W-CC

CODS
WINTER CHEMISTRY OLYMPIAD
Silver Tier

TEAM NAME			
DATE		PROCTOR'S NAME	
CIN			

Team Round (Free Response) January 16 – January 19, 2025
Maximum: 2 hours

Additional Materials: Answer Sheet, PEC Packet or USNCO Data Sheet

READ THESE INSTRUCTIONS FIRST

You are allowed to use only a pen to write the answer.
Do not use staples, paper clips, glue or correction fluid.
Write your name, date, CIN, and your proctor's name in the spaces at the top of this page.

This examination has **6 problems**. You may solve the problems in any order.
You will have **2 hours** to solve all problems.

Write your answers on the answer sheet provided.
Read the instructions on the answer sheet very carefully.

All results must be written in the appropriate answer boxes on the **answer sheets**. Write relevant calculations in the appropriate boxes when necessary. Full marks will be given for correct answers only when your work is shown, unless explicitly stated otherwise.

Use the back of the question sheets if you need scratch paper. Remember that answers written outside the answer boxes will not be graded.

You must stop working when the **STOP** command is given. Failure to stop writing will lead to the nullification of your examination.

The use of an approved, non-programmable scientific calculator is expected, where appropriate.
The number of marks is given in the table at the top of each question.

This document consists of **31** printed pages.

Problems & Grading Information

	Title	Author(s)	Total score	Percentage
1	Geometry Dash!	Pin-Jui Lin	21.5	16
2	Onsens	Dillion Lim and Ranen Yong	17	16
3	Curvy potentials, and other titration fun	Daniil Kargin	50	16
4	I'm a firestarter, a twisted firestarter	Pin-Jui Lin	28	17
5	Cyclodextrins	Ranen Yong	55	21
6	Nice-smelling Chemistry	Ranen Yong	38	14
		Total		100

Authors:

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- Dillion Lim, Singapore
- Pin-Jui Lin, Taiwan
- Ranen Yong, Singapore
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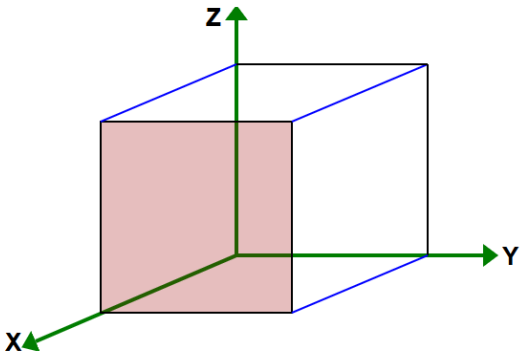
Problem 1 (16% of total)	Question	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	Total
	Points	3	3	2	1	2	1.5	3	3	3	21.5

Problem 1: Geometry dash!

by Pin-Jui Lin (nightlight_1201), Taiwan

Part 1: Miller index

The Miller indices (hkl) are a set of integers describing planes' orientation within a crystal lattice. These indices are determined by taking the reciprocals of the intercepts a plane makes with the crystal axes and reducing them to the smallest integers. The following is a simplified procedure for determining the Miller indices, specifically for a cubic crystal system (a unit cell with dimensions $a \times a \times a$). Consider the following example:



Step 1: Identify the intercepts on the *x*, *y*, and *z* axes

Determine where the plane intersects the crystal axes. For example, if the plane intersects the x-axis at x = a (point (a, 0, 0)) and is parallel to the y- and z-axes, the intercepts are: a, ∞, ∞.(Parallel axes are considered to have intercepts at infinity ∞.)

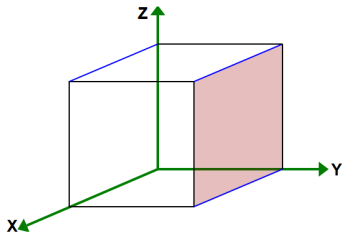
Step 2: Convert to fractional coordinates

Divide each intercept by the corresponding unit cell dimension. For a cubic unit cell, divide by the side length a. So Fractional intercepts are (a/a, ∞/a, ∞/a) = (1, ∞, ∞)

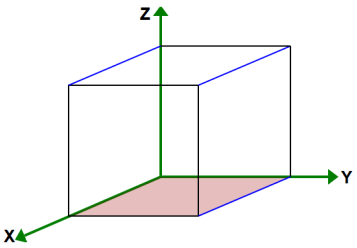
Step 3: Take the reciprocals of the fractional intercepts

Calculate the reciprocals of the fractional intercepts to obtain the Miller indices. Miller indices are written in parentheses with no spaces between numbers. Negative values (such as –1) are indicated by an overbar (such as $\bar{1}$). Hence, the Miller index is (100).

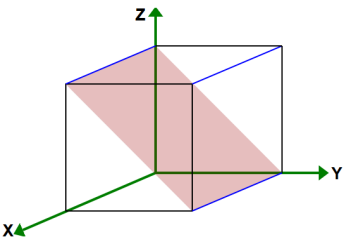
1.1 **Determine** the Miller indices for planes 1 to 3 in the diagram below.



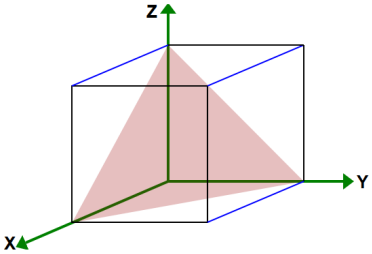
(010)



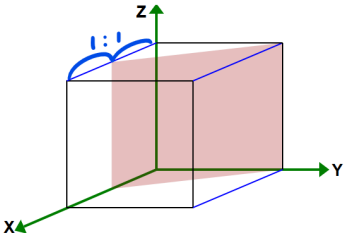
(00$\bar{1}$)



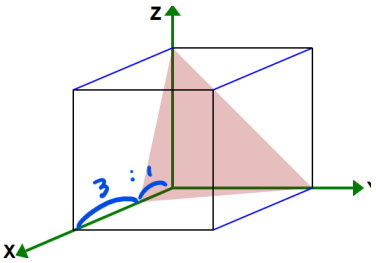
1. _____



4.(111)



2. _____



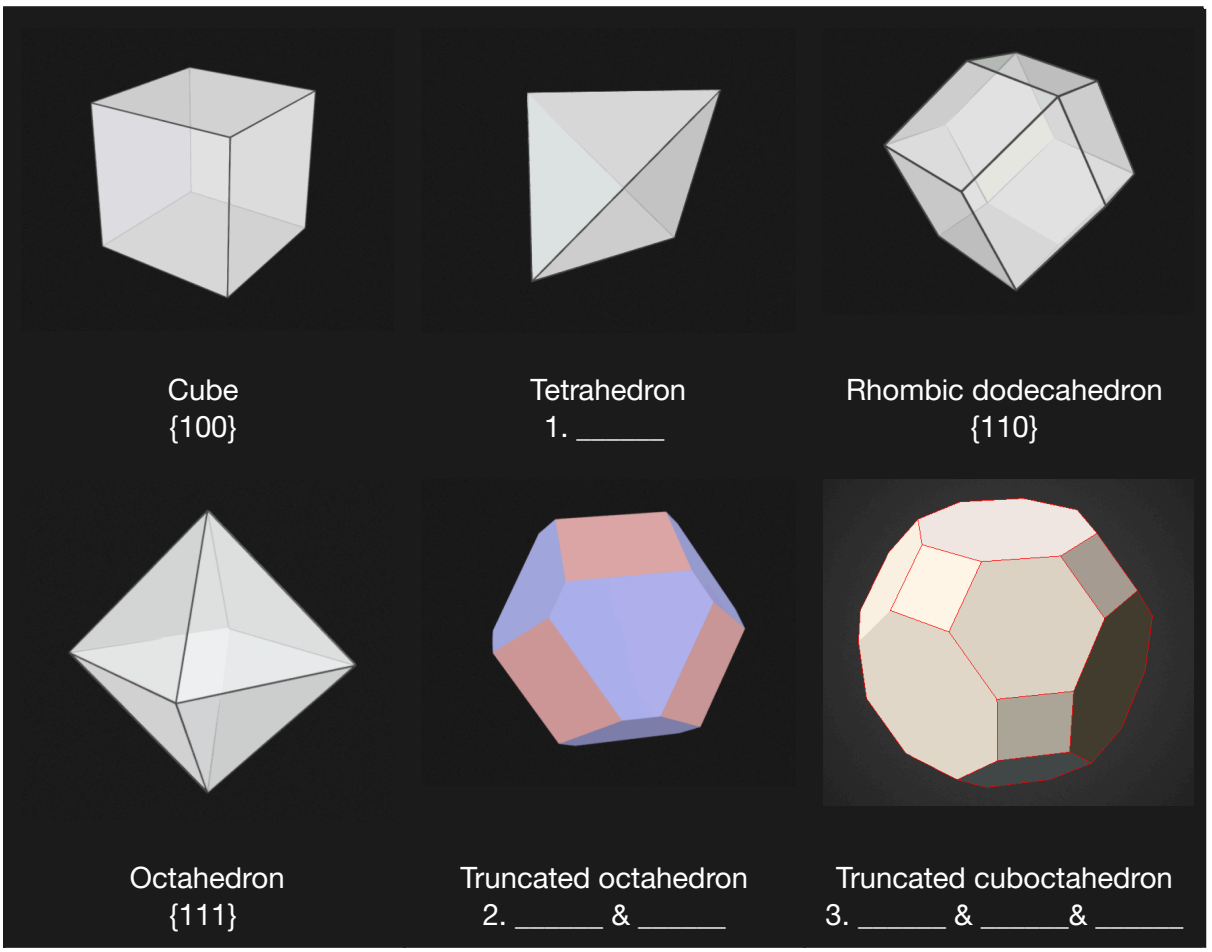
3. _____

Part 2: Crystal form

A crystal form refers to a set of crystal faces that are symmetrically related. To designate a crystal form (which can include multiple equivalent faces), we use the Miller Index notation {hkl}, often called a form symbol. For example,

$$(100), (010), (001), (\bar{1}00), (0\bar{1}0), (00\bar{1}) \in \{100\}$$
$$(113), (1\bar{1}3), (11\bar{3}), (1\bar{1}\bar{3}), (\bar{1}13), (\bar{1}\bar{1}3), (\bar{1}1\bar{3}), (\bar{1}\bar{1}\bar{3}) \in \{113\}$$
$$(111), (11\bar{1}), (1\bar{1}1), (1\bar{1}\bar{1}), (\bar{1}11), (\bar{1}\bar{1}1), (\bar{1}\bar{1}1), (\bar{1}\bar{1}\bar{1}) \in \{111\}$$

1.2 **Identify** all crystal forms present in solids 1 to 3.



