Indian National Chemistry Olympiad 2017
Theory (3 hours)

Roll No. ☐☐☐☐☐–☐☐☐☐☐–☐☐☐☐☐

I permit/do not permit (*strike out one*) HBCSE to make my INO academic performance and personal details public unless I communicate my consent in writing.

I have read the Procedural Rules of the INOs and agree to abide by them.

Name of student: _____

Signature: _____ **Exam Centre:**_____**Date:** January 28, 2017

Do not write anything below this line

Question No	1	2	3	4	5	Total
Marks	17	26	23	26	21	113
Marks Obtained						
Signature of Examiner						

Instructions for students
- Write your Roll No. at the top of all pages.
- This examination paper consists of **29** pages of problems including answer boxes.
- Kindly check that the booklet has all the pages.
- Blank space for rough work has been provided at the end of the paper.
- **Use only a pen to write the answers in the answer boxes. Anything written by pencil will not be considered for assessment.**
- All answers must be written in the appropriate boxes. **Anything written elsewhere will not be considered for assessment.**
- You **must** show the main steps in the calculations.
- For objective type question, mark **X** in the correct box. Some of the objective questions may have more than one correct answer.
- A copy of the Periodic Table of the Elements is provided on the 2nd page of the paper.
- Do not leave the examination room until you are directed to do so.
- The question paper will be uploaded on the HBCSE website on **31st January 2017**.

Fundamental Constants

Avogadro number	$N_A = 6.022 \times 10^{23}$ mol^{-1}	Mass of electron	$m_e = 9.109 \times 10^{-31}$ kg
Electronic charge	$e = 1.602 \times 10^{-19}$ C	Speed of light	$c = 2.998 \times 10^8$ ms^{-1}
Molar gas constant	$R = 8.314$ J K^{-1} mol^{-1}	Rydberg constant	$R_H = 2.179 \times 10^{-18}$ J
Faraday constant	$F = 96485$ C mol^{-1}	Plancks constant	$h = 6.625 \times 10^{-34}$ Js
Temperature	$0°C = 273.15$ K	Pressure	1 mm Hg $= 133.33$ Pa

Roots of a quadratic equation ($ax^2 + bx + c = 0$) are : $x = -\dfrac{b \pm \sqrt{b^2 - 4ac}}{2a}$

Periodic Table of the Elements

1 IA 11A	2 IIA 2A	3 IIIB 3B	4 IVB 4B	5 VB 5B	6 VIB 6B	7 VIIB 7B	8 VIII 8	9 VIII	10 VIII	11 IB 1B	12 IIB 2B	13 IIIA 3A	14 IVA 4A	15 VA 5A	16 VIA 6A	17 VIIA 7A	18 VIIIA 8A
1 **H** Hydrogen 1.008																	2 **He** Helium 4.003
3 **Li** Lithium 6.941	4 **Be** Beryllium 9.012											5 **B** Boron 10.811	6 **C** Carbon 12.011	7 **N** Nitrogen 14.007	8 **O** Oxygen 15.999	9 **F** Fluorine 18.998	10 **Ne** Neon 20.180
11 **Na** Sodium 22.990	12 **Mg** Magnesium 24.305											13 **Al** Aluminum 26.982	14 **Si** Silicon 28.086	15 **P** Phosphorus 30.974	16 **S** Sulfur 32.066	17 **Cl** Chlorine 35.453	18 **Ar** Argon 39.948
19 **K** Potassium 39.098	20 **Ca** Calcium 40.078	21 **Sc** Scandium 44.956	22 **Ti** Titanium 47.88	23 **V** Vanadium 50.942	24 **Cr** Chromium 51.996	25 **Mn** Manganese 54.938	26 **Fe** Iron 55.933	27 **Co** Cobalt 58.933	28 **Ni** Nickel 58.693	29 **Cu** Copper 63.546	30 **Zn** Zinc 65.39	31 **Ga** Gallium 69.732	32 **Ge** Germanium 72.61	33 **As** Arsenic 74.922	34 **Se** Selenium 78.09	35 **Br** Bromine 79.904	36 **Kr** Krypton 84.80
37 **Rb** Rubidium 84.468	38 **Sr** Strontium 87.62	39 **Y** Yttrium 88.906	40 **Zr** Zirconium 91.224	41 **Nb** Niobium 92.906	42 **Mo** Molybdenum 95.94	43 **Tc** Technetium 98.907	44 **Ru** Ruthenium 101.07	45 **Rh** Rhodium 102.906	46 **Pd** Palladium 106.42	47 **Ag** Silver 107.868	48 **Cd** Cadmium 112.411	49 **In** Indium 114.818	50 **Sn** Tin 118.71	51 **Sb** Antimony 121.760	52 **Te** Tellurium 127.6	53 **I** Iodine 126.904	54 **Xe** Xenon 131.29
55 **Cs** Cesium 132.905	56 **Ba** Barium 137.327	57-71	72 **Hf** Hafnium 178.49	73 **Ta** Tantalum 180.948	74 **W** Tungsten 183.85	75 **Re** Rhenium 186.207	76 **Os** Osmium 190.23	77 **Ir** Iridium 192.22	78 **Pt** Platinum 195.08	79 **Au** Gold 196.967	80 **Hg** Mercury 200.59	81 **Tl** Thallium 204.383	82 **Pb** Lead 207.2	83 **Bi** Bismuth 208.980	84 **Po** Polonium [208.982]	85 **At** Astatine 209.987	86 **Rn** Radon 222.018
87 **Fr** Francium 223.020	88 **Ra** Radium 226.025	89-103	104 **Rf** Rutherfordium [261]	105 **Db** Dubnium [262]	106 **Sg** Seaborgium [266]	107 **Bh** Bohrium [264]	108 **Hs** Hassium [269]	109 **Mt** Meitnerium [268]	110 **Ds** Darmstadtium [269]	111 **Rg** Roentgenium [272]	112 **Cn** Copernicium [277]	113 **Uut** Ununtrium unknown	114 **Fl** Flerovium [289]	115 **Uup** Ununpentium unknown	116 **Lv** Livermorium [298]	117 **Uus** Ununseptium unknown	118 **Uuo** Ununoctium unknown

Lanthanide Series

57 **La** Lanthanum 138.906	58 **Ce** Cerium 140.115	59 **Pr** Praseodymium 140.908	60 **Nd** Neodymium 144.24	61 **Pm** Promethium 144.913	62 **Sm** Samarium 150.36	63 **Eu** Europium 151.966	64 **Gd** Gadolinium 157.25	65 **Tb** Terbium 158.925	66 **Dy** Dysprosium 162.50	67 **Ho** Holmium 164.930	68 **Er** Erbium 167.26	69 **Tm** Thulium 168.934	70 **Yb** Ytterbium 173.04	71 **Lu** Lutetium 174.967

Actinide Series

89 **Ac** Actinium 227.028	90 **Th** Thorium 232.038	91 **Pa** Protactinium 231.036	92 **U** Uranium 238.029	93 **Np** Neptunium 237.048	94 **Pu** Plutonium 244.064	95 **Am** Americium 243.061	96 **Cm** Curium 247.070	97 **Bk** Berkelium 247.070	98 **Cf** Californium 251.080	99 **Es** Einsteinium [254]	100 **Fm** Fermium 257.095	101 **Md** Mendelevium 258.1	102 **No** Nobelium 259.101	103 **Lr** Lawrencium [262]

**Problem 1**   **17 Marks**

Barbiturates in our lives

Guano, the excreta of sea birds and bats was a major export item from colonial America to Europe in the 19th century used for making fertilizers and extracting uric acid, which was used to produce many commercial chemicals including the valuable dye Murexide. Uric acid is a metabolic by-product of proteins and nucleic acids. German chemist Adolf von Baeyer in 1864, while studying the chemistry of uric acid, discovered barbituric acid **C**. Derivatives of this compound were very effective in inducing sleep in animals. Later, this family of compounds turned out to be very effective drugs for human psychological disorders.

In a few years, a simple procedure to produce **C** was found using $POCl_3$ mediated condensation of compound **A** ($C_3H_4O_4$) derived from apple juice and compound **B** (CH_4N_2O), abundant in animal excreta.

**1.1**   Draw structures for **A** and **B**.

C

A

B
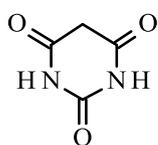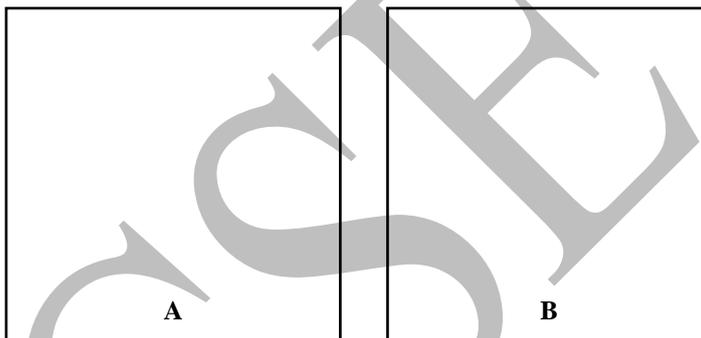
Thiopental, popularly known as "truth serum", which makes people to speak more (often revealing the truth) was soon discovered. It has a ring structure similar to **C**. Its preparation involves reacting 2-ethyl-propanedioic acid diethyl ester with racemic 2-bromopentane in the presence of sodium ethoxide to form product **D** ($C_{14}H_{26}O_4$). **D** obtained, is a racemic mixture, which condenses with thiourea to give Thiopental (**E**) ($C_{11}H_{18}N_2O_2S$). The 'R' isomer of Thiopental is a mood elevator and the 'S' isomer causes neurological depression.

1.2   Draw the structure of **D** and the two isomers of **E** and label them with 'R' and 'S' configuration.
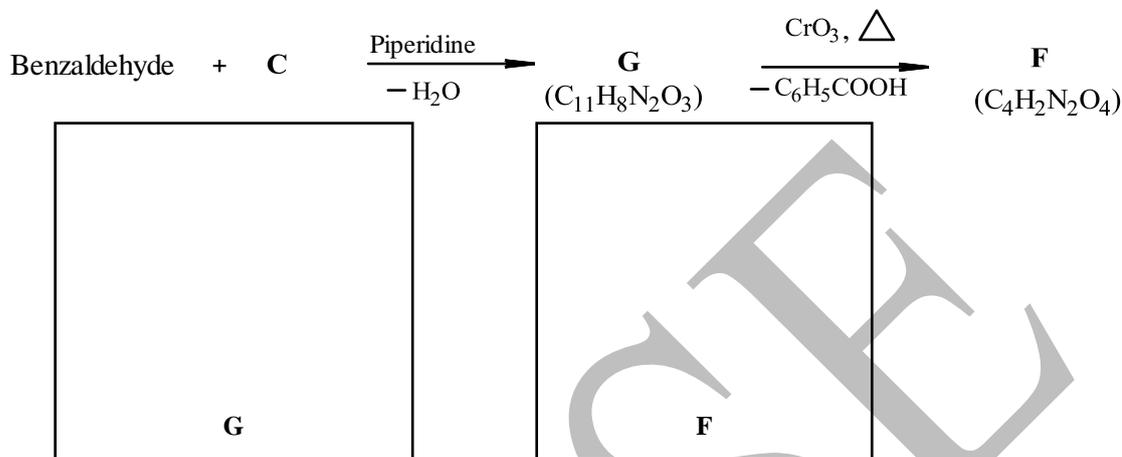
D

