PREPARATORY PROBLEMS & SOLUTIONS

52nd International Chemistry Olympiad
Istanbul, Turkey

Preparatory Problems & Solutions

52nd IChO 2020

International Chemistry Olympiad

Istanbul, Turkey

CHEMISTRY FOR A BETTER TOMORROW

Fifth edition (04.08.2020)

Preface

We are very glad to provide Preparatory Problems for the 52nd International Chemistry Olympiad, which will be held in 2020 in Istanbul, Turkey. We prepared these problems with the intention of facilitating the training and preparation of participants. The contents of the problems have been carefully selected so as to cover a broad range of challenging topics that can be encountered in modern as well as classical chemistry. The problems can be solved by applying the fundamental principles of chemistry covered at high school level along with 6 topics of advanced difficulty for the theoretical section, and 3 topics of advanced difficulty for the practical section. These advanced topics are listed explicitly under "Topics of Advanced Difficulty" and their applications are demonstrated in the tasks. We expect the participants to be familiar with these advanced topics.

The problems listed in this booklet consist of 25 theoretical and 8 practical tasks. The solutions were sent to the Head Mentor of each country by e-mail by February 10th, 2020 and published by June 01st, 2020 on our IChO 2020 website. We welcome any comments, suggestions, corrections, or questions about the problems at icho2020@tubitak.gov.tr.

The International Chemistry Olympiad presents a great opportunity to inspire younger generations to pursue a career in fundamental sciences and make a positive influence on public attitudes towards science, and in particular chemistry. We hope you will enjoy solving these problems and we look forward to seeing you in July in Istanbul, Turkey.

Acknowledgments

I would like to express my deep gratitude to all the authors for their dedication and effort in contributing to the Preparatory Problems as well as the members of the International Steering Committee for their valuable comments and suggestions. We are also highly appreciative of the Scientific and Technological Research Council of Turkey (TUBITAK), in collaboration with the Faculty of Science, Istanbul Technical University (ITU), for facilitating all organizational tasks before and during IChO 2020.

On behalf of the Scientific Committee,
Dr. Arif DAŞTAN

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Edited by: SARAÇOĞLU, Nurullah, *Atatürk University*

Physical Constants and Equations

Avogadro's number, $N_A = 6.0221 \times 10^{23} mol^{-1}$
Boltzmann constant, $k_B = 1.3807 \times 10^{-23} JK^{-1}$
Universal gas constant, $R = 8.3145\ JK^{-1}mol^{-1} = 0.08205\ atm\ L\ K^{-1}mol^{-1}$
Speed of light, $c = 2.9979 \times 10^{8} ms^{-1}$
Planck's constant, $h = 6.6261 \times 10^{-34}\ J\ s$
Faraday's constant, $F = 9.6485 \times 10^{4}\ C\ mol^{-1}$
Mass of electron, $m_e = 9.10938215 \times 10^{-31}\ kg$
Standard pressure, $P = 1\ bar = 10^{5}\ Pa$
Atmospheric pressure, $P_{atm} = 1.01325 \times 10^{5}\ Pa = 760\ mmHg = 760\ torr$
Zero of the Celsius scale, $273.15\ K$
1 picometer (pm) = $10^{-12}\ m$; $1Å = 10^{-10}\ m$; 1 nanometer (nm) = $10^{-9}\ m$
$1\ eV = 1.6 \times 10^{-19}\ J$
$1\ cal = 4.184\ J$
$1\ amu = 1.66053904 \times 10^{-27}\ kg$
Charge of an electron: $1.6 \times 10^{-19}\ C$
Ideal gas equation: $PV = nRT$
Enthalpy: $H = U + PV$
Gibbs free energy: $G = H - TS$

$$\Delta G = \Delta G^0 + RTlnQ$$

$$\Delta G^0 = -RTlnK = -nFE^0_{cell}$$

Entropy change:

$\Delta S = \frac{q_{rev}}{T}$, where q_{rev} is heat for the reversible process

$\Delta S = nRln\frac{V_2}{V_1}$ (for isothermal expansion of an ideal gas)

Nernst equation: $E = E^0 + \frac{RT}{nF} ln \frac{C_{ox}}{C_{red}}$

Energy of a photon: $E = \frac{hc}{\lambda}$

Integrated rate law

Zeroth order: $[A] = [A]_0 - kt$

First order:

$$ln[A] = ln[A]_0 - kt$$

Second order:

$$\frac{1}{[A]} = \frac{1}{[A]_0} + kt$$

Arrhenius equation: $k = Ae^{-E_a/RT}$

Equation of linear calibration curve: $y = mx + n$

Standard deviation:

$$s = \sqrt{\frac{\sum_{x=1}^{N}(x_1 - \bar{x})^2}{N-1}}$$

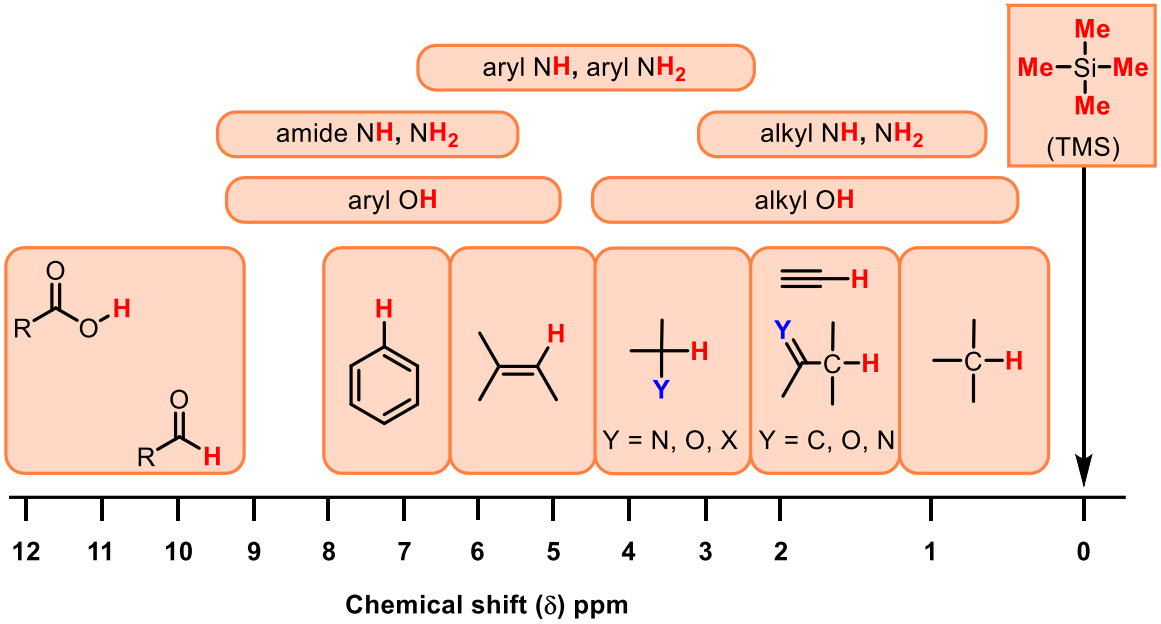
Lambert–Beer equation: $A = \varepsilon l c$

Periodic Table of Elements

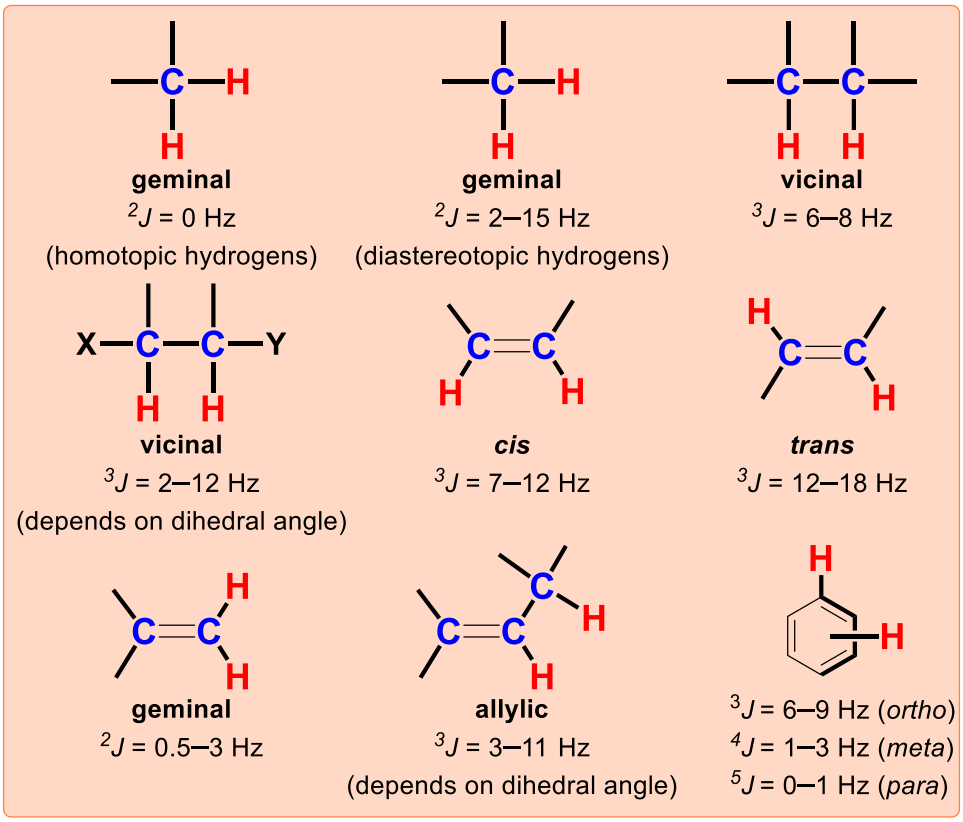
1																	18
1 H 1.008	2		atomic number Symbol atomic weight									13	14	15	16	17	2 He 4.003
3 Li 6.94	4 Be 9.01											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
11 Na 22.99	12 Mg 24.31	3	4	5	6	7	8	9	10	11	12	13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.06	17 Cl 35.45	18 Ar 39.95
19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.87	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.38	31 Ga 69.72	32 Ge 72.63	33 As 74.92	34 Se 78.97	35 Br 79.90	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.95	43 Tc -	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
55 Cs 132.9	56 Ba 137.3	57-71	72 Hf 178.5	73 Ta 180.9	74 W 183.8	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po -	85 At -	86 Rn -
87 Fr -	88 Ra -	89-103	104 Rf -	105 Db -	106 Sg -	107 Bh -	108 Hs -	109 Mt -	110 Ds -	111 Rg -	112 Cn -	113 Nh -	114 Fl -	115 Mc -	116 Lv -	117 Ts -	118 Og -

57 La 138.9	58 Ce 140.1	59 Pr 140.9	60 Nd 144.2	61 Pm -	62 Sm 150.4	63 Eu 152.0	64 Gd 157.3	65 Tb 158.9	66 Dy 162.5	67 Ho 164.9	68 Er 167.3	69 Tm 168.9	70 Yb 173.0	71 Lu 175.0
89 Ac -	90 Th 232.0	91 Pa 231.0	92 U 238.0	93 Np -	94 Pu -	95 Am -	96 Cm -	97 Bk -	98 Cf -	99 Es -	100 Fm -	101 Md -	102 No -	103 Lr -

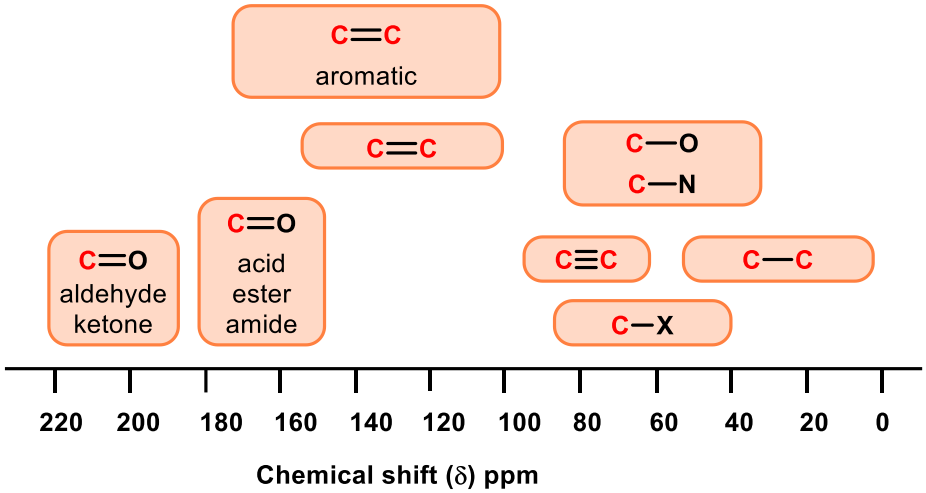
^{1}H NMR Chemical Shifts



Typical Coupling Constants



^{13}C NMR Chemical Shifts



IR Absorption Frequency Table

Functional Group	Type of Vibration	Absorption Frequency Region (cm^{-1})	Intensity
Alcohol			
O–H	(stretch, H–bonded)	3600–3200	strong, broad
	(stretch, free)	3700–3500	strong, sharp
C–O	(stretch)	1150–1050	strong
Alkane			
C–H	stretch	3000–2850	strong
	bending	1480–1350	variable
Alkene			
=C–H	stretch	3100–3010	medium
	bending	1000–675	strong
C=C	stretch	1680–1620	variable
Alkyl Halide			
C–F	stretch	1400–1000	strong
C–Cl	stretch	800–600	strong
C–Br	stretch	600–500	strong
C–I	stretch	500	strong
Alkyne			
C–H	stretch	3300	strong, sharp
C≡C	stretch	2260–2100	variable, not present in symmetrical alkynes
Amine			
N–H	stretch	3500–3300	medium (primary amines have two bands; secondary have one band, often very weak)
C–N	stretch	1360–1080	medium-weak

N–H	bending	1600	medium
Aromatic			
C–H	stretch	3100–3000	medium
C=C	stretch	1600–1400	medium-weak, multiple bands
Carbonyl			
C=O	stretch	1820–1670	strong
Acid			
C=O	stretch	1725–1700	strong
O–H	stretch	3300–2500	strong, very broad
C–O	stretch	1320–1210	strong
Aldehyde			
C=O	stretch	1740–1720	strong
C–H	stretch	2850–2820 & 2750–2720	medium, two peaks
Amide			
C=O	stretch	1690–1640	strong
N–H	stretch	3500–3100	unsubstituted have two bands
	bending	1640–1550	
Anhydride			
C=O	stretch	1830–1800 &1775–1740	two bands
Ester			
C=O	stretch	1750–1735	strong
C–O	stretch	1300–1000	two bands or more
Ketone			
acyclic	stretch	1725–1705	strong
cyclic	stretch	3-membered - 1850	strong
	stretch	4-membered - 1780	strong
	stretch	5-membered - 1745	strong
	stretch	6-membered - 1715	strong
	stretch	7-membered - 1705	strong
α,β-unsaturated	stretch	1685–1665	strong
conjugation moves absorptions to lower wavenumbers			
aryl ketone	stretch	1700–1680	strong
Ether			
C–O	stretch	1300–1000 (1150–1070)	strong
Nitrile			
C≡N	Stretch	2260–2210	medium
Nitro			
N–O	stretch	1560–1515 & 1385–1345	strong, two bands

Fields of Advanced Difficulty

Theoretical

1. Pericyclic reactions (Cycloaddition and electrocyclization reactions).
2. Nucleophilic substitution reactions at sp^2 carbon centers.
3. *Spectroscopy*: Basic ^{1}H and ^{13}C NMR spectroscopy (chemical shifts, signal multiplicity, intensity and coupling constants); simple IR spectroscopy.
4. *Kinetics*: Rate constant models and kinetic isotope effect.
5. *Basic quantum chemistry:* Electronic energy levels, transitions applied to conjugated systems, vibrational and rotational motions of molecules (formulas provided), and simple theories of conjugated systems.
6. *Inorganic chemistry:* Coordination chemistry (crystal structure, crystal field theory, and isomerism) and molecular orbital energy diagrams of homo/heteronuclear diatomic molecules.

Notes:

i) The following topics WILL NOT appear in the exam set:

- Metal-catalyzed cross-coupling reactions and olefin metathesis reactions.
- Use of Microsoft Excel or any related computer software.
- Use of derivatives and integrals.
- Although a few examples in the preparatory problems are related to biomolecules, students are not expected to cover any biochemistry or carbohydrate chemistry as advanced topics.
- Inorganic reaction mechanisms.
- Molecular orbital diagrams of polyatomic molecules.

ii) Unless important, the reaction conditions such as solvent and temperature have not been shown on the arrows in the reaction schemes.