[Turn Over

Part 3: Seed-mediated synthesis of gold nanoparticles

Seed-mediated synthesis is widely used to produce gold nanoparticles (AuNPs). It is divided into two steps: seed formation and growth phase.

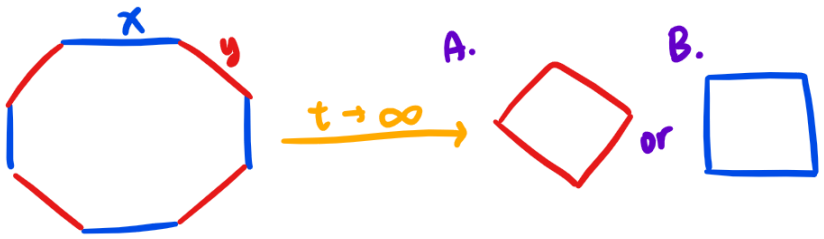
In the seed formation step, gold ions (Au^{3+}) are rapidly reduced into small, uniform nanoparticles (~3–7 nm) using a strong reducing agent like **X** in the presence of stabilizers such as cetyltrimethylammonium bromide (CTA-Br) or sodium citrate.

In the growth phase, **Y** is commonly used as the reducing agent. **Y** first reduces Au^{3+} to Au^{+} rapidly, but the subsequent reduction of Au^{+} to metallic gold (Au^{0}) is much slower, especially at low pH values. This slow reduction ensures that gold deposition occurs only on the surface of seed particles, which act as catalysts for reducing Au^{+} to Au^{0}. Without the catalytic surface provided by the seeds, the reduction of Au^{+} to Au^{0} is negligible.

1.3 Given that **X** and **Y** are either ascorbic acid or sodium borohydride, **deduce** what **X** and **Y** are.

Part 4: Kinetic control

Consider an imaginary 2D octagonal crystal with alternating fast- and slow-growing edges. The octagonal crystal is unstable and will eventually transform the crystal into a more stable shape over time, such as a rhombus or a square.



1.4 If a crystal grows faster along the y-edges than the x-edges, **determine** the final shape that the octagonal crystal will develop into.

Consider a 3D gold nanocube with only {100} facets (where facets refer to the faces of the nanostructure).

1.5 If metallic gold is deposited only onto the {100} facets, **determine** the final shape that this particle will grow into (Hint: see problem 1.2)

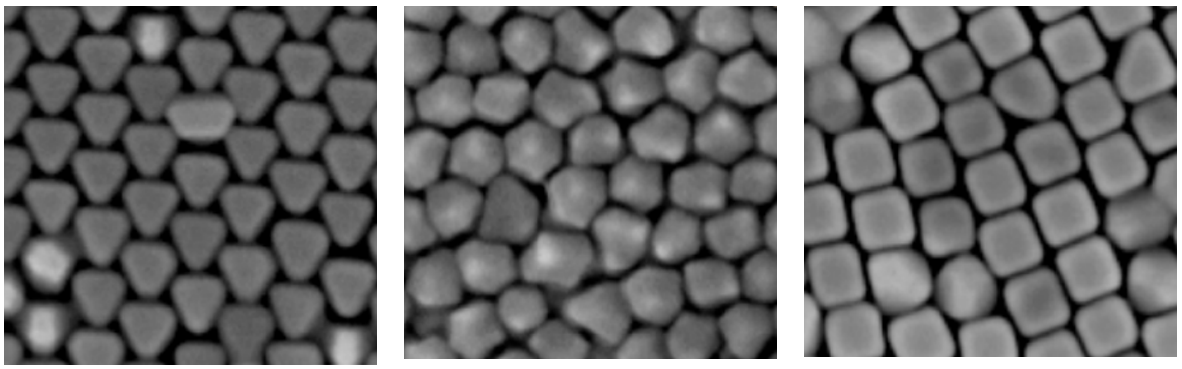
It is known that gold adopts the face-centered cubic structure (fcc),

1.6 **Draw** the (100), (111), and (110) facets of a gold unit cell. Additionally, **determine** the number of atoms on each facet per unit cell. (Hint: see problem **1.1**)

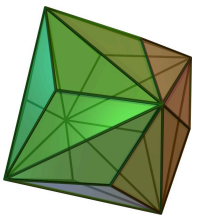
1.7 Consider the {100}, {111}, and {110} facets in a gold nanoparticle. **Rank** these facets in order of their thermodynamic stability and briefly **explain** your reasoning.

Here are SEM images of reaction products obtained from growth solutions containing 10 mM CTA-Br (cetyltrimethylammonium bromide) and varying concentrations of **Y**: (A) 0.5 mM, (B) 2.0 mM, and (C) 10.0 mM.

1. 2. 3.



1.8 **Label** each image as (A), (B), or (C), and **identify** the shape of the nanoparticles observed in each image. (Hint: the shape to the right is called trisoctahedron)



Different concentrations of halides can significantly influence the growth rate of gold nanoparticles. Below is some data that may be useful.

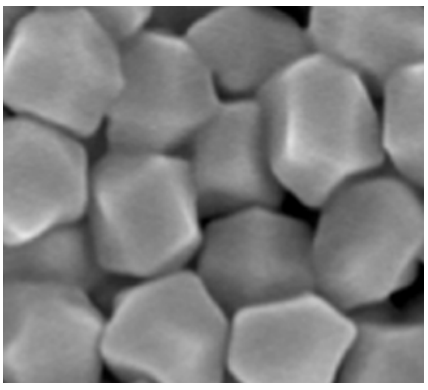
standard electrode potential	E° (V)
$[AuCl_2]^-$	1.15
$[AuBr_2]^-$	0.96
$[AuI_2]^-$	0.58

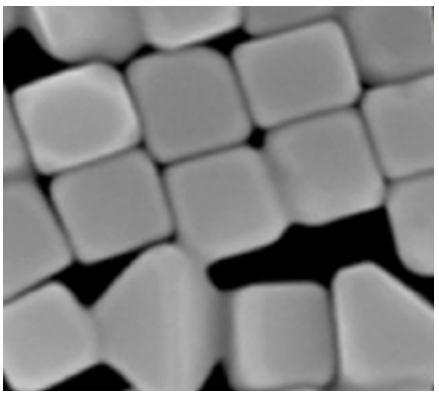
$$\text{solubilities: } [AuCl_2]^- > [AuBr_2]^- > [AuI_2]^-$$

The relative binding strength of the halides to the Au nanoparticle surface:

$$\text{binding strength: } I^- > Br^- > Cl^-$$

Here are SEM images of reaction products obtained from growth solutions containing 50 mM CTA-Cl, 0.5 mM $HAuCl_4$,1.0 mM ascorbic acid, and varying concentrations of NaBr : (A) 0.0 mM and (B) 5.0 mM.

1. 

2. 

1.9 **Label** each image as (A) or (B), and **identify** the shape of the nanoparticles observed in each image.

Problem 2 (16% of total)	Question	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9	Total
	Points	1	9	3	3	1	1	1	3	1	20

Problem 2: Onsens…

By Dillion Lim and Ranen Yong, Singapore

Authors' Note: *It is* ***highly recommended*** *for different members of the team to work on different parts of the problem at the same time. The problem has been structured such that individual parts can largely be done independent of each other, except for the ending.*

Fig. 2.1: rymh's quirky obsession with onsens

Rymh received an unknown package in his mail. Despite the risk of getting Anthrax from frustrated ACOT participants, he believed that it was the Japanese onsen concentrate, *Yunomoto*, that he ordered from a Yahoo! auction on Buyee. So he rips the package open — fortunately, there's no Anthrax in there.

When preparing the bath for the first time, rymh accidentally spilled a few drops onto his fingers. The concentrate turned out to be pretty corrosive, as rymh found out the hard way (it stung his fingers).

Curious, rymh decided to search up the ingredients list to figure out the ingredient responsible for the concentrate's corrosive properties. However, a quick google search in Japanese brings up only two active ingredients in the product:

■有効成分
多硫化態硫黄・酸化カルシウム

■ **Active ingredients**
Polysulfide sulfur/calcium oxide

**Powered by Google Translate.*

Rymh figures that the mixture cannot just be made from these two ingredients alone, and decides to conduct some tests on it to ascertain the identity of other ingredients in there. Of course, "polysulfide sulfur" also sounds very suspicious, so he decides to determine the *actual* sulfur-containing compounds present in the concentrate.

