.3 We wish to synthesize a linear polyene for which the excitation of a π electron from the HOMO to the LUMO requires an absorption wavelength of close to 600 nm. Using your expression from part 2, determine the number of conjugated double bonds (k) in this polyene and give its structure. [If you did not solve Part 2, use the semi-empirical Equation 1 with $B = 65.01 \text{ nm}$ to complete Part 3.]

1.4 For the polyene molecule found in Part 3, calculate the difference in energy between the HOMO and the LUMO, ΔE , (kJ mol^{-1}).

In case that Part 3 was not solved, take $k = 5$ to solve this problem.

The model for a particle in a one-dimensional box can be extended to a three dimensional rectangular box of dimensions L_x , L_y and L_z , yielding the following expression for the allowed energy levels:

$$E_{n_x, n_y, n_z} = \frac{h^2}{8m} \left(\frac{n_x^2}{L_x^2} + \frac{n_y^2}{L_y^2} + \frac{n_z^2}{L_z^2} \right)$$

1.2

Each conjugated double bond contributes two π electrons, giving $2k$ electrons altogether. Each spatial orbital accommodates two electrons of opposite spin. In the ground state, the levels $n = 1, \dots, k$ are therefore filled:

$$n_{\text{HOMO}} = k, \quad n_{\text{LUMO}} = k + 1.$$

The excitation energy is

$$\begin{aligned} \Delta E &= E_{k+1} - E_k \\ &= \frac{h^2}{8mL^2} [(k+1)^2 - k^2] \\ &= \frac{h^2(2k+1)}{8mL^2}. \end{aligned}$$

Equating this to the photon energy,

$$\frac{hc}{\lambda} = \frac{h^2(2k+1)}{8mL^2},$$

gives

$$\lambda = \frac{8mcL^2}{h(2k+1)}.$$

Let $a = 1.40 \text{ \AA} = 1.40 \times 10^{-10} \text{ m}$. Substituting $L = (k+2)a$,

$$\lambda = \frac{8mca^2}{\underbrace{h}_{B_{\text{calc}}}} \frac{(k+2)^2}{2k+1}.$$

The problem does not tabulate fundamental constants. Using the standard values

$$h = 6.62607015 \times 10^{-34} \text{ J s}, \quad m = 9.1093837 \times 10^{-31} \text{ kg}, \quad c = 2.99792458 \times 10^8 \text{ m s}^{-1},$$

we obtain

$$B_{\text{calc}} = \frac{8mca^2}{h} = 6.46249 \times 10^{-8} \text{ m} = 64.6249 \text{ nm}.$$

Thus, to three significant figures,

$$B_{\text{calc}} = 64.6 \text{ nm}.$$

1.3

Using the theoretical constant, with additional digits retained during calculation,

$$600 = 64.6249 \frac{(k+2)^2}{2k+1}.$$

Define $r = 600/64.6249$. Rearrangement gives

$$k^2 + (4 - 2r)k + (4 - r) = 0.$$

The positive root is

$$k = r - 2 + \sqrt{r(r-3)} \approx 14.923.$$

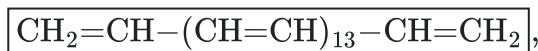
The number of double bonds must be an integer. Checking nearby values,

$$\lambda(14) = 570.5 \text{ nm}, \quad \lambda(15) = 602.5 \text{ nm}, \quad \lambda(16) = 634.5 \text{ nm}.$$

Hence,

$$\boxed{k = 15}.$$

The structure is



an unbranched chain of 30 carbon atoms with 15 alternating double bonds and molecular formula $\text{C}_{30}\text{H}_{32}$.

Its name is **triaconta-1,3,5,7,9,11,13,15,17,19,21,23,25,27,29-pentadecaene**.

SMILES: C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C-C=C

The model approximates the conjugated chain as one-dimensional. It does not specify double-bond stereochemistry, so the SMILES leaves *E/Z* configurations unspecified.

1.4

For $k = 15$, the HOMO and LUMO have $n = 15$ and $n = 16$, respectively, and

$$L = (15 + 2)(1.40 \text{ Å}) = 23.8 \text{ Å} = 2.38 \times 10^{-9} \text{ m}.$$

The energy gap per molecule is

$$\begin{aligned} \Delta E_{\text{molecule}} &= \frac{h^2(16^2 - 15^2)}{8mL^2} \\ &= \frac{31h^2}{8m(2.38 \times 10^{-9} \text{ m})^2} \\ &= 3.29717 \times 10^{-19} \text{ J}. \end{aligned}$$

Using $N_A = 6.02214076 \times 10^{23} \text{ mol}^{-1}$,

$$\begin{aligned} \Delta E_{\text{molar}} &= N_A \Delta E_{\text{molecule}} \\ &= 1.98560 \times 10^5 \text{ J mol}^{-1} \\ &= 198.560 \text{ kJ mol}^{-1}. \end{aligned}$$

Therefore,

$$\boxed{\Delta E \approx 1.99 \times 10^2 \text{ kJ mol}^{-1}}.$$

Using the target wavelength of exactly 600 nm gives the close approximation $199.4 \text{ kJ mol}^{-1}$; the calculation above uses the actual model prediction for $k = 15$.

1.5

For a cubic box, $L_x = L_y = L_z = L$, so

$$E_{n_x, n_y, n_z} = \frac{h^2}{8mL^2} (n_x^2 + n_y^2 + n_z^2).$$

The quantum numbers are positive integers: zero would give an identically zero wavefunction rather than an allowed state. The three smallest distinct sums of squares are

$$1^2 + 1^2 + 1^2 = 3, \quad 2^2 + 1^2 + 1^2 = 6, \quad 2^2 + 2^2 + 1^2 = 9.$$

Consequently,

$$\begin{aligned}
 E_{1,1,1} &= \frac{3h^2}{8mL^2}, \\
 E_{2,1,1} = E_{1,2,1} = E_{1,1,2} &= \frac{6h^2}{8mL^2}, \\
 E_{2,2,1} = E_{2,1,2} = E_{1,2,2} &= \frac{9h^2}{8mL^2}.
 \end{aligned}$$

1.6

Let $A = h^2/(8mL^2)$. Restricting each quantum number to 1 or 2 gives $2^3 = 8$ spatial states:

Energy	Quantum-number triples (n_x, n_y, n_z)	Spatial degeneracy
$12A$	$(2, 2, 2)$	1
$9A$	$(2, 2, 1), (2, 1, 2), (1, 2, 2)$	3
$6A$	$(2, 1, 1), (1, 2, 1), (1, 1, 2)$	3
$3A$	$(1, 1, 1)$	1

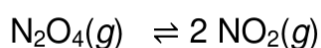
The sketch has an upward energy axis and four equally spaced heights at $3A$, $6A$, $9A$, and $12A$. From bottom to top, there are one, three, three, and one horizontal level lines. Degenerate lines lie side by side at the same height, each labelled with its quantum-number triple from the table.

These degeneracies count spatial states; electron spin is not included.

The solution was checked against the official solution.

Problem 2: Dissociating gas cycle

Dinitrogen tetroxide forms an equilibrium mixture with nitrogen dioxide:



1.00 mol of N_2O_4 was put into an empty vessel with a fixed volume of 24.44 dm^3 . The equilibrium gas pressure at 298 K was found to be 1.190 bar. When heated to 348 K, the gas pressure increased to its equilibrium value of 1.886 bar.

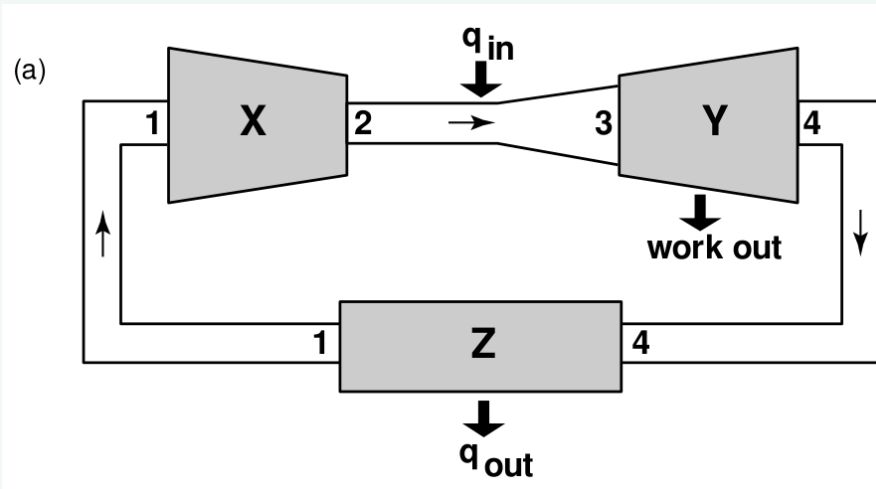
2.1 Calculate ΔG^0 of the reaction at 298K, assuming the gases are ideal.

2.2 Calculate ΔH^0 and ΔS^0 of the reaction, assuming that they do not change significantly with temperature.

Note: If you cannot calculate ΔH^0 , use $\Delta H^0 = 30.0 \text{ kJ mol}^{-1}$ for further calculations.

The tendency of N_2O_4 to dissociate reversibly into NO_2 enables its potential use in advanced power generation systems. A simplified scheme for one such system is shown below in Figure (a). Initially, "cool" N_2O_4 is compressed ($1 \rightarrow 2$) in a compressor (X), and heated ($2 \rightarrow 3$). Some N_2O_4 dissociates into NO_2 . The hot mixture is expanded ($3 \rightarrow 4$) through a turbine (Y), resulting in a decrease in both temperature and pressure. The mixture is then cooled further ($4 \rightarrow 1$) in a

heat sink (Z), to promote the reformation of N_2O_4 . This recombination reduces the pressure, thus facilitates the compression of N_2O_4 to start a new cycle. All these processes are assumed to take place reversibly.



To understand the benefits of using reversible dissociating gases such as N_2O_4 , we will focus on step $3 \rightarrow 4$ and consider an ideal gas turbine working with 1 mole of air (which we assume to be an inert, non-dissociating gas). During the reversible adiabatic expansion in the turbine, no heat is exchanged.

2.3 Give the equation to calculate the work done by the system $w(\text{air})$ during the reversible adiabatic expansion for 1 mol of air during stage $3 \rightarrow 4$. Assume that $C_{v,m}(\text{air})$ (the isochoric molar heat capacity of air) is constant, and the temperature changes from T_3 to T_4 .

2.4 Estimate the ratio $w_{\text{N}_2\text{O}_4}/w(\text{air})$, in which $w_{\text{N}_2\text{O}_4}$ is the work done by the gas during the reversible adiabatic expansion process $3 \rightarrow 4$ with the cycle working with 1 mol of N_2O_4 , T_3 and T_4 are the same as in part 2. Take the conditions at stage 3 to be $T_3 = 440 \text{ K}$ and $p_3 = 12.156 \text{ bar}$ and assume that:

- (i) the gas is at its equilibrium composition at stage 3;
- (ii) $C_{v,m}$ for the gas is the same as for air;
- (iii) the adiabatic expansion in the turbine takes place in a way that the composition of the gas mixture ($\text{N}_2\text{O}_4 + \text{NO}_2$) is unchanged until the expansion is completed.

Official English text of the problem.

Answers

- **2.1:** $\Delta G_{298}^\circ = +4.73 \text{ kJ mol}^{-1}$.
- **2.2:** $\Delta H^\circ = +57.2 \text{ kJ mol}^{-1}$, $\Delta S^\circ = +176 \text{ J mol}^{-1} \text{ K}^{-1}$.
- **2.3:** For the closed-system expansion-work interpretation,

$$w(\text{air}) = (1.00 \text{ mol}) C_{v,m}(\text{air})(T_3 - T_4),$$

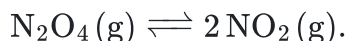
positive for work done by the gas.

- 2.4: $w_{(\text{N}_2\text{O}_4)}/w_{(\text{air})} \approx 1.92$.

Solution

2.1 — Standard Gibbs energy of dissociation

The balanced reaction is



The species are dinitrogen tetroxide, $\text{O}=[\text{N}^+](\text{O}^-)[\text{N}^+](=\text{O})(\text{O}^-)$, and nitrogen dioxide, $\text{O}=[\text{N}^+](\text{O}^-)$. Nitrogen dioxide is an odd-electron radical; its SMILES represents one Lewis form and does not depict resonance delocalization.

Use

$$R = 8.314 \text{ J mol}^{-1} \text{ K}^{-1} = 0.08314 \text{ bar dm}^3 \text{ mol}^{-1} \text{ K}^{-1}, \quad p^\circ = 1 \text{ bar}.$$

Let α be the fraction of the original $n_0 = 1.00 \text{ mol}$ of N_2O_4 that dissociates. At equilibrium,

$$n(\text{N}_2\text{O}_4) = n_0(1 - \alpha), \quad n(\text{NO}_2) = 2n_0\alpha,$$

so

$$n_{\text{tot}} = n_0(1 + \alpha).$$

The ideal-gas equation therefore gives

$$\alpha = \frac{pV}{n_0RT} - 1.$$

At 298 K,

$$\alpha_{298} = \frac{(1.190 \text{ bar})(24.44 \text{ dm}^3)}{(1.00 \text{ mol})(0.08314 \text{ bar dm}^3 \text{ mol}^{-1} \text{ K}^{-1})(298 \text{ K})} - 1 = 0.173875.$$

The partial pressures are

$$p(\text{NO}_2) = \frac{2\alpha}{1 + \alpha}p = 0.352527 \text{ bar},$$

$$p(\text{N}_2\text{O}_4) = \frac{1 - \alpha}{1 + \alpha}p = 0.837473 \text{ bar}.$$

The dimensionless equilibrium constant is

$$K_p = \frac{[p(\text{NO}_2)/p^\circ]^2}{p(\text{N}_2\text{O}_4)/p^\circ} = \frac{4\alpha^2}{1 - \alpha^2} \frac{p}{p^\circ}.$$

Thus,

$$K_p(298) = \frac{(0.352527)^2}{0.837473} = 0.148393.$$

Consequently,

$$\Delta G_{298}^\circ = -RT \ln K_p(298) = -(8.314)(298) \ln(0.148393) \text{ J mol}^{-1},$$

$$\boxed{\Delta G_{298}^\circ = +4.73 \text{ kJ mol}^{-1}}.$$

2.2 — Standard enthalpy and entropy of dissociation

At 348 K, the same calculation gives

$$\alpha_{348} = \frac{(1.886)(24.44)}{(1.00)(0.08314)(348)} - 1 = 0.593139,$$

and hence

$$K_p(348) = \frac{4(0.593139)^2}{1 - (0.593139)^2} \frac{1.886 \text{ bar}}{1 \text{ bar}} = 4.09463.$$

For temperature-independent ΔH° , the integrated van 't Hoff equation is

$$\ln \frac{K_p(T_2)}{K_p(T_1)} = \frac{\Delta H^\circ}{R} \left(\frac{1}{T_1} - \frac{1}{T_2} \right).$$

Therefore,

$$\Delta H^\circ = \frac{(8.314 \text{ J mol}^{-1} \text{ K}^{-1}) \ln(4.09463/0.148393)}{\frac{1}{298 \text{ K}} - \frac{1}{348 \text{ K}}} = 57207.8 \text{ J mol}^{-1},$$

$\Delta H^\circ = +57.2 \text{ kJ mol}^{-1}.$

Using $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$,

$$\Delta S^\circ = \frac{\Delta H^\circ - \Delta G_{298}^\circ}{298 \text{ K}} = \frac{(57207.8 - 4726.93) \text{ J mol}^{-1}}{298 \text{ K}},$$

$\Delta S^\circ = +176 \text{ J mol}^{-1} \text{ K}^{-1}.$

Dissociation is endothermic and increases entropy, consistent with converting one gas molecule into two.

2.3 — Adiabatic expansion work

Take $w > 0$ for work done by the gas. For a closed system, the first law is

$$\Delta U = q - w.$$

Since the expansion is adiabatic, $q = 0$, so $w = -\Delta U$. For a fixed amount of ideal gas with constant molar heat capacity,

$$\Delta U = nC_{v,m}(T_4 - T_3).$$

For $n = 1.00 \text{ mol}$ of air,

$w(\text{air}) = (1.00 \text{ mol}) C_{v,m}(\text{air})(T_3 - T_4).$

The temperature decreases during expansion, so this work is positive.

2.4 — Work ratio for the dissociating gas

First calculate the equilibrium constant at stage 3:

$$\ln \frac{K_p(440)}{K_p(298)} = \frac{\Delta H^\circ}{R} \left(\frac{1}{298 \text{ K}} - \frac{1}{440 \text{ K}} \right).$$

Using the unrounded results above,

$$K_p(440) = 0.148393 \exp \left[\frac{57207.8}{8.314} \left(\frac{1}{298} - \frac{1}{440} \right) \right] = 255.690.$$

Let α_3 be the dissociation fraction at $p_3 = 12.156$ bar. From the equilibrium expression derived in 2.1,

$$K_p(440) = \frac{4\alpha_3^2}{1 - \alpha_3^2} \frac{p_3}{p^\circ}.$$

Solving,

$$\alpha_3 = \sqrt{\frac{K_p(440)}{K_p(440) + 4p_3/p^\circ}} = \sqrt{\frac{255.690}{255.690 + 4(12.156)}} = 0.916634.$$

Thus, starting with 1.00 mol of N_2O_4 , the stage-3 mixture contains

$$n(\text{N}_2\text{O}_4) = 0.083366 \text{ mol}, \quad n(\text{NO}_2) = 1.833268 \text{ mol},$$

and

$$n_3 = (1.00 \text{ mol})(1 + \alpha_3) = 1.916634 \text{ mol}.$$

The composition is unchanged during expansion, so there is no reaction contribution to the change in internal energy during $3 \rightarrow 4$. With the same molar heat capacity and temperature change as for air,

$$w(\text{N}_2\text{O}_4) = n_3 C_{v,m}(\text{air})(T_3 - T_4).$$

Therefore,

$$\frac{w(\text{N}_2\text{O}_4)}{w(\text{air})} = \frac{n_3}{1.00 \text{ mol}} = 1 + \alpha_3,$$

$$\frac{w(\text{N}_2\text{O}_4)}{w(\text{air})} = 1.916634 \approx 1.92.$$

The increased work comes from the larger number of gas molecules produced by dissociation.

The solution was checked against the official solution.

Problem 3: High-valent silver compounds

Silver chemistry is dominated by Ag (I) compounds. Compounds of silver in higher oxidation state (from +2 to +5) are not very abundant due to their instability with respect to reduction. High-valent silver compounds are very reactive and can be synthesized from Ag(I) compounds in electro-chemical oxidations or in chemical oxidations using powerful oxidizing agents.

In some peroxydisulfate ($\text{S}_2\text{O}_8^{2-}$) oxidations catalyzed by Ag^+ , black solid (**A**) with the composition AgO can be isolated.

3.1 Choose the appropriate magnetic behavior of **A** if it exists as $\text{Ag}^{\text{II}}\text{O}$.

Single crystal X - ray studies reveal that the lattice of **A** contains two nonequivalent Ag atom sites (in equal proportions) of which one denoted as Ag1 and the other denoted as Ag2. Ag1 shows a linear O atom coordination ($\text{O}-\text{Ag}-\text{O}$) and Ag2 shows a square-planar O atom coordination. All O atoms are in equivalent environments in the structure. Thus, **A** should be assigned as $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$ rather than $\text{Ag}^{\text{II}}\text{O}$.

3.2. Assign the oxidation number of Ag^I and Ag^{III}.

3.3 What is the coordination number of O atoms in the lattice of **A**?

3.4 How many Ag^I and Ag^{III} bond to one O atom in the lattice of **A**?

3.5 Predict the magnetic behavior of **A**. Check the appropriate box below.

3.6 The compound **A** can also be formed on warming a solution of Ag⁺ with peroxydisulfate. Write down the equation for the formation of **A**.