E

1.3   Compound **C** is quite acidic (pKa = 4.01). Draw the structures of the most stable tautomers of the conjugate base of **C**. The tautomers should be unique and not resonance structures of each other.
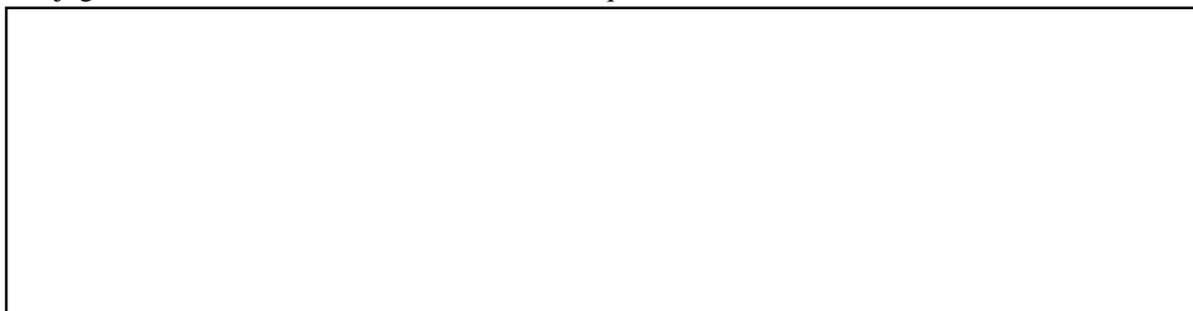
Compound **F** ($C_4H_2N_2O_4$) is one of the oldest synthesised organic compounds, discovered by Justus von Liebig and Friedrich Wöhler in 1938. It was used to produce the dye murexide. When ingested, it accumulates in the pancreas damaging insulin-producing cells and causing Type II diabetes mellitus. Due to this, it is used to induce diabetes in laboratory rats in diabetes research.
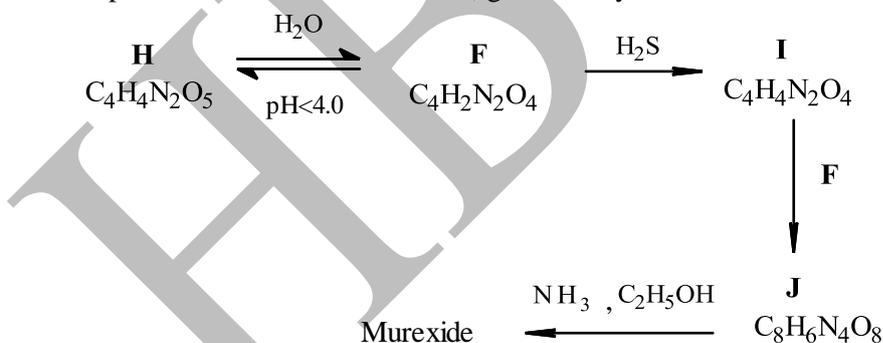
1.4   **F** is formed in the CrO_3 oxidation of the condensation product **G** of benzaldehyde and **C** in the presence of piperidine (a base). Draw the structures of **F** and **G.**
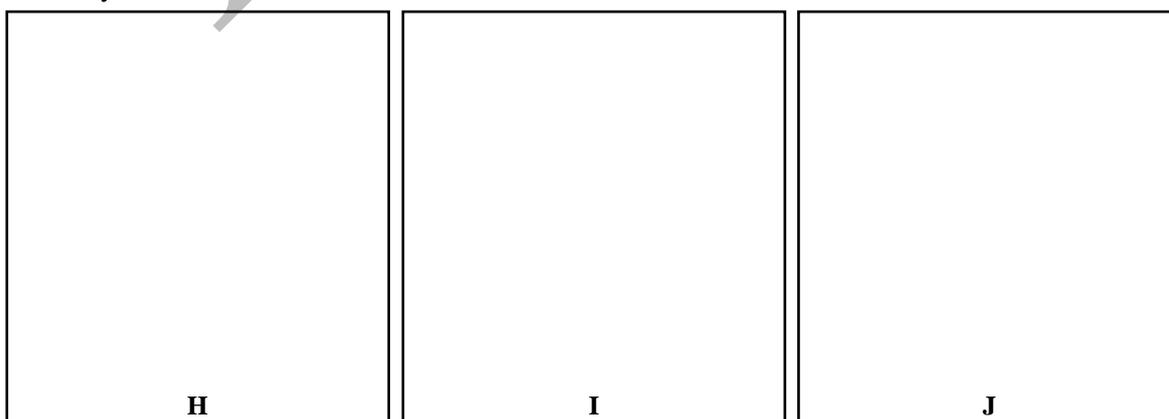
Benzaldehyde + **C** $\xrightarrow[-H_2O]{\text{Piperidine}}$ **G** ($C_{11}H_8N_2O_3$) $\xrightarrow[-C_6H_5COOH]{CrO_3, \triangle}$ **F** ($C_4H_2N_2O_4$)

G	**F**

1.5   The condensation reaction above giving **G** proceeds well. This shows that the pKa of the conjugate acid of piperidine is (mark **X** in the correct box)

a) < 4.01 ☐   b) > 4.01 ☐   c) $= 4.01$ ☐

In neutral aqueous solution, **F** exists as a ketal **H**. At acidic pH, **H** reverts to **F**. When   reduced with hydrogen sulphide, **F** gave **I,** which in the presence of excess **F** gives hemiketal **J**. Compound **J** on treatment with NH_3 gives the dye murexide.

H $C_4H_4N_2O_5$ $\underset{\text{pH}<4.0}{\overset{H_2O}{\rightleftharpoons}}$ **F** $C_4H_2N_2O_4$ $\xrightarrow{H_2S}$ **I** $C_4H_4N_2O_4$

$\downarrow$ **F**

Murexide $\xleftarrow{NH_3, C_2H_5OH}$ **J** $C_8H_6N_4O_8$

1.6   Identify the structures **H** to **J**.
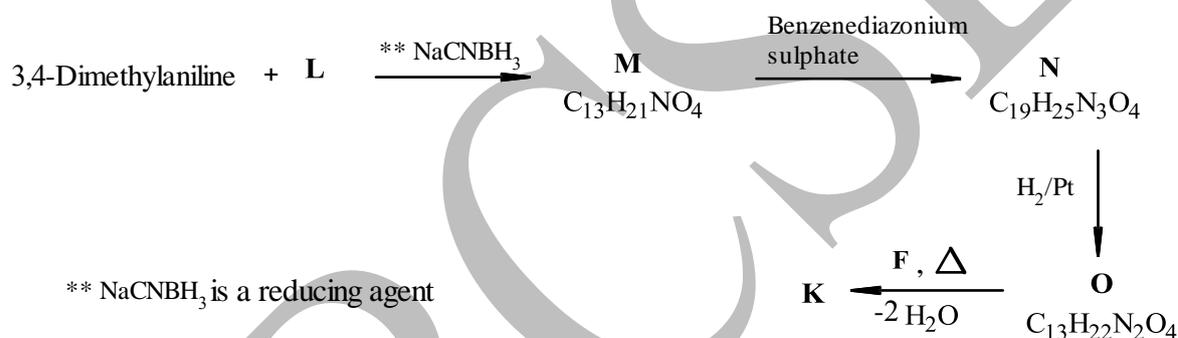
H	**I**	**J**

In 1933, Paul György and Richard Kuhn isolated a yellow pigment which turned out to be an essential vitamin and a cure for many diseases. Later, it was identified as Compound **K** ($C_{17}H_{20}N_4O_6$) with a D-aldopentose (**L**) derived side chain. In **L**, C3 carbon has 'R' configuration.
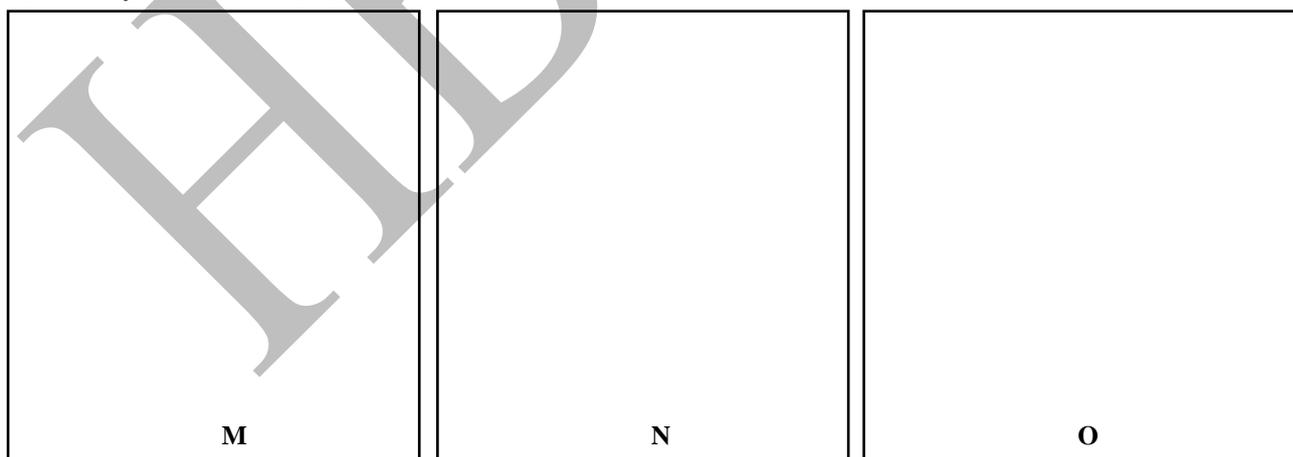
1.7   **L** ($C_5H_{10}O_5$) on reduction with sodium borohydride ($NaBH_4$) gives an optically inactive alditol. Draw the Fischer projection formula of **L** with correct configuration at all chiral carbons**.**

L
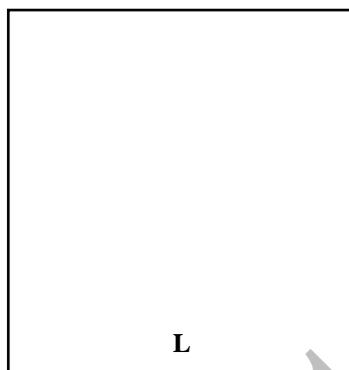
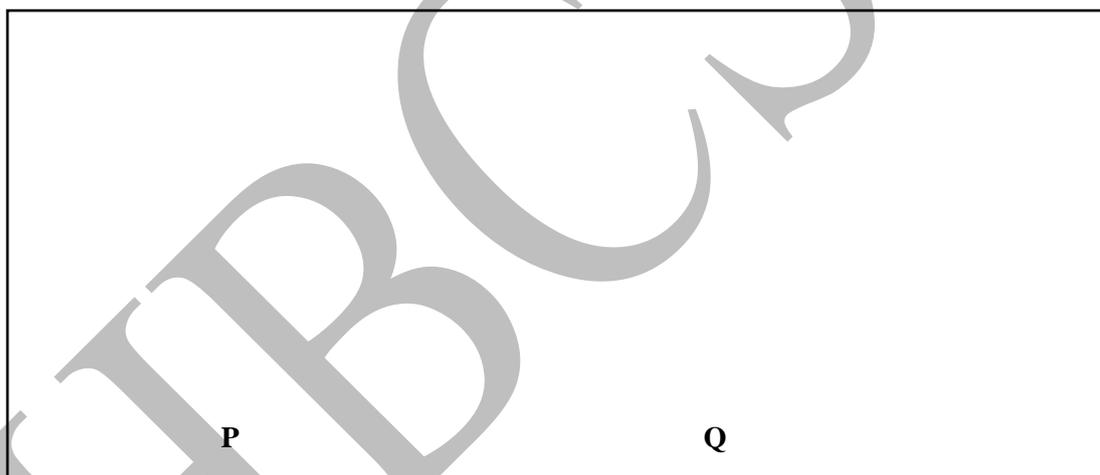**1.8**   One of the chemical syntheses of **K** involves a series of reactions as given below.