Introduction: Strange Smells and White Powder

Before even beginning proper tests to figure out the identity (or identities) of any compounds present, he first decided to enjoy a good, long, soak in the bathtub. Of course, he added a capful of *Yunomoto* to the bathtub, as per the directions stated on the packaging. There was a faint but familiarly unpleasant smell, but he paid it no mind and went ahead. *After all, since it's one of the highest-rated bath additives in Japan, it's probably still safe to use, right?*

When the concentrate was added to the tub, it formed a slightly murky yellowish-green solution. Interestingly, rymh noted that the yellowish-green colour faded, and a white precipitate formed over time.

2.1 **<u>What</u>** is the identity of the compound most likely responsible for the 'faint but familiarly unpleasant smell'?

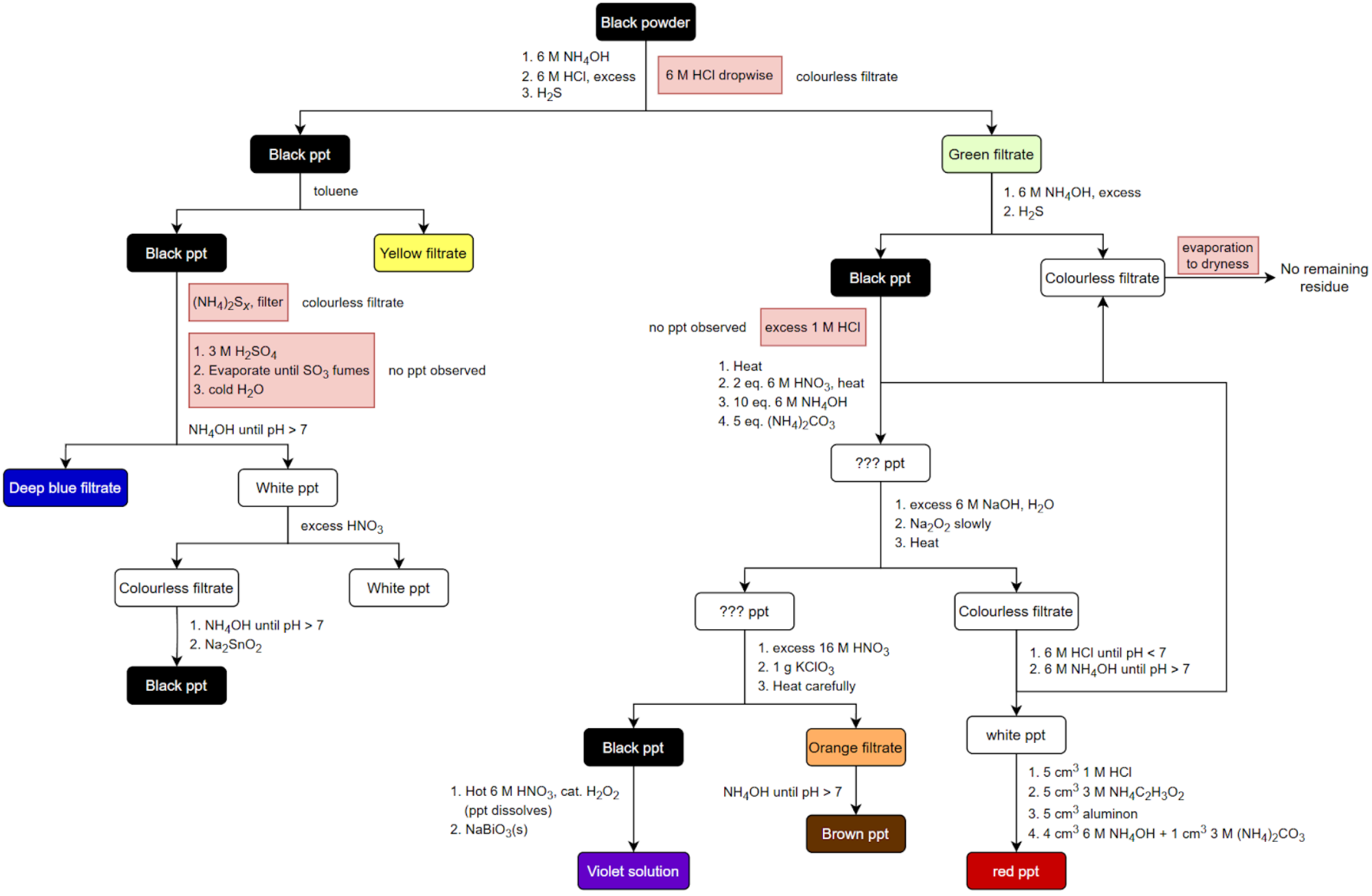
Before stepping into the bath, rymh decided to scoop a sufficiently large sample of the now-white and murky solution. He poured the mixture over a large coffee filter, and left it alone while he enjoyed the nice bath.

After finishing his bath, he came back to the filtration setup and discovered that the mixture separated into a colourless filtrate and a white residue. He washed the white residue with deionized water and left it to dry for a full day.

Part 1: Elucidation Fun

By the following day, the white residue had dried into a white powder. Knowing that Ca^{2+} was present in the sample, he decided to separate it out before performing further tests, which he thankfully managed to do (with the help of some black magic).

Upon strong heating, the white powder turned black, and there was a notable loss in mass. To determine the identity of the ions present in the sample, he then performed a series of tests as shown on the next page.


Black powder
1. 6 M NH_4OH
2. 6 M HCl, excess
3. H_2S
6 M HCl dropwise
colourless filtrate
Black ppt
toluene
Black ppt
Yellow filtrate
$(NH_4)_2S_x$, filter
colourless filtrate
1. 3 M H_2SO_4
2. Evaporate until SO_3 fumes
3. cold H_2O
no ppt observed
NH_4OH until pH > 7
Deep blue filtrate
White ppt
excess HNO_3
Colourless filtrate
White ppt
1. NH_4OH until pH > 7
2. Na_2SnO_2
Black ppt
Green filtrate
1. 6 M NH_4OH, excess
2. H_2S
Black ppt
Colourless filtrate
evaporation to dryness
No remaining residue
no ppt observed
excess 1 M HCl
1. Heat
2. 2 eq. 6 M HNO_3, heat
3. 10 eq. 6 M NH_4OH
4. 5 eq. $(NH_4)_2CO_3$
??? ppt
1. excess 6 M NaOH, H_2O
2. Na_2O_2 slowly
3. Heat
??? ppt
Colourless filtrate
1. excess 16 M HNO_3
2. 1 g $KClO_3$
3. Heat carefully
1. 6 M HCl until pH < 7
2. 6 M NH_4OH until pH > 7
Black ppt
Orange filtrate
white ppt
1. Hot 6 M HNO_3, cat. H_2O_2
(ppt dissolves)
2. $NaBiO_3$(s)
NH_4OH until pH > 7
1. 5 cm^3 1 M HCl
2. 5 cm^3 3 M $NH_4C_2H_3O_2$
3. 5 cm^3 aluminon
4. 4 cm^3 6 M NH_4OH + 1 cm^3 3 M $(NH_4)_2CO_3$
Violet solution
Brown ppt
red ppt

[Turn Over

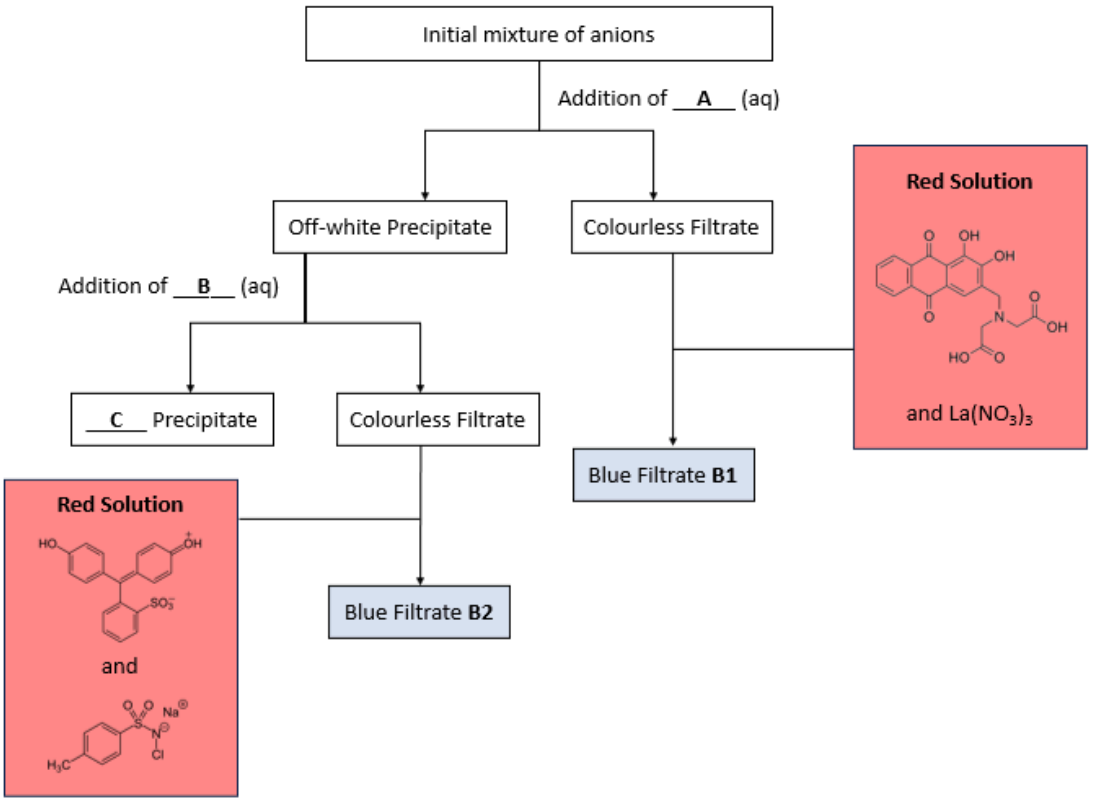
He determined that the heated black powder consisted of a relatively inert macromolecule and 5 other cations of different elements, one of which is Bi^{3+}.