Among the silver oxides which have been crystallographically characterized, the most surprising is probably that compound **A** is not a Ag^{II}O. Thermochemical cycles are useful to understand this fact. Some standard enthalpy changes (at 298 K) are listed:

Atom	Standard enthalpy of formation (kJ mol ⁻¹)	1st ionization (kJ mol ⁻¹)	2nd ionization (kJ mol ⁻¹)	3rd ionization (kJ mol ⁻¹)	1st electron affinity (kJ mol ⁻¹)	2nd electron affinity (kJ mol ⁻¹)
Cu(g)	337.4	751.7	1964.1	3560.2		
Ag(g)	284.9	737.2	2080.2	3367.2		
O(g)	249.0				-141.0	844.0

Compounds	ΔH_f° (kJ mol ⁻¹)
Ag ^I Ag ^{III} O ₂ (s)	-24.3
Cu ^{II} O (s)	-157.3

The relationship between the lattice dissociation energy (U_{lat}) and the lattice dissociation enthalpy (ΔH_{lat}) for monoatomic ion lattices is: $\Delta H_{\text{lat}} = U_{\text{lat}} + nRT$, where n is the number of ions in the formula unit.

3.7 Calculate U_{lat} at 298 K of Ag^IAg^{III}O₂ and Cu^{II}O. Assume that they are ionic compounds.

The lattice dissociation energies for a range of compounds may be estimated using this simple formula:

$$U_{\text{lat}} = C \times \left(\frac{1}{V_m} \right)^{1/3}$$

where: V_m (nm³) is the volume of the formula unit and C (kJ nm mol⁻¹) is an empirical constant which has a particular value for each type of lattice with ions of specified charges.

The formula unit volumes of some oxides are calculated from crystallographic data as the ratio between the unit cell volume and the number of formula units in the unit cell and listed as below:

Oxides	V_m (nm ³)
Cu ^{II} O	0.02030
Ag ^{III} ₂ O ₃	0.06182
Ag ^{II} Ag ^{III} ₂ O ₄	0.08985

3.8 Calculate U_{lat} for the hypothetical compound Ag^{II}O. Assume that Ag^{II}O and Cu^{II}O have the same type of lattice, and $V_m(\text{Ag}^{\text{II}}\text{O}) = V_m(\text{Ag}^{\text{II}}\text{Ag}^{\text{III}}_2\text{O}_4) - V_m(\text{Ag}^{\text{III}}_2\text{O}_3)$.

3.9 By constructing an appropriate thermodynamic cycle or otherwise, estimate the enthalpy change for the solid-state transformation from $\text{Ag}^{\text{II}}\text{O}$ to 1 mole of $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$.

Note: Use $U_{\text{lat}}(\text{Ag}^{\text{II}}\text{O}) = 3180.0 \text{ kJ mol}^{-1}$ and $U_{\text{lat}}(\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2) = 8310.0 \text{ kJ mol}^{-1}$ if you cannot calculate $U_{\text{lat}}(\text{Ag}^{\text{II}}\text{O})$ in Part 3.8).

3.10 Indicate which compound ($\text{Ag}^{\text{II}}\text{O}$ or $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$) is thermodynamically more stable.

(Check the corresponding box.)

3.11 When $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$ is dissolved in aqueous HClO_4 solution, a paramagnetic compound (**B**) is first formed then slowly decomposes to form a diamagnetic compound (**C**). Given that **B** and **C** are the only compounds containing silver formed in these reactions, write down the equations for the formation of **B** and **C**.

Oxidation of Ag^+ with powerful oxidizing agents in the presence of appropriate ligands can result in the formation of high-valent silver complexes. A complex **Z** is synthesized and analyzed by the following procedures:

An aqueous solution containing 0.500 g of AgNO_3 and 2 cm^3 of pyridine ($d = 0.982 \text{ g cm}^{-3}$) is added to a stirred, ice-cold aqueous solution of 5.000 g of $\text{K}_2\text{S}_2\text{O}_8$. The reaction mixture becomes yellow, then an orange solid (**Z**) is formed which has a mass of 1.719 g when dried.

Elemental analysis of **Z** shows the mass percentages of C, H, N elements are 38.96 %, 3.28 %, 9.09 %, respectively.

A 0.6164 g **Z** is added to aqueous NH_3 . The suspension is boiled to form a clear solution during which stage the complex is destroyed completely. The solution is acidified with excess aqueous HCl and the resulting suspension is filtered, washed and dried (in darkness) to obtain 0.1433 g of white solid (**D**). The filtrate is collected and treated with excess BaCl_2 solution to obtain 0.4668 g (when dry) of white precipitate (**E**).

3.12 Determine the empirical formula of **Z** and calculate the percentage yield in the preparation.

3.13 Ag (IV) and Ag (V) compounds are extremely unstable and found only in few fluorides. Thus, the formation of their complexes with organic ligands in water can be discounted. To confirm the oxidation number of silver in **Z**, the effective magnetic moment (μ_{eff}) of **Z** was determined and found to be 1.78 BM. Use the spin only formula to determine the number of unpaired electrons in **Z** and the molecular formula of **Z**. (**Z** contains a mononuclear complex with only one species of Ag and only one type of ligand in the ligand sphere.)

3.14 Write down all chemical equations for the preparation of **Z**, and its analysis.

Official English text of the problem.

Answers

Names and SMILES representations are provided in the solution.

- **3.1: Paramagnetic**, with one unpaired electron per Ag^{II} , $4d^9$.
- **3.2:** Ag1: **+1**; Ag2: **+3**.
- **3.3:** Oxygen coordination number: **3**.
- **3.4:** Each oxygen is bonded to **one** Ag^{I} and **two** Ag^{III} .

- **3.5: Diamagnetic.**

- **3.6:**



- **3.7:**

$$U_{\text{lat}}(\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2) = 9410.0 \text{ kJ mol}^{-1}$$

$$U_{\text{lat}}(\text{Cu}^{\text{II}}\text{O}) = 4157.5 \text{ kJ mol}^{-1}$$

- **3.8:**

$$U_{\text{lat}}(\text{Ag}^{\text{II}}\text{O}) = 3733.6 \text{ kJ mol}^{-1}$$

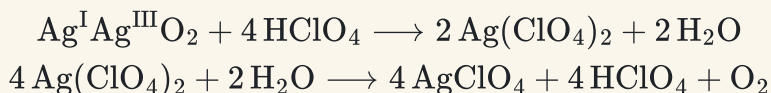
- **3.9:** For $2 \text{Ag}^{\text{II}}\text{O}(\text{s}) \longrightarrow \text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2(\text{s})$,

$$\Delta H = -655.8 \text{ kJ mol}^{-1}$$

per mole of product. Using the permitted fallback values gives $-663.0 \text{ kJ mol}^{-1}$.

- **3.10:** $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$ is the favored solid.

- **3.11:** **B** is silver(II) perchlorate, $\text{Ag}(\text{ClO}_4)_2$; **C** is silver(I) perchlorate, AgClO_4 :



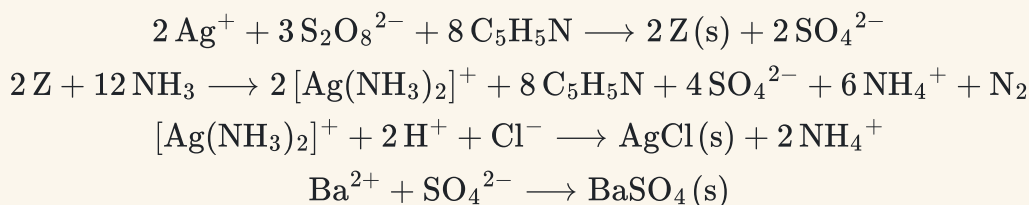
- **3.12:** Empirical formula: $\text{C}_{20}\text{H}_{20}\text{AgN}_4\text{O}_8\text{S}_2$. Percentage yield: **94.7%**.

- **3.13:** **One unpaired electron**; silver is **+2**:



tetrakis(pyridine)silver(II) peroxydisulfate.

- **3.14:** The principal preparation and analysis equations are:

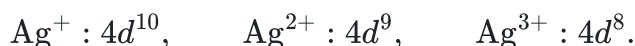


Excess ammonia and released pyridine are also protonated during acidification.

Solution

3.1 — Hypothetical silver(II) oxide

Neutral silver has the configuration $[\text{Kr}] 4d^{10}5s^1$. Its relevant ions therefore have configurations



A d^9 ion necessarily has one unpaired electron. Hypothetical silver(II) oxide is therefore **paramagnetic**. Select the paramagnetic option on the answer sheet.

The spin-only moment for an isolated d^9 center would be

$$\mu_{\text{so}} = \sqrt{1(1+2)} = \sqrt{3} = 1.73 \text{ BM}.$$

3.2 — Oxidation states of the two silver sites

The linear, two-coordinate site is characteristic of d^{10} silver(I), while square-planar coordination stabilizes d^8 silver(III). Thus,

$$\boxed{\text{Ag1} = +1, \quad \text{Ag2} = +3.}$$

Charge balance confirms the assignment:

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

3.3 — Oxygen coordination number

One formula unit of $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$ contains one two-coordinate silver(I) and one four-coordinate silver(III). Consequently, it contains

$$2 + 4 = 6$$

silver–oxygen contacts distributed over two equivalent oxygen atoms. Hence

$$\boxed{\text{CN}(\text{O}) = \frac{6}{2} = 3.}$$

3.4 — Types of silver neighbors around oxygen

The two silver(I)–oxygen contacts per formula unit give

$$\frac{2}{2} = 1$$

silver(I) neighbor per oxygen. The four silver(III)–oxygen contacts give

$$\frac{4}{2} = 2$$

silver(III) neighbors per oxygen.

Thus every oxygen is attached to **one silver(I) and two silver(III) centers**. The supplied information fixes these neighbor counts but does not specify the oxygen-centered bond angles.

3.5 — Magnetism of the actual oxide

Silver(I) is $4d^{10}$, with all electrons paired. Square-planar silver(III) is $4d^8$: its four lower-energy d orbitals are doubly occupied, and the highest-energy $d_{x^2-y^2}$ orbital is empty.

Both sites are therefore diamagnetic, so **A is diamagnetic**. Select the diamagnetic box.

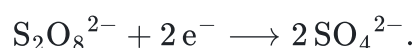
Its structural description is an extended lattice with linear $\text{O} - \text{Ag}^{\text{I}} - \text{O}$ units and square-planar $\text{Ag}^{\text{III}}\text{O}_4$ coordination units, joined through the oxygen atoms.

3.6 — Formation of A with peroxydisulfate

Formation of one formula unit oxidizes one of two silver(I) ions to silver(III), releasing two electrons:



Peroxydisulfate accepts these electrons:



Adding the half-reactions gives



3.7 — Lattice dissociation energies

Use a Born–Haber cycle:

$$\Delta H_f^\circ(\text{solid}) = \Delta H^\circ(\text{elements} \rightarrow \text{gaseous ions}) - \Delta H_{\text{lat}}.$$

The energy needed to form one gaseous oxide ion from oxygen in its standard state is



with total enthalpy

$$249.0 - 141.0 + 844.0 = 952.0 \text{ kJ mol}^{-1}.$$

Using $R = 8.314 \times 10^{-3} \text{ kJ mol}^{-1} \text{ K}^{-1}$,

$$RT = 2.4776 \text{ kJ mol}^{-1} \quad \text{at } 298 \text{ K}.$$

For $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$, the gaseous ions are Ag^+ , Ag^{3+} , and two O^{2-} . Their formation requires

$$\begin{aligned} \Delta H_{\text{ions}}^\circ &= 2(284.9) + [737.2 + (737.2 + 2080.2 + 3367.2)] + 2(952.0) \\ &= 9395.6 \text{ kJ mol}^{-1}. \end{aligned}$$

Therefore,

$$\Delta H_{\text{lat}} = 9395.6 - (-24.3) = 9419.9 \text{ kJ mol}^{-1}.$$

There are four ions per formula unit, so

$$U_{\text{lat}} = 9419.9 - 4RT = 9410.0 \text{ kJ mol}^{-1}.$$

For $\text{Cu}^{\text{II}}\text{O}$, formation of gaseous Cu^{2+} and O^{2-} requires

$$337.4 + 751.7 + 1964.1 + 952.0 = 4005.2 \text{ kJ mol}^{-1}.$$

Thus,

$$\Delta H_{\text{lat}} = 4005.2 - (-157.3) = 4162.5 \text{ kJ mol}^{-1}.$$

There are two ions per formula unit:

$$U_{\text{lat}}(\text{Cu}^{\text{II}}\text{O}) = 4162.5 - 2RT = 4157.5 \text{ kJ mol}^{-1}.$$

These are positive dissociation energies; lattice formation has the opposite sign.

3.8 — Estimated lattice energy of hypothetical silver(II) oxide

The prescribed volume difference gives

$$V_m(\text{Ag}^{\text{II}}\text{O}) = 0.08985 - 0.06182 = 0.02803 \text{ nm}^3.$$

Because the two $2+ / 2-$ oxides are assumed to have the same lattice type, they share the constant C .

Therefore,

$$\frac{U_{\text{lat}}(\text{Ag}^{\text{II}}\text{O})}{U_{\text{lat}}(\text{Cu}^{\text{II}}\text{O})} = \left[\frac{V_m(\text{Cu}^{\text{II}}\text{O})}{V_m(\text{Ag}^{\text{II}}\text{O})} \right]^{1/3}.$$

Substitution gives

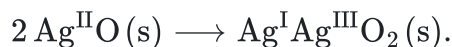
$$\begin{aligned} U_{\text{lat}}(\text{Ag}^{\text{II}}\text{O}) &= 4157.5449 \left(\frac{0.02030}{0.02803} \right)^{1/3} \\ &= \boxed{3733.6 \text{ kJ mol}^{-1}}. \end{aligned}$$

The corresponding empirical constant is approximately

$$C = 1134.1 \text{ kJ nm mol}^{-1}.$$

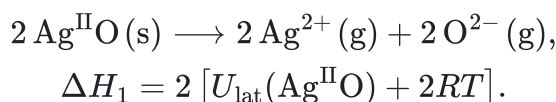
3.9 — Solid-state disproportionation enthalpy

The balanced transformation producing one mole of A is

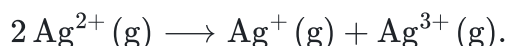


Construct the following cycle.

First dissociate the two hypothetical oxide formula units:



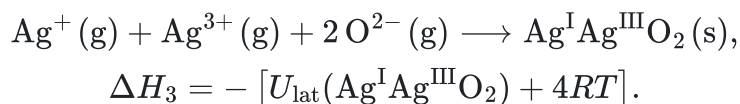
Next disproportionate the gaseous silver(II) ions:



One ion gains an electron, reversing the second ionization; the other loses an electron in the third ionization. Hence

$$\Delta H_2 = I_3 - I_2 = 3367.2 - 2080.2 = 1287.0 \text{ kJ mol}^{-1}.$$

Finally form the mixed-valence lattice:



The RT terms cancel:

$$\begin{aligned} \Delta H &= 2U_{\text{lat}}(\text{Ag}^{\text{II}}\text{O}) + (I_3 - I_2) - U_{\text{lat}}(\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2) \\ &= 2(3733.6009) + 1287.0 - 9409.9897 \\ &= \boxed{-655.8 \text{ kJ mol}^{-1}}. \end{aligned}$$

Thus, the additional stabilization of the mixed-valence lattice outweighs the energetic cost of gaseous-ion disproportionation.

If the permitted fallback values are used instead,

$$\Delta H = 2(3180.0) + 1287.0 - 8310.0 = \boxed{-663.0 \text{ kJ mol}^{-1}}.$$

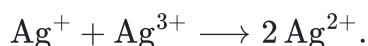
3.10 — Relative stability

Select $\text{Ag}^{\text{I}}\text{Ag}^{\text{III}}\text{O}_2$.

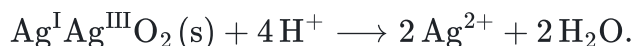
Its formation from two formula units of hypothetical $\text{Ag}^{\text{II}}\text{O}$ is strongly exothermic. This is the stability conclusion intended by the thermochemical comparison. Strictly, a complete Gibbs-energy comparison would also require the entropy change; the conclusion assumes solid-state entropy effects do not reverse this large enthalpy advantage.

3.11 — Silver compounds formed in perchloric acid

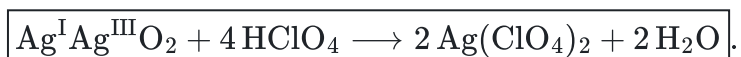
Dissolution allows silver(I) and silver(III) to comproportionate to silver(II):



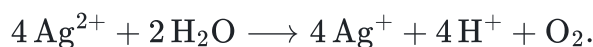
Simultaneously, oxide ions are protonated to water. The overall ionic equation is



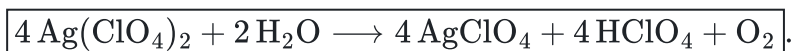
Thus **B is silver(II) perchlorate**, $\text{Ag}(\text{ClO}_4)_2$, containing paramagnetic $4d^9$ silver:



Silver(II) subsequently oxidizes water and is reduced to diamagnetic $4d^{10}$ silver(I):



Therefore **C is silver(I) perchlorate**, AgClO_4 :



These formulas describe the aqueous salts without assigning a particular hydration number to the silver ions.

3.12 — Empirical formula and percentage yield

The white chloride precipitate **D** is silver(I) chloride, AgCl . Therefore,

$$n(\text{Ag}) = n(\text{AgCl}) = \frac{0.1433}{143.32} = 9.9986 \times 10^{-4} \text{ mol}.$$

The white barium precipitate **E** is barium sulfate, BaSO_4 . Complete digestion converts the sulfur to sulfate, so

$$n(\text{S}) = n(\text{BaSO}_4) = \frac{0.4668}{233.40} = 2.0000 \times 10^{-3} \text{ mol}.$$

For the 0.6164 g sample, the elemental analysis gives

$$n(\text{C}) = \frac{0.6164(0.3896)}{12.01} = 1.9996 \times 10^{-2} \text{ mol},$$

$$n(\text{H}) = \frac{0.6164(0.0328)}{1.008} = 2.0057 \times 10^{-2} \text{ mol},$$

$$n(\text{N}) = \frac{0.6164(0.0909)}{14.01} = 3.9993 \times 10^{-3} \text{ mol}.$$

The masses of silver and sulfur are

$$m(\text{Ag}) = (9.9986 \times 10^{-4})(107.87) = 0.107855 \text{ g},$$

$$m(\text{S}) = (2.0000 \times 10^{-3})(32.07) = 0.064140 \text{ g}.$$

Assigning the remaining mass to oxygen,

$$\begin{aligned} m(\text{O}) &= 0.6164 - 0.6164(0.3896 + 0.0328 + 0.0909) \\ &\quad - 0.107855 - 0.064140 \\ &= 0.128007 \text{ g}, \end{aligned}$$

so

$$n(\text{O}) = \frac{0.128007}{16.00} = 8.0004 \times 10^{-3} \text{ mol}.$$

The ratios are consequently:

Element	Amount in sample (mmol)	Ratio to silver	Assigned integer
C	19.996	19.999	20
H	20.057	20.060	20

Element	Amount in sample (mmol)	Ratio to silver	Assigned integer
Ag	0.99986	1	1
N	3.9993	3.9999	4
O	8.0004	8.0015	8
S	2.0000	2.0003	2

Thus,

$$\text{Empirical formula of Z: } \text{C}_{20}\text{H}_{20}\text{AgN}_4\text{O}_8\text{S}_2.$$

Its formula mass is approximately 616.4 g mol^{-1} .

The initial amount of silver is

$$n_0(\text{Ag}) = \frac{0.500}{169.88} = 2.9433 \times 10^{-3} \text{ mol.}$$

As established in parts 3.13–3.14, each formula unit requires four pyridines and, overall, $3/2$ peroxydisulfates. The available quantities are

$$n_0(\text{pyridine}) = \frac{2(0.982)}{79.10} = 0.02483 \text{ mol,}$$

$$n_0(\text{K}_2\text{S}_2\text{O}_8) = \frac{5.000}{270.34} = 0.01850 \text{ mol.}$$

These exceed the respective requirements of 0.01177 and 0.004415 mol. Silver nitrate is therefore limiting.