3,4-Dimethylaniline + **L** $\xrightarrow{\text{** NaCNBH}_3}$ **M** $C_{13}H_{21}NO_4$ $\xrightarrow{\text{Benzenediazonium sulphate}}$ **N** $C_{19}H_{25}N_3O_4$

$\downarrow$ H$_2$/Pt

** NaCNBH$_3$ is a reducing agent   **K** $\xleftarrow[-2\ H_2O]{\text{F, }\triangle}$ **O** $C_{13}H_{22}N_2O_4$

a) Identify structures **M**, **N**, and **O**.

M	**N**	**O**

b)   **K** ($C_{17}H_{20}N_4O_6$), obtained by condensation of **O** and **F** has a ring structure. The template of the structure of **K** is shown below. Using the given template, complete the structure of **K**.

K
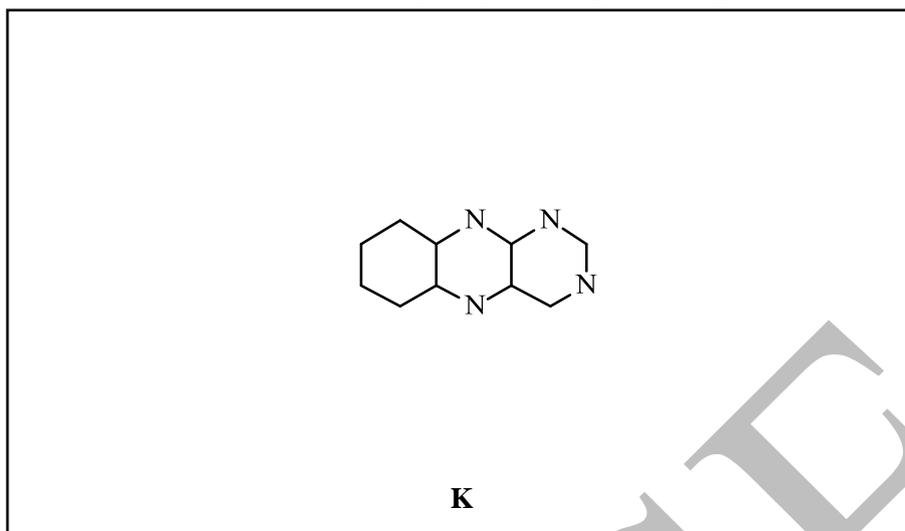
1.9   Degradation studies of **K** had played an important role in its identification. Alkaline hydrolysis of **K** with 1 M NaOH at 100^oC gave **P** ($C_{16}H_{19}N_2NaO_7$) by losing a mole of **B.** Further   hydrolysis of **P** by 5M NaOH at 100^oC gave **Q** ($C_{13}H_{22}N_2O_4$). Draw structure of **P** and **Q**.

P   **Q**

Problem 2   **26 Marks**

Chemistry of Iron
Part A: Iron Sulphur proteins

Iron is the most prevalent transition metal in living systems. Let us look at proteins containing iron that play an important role in electron transfer (i.e., oxidation–reduction) reactions in living systems.

Fe–S protein(s) is an important class of proteins, containing iron and sulphur in their core. These proteins have been discovered in last mid-century and seem to be highly abundant in living systems. Their core Fe-S clusters can be synthesized in laboratory in absence of oxygen. Their properties make one to believe that they could have been the biomolecules shaping the origins of life on earth when anaerobic conditions were most prevalent.

The simplest Fe-S unit is found in *rubredoxin protein* that contains one iron and four cysteine amino acid [$HOOCCH(NH_2)CH_2SH$] units. In 1981, Hagen and co-workers in USA synthesized an analogue of *rubredoxin,* $(Et_4N)_2[Fe(SPh)_4]$, where $Et = -C_2H_5$, $Ph = -C_6H_5$. (In the following questions, consider sulphur as a weak field ligand.)

2.1   Predict the geometry of $[Fe(SPh)_4]^{2-}$ and draw its appropriate structure. Calculate its magnetic moment.

Structure of $[Fe(SPh)_4]^{2-}$	Calculation for magnetic moment:
Geometry:	

The next simplest Fe-S units found in proteins are *2Fe-2S, 4Fe-4S* and *3Fe-4S*. These units have **two** types of Fe-S bonds and no Fe-Fe bonds.

a) *2Fe-2S* –This unit has two sulphide ions (S^{2-}) and four cysteine residues bonded to two iron centers. Hagen and co-workers synthesized an analogue of this cluster, $[Fe_2S_2(SPh)_4]^{2-}$ from $[Fe(SPh)_4]^{2-}$ and elemental sulphur.

2.2   Complete and balance the chemical equation given below.

$$[Fe(SPh)_4]^{2-} + \quad S \rightarrow \quad [Fe_2S_2(SPh)_4]^{2-} + \quad PhSSPh +$$

$$(X)$$

2.3   Draw the structure of $[Fe_2S_2(SPh)_4]^{2-}$ unit.

b) *4Fe-4S–* This unit has four sulphide ions and four cysteine residues bonded to four iron centers. The analogue, $[Fe_4S_4(SPh)_4]^{2-}$ was spontaneously obtained from $[Fe_2S_2(SPh)_4]^{2-}$ using suitable reaction medium.

2.4   Give the balanced chemical equation for the synthesis of $[Fe_4S_4(SPh)_4]^{2-}$ from $[Fe_2S_2(SPh)_4]^{2-}$.

$[Fe_2S_2(SPh)_4]^{2-} \rightarrow [Fe_4S_4(SPh)_4]^{2-} +$ 　　　　　　 $+$

　　　　　　　　　　　　　　　　　　 (Y) 　　　　　　　　 (Z)
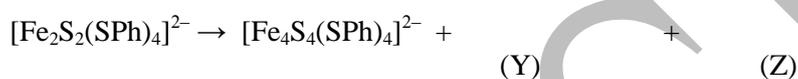
2.5   Draw the structure of $[Fe_4S_4(SPh)_4]^{2-}$ that has a cubic core.

2.6   The number of Fe (III) and Fe (II) ions in $[Fe_2S_2(SPh)_4]^{2-}$ and $[Fe_4S_4(SPh)_4]^{2-}$ are– **(Indicate the numbers in the boxes):**

a) Fe (III) in $[Fe_2S_2(SPh)_4]^{2-}$ ☐   b) Fe (II) in $[Fe_2S_2(SPh)_4]^{2-}$ ☐

c) Fe (III) in $[Fe_4S_4(SPh)_4]^{2-}$ ☐   d) Fe (II) in $[Fe_4S_4(SPh)_4]^{2-}$ ☐

2.7   Using the above cubic structure of $[Fe_4S_4(SPh)_4]^{2-}$ as reference, draw the structure of $[Fe_3S_4(SPh)_3]^{2-}$, another analogue unit of iron-sulphur proteins, labeled as *3Fe-4S*.
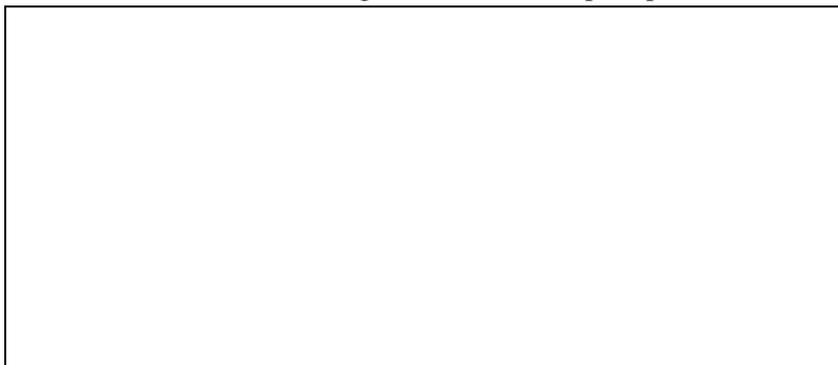
2.8   At pH > 9 and with availability of excess thiophenol, $[Fe_3S_4(SPh)_3]^{2-}$ gets converted to a linear structure with a molecular formula of $[Fe_3S_4(SPh)_4]^{3-}$. Draw the structure of $[Fe_3S_4(SPh)_4]^{3-}$.

2.9   Following are different types of Fe-S bonds in the above clusters. Mark **X** for—

	the most ionic Fe-S bond	the least ionic Fe-S bond
a) C_6H_5S-Fe(III)	⬚	⬚
b) C_6H_5S-Fe(II)	⬚	⬚
c) S-Fe(III)	⬚	⬚
d) S-Fe(II)	⬚	⬚

Generally, Fe compounds have very high magnetic moments due to which they are often used in magnetic applications. Some of the Fe-S units, however, exhibit low or no magnetic moments. This observation is attributed to opposite spin orientations of electrons in neighbouring metal centres within the same unit — a property also known as antiferromagnetic coupling.

2.10   In which of the following units (R = cysteine group), it is possible to have **zero** net magnetic moment due to antiferromagnetic coupling? (Mark **X** in the correct box (es))

a) $[Fe_2S_2(SR)_4]^{3-}$ ⬚   b) $[Fe_2S_2(SR)_4]^{2-}$ ⬚   c) $[Fe_4S_4(SR)_4]^{2-}$ ⬚

Redox potential of $[Fe_2S_2(SR)_4]^{3-}/[Fe_2S_2(SR)_4]^{2-}$ couple (R= cysteine group) changes as the charges on the peptide chain in the extended part of the protein change through protonation/deprotonation of various groups such as amide –NH–groups. The following simplified schematic figures indicate two possible charge distribution on the peptide chain around $[Fe_2S_2(SR)_4]^{3-}$.

2.11   In which of these two systems, the iron centres are less prone to oxidation? (Mark **X** in correct box)
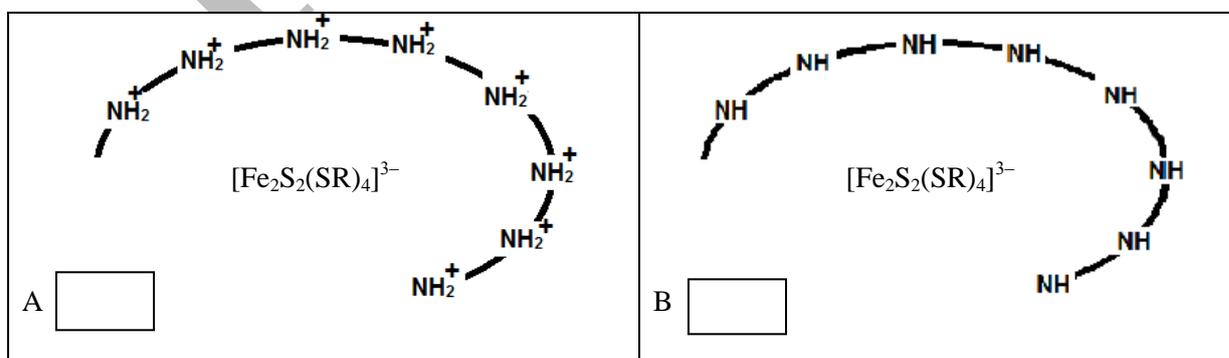
In respiration cycle, O_2 gets converted to H_2O. In this process, superoxide, O_2^- is generated, which is believed to be responsible for the process of ageing by damaging cell membranes. Body cells have an enzyme called superoxide dismutase (SOD), which converts O_2^- into O_2 by abstracting an electron. SOD has two 3d transition metal ions (**A** and **B**) in +2 oxidation state. Some features of **A** and **B** are –

	A	**B**
Colour in +2 state in octahedral coordination	Yes	No
Other possible oxidation states	+1	No

2.12   **A** is [   ]   **B** is [   ]

2.13   The ion that can convert O_2^- into O_2 is (Mark **X** in correct box)

  A^{2+} [   ] B^{2+} [   ]

Part B: Use of iron in "blue" colours

British astronomer and photographer John Hershel used Fe-based reagents to obtain a blue pigment (known as Turnbull's Blue) to develop the blue printing technique in 1842. Now, blue printing can be easily carried out using photochemical redox chemistry of potassium ferrioxalate.