2.2 **Determine** the identities of the 4 remaining cations present in the black solid, explaining your reasoning clearly. **What** is the most likely identity of the macromolecule present?
[Hint: Don't overthink about why the pre-heated powder is white.]

2.3 **State** a possible reason for the presence of the yellow filtrate in the scheme, and **cite** a piece of evidence from the scheme to support your reasoning. **Write** down the relevant equation(s) responsible for its formation.

Part 2: More elucidation fun

It is known that onsens should probably contain bromide, iodide and fluoride anions. So, rymh proceeded to confirm their presence using the scheme below.



2.4 If it is known that Br^-, I^- and F^- are all present in the initial mixture, **fill in the blanks** for **A**, **B** and **C** respectively.

To arrive at blue filtrate **B1**, the colourless filtrate was mixed with a red solution comprising alizarin complexone and $La(NO_3)_3$.

2.5 **Suggest** the product formed (yielding the red solution) when alizarin complexone and $La(NO_3)_3$ is mixed together.

2.6 Hence, **suggest** the identity of the blue filtrate **B1**, given that a **single** ligand exchange occurred.

To arrive at blue filtrate **B2**, the colourless filtrate was mixed with a red solution comprising phenol red and chloramine-T.

2.7 **Suggest** the product formed when chloramine-T reacts with the colourless filtrate.

2.8 Hence, **draw** the mechanism for the formation of the blue filtrate **B2**.

It is known from the research done by Serbulea and Payyappallimana (2012) that the composition of onsens are:

Name of the substance	**Quantity / kg**
Lithium (Li^+) ions	1 mg
Strontium (Sr^{2+}) ions	10 mg
Barium (Ba^{2+}) ions	5 mg
Iron ($Fe^{2+/3+}$) ions	10 mg
Manganese (Mn^{2+}) ions	10 mg
Bromide (Br^-) ions	5 mg
Iodide (I^-) ions	1 mg
Fluoride (F^-) ions	2 mg

2.9 Based on the information above, **suggest** whether the onsen bath additives accurately represent the composition of a real onsen.

Epilogue

After this adventure, rymh was slightly addicted to Onsen bath salts. He then notices that when adding Onsen balt salts to water, some white precipitate forms. He then aspires to investigate the white precipitate known as 湯の花 (Yunohana), typically found in Onsens, in more detail. To continue with his adventures, see Bronze Tier, Team Round, Problem 2! For a slightly buffed version of this question, see Gold Tier, Team Round, Problem 3!

Problem 3 *(16% of total)*	Question	3.1	3.2	3.3	3.4	3.5	Total
	Points	12	12	10	8	8	50

Problem 3: Curvy potentials, and other titration fun

by Daniil Kargin (kuravax#1810), Latvia / Singapore

Note: YOU DO NOT NEED CALCULUS to solve this problem, basic log property knowledge and solving quadratic equations is sufficient.

How to improve one's titration experience? Correct, stick a bunch of electrodes in your titration flask and get even more anxiety while dealing with your burette!

But don't worry nevertheless, those practical chemists still make it out easily – they just look at a reading until it jumps like crazy. That's the essence of potentiometric titration.

In this problem, we'll discuss some theoretical aspects behind general and specifically potentiometric titration curves, derive a bunch of equations and show a couple nice things about them. Brace for the ride and stay with us!

Let us begin with the simplest example possible. We just mix water and HCl.

3.1 **Derive** an equation that describes the pH of a mixture of V L of c molar HCl solution to V_0 L of pure deionised water. Assume water has an autodissociation constant K_w and HCl dissociates completely.
If you plot this equation as a function of pH / V, you obtain the titration curve graph.
Draw a rough sketch of how the graph behaves.

3.2 **Write** down an equation of a titration curve that describes titration of V_B litres of c_B molar solution of NaOH with V litres of c_A molar solution of HCl. Take that all acids and bases dissociate completely and water autoprotolysis constant is K_w. This looks more like an actual titration curve, plot a quick sketch and indicate the equivalence point!

The math you just did explains and justifies mathematically the commonly known fact of the titration curve having an inflection point at the equivalence point.

3.3 Using the equation you derived in **3.2,** show why a simple titration curve indeed experiences an inflection at equivalence point. **Calculus isn't required – basic algebraic manipulation will suffice.**

Assume we put some reference electrode that doesn't interfere with neither pH, nor [Na^+], nor [Cl^-], and a pH-sensitive electrode in the titration mixture, and measure the potential difference between the electrodes.

3.4 Assuming the same conditions as in **3.2** and using your results from **3.2** and **3.3**, standard potential of reference electrode E_{ref} and standard reduction potential for pH electrode as E^0, **write** down an equation of the curve that describes the measured voltage $U = E - E_{ref}$ as a function of V. At experiment conditions, $\frac{RT}{F} = N$.

Potentiometric curves behave remarkably similar to pH / V titration curves if you have a keen eye.

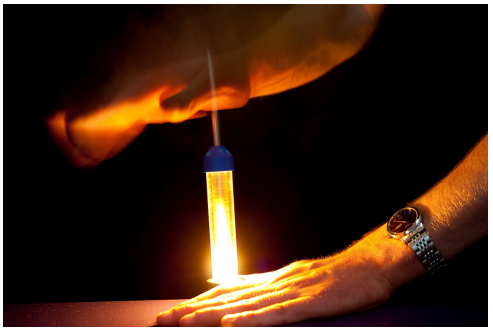
3.5 **Show** that *U* is linearly dependent to pH, i.e. $U = a * pH + b$. Find the linear coefficients. Hint: remember about the fabled 0.0592 factor.

Having done all that, the author hopes you understand much more the maths that dictate titration equilibria and would apply them in many different settings that require solid understanding of the fundamentals.

Problem 4 (17% of total)	Question	4.1	4.2	4.3	4.4	4.5	4.6	4.7	4.8	4.B	Total
	Points	2	2	2	5	3	2	2	10	3	28

Problem 4: I'm a firestarter, a twisted firestarter

by Pin-Jui Lin (nightlight_1201), Taiwan



A fire piston is a simple tool used to create fire through the principle of rapid air compression. It consists of a hollow cylinder and a tightly fitting piston. When the piston is quickly forced into the cylinder, the air inside is compressed nearly adiabatically, causing its temperature to rise dramatically—often reaching over 260 °C (500 °F). This sudden heat ignites a small tinder at the piston's end. The ignited tinder can then be used to start a fire.

This problem examines how the temperature inside a fire piston changes during rapid compression, igniting the tinder. The fire piston is a perfectly adiabatic and frictionless cylinder with a diameter of 1 cm, an initial height of 20 cm, and an initial state of 298 K at 1 atm. The air inside consists of a mixture of 80% nitrogen and 20% oxygen, which behaves ideally and has a constant-volume molar heat capacity of 5/2 R. When a constant force of 50 N strikes the piston, the air undergoes adiabatic compression, causing a significant temperature rise.

4.1 **Explain** why the heat capacity at constant volume is 5/2 R.

4.2 **Calculate** the final pressure of the gas.

4.3 **Determine** the system's sign of work and heat (positive, negative, or zero) during this process, and briefly **explain** your answer.

The change in internal energy of the ideal gas is given by:

$$\Delta U = C_V \Delta T = C_V (T_2 - T_1)$$

where C_v is the constant-volume heat capacity of the entire system, ΔU is the change in internal energy, and ΔT is the temperature change.

When the external pressure is constant, work is calculated as follows:

$$w = -P_{\text{ext}} \Delta V = -P_{\text{ext}} (V_2 - V_1)$$

where P_{ext} is external pressure, and ΔV is the change in volume.

4.4 **Calculate** the final temperature of the gas inside the fire piston.

4.5 **Determine** whether the final temperature of the system will be **higher, lower, or equal** if the compression process is carried out reversibly, assuming the final pressure remains the same as in the process above. **Provide** a brief explanation for your answer.

In the following problems, we investigate the temperature changes during the combustion of a substance inside a fire piston. A stoichiometric amount of solid adamantane ($C_{10}H_{16}$) with respect to the oxygen in the piston ignites upon reaching the equilibrium temperature (as determined in Problem 4.3). Once ignited, the adamantane combusts completely while the external pressure of 50 N remains constant throughout the combustion.