The theoretical product mass is

$$m_{\text{theor}} = (2.9433 \times 10^{-3})(616.4) = 1.814 \text{ g.}$$

Hence,

$$\text{Yield} = \frac{1.719}{1.814} \times 100 = 94.7\%.$$

3.13 — Magnetic moment and coordination formula

The spin-only formula for n unpaired electrons is

$$\mu_{\text{eff}} = \sqrt{n(n+2)} \text{ BM.}$$

The measured moment gives

$$n(n+2) = 1.78^2 = 3.1684.$$

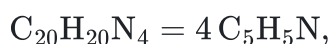
The physically appropriate integer is

$$n = 1,$$

for which the spin-only prediction is 1.73 BM, close to the observed 1.78 BM.

Among the relevant silver oxidation states, silver(I) is d^{10} , silver(II) is d^9 , and silver(III) is d^8 . One unpaired electron identifies **silver(II)**.

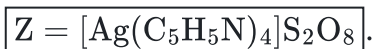
The organic portion of the empirical formula is



corresponding to four neutral pyridine ligands. The complex cation is therefore



The remaining composition is S_2O_8 . Two sulfate ions would require a $4+$ cation; a peroxydisulfate ion has the required $2-$ charge. Thus,



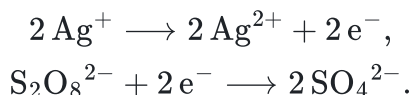
The name is **tetrakis(pyridine)silver(II) peroxydisulfate**. A coordination SMILES representation is:

[Ag+2](<-n1cccc1)(<-n2cccc2)(<-n3cccc3)<-n4cccc4.[O-]S(=O)(=O)OOS(=O)(=O)[O-]

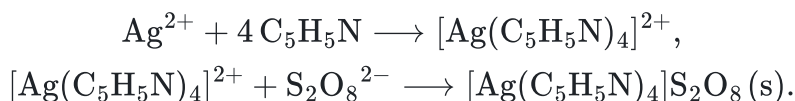
The four pyridines bind through their nitrogen atoms. The peroxydisulfate counterion contains an $\text{S}-\text{O}-\text{O}-\text{S}$ linkage. This SMILES records the coordination connections and formal charges; it does not establish metal-centered geometry. The given data do not independently determine exact bond angles.

3.14 — Preparation and analysis equations

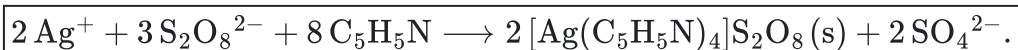
For preparation, oxidation of two silver(I) ions supplies the two electrons consumed by one peroxydisulfate:



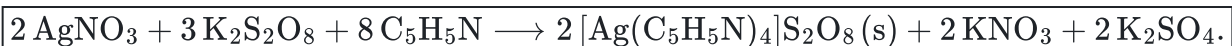
Coordination and salt formation are represented by



The overall preparation equation is therefore

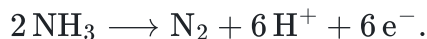


Including the reagent counterions gives



During hot ammoniacal digestion, silver(II) is reduced to silver(I), peroxydisulfate is reduced to sulfate, and pyridine is displaced. Taking ammonia oxidation to nitrogen as the digestion pathway, each formula unit accepts three electrons: one at silver and two at peroxydisulfate.

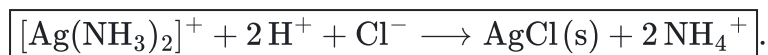
The ammonia oxidation half-reaction is



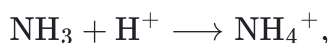
For two formula units, this supplies exactly the six electrons required. Additional ammonia coordinates silver(I) and accepts the released protons. The combined equation is

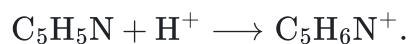


On acidification, protonation removes ammonia from the silver complex, and chloride precipitates silver(I):

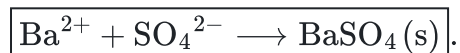


The additional acid–base reactions are





Finally, addition of barium chloride precipitates sulfate:



These equations explain why the analytical precipitates measure one silver atom and two sulfur atoms per formula unit of Z.

Names and SMILES for the species used

For ionic solids, the dot-separated SMILES below specify ionic formula units, not extended crystal structures. SMILES do not encode magnetic spin states. Dative arrows denote donor-to-metal coordination.

Species or name	SMILES
Silver(I), silver(II), and silver(III) ions	[Ag+], [Ag+2], [Ag+3]
Copper(II) ion	[Cu+2]
Oxide ion	[O-2]
Singly charged atomic oxygen anion, O [−]	[O-]
Proton, chloride ion	[H+], [Cl-]
Potassium ion, barium ion	[K+], [Ba+2]
A , silver(I,III) oxide	[Ag+] . [Ag+3] . [O-2] . [O-2]
Hypothetical silver(II) oxide	[Ag+2] . [O-2]
Copper(II) oxide	[Cu+2] . [O-2]
Sulfate ion	[O-]S(=O)(=O)[O-]
Peroxydisulfate ion	[O-]S(=O)(=O)OOS(=O)(=O)[O-]
Perchlorate ion	[O-]Cl(=O)(=O)=O
Nitrate ion	[O-][N+](=O)[O-]
B , silver(II) perchlorate	[Ag+2] . [O-]Cl(=O)(=O)=O . [O-]Cl(=O)(=O)=O
C , silver(I) perchlorate	[Ag+] . [O-]Cl(=O)(=O)=O
D , silver(I) chloride	[Ag+] . [Cl-]
E , barium sulfate	[Ba+2] . [O-]S(=O)(=O)[O-]
Silver nitrate	[Ag+] . [O-][N+](=O)[O-]
Potassium peroxydisulfate	[K+] . [K+] . [O-]S(=O)(=O)OOS(=O)(=O)[O-]
Potassium nitrate	[K+] . [O-][N+](=O)[O-]
Potassium sulfate	[K+] . [K+] . [O-]S(=O)(=O)[O-]
Barium chloride	[Ba+2] . [Cl-] . [Cl-]
Pyridine	n1ccccc1
Pyridinium ion	[nH+]1ccccc1
Ammonia, ammonium ion	N, [NH4+]
Diamminesilver(I) ion	N->[Ag+]<-N
Water	O

Species or name	SMILES
Dioxygen	O=O
Dinitrogen	N#N
Perchloric acid	OC1(=O)(=O)=O
Hydrogen chloride	Cl

The diamminesilver(I) ion has linear N—Ag—N coordination. The specified linear and square-planar geometries in A must likewise be supplied in words alongside its ionic SMILES.

The solution was checked against the official solution.

Problem 4: Zeise's salt

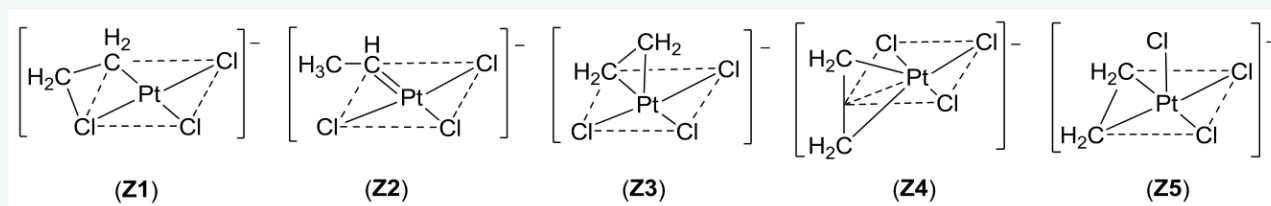
Zeise's salt, $K[PtCl_3C_2H_4]^-$, was one of the first organometallic compounds to be reported. W. C. Zeise, a professor at the University of Copenhagen, prepared this compound in 1827 by reacting $PtCl_4$ with boiling ethanol and then adding potassium chloride (Method 1). This compound may also be prepared by refluxing a mixture of $K_2[PtCl_6]$ and ethanol (Method 2). The commercially available Zeise's salt is commonly prepared from $K_2[PtCl_4]$ and ethylene (Method 3).

4.1 Write balanced equations for each of the above mentioned preparations of Zeise's salt, given that in methods 1 and 2 the formation of 1 mole of Zeise's salt consumes 2 moles of ethanol.

4.2 Mass spectrometry of the anion $[PtCl_3C_2H_4]^-$ shows one set of peaks with mass numbers 325–337 *au* and various intensities. Calculate the mass number of the anion which consists of the largest natural abundance isotopes (using given below data).

Isotope	$^{192}_{78}Pt$	$^{194}_{78}Pt$	$^{195}_{78}Pt$	$^{196}_{78}Pt$	$^{198}_{78}Pt$	$^{35}_{17}Cl$	$^{37}_{17}Cl$	$^{12}_6C$	$^{13}_6C$	^1_1H
Natural abundance, %	0.8	32.9	33.8	25.3	7.2	75.8	24.2	98.9	1.1	99.99

Some early structures proposed for Zeise's salt anion were:



In structure **Z1**, **Z2**, and **Z5** both carbons are in the same plane as dashed square.

[You should assume that these structures do not undergo any fluxional process by interchanging two or more sites.]

NMR spectroscopy allowed the structure for Zeise's salt to be determined as structure **Z4**.

4.3 For each structure **Z1 – Z5**, indicate in the table below how many hydrogen atoms are in different environments, and how many different environments of hydrogen atoms there are, and how many different environments of carbon atoms there are?

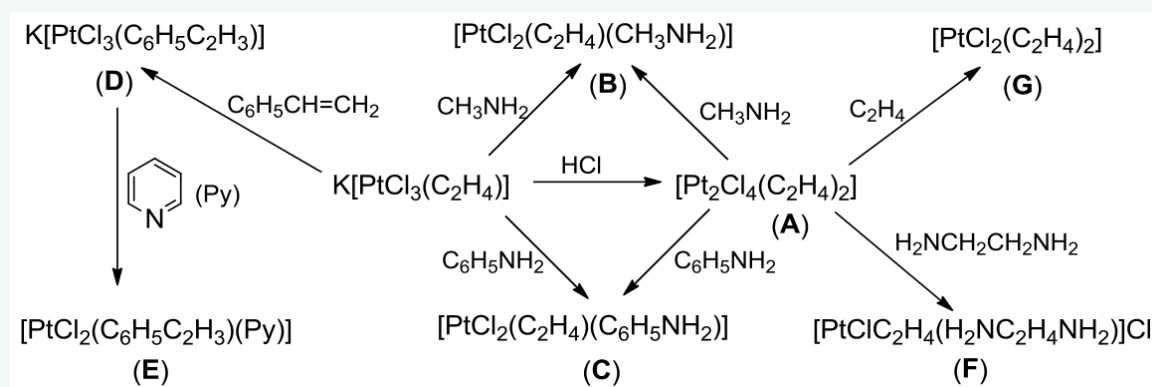
Structure	Number of different environments of hydrogen	Number of different environments of carbon
Z1		
Z2		
Z3		
Z4		
Z5		

For substitution reactions of square platinum(II) complexes, ligands may be arranged in order of their tendency to facilitate substitution in the position *trans* to themselves (the *trans effect*). The ordering of ligands is:

$\text{CO}, \text{CN}^-, \text{C}_2\text{H}_4 > \text{PR}_3, \text{H}^- > \text{CH}_3^-, \text{C}_6\text{H}_5^-, \text{I}^-, \text{SCN}^- > \text{Br}^- > \text{Cl}^- > \text{Py} > \text{NH}_3 > \text{OH}^-, \text{H}_2\text{O}$

In above series a left ligand has a stronger *trans effect* than that of the right ligand.

Some reactions of Zeise's salt and the complex $[\text{Pt}_2\text{Cl}_4(\text{C}_2\text{H}_4)_2]$ are given below.



4.4 Draw the structure of **A**, given that the molecule of this complex has a centre of symmetry, no Pt-Pt bond, and no bridging alkene.

4.5 Draw the structures of **B**, **C**, **D**, **E**, **F** and **G**.

4.6 Suggest the driving force(s) for the formation of **D** and **F** by choosing one or more of the following statements (for example, i and ii):

- i) formation of gas,
- ii) formation of liquid,
- iii) *trans effect*,
- iv) chelate effect.

Official English text of the problem.

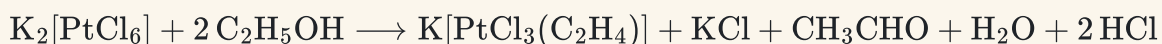
Answers

• 4.1

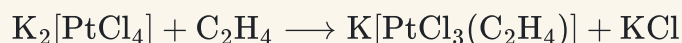
Method 1:



Method 2:



Method 3:



- **4.2** The isotopes are ^{195}Pt , ^{35}Cl , ^{12}C , and ^1H . The **mass number is 328**, corresponding to a nominal mass of 328 u.
- **4.3**

Structure	Number of H environments	H atoms in each environment	Number of C environments
Z1	2	2 + 2	2
Z2	2	3 + 1	2
Z3	2	2 + 2	2
Z4	1	4	1
Z5	2	2 + 2	1

- **4.4 A is Zeise's dimer**, $[\text{Pt}_2\text{Cl}_4(\text{C}_2\text{H}_4)_2]$: two chloride bridges join the Pt atoms. Each Pt additionally carries one terminal chloride and one terminal η^2 -ethene. The two halves are related by inversion; there is no Pt–Pt bond.
- **4.5** All Pt centers have square-planar arrangements of four ligand sites. Every alkene is coordinated through its double bond, η^2 .

Product	Formula	Required arrangement
B	$[\text{PtCl}_2(\text{C}_2\text{H}_4)(\text{CH}_3\text{NH}_2)]$	Methylamine trans to ethene; chlorides mutually trans
C	$[\text{PtCl}_2(\text{C}_2\text{H}_4)(\text{C}_6\text{H}_5\text{NH}_2)]$	Aniline trans to ethene; chlorides mutually trans
D	$\text{K}[\text{PtCl}_3(\text{C}_6\text{H}_5\text{CH}=\text{CH}_2)]$	Styrene occupies the alkene site of Zeise's salt
E	$[\text{PtCl}_2(\text{C}_6\text{H}_5\text{CH}=\text{CH}_2)(\text{Py})]$	Pyridine trans to styrene; chlorides mutually trans
F	$[\text{PtCl}(\text{C}_2\text{H}_4)(\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2)]\text{Cl}$	The two N donors are cis; ethene and coordinated chloride are cis
G	$[\text{PtCl}_2(\text{C}_2\text{H}_4)_2]$	Ethenes mutually trans; chlorides mutually trans

Names and SMILES are given with the structural explanations below.

- **4.6 D: i only. F: iii and iv.**

Solution

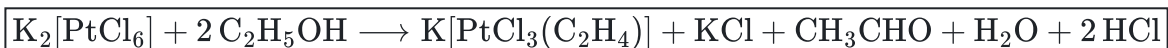
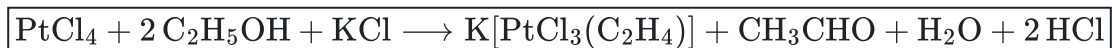
The coordination SMILES below use the dative-bond extension $\rightarrow$ or $\leftarrow$. Two carbon-to-Pt dative bonds represent an η^2 -alkene, which occupies **one ligand site**. The required coordination geometry is specified in words because these strings do not encode it. Formula-unit SMILES for inorganic compounds do not specify their crystal structures.

4.1 — Preparation of Zeise's salt

In methods 1 and 2, platinum is reduced from oxidation state +4 to +2. Of the two ethanol molecules consumed:

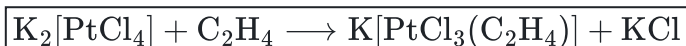
- One is oxidized to ethanal, supplying the two electrons required for this reduction.
- One supplies ethene by loss of water.

Thus the balanced overall equations are:



Each equation consumes exactly two ethanol molecules per formula unit of Zeise's salt. For example, the twelve ethanol hydrogen atoms appear as four in coordinated ethene, four in ethanal, two in water, and two in hydrogen chloride.

Method 3 is ligand substitution without a change in the platinum oxidation state: ethene replaces one coordinated chloride.



The species used in these equations are:

Species	Name	SMILES
$\text{C}_2\text{H}_5\text{OH}$	Ethanol	CCO
C_2H_4	Ethene, or ethylene	C=C
CH_3CHO	Ethanal, or acetaldehyde	CC=O
H_2O	Water	O
HCl	Hydrogen chloride	Cl
KCl	Potassium chloride	[K+] . [Cl-]
PtCl_4	Platinum(IV) chloride	[Cl-]->[Pt+4](<-[Cl-])(<-[Cl-])<-[Cl-]
$\text{K}_2[\text{PtCl}_6]$	Potassium hexachloridoplatinate(IV)	[K+] . [K+] . [Cl-]->[Pt+4](<-[Cl-])(<-[Cl-])(<-[Cl-])(<-[Cl-])(<-[Cl-])<-[Cl-]
$\text{K}_2[\text{PtCl}_4]$	Potassium tetrachloridoplatinate(II)	[K+] . [K+] . [Cl-]->[Pt+2](<-[Cl-])(<-[Cl-])<-[Cl-]
$\text{K}[\text{PtCl}_3(\text{C}_2\text{H}_4)]$	Potassium trichlorido(η^2 -ethene)platinate(II), Zeise's salt	[K+] . C1=C->[Pt+2](<-[Cl-])(<-[Cl-])(<-[Cl-])<-1

4.2 — Isotopic mass number

Select the most abundant isotope **of each element**, rather than using abundance-weighted atomic masses:

Element	Selected isotope	Given abundance
Pt	^{195}Pt	33.8%
Cl	^{35}Cl	75.8%
C	^{12}C	98.9%

Element	Selected isotope	Given abundance
H	^1H	99.99%

The mass-number sum is

$$A = 195 + 3(35) + 2(12) + 4(1) = \boxed{328}.$$

Mass number is dimensionless; the corresponding nominal ionic mass is 328 u. An exact isotopic mass cannot be calculated from mass numbers alone.

The selected **trichlorido(η^2 -ethene)platinate(II) isotopologue anion** has the explicitly isotope-labelled SMILES:

[1H][12C]1([1H])=[12C]([1H])([1H])>[195Pt+2](<-[35Cl-])(<-[35Cl-])(<-[35Cl-])<-1

4.3 — NMR environments

Count chemically distinct environments, not the individual lines arising from spin–spin coupling. Symmetry-related nuclei have the same chemical shift in the usual achiral NMR environment.

For reference, the proposed structures have the following connectivity descriptions. In the covalent SMILES for Z1–Z3 and Z5, the Pt formal charge is SMILES bookkeeping, not a statement of its oxidation state.

Structure	Name or structural description	SMILES
Z1	Proposed dichlorido(2-chloroethyl)platinate anion, chelated through carbon and chlorine	<chem>C1CC1->[Pt-]1(Cl)Cl</chem>
Z2	Proposed trichlorido(ethylidene)platinum anion, with a $\text{Pt}=\text{CHCH}_3$ group	<chem>CC=[Pt-](Cl)(Cl)Cl</chem>
Z3	Proposed trichlorido(ethane-1,2-diyl)platinate anion; a platinacyclopropane with one carbon basal and one apical	<chem>C1C[Pt-]1(Cl)(Cl)Cl</chem>
Z4	Trichlorido(η^2 -ethene)platinate(II), the Zeise anion	<chem>Cl=C->[Pt+2](<-[Cl-])(<-[Cl-])(<-[Cl-])<-1</chem>
Z5	Proposed trichlorido(ethane-1,2-diyl)platinate anion; both carbons basal and one chloride apical	<chem>C1C[Pt-]1(Cl)(Cl)Cl</chem>

The distinction between Z3 and Z5 is geometrical and therefore is not conveyed by their identical connectivity SMILES.

- **Z1:** The two carbons have different connectivities: one is bonded directly to Pt, while the other is bonded to the coordinating chlorine. They therefore give **two carbon environments**. Reflection in the plane of the heavy-atom framework exchanges the two hydrogens on each methylene, giving **two hydrogen environments**, $2 + 2$.
- **Z2:** The methyl carbon and the Pt-bound methine carbon are different. The methyl hydrogens form the usual equivalent three-proton set, while the methine hydrogen is distinct. Thus there are **two hydrogen environments**, $3 + 1$, and **two carbon environments**. Ordinary methyl-group averaging is used here; distinct coordination sites are not interchanged.