Practical

1. Use of a spectrophotometer (mono/double-wavelength measurements).
2. Basic techniques in organic synthesis: recrystallization, thin layer chromatography (TLC), filtration, and drying of precipitates following the described procedures.
3. Distillation and extraction.

Notes:

During the practical exam, students WILL NOT be expected to:

⇒ Determine melting points.
⇒ Use a rotary evaporator.
⇒ Handle and work up moisture-sensitive compounds (using syringes and balloons).
⇒ Perform column chromatography.
⇒ Produce the hydrogel system by polymerization through the experiments.

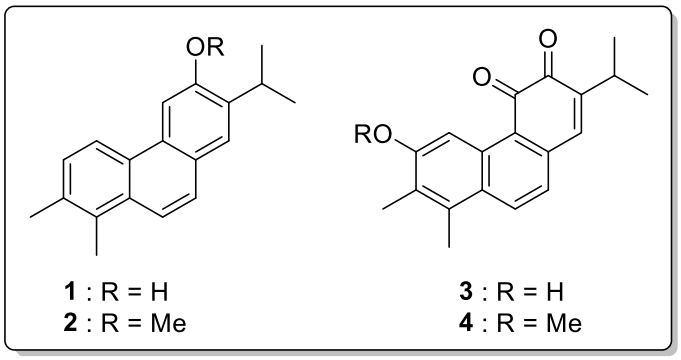
Part I: Theoretical Problems

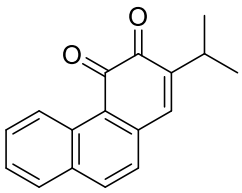
Problem 1. *Salvia* Species Growing in Turkey: Isolation and Total Synthesis of Abietane Diterpenoids

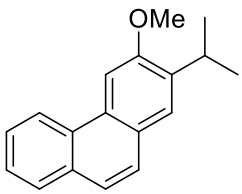
The genus *Salvia*, named after a Latin word, salvare ("healer"), has a variety of species with important medicinal activities. They have been used for the treatment of colds, flu, and menstrual disorders in most regions of the world since ancient times. In Turkish folk medicine, *Salvia* L. species have also been used as a carminative, diuretic, hemostatic, spasmolitic, and stomachic, and in the treatment of mouth and throat irritations due to their antibacterial and wound healing properties. The genus *Salvia* includes over 900 species across the world, 58 of which are endemic in Turkey.

Female Turkish scientists Ulubelen & Topçu with co-workers have studied Anatolian *Salvia* plants growing in Turkey, and isolated and characterized more than 320 natural products, most of which are terpenoids, while one third are new diterpenoids.

In one of their studies on *Salvia multicaulis* Vahl., Ulubelen & Topçu isolated four new aromatic abietane norditerpenoids (**1**–**4**), which showed strong antituberculous activity. In addition to the antibacterial and antifungal activities of the isolated diterpenoids, the plant extracts also showed antioxidant, antiinflammatory, and cholinesterase inhibitory activities. *S. multicaulis* has folkloric use in Anatolia, such as an appetizer, for wound healing, against scorpion stings, and in the treatment of respiratory and urinary infections and diabetes.



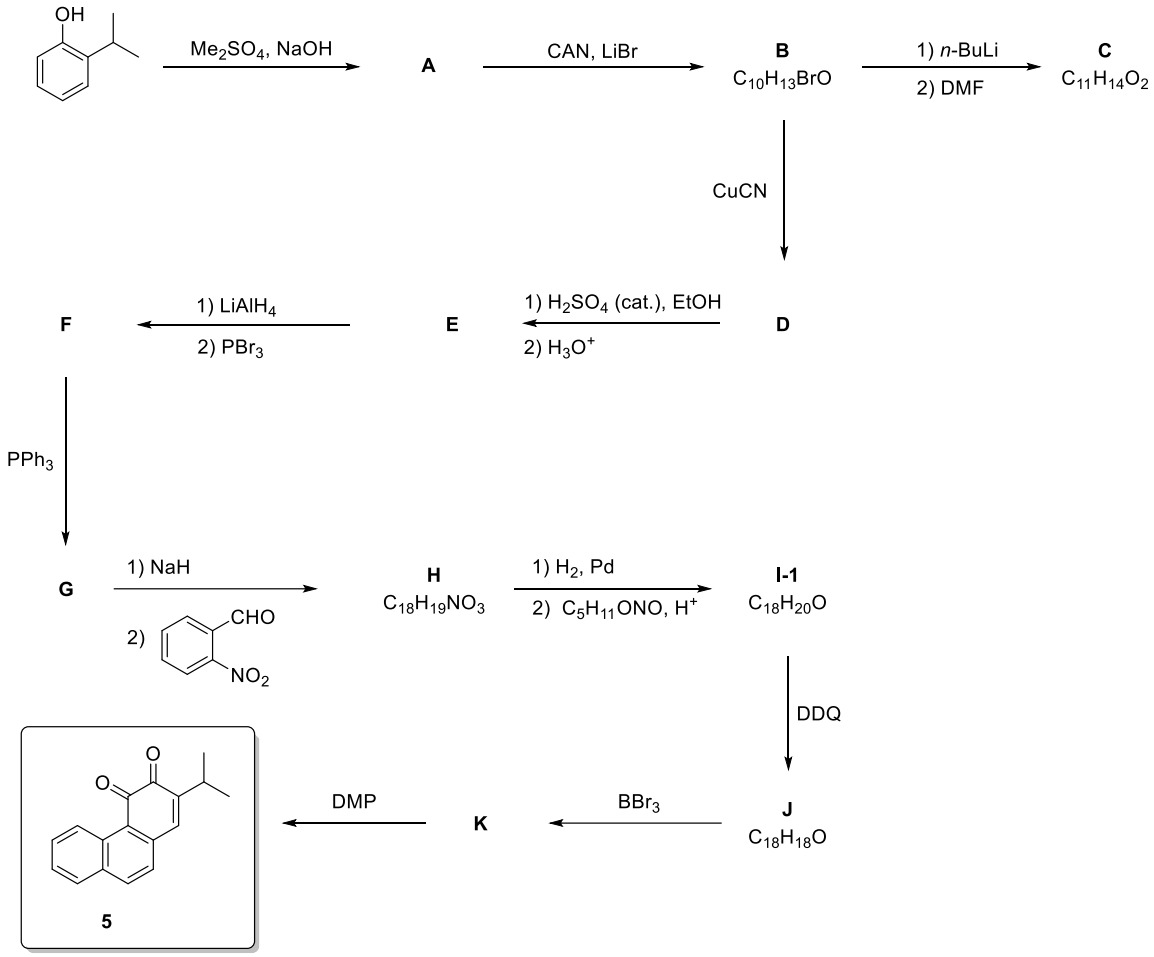


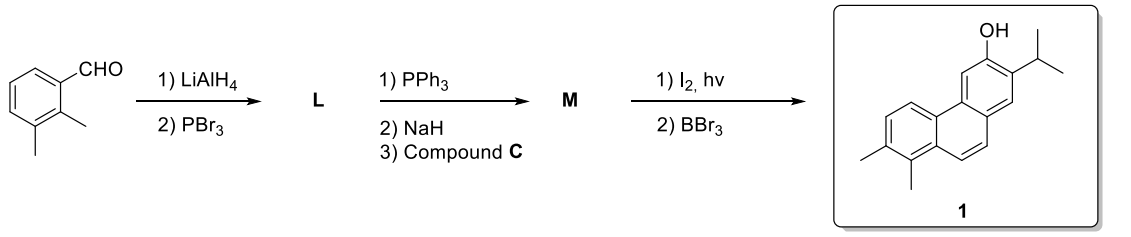


Later, a research group in Turkey developed a synthetic route to obtain derivatives of natural products **1**–**4**. This problem covers the synthesis of related compounds. The following reaction schemes illustrate the total synthesis of diterpenoids **1** and **5**.

1.1. **Draw** the structure of the products **A**–**M**, without any stereochemical detail. **Hint:** In second step (**A** → **B**), combination of lithium bromide and cerium(IV) ammonium nitrate (CAN) is used as a brominating reagent. Compound **C** is a benzaldehyde derivative and used in the synthesis step of compound **M**.

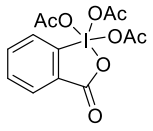
1.2. During the cyclization of **H** to **I-1**, another isomeric compound, **I-2**, with the formula $C_{18}H_{20}O$, is also formed. **Draw** the structure of **I-2**.

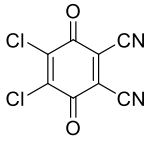




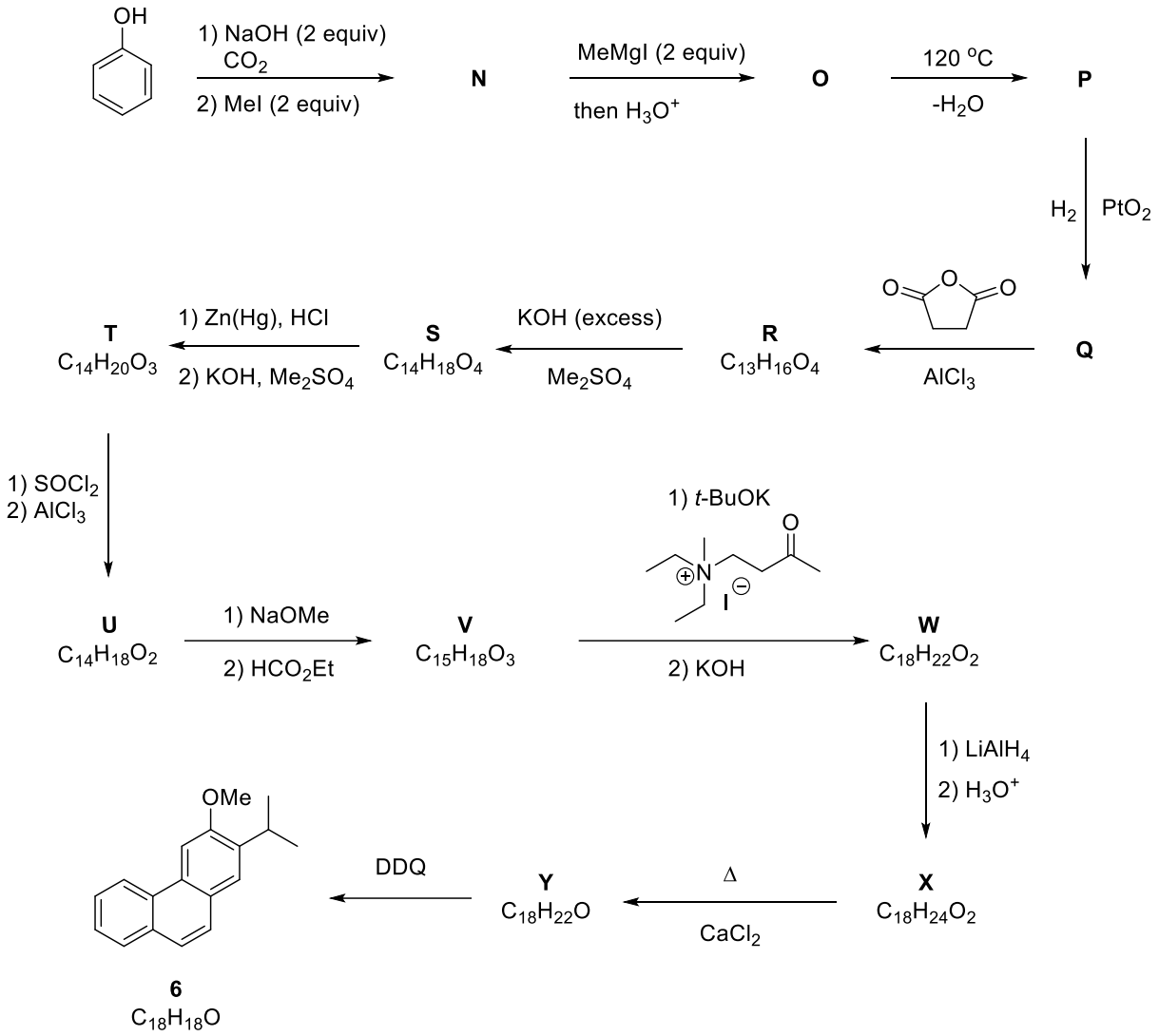
CAN = Ceric ammonium nitrate ($(NH_4)_2Ce(NO_3)_6$) ; DMF = Dimethylformamide (Me_2NCHO) ;

DMP = Dess-Martin Periodinane ($C_{13}H_{13}IO_8$) ; DDQ = 2,3-Dichloro-4,5-dicyano-1,4-benzoquinone





1.3. The following reaction scheme is related to the synthesis of **6**, a desmethyl derivative of the diterpenoids **1** and **2**. **Draw** the structures of products **N**–**Y**, without any stereochemical detail. **Hint:** Compounds **R**, **S** and **T** exhibit acidic character. The transformation of compound **V** to **W** includes Robinson annulation and a possible deformylation reaction steps.



1.4. During the transformation of compound **V** to **W** (Robinson annulation step), the use of a precursor of the *α*,*β*-unsaturated ketone, such as a *β*-chloroketone or *N*,*N*,*N*,-trialkyl-3-oxobutan-1-aminium halide (as used in the reaction scheme), can be more favorable. **Explain**.

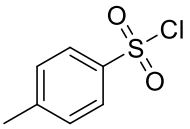
1.5. **Draw** possible tautomeric forms of compound **V**.

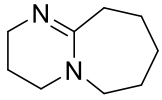
1.6. Compound **Y** can be also obtained via ring-closing (electrocyclization) of the compound **Z**. **Draw** structure of **Z**.

1.7. For the transformation of **X** to **Y**, which of the following reagents can also be used? (Ignore S_N2' type reactions).

- ☐ i) PBr_3/pyridine; ii) *n*-Bu_3SnH/AIBN
- ☐ i) PBr_3/pyridine; ii) Na/*t*-BuOH
- ☐ i) MnO_2; ii) DDQ
- ☐ i) TsCl/pyridine; ii) $LiAlH_4$
- ☐ i) TsCl/pyridine; ii) DBU

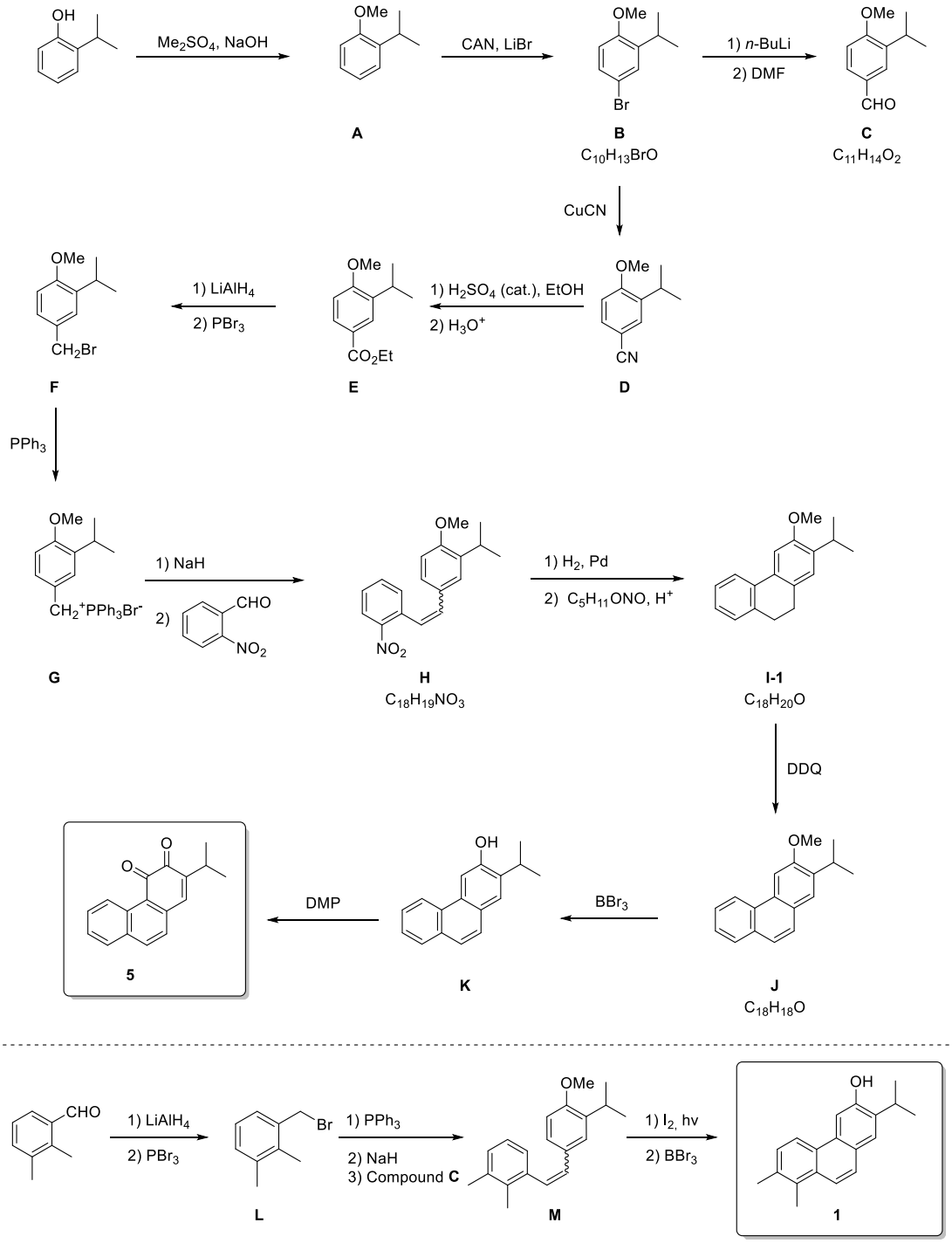
TsCl = *p*-Toluenesulfonyl chloride DBU = 1,8-Diazabcyclo[5,4,0]undec-7-ene



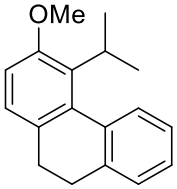


Solution:

1.1.