4.6 **Write** down the balance equation for the complete combustion of adamantane ($C_{10}H_{16}$)

4.7 **Calculate** moles of adamantane ($C_{10}H_{16}$) needed to react with all oxygen inside the piston completely

Here is some helpful info for the following problem, assuming heat capacity and enthalpy of combustion are independent of temperature:

$\Delta H_{\text{combustion, } C_{10}H_{16}}$	$-6030\ \text{KJ} \cdot \text{mol}^{-1}$
$\overline{C}_P(H_2O)$	$36.5\ \text{J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$
$\overline{C}_P(N_2)$	$29.1\ \text{J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$
$\overline{C}_P(CO_2)$	$36.9\ \text{J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$

4.8 **Calculate** the temperature after combustion is complete. Ignore the heat capacity of adamantane. If the solution to Problem **4.3** is unavailable, calculate only the temperature difference.
[Hint 1: For the entire system, ΔH = 0 because the fire piston is an adiabatic system]
[Hint 2: How does the enthalpy of a reaction change with temperature?]

4.B Prove that for an adiabatic and isobaric process, the change in enthalpy is zero (dH = 0).

Problem 5 *(21% of total)*	Question	5.1	5.2	5.3	5.4	5.5	5.6	5.7	5.8	Total
	Points	2	7	4	1	1	2	1	4	55
		5.9	5.10	5.11	5.12	5.13	5.14	5.15		
		2	4	8	1	3	10	5		

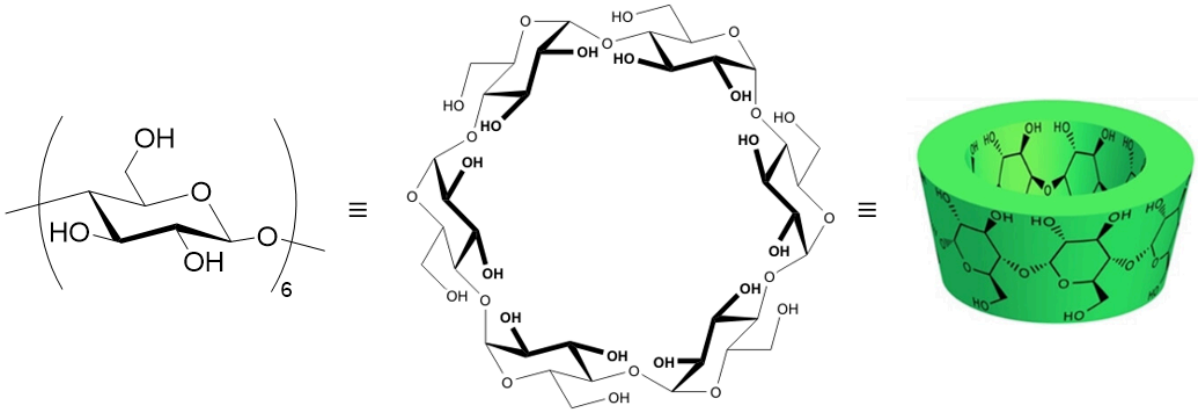
Problem 5: Cyclodextrins

By Ranen Yong, Singapore

Cyclodextrins are a family of cyclic oligosaccharides consisting of glucose subunits joined by *α*-1,4 glycosidic bonds. Cyclodextrins are commonly used in food, pharmaceutical and drug delivery. Typically, cyclodextrins contain a number of glucose monomers ranging from 6 to 8 units in a ring.

Part 1: *α*-cyclodextrin

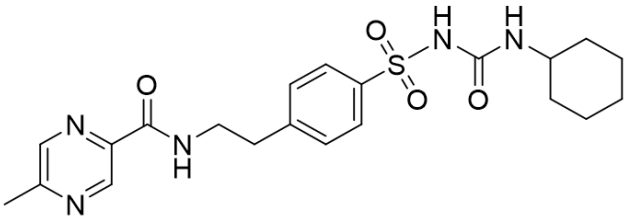
In *α*-cyclodextrin (*α*-CD), the 6 glucose subunits are linked end to end via *α*-1,4 linkages. The resulting three-dimensional structure of *α*-CD has the shape of a tapered cylinder. The structure of *α*-CD is shown below.



It is known that one face of the tapered cylinder of *α*-CD is somewhat hydrophilic, whereas the other face is hydrophobic.

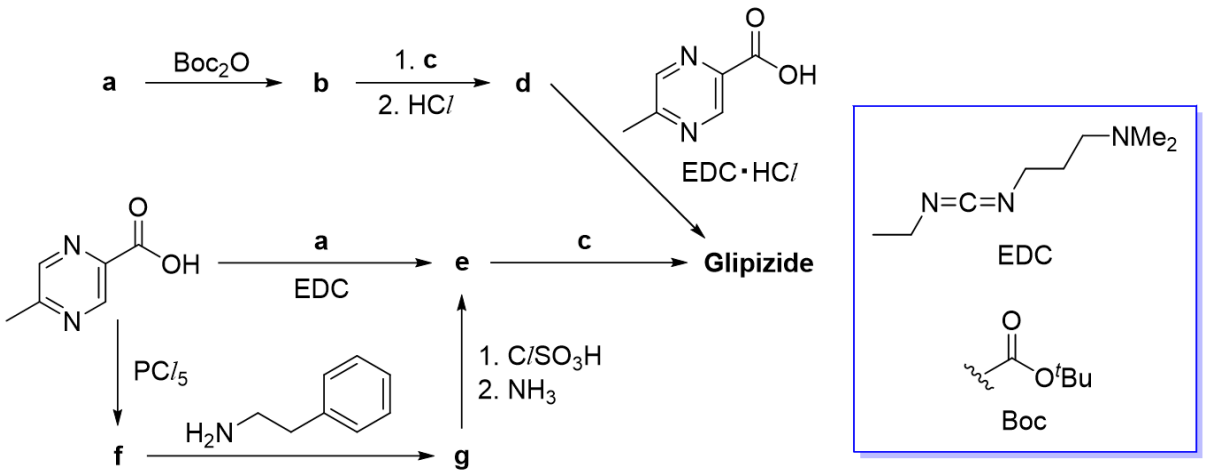
5.1 **State** whether the interior core of *α*-CD is hydrophilic or hydrophobic. Hence, **explain** if *α*-CD is soluble or insoluble in water.

In 2017, researchers Roselet and Kumari found that Glipizide can form inclusion complexes with *α*-CD, in which Glipizide is contained in the cavity of *α*-CD. Glipizide is a second-generation sulfonylurea drug for the treatment of type 2 diabetes mellitus, an endocrinological disorder that causes high blood sugar. Although there are several anti-diabetic agents on the market, sulfonylureas remain one of the most prescribed due to their affordability. The structure of Glipizide is shown below.



Glipizide

Three different synthetic routes for Glipizide are shown in the diagram below.



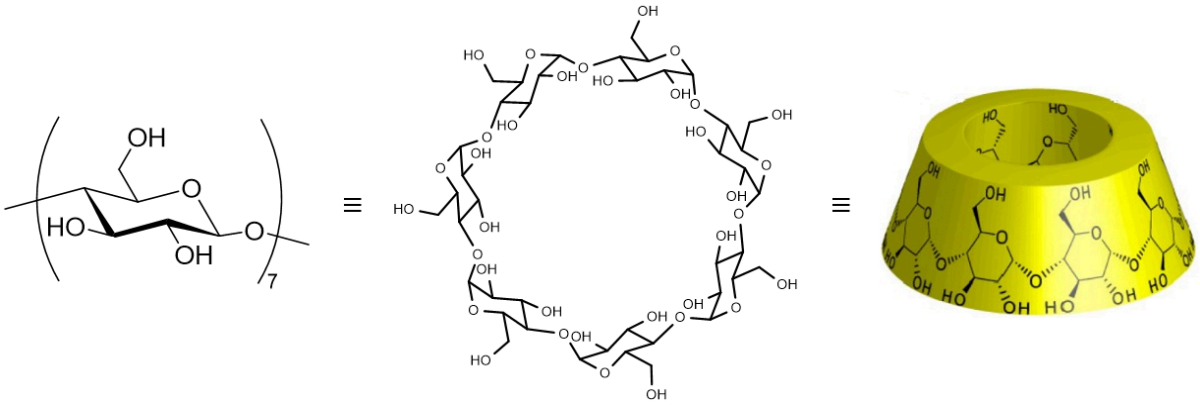
5.2 **<u>Deduce</u>** the structures of compounds **a** to **g**.

5.3 **<u>Draw</u>** the mechanism showing the reaction between compounds **a**, **e** and EDC • HC*l*, showing clearly all side product(s) formed.

5.4 Briefly **<u>explain</u>** the advantage of using an *α*-CD-Glipizide inclusion complex over using just Glipizide alone for the treatment of type 2 diabetes mellitus.

Part 2: *β*-cyclodextrin

β-cyclodextrin (*β*-CD) consists of 7 glucose molecules linked together to form a structure that resembles a truncated cone.

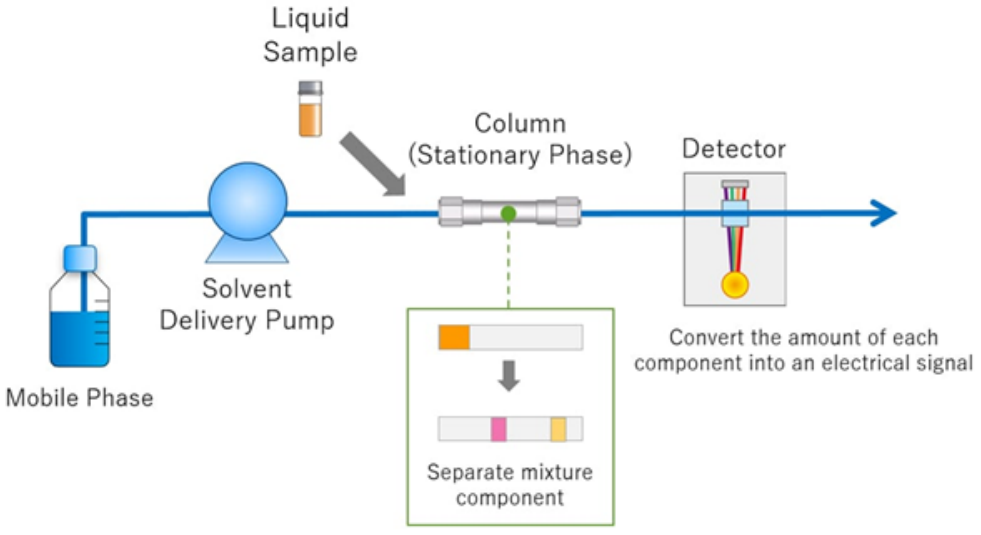


β-CD is a chiral mobile phase additive that can separate two enantiomers of a drug compound by high-performance liquid chromatography (HPLC), such that an optically pure drug can be obtained.