- **Z3:** One carbon occupies a basal position and the other an apical position, so the carbons are inequivalent. A mirror plane through Pt and the two carbons exchanges the two hydrogens on each carbon. Thus there are **two hydrogen environments**, $2 + 2$, and **two carbon environments**.
- **Z4:** The ethene C–C axis is perpendicular to the square coordination plane. The symmetry operations exchange the two carbons and also the two hydrogens on each carbon. Consequently, **all four hydrogens are equivalent**, and **both carbons are equivalent**.
- **Z5:** A symmetry plane exchanges the two carbon positions, so there is **one carbon environment**. However, the apical chloride distinguishes the two sides of the basal plane. Hydrogens on opposite sides are inequivalent, giving **two hydrogen environments**, $2 + 2$.

Therefore:

Structure	H environments	H atoms per environment	C environments
Z1	2	$2 + 2$	2
Z2	2	$3 + 1$	2
Z3	2	$2 + 2$	2
Z4	1	4	1
Z5	2	$2 + 2$	1

4.4 — Structure of A

Each square-planar Pt center has one ethene ligand and therefore requires three chloride contacts. The two Pt centers require six Pt–Cl contacts in total, but A contains only four chloride atoms.

Let b be the number of bridging chlorides and t the number of terminal chlorides. Then

$$b + t = 4, \quad 2b + t = 6,$$

so

$$b = 2, \quad t = 2.$$

Thus **A is di- μ -chlorido-bis[chlorido(η^2 -ethene)platinum(II)]**, commonly called **Zeise's dimer**.

SMILES:

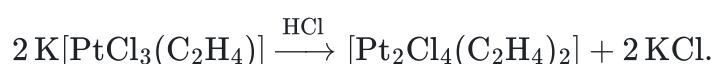
C1=C->[Pt+2]2<-1(<-[Cl-])<-[Cl-]->[Pt+2]3(<-[Cl-])(<-C=C->3)<-[Cl-]->2

To draw it precisely:

1. Draw a four-membered ring whose successive vertices are Pt_1 , bridging Cl_a , Pt_2 , and bridging Cl_b .
2. Attach one terminal chloride and one terminal η^2 -ethene to each Pt.
3. At Pt_1 , place ethene trans to Cl_a and terminal chloride trans to Cl_b .
4. At Pt_2 , place ethene trans to Cl_b and terminal chloride trans to Cl_a .

The center of the ring is then an inversion center. The two ethenes are terminal and inversion-related, as are the two terminal chlorides. **Do not draw a Pt–Pt bond.**

The balanced net formation reaction is



Here HCl is the stated reaction condition and is not consumed in the net equation.

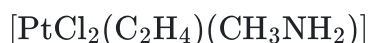
4.5 — Structures of B–G

Ethene has a stronger trans effect than chloride. Consequently, substitution preferentially occurs at the chloride site **trans to ethene**. In A, this is a bridging Pt–Cl bond; its cleavage allows the incoming ligand to occupy that site.

The incoming molecular ligands are:

Ligand	Name	SMILES
CH ₃ NH ₂	Methylamine	CN
C ₆ H ₅ NH ₂	Aniline	Nc1ccccc1
C ₆ H ₅ CH=CH ₂	Styrene, or ethenylbenzene	C=Cc1ccccc1
Py, C ₅ H ₅ N	Pyridine	n1ccccc1
H ₂ NCH ₂ CH ₂ NH ₂	Ethane-1,2-diamine, or ethylenediamine	NCCN

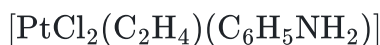
B — trans-Dichlorido(η^2 -ethene)(methylamine)platinum(II)



SMILES: CN->[Pt+2]1(<-[Cl-])(<-[Cl-])<-C=C->1

Draw methylamine coordinated through N **trans to ethene**. The two chlorides occupy the remaining mutually trans sites.

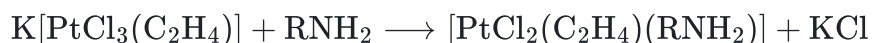
C — trans-Dichlorido(η^2 -ethene)(aniline)platinum(II)



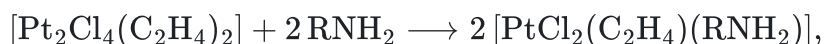
SMILES: c1ccccc1N->[Pt+2]2(<-[Cl-])(<-[Cl-])<-C=C->2

Draw aniline coordinated through its amino N **trans to ethene**, with the two chlorides mutually trans.

Both preparations of B and C are represented by the balanced equations

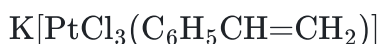


and



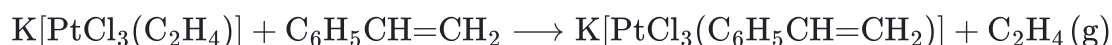
where $R = \text{CH}_3$ gives B and $R = \text{C}_6\text{H}_5$ gives C.

D — Potassium trichlorido(η^2 -styrene)platinate(II)

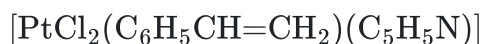


SMILES: [K+] . c1ccccc1C2=C->[Pt+2](<-[Cl-])(<-[Cl-])(<-[Cl-])<-2

Replace the ethene in Zeise's salt by styrene, coordinated through the two carbons of its **vinyl double bond**. The phenyl ring is not the coordinating group. The other three ligand sites remain occupied by chlorides.

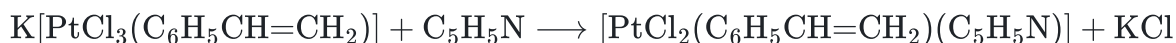


E — trans-Dichlorido(pyridine)(η^2 -styrene)platinum(II)



SMILES: c1ccccc1C2=C->[Pt+2]<-2(<-[Cl-])(<-[Cl-])<-n3ccccc3

Pyridine coordinates through N at the chloride position **trans to styrene**. The remaining chlorides are mutually trans.



F — Chlorido(η^2 -ethene)(ethane-1,2-diamine- $\kappa^2\text{N}, \text{N}'$)platinum(II) chloride



SMILES: [Cl-].[C1=C->[Pt+2]2<-1(<-[Cl-])<-NCCN->2

Draw both nitrogen atoms of one ethylenediamine coordinated to **adjacent Pt sites**, producing a five-membered Pt–N–C–C–N chelate ring. Ethene and the coordinated chloride occupy the other two adjacent sites.

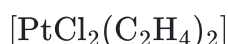
Thus:

- One N donor is trans to ethene.
- The other N donor is trans to coordinated chloride.
- The complex ion has charge +1, with one external chloride counterion.

The balanced reaction is

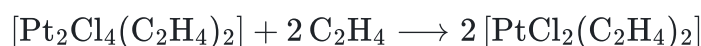


G — trans-Dichloridobis(η^2 -ethene)platinum(II)



SMILES: C1=C->[Pt+2]2<-1(<-[Cl-])(<-[Cl-])<-C=C->2

Incoming ethene replaces the bridging chloride contact trans to the original ethene. Therefore the **two ethene ligands are mutually trans**, and the two chlorides are mutually trans.



4.6 — Driving forces

Formation of D: i only — formation of gas.

Styrene replaces coordinated ethene, releasing $\text{C}_2\text{H}_4(\text{g})$. Escape of ethene from the reaction mixture favors formation of D. Thus only **i** applies to this alkene-exchange reaction.

Formation of F: iii and iv — trans effect and chelate effect.

The strong trans effect of coordinated ethene facilitates cleavage of the Pt–Cl bridge trans to it. One nitrogen of ethylenediamine binds at that position. The second nitrogen then binds at an adjacent site, replacing another chloride contact and closing the five-membered chelate ring.

Thus the **trans effect directs the substitution**, and the **chelate effect favors binding both N donors of the same ligand**. In the sense used by the question, both **iii and iv** apply.

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

Problem 5: Acid-base equilibria in water

A solution (**X**) contains two weak monoprotic acids (those having *one* acidic proton); **HA** with the acid dissociation constant of $K_{\text{HA}} = 1.74 \times 10^{-7}$, and **HB** with the acid dissociation constant of $K_{\text{HB}} = 1.34 \times 10^{-7}$. The solution **X** has a pH of 3.75.

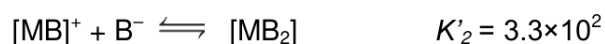
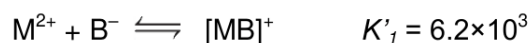
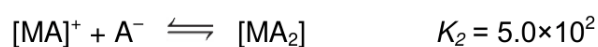
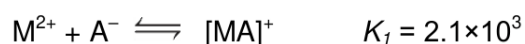
5.1 Titration of 100 cm^3 of solution **X** requires 100 cm^3 of **NaOH** solution ($c = 0.220 \text{ mol} \cdot \text{dm}^{-3}$) for completion. Calculate the initial (total) concentration ($\text{mol} \cdot \text{dm}^{-3}$) of each acid in the solution **X**.

Use reasonable approximations where appropriate. [$K_w = 1.00 \times 10^{-14}$ at 298 K]

5.2 Calculate the pH of the solution **Y** in which the concentration of **NaA** initially was $6.00 \times 10^{-2} \text{ mol} \cdot \text{dm}^{-3}$ and that of **NaB** $4.00 \times 10^{-2} \text{ mol} \cdot \text{dm}^{-3}$.

5.3 Adding large amounts of distilled water to solution **X** gives a very (infinitely) dilute solution where the total concentrations of the acids are close to zero. Calculate the percentage of dissociation of each acid in this dilute solution.

5.4. A buffer solution is added to solution **Y** to maintain a pH of 10.0. Assume no change in volume of the resulting solution **Z**. Calculate the solubility (in $\text{mol} \cdot \text{dm}^{-3}$) of the substance $\text{M}(\text{OH})_2$ in **Z**, taking into consideration that the anions A^- and B^- can form complexes with M^{2+} :



Official English text of the problem.

Answers

- 5.1:** Using the full equilibrium balances,

$$C_{\text{HA}} \approx 5.42 \times 10^{-2} \text{ mol dm}^{-3}, \quad C_{\text{HB}} \approx 1.66 \times 10^{-1} \text{ mol dm}^{-3}.$$

The permitted weak-dissociation approximation gives 5.36×10^{-2} and $1.66 \times 10^{-1} \text{ mol dm}^{-3}$, respectively.

- 5.2:** $\text{pH} = 9.90$.
- 5.3:** $\text{HA} : 63.5\%, \quad \text{HB} : 57.3\%$.
- 5.4:** $s(\text{M}(\text{OH})_2) \approx 5.1 \times 10^{-2} \text{ mol dm}^{-3}$.

Solution

The acids, conjugate bases, salts and metal complexes are specified only by generic symbols. Their chemical identities, unique SMILES and coordination geometries cannot be inferred. The explicitly identified species used below are water O, hydronium ion $[\text{OH}_3^+]$, hydroxide ion $[\text{OH}^-]$, sodium ion $[\text{Na}^+]$, and sodium hydroxide $[\text{Na}^+][\text{OH}^-]$.

Write $K_A = K_{\text{HA}}$, $K_B = K_{\text{HB}}$, and $h = [\text{H}_3\text{O}^+]$.

5.1 — Initial total concentrations

Both acids are monoprotic, so their neutralization reactions are



Thus, the amount of hydroxide required equals the combined amount of the two acids:

$$n_{\text{acids}} = (0.100 \text{ dm}^3)(0.220 \text{ mol dm}^{-3}) = 0.0220 \text{ mol}.$$

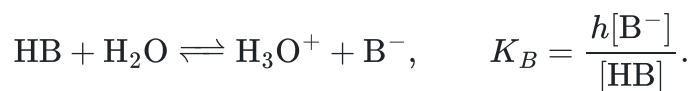
Define the analytical concentrations

$$C_A = [\text{HA}] + [\text{A}^-], \quad C_B = [\text{HB}] + [\text{B}^-].$$

Since the original sample volume is 0.100 dm^3 ,

$$C_A + C_B = 0.220 \text{ mol dm}^{-3}. \quad (1)$$

The acid equilibria are



The specified pH gives

$$h = 10^{-3.75} = 1.77828 \times 10^{-4} \text{ mol dm}^{-3}.$$

Combining each dissociation equilibrium with its material balance gives

$$[\text{A}^-] = \frac{K_A C_A}{h + K_A}, \quad [\text{B}^-] = \frac{K_B C_B}{h + K_B}.$$

Electroneutrality requires

$$h = [\text{A}^-] + [\text{B}^-] + [\text{OH}^-],$$

hence

$$h - \frac{K_w}{h} = \frac{K_A C_A}{h + K_A} + \frac{K_B C_B}{h + K_B}. \quad (2)$$

Solving (1) and (2) gives

$$C_A = 0.0542179 \text{ mol dm}^{-3}, \quad C_B = 0.1657821 \text{ mol dm}^{-3}.$$

Therefore,

$$\boxed{C_{\text{HA}} \approx 5.42 \times 10^{-2} \text{ mol dm}^{-3}},$$
$$\boxed{C_{\text{HB}} \approx 1.66 \times 10^{-1} \text{ mol dm}^{-3}}.$$

For the permitted approximation, $h \gg K_A, K_B$, so each acid is only slightly dissociated and hydroxide is negligible. Equation (2) then becomes

$$h^2 \approx K_A C_A + K_B C_B.$$

Using $C_B = 0.220 - C_A$,

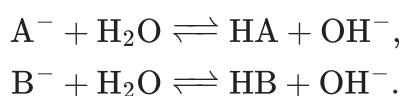
$$C_A \approx \frac{10^{-7.50} - (1.34 \times 10^{-7})(0.220)}{1.74 \times 10^{-7} - 1.34 \times 10^{-7}} = 0.0535694 \text{ mol dm}^{-3},$$

$$C_B \approx 0.166431 \text{ mol dm}^{-3}.$$

The small difference from the full calculation is amplified because the two acid dissociation constants are close.

5.2 — pH of solution Y

The anions undergo base hydrolysis:



Their base dissociation constants are

$$\begin{aligned} K_{b,A} &= \frac{K_w}{K_A} = \frac{1.00 \times 10^{-14}}{1.74 \times 10^{-7}} = 5.7471 \times 10^{-8}, \\ K_{b,B} &= \frac{K_w}{K_B} = \frac{1.00 \times 10^{-14}}{1.34 \times 10^{-7}} = 7.4627 \times 10^{-8}. \end{aligned}$$

Let $x = [\text{OH}^-]$. Because hydrolysis is slight,

$$[\text{A}^-] \approx 0.0600 \text{ mol dm}^{-3}, \quad [\text{B}^-] \approx 0.0400 \text{ mol dm}^{-3}.$$

Both hydrolysis reactions share the same hydroxide concentration:

$$[\text{HA}] \approx \frac{K_{b,A}(0.0600)}{x}, \quad [\text{HB}] \approx \frac{K_{b,B}(0.0400)}{x}.$$

Material and charge balances give

$$x = [\text{HA}] + [\text{HB}] + h \approx [\text{HA}] + [\text{HB}],$$

so

$$x^2 \approx K_{b,A}(0.0600) + K_{b,B}(0.0400).$$

Consequently,

$$x = \sqrt{(5.7471 \times 10^{-8})(0.0600) + (7.4627 \times 10^{-8})(0.0400)} = 8.0208 \times 10^{-5} \text{ mol dm}^{-3}.$$

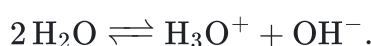
Thus,

$$\begin{aligned} \text{pOH} &= 4.0958, & \text{pH} &= 14.0000 - 4.0958 = 9.9042, \\ & & \boxed{\text{pH} &= 9.90}. \end{aligned}$$

Less than 0.1% of either anion is protonated, validating the approximation.

5.3 — Dissociation at infinite dilution

Water undergoes autoionization:



As both acid concentrations approach zero, their contributions to the charge balance vanish. Therefore,

$$h \longrightarrow \sqrt{K_w} = 1.00 \times 10^{-7} \text{ mol dm}^{-3}.$$

For either acid, the fraction dissociated is

$$\alpha = \frac{[\text{conjugate base}]}{[\text{acid}] + [\text{conjugate base}]} = \frac{K_a}{K_a + h}.$$

Hence,

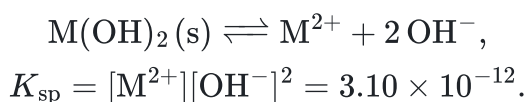
$$100\alpha_A = 100 \frac{1.74 \times 10^{-7}}{1.74 \times 10^{-7} + 1.00 \times 10^{-7}} = \boxed{63.5\%},$$

$$100\alpha_B = 100 \frac{1.34 \times 10^{-7}}{1.34 \times 10^{-7} + 1.00 \times 10^{-7}} = \boxed{57.3\%}.$$

Neither limiting percentage is 100%, because water maintains a nonzero hydronium concentration comparable to the given acid dissociation constants.

5.4 — Solubility in buffered solution Z

The dissolution equilibrium is



At the maintained pH of 10.0,

$$h = 1.00 \times 10^{-10} \text{ mol dm}^{-3}, \quad [\text{OH}^-] = \frac{K_w}{h} = 1.00 \times 10^{-4} \text{ mol dm}^{-3}.$$

Therefore, the free metal-ion concentration is fixed:

$$m = [\text{M}^{2+}] = \frac{3.10 \times 10^{-12}}{(1.00 \times 10^{-4})^2} = 3.10 \times 10^{-4} \text{ mol dm}^{-3}. \quad (3)$$

The complex-formation equilibria are

Reaction	Stepwise formation constant
$\text{M}^{2+} + \text{A}^- \rightleftharpoons [\text{MA}]^+$	$K_1 = 2.1 \times 10^3$
$[\text{MA}]^+ + \text{A}^- \rightleftharpoons [\text{MA}_2]$	$K_2 = 5.0 \times 10^2$
$\text{M}^{2+} + \text{B}^- \rightleftharpoons [\text{MB}]^+$	$K'_1 = 6.2 \times 10^3$
$[\text{MB}]^+ + \text{B}^- \rightleftharpoons [\text{MB}_2]$	$K'_2 = 3.3 \times 10^2$

Let $a = [\text{A}^-]$ and $b = [\text{B}^-]$. Then

$$[\text{MA}]^+ = K_1 m a, \quad [[\text{MA}_2]] = K_1 K_2 m a^2,$$

$$[\text{MB}]^+ = K'_1 m b, \quad [[\text{MB}_2]] = K'_1 K'_2 m b^2.$$

Complex formation consumes substantial quantities of both ligands, so their free concentrations must be obtained from their material balances. With no volume change,

$$0.0600 = a + [\text{HA}] + [[\text{MA}]^+] + 2[[\text{MA}_2]],$$

$$0.0400 = b + [\text{HB}] + [[\text{MB}]^+] + 2[[\text{MB}_2]].$$

The factors of two account for the two ligands in each neutral complex. Since

$$[\text{HA}] = \frac{h}{K_A}a, \quad [\text{HB}] = \frac{h}{K_B}b,$$

the balances become

$$2K_1K_2ma^2 + \left(1 + \frac{h}{K_A} + K_1m\right)a = 0.0600,$$

$$2K'_1K'_2mb^2 + \left(1 + \frac{h}{K_B} + K'_1m\right)b = 0.0400.$$

Numerically, with concentrations entered in mol dm^{-3} ,

$$651.0a^2 + 1.651575a - 0.0600 = 0,$$

$$1268.52b^2 + 2.922746b - 0.0400 = 0.$$

The positive roots are

$$a = 8.41526 \times 10^{-3} \text{ mol dm}^{-3}, \quad b = 4.58033 \times 10^{-3} \text{ mol dm}^{-3}.$$

Substitution into the formation expressions gives the dissolved metal concentrations below; extra digits are retained for summation.