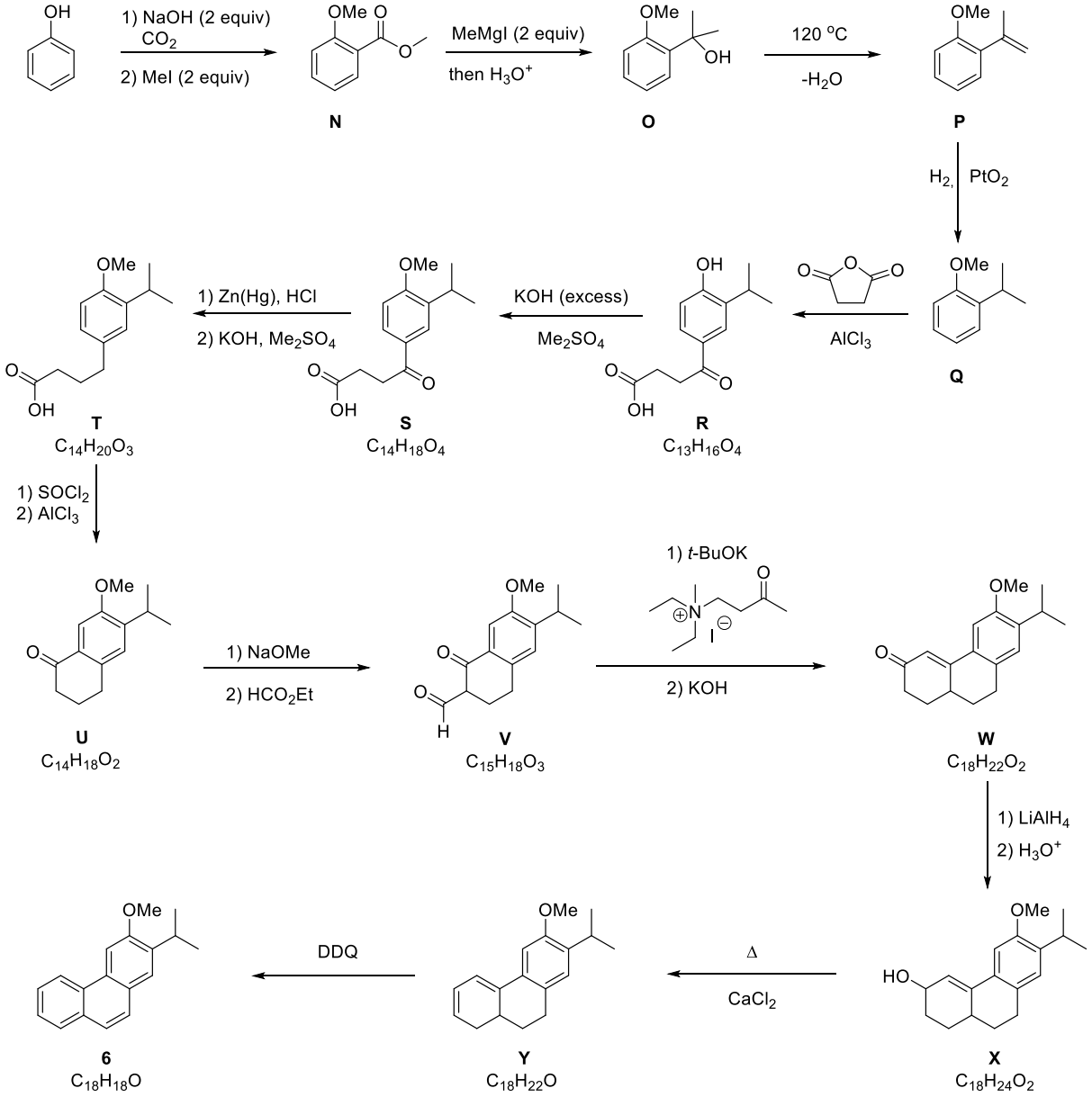

OH
Me2SO4, NaOH
OMe
CAN, LiBr
OMe
Br
1) n-BuLi
2) DMF
OMe
CHO
A
B
C10H13BrO
C
C11H14O2
CuCN
OMe
CN
D
1) H2SO4 (cat.), EtOH
2) H3O+
OMe
CO2Et
E
1) LiAlH4
2) PBr3
OMe
CH2Br
F
PPh3
OMe
CH2+PPh3Br-
1) NaH
2)
CHO
NO2
OMe
NO2
G
H
C18H19NO3
1) H2, Pd
2) C5H11ONO, H+
OMe
I-1
C18H20O
DDQ
OMe
J
C18H18O
BBr3
OH
K
DMP
O
O
5
CHO
1) LiAlH4
2) PBr3
Br
L
1) PPh3
2) NaH
3) Compound C
OMe
M
1) I2, hv
2) BBr3
OH
1

1.2.



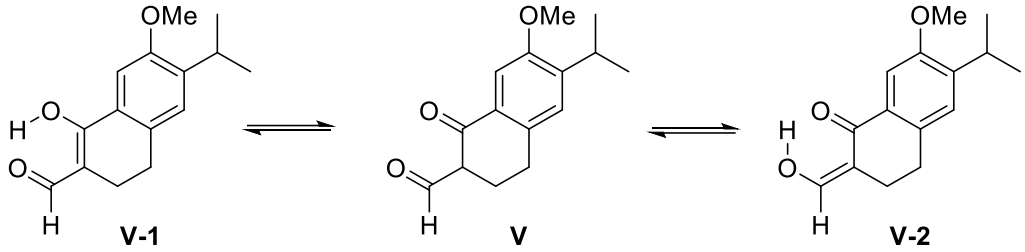
I-2
$C_{18}H_{20}O$

1.3.

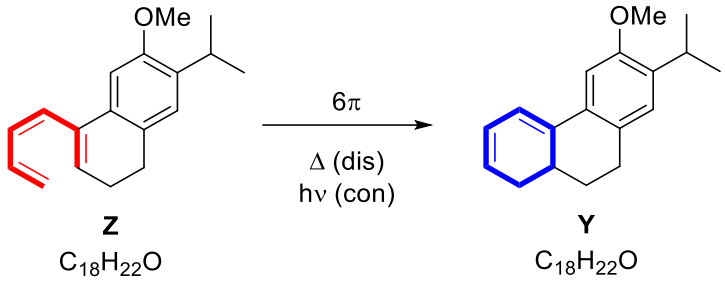


1.4. The use of a precursor of the α,β-unsaturated ketone, such as a *β*-chloroketone or *N*,*N*,*N*-trialkyl-3-oxobutan-1-aminium halide, can reduce the steady-state concentration of enone and decrease the possible side reactions of precursors such as self-condensation or polymerization reactions.

1.5.



1.6.



1.7.

☐ i) PBr_3/pyridine; ii) *n*-Bu_3SnH/AIBN

☐ i) PBr_3/pyridine; ii) Na/*t*-BuOH

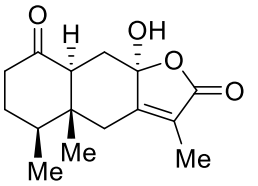
☐ i) MnO_2; ii) DDQ

☐ i) TsCl/pyridine; ii) $LiAlH_4$

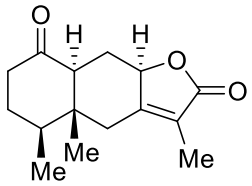
☒ i) TsCl/pyridine; ii) DBU

Problem 2. Istanbulins and Related Sesquiterpene Natural Products

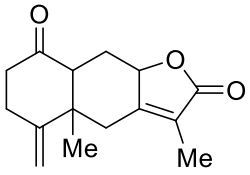
Some elements received their names from different places around the world. In this respect, the record belongs to the Swedish village of Ytterby, after which four elements were named: ytterbium (Yb), yttrium (Y), erbium (Er), and terbium (Tb). However, elements are not the only chemical entities that owe their names to such places. Interestingly, a class of natural products, **istanbulins A**–**E**, received their names from the city of Istanbul. The first two members of this family, istanbulins A and B, were first isolated by Prof. Dr. Ayhan Ulubelen and co-workers from the plant *Smyrnium olusatrum* in 1971. The isolation of the remaining members, istanbulins C–E, was reported by Ulubelen and co-workers between 1979 and 1982.



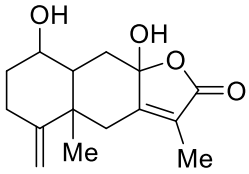
Istanbulin A



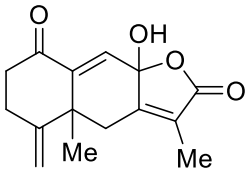
Istanbulin B



Istanbulin C



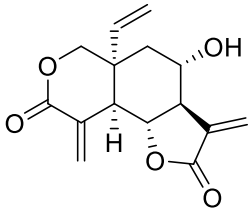
Istanbulin D



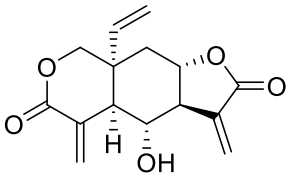
Istanbulin E

Istanbulins constitute a subclass of a much larger family of natural products called sesquiterpenes. Two important sesquiterpene natural products with a similar 6-6-5 fused ring system are vernolepin (**1**) and vernomenin (**2**). Danishefsky and co-workers reported an elegant total synthesis of these two natural products in 1976 via the utilization of the Diels–Alder (DA) chemistry of the so-called Danishefsky's diene.

Please note that all formulae depicting chiral molecules in this question refer to racemic mixtures.

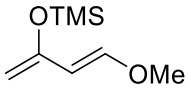


Vernolepin
1

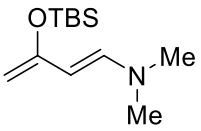


Vernomenin
2

In this context, Danishefsky's diene (**3**) and the Rawal–Kozmin diene (**4**) are two electron-rich dienes that found widespread use in organic synthesis, and their structures are shown below.



Danishefsky's diene
3

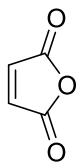


Rawal-Kozmin diene
4

TMS: trimethylsilyl; TBS: *tert*-butyldimethylsilyl

2.1. **Draw** the major resonance structures of dienes **3** and **4**. **Indicate** the carbon atoms with higher electron density on each diene.

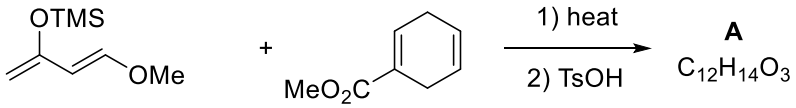
2.2. Compounds **3** and **4** have been extensively used as diene components in Diels–Alder reactions. **Draw** the conformations of **3** and **4** required to be able to enter a DA reaction. **Predict** which compound is a more reactive diene in a DA reaction with maleic anhydride (**5**).



maleic anhydride
5

2.3. When a mixture of Danishefsky's diene (**3**) and compound **6** was heated followed by treatment with acid (TsOH, *p*-toluenesulfonic acid), compound **A** was obtained as the major product.

Draw the structures of **all** possible Diels–Alder products with the molecular formula of $C_{12}H_{14}O_3$ that can be obtained from the reaction of **3** and **6**. Drawing only one enantiomer of an enantiomeric pair is sufficient.

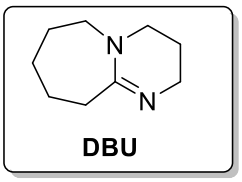


3 **6**

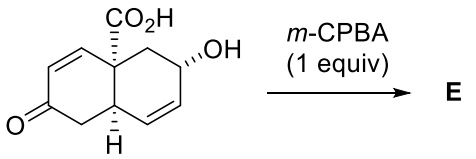
2.4. **Determine** the structure of the major product **A**.

2.5. Diels–Alder adduct **A** was converted to compound **7** via a sequence of 4 steps as shown below. Compound **B** is known to be acidic. **Draw** the structures of **B**–**D**.

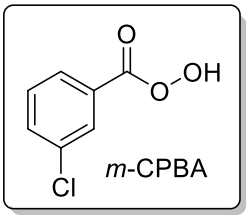
7



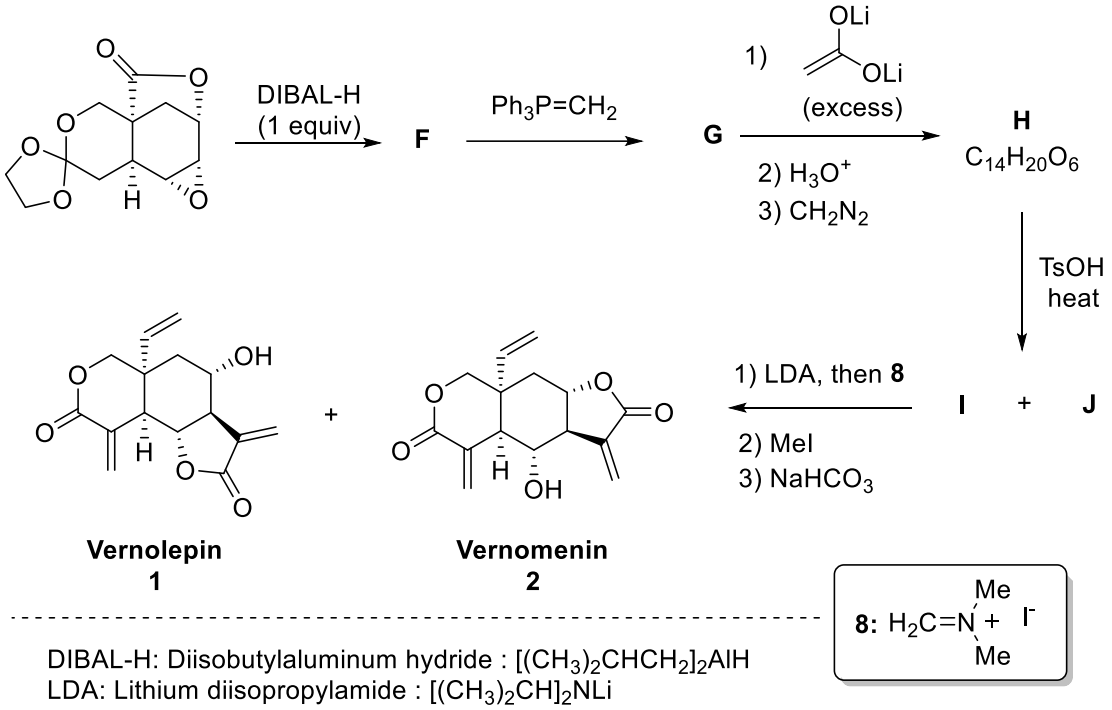
2.6. When compound **7** is reacted with 1 equiv of *m*-CPBA, product **E** was obtained as a major product. **Circle** the functional group that reacts selectively with *m*-CPBA, and **draw** the structure of **E**.