Potassium ferrioxalate is synthesized by adding aqueous ferric nitrate to hot aqueous potassium oxalate. To optimize this process, it is important to determine the molar ratio of iron and oxalate in the complex that can be done using redox titrations. In one such analysis, 0.250 g of potassium ferrioxalate sample was taken to a flask and 25 mL of 4M H_2SO_4 was added to it. After making the solution hot, it was titrated with 0.0196 M $KMnO_4$ till light pink colour was obtained. The observed burette reading was 31.1 mL which indicates oxalate content present in the complex.

2.14   Write the balanced half-cell equations for the reaction involved in the titration of oxalate with $KMnO_4$.

After this titration, excess of zinc powder was added to the same flask that led to effervescence in the solution. When the effervescence subsided, the solution was boiled for 10-15 minutes. The flask was cooled to room temperature and was titrated with the same $KMnO_4$ solution. (The solution was still acidic). The observed burette reading was 5.1 mL. This will give the iron content in the sample.

2.15   Write the possible balanced chemical equation (s) for reaction (s) taking place after Zn dust is added to the flask.

2.16   Write the balanced half cell equations for the reaction involved in the titration of iron with $KMnO_4$.

2.17   Calculate the moles of iron and oxalate present in the sample and their molar ratio. (Show the main steps in your calculation).

Calculations for oxalate content:

Calculations for iron content:

Molar ratio of iron: oxalate (to the nearest whole number):

2.18   a) Based on the above calculations draw the structure of the ferrioxalate complex ion formed. Represent the **oxalate** ligand as

b) How many isomers are possible for this complex? (Mark **X** in correct box (es))

i)   two *cis*, one *trans* and *trans* giving two optical isomers   ☐

ii) only two optical isomers   ☐

iii) two *cis*, one *trans* and each of the *cis* forming two optical isomers each   ☐

iv) one *cis*, one *trans* and *trans* giving two optical isomers   ☐

2.19   In blue printing, a ferrioxalate salt is coated on a surface. Light is shone on this surface through a template of design that is to be printed. On regions of surface exposed to light, ferrioxalate ion undergoes photochemical reduction with the evolution of a gas which is acidic in aqueous solution.

a) Write the balanced chemical equation for this photochemical reaction.

This surface when dipped in potassium ferricyanide solution produces a blue coloured ferroferricyanide complex.

b) Write the balanced chemical equation for this reaction.

Alkaloids

The chemical constituents in plants and fungi world that had active biological effects in humans were often found to be N-containing bases. These N-containing compounds were termed as alkaloids and became basis for several medicines, dyes and agrochemicals.

Several methods are available for the synthesis of such nitrogenous bases. One of them is reductive amination where a carbonyl compound is reacted with a primary or secondary amine and the intermediate formed is reduced.

3.1   Identify **A** and **B** in the following reaction.

Mannich reaction (named after Carl Ulrich Franz Mannich who discovered it in 1912) is a commonly used synthetic method for the preparation of β-amino carbonyl compounds. Here an enolisable aldehyde or ketone, another aldehyde and a primary or secondary amine, react under acidic conditions to a β-amino carbonyl compound.

The skeletal framework of **D** is found in alkaloids present in shrubs and is known to cause liver damage in animals which feed on them.

D

3.2   Identify the starting compound **C** ($C_8H_{15}NO_2$) which would yield compound **D** on Mannich reaction.

C

One of the methods for structure determination of alkaloids is Hoffman elimination represented below. Here the alkaloid is converted to the quaternary ammonium hydroxide, which on heating gives an olefin and a tertiary amine.

$$CH_3CH_2CH_2CH_2NH_2 \xrightarrow[\text{ii) Ag}_2\text{O, H}_2\text{O, iii) }\Delta]{\text{i) excess CH}_3\text{I/K}_2\text{CO}_3\text{, H}_2\text{O}} CH_3CH_2CH=CH_2 \; + \; (CH_3)_3N$$
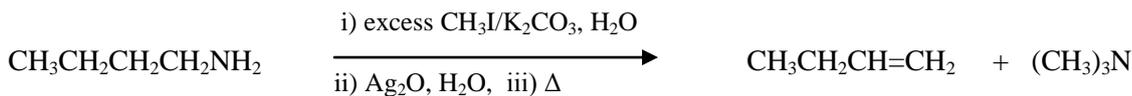
3.3　Draw the structure of the product obtained on Hoffman elimination of the following compound.

E
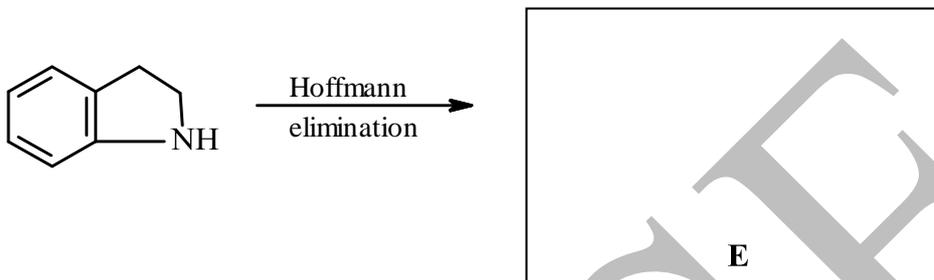
Pethidine ($C_{15}H_{21}NO_2$) is a synthetic analogue of natural alkaloid (morphine) and is used as pain reliever. Consider the following sequence of reactions.

Pethidine ($C_{15}H_{21}NO_2$) $\xrightarrow[\text{elimination}]{\text{Hoffmann}}$ **F** ($C_{16}H_{23}NO_2$) $\xrightarrow[\text{elimination}]{\text{Hoffmann}}$ **G** ($C_{14}H_{16}O_2$)

$\downarrow$ i) O_3
　ii) Zn/H_2O

CH_2O (2 eqv) **+**

OHC—(C)(COOC$_2$H$_5$)—CHO
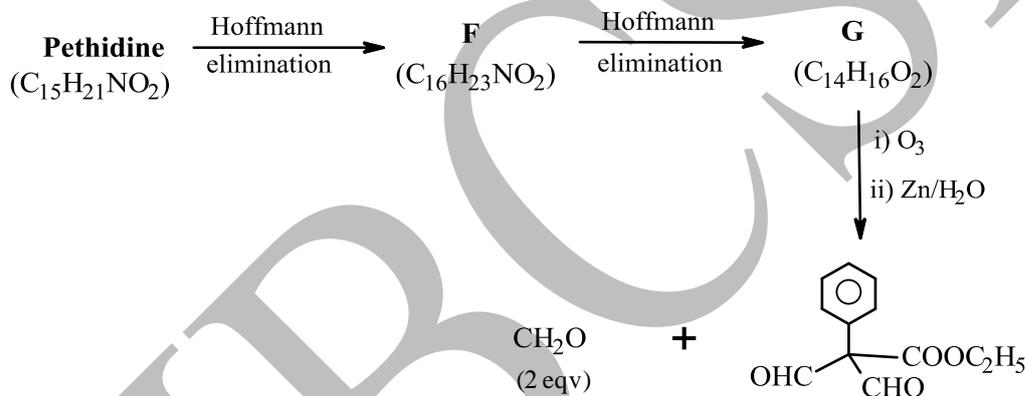
3.4　Draw the structures of intermediates **F**, **G** and Pethidine.

F	**G**	**Pethidine**
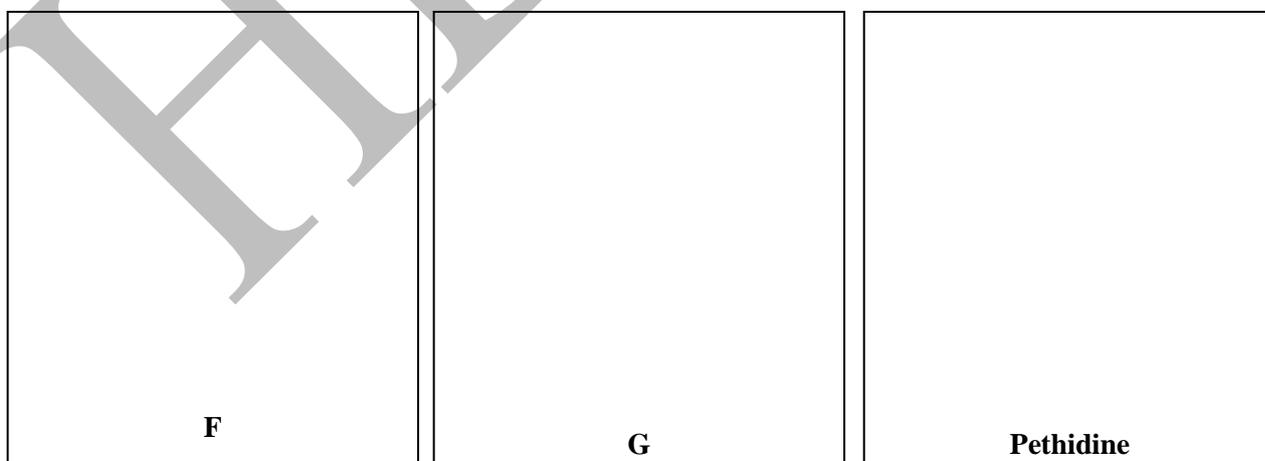
Pseudoephedrin, a natural alkaloid used as nasal decongestant, on Hoffman elimination gives **H** ($C_9H_{10}O$). However **H** does not decolorize Br_2 water and does not form an oxime derivative.

3.5 Draw the structure of **H** with the correct stereochemistry.

Pseudoephedrin   **H**
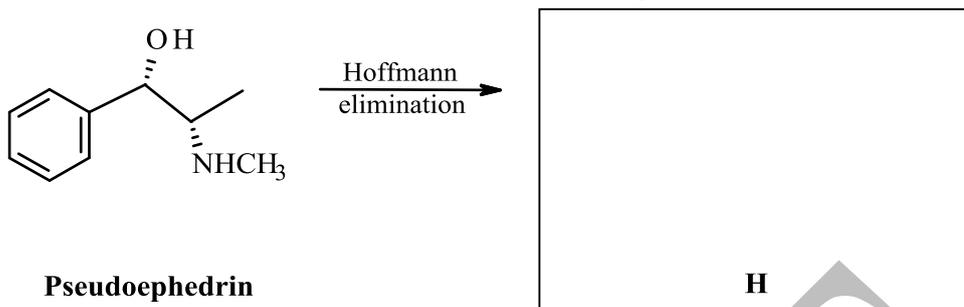
Indole is a nitrogen heterocycle found in many alkaloids, one of them being indole-3-acetic acid, a plant growth regulator. Indole can undergo protonation at different positions on the pyrole ring.