Metal-containing species	Concentration (mol dm^{-3})
M^{2+}	0.000310000
$[\text{MA}]^+$	0.00547833
$[\text{MA}_2]$	0.0230508
$[\text{MB}]^+$	0.00880340
$[\text{MB}_2]$	0.0133064

Each species contains one metal atom. The solubility is therefore

$$\begin{aligned} s &= [\text{M}^{2+}] + [[\text{MA}]^+] + [[\text{MA}_2]] \\ &\quad + [[\text{MB}]^+] + [[\text{MB}_2]] \\ &= 0.0509489 \text{ mol dm}^{-3}. \end{aligned}$$

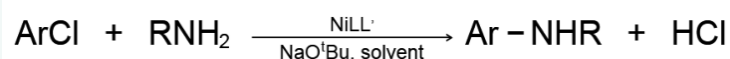
Thus,

$$s(\text{M}(\text{OH})_2) \approx 5.1 \times 10^{-2} \text{ mol dm}^{-3}.$$

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

Problem 6: Chemical kinetics

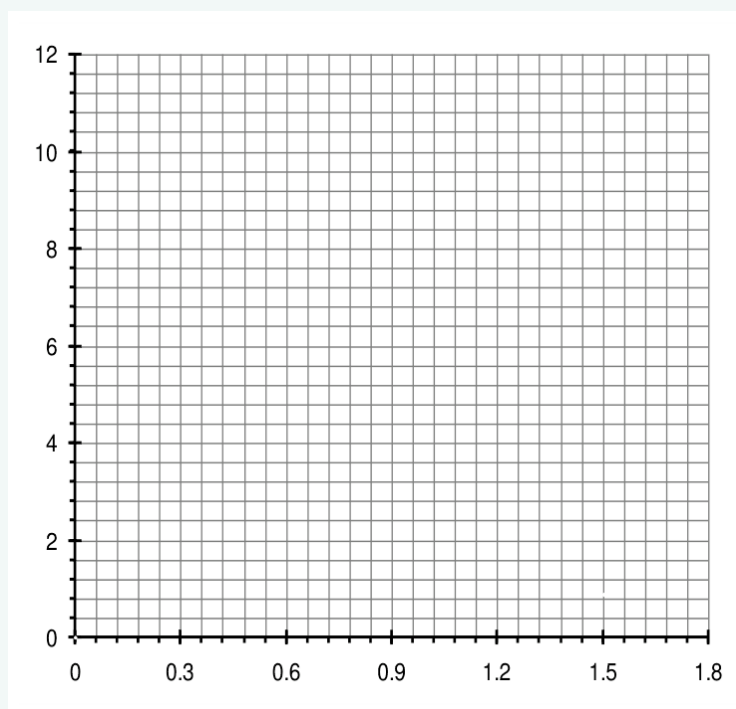
The transition-metal-catalyzed amination of aryl halides has become one of the most powerful methods to synthesize arylamines. The overall reaction for the nickel-catalyzed amination of aryl chloride in basic conditions is:



in which NiLL' is the nickel complex catalyst. The reaction goes through several steps in which the catalyst, reactants, and solvent may be involved in elementary steps.

To determine the reaction order with respect to each reactant, the dependence of the initial rate of the reaction on the concentrations of each reagent was carried out with all other reagents present in large excess. Some kinetic data at 298 K are shown in the tables below. (Use the grids if you like.)

$[\text{ArCl}] \text{ (mol dm}^{-3}\text{)}$	0.1	0.2	0.4	0.6
Initial rate $\text{(mol dm}^{-3}\text{ s}^{-1}\text{)}$	1.88×10^{-5}	4.13×10^{-5}	9.42×10^{-5}	1.50×10^{-4}

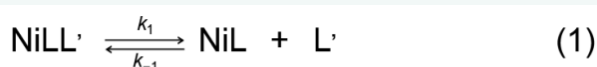


$[\text{NiLL}'] \text{ (mol dm}^{-3}\text{)}$	6×10^{-3}	9×10^{-3}	1.2×10^{-2}	1.5×10^{-2}
Initial rate $\text{(mol dm}^{-3}\text{ s}^{-1}\text{)}$	4.12×10^{-5}	6.01×10^{-5}	7.80×10^{-5}	1.10×10^{-4}

$[\text{L}'] \text{ (mol dm}^{-3}\text{)}$	0.06	0.09	0.12	0.15
Initial rate $\text{(mol dm}^{-3}\text{ s}^{-1}\text{)}$	5.8×10^{-5}	4.3×10^{-5}	3.4×10^{-5}	2.8×10^{-5}

6.1 Determine the order with respect to the reagents assuming they are integers.

To study the mechanism for this reaction, ^1H , ^{31}P , ^{19}F , and ^{13}C NMR spectroscopy have been used to identify the major transition metal complexes in solution, and the initial rates were measured using reaction calorimetry. An intermediate, $\text{NiL}(\text{Ar})\text{Cl}$, may be isolated at room temperature. The first two steps of the overall reaction involve the dissociation of a ligand from NiLL' (step 1) at 50°C , followed by the oxidation addition (step 2) of aryl chloride to the NiL at room temperature (rt):



6.2 Using the steady state approximation, derive an expression for the rate equation for the formation of $[\text{NiL}(\text{Ar})\text{Cl}]$.

The next steps in the overall reaction involve the amine (RNH_2) and $^t\text{BuONa}$. To determine the order with respect to RNH_2 and $^t\text{BuONa}$, the dependence of the initial rates of the reaction on the concentrations of these two reagents was carried with the other reagents present in large excess. Some results are shown in the tables below.

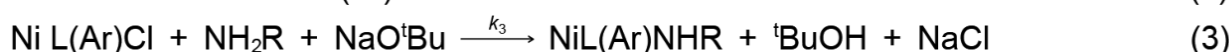
$[\text{NaO}^t\text{Bu}] \text{ (mol dm}^{-3}\text{)}$	0.2	0.6	0.9	0.12
Initial rate ($\text{mol dm}^{-3} \text{ s}^{-1}$)	4.16×10^{-5}	4.12×10^{-5}	4.24×10^{-5}	4.20×10^{-5}

$[\text{RNH}_2] \text{ (mol dm}^{-3}\text{)}$	0.3	0.6	0.9	1.2
Initial rate ($\text{mol dm}^{-3} \text{ s}^{-1}$)	4.12×10^{-5}	4.26×10^{-5}	4.21×10^{-5}	4.23×10^{-5}

6.3 Determine the order with each of these reagents, assuming each is an integer.

(Use the grids if you like)

During a catalytic cycle, a number of different structures may be involved which include the catalyst. One step in the cycle will be rate-determining. A proposed cycle for the nickel-catalyzed coupling of aryl halides with amines is as follows:



6.4 Use the steady-state approximation and material balance equation to derive the rate law for $d[\text{ArNHR}]/dt$ for the above mechanism in terms of the initial concentration of the catalyst $[\text{NiLL}']_0$ and concentrations of $[\text{ArCl}]$, $[\text{NH}_2\text{R}]$, $[\text{NaO}^t\text{Bu}]$, and $[\text{L}']$.

6.5 Give the simplified form of the rate equation in 6.4 assuming that k_1 is very small.

Official English text of the problem.

Answers

- **6.1:** First order in ArCl , first order in NiLL' , and order -1 in L' .

- **6.2:**

$$\frac{d[\text{NiL}(\text{Ar})\text{Cl}]}{dt} = \frac{k_1 k_2 [\text{NiLL}'] [\text{ArCl}]}{k_{-1} [\text{L}'] + k_2 [\text{ArCl}]}$$

- **6.3:** Zero order in both RNH_2 and NaO^tBu .

• 6.4:

$$\frac{d[\text{ArNHR}]}{dt} = \frac{k_1 k_2 [\text{NiLL}']_0 [\text{ArCl}]}{k_{-1} [\text{L}'] + k_1 \left(1 + \frac{k_2 [\text{ArCl}]}{k_3 [\text{NH}_2\text{R}] [\text{NaO}^t\text{Bu}]} + \frac{k_2 [\text{ArCl}]}{k_4} \right)}$$

- 6.5: When k_1 is sufficiently small that $k_{-1} [\text{L}']$ dominates the denominator,

$$\frac{d[\text{ArNHR}]}{dt} \simeq \frac{k_1 k_2}{k_{-1}} \frac{[\text{NiLL}']_0 [\text{ArCl}]}{[\text{L}']}$$

Solution

The groups Ar, R, L, and L' are unspecified, so unique molecular structures and complete molecular SMILES cannot be assigned. The following wildcard templates identify the species used below. The mapped wildcards [*:1], [*:2], [*:3], and [*:4] represent the unspecified aryl, organic, ligand L, and ligand L' fragments, respectively.

Species	Name or description	SMILES or schematic SMILES template
ArCl	Aryl chloride	[*:1]Cl
RNH ₂ , also written NH ₂ R	Primary amine	[*:2]N
ArNHR	N-substituted arylamine	[*:1]N[*:2]
L, L'	Unspecified ligands	[*:3], [*:4]
NiLL'	Nickel catalyst bearing both ligands	[*:3]->[Ni]<- [*:4]
NiL	Nickel complex after ligand dissociation	[*:3]->[Ni]
NiL(Ar)Cl	Aryl-chlorido nickel intermediate bearing L	[*:3]->[Ni] ([*:1]) Cl
NiL(Ar)NHR	Aryl-amido nickel intermediate bearing L	[*:3]->[Ni] ([*:1]) N[*:2]
NaO ^t Bu	Sodium tert-butoxide	[Na+] . [O-] C (C) (C) C
^t BuOH	tert-Butanol, or 2-methylpropan-2-ol	CC (C) (C) O
NaCl	Sodium chloride	[Na+] . [Cl-]
HCl	Hydrogen chloride	[H] Cl

The nickel templates show only schematic connectivity. They do not establish ligand denticity, metal oxidation states, conformation, or coordination geometry. Individual SMILES also do not describe the mechanism's electron flow.

6.1 — Orders in aryl chloride, catalyst, and free ligand

With all other concentrations fixed, write the initial rate as

$$r = Kc^n.$$

For two measurements,

$$n = \frac{\ln(r_2/r_1)}{\ln(c_2/c_1)}.$$

Using the first and last measurements in each table gives:

Varied reagent	Concentration ratio c_2/c_1	Rate ratio r_2/r_1	Calculated n	Integer assignment
ArCl	6.00	7.98	1.16	+1
NiLL'	2.50	2.67	1.07	+1
L'	2.50	0.483	-0.795	-1

For example,

$$n_{\text{ArCl}} = \frac{\ln[(1.50 \times 10^{-4})/(1.88 \times 10^{-5})]}{\ln(0.6/0.1)} = 1.16.$$

The measurements do not follow exact integer power laws, but under the stipulated integer-order assumption they give

$$n_{\text{ArCl}} = 1, \quad n_{\text{NiLL}'} = 1, \quad n_{\text{L}'} = -1.$$

Thus, under the measured conditions,

$$r \propto \frac{[\text{NiLL}'] [\text{ArCl}]}{[\text{L}']}.$$

The negative order means that adding free ligand inhibits the reaction.

6.2 — Steady-state treatment of the first two steps

Define

$$c = [\text{NiLL}'], \quad x = [\text{NiL}], \quad a = [\text{ArCl}], \quad \ell = [\text{L}'].$$

The intermediate NiL is formed by ligand dissociation and consumed by ligand reassociation and oxidative addition. Therefore,

$$\frac{dx}{dt} = k_1 c - k_{-1} x \ell - k_2 x a.$$

Applying the steady-state approximation to NiL,

$$0 \simeq k_1 c - (k_{-1} \ell + k_2 a) x,$$

so

$$x \simeq \frac{k_1 c}{k_{-1} \ell + k_2 a}.$$

The formation rate of the aryl-chlorido nickel intermediate is the rate of step (2):

$$\frac{d[\text{NiL}(\text{Ar})\text{Cl}]}{dt} = k_2 x a.$$

Consequently,

$$\frac{d[\text{NiL}(\text{Ar})\text{Cl}]}{dt} = \frac{k_1 k_2 [\text{NiLL}'] [\text{ArCl}]}{k_{-1} [\text{L}'] + k_2 [\text{ArCl}]}.$$

Here $[\text{NiLL}']$ is the concentration of that particular catalyst species; it has not yet been replaced by the conserved total nickel concentration.

6.3 — Orders in amine and base

Changing the base concentration across the listed values changes the rate only from 4.12×10^{-5} to $4.24 \times 10^{-5} \text{ mol dm}^{-3} \text{ s}^{-1}$, approximately a 3% variation.

Likewise, a fourfold increase in amine concentration leaves the rate approximately unchanged at

$$r \simeq 4.2 \times 10^{-5} \text{ mol dm}^{-3} \text{ s}^{-1}.$$

Thus neither reagent has an appreciable rate dependence over the measured ranges. The integer orders are

$$\boxed{n_{\text{RNH}_2} = 0, \quad n_{\text{NaO}^t\text{Bu}} = 0.}$$

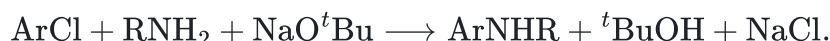
Zero order does not mean these reagents are absent from the mechanism; their concentrations do not control the rate in this kinetic regime.

6.4 — Full catalytic-cycle rate law

In addition to the notation above, define

$$\begin{aligned} y &= [\text{NiL}(\text{Ar})\text{Cl}], & z &= [\text{NiL}(\text{Ar})\text{NHR}], \\ n &= [\text{NH}_2\text{R}], & b &= [\text{NaO}^t\text{Bu}], & C_T &= [\text{NiLL}']_0. \end{aligned}$$

The balanced net reaction obtained by adding steps (2)–(4) is



For the full cycle, the steady-state balances of the three intermediates are

$$\begin{aligned} 0 &\simeq \frac{dx}{dt} = k_1c - k_{-1}\ell x - k_2ax + k_4z, \\ 0 &\simeq \frac{dy}{dt} = k_2ax - k_3nby, \\ 0 &\simeq \frac{dz}{dt} = k_3nby - k_4z. \end{aligned}$$

The term $+k_4z$ in the first equation is essential: step (4) regenerates NiL.

The last two equations show that the forward fluxes through steps (2), (3), and (4) are equal:

$$r = \frac{d[\text{ArNHR}]}{dt} = k_4z = k_3nby = k_2ax.$$

Hence,

$$y = \frac{k_2a}{k_3nb} x, \quad z = \frac{k_2a}{k_4} x.$$

Substituting $k_4z = k_2ax$ into the first steady-state equation gives

$$k_1c = k_{-1}\ell x, \quad c = \frac{k_{-1}\ell}{k_1} x.$$

Each catalyst species contains one nickel atom, so conservation of nickel gives

$$C_T = c + x + y + z.$$

Substitution yields

$$C_T = x \left(\frac{k_{-1}\ell}{k_1} + 1 + \frac{k_2a}{k_3nb} + \frac{k_2a}{k_4} \right).$$

Solving for x and using $r = k_2ax$,

$$r = \frac{k_1k_2aC_T}{k_{-1}\ell + k_1 \left(1 + \frac{k_2a}{k_3nb} + \frac{k_2a}{k_4} \right)}.$$

Therefore,

$$\frac{d[\text{ArNHR}]}{dt} = \frac{k_1k_2[\text{NiLL}']_0[\text{ArCl}]}{k_{-1}[\text{L}'] + k_1 \left(1 + \frac{k_2[\text{ArCl}]}{k_3[\text{NH}_2\text{R}][\text{NaO}^t\text{Bu}]} + \frac{k_2[\text{ArCl}]}{k_4} \right)}.$$

For the elementary steps as written, the rate-constant units are

$$\begin{aligned} &= [k_4] = \text{s}^{-1}, \\ [k_{-1}] &= [k_2] = \text{dm}^3 \text{mol}^{-1} \text{s}^{-1}, \\ [k_3] &= \text{dm}^6 \text{mol}^{-2} \text{s}^{-1}. \end{aligned}$$

Every denominator term therefore has units s^{-1} , and the resulting rate has units $\text{mol dm}^{-3} \text{s}^{-1}$.

6.5 — Small- k_1 limit

At fixed, nonzero free-ligand concentration, the required approximation is

$$k_1 \left(1 + \frac{k_2a}{k_3nb} + \frac{k_2a}{k_4} \right) \ll k_{-1}\ell.$$

The denominator in 6.4 then reduces to $k_{-1}\ell$, giving

$$r \simeq \frac{k_1k_2}{k_{-1}} \frac{[\text{NiLL}']_0[\text{ArCl}]}{[\text{L}']}.$$

In this limit, most nickel remains as NiLL' , and

$$[\text{NiL}] \simeq \frac{k_1}{k_{-1}} \frac{[\text{NiLL}']_0}{[\text{L}']}.$$

The simplified rate law predicts precisely the assigned experimental orders:

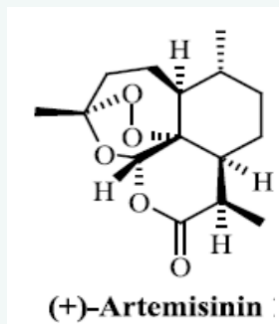
Reagent	Predicted order
Aryl chloride	+1
Total nickel catalyst	+1
Free ligand	−1
Amine	0
Sodium tert-butoxide	0

The effective coefficient k_1k_2/k_{-1} has units s^{-1} .

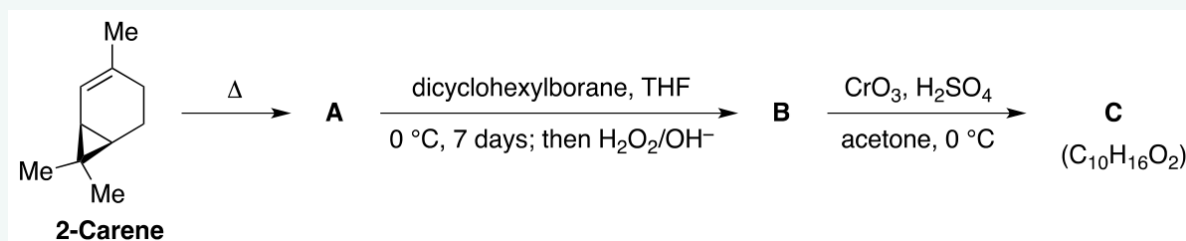
The solution was checked against the official solution.

Problem 7: Synthesis of artemisinin

(+)-Artemisinin, isolated from *Artemisia annua* L. (Qinghao, *Compositae*) is a potent antimalarial effective against resistant strains of *Plasmodium*. A simple route for the synthesis of Artemisinin is outlined below.

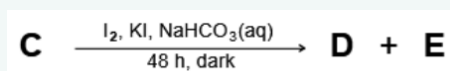


First, pyrolysis of (+)-2-Carene broke the cyclopropane ring forming, among other products, (1R)-(+)-*trans*-isolimnonene **A** ($C_{10}H_{16}$), which then was subjected to regioselective hydroboration using dicyclohexylborane to give the required alcohol **B** in 82% yield as a mixture of diastereoisomers. In the next step, **B** was converted to the corresponding γ, δ -unsaturated acid **C** in 80% yield by Jones' oxidation.



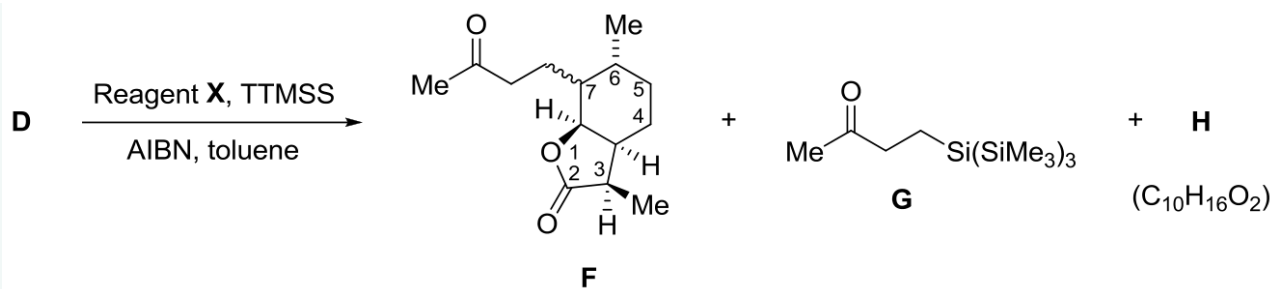
7.1 Draw the structures (with stereochemistry) of the compounds **A - C**.