5.5 **Why** is it desirable to use optically pure drugs?

HPLC is a technique in analytical chemistry used to separate, identify, and quantify specific components in liquid mixtures.

HPLC relies on high pressure pumps which deliver mixtures of various solvents (mobile phase). The mobile phase flows through the system, collecting the sample mixture on the way. The mixture is then delivered into a cylinder (column) filled with solid particles made of adsorbent material (stationary phase). Each component in the sample interacts slightly differently with the adsorbent material, causing different migration rates for each component across the column. This leads to their separation as they flow out of the column into a specific detector. This process is illustrated in the diagram below.



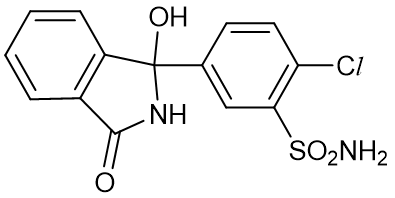
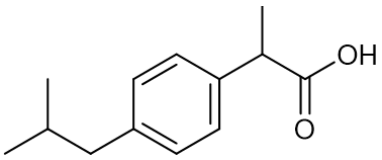
[Turn Over

There are many different types of HPLC. One of the first kinds of HPLC developed was the normal-phase HPLC. In normal-phase HPLC, the stationary phase is polar (usually silica) while the mobile phase is non-polar solvent such as chloroform. The mechanism of separation is liquid-solid adsorption.

5.6 **Suggest** a reason for why normal-phase HPLC cannot separate two enantiomers of a drug molecule.

The separation mechanism of the enantiomers is thought to involve formation of an inclusion complex, in which a molecule is contained in the cavity of *β*-CD. One of the enantiomers can form a more stable complex with *β*-CD than the other. This forms the basis of the separation. This technique is known as the chiral mobile-phase additive (CMPA) technique, where the chiral selector (*β*-CD) is dissolved in the mobile phase while the stationary phase is achiral.

The table below shows the effectiveness of separation of enantiomers of two different drugs using *β*-CD as the chiral mobile phase additive.

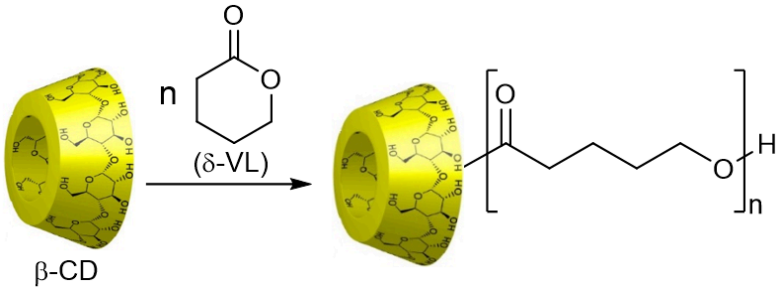
Drug	Effectiveness of separation
 **A**	very effective
 **B**	not effective

5.7 **State** the stereochemical relationship of the inclusion complexes formed between *β*-CD and the respective enantiomers of drug **A**.

5.8 **Suggest** the type(s) of intermolecular force(s) that exist between drug **A** and *β*-CD in an inclusion complex, stating the groups of atoms that are involved in these interaction(s).

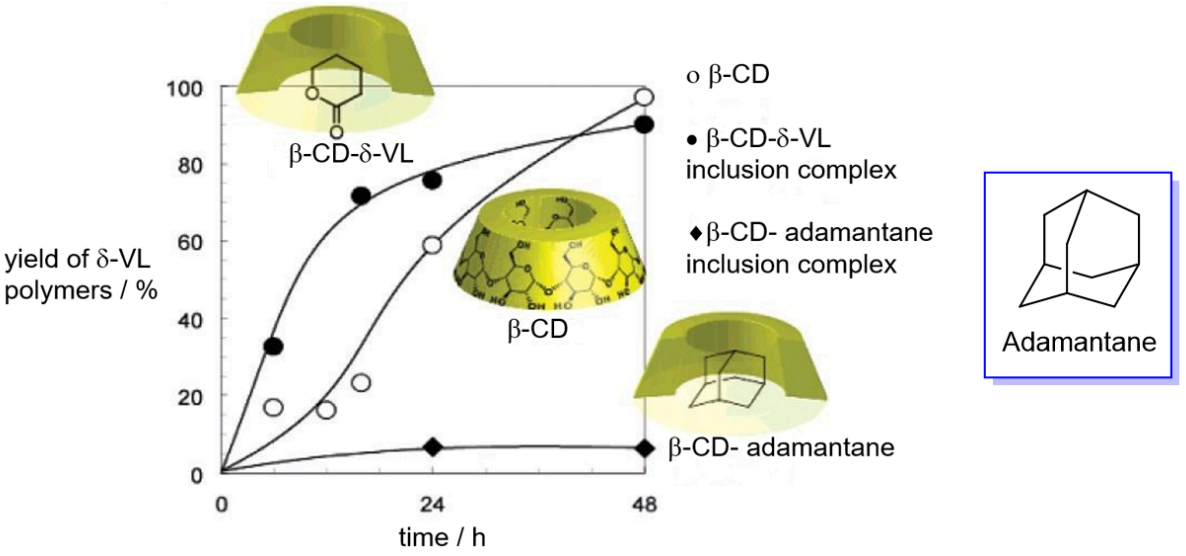
5.9 **Suggest** why enantiomers of drug **B** are poorly separated using *β*-CD unlike drug **A**.

Besides being used in chiral chromatography, *β*-CD can also act as a catalyst to initiate the polymerisation of lactones to give polyesters. The diagram below illustrates the polymerisation of *δ*-valerolactone (*δ*-VL) using *β*-CD as the catalyst.



The catalysis process involves *β*-CD-lactone inclusion complex, similar to the one in the separation of enantiomers, as an initiator for the polymerisation of the lactone.

To show that *β*-CD-lactone inclusion complex acts as an initiator, a series of experiments was carried out by adding different kinds of initiator to *δ*-VL. The diagram below shows a graph of yield of *δ*-VL polymers against time for three different experiments.



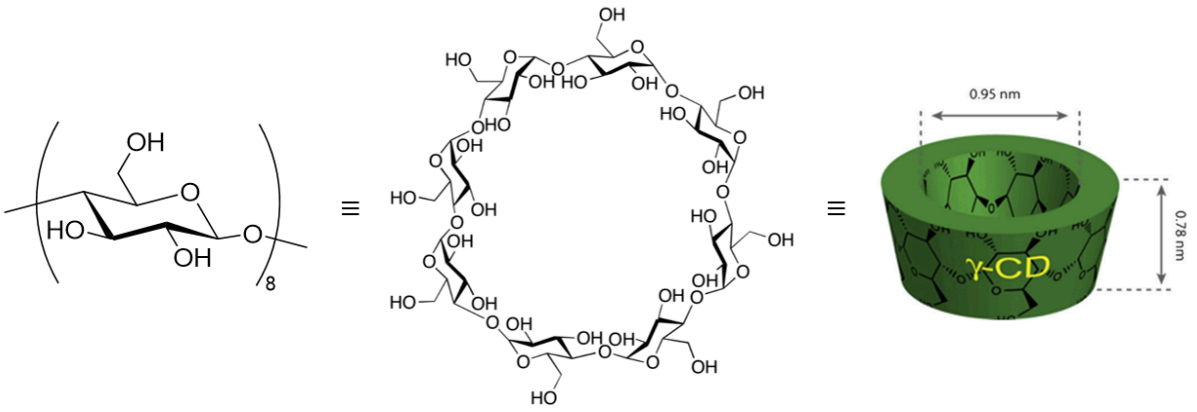
5.10 Use **all** the information in the graph above to **show** that the *β*-CD-*δ*-VL inclusion complex is essential in initiating the polymerisation.

The polymerisation catalysed by *β*-CD goes through many steps, of which the formation of inclusion complex **C** occurred after the initial few steps. The lactone is then attacked by the same *β*-CD, forming a disubstituted *β*-CD. Subsequent reactions will lead to product **D**, where the top chain is analogous to a dimer. This chain will continue to grow, leading to a polyester chain.

5.11 **Draw** the mechanism to illustrate the polymerisation that leads to product **D** from inclusion complex **C**. In your response, you may use an oval to represent *β*-CD.

Part 3: *γ*-cyclodextrin

γ-cyclodextrin (*γ*-CD) consists of 8 glucose molecules linked together to form a structure that resembles a truncated cone.