3.6 Draw the most stable cation **I,** resulting from the protonation of Indole.
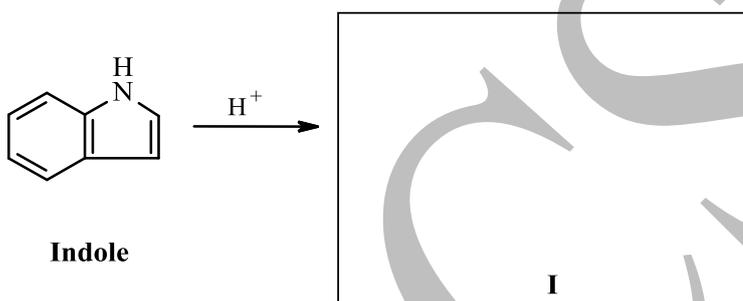
Indole   **I**

Indoles are easily oxidized by air and a variety of other oxidants to give compound **O**. Compound **O** can be synthesized from o-xylene by the following route.
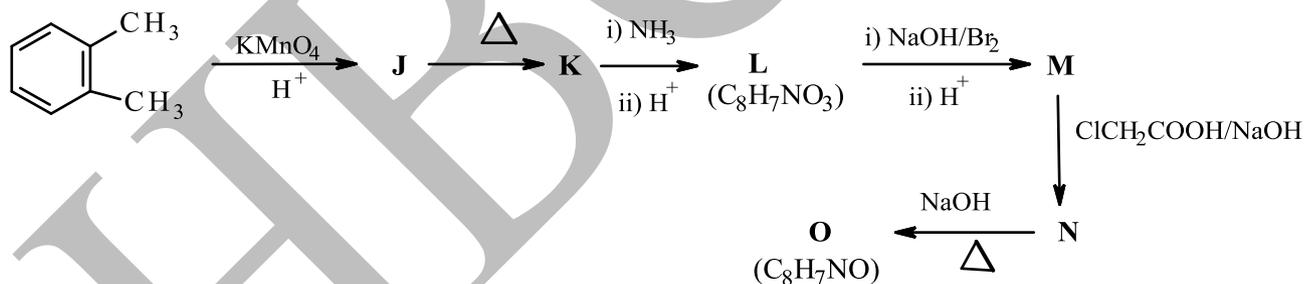
3.7 Draw the structures of **J-O**.

J	**K**	**L**

M	N	O
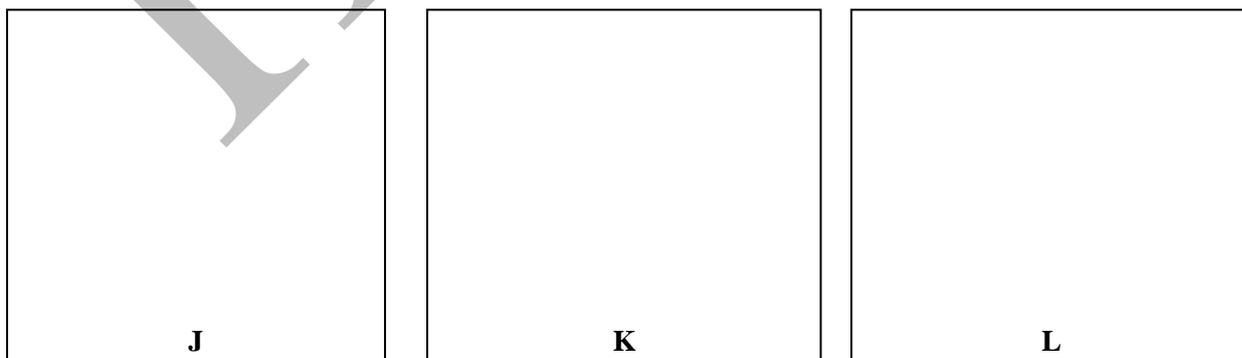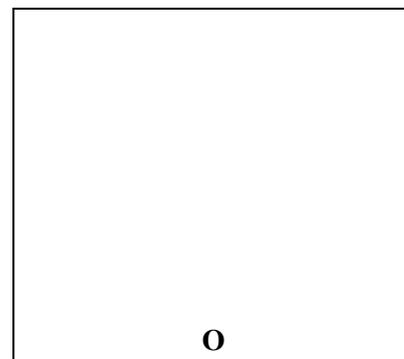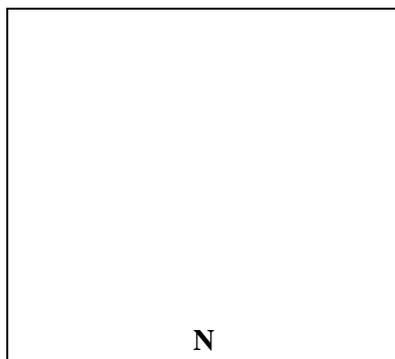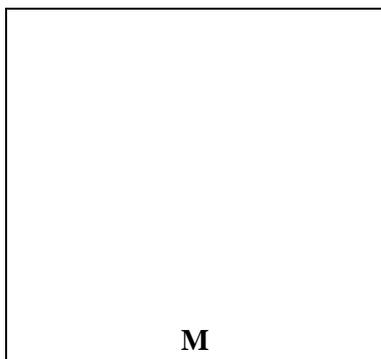
Oxidative dimerisation of **O** produces **P**, which can theoretically form three stereosiomers.

3.8   Draw the structure of **P.**

P
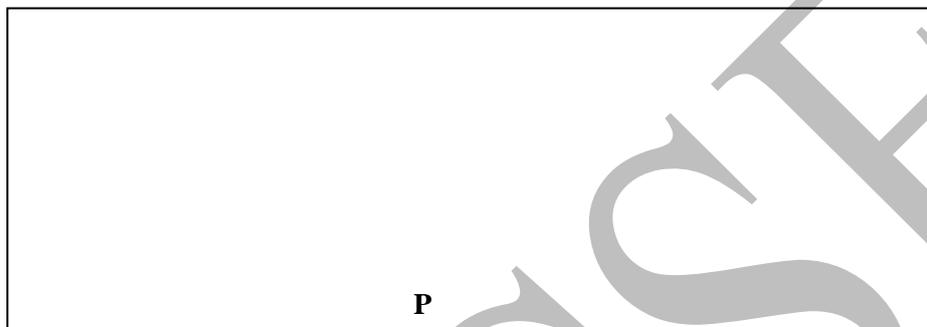
P undergoes oxidation to give compound **Q** ($C_{16}H_{10}N_2O_2$) which is an important dye in the textile industry.

3.9   Draw the structure of **Q.**

Q
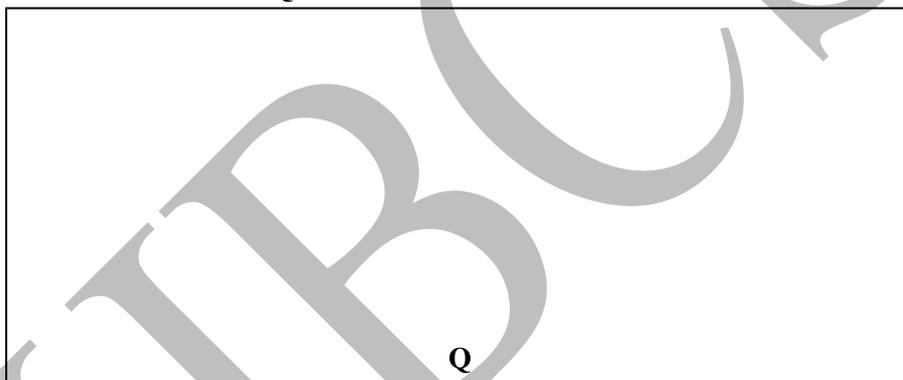
3.10   How many stereoisomers are possible for **Q**?

3.11   Indirubin **R** an isomer of **Q**, is a by-product of bacterial metabolism. **R** is obtained by reaction of **O** with isatin. Draw the structure of **R**.

Isatin + **O** $\xrightarrow{\text{base}}$

R
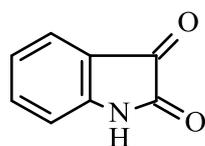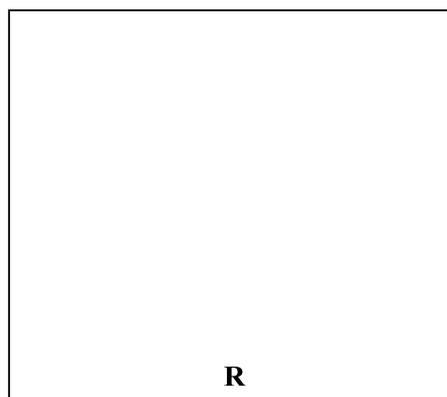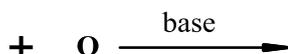
Imidazole is a heterocycle with two nitrogen atoms.
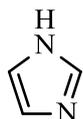
Imidazole

3.12   The following statements that is/are true (Mark **X** in the correct box)

i) Imidazole is a weaker base compared to pyridine and a stronger acid   compared to pyrrole. ⬚

ii) Imidazole is a stronger base compared to pyridine and a weaker acid   compared to pyrrole. ⬚

iii) Imidazole is a stronger base compared to pyridine and a stronger acid compared to pyrrole. ⬚

iv) Imidazole is a weaker base compared to pyridine and a weaker acid compared to pyrrole. ⬚