The acid **C** was subjected to iodolactonization using KI , I_2 in aqueous. NaHCO_3 solution to afford diastereomeric iodolactones **D** and **E** (which differ in stereochemistry only at C_3) in 70% yield.



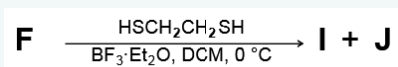
7.2 Draw the structures (with stereochemistry) of the compounds **D** and **E**.

The iodolactone **D** was subjected to an intermolecular radical reaction with ketone **X** using tris(trimethylsilyl)silane (TTMSS) and AIBN (azobisisobutyronitrile) in a catalytic amount, refluxing in toluene to yield the corresponding alkylated lactone **F** in 72% yield as a mixture of diastereoisomers which differ only in stereochemistry at C_7 along with compound **G** (~10%) and the reduced product **H**, $C_{10}H_{16}O_2$ (<5%).



7.3 Draw the structures (with stereochemistry) of compound **H** and the reagent **X**.

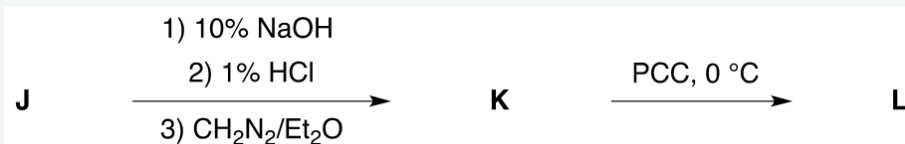
The keto group of **F** reacted with ethanedithiol and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in dichloromethane (DCM) at 0°C to afford two diastereomers: thioketal lactones **I** and **J** in nearly quantitative yield (98%). The thioketalization facilitated the separation of the major isomer **J** in which the thioketal group is on the opposite face of the ring to the adjacent methyl group.



7.4 Draw the structures (with stereochemistry) of the compounds **I** and **J**.

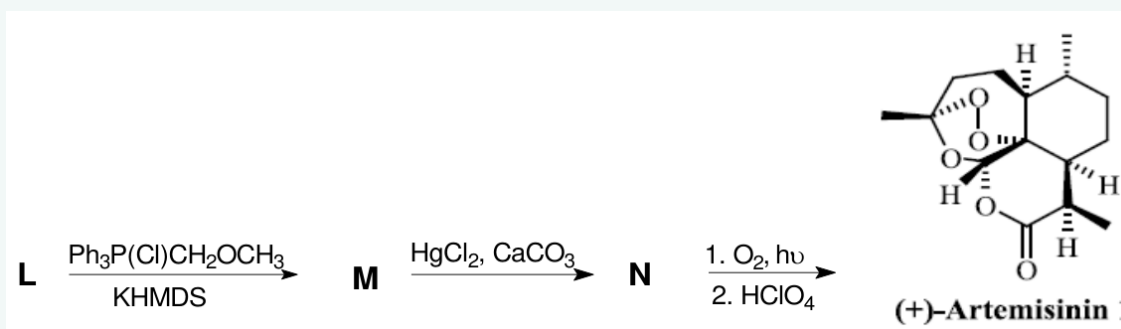
The isomer **J** was further subjected to alkaline hydrolysis followed by esterification with diazomethane providing hydroxy methyl ester **K** in 50% yield. The hydroxy methyl ester **K** was transformed into the keto ester **L** using PCC (Pyridium ChloroChromate) as the oxidizing agent in dichloromethane (DCM).

A two-dimensional NMR study of the compound **L** revealed that the two protons adjacent to the newly-formed carbonyl group are *cis* to each other and confirmed the structure of **L**.



7.5 Draw the structures (with stereochemistry) of the compounds **K** and **L**.

The ketone **L** was subjected to a Wittig reaction with methoxymethyl triphenyl-phosphonium chloride and KHMDS (Potassium HexaMethylDiSilazid - a strong, non-nucleophilic base) to furnish the required methyl vinyl ether **M** in 45% yield. Deprotection of thioketal using HgCl_2 , CaCO_3 resulted in the key intermediate **N** (80%). Finally, the compound **N** was transformed into the target molecule Artemisinin by photo-oxidation followed by acid hydrolysis with 70 % HClO_4 .



7.6 Draw the structures (with stereochemistry) of the compounds **M** and **N**.

Answers

The lactone names below use the benzofuran numbering shown in **F**. All specified stereocentres are encoded in the SMILES.

• 7.1 — A, B and C

A: (1R,4R)-*trans*-isolimonene, or (1R,4R)-*p*-mentha-2,8-diene.

C[C@H]1C=C[C@H](C(=C)C)CC1

B: A mixture of the (2S) and (2R) forms of 2-[(1R,4R)-4-methylcyclohex-2-en-1-yl]propan-1-ol.

(2S): C[C@H]1C=C[C@H]([C@H](C)CO)CC1

(2R): C[C@H]1C=C[C@H]([C@@H](C)CO)CC1

C: A mixture of the (2S) and (2R) forms of 2-[(1R,4R)-4-methylcyclohex-2-en-1-yl]propanoic acid.

(2S): C[C@H]1C=C[C@H]([C@H](C)C(=O)O)CC1

(2R): C[C@H]1C=C[C@H]([C@@H](C)C(=O)O)CC1

• 7.2 — D and E

D: (3R,3aS,6R,7R,7aR)-7-Iodo-3,6-dimethylhexahydrobenzofuran-2(3H)-one.

C[C@H]1[C@@H](I)[C@@H]2OC(=O)[C@H](C)[C@@H]2CC1

E: (3S,3aS,6R,7R,7aR)-7-Iodo-3,6-dimethylhexahydrobenzofuran-2(3H)-one.

C[C@H]1[C@@H](I)[C@@H]2OC(=O)[C@@H](C)[C@@H]2CC1

• 7.3 — H and X

H: (3R,3aS,6R,7aS)-3,6-Dimethylhexahydrobenzofuran-2(3H)-one.

C[C@H]1C[C@@H]2OC(=O)[C@H](C)[C@@H]2CC1

X: Methyl vinyl ketone, or but-3-en-2-one.

C=CC(C)=O

• 7.4 — I and J

I: (3R,3aS,6R,7R,7aS)-3,6-Dimethyl-7-[2-(2-methyl-1,3-dithiolan-2-yl)ethyl]hexahydrobenzofuran-2(3H)-one. Its side chain and the C_6 methyl group are **cis**.

C[C@H]1[C@@H](CCC3(C)SCCS3)[C@@H]2OC(=O)[C@H](C)[C@@H]2CC1

J: (3R,3aS,6R,7S,7aS)-3,6-Dimethyl-7-[2-(2-methyl-1,3-dithiolan-2-yl)ethyl]hexahydrobenzofuran-2(3H)-one. Its side chain and the C_6 methyl group are **trans**.

C[C@H]1[C@H](CCC3(C)SCCS3)[C@@H]2OC(=O)[C@H](C)[C@@H]2CC1

• 7.5 — K and L

K: Methyl (2R)-2-[(1S,2S,3S,4R)-2-hydroxy-4-methyl-3-[2-(2-methyl-1,3-dithiolan-2-yl)ethyl]cyclohexyl]propanoate.

C[C@H]1[C@H](CCC2(C)SCCS2)[C@H](O)[C@H]([C@@H](C)C(=O)OC)CC1

L: Methyl (2R)-2-[(1S,3S,4R)-4-methyl-3-[2-(2-methyl-1,3-dithiolan-2-yl)ethyl]-2-oxocyclohexyl]propanoate.

C[C@H]1[C@H](CCC2(C)SCCS2)C(=O)[C@H]([C@@H](C)C(=O)OC)CC1

• 7.6 — M and N

M: Methyl (2R)-2-[(1S,3S,4R)-2-(methoxymethylidene)-4-methyl-3-[2-(2-methyl-1,3-dithiolan-2-yl)ethyl]cyclohexyl]propanoate.

C[C@H]1[C@H](CCC2(C)SCCS2)C(=COC)[C@H]([C@@H](C)C(=O)OC)CC1

N: Methyl (2R)-2-[(1S,3S,4R)-2-(methoxymethylidene)-4-methyl-3-(3-oxobutyl)cyclohexyl]propanoate.

C[C@H]1[C@H](CCC(C)=O)C(=COC)[C@H]([C@@H](C)C(=O)OC)CC1

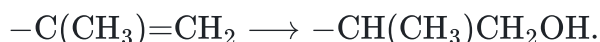
Solution

7.1 — Ring opening, selective hydroboration and oxidation

Opening the cyclopropane ring gives the *p*-menthane skeleton of **A**, with an internal cyclohexene double bond and an isopropenyl substituent. The specified *trans* relationship places the ring methyl and isopropenyl groups on opposite faces. Together with the stated *1R* configuration, this gives the **(1R,4R)** structure listed above.

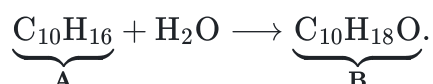
To sketch **A**, use the cyclohexane orientation in **F**: put the methyl group at the top behind the page and the isopropenyl group at the opposite ring carbon in front. The internal double bond occupies the left-hand ring bond, corresponding to $C_7 = C_{7a}$ in the later lactone numbering.

Dicyclohexylborane preferentially hydroborates the less hindered, terminal double bond. Boron attaches to its terminal carbon, and oxidative workup replaces the C–B bond by C–O with retention. Thus the side-chain transformation is



Hydrogen and boron add **syn**, but addition can create either configuration at the new side-chain stereocentre. Consequently, **B** is the stated mixture of two diastereomers; the existing ring stereocentres remain unchanged.

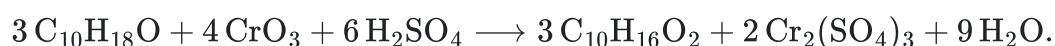
The formal net hydration balance is



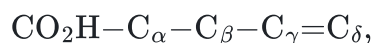
Jones' reagent oxidizes the primary alcohol to a carboxylic acid:



A balanced equation using the supplied chromium reagent is



This gives **C**, retaining the two side-chain configurations. Counting outward from its carboxyl carbon gives



so the remaining ring alkene is correctly γ, δ -**unsaturated**.

7.2 — Iodolactonization

The carboxylate attacks the nearer carbon of the iodine-activated ring double bond. This forms a **five-membered γ -lactone**, with oxygen bonded to the former γ -carbon and iodine bonded to the former δ -carbon.

Opening of the iodine bridge occurs from the opposite face, so the new C–O and C–I bonds are **anti**. The side chain already fixes the face from which the intramolecular oxygen attack occurs.

Using the orientation of **F**, the required drawing has:

- The C_6 methyl group behind the page.
- Both bridgehead hydrogens, at C_{3a} and C_{7a} , behind the page: the ring fusion is **cis**.
- The lactone C–O bond at C_{7a} toward the viewer.
- Iodine at C_7 behind the page.
- The C_3 methyl group toward the viewer in **D**, and behind the page in **E**.

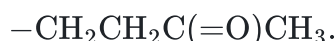
The identity of **D** is fixed by the C_3 stereochemistry subsequently shown in **F**. Thus **D** is the $3R$ isomer and **E** the $3S$ isomer.

For either epimer, the balanced net reaction is



7.3 — Radical coupling and reduction

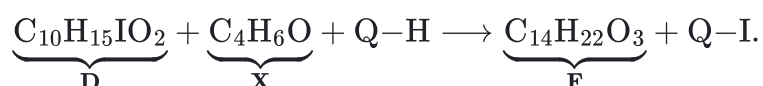
The side chain drawn in **F** is



It results from addition of the lactone radical to the terminal carbon of **methyl vinyl ketone**, **X**, $\text{C}=\text{CC}(\text{C})=\text{O}$.

A silyl radical abstracts iodine from **D**, producing a radical at C_7 . Addition to **X** creates a radical adjacent to its carbonyl group; hydrogen-atom transfer from TTMSS then gives **F**. The approximately planar C_7 radical explains why both configurations at that carbon are obtained.

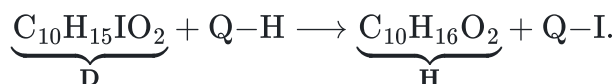
Writing $Q = (\text{Me}_3\text{Si})_3\text{Si}$, the balanced coupling is



The two forms of **F** are the $7R$ and $7S$ epimers of (3*R*,3*aS*,6*R*,7*aS*)-3,6-dimethyl-7-(3-oxobutyl)hexahydrobenzofuran-2(3*H*)-one:

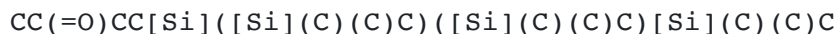
- $7R$: $\text{C}[\text{C@H}]1[\text{C@@H}](\text{CCC}(\text{C})=\text{O})[\text{C@@H}]2\text{OC}(=\text{O})[\text{C@H}](\text{C})[\text{C@@H}]2\text{CC}1$
- $7S$: $\text{C}[\text{C@H}]1[\text{C@H}](\text{CCC}(\text{C})=\text{O})[\text{C@@H}]2\text{OC}(=\text{O})[\text{C@H}](\text{C})[\text{C@@H}]2\text{CC}1$

Direct hydrogen-atom transfer to the lactone radical instead produces **H**:



Thus **H** is simply **D with iodine replaced by hydrogen**. Carbon C_7 becomes a methylene group, and all other stereocentres retain their spatial configurations.

The side product **G** independently confirms **X**: it is 4-[tris(trimethylsilyl)silyl]butan-2-one,



formed by net addition of the silane across the double bond:



The change from $7aR$ in **D** to $7aS$ in **H** reflects a change in CIP priorities after iodine removal, **not inversion at that stereocentre**.

7.4 — Thioketal formation

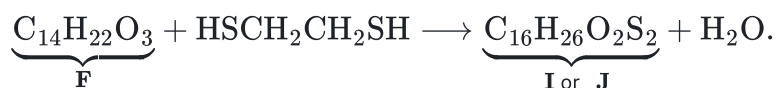
Ethane-1,2-dithiol, **SCCS**, converts the side-chain ketone into a cyclic **1,3-dithiolane**. Lewis-acid activation of the carbonyl allows sulfur attack, followed by ring closure and loss of water.

The side-chain change is



where both sulfur atoms in the product are bonded to the same former carbonyl carbon, closing the five-membered ring.

The balanced condensation is



The thioketal carbon is not a new stereocentre because the two paths through the unsubstituted dithiolane ring are equivalent. **I** and **J** therefore retain the C_7 epimerism already present in **F**.

The stated relationship identifies **J**:

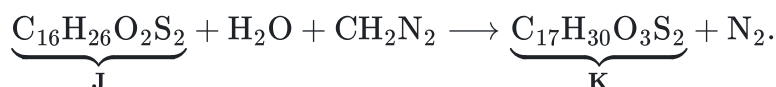
- In **J**, draw the protected side chain at C_7 toward the viewer, opposite the backward C_6 methyl group.
- In **I**, draw that side chain behind the page, on the same face as the C_6 methyl group.

These are respectively the $7S$ and $7R$ structures given in the answers.

7.5 — Lactone opening and oxidation

Alkaline hydrolysis cleaves the lactone's **acyl–oxygen bond**. It therefore gives a hydroxy carboxylate without breaking the bond between oxygen and the stereogenic ring carbon.

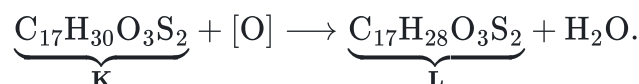
After acidification, diazomethane, $\text{C}=[\text{N}^+]=[\text{N}^-]$, converts the carboxylic acid into its methyl ester. The net organic balance is



To draw **K**, open the five-membered lactone of **J**:

- Replace the lactone oxygen connection at the former C_{7a} by an **OH group pointing toward the viewer**.
- Replace the lactone carbonyl terminus by CO_2Me .
- Retain the configuration of the adjacent methyl-bearing side-chain carbon and all ring stereocentres.

PCC oxidizes this secondary alcohol to a ring ketone, giving **L**. Using $[\text{O}]$ for one formal oxygen-atom equivalent supplied by the oxidant,

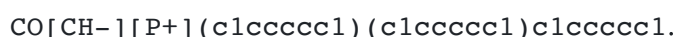


Only the stereocentre bearing OH disappears.

The hydrogens on the two carbons flanking the new carbonyl—the former C_{3a} and C_7 —both point behind the page. They are therefore **cis**, exactly as required by the NMR observation. No epimerization is needed to explain the result.

7.6 — Wittig reaction and thioacetal deprotection

KHMDS removes a proton from the methoxymethylphosphonium salt to form **(methoxymethylene)triphenylphosphorane**, represented in its charge-separated form by



Its carbon attacks the ring ketone of **L**. Collapse of the Wittig intermediate replaces the carbonyl oxygen by $=\text{CHOMe}$, producing **M**:



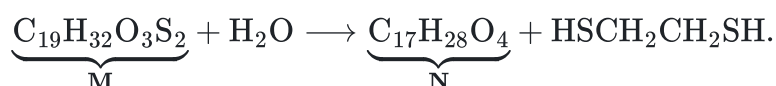
The phosphorus-containing product is **triphenylphosphine oxide**, $\text{O}=\text{P}(\text{c1ccccc1})(\text{c1ccccc1})\text{c1ccccc1}$.

Thus, when drawing **M**, replace only the ring $\text{C}=\text{O}$ of **L** by an exocyclic $\text{C}=\text{CH}-\text{OCH}_3$ group. The methyl ester, protected side-chain ketone and existing stereocentres remain as shown in **L**.

Mercury(II)-assisted deprotection then restores the side-chain ketone:



This gives **N**. The formal hydrolysis balance, before accounting for mercury binding to the sulfur-containing product, is

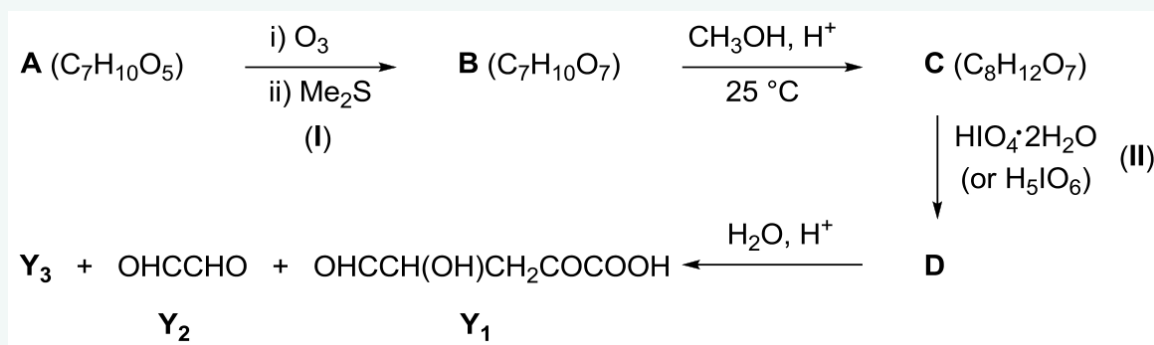


The exocyclic enol ether and methyl ester are retained in **N**, ready for the final photo-oxidation and acid treatment.

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

Problem 8: Star anise

Illicium verum, commonly called *Star anise*, is a small native evergreen tree grown in northeast Vietnam. *Star anise* fruit is used in traditional Vietnamese medicine. It is also a major ingredient in the making the flavor of 'phở', a Vietnamese favorite soup. Acid **A** is isolated from the *star anise* fruit. The constitutional formula of **A** has been deduced from the following sequence of reactions:

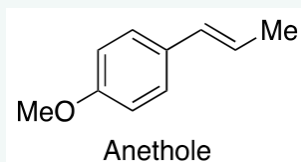


(I): this overall process results in an alkene cleavage at the C=C bond, with each carbon of this becoming doubly bonded to an oxygen atom.