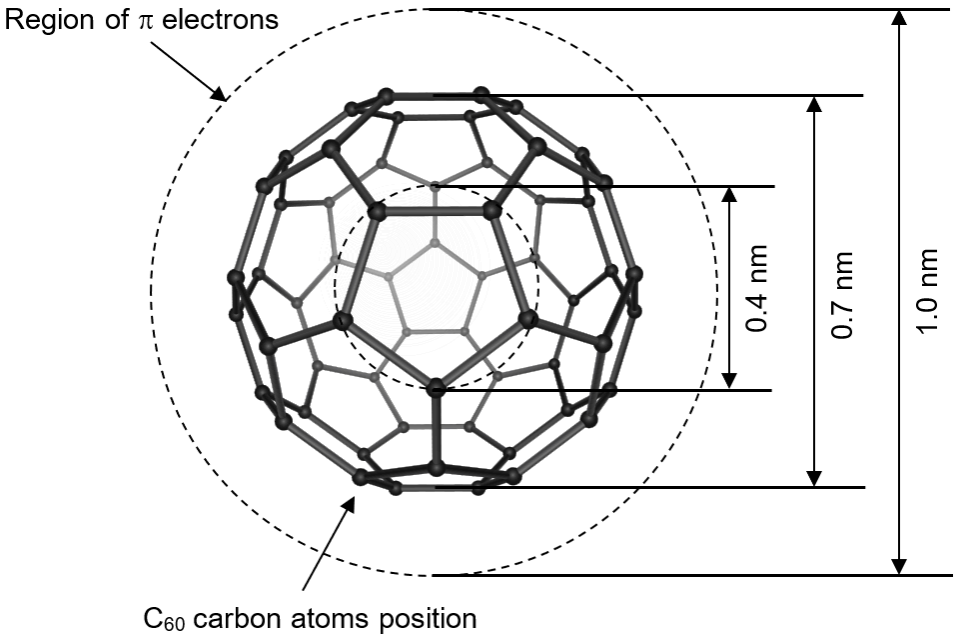
A study by Komatsu et al. found that *γ*-CD is able to form complexes with buckminsterfullerene, C_{60}. This was achieved via high-speed vibrational milling (HSVM).

Ball milling is a mechanical technique that is broadly used to grind powders into fine particles. Traditionally, reactants are generally broken apart using solvent molecules. However, in ball milling, reactants are broken by using mechanical forces.

Recently, solvent-free ball milling in organic synthesis has attracted growing interest, partly due to cost-savings since no solvent is needed.

5.12 **State** another advantage of solvent-free ball milling unrelated to cost-savings.

The dimensions of buckminsterfullerene are shown in the diagram below.

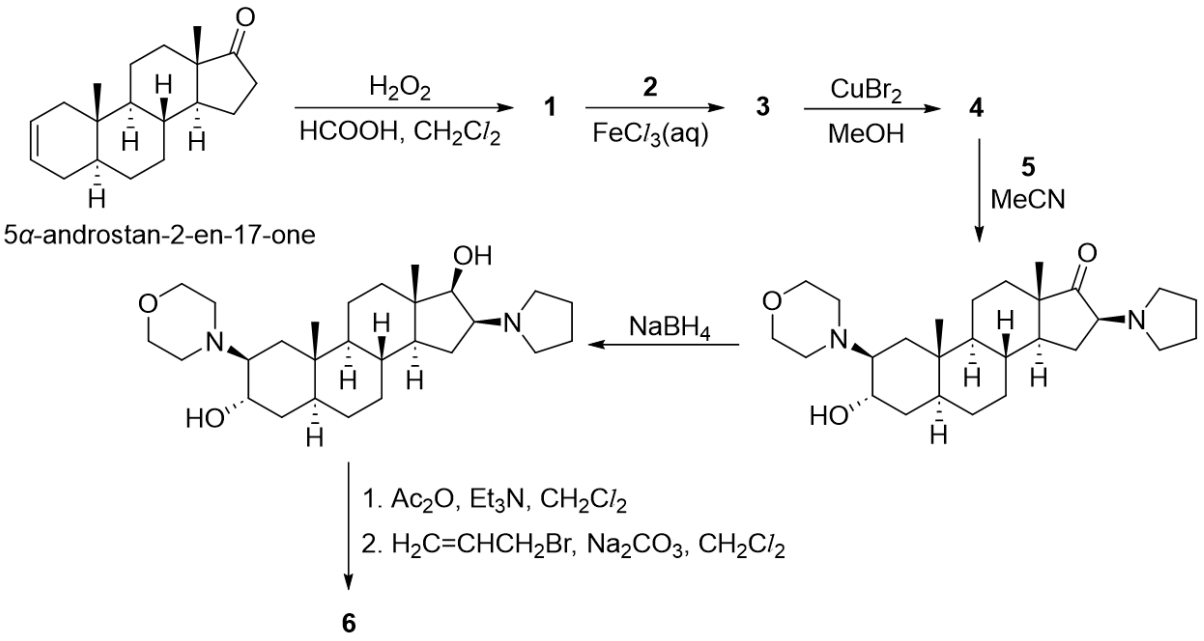


5.13 **Suggest** the stoichiometric ratio in which buckminsterfullerene reacts with γ-CD. **Draw** a well-labelled diagram to illustrate the overall structural appearance of the product formed.

In 2002, Cameron et al. found that modified *γ*-CDs could serve as synthetic host molecules for rocuronium bromide.

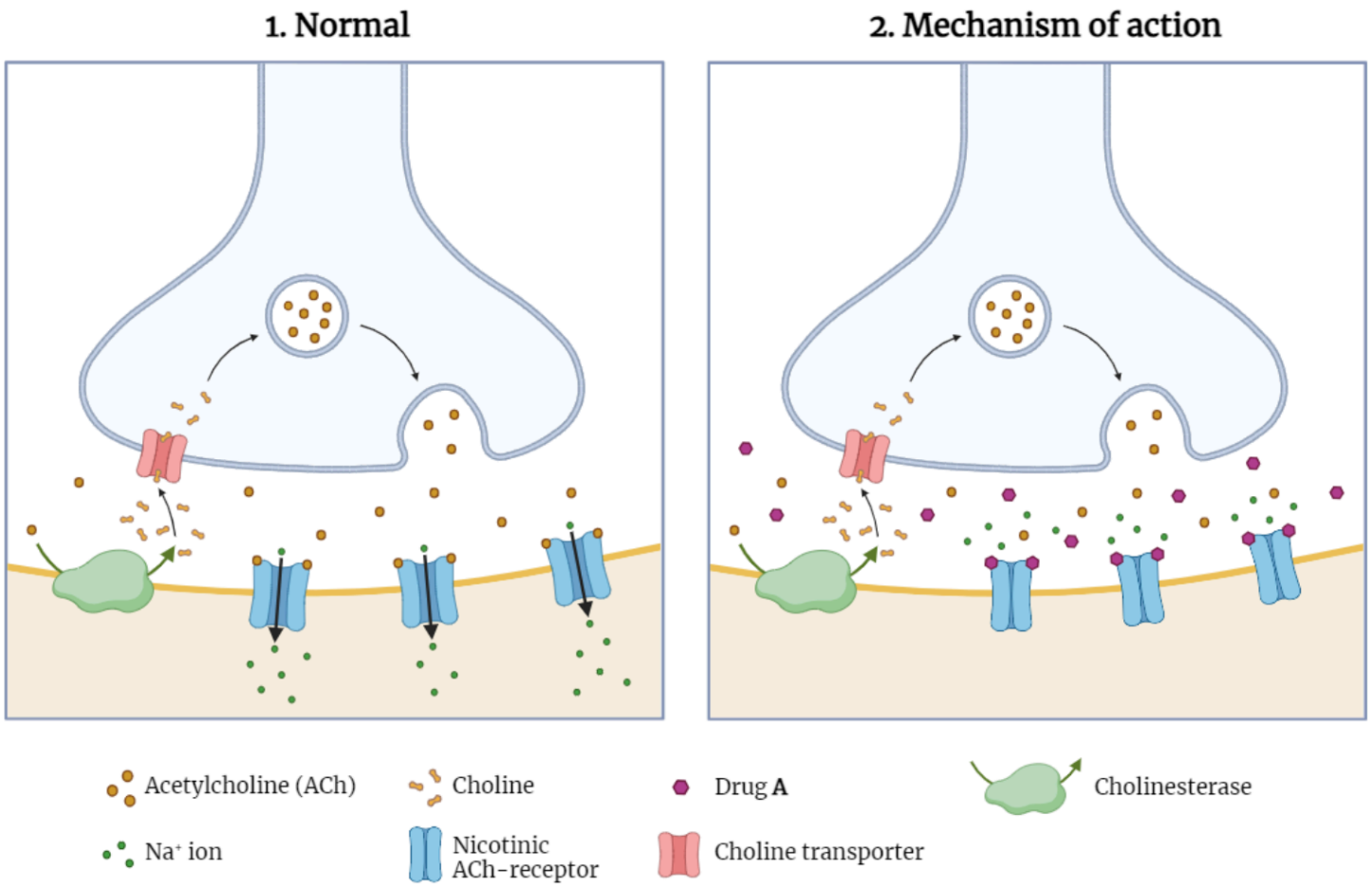
Rocuronium bromide is a non-depolarizing neuromuscular blocker widely used to produce muscle relaxation to help facilitate surgeries. It is one of the many non-depolarising neuromuscular blockers that is used but has the distinct advantage of being fast-acting.

The total synthesis of rocuronium bromide (**6**) is shown below, starting from 5*α*-androstan-2-en-17-one.



5.14 **Draw** the structures of compounds **1** to **6** with stereochemistry.

The mechanism of action of nondepolarizing neuromuscular blockers like rocuronium bromide (labelled 'drug **A**') is shown in the diagram below.



You are given the following further information:

- Acetylcholine (Ach) is a neurotransmitter. Ach causes the conduction of muscle action potential to occur which subsequently induces skeletal muscle contraction.
- Choline is an essential nutrient required to make acetylcholine.
- Nicotinic acetylcholine receptors (nAchR) are receptor polypeptides that respond to acetylcholine.
- Cholinesterase is an enzyme that catalyses the hydrolysis of choline-based esters.

5.15 Briefly **describe** the mode of action of rocuronium bromide. Hence, **explain** the significance of Cameron's findings on surgery.

Problem 6 *(14% of total)*	Question	6.1	6.2	6.3	6.4	6.5	6.6	6.7	6.8	Total
	Points	15	2	4	5	2	6	2	2	38

Problem 6: Nice-smelling Chemistry

By Ranen Yong, Singapore

Ever wanted to smell nice?

While body odor is often taken care of with good hygiene and deodorants, some want to go an extra step further – by smelling unique and pleasant. Be it for special occasions or for daily use, perfumes have been used since ancient times to help people smell great. Today, modern perfumes aim to do the same, except that they now largely consist of manmade mixtures of aromatic chemicals and essential oils.

Today's perfumes contain multiple scent molecules that vary in volatility. In marketing lingo, the scents are compared to the notes in a musical chord. The molecules that evaporate first and create the first impression for the user's sense of smell are known as the "head notes"; the ones that hit the user next are known as the "middle notes"; the ones that linger for a long time are known as the "bottom notes".

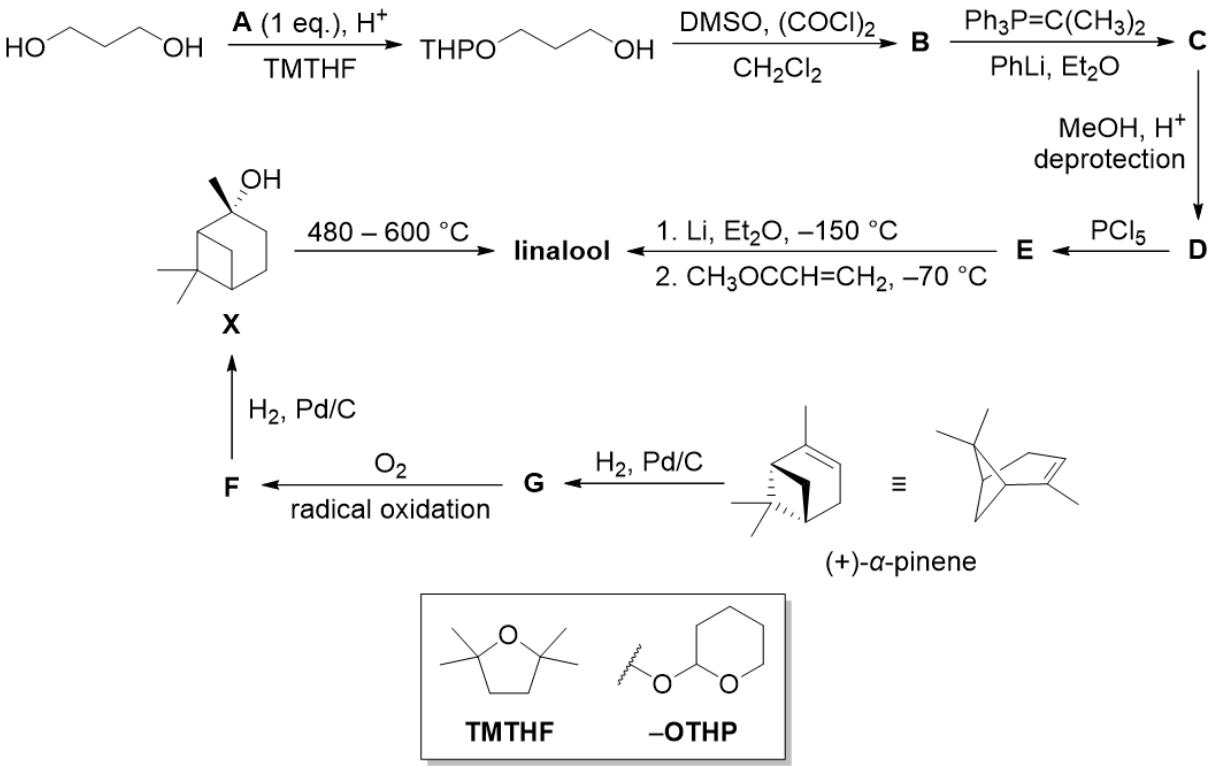
<u>Part 1: A classic modern fragrance</u>

The first abstract perfume in history (i.e. not based on a single note) is *Jicky*, a unisex perfume originally created by Aimé Guerlain in 1889. It is also currently the oldest continuously produced perfume in the world. The scent composition of the fragrance is shown below.

Top notes: Bergamot, Lavender
Middle notes: Jasmine, Rose
Base notes: Vanilla, Tonka Bean, Resins

Bergamot is a scent note commonly found in various modern perfumes. Its crisp and floral qualities are largely attributed to two compounds: linalool and linalyl acetate.

Two synthesis methods for linalool are shown below. The synthesis beginning with 1,3-propanediol forms racemic linalool as the final product mixture, but the other synthesis beginning with *α*-pinene produces (–)-linalool as the main product.



6.1 **Draw** the structures of compounds **A** to **G** and linalool. Stereochemistry is not required.

6.2 **Draw** a mechanism illustrating the transformation from compound **X** to (–)-linalool.

The reactions of *α*-pinene to compound **G** and compounds **G** to **X** both involve the use of Pd/C. In this process, Pd acts as a catalyst by activating H_2 molecules on its surface by oxidative addition reaction, including homolytic cleavage of the H–H bond as shown in the diagram below.

Fig. 6.1: Activation of H_2 molecules on Pd catalyst surface

Let's consider the reaction of *α*-pinene to compound **H**.

Mechanistic studies of the reaction found that the substrate (*α*-pinene) binds to the surface of the Pd catalyst by forming π-complexes with the Pd surface atoms. There are two different orientations of adsorption, which results in two different π-complexes formed.

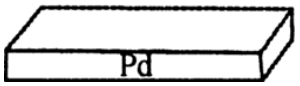


Fig. 6.2: Three-dimensional representation of the Pd catalyst surface

6.3 With reference to Fig. 6.2, **<u>illustrate</u>** the two **orientations of adsorption** by drawing **two different ways** in which *α*-pinene would **approach** the Pd catalyst surface.
[Hint: consider the three-dimensional conformation of α-pinene drawn in the synthesis scheme.]

After the π-complex is formed, hydrogenation of the π-complex occurs, and compound **G** is de-adsorped from the Pd catalyst surface. Both hydrogenation and de-adsorption can be assumed to occur in a single step. The reaction was found to produce both *cis* and *trans* isomers of compound **G**, but in unequal proportions.

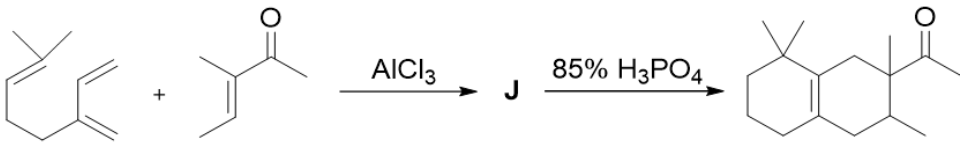
6.4 **<u>Draw</u>** a catalytic cycle for the formation of **either** the *cis* **or** *trans* products of compound **G** from *α*-pinene. Arrow-pushing mechanisms that illustrate the flow of electrons are **not** required.

6.5 Using your answers in 6.4 and 6.5, briefly **<u>explain</u>** which isomer would be the major product.

Part 2: A simple but modern fragrance

Many modern perfumes contain intricate blends of various natural and synthetic fragrance oils diluted in alcohol and water. However, in 2006, German perfumer Geza Schön developed a unique perfume known as "Molecule 01" that features just one fragrance ingredient: Iso E Super. Owing to its simplicity, Molecule 01 has been widely regarded as a perfume highly suitable for perfume layering, the practice of strategically spraying multiple perfumes (often not more than two) around the body to create a unique scent.

Iso E Super is produced commercially by Diels-Alder reaction of myrcene with 3-methyl-3-penten-2-one catalyzed by $AlCl_3$ to give a monocyclic intermediate **J**. This monocyclic intermediate is then cyclized in the presence of 85% phosphoric acid to form Iso E Super, as shown below.



myrcene Iso E Super

The Diels-Alder reaction can be understood by analyzing the frontier molecular orbitals (MOs) of π-symmetry of both reactants, where the HOMO of myrcene interacted with the LUMO of the 3-methyl-3-penten-2-one-$AlCl_3$ adduct.

6.6 **Draw** the transition state illustrating this Diels-Alder reaction, using dotted lines ('-----') to indicate the bonds that are being broken and formed. Hence, by drawing in the appropriate frontier MOs on the transition state, **explain** why the two reactants approach each other in this manner and how this leads to the formation of two new σ bonds.

6.7 **Draw** a possible structure of compound **J** with stereochemistry.

6.8 **Draw** the mechanism illustrating the transformation of compound **J** to Iso E Super.

END OF PAPER