3.13   Orientation of an incoming electrophile in a heterocycle is governed by the existing substituent similar to its effect on a benzene system. Complete the following reactions by identifying **S** and **T** in the following synthesis.
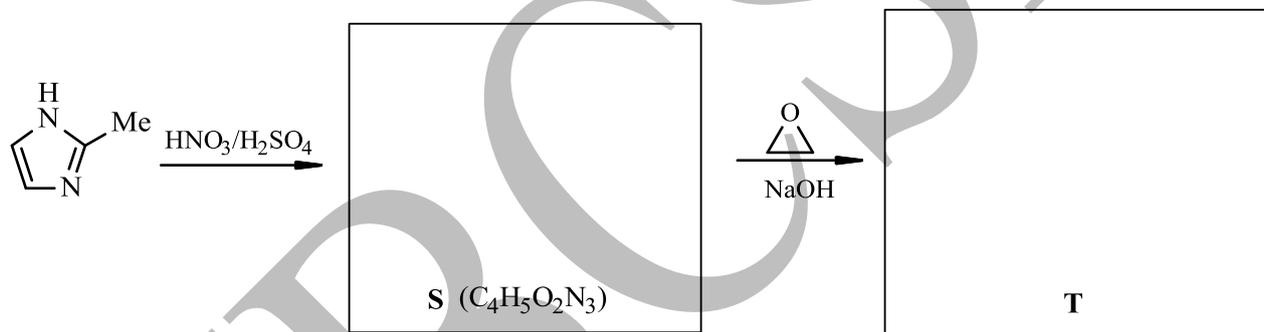
Sulfur ylides **U** are species in which a negatively charged carbon is attached to a positively charged sulfur atom. They react with carbonyl compounds to give the simplest oxygen heterocycle viz. the oxirane or epoxides. **U** is formed when a compound containing sulphonium ion (sulphur with + ve charge) with α-H is reacted with a base.
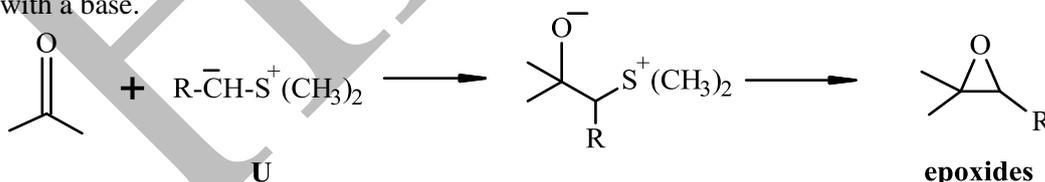
3.14   Identify **V-X** in the synthesis of the antifungal agent fluconazole **X** ($C_{13}H_{12}OF_2N_6$).
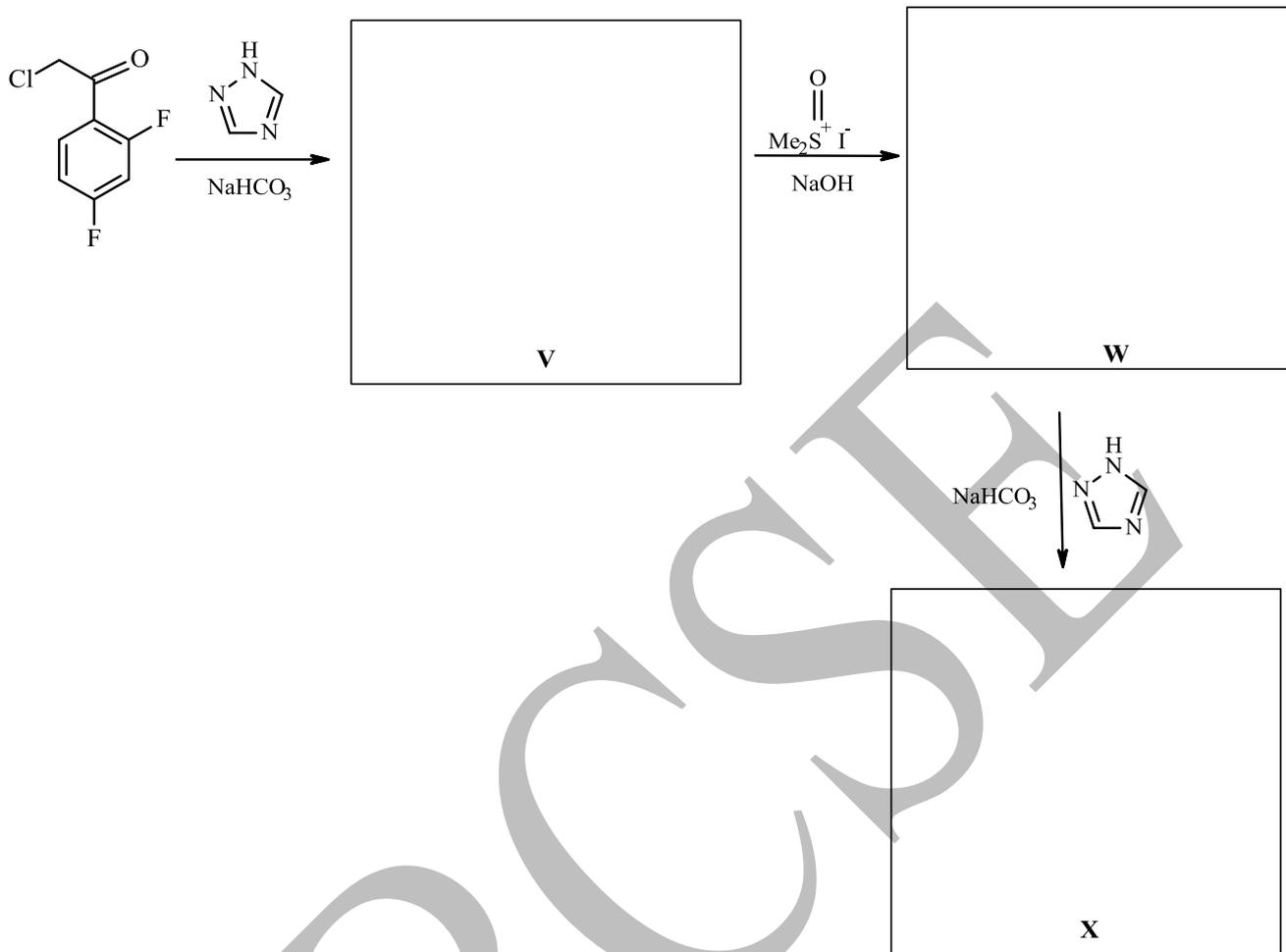
Problem 4   **26 marks**

Understanding Milk

Milk is regarded as a complete food for infants of mammals as it contains all the nutrients like carbohydrates, proteins, fats, minerals and vitamins required by them.

Part A: Proteins in Milk

Milk proteins are categorized into two groups:

    (i) the water soluble whey proteins and

    (ii) the caseins that have low aqueous solubility and exist in milk as micelles.

Adding a mild acid or alcohol leads to precipitation of casein, while whey proteins remain soluble. Caseins act as carriers of (otherwise insoluble) calcium phosphate through amino acids serine and threonine (in its peptide chains), whose side groups form ester linkages with the phosphate units of calcium phosphate.

Serine   **Threonine**
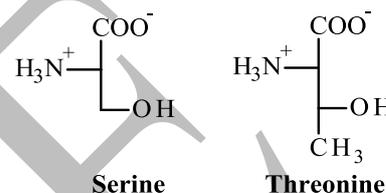
Phospho-ester groups in proteins typically have a pK_{a1} of about 2.0 and pK_{a2} of about 7.0. The isoelectric point (the pH at which net charge on the species is zero) of caseins is at pH 4.6. A generalized polypeptide sequence can be represented as
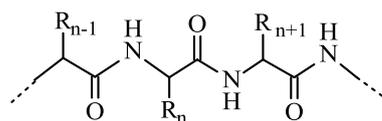
where 'R_n' represents side chains present in amino acids.

4.1   If the amino acid bearing R_n in a casein protein is threonine, draw the structure of R_n in the templates given below (assuming that ester linkages are not broken due to hydrolysis).
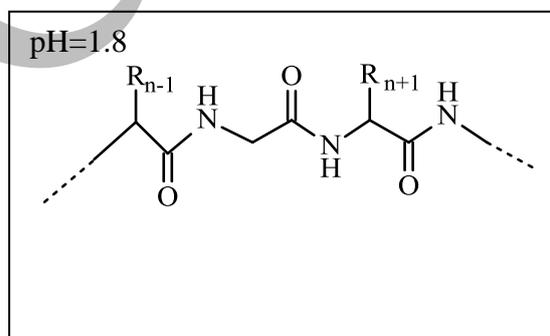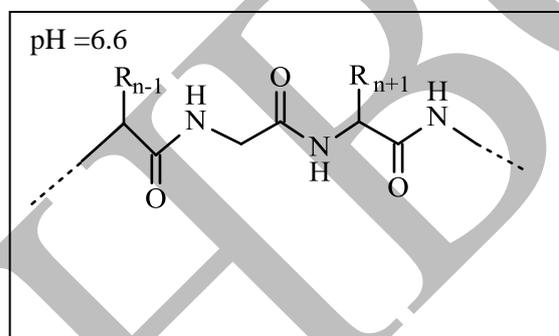
Casein proteins have hydrophobic as well as polar parts. Clustering of these proteins form micellar structures which, in fresh milk, have a net negative charge. Repulsion between these micelles stabilizes them in aqueous phase. Fresh milk has a pH of ~ 6.4 - 6.8. With time, milk tends to turn sour. Acidification tends to break phosphoester linkages. Baking soda ($NaHCO_3$) is sometimes added to souring milk to increase its shelf life.

4.2.   Identify the correct statements from the following (Mark **X** in the appropriate box):

    (a) Caseins would coagulate at pH < 6.4.   ☐

    (b) Caseins would coagulate at pH < 4.6.   ☐

    (c) Caseins would coagulate only at pH ~ <2.0.   ☐

    (d) At pH < 4.6, $Ca_3(PO_4)_2$ would precipitate out.   ☐

(e) At pH < 2.0, both Ca^{2+} and PO_4^{3-} would tend to dissociate from casein ☐

      micelles and dissolve in the aqueous phase.

(f) Adding baking soda prevents coagulation of casein by consuming H^+. ☐

Protein content of a milk sample is usually estimated by two methods:

(i) *Kjeldahl method (estimation of total N in sample)***:** This is the commonly used method by food inspection agencies. Milk sample is heated with concentrated H_2SO_4 with a catalyst, when all N is converted to ammonium ions. Then, this solution is made alkaline and ammonia is distilled into an excess of boric acid (H_3BO_3) solution. The resultant solution is then titrated with a standard acid using a suitable indicator. From the amount of ammonia liberated, the N content is determined.

4.3 In the Kjeldahl's method, write balanced equations of the reaction of ammonia and boric acid, and that involved in the titration with HCl.

(ii) *Biuret test (estimation of the amount of proteins)***:** The sample is mixed with an **excess** of Biuret reagent ($CuSO_4$ in an alkaline solution). The amide units in proteins coordinate with Cu^{2+} ions to form a violet coloured complex, which absorbs light of wavelength 540 nm. This phenomenon of absorption is used to estimate the amount of complex formed which indicates the amount of protein. Aqueous Cu^{2+} does not absorb at this wavelength.
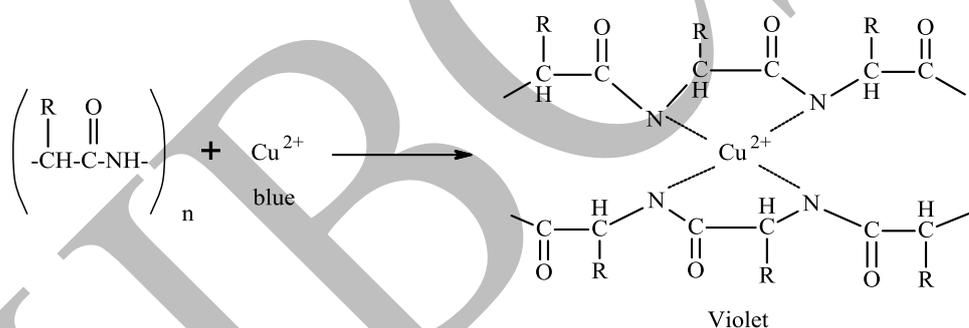
Violet

4.4 In Biuret test, addition of excess reagent is needed to ensure that (Mark **X** in the correct box):

a) all amide N in protein complex with Cu^{2+}. ☐

b) all Cu^{2+} ions in the mixture are bound to proteins. ☐

c) the violet colour developed is intense (to be detectable). ☐

Milk suppliers often dilute milk with water to make profit. This reduces the protein content of the milk and can be easily caught by the Kjeldahl test. To get the diluted milk samples pass the Kjeldahl test, these suppliers add water soluble N-rich compounds as adulterants.

A food analysis lab received a milk sample **M** that was suspected to be adulterated.

4.5 A 10 mL portion of **M** was subjected to Kjeldahl analysis. When the ammonia collected into boric acid (aq.) was titrated with HCl solution (0.140 mol L^{-1}), 35.0 mL of HCl was consumed. Calculate the protein content (in g L^{-1}) that would be reported for this sample based on this analysis. (In general, milk proteins contain 15.65% N.)

4.6. To another 10 mL portion of **M**, sufficient amount of acetic acid was added to ensure coagulation of casein. After filtering off the solid part, the filtrate was subjected to Kjeldahl analysis as above. In the titration, 7.6 mL of HCl solution (0.140 mol L^{-1}) was consumed. Calculate the casein content (in g L^{-1}) in the milk sample.

The sample was further taken for Biuret analysis.