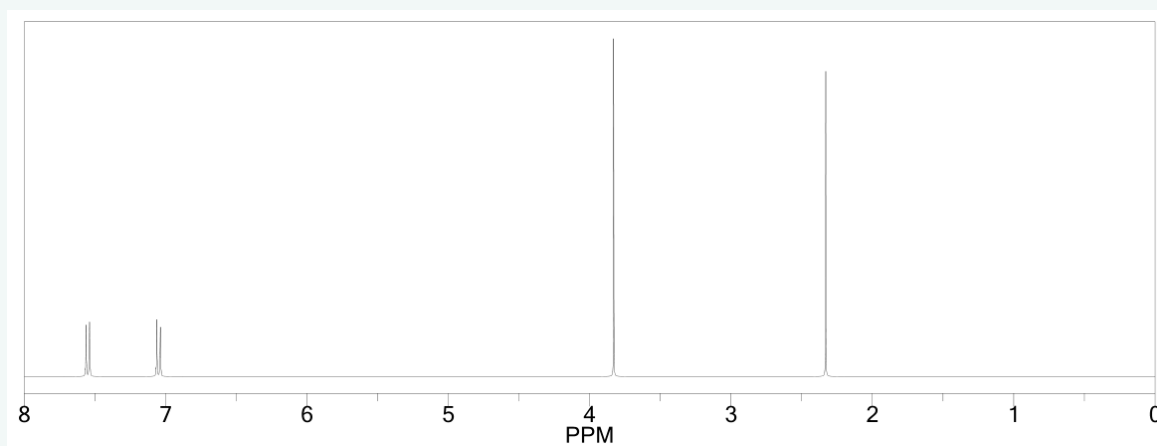
(II): this oxidative cleavage process of 1,2-diols breaks C(OH)–C(OH) bond and produces corresponding carbonyl compounds.

8.1 Draw the structures for the compounds **Y**₁ and **Y**₂ and hence deduce the structure of **Y**₃ and **A**, **B**, **C**, **D**, given that in **A** there is only one ethylenic hydrogen atom.

Anethole, a main component of star anise oil, is an inexpensive chemical precursor for the production of many pharmaceutical drugs.



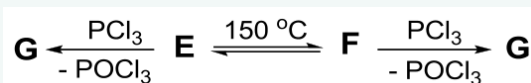
Treating anethole with sodium nitrite in acetic acid gives a crystalline solid **E** (C₁₀H₁₀N₂O₃). The IR spectrum of **E** shows there is no non-aromatic C=C double bond. The ¹H NMR spectrum of **E** is given below.



8.2 What differences in the structure between **E** and anethole can be obtained from the ^1H NMR data? Pick one of the following statements.

- i) **E** contains a *cis*-C=C ethylenic bond while that of anethole is *trans*.
- ii) **E** cannot contain a non-aromatic C=C bond.
- iii) **E** is the adduct of anethole and N_2O_2 .
- iv) **E** is the adduct of anethole and N_2O_3 .
- v) **E** does not contain two *trans* ethylenic protons as anethole.

On heating at $150\text{ }^\circ\text{C}$ for several hours, **E** is partially isomerized into **F**. Under the same conditions, **F** gives the identical equilibrium mixture to that obtained from **E**. On heating with phosphorus trichloride, both **E** and **F** lose one oxygen atom giving compound **G**. Compounds **E** and **F** have the same functional groups.



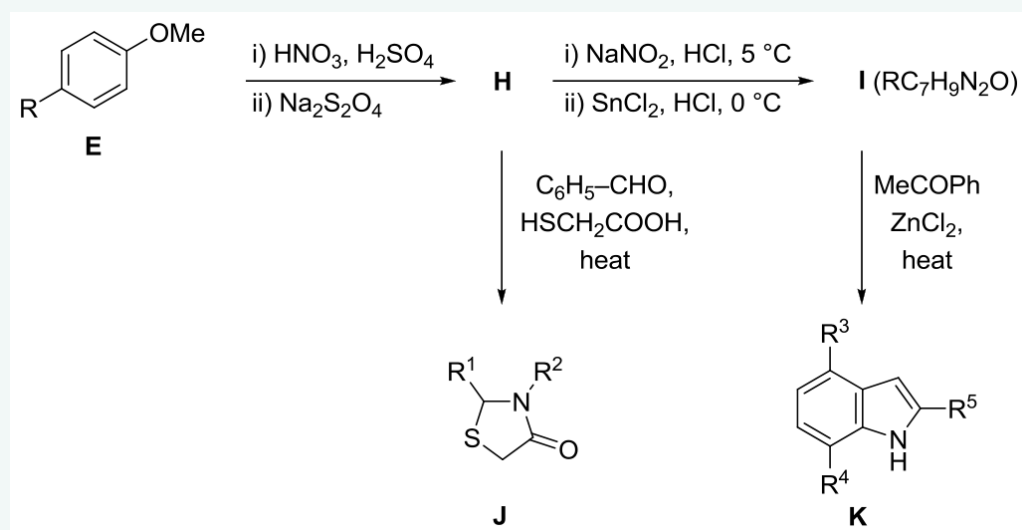
The chemical shifts of methyl protons in **E**, **F** and **G** are given below.

	E	F	G
$\text{CH}_3\text{—O}$	3.8 ppm	3.8 ppm	3.8 ppm
$\text{CH}_3\text{—C}$	2.3 ppm	2.6 ppm	2.6 ppm

8.3 Suggest structures for **E**, **F** and **G**, assuming that they do NOT contain three-membered rings.

A simplified structure for compound **E** is shown below; the R group does not change throughout the rest of this question. Compound **E** is nitrated and subsequently reduced with sodium dithionite to **H**. Treatment of **H** with sodium nitrite and hydrochloric acid at $0\text{--}5\text{ }^\circ\text{C}$ and subsequently reduced with stannous chloride to provide **I** ($\text{R—C}_7\text{H}_9\text{N}_2\text{O}$). One-pot reaction (three component reaction) of **H**, benzaldehyde and thioglycolic acid ($\text{HSCH}_2\text{CO}_2\text{H}$) leads to the formation of **J**. Reaction of **I** and methyl phenyl ketone in the presence of ZnCl_2 affords **K**.

8.4 Give the structures for **H**, **I**, **J** and **K** in the following scheme:



Official English text of the problem.

Answers

- **8.1.** The structures are given below. Stereochemistry is left unspecified because the question determines constitution.

Compound	Name	SMILES
Y₁	4-Hydroxy-2,5-dioxopentanoic acid	<chem>O=CC(=O)CC(=O)C(=O)O</chem>
Y₂	Glyoxal (ethanedial)	<chem>O=CC=O</chem>
Y₃	Methanol	<chem>CO</chem>
A	3,4,5-Trihydroxycyclohex-1-ene-1-carboxylic acid —the constitution of shikimic acid	<chem>O=C(O)C1=CC(O)C(O)C(O)C1</chem>
B, open form	4,5,6-Trihydroxy-2,7-dioxoheptanoic acid	<chem>O=CC(=O)C(O)C(O)CC(=O)C(=O)O</chem>
B, cyclic hemiacetal	3-(3,4,5-Trihydroxyoxolan-2-yl)-2-oxopropanoic acid	<chem>O=C(O)C(=O)CC1OC(O)C(O)C1O</chem>
C	3-(3,4-Dihydroxy-5-methoxyoxolan-2-yl)-2-oxopropanoic acid	<chem>O=C(O)C(=O)CC1OC(OC)C(O)C1O</chem>
D	4-(1-Methoxy-2-oxoethoxy)-2,5-dioxopentanoic acid	<chem>O=C(O)C(=O)CC(C=O)OC(OC)C=O</chem>

- **8.2. v)** E does not contain two *trans* ethylenic protons as anethole.
- **8.3.** E and F are the two N-oxide regioisomers of the same substituted furazan. *Furoxan* means 1,2,5-oxadiazole 2-oxide; *furazan* means 1,2,5-oxadiazole.

Compound	Name	SMILES
E	4-(4-Methoxyphenyl)-3-methylfuroxan	<chem>COc1ccc(C2=NO[N+]([O-])=C2C)cc1</chem>
F	3-(4-Methoxyphenyl)-4-methylfuroxan	<chem>COc1ccc(C2=[N+]([O-])ON=C2C)cc1</chem>
G	3-(4-Methoxyphenyl)-4-methylfurazan	<chem>COc1ccc(C2=NON=C2C)cc1</chem>

In **E**, the N-oxide is adjacent to the methyl-bearing ring carbon; in **F**, it is adjacent to the aryl-bearing ring carbon.

- **8.4.** Here *R* is **3-methylfuroxan-4-yl**, with attachment-point SMILES *C1=NO[N+]([O-])=C1C; * marks attachment to the aromatic ring.

Compound	Name	SMILES
H	4-(3-Amino-4-methoxyphenyl)-3-methylfuroxan	<chem>COc1ccc(C2=NO[N+]([O-])=C2C)cc1N</chem>
I	4-(3-Hydrazinyl-4-methoxyphenyl)-3-methylfuroxan	<chem>COc1ccc(C2=NO[N+]([O-])=C2C)cc1NN</chem>
J	3-[2-Methoxy-5-(3-methylfuroxan-4-yl)phenyl]-2-phenyl-1,3-thiazolidin-4-one	<chem>COc1ccc(C2=NO[N+]([O-])=C2C)cc1N1C(=O)CSC1c1ccccc1</chem>
K	7-Methoxy-4-(3-methylfuroxan-4-yl)-2-phenyl-1H-indole	<chem>COc1ccc(C2=NO[N+]([O-])=C2C)c2cc(-c3ccccc3)[nH]c12</chem>

The labels on the printed templates are:

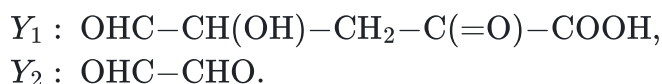
$$R^1 = \text{phenyl}, \quad R^2 = 2\text{-methoxy-5-}R\text{-phenyl}, \quad R^3 = R, \quad R^4 = \text{methoxy}, \quad R^5 = \text{phenyl}.$$

J has a new stereocentre at thiazolidinone C2; a racemic product is expected under the stated achiral conditions.

Solution

8.1

The explicitly supplied degradation products are



Thus Y_1 contains five carbons and Y_2 contains two. Together they account for all seven carbons originally present in A. The additional carbon introduced when B reacts with methanol must therefore leave during hydrolysis as **Y_3 , methanol**.

The important feature of C is its **cyclic methyl acetal**, which protects both an aldehyde and one hydroxyl group during periodate oxidation.

Reversing the carbon-carbon cleavage that produces Y_1 and Y_2 gives the open-chain structure of B:



The aldehyde reacts intramolecularly with the third hydroxyl group counted from the aldehyde end. This forms a **five-membered hemiacetal ring**: four carbon atoms and one oxygen atom. Methanol then converts the hemiacetal hydroxyl group into a methoxy group, giving C.

Consequently, C has:

- one cyclic acetal carbon bearing hydrogen and methoxy;
- two adjacent, unprotected secondary hydroxyl groups;
- a side chain $-\text{CH}_2-\text{C}(=\text{O})-\text{COOH}$.

Periodate cleaves the bond between the two unprotected hydroxyl-bearing carbons. The resulting structure is



which is D. Its acetal linkage still connects the future five-carbon and two-carbon fragments.

Acidic hydrolysis restores the hydroxyl group of Y_1 and the second aldehyde group of glyoxal, while releasing methanol:



To recover A, reverse the ozonolysis of B. The aldehyde carbon at one end and the ketone carbon adjacent to the carboxyl group were the two alkene carbons. Reconnecting them produces a six-membered ring.

The constitution of A is therefore a cyclohexene bearing:

- COOH at alkene carbon C1;
- the sole ethylenic hydrogen at C2;

- hydroxyl groups at C3, C4 and C5;
- a methylene group at C6.

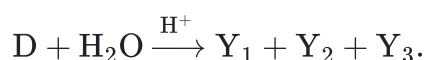
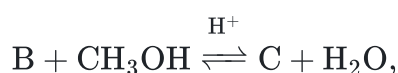
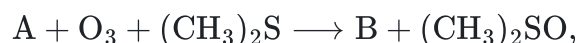
This is the **shikimic-acid constitution**.

The degree of unsaturation provides a check:

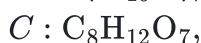
$$\text{DBE}(A) = \frac{2(7) + 2 - 10}{2} = 3,$$

accounted for by one carboxyl carbonyl, one alkene and one ring.

Using the compound labels for the organic structures, the balanced transformations are



The formulas also agree throughout:



A methyl ester alone would not provide the required protection of the adjacent hydroxyl groups; the degradation requires the methyl acetal described above.

8.2

The starting material is **trans-anethole**, or (*E*)-anethole, COc1ccc(/C=C/C)cc1.

Its side chain contains two ethylenic hydrogens. In E, the displayed spectrum instead shows two aromatic proton sets and the methoxy and carbon-bound methyl signals. Together with the molecular formula, these account for four aromatic hydrogens and two three-hydrogen methyl groups. The original pair of ethylenic proton signals is absent.

Therefore the conclusion supported by the proton NMR is

v) E does not contain two trans ethylenic protons as anethole.

Option ii is stronger than proton NMR alone permits: a double bond bearing no hydrogens need not produce an ethylenic proton signal. The IR observation supplies the separate information about the absence of a non-aromatic alkene.

Options iii and iv also fail as simple addition formulas. Addition of either N_2O_2 or N_2O_3 to anethole would retain twelve hydrogens, whereas E has ten.

8.3

For E,

$$\text{DBE}(E) = \frac{2(10) + 2 + 2 - 10}{2} = 7.$$

The benzene ring accounts for four degrees of unsaturation. The remaining three can be accommodated by a five-membered ring containing two double bonds.

The retained methoxyphenyl and methyl groups leave two additional carbon atoms, two nitrogen atoms and two oxygen atoms to form the transformed side-chain unit. A **furoxan ring** satisfies these constraints:

- its ring sequence is O–N–C–C–N;
- its Kekulé structure has two C=N bonds;
- one nitrogen bears an exocyclic N-oxide oxygen;
- its two carbon atoms carry methyl and 4-methoxyphenyl substituents.

The SMILES in the answer explicitly show the N-oxide as N⁺–O[–].

Removal of the exocyclic oxygen gives the corresponding **furazan**, G. Because the methyl and aryl substituents make the two nitrogen sites inequivalent, oxidation at either nitrogen gives a different furoxan. These are E and F, and removal of either N-oxide oxygen gives the same G.

The methyl shifts distinguish their assignments. Relative to G,

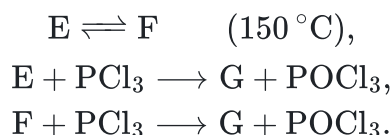
$$\Delta\delta_E = 2.3 - 2.6 = -0.3 \text{ ppm}, \quad \Delta\delta_F = 2.6 - 2.6 = 0.0 \text{ ppm}.$$

The methyl group is appreciably shielded only in E. Accordingly, E is assigned the N-oxide adjacent to the methyl-bearing carbon; F has the N-oxide adjacent to the aryl-bearing carbon.

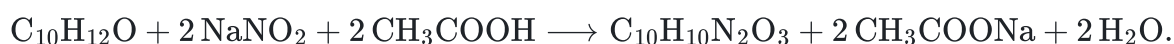
For a precise drawing, number the furoxan ring consecutively O1–N2–C3–C4–N5, with N2 bearing the exocyclic oxygen:

- **E**: methyl at C3 and 4-methoxyphenyl at C4.
- **F**: 4-methoxyphenyl at C3 and methyl at C4.
- **G**: the corresponding ring without the exocyclic N-oxide oxygen.

The thermal interconversion and deoxygenations are



A balanced overall equation for formation of E from anethole under the stated nitrite/acetic-acid conditions is



This is an overall material balance, rather than an elementary mechanistic step.

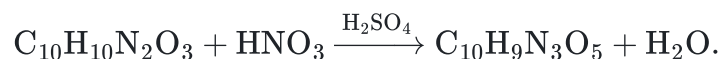
8.4

Throughout this part, *R* remains the furoxan substituent identified above. For the following equations, let Ar denote **2-methoxy-5-*R*-phenyl**.

Formation of H. Methoxy directs electrophilic nitration ortho and para. Its para position is occupied by *R*, and its two ortho positions are equivalent in E. Nitration therefore introduces the nitro group ortho to methoxy.

The intermediate is **4-(4-methoxy-3-nitrophenyl)-3-methylfuroxan**, COc1ccc(C2=NO[N+]([O-])=C2C)cc1[N+]([O-])=O.

Its formation is balanced by



Dithionite reduces the nitro group to an amino group, giving H, equivalently **2-methoxy-5-*R*-aniline**. A balanced net reduction, expressing the oxidized sulfur product as hydrogen sulfite, is



Formation of I. Diazotization replaces the amino group by a diazonium group:



The intermediate is the **2-methoxy-5-*R*-benzenediazonium ion**, COc1ccc(C2=NO[N+])([O-])=C2C)cc1[N+].

Reduction by tin(II) gives the arylhydrazine I:



The displayed organic structure is the neutral hydrazine after work-up. Its substituent formula is correctly



Formation of J. Benzaldehyde, O=Cc1ccccc1, first condenses with H to form its imine. This intermediate is **N-benzylidene-2-methoxy-5-*R*-aniline**, COc1ccc(C2=NO[N+])([O-])=C2C)cc1N=Cc1ccccc1.

The sulfur of **thioglycolic acid**, O=C(O)CS, adds to the imine carbon. Subsequent intramolecular amide formation closes the five-membered thiazolidin-4-one ring.

Consequently:

- the benzaldehyde-derived phenyl group is attached to ring C2, so $R^1 = \text{phenyl}$;
- the original aryl group of H remains attached to nitrogen, so $R^2 = 2\text{-methoxy-5-}R\text{-phenyl}$;
- the thioglycolic-acid carboxyl group becomes the ring carbonyl;
- its methylene becomes ring C5.

The balanced overall condensation is



The product has formula C_{19}H_{17}N_3O_4S. Its newly formed C2 stereocentre is not assigned an absolute configuration.

Formation of K. I reacts with **acetophenone**, CC(=O)c1ccccc1, through a **Fischer indole synthesis**.

The initial condensation product is **acetophenone (2-methoxy-5-*R*-phenyl)hydrazone**, COc1ccc(C2=NO[N+])([O-])=C2C)cc1NN=C(C)c1ccccc1. Its geometrical configuration is not specified by the problem.

During indole formation:

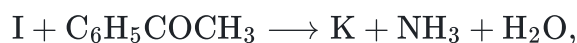
- the nitrogen originally bonded to the aromatic ring becomes the indole nitrogen;
- the other nitrogen is eliminated as ammonia;
- the acetophenone carbonyl carbon becomes indole C2 and retains phenyl;
- the acetophenone methyl carbon becomes indole C3.

One position ortho to the hydrazine group is occupied by methoxy. Cyclization therefore occurs at the other, unsubstituted ortho position. Mapping the original aromatic ring onto the indole gives methoxy at C7 and *R* at C4.

Thus the printed template requires

$$R^3 = R, \quad R^4 = \text{OCH}_3, \quad R^5 = \text{C}_6\text{H}_5.$$

The balanced overall reaction is

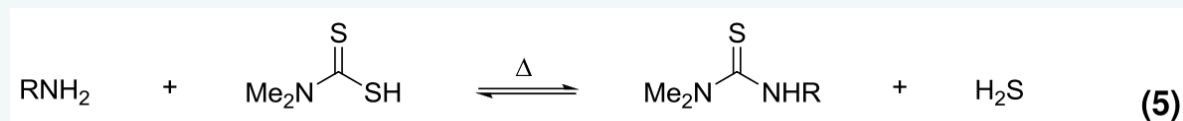
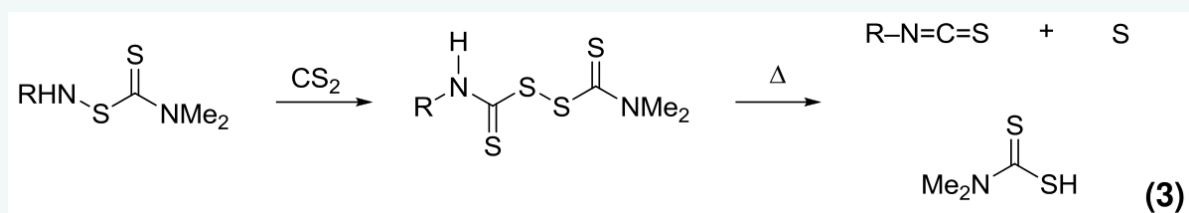
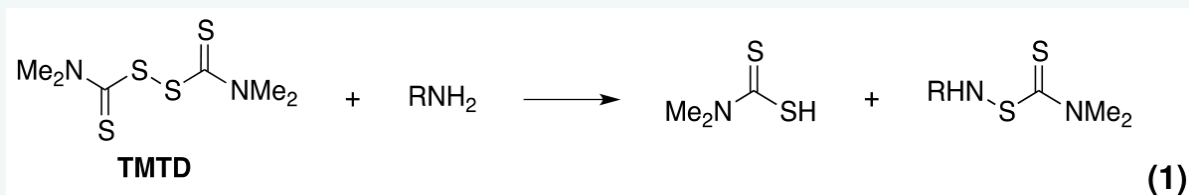


with ZnCl_2 and heat. The resulting formula, $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_3$, agrees with the structure given for K.