7



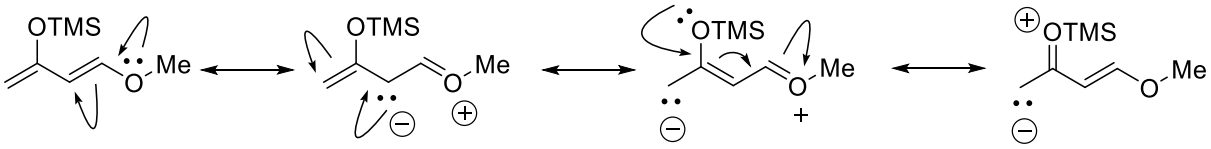
2.7. The syntheses of vernolepin (**1**) and vernomenin (**2**) were completed as shown in the scheme below. **Draw** the structures of compounds **F**–**J**. In the final step, compound **I** is the precursor of **1**.



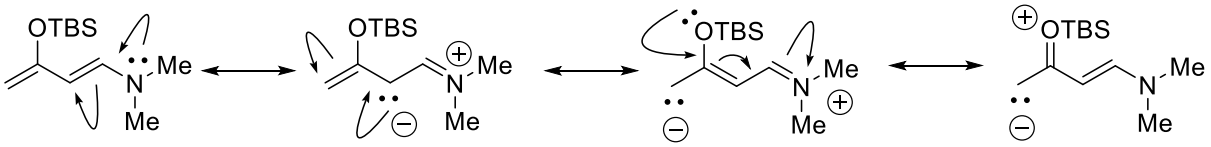
Solution:

2.1.

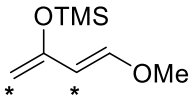
Danishefsky's diene (3):



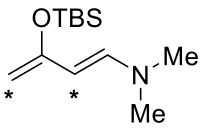
Rawal–Kozmin diene (4):



Carbon atoms with higher electron density are indicated by the * symbol.

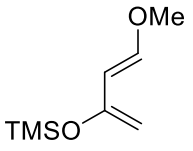


3

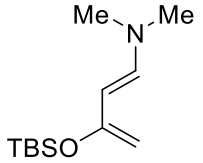


4

2.2. Compound **4** is a more reactive diene in a DA reaction with maleic anhydride due to the higher electron-donating ability of nitrogen compared to oxygen.

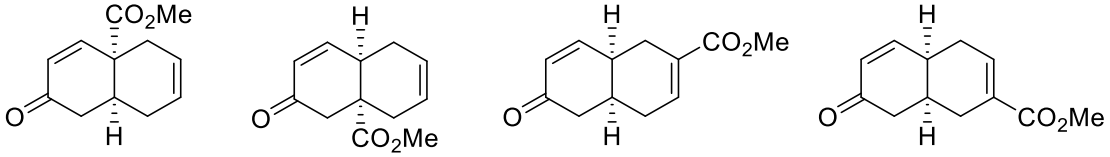


3
s-cis conformation

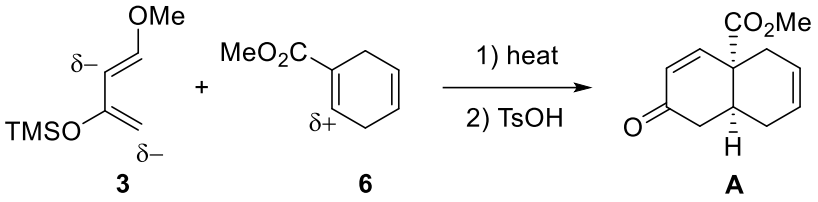


4
s-cis conformation

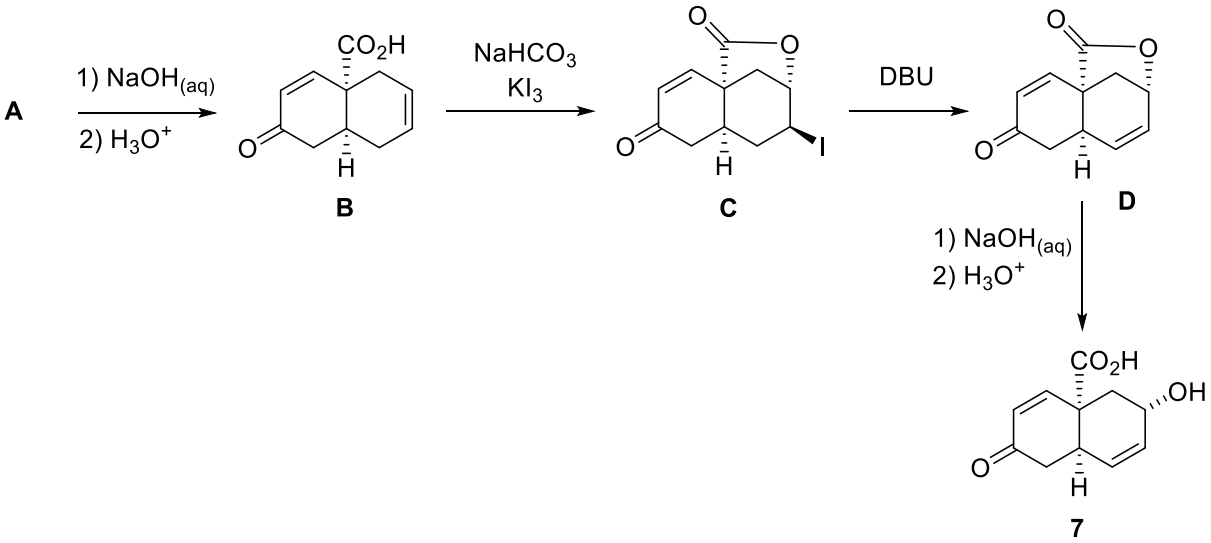
2.3.



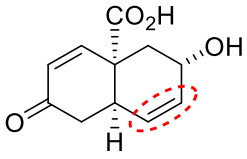
2.4.



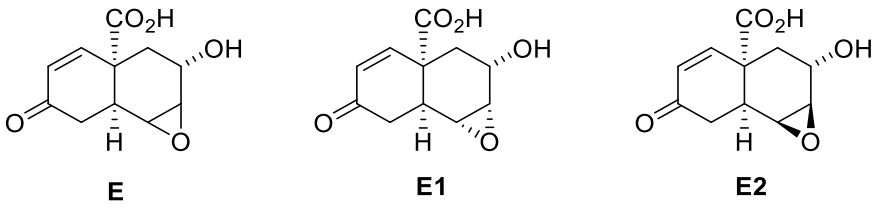
2.5.



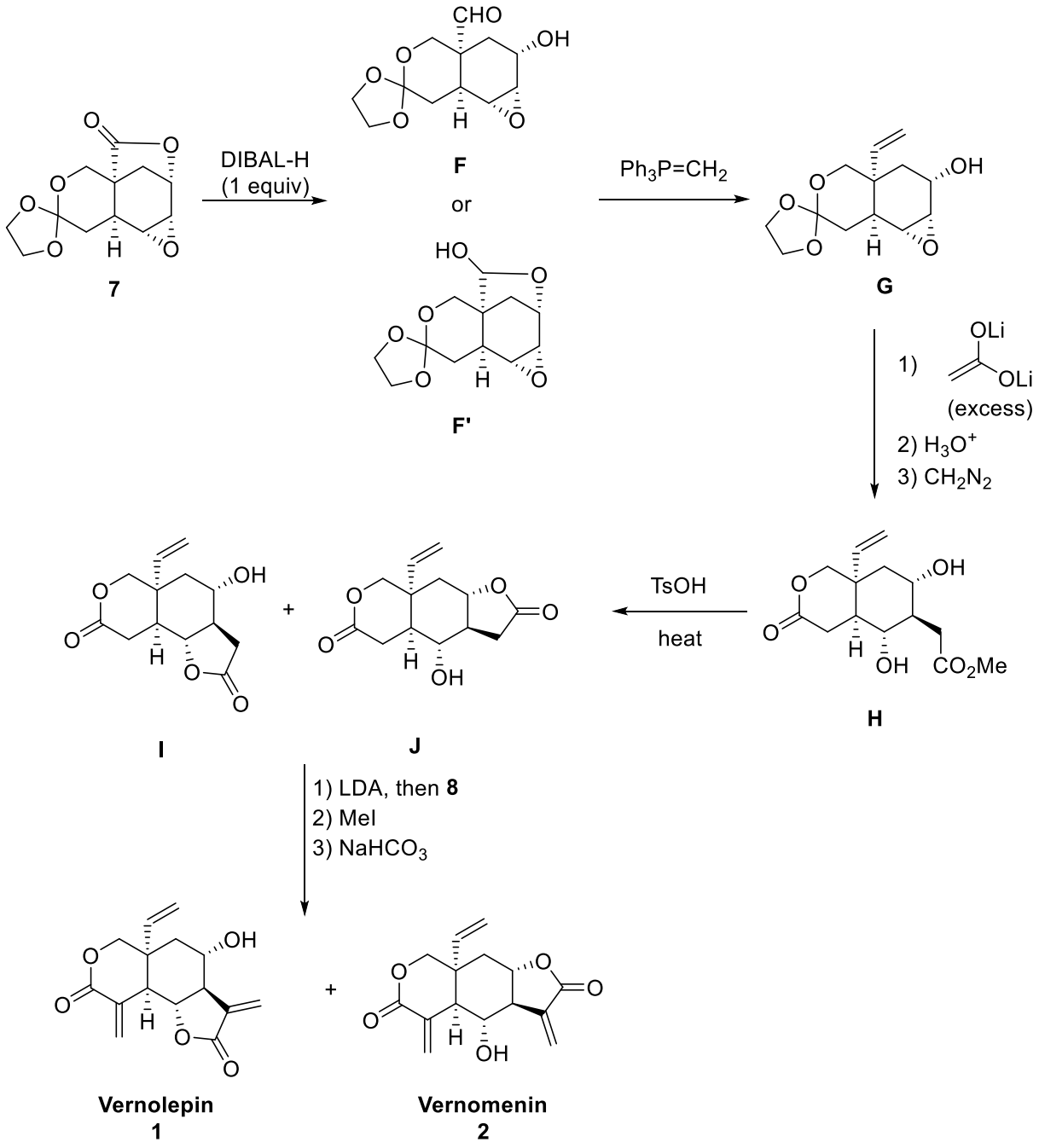
2.6. The circled alkene reacts selectively with *m*-CPBA as it is the more electron-rich alkene.



All of the following structures are acceptable answers (**E**, **E1**, or **E2**).



2.7.


7
DIBAL-H
(1 equiv)
F
or
F'
Ph3P=CH2
G
1)
OLi
OLi
(excess)
2) H3O+
3) CH2N2
H
TsOH
heat
I
J
1) LDA, then 8
2) MeI
3) NaHCO3
Vernolepin
1
Vernomenin
2

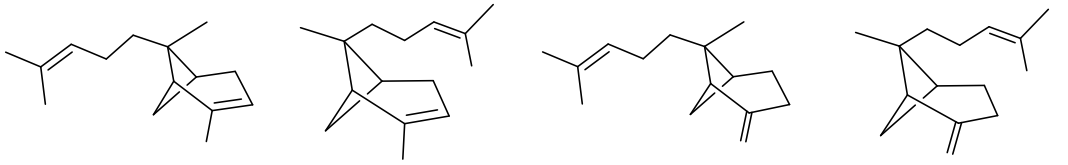
Problem 3. Çay, Cha, Chai, Te, Tea, Tee, Thé, Thee, and Earl Grey Tea Flavor: Bergamot

Cha	Chinese, Japanese, Korean, Portuguese…..
Chai	Russian, Persian…
Çay	Turkish, Azerbaijani…
čaj	Bosnian, Croatian, Czech, Serbian, Slovak..
Shay	Arabic…
Te	Italian, Spanish…
Tea	English…
Tee	German…
Thé	French…
Thee	Dutch…
Chaay	Hindi…
…..	…

Tea (in Turkish: *çay*) is popular throughout Turkey and the Turkish diaspora. Turkish tea culture also extends from Azerbaijan to some countries in the Balkan Peninsula. Turkey has the highest per capita tea consumption in the world, i.e. 2.5 kg/person per year, followed by the United Kingdom (2.1 kg/person per year).

Bergamotene and derivatives (**1-4**), sesquiterpenes, are analogues of pinnae monoterpenes.

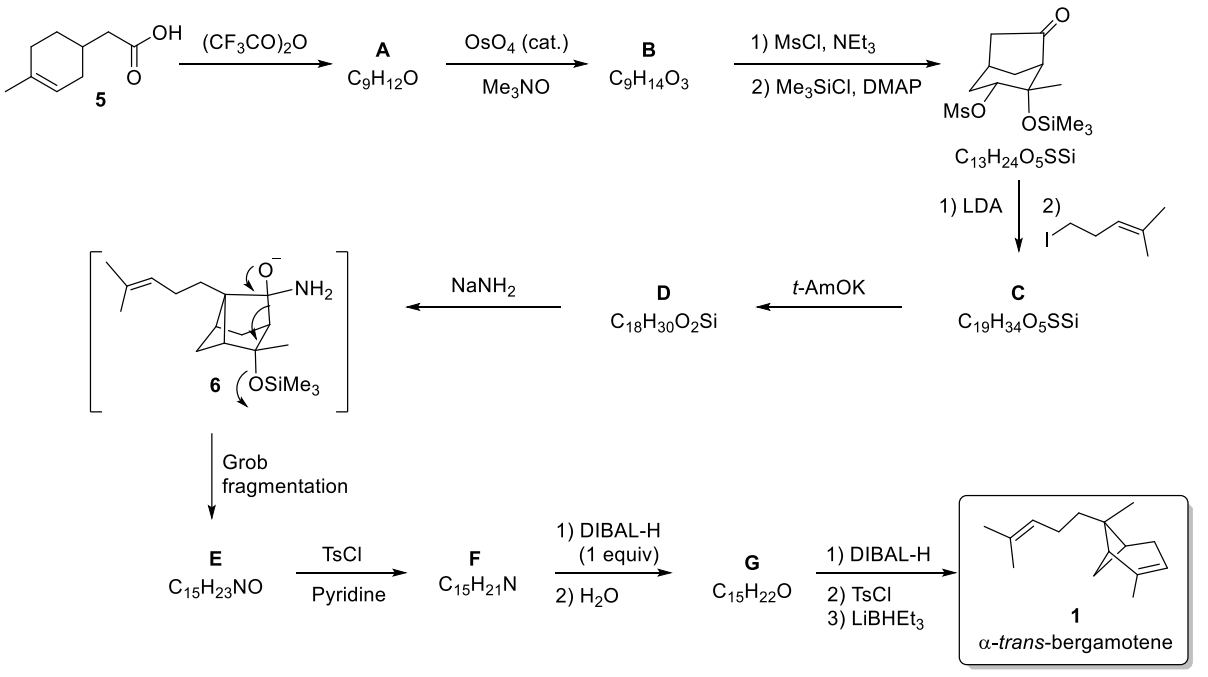
Found in bergamot oil, the bergamotenes contribute to the aroma and flavor of Earl Grey tea.



1 α-*trans*-bergamotene | **2** α-*cis*-bergamotene | **3** β-*trans*-bergamotene | **4** β-*cis*-bergamotene

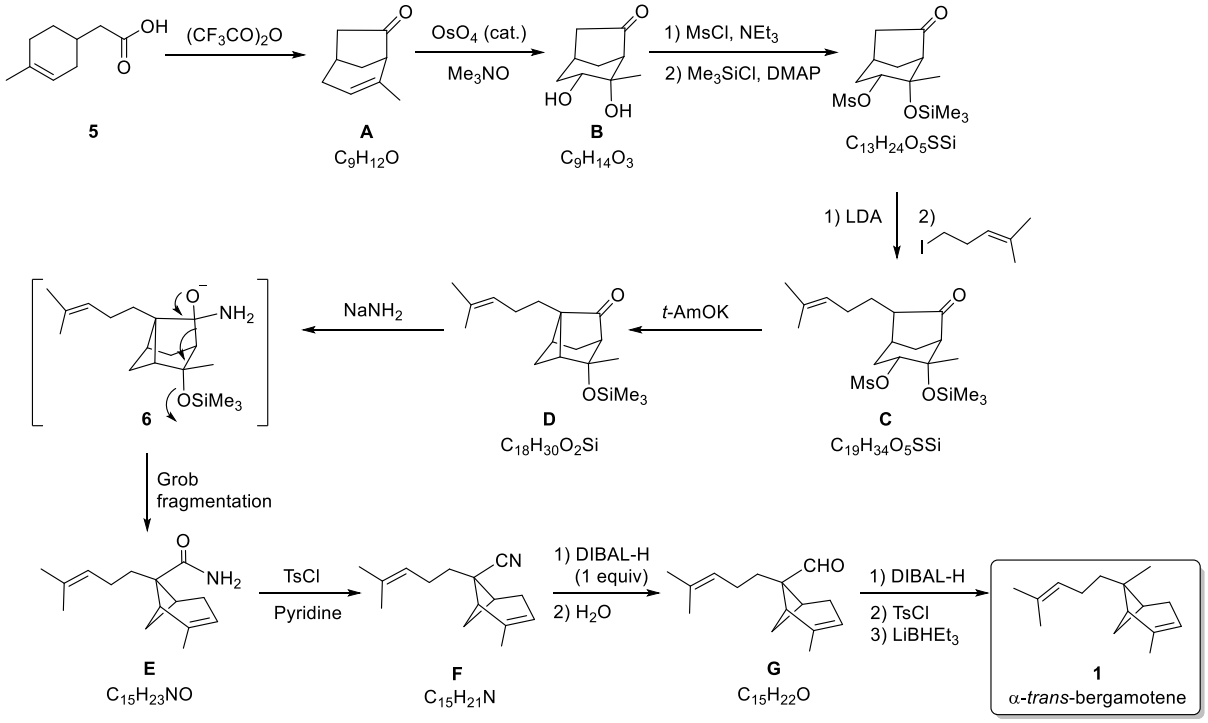
3.1. The following reaction scheme illustrates the synthesis of α-*trans*-bergamotene (**1**). **Draw** the structures of products **A–G**.