4.7 A series of standard solutions of milk proteins of known concentrations 0.1, 0.5, 1.2 and 2.4 mg mL^{-1} were prepared. To 2 mL of each of the above solutions, excess   Biuret reagent (constant amount for each solution) was added. After 30 min, the absorbance values of   these mixtures was measured at 540 nm, which is proportional to concentration of the light-   absorbing species. Following plot shows the absorbance values for the protein concentration of   solutions taken.
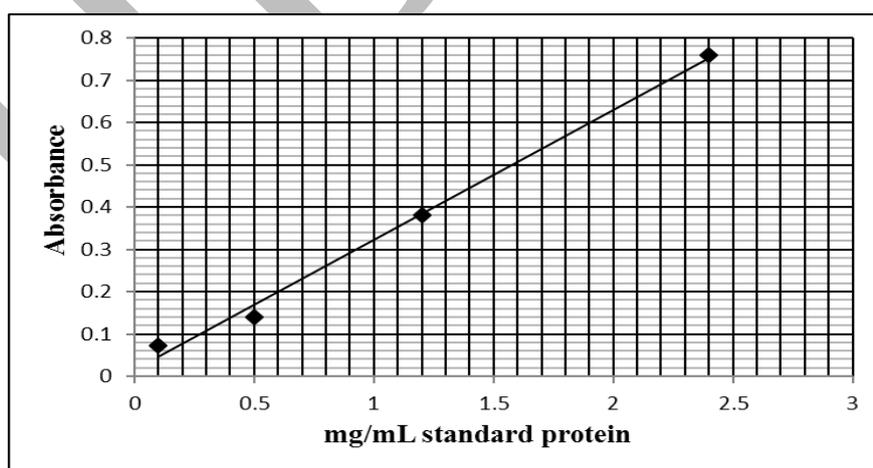
To another 10 mL of milk sample **M**, sufficient amount of acetic acid was added to coagulate casein. This mixture was filtered and 8 mL filtrate was obtained. 2 mL of this filtrate on reaction with the same amount of Biuret reagent (as added to standard solutions above) gave an absorbance value of 0.66 at 540 nm.

Using this data, calculate the concentration of non-protein N (if present) in g L^{-1} in the milk sample.

The remaining filtrate in part **4.7** was subjected to the following qualitative tests to check presence of any adulterant.

  a. On heating with concentrated NaOH evolved a gas which turned moist turmeric paper deep red.
  b. Addition of barium nitrate solution gave a white precipitate which was insoluble in dilute nitric acid.

4.8.   Identify the possible adulterant(s) in the milk sample **M** based on above observations.
(Mark **X** in the appropriate box):

a) Urea ☐   b) $(NH_4)_2SO_4$ ☐   c) $NaHCO_3$ ☐   d) $NaNO_3$ ☐

Part B: Carbohydrates in Milk

Lactose is the major carbohydrate present in milk, which is produced in mammary glands by α-lacto albumin— a major component of whey proteins. Natural milk does not contain sucrose, starch, maltose, etc found in plant sources. Lactose is a disaccharide formed from D(+) galactose and D(+)glucose. The Haworth formulae for α anomers of glucose and galactose are given below.

Glucose   **Galactose (P)**
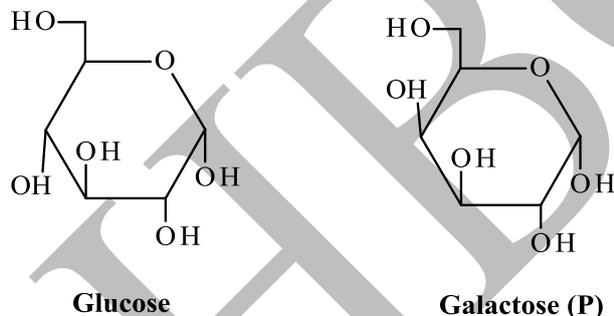
On reaction with concentrated HNO_3, galactose (**P**) gives compound **Q** ($C_6H_{10}O_8$).

4.9   Draw Fisher projection of **Q** and determine if it would be optically active or inactive.   (Mark **X** in the appropriate box)
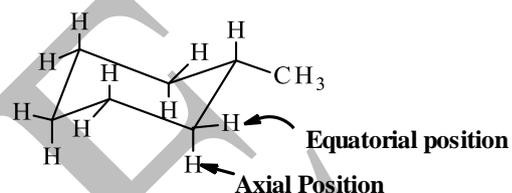
Optically active ☐

Optically inactive ☐

Q

**4.10** Draw the Haworth formula of the anomer of galactose **P**.

Usually, 6-membered rings are more stable in chair conformations. Substitutents on ring, such as methyl group in methyl cyclohexane shown here, are more stable in equatorial position.


Generally, in case of multiple substituents, a conformation with more substituents in equatorial positions is more stable.

4.11 Lactose has two anomeric structures **L₁** and **L₂**. Haworth formula for **L₁** is given below. Complete the partial structure of the stable conformation of **L₁** with the two rings in chair forms (template for one of the rings is given).
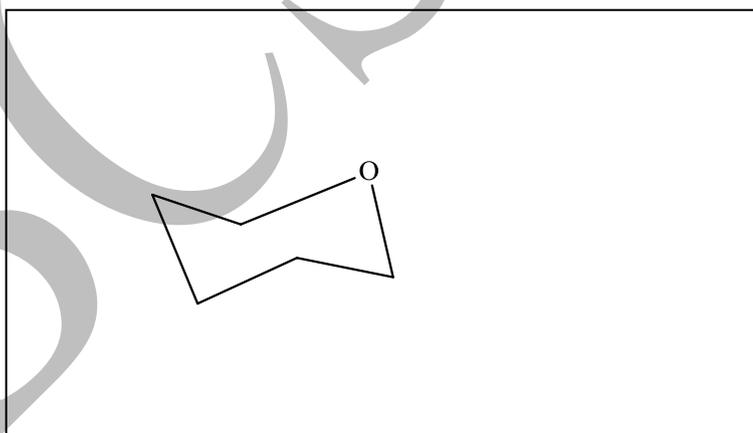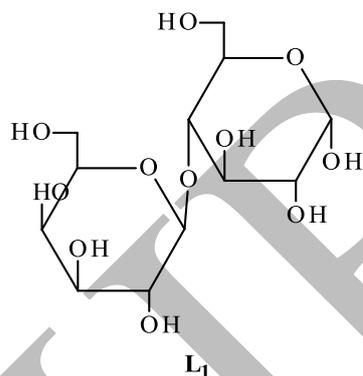
Lactose **L₁** reacts with NH_2OH to give compound **R** ($C_{12}H_{23}NO_{11}$).

4.12 Draw the Haworth formula of **R**.

R
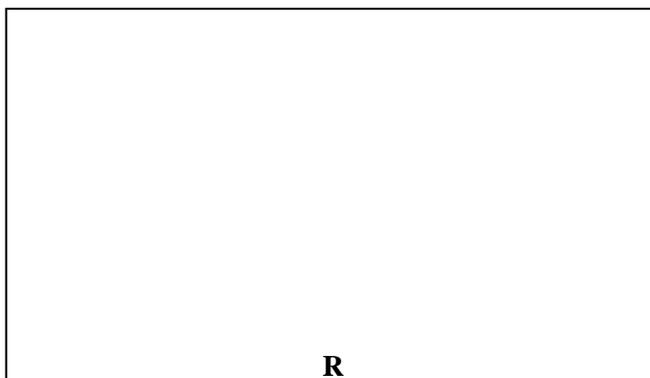
Lactose forms L_1 and L_2 have specific optical rotations, $+89.4°$ and $+35°$, respectively at 20°C, while lactose solution at equilibrium (having these two forms) has specific optical rotation $+55.7°$.

4.13   From this data, determine the percentages of L_1 and L_2 in a lactose solution at equilibrium.

4.14 L_1 and L_2 have solubilities of 70 g and 500 g, respectively in 1 kg of water at 20°C. A student dissolved 400 g of L_2 crystals in 1 kg of water and kept this solution in a closed bottle at 20°C. The next day she found white crystals growing in the bottle indicating some lactose has solidified out of the solution. Determine the total amount of lactose in the solution at this stage.

In recent decades, synthetic milk is being prepared by mixing cheap proteins, oils and surfactants with carbohydrates such as sucrose or starch. Two samples of milk, Y_1 and Y_2, were received in a laboratory, which were suspected of adulteration with synthetic milk.

These samples were taken through a process in which carbohydrates can be selectively extracted. From Y_1 and Y_2, respectively, carbohydrates were obtained as white crystalline solids Y_{1S} and Y_{2S}, both of which were completely soluble in water. Solutions of both Y_{1S} and Y_{2S} had +ve optical rotations, but after adding small amount of HCl (aq) to both, Y_{1S} solution had –ve optical rotation while Y_{2S} solution had still +ve optical rotation. The analyst knew that sucrose is made of D (+) glucose and D(−) fructose, while starch is a polymer of D (+) glucose.

4.15   Based on this data, the analyst can **conclude** that (For each statement, mark **X** in correct box).

	Yes	No
a) Y_1 had synthetic milk added to it.	☐	☐
b) No synthetic milk was present in Y_2.	☐	☐
c) Y_1 had no lactose in it.	☐	☐
d) Y_1 had sucrose in it.	☐	☐
e) No starch was present in Y_1.	☐	☐
f) Y_2 had starch in it.	☐	☐

Problem 5   **21 Marks**

Isotope Effects

In the last century, the discovery of deuterium has contributed most remarkably to our understanding of isotopes and expanded the limits of isotope applications. Deuterated compounds serve as non-radioactive isotopic tracers to study chemical reactions, particularly in biological systems, as deuterium substitution can change the physico-chemical properties of compounds.

The discovery of deuterium in 1931 is credited to American chemist Harold Urey, who observed the atomic spectrum of deuterium as faint lines accompanying the Balmer series lines of atomic hydrogen.

5.1   For a H atom with a nucleus of mass M and an electron of mass m, the wavelength of light emitted corresponding to Balmer series is inversely proportional to the 'reduced mass' μ of the atom, defined as:

$$\mu = \frac{mM}{(m+M)}$$

If the wavelength of the first line of the Balmer series for hydrogen (λ_H) is 6564.74 Å, what would be the difference in wavelengths of the first lines in Balmer series for deuterium and hydrogen (i.e., $\lambda_H - \lambda_D$) as observed by Urey? (Note that $M_H = 1.6737 \times 10^{-27}$ kg and $M_D = 3.3436 \times 10^{-27}$ kg)

The lines observed by Urey for D spectrum were faint because of the low amounts of D naturally present in hydrogen gas samples (average 0.1998 mol% HD and negligible D_2). To establish that the faint lines were not the result of impurities, Urey tried to increase the proportion of D in the hydrogen gas samples –a process known as 'isotopic enrichment'.

This was achieved by slow evaporation, which exploited the difference in the vapour pressure of liquid H_2 and HD. At 14.1 K and 53 mm Hg, Urey theoretically estimated the ratio of vapour pressures of pure liquids $p^\circ_{HD} / p^\circ_{H2} = 0.4$ (use this information for question below).

Consider 2.002 g of liquid hydrogen (0.20 mol% HD; density = 0.077 g cm^{-3}) introduced in an evacuated sealed 12 L flask at 14 K. It is allowed to slowly evaporate and attain equilibrium when the pressure measured was 53 mm Hg.