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

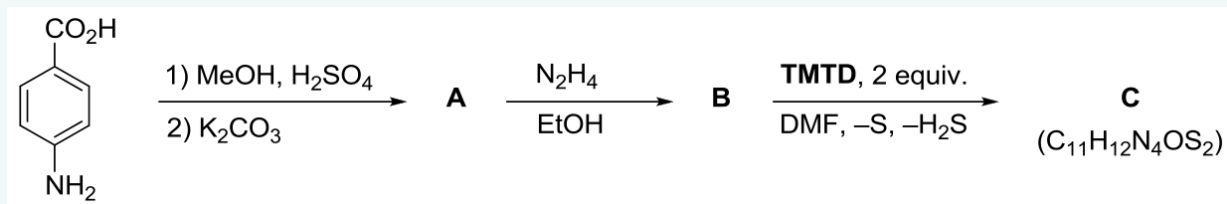
Problem 9: Heterocycle preparation

Tetramethylthiurame disulfide (**TMTD**) is emerging as a useful reagent to prepare many sulfur-nitrogen functional groups and heterocycles in organic chemistry. The reactions of **TMTD** with primary amines, as well some corresponding post-transformations of the resulting product(s) are presented in the following schemes:

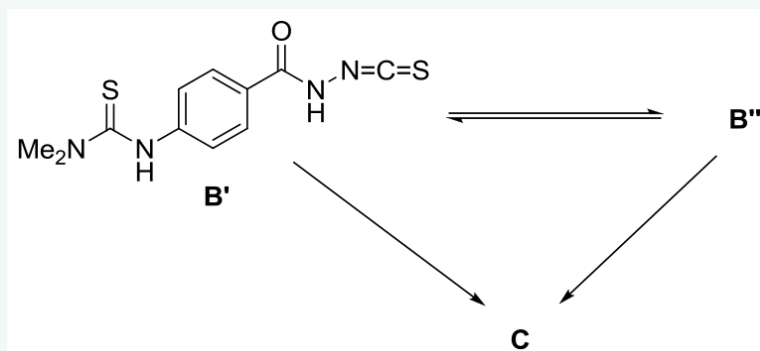


Similar transformations of benzohydrazides (containing nucleophilic NH_2 group) and **TMTD** have been observed.

In the synthetic scheme below, the thiocarbamoylation reaction of an aroyl hydrazine with **TMTD** produces compound **C** containing a heterocyclic moiety from *p*-aminobenzoic acid.



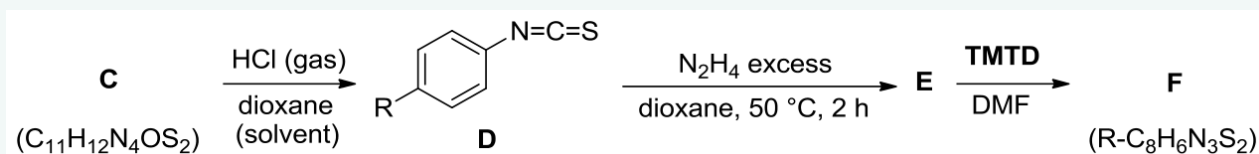
During the formation of **C** from **B**, an intermediate **B'** was observed. This intermediate tautomerizes to **B''**. **C** can be formed from **B'** or **B''**.



9.1 Give the structures of **A**, **B**, and **C**.

9.2 Suggest a structure for the tautomer **B''** and give a curly-arrow mechanism for the formation of **C**.

Compound **C** was then converted to **F** by the following pathway:



[The group R remains exactly the same throughout the rest of the question.]

9.3 Draw the structures of **E**, and **F**. (You do not need to draw the structure for the R group from this point.)

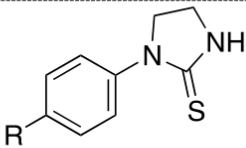
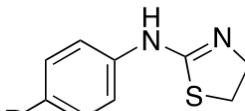
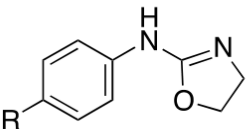
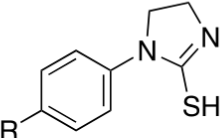
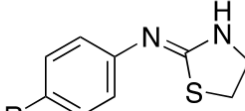
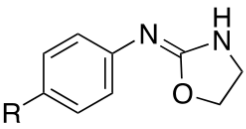
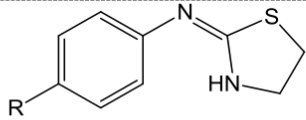
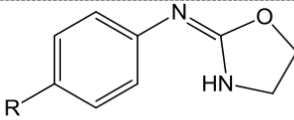
E was only obtained when **D** was slowly added to the solution of excess N_2H_4 in dioxane. If N_2H_4 was added to the solution of **D** in dioxane instead, a major side product **D'** ($\text{R}_2\text{C}_{14}\text{H}_{12}\text{N}_4\text{S}_2$) was formed.

9.4 Give the structure of **D'**.

Slightly heating of **D** with ethanolamine ($\text{HOCH}_2\text{CH}_2\text{NH}_2$) in dioxane for 2 hours yielded **G** ($\text{R}-\text{C}_9\text{H}_{11}\text{N}_2\text{OS}$).

9.5 Draw the structural formula of **G**.

9.6 Heating **G** in the presence of *p*-toluenesulfonic acid as the catalyst could form a number of different five-membered heterocyclic products:

H₁	H₂	H₃
		
H₄	H₅	H₆
		
H₇	H₈	
		

- i) Draw 2 structures that have different molecular formulae.
- ii) Draw 2 structures that are constitutional isomers.
- iii) Draw 2 structures that are stereoisomers.

Official English text of the problem.

Answers

For **C** and **F**, the structures below use the **thiol tautomer**; their thione tautomers are given in the solution. In subsequent abbreviated SMILES, each * represents the same unchanged group **R**.

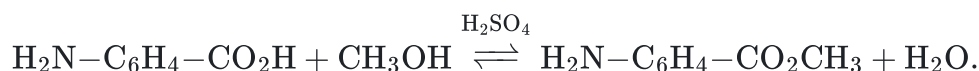
- **9.1 — A:** Methyl 4-aminobenzoate: COC(=O)c1ccc(N)cc1.
- **9.1 — B:** 4-Aminobenzohydrazide: NNC(=O)c1ccc(N)cc1.
- **9.1 — C:** 5-[4-(3,3-Dimethylthioureido)phenyl]-1,3,4-oxadiazole-2-thiol: CN(C)C(=S)Nc1ccc(-c2nnc(S)o2)cc1.
- **9.2 — B'':** The imidic-acid tautomer of **B'**, N-isothiocyanato-4-(3,3-dimethylthioureido)benzimidic acid. A geometry suitable for cyclization is: CN(C)C(=S)Nc1ccc(/C(O)=N/N=C=S)cc1. Intramolecular oxygen attack on the isothiocyanate carbon, followed by proton transfer, gives **C**.
- **9.3 — E:** 4-(4-R-Phenyl)thiosemicarbazide: *c1ccc(NC(=S)NN)cc1.
- **9.3 — F:** 5-[(4-R-Phenyl)amino]-1,3,4-thiadiazole-2-thiol: *c1ccc(Nc2nnc(S)s2)cc1.

- **9.4 — D':** 1,2-Bis[N-(4-R-phenyl)carbamothioyl]hydrazine:
c1ccc(NC(=S)NNC(=S)Nc2ccc()cc2)cc1.
- **9.5 — G:** 1-(2-Hydroxyethyl)-3-(4-R-phenyl)thiourea: *c1ccc(NC(=S)NCCO)cc1.
- **9.6(i): H₁ and H₃,** with different molecular formulae:
 - **H₁,** 1-(4-R-phenyl)imidazolidine-2-thione: *c1ccc(N2CCNC2=S)cc1; formula R–C₉H₉N₂S.
 - **H₃,** N-(4-R-phenyl)-4,5-dihydro-1,3-oxazol-2-amine: *c1ccc(NC2=NCCO2)cc1; formula R–C₉H₉N₂O.
- **9.6(ii): H₁ and H₂,** constitutional isomers:
 - **H₁** is specified above.
 - **H₂,** N-(4-R-phenyl)-4,5-dihydro-1,3-thiazol-2-amine: *c1ccc(NC2=NCCS2)cc1.
 - Both have formula R–C₉H₉N₂S.
- **9.6(iii): H₅ and H₇,** geometrical stereoisomers:
 - **H₅,** (Z)-N-(4-R-phenyl)-1,3-thiazolidin-2-imine: *c1ccc(/N=C2\SCCN2)cc1.
 - **H₇,** (E)-N-(4-R-phenyl)-1,3-thiazolidin-2-imine: *c1ccc(/N=C2/SCCN2)cc1.

Solution

9.1 — Identification of A, B, and C

The starting material, 4-aminobenzoic acid, is Nc1ccc(C(=O)O)cc1. Methanol, CO, and sulfuric acid, OS(=O)(=O)O, effect Fischer esterification:



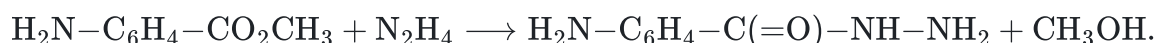
The amino and carboxyl-derived substituents remain para throughout. Water is O.

Potassium carbonate, [K+].[K+].[O-]C(=O)[O-], neutralizes the acid during work-up, giving the free amino ester **A**. The acid-neutralization balance is



Here potassium sulfate is [K+].[K+].[O-]S(=O)(=O)[O-], and carbon dioxide is O=C=O.

Hydrazine, NN, then attacks the ester carbonyl. Nucleophilic acyl substitution replaces methoxy by hydrazino, producing **B**:



Thus **B** contains two primary amino groups: the aromatic amino group and the terminal hydrazide amino group.

TMTD, tetramethylthiuram disulfide, has SMILES CN(C)C(=S)SSC(=S)N(C)C. The supplied transformations account for the two different modifications:

- The aromatic amino group becomes –NH–C(=S)–N(CH₃)₂.
- The terminal hydrazide amino group becomes an isothiocyanate group, giving –C(=O)–NH–N=C=S.

The resulting **B'** is **N-isothiocyanato-4-(3,3-dimethylthioureido)benzamide**,
CN(C)C(=S)Nc1ccc(C(=O)NN=C=S)cc1, exactly matching the supplied intermediate.

For completeness, the supplied reactions give an atom-balanced route to **B'**, and hence **C**. At the hydrazide end, reactions (1) and (3) generate the isothiocyanate and two molecules of **dimethyldithiocarbamic acid**, CN(C)C(=S)S. One acid molecule decomposes by reaction (2), supplying the carbon disulfide needed in reaction (3); the other converts the aromatic amino group into the thiourea by reaction (5).

After cancellation of these intermediates, a balanced net equation is

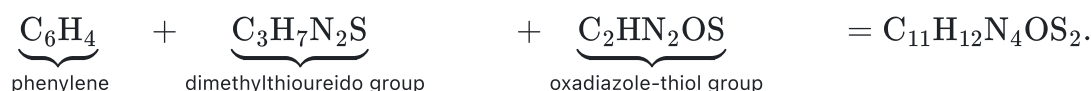


The first reactant is **B**, and the first product is **C**. The "2 equiv." in the experimental scheme specifies reagent loading; the equation above expresses the minimum net consumption along this route.

The small products are dimethylamine, CNC, hydrogen sulfide, S, and elemental sulfur. Carbon disulfide is S=C=S. As in the problem, *S* denotes an atomic equivalent of elemental sulfur; its usual molecular form, octasulfur, is S1SSSSSSS1.

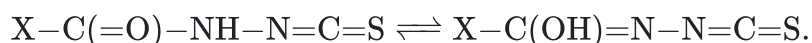
Cyclization of **B'** produces a five-membered ring containing the original carbonyl oxygen, the two hydrazide nitrogens, and the two relevant carbon atoms. This is the **1,3,4-oxadiazole** ring in **C**.

The formula follows directly by adding its structural fragments:



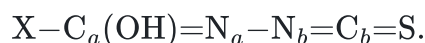
9.2 – Tautomer B'' and electron-flow mechanism

Let **X** denote the 4-(3,3-dimethylthioureido)phenyl group. The relevant tautomerization is



This is **amide–imidic-acid tautomerism**: the acyl nitrogen loses its proton, oxygen gains that proton, and the carbonyl double bond is replaced by a carbon–nitrogen double bond. Acid/base-assisted proton transfer can accomplish this change.

For the cyclization, label the original carbonyl carbon C_a , its adjacent nitrogen N_a , the terminal nitrogen N_b , and the isothiocyanate carbon C_b . The chain in **B''** is therefore



The precise curly-arrow sequence from **B''** is:

1. **Ring closure**: Draw an arrow from a lone pair on the hydroxyl oxygen to C_b . Simultaneously, draw an arrow from the $C_b=\text{S}$ π bond onto sulfur. This forms the five-membered ring with atom order



2. The resulting **cyclic oxonium–thiolate zwitterion** has SMILES

CN(C)C(=S)Nc1ccc(C2=NN=C([S-])[OH+]2)cc1. Oxygen bears a positive charge and still carries hydrogen; the exocyclic sulfur bears a negative charge.

3. **Proton transfer**: Draw an arrow from the negatively charged sulfur to the oxygen-bound hydrogen, and an arrow from the $\text{O}-\text{H}$ bond back to oxygen. A proton shuttle may mediate this transfer. The product is the neutral oxadiazole-2-thiol **C**.

The configuration specified for **B''** places the hydroxyl oxygen and the continuing nitrogen chain on the same side of the imidic C=N bond, allowing this five-membered closure.

Direct formation from B' is also possible. The carbonyl oxygen attacks C_b , while the $C_b=S$ π electrons move to sulfur. The resulting **carbonyl-derived cyclic oxonium-thiolate** is CN(C)C(=S)Nc1ccc(C2=[O+]C([S-])=NN2)cc1.

Transfer of the acyl N-H proton to sulfur, followed by donation of the nitrogen lone pair into the C_a-N_a bond and movement of the $C_a=O$ π electrons onto oxygen, gives the same **C**.

The thiol form of **C** is tautomeric with **5-[4-(3,3-dimethylthioureido)phenyl]-1,3,4-oxadiazole-2(3H)-thione**, CN(C)C(=S)Nc1ccc(C2=NNC(=S)O2)cc1. In that representation, the proton is on ring nitrogen and the exocyclic sulfur is double-bonded to carbon.

9.3 — Identification of E and F

From this point, write Ar for the 4-R-phenyl group. In the thiol representation used above, **R** is the 5-sulfanyl-1,3,4-oxadiazol-2-yl substituent.

Hydrogen chloride, Cl, promotes cleavage of the dimethylthiourea group in **C**. Protonation traps the departing dimethylamine as **dimethylammonium chloride**, C[NH2+]C.[Cl-]:



Thus **D** is **5-(4-isothiocyanatophenyl)-1,3,4-oxadiazole-2-thiol**, S=C=Nc1ccc(-c2nnc(S)o2)cc1.

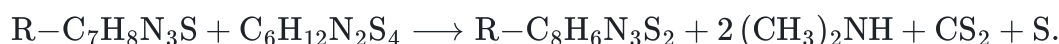
Hydrazine attacks the electrophilic carbon of the isothiocyanate. Proton transfer gives the thiosemicarbazide **E**, without elimination of a small molecule:



Treatment of **E** with TMTD converts its terminal $-\text{NH}_2$ group into $-\text{N}=\text{C}=\text{S}$. The intermediate is **N-isothiocyanato-N'-(4-R-phenyl)thiourea**, *c1ccc(NC(=S)NN=C=S)cc1.

This intermediate cyclizes analogously to **B'**, but the original thiocarbonyl **sulfur** now becomes the ring heteroatom. The product therefore contains a **1,3,4-thiadiazole** ring, giving **F**.

An atom-balanced net equation, with the generated dimethyldithiocarbamic acid written in its decomposed form, is



The formula of **F**, excluding unchanged R, is

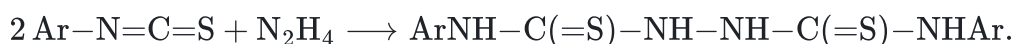


as required.

The corresponding thione tautomer is **5-[(4-R-phenyl)amino]-1,3,4-thiadiazole-2(3H)-thione**, *c1ccc(NC2=NNC(=S)S2)cc1.

9.4 — Identification of D' and the addition-order effect

Both nitrogen atoms of hydrazine can react with isothiocyanate molecules. Addition of two equivalents of **D** gives



This is **D'**, the bis-adduct specified in the answers.

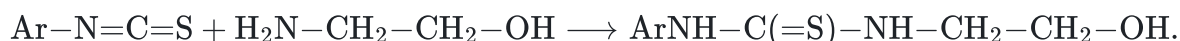
Its formula contains two para-disubstituted phenyl groups, two thiocarbonyl carbons, and four NH groups:



When **D** is added slowly to excess hydrazine, an incoming molecule of **D** preferentially encounters free hydrazine, forming **E**. When hydrazine is added to a solution rich in **D**, the initially formed **E** can react again through its remaining terminal amino group, producing **D'**.

9.5 — Identification of G

Ethanolamine, **2-aminoethan-1-ol**, has SMILES NCCO. Its amino group attacks the isothiocyanate carbon more readily than its hydroxyl group. Addition and proton transfer give **G**:



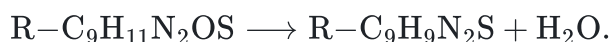
No atoms are lost. The formula, excluding R, is consequently



9.6 — Classification of the heterocyclic products

The catalyst, *p*-toluenesulfonic acid, has SMILES Cc1ccc(S(=O)(=O)O)cc1.

Formation of the selected sulfur-containing products can be balanced as dehydration:



Formation of the oxygen-containing product **H₃** instead corresponds to loss of hydrogen sulfide:



9.6(i): Different molecular formulae — **H₁** and **H₃**.

H₁ contains sulfur and has formula $R-C_9H_9N_2S$. **H₃** contains oxygen in its place and has formula $R-C_9H_9N_2O$. Their molecular formulae therefore differ.

9.6(ii): Constitutional isomers — **H₁** and **H₂**.

Both have formula $R-C_9H_9N_2S$, but their atom connectivity differs:

- In **H₁**, both nitrogen atoms are ring members, and sulfur is an exocyclic thione sulfur.
- In **H₂**, sulfur and one nitrogen are ring members, while the aryl-bearing nitrogen is exocyclic.

They are therefore constitutional isomers.

9.6(iii): Stereoisomers — **H₅** and **H₇**.

Both have the same thiazolidine-ring connectivity and an exocyclic $C=N-Ar$ bond. They differ in configuration about that double bond.

At the imine carbon, sulfur has higher CIP priority than nitrogen. At the imine nitrogen, the aryl group has higher priority than the lone-pair position. In the supplied drawings:

- **H₅**: The aryl group and ring sulfur are on the **same side** of the exocyclic double bond, giving the **Z** configuration.
- **H₇**: They are on **opposite sides**, giving the **E** configuration.

The directional bonds in their answer SMILES encode this distinction.

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