3.2. What is the function of Me_3NO reagent in the transformation of **A** to **B**?



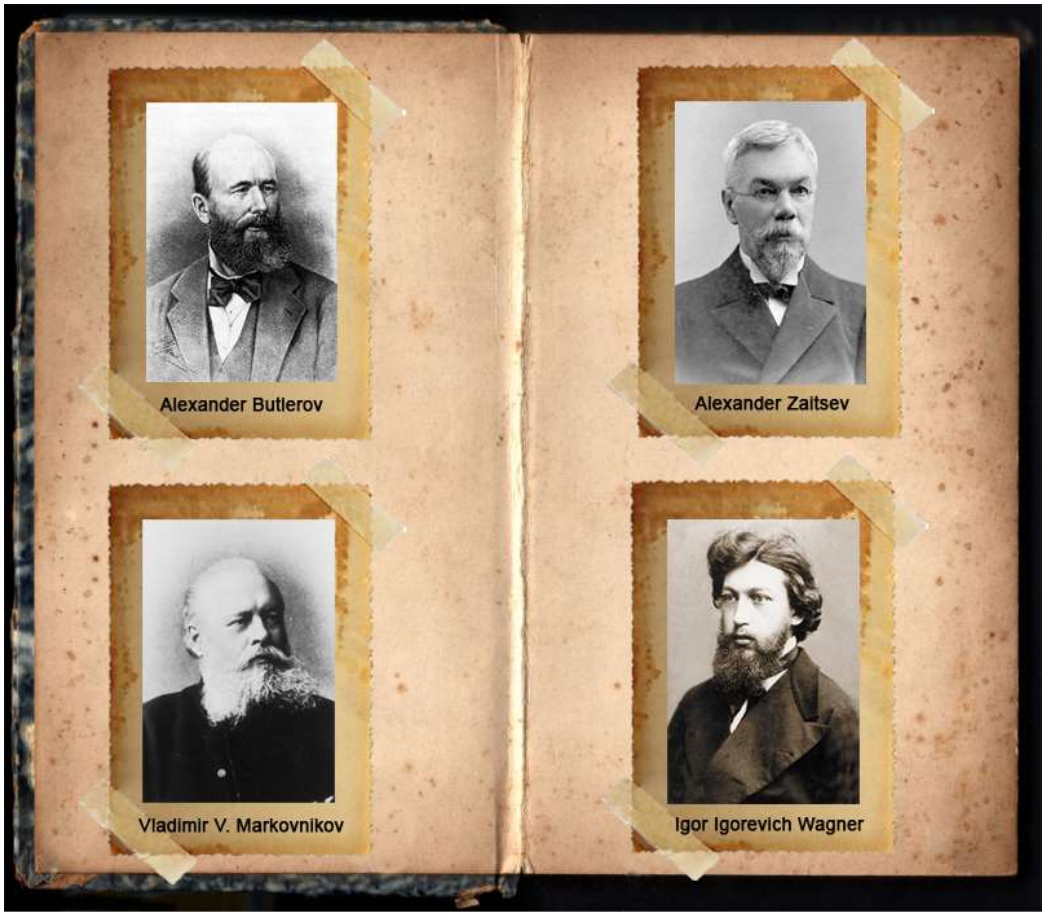
Solution:

3.1.



3.2. OsO_4 is an expensive and very toxic reagent. Thus, instead of using a large amount of OsO_4, the cheap and mild oxidation agent Me_3NO is used to oxidize the reduced osmium reagent to OsO_4 reagent for reuse.

Problem 4. Early Russian Organic Chemists and Markovnikov's Rule

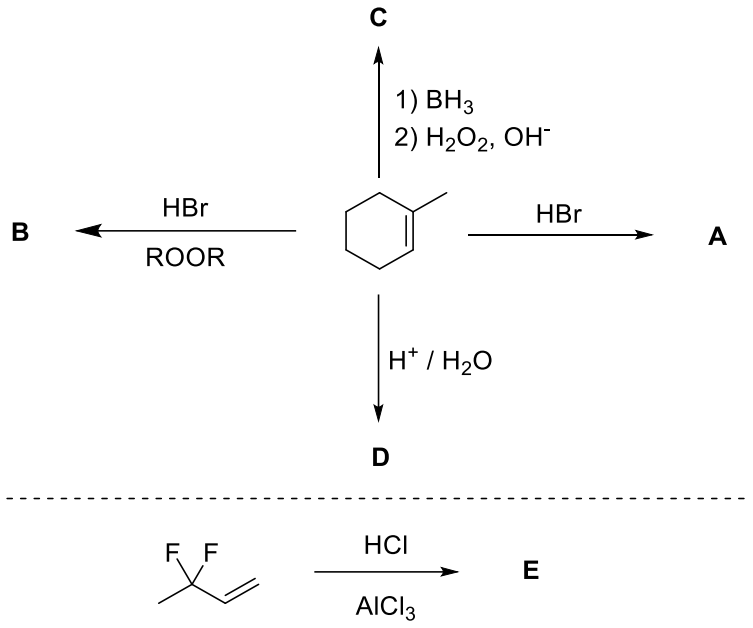


The last year was devoted to the 150th anniversary of the discovery of Markovnikov's rule, formulated by Vladimir V. Markovnikov in 1869. Markovnikov was a PhD student of the famous early Russian scientist Alexander Butlerov. In his PhD thesis in 1869, Markovnikov discovered the famous rule that exists in almost every textbook on organic chemistry. According to Markovnikov's rule, when an unsymmetrical alkene or alkyne reacts with a hydrogen halide (hydrogen chloride, hydrogen bromide, or hydrogen iodide), the hydrogen atom of HX adds to the carbon atom having the highest number of hydrogen atoms. However, depending on the reagent or substrate, in some cases, opposite results could also be possible, and these kinds of reactions are called *anti*-Markovnikov addition. Although Markovnikov's rule was developed for and is specifically applied to the addition of hydrogen halides to alkenes or alkynes, many other additions are also described as Markovnikov or *anti*-Markovnikov depending on the regioselectivity of the addition reaction.

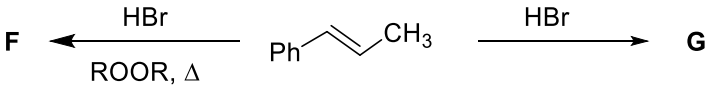
Actually, the rule should be revised as follows: "*addition to this kind of double or triple bond proceeds through more stable intermediates*". In some cases, besides electronic effects, steric effects can also affect the formation of Markovnikov or *anti*-Markovnikov addition products.

The following problems are mainly related to discoveries described by the student of the more distinguished organic chemist Alexander Butlerov or his colleagues at Kazan University, Tatarstan, Russia.

4.1. **Draw** the structures of major products **A**-**E**, including the appropriate stereochemistry (ignore optical isomerism).



4.2. **Draw** the structures of major products **F** and **G** for the following reactions.

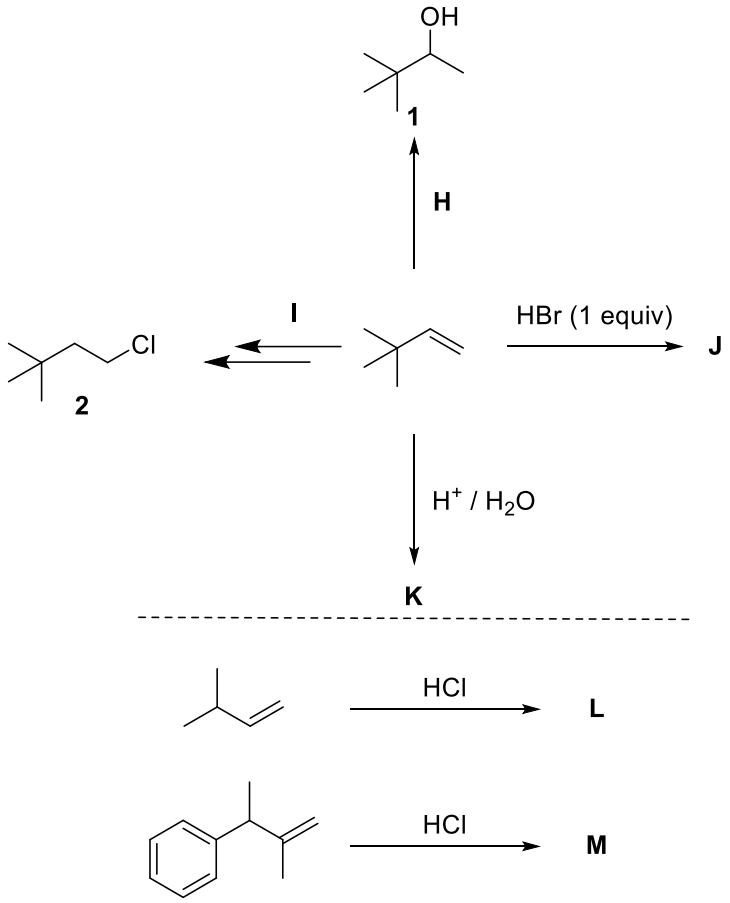


Wagner–Meerwein Rearrangement (WMR)

Wagner is another famous scientist who worked at Kazan University contemporaneously with Butlerov and Markovnikov. Wagner proposed that bornyl chloride undergoes an internal rearrangement to form pinene. Meerwein then generalized this type of rearrangement. Thus, this kind of reaction was named Wagner–Meerwein rearrangement. These reactions take place when a carbocation is formed. Generally, a carbocation is rearranged to a more stable

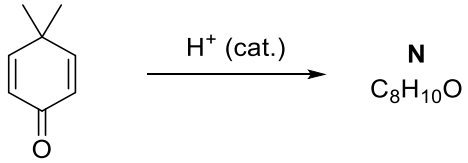
carbocation, if possible, by neighboring group migration. In addition, if the reaction does not proceed through a carbocation or borderline carbocation intermediates, rearrangements do not take place.

4.3. Considering the formation of intermediates for every reaction, **draw** the structures of reagents **H** and **I** and major products **J**–**M**.



Acid-catalyzed Wagner–Meerwein Rearrangement

The acid-catalyzed reaction of 4,4-dimethylcyclohexa-2,5-dien-1-one resulted in the formation of a compound, the NMR data of which are given below.



For **N**; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.95 (d, *J* = 8.0 Hz, 1H), 6.61 (d, *J* = 2.8 Hz, 1H), 6.57 (dd, *J* = 8.0, 2.8 Hz, 1H), 5.39 (bs, 1H), 2.16 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 137.9, 130.4, 128.6, 116.6, 112.3, 19.8, 18.7.

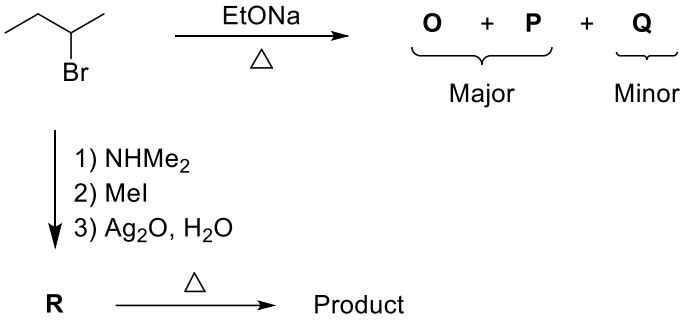
4.4. Find the structure of product **N** and **propose** a plausible mechanism.

4.5. What kind of difference do you expect in the ^{1}H NMR spectrum after a drop of D_2O is added to the solution in the NMR tube?

Zaitsev's Rule

Zaitsev, who described a rule named after him (Zaitsev's or Saytzeff's or Saytzev's rule), was another PhD student of Butlerov's. Zaitsev's rule is an empirical rule for estimating preferred alkene product(s) in elimination reactions. At Kazan University, the chemist Alexander Zaitsev studied various elimination reactions and observed a general trend in the resulting alkenes. More generally, Zaitsev's rule stipulates that in an elimination reaction the most substituted product will be formed. The following problem is mainly related to Zaitsev's rule.

4.6. Draw the structures of elimination products **O**–**Q** and compound **R**. What is the major product formed by the thermal reaction of **R** described in the following scheme?

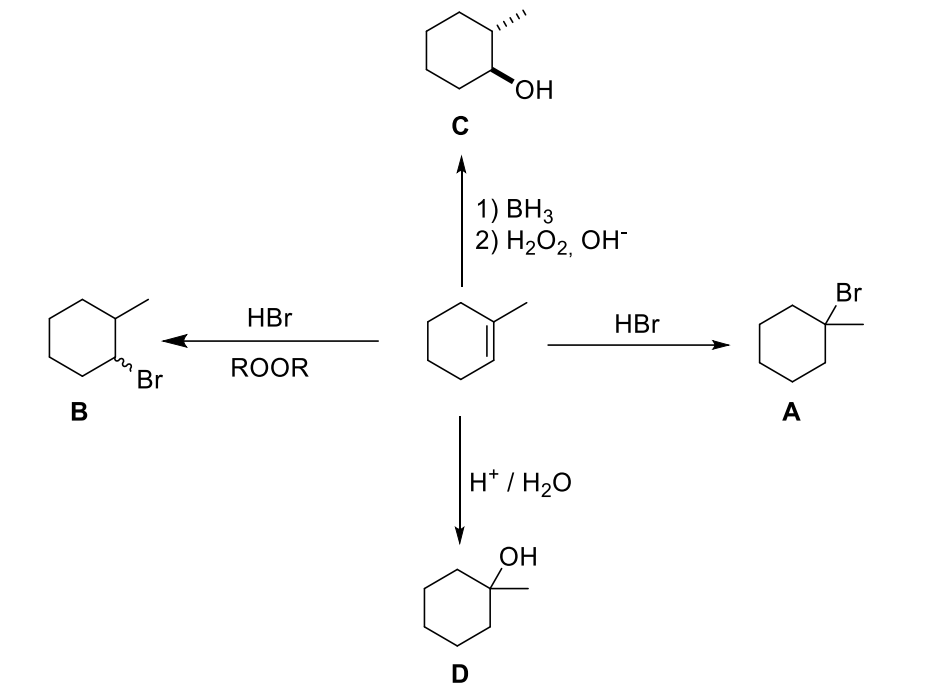


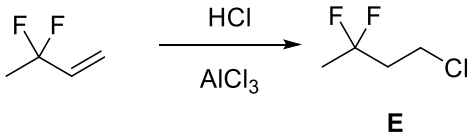
4.7. Which base(s) can be used to increase the ratio of **Q** relative to EtONa?

- ☐ NaOMe
- ☐ KOMe
- ☐ *i*-PrOK
- ☐ *t*-BuOK
- ☐ NH_3
- ☐ DBU
- ☐ *i*-Pr_2NEt

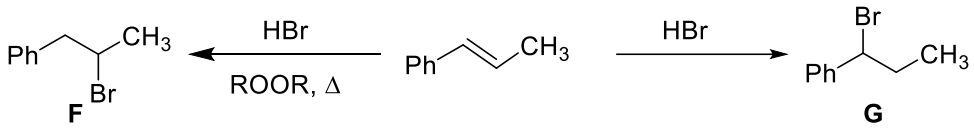
Solution:

4.1.

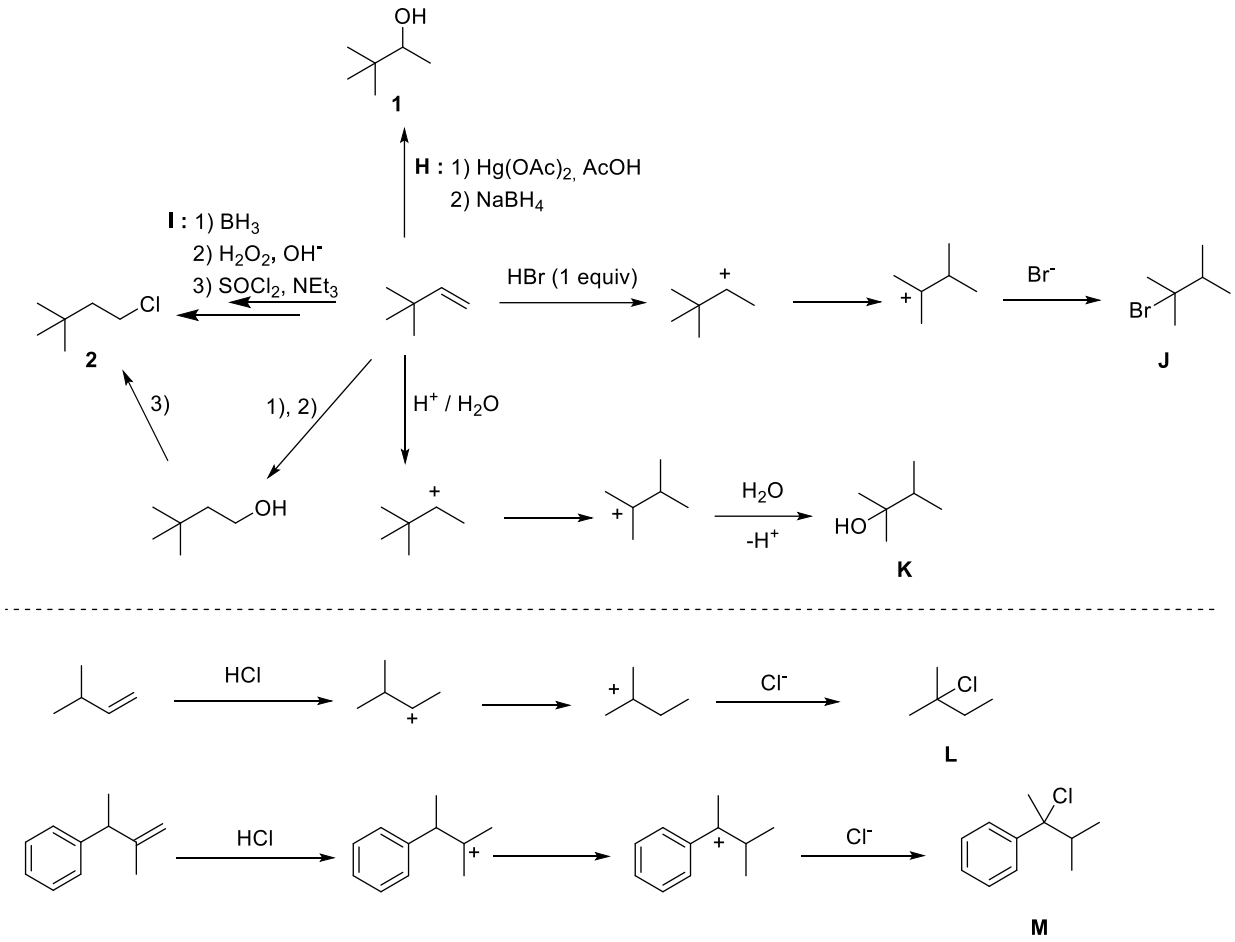




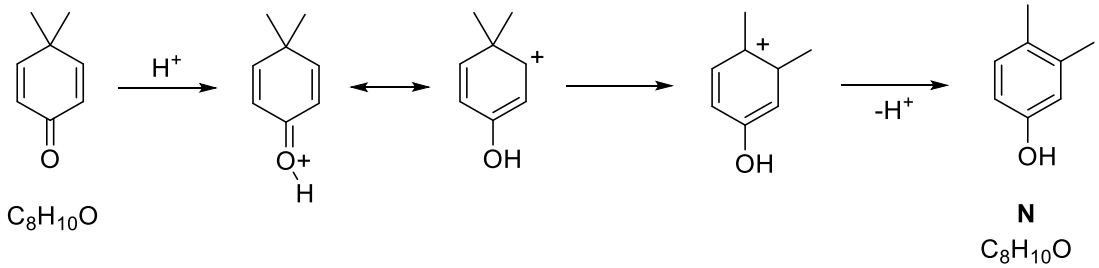
4.2.



4.3.

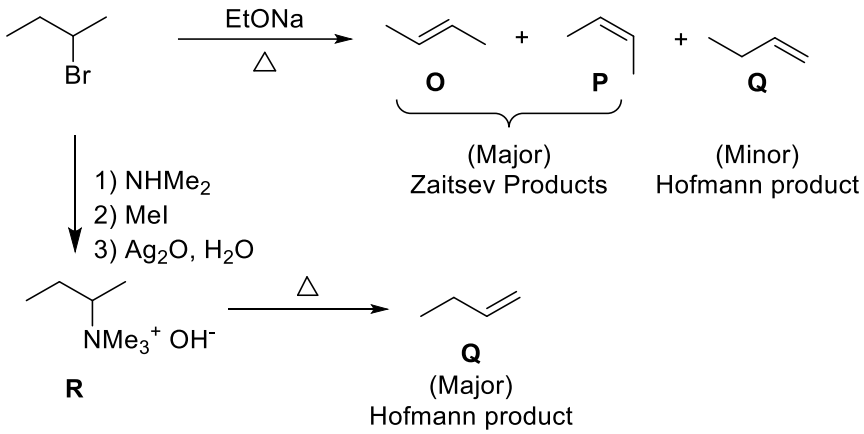


4.4.



4.5. The phenolic proton at 5.39 ppm (bs, 1H) will exchange with the deuterium in the D_2O and disappear from the spectrum.

4.6.

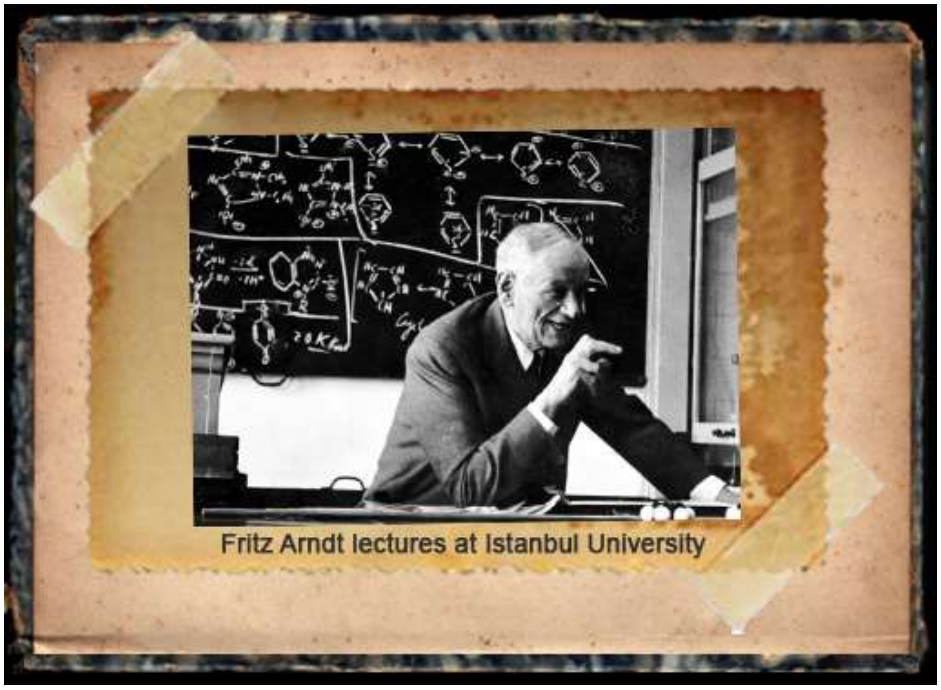


4.7.

- ☐ NaOMe
- ☐ KOMe
- ☒ *i*-PrOK
- ☒ *t*-BuOK
- ☐ NH_3
- ☒ DBU
- ☒ *i*-Pr_2NEt

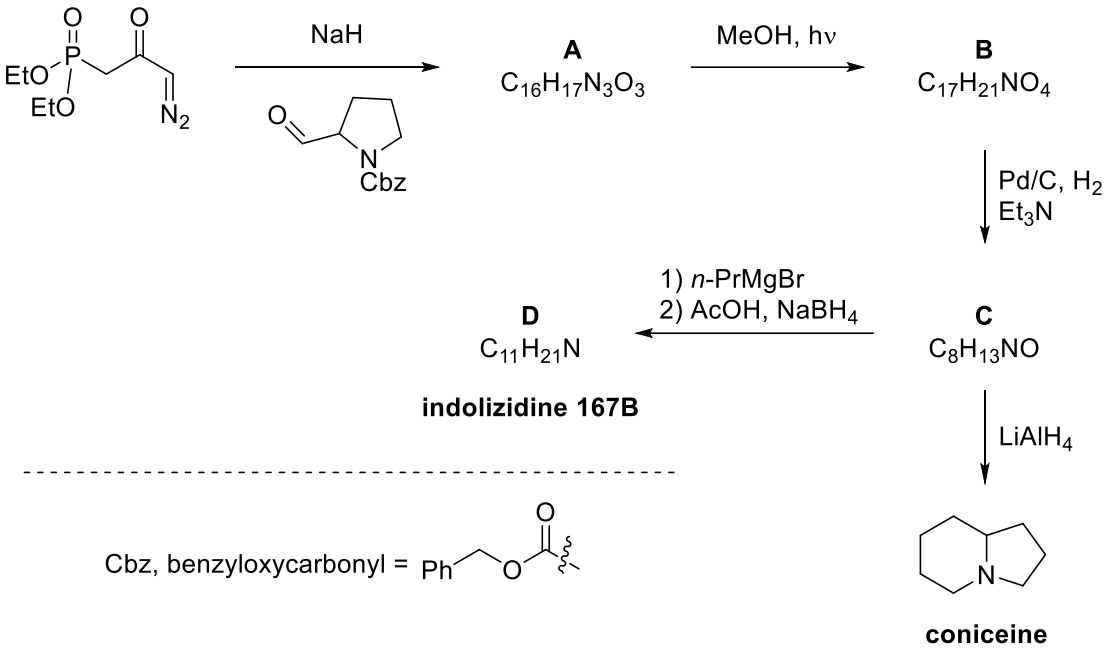
Problem 5. Arndt–Eistert Homologation

Fritz Georg Arndt (6 July 1885–8 December 1969) was a German chemist who had a great influence on the development of chemistry in Turkey. He was employed for two decades of his professional life at Istanbul University in two distinct periods. He discovered the Arndt–Eistert synthesis with Bernd Eistert. The Arndt–Eistert synthesis is the chemical reaction for one-carbon homologation (i.e. the conversion of RCO_2H to RCH_2CO_2H) of carboxylic acids and is called the homologation process. In the Arndt–Eistert homologation, the key step is the Wolff rearrangement of diazoketones to ketenes, which can be achieved thermally, photochemically, or by silver (I) catalysis. The reaction is conducted in the presence of nucleophiles such as water, alcohols, or amines to capture the ketene intermediate to yield carboxylic acids, esters, or amides, respectively. In this problem, synthesis of indolizidine alkaloids is studied.



5.1. As depicted in the scheme below, the synthesis of indolizidines 167B and coniceine could be easily and concisely achieved from β,γ-unsaturated ester **B**. The key step (**A** → **B**) is the Wolff rearrangement. Compound **C** has a lactam core, which is a bicyclic heterocycle containing a six-membered ring fused to a saturated five-membered ring, one of the bridging atoms being nitrogen.

Draw the structures of **A**–**D** without any stereochemical detail.



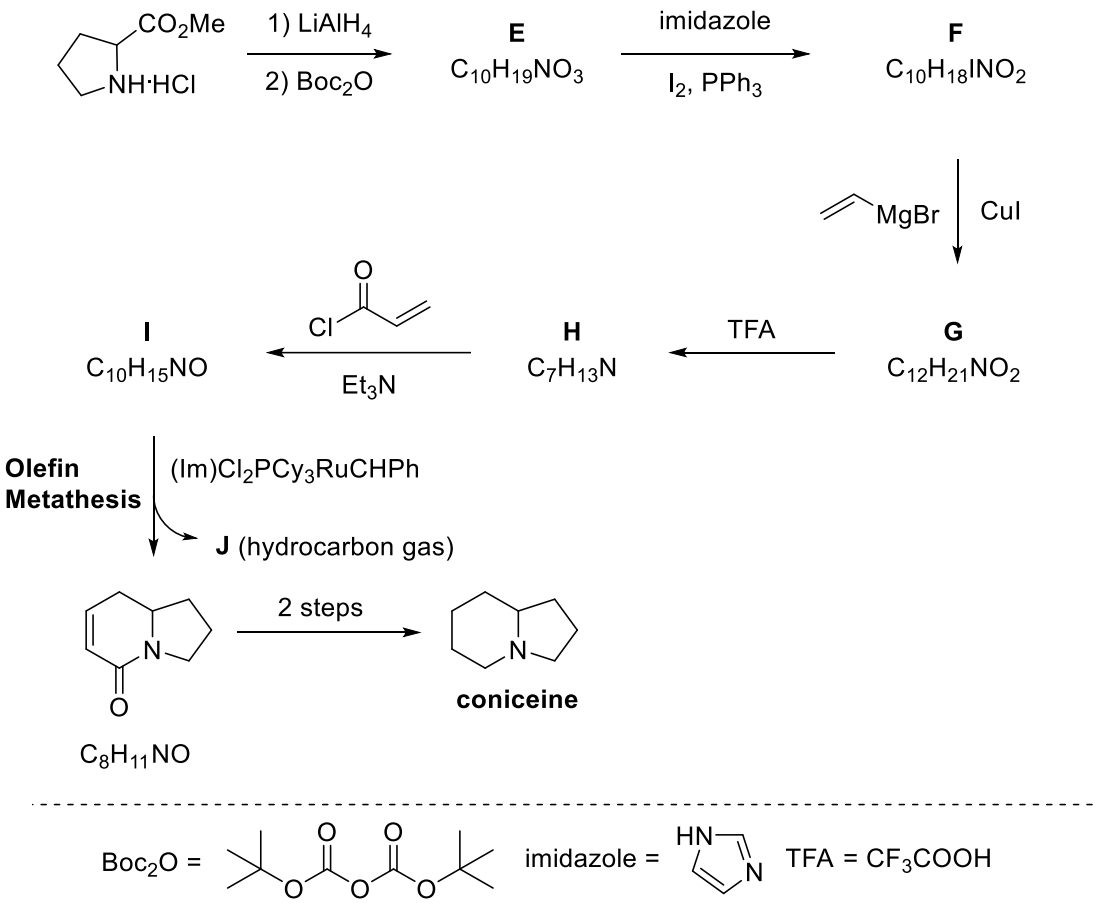
5.2. In the Arndt–Eistert homologation reaction, an α-diazo ketone can undergo photochemical Wolff rearrangement to form α-ketocarbene via nitrogen extrusion. This intermediate undergoes a 1,2-alkyl shift to give the ketene product.

Draw the structures of the α-ketocarbene and ketene intermediates in the second step (**A → B**).

5.3. Addition of propylmagnesium bromide to compound **C**, followed by AcOH/$NaBH_4$, is the last step in the total synthesis of indolizidine 167B.

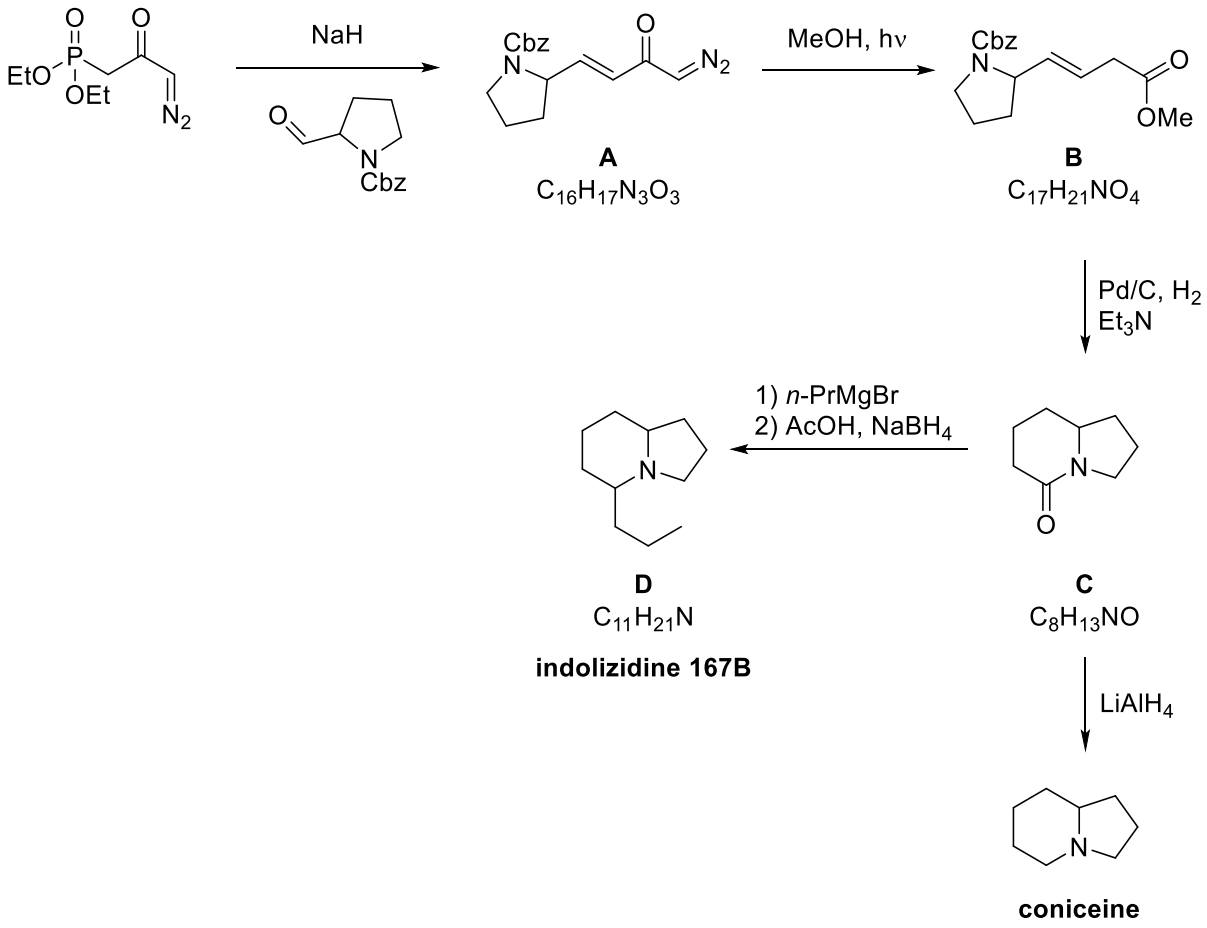
Draw the structure of an intermediate ($\mathbf{C_{11}H_{20}N^+}$) in the fourth step (**C → D**).

5.4. An alternative synthesis of coniceine is depicted below. **Draw** the structures of **E**–**J**.

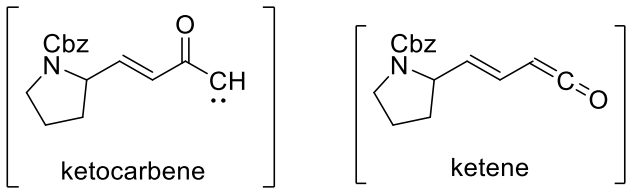

CO2Me
NH·HCl
1) LiAlH4
2) Boc2O
E
C10H19NO3
imidazole
I2, PPh3
F
C10H18INO2
MgBr
CuI
G
C12H21NO2
TFA
H
C7H13N
Cl
Et3N
I
C10H15NO
Olefin Metathesis
(Im)Cl2PCy3RuCHPh
J (hydrocarbon gas)
2 steps
coniceine
C8H11NO
Boc2O =
imidazole =
TFA = CF3COOH

Solution:

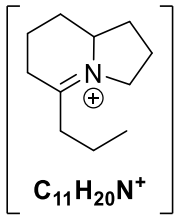
5.1.



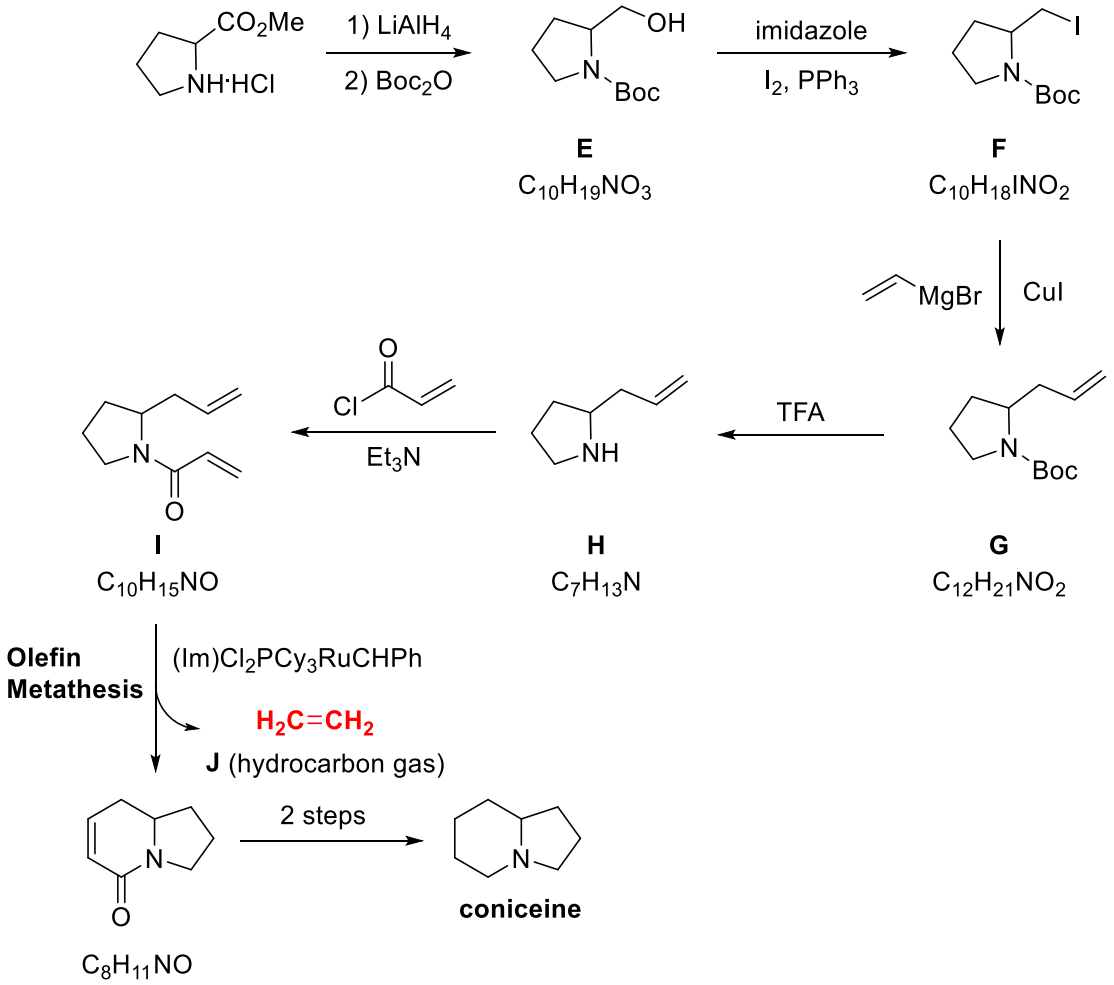
5.2.



5.3.

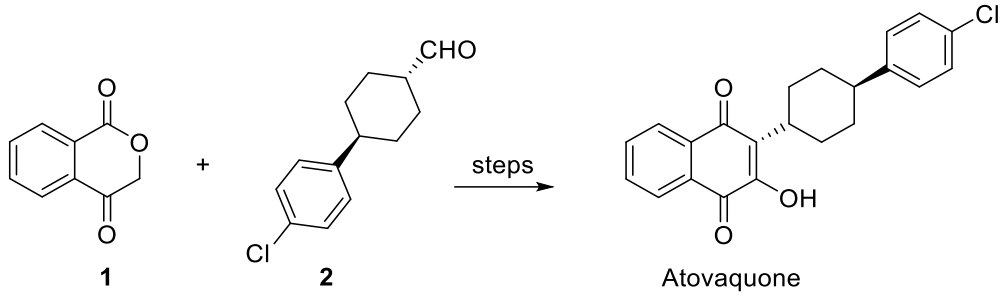


5.4.


CO2Me
NH·HCl
1) LiAlH4
2) Boc2O
OH
N
Boc
imidazole
I2, PPh3
I
N
Boc
E
C10H19NO3
F
C10H18INO2
MgBr
CuI
O
Cl
Et3N
TFA
N
NH
N
Boc
N
O
I
C10H15NO
H
C7H13N
G
C12H21NO2
Olefin Metathesis
(Im)Cl2PCy3RuCHPh
H2C=CH2
J (hydrocarbon gas)
2 steps
N
O
C8H11NO
N
coniceine

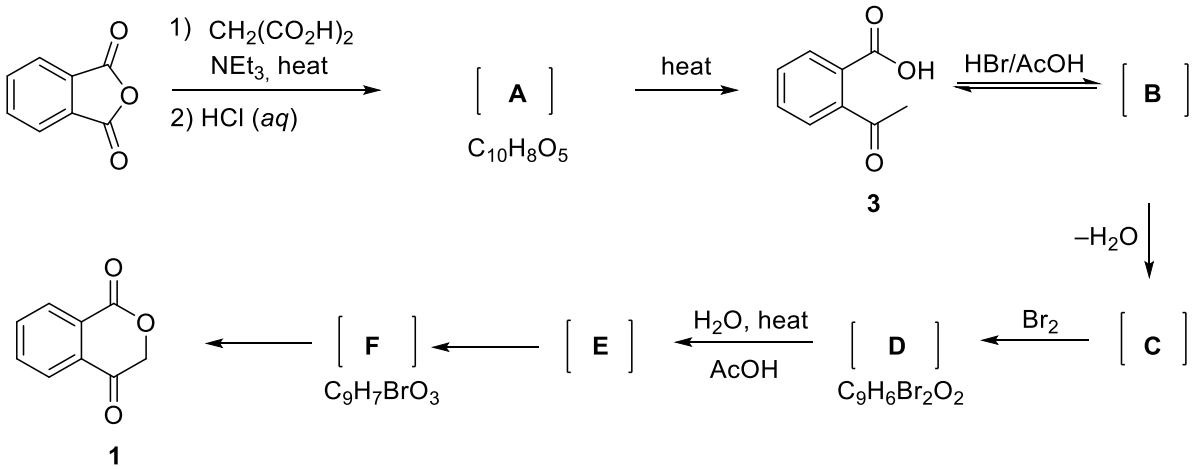
Problem 6. Atovaquone

Atovaquone, an approved drug, is used to treat pneumocystosis and malaria. Ketoester **1** and aldehyde **2** are key compounds in the synthetic process of atovaquone.



6.1. The synthesis of key compound ketoester **1** is shown below. A mixture of phthalic anhydride and Et_3N is treated with diacid. Gas evolution is observed during this period. Treatment of the reaction mixture with *aq*. HCl solution provides formation of acid **3** through intermediate **A** with two carboxylic acid groups. Acid **3** is converted to the isomeric intermediate **B**, containing both hemiacetal and ester functionalities, followed by dehydration to the alkene **C**, which is then brominated to give **D** under acidic condition. Dibromide **D** undergoes solvolysis in a hot mixture of H_2O/AcOH to give tertiary carbocation intermediate **E**, which is then trapped with water to give intermediate hemiacetal **F**. Finally, rearrangement of intermediate hemiacetal **F** provides key compound **1**.

*Note: The square brackets denote that the product was not isolated but reacted further without purification. The conversion of **3** to **1** is a one-pot reaction that involves a series of reactions occurring one after another in the same vessel without isolation and purification of intermediates.*

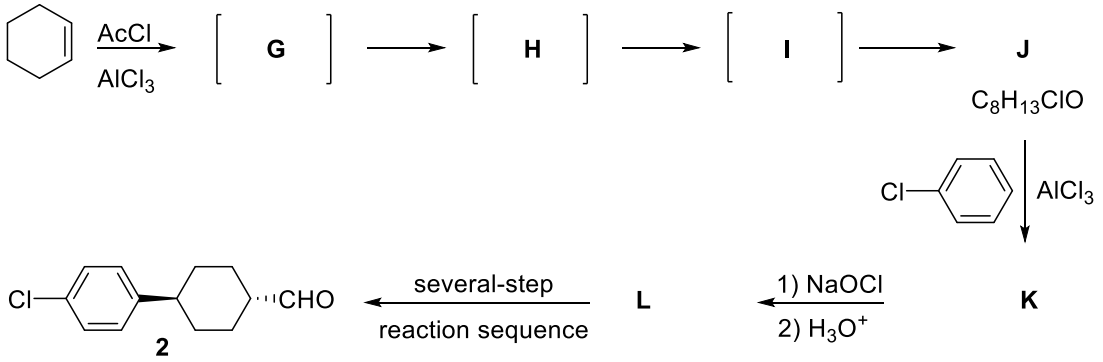


Spectroscopic data for intermediates **B** and **C**: **B:** ^{1}H NMR δ = 7.86–7.52 (4H), 4.13 (bs, 1H, exchangeable with D_2O), 1.97 (s, 3H). **C:** ^{1}H NMR δ = 7.92–7.58 (4H), 5.24 (m, 2H); ^{13}C NMR δ = 166.8, 151.8, 139.0, 134.4, 130.4, 125.3, 125.1, 120.6, 91.3; MS m/z = 146.0

Draw the structure of intermediates **A**–**F** in the synthesis of **1**.

6.2. The synthesis of aldehyde **2** starts from cyclohexene by key steps including Friedel–Crafts acylations, haloform, reduction, and oxidation. Friedel–Crafts acylation of cyclohexene with acetyl chloride yields chlorocyclohexyl methyl ketone **J.** Reaction of cyclohexene with acetyl chloride produces an initial carbocation **G** that undergoes two successive Wagner–Meerwein hydride migrations to form isomeric carbocations **H** and **I**, respectively. Trapping of carbocation **I** with chloride ion produces **J**, the Friedel–Crafts reaction of which with chlorobenzene provides **K**. Haloform reaction of methyl ketone **K** using sodium hypochlorite (NaOCl) gives the corresponding acid **L**. Acid **L** is converted into the aldehyde **2** in a several-step reaction sequence.

Draw structure of isomeric carbocations **G**–**I** formed in this reaction.



6.3. Are these carbocations chiral?

G	☐	Yes
	☐	No
H	☐	Yes
	☐	No
I	☐	Yes
	☐	No

6.4. Draw the structure of **J**–**L**.

6.5. **Choose** all correct statements for **L**.

- ☐ **L** has 4 stereoisomers.
- ☐ **L** is a chiral compound.
- ☐ **L** is an achiral compound.
- ☐ **L** is a meso compound.
- ☐ **L** has 2 stereoisomers.
- ☐ Stereoisomers of **L** are diastereomers of each other.
- ☐ Stereoisomers of **L** are enantiomers of each other.

6.6. Which of the following compound(s) result(s) in the haloform reaction of **K**?

- ☐ CH_2Cl_2
- ☐ CH_3Cl
- ☐ $CHCl_3$
- ☐ CCl_4

6.7. Which of the following reagents are appropriate to form aldehyde **2** from **L**?

Choose all correct reactions.

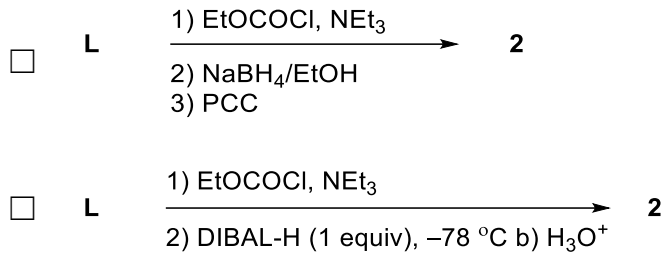
☐ **L** $\xrightarrow[2)\ (COCl)_2,\ DMSO,\ NEt_3]{1)\ a)\ LiAlH_4\ b)\ H_3O^+}$ **2**

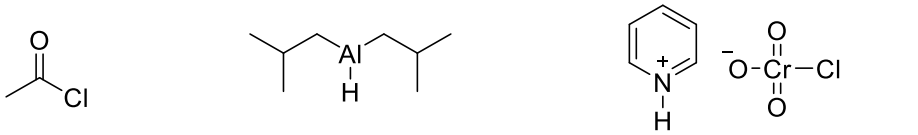
☐ **L** $\xrightarrow[2)\ a)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^oC\ b)\ H_3O^+]{1)\ CH_3OH/H^+}$ **2**

☐ **L** $\xrightarrow[2)\ CrO_3/H_3O^+]{1)\ NaBH_4/EtOH}$ **2**

☐ **L** $\xrightarrow[2)\ HONHMe\cdot HCl,\ NEt_3\ 3)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^oC\ b)\ H_3O^+]{1)\ SOCl_2}$ **2**

☐ **L** $\xrightarrow[2)\ CrO_3/H_3O^+]{1)\ EtOCOCl,\ NEt_3}$ **2**





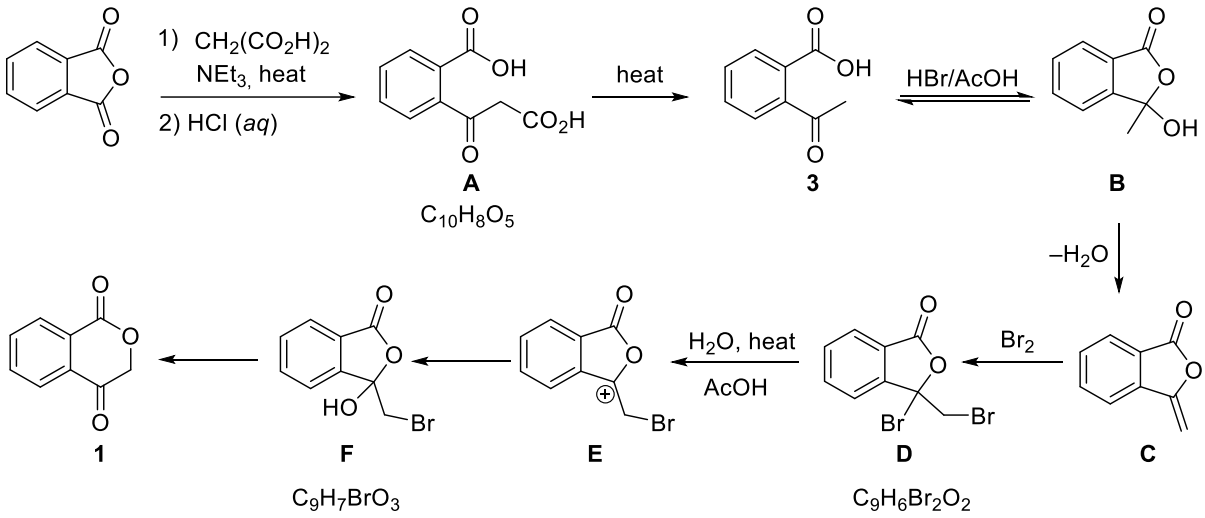
AcCl
Acetyl chloride

DIBAL-H
Diisobutylaluminium hydride

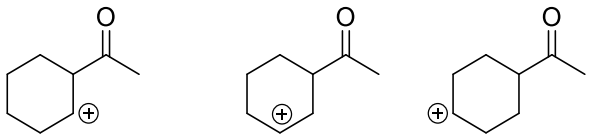
PCC
Pyridinium chlorochromate

Solution:

6.1.



6.2.

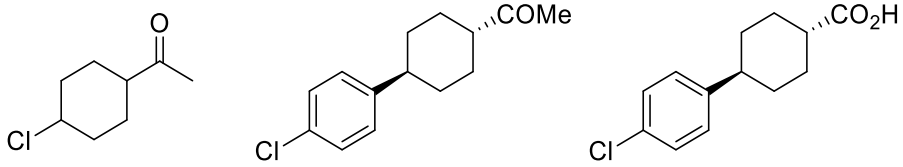


G **H** **I**

6.3.

G	☒	Yes
	☐	No
H	☒	Yes
	☐	No
I	☐	Yes
	☒	No

6.4.



J **K** **L**

6.5.

- ☐ **L** has 4 stereoisomers.
- ☐ **L** is a chiral compound.
- ☒ **L** is an achiral compound.
- ☐ **L** is a meso compound.
- ☒ **L** has 2 stereoisomers.
- ☒ Stereoisomers of **L** are diastereomers of each other.
- ☐ Stereoisomers of **L** are enantiomers of each other.

6.6.

- ☐ CH_2Cl_2
- ☐ CH_3Cl
- ☒ $CHCl_3$
- ☐ CCl_4

6.7.

☒ **L** $\xrightarrow[2)\ (COCl)_2,\ DMSO,\ NEt_3]{1)\ a)\ LiAlH_4\ b)\ H_3O^+}$ **2**

☒ **L** $\xrightarrow[2)\ a)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^oC\ b)\ H_3O^+]{1)\ CH_3OH/H^+}$ **2**

☐ **L** $\xrightarrow[2)\ CrO_3/H_3O^+]{1)\ NaBH_4/EtOH}$ **2**

☒ **L** $\xrightarrow[2)\ HONHMe\cdot HCl,\ NEt_3\ 3)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^oC\ b)\ H_3O^+]{1)\ SOCl_2}$ **2**

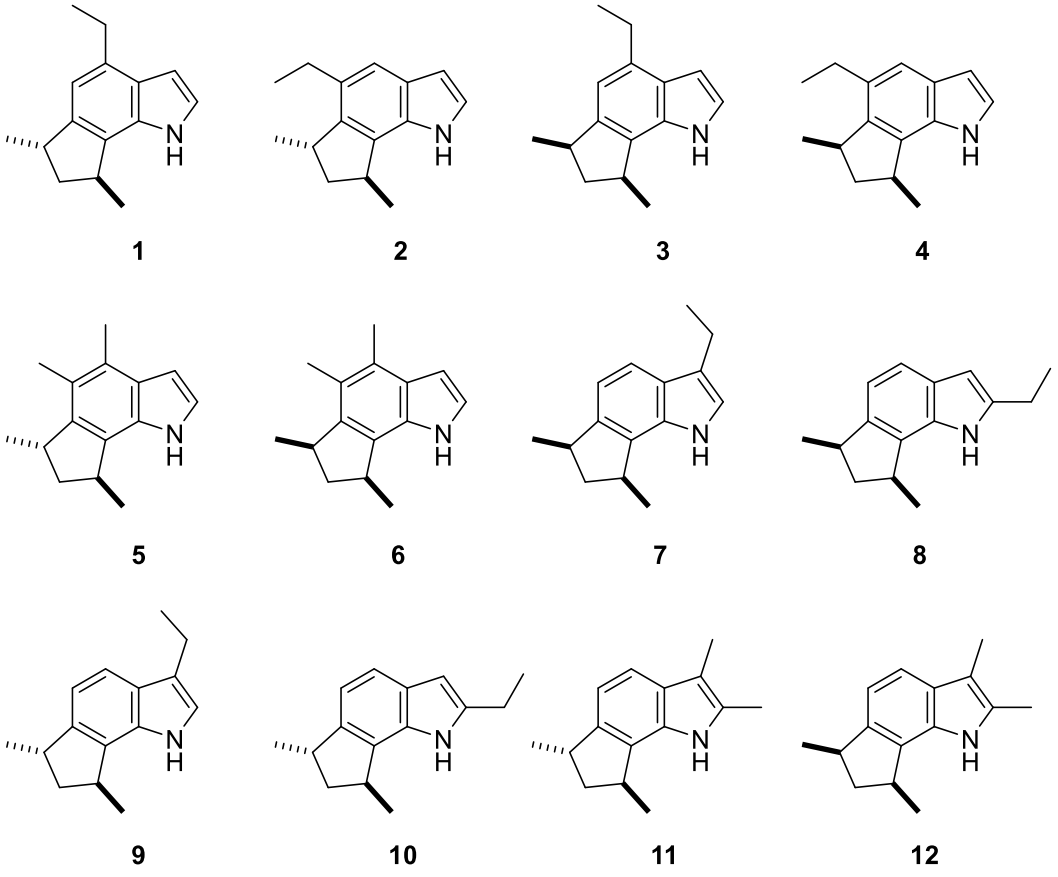
☐ **L** $\xrightarrow[2)\ CrO_3/H_3O^+]{1)\ EtOCOCl,\ NEt_3}$ **2**

☒ **L** $\xrightarrow[2)\ NaBH_4/EtOH\ 3)\ PCC]{1)\ EtOCOCl,\ NEt_3}$ **2**

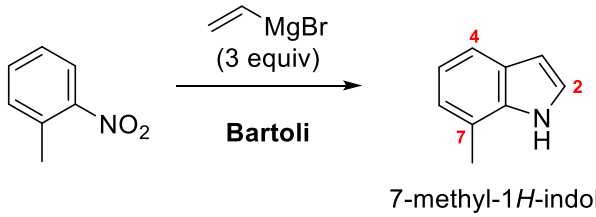
☒ **L** $\xrightarrow[2)\ DIBAL\text{-}H\ (1\ equiv),\ -78\ ^oC\ b)\ H_3O^+]{1)\ EtOCOCl,\ NEt_3}$ **2**

Problem 7. Which is (±)-Trikentrin A?

Although the indole skeleton is ubiquitous in nature, annulated indoles at any of the benzenoid positions are uncommon. The trikentrins and the structurally similar herbindoles represent fascinating such examples of 6,7-annulated indole or polyalkylated cyclopent[*g*]indole natural products. The trikentrins were isolated from the marine sponge *Trikentrion flabelliforme* and possess antibacterial activity. Possible structures for trikentrin A are shown in the Figure below. In this problem, we will find out which of these structures is trikentrin A.



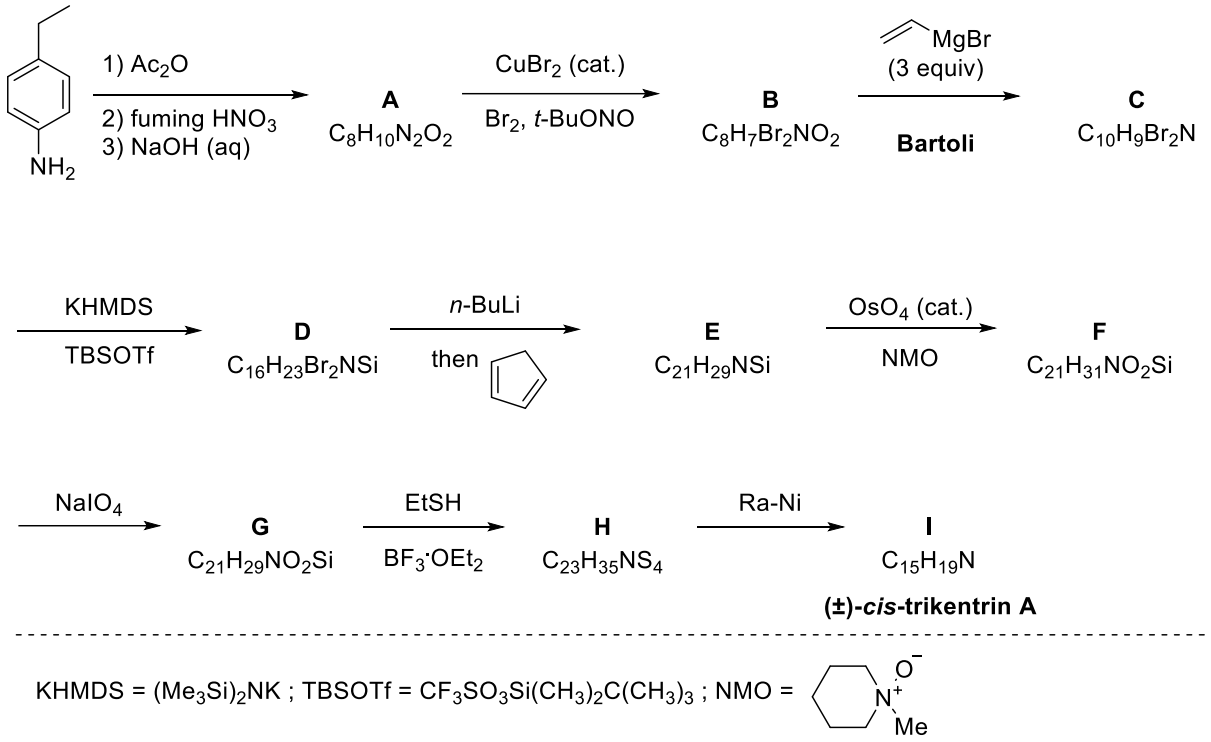
There are several ways to synthesize trikentrin A. Two routes below involve aryne-based and hydrovinylation strategies and both finally lead to the formation of trikentrin A. The first step for problems 8.1 and 8.2 is the Bartoli reaction or Bartoli indole synthesis, which is the organic reaction of *ortho*-substituted nitroarenes with vinyl Grignard reagents to yield substituted indoles. In particular, it is the most efficient route to 7-substituted indoles.



7-methyl-1*H*-indole

(±)-Trikentrin A: ^{13}C NMR ($CDCl_3$): δ 143.4–101.6 (8 signals), 44.8–15.1 (7 signals).

Aryne-based strategy

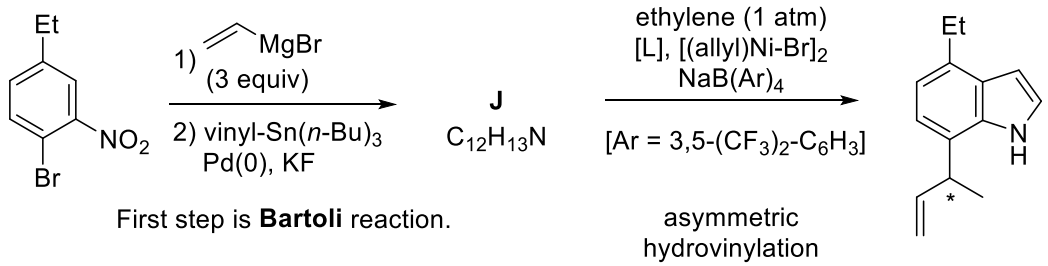


KHMDS = $(Me_3Si)_2NK$; TBSOTf = $CF_3SO_3Si(CH_3)_2C(CH_3)_3$; NMO =

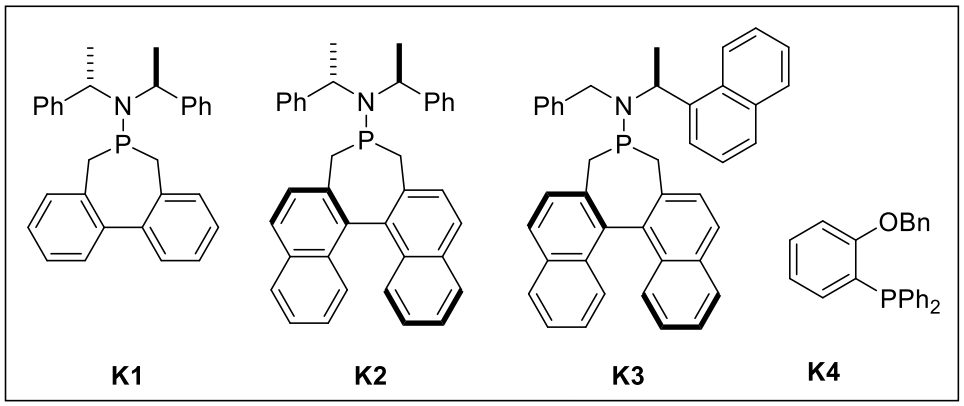
7.1. **Draw** the structures of **A**–**I**.

7.2. **Draw** the structure of the aryne involved as a reaction intermediate in step **D** → **E**.

Hydrovinylation strategy



ligand	yield (%) / ee%
K1	96 / 86
K2	95 / 87
K3	99 / 96
K4	90 / 0



7.3. Chemical transformation of bromo-nitrobenzene to corresponding 7-vinylindole **J** includes in Bartoli reaction followed by the vinylation step with vinylstannane. **Draw** the structure of **J**.

7.4. The second step is the Ni(II)-catalyzed asymmetric hydrovinylation of **J**. The ligands (**K1**–**K4**) used for hydrovinylation are given above.

Note: ee = enantiomeric excess; % ee = % major enantiomer - % minor enantiomer