5.2   Determine the moles of gas molecules present in the flask at equilibrium. Assume that both H_2 and HD show ideal gas behavior. Note that volume changes in liquid   hydrogen during evaporation are negligible compared to the gaseous volume. (For all   calculations in this part, take numbers upto 4th decimal)
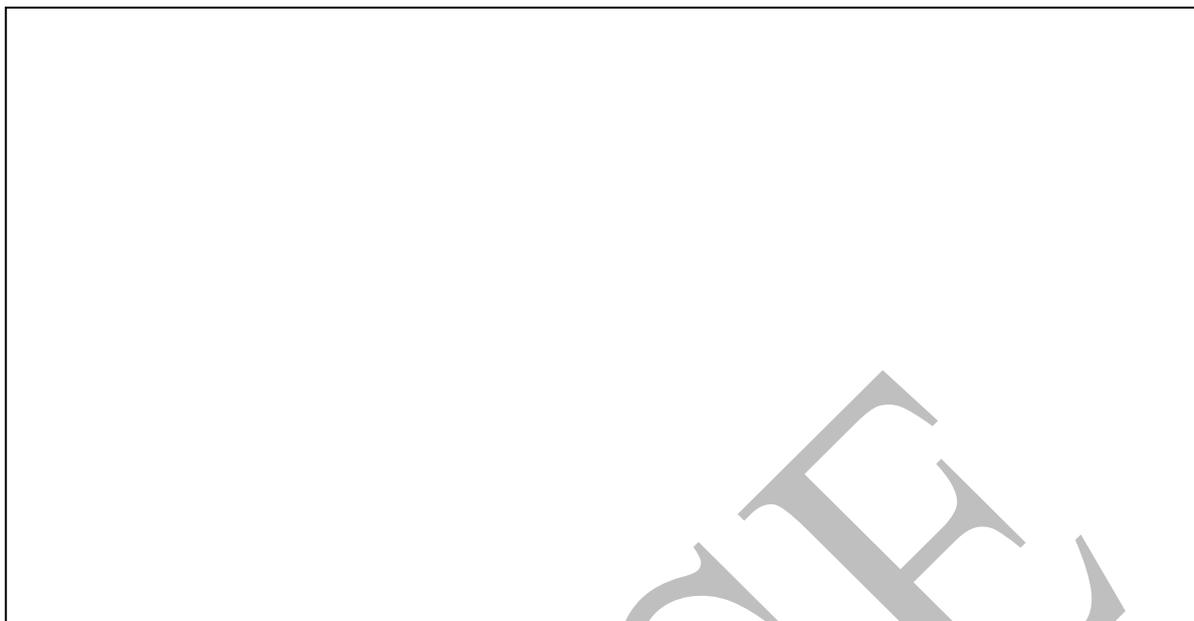
5.3   What would be the mol% of HD in the liquid phase at equilibrium?
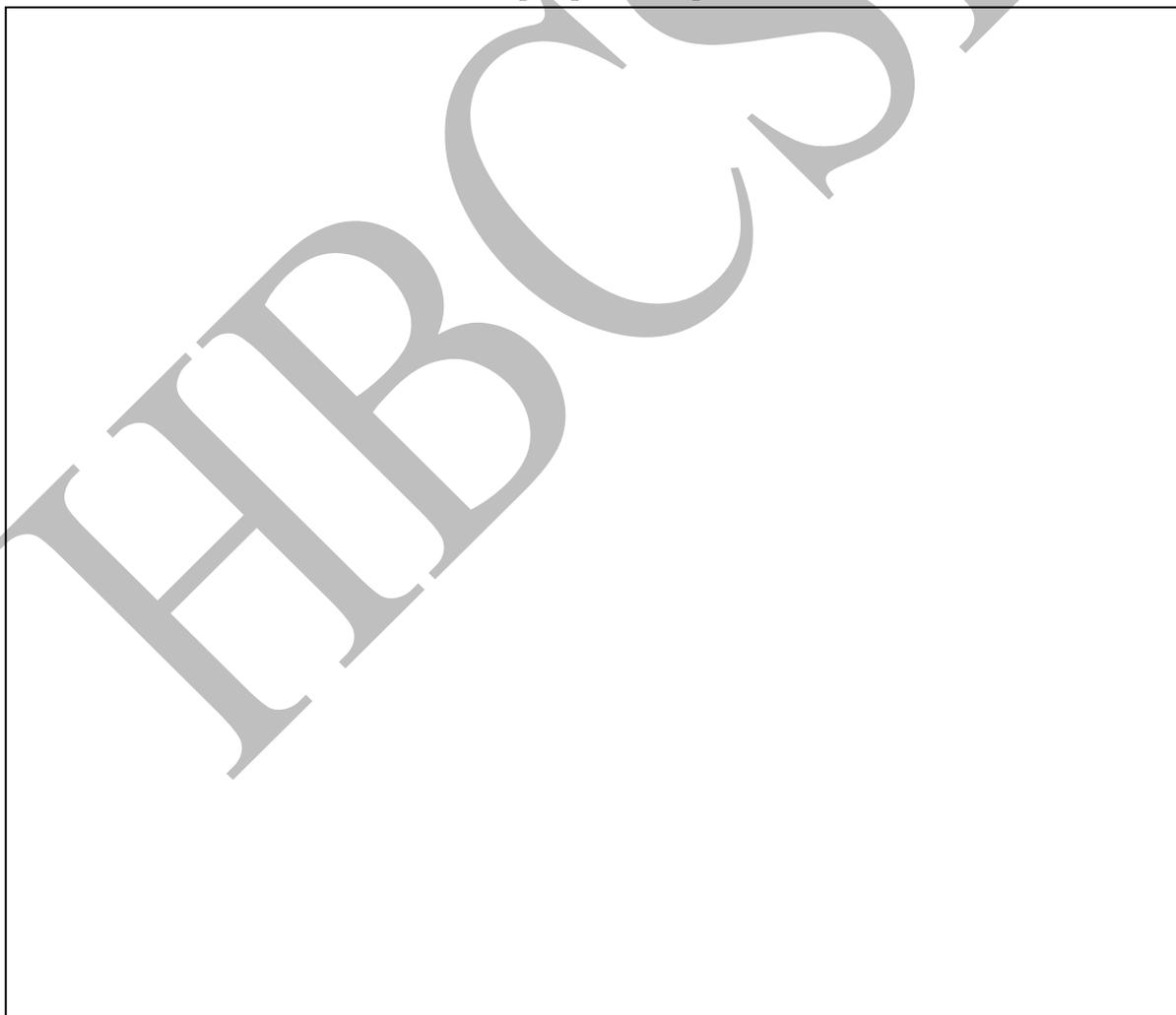
5.4   Efficiency of an enrichment process is gauged by the separation factor (α), defined as

$$\alpha = \frac{x'_{HD} / x'_{H2}}{x_{HD} / x_{H2}}$$

(where, x_{HD} and x'_{HD} represents the mole fraction of HD in the sample before and after processing, respectively. Similarly, x_{H2} and x'_{H2} represents the corresponding mole fractions of H_2). For the evaporation process described above, what is the enrichment   factor of HD in the residual liquid?

5.5   Density of a gas often reflects its isotopic composition. Consider a gas sample containing H_2 and HD mixed in a 1000 cm^3 container. The gas weighs 0.1105 g at standard temperature and pressure. Determine the mol percentage of HD in the sample. (Assume ideal gas behavior for both HD and H_2).

Deuterium enrichment in liquid water can also be achieved by prolonged electrolysis of water, using the small difference in electrode potentials for reduction of H$^+$ and D$^+$. For the electrode reaction:

$H^+(aq) + D^+(aq) + 2e^- \rightleftharpoons HD(g)$, $E^0 = -0.0076V$ with reference to Standard Hydrogen Electrode

5.6   For the following statements, mark **X** in the appropriate box.

	True	**False**
a) HD has a lower tendency to get oxidized as compared to H_2.	☐	☐
b) Deuterium enrichment will occur in the aqueous phase.	☐	☐
c) H$^+$ has a greater tendency to get reduced as compared to D$^+$.	☐	☐
d) HD will not form at cathode.	☐	☐

5.7   Write the half-cell reaction possible at the anode with HDO as reacting species.

5.8   In the following cell meant for electrolysis of water, if the solution is not stirred, in which part of cell (**A** or **B**) one can expect a   higher concentration of HDO once electrolysis has started?
(Mark **X** in the appropriate box)
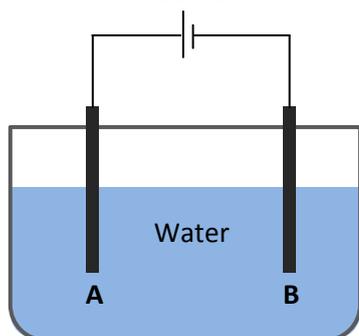
(i) **A**   ☐

(ii) **B**   ☐

(iii) equal in **A** and **B**   ☐

Water

A   B

Water chemistry becomes more interesting and challenging when isotopes are considered. For   example, artificial mixtures of 'light' water (H_2O) and heavy water (D_2O) undergo self-dissociation and recombination process to yield a mixture of H_2O, D_2O and HDO. The equilibrium can be represented as:

$$H_2O\ (l) + D_2O\ (l) \rightleftharpoons 2HDO\ (l)\ (K_{eq} = 3.86\ at\ 298\ K)$$

Note that here K_{eq} = [HDO (l)] / [H_2O (l)][D_2O (l)], where [X] = molarity of X in mol dm^{-3}.

5.9   What would be the equilibrium composition of a mixture prepared by mixing 20 mL D_2O with 80 mL H_2O at 298 K?
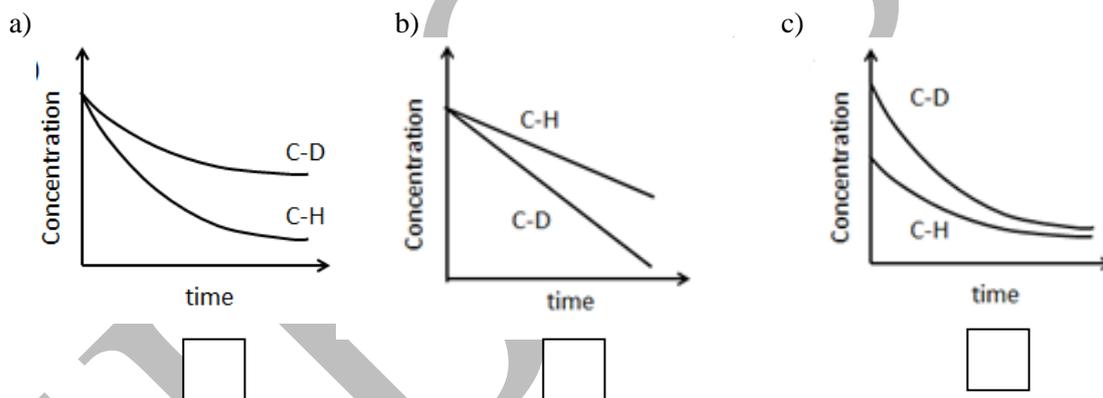Densities of pure H_2O and D_2O at 298 K are 997.05 and 1104.36 kg m^{-3}, respectively. Assume ideal behavior of solution so that volumes are additive.

5.10 The self-dissociation constant of D_2O is 1.1×10^{-15} as compared to 1×10^{-14} for H_2O. Here, the the activities of the bulk liquids (not molarities) are used to determine dissociation constant. This shows that: (Mark **X** in the correct boxes)

a) O-H bond is stronger than O-D bond.

b) O-D bond is stronger than O-H bond.

c) D_2O is a weaker acid than H_2O.

d) D_2O is a stronger acid than H_2O.

Isotopic substitution, ideally, should not affect the chemical properties of the molecules since it does not affect the electronic configuration of the molecule. But in reality, the change of nucleus affects the strength of bonding. Changes in the rate of a reaction involving breaking of a bond involving H atoms versus the same bond involving D atom is known as the *kinetic isotope effect*.

5.11 Consider a reaction involving breaking of a C-H bond in a compound **Z** in the rate determining step. Which of the following would correctly represent the effect of deuterium substitution on concentration vs time profile of **Z** for the above reaction, keeping all other parameters constant? (Mark **X** in the correct box)

a)

b)

c)

Rough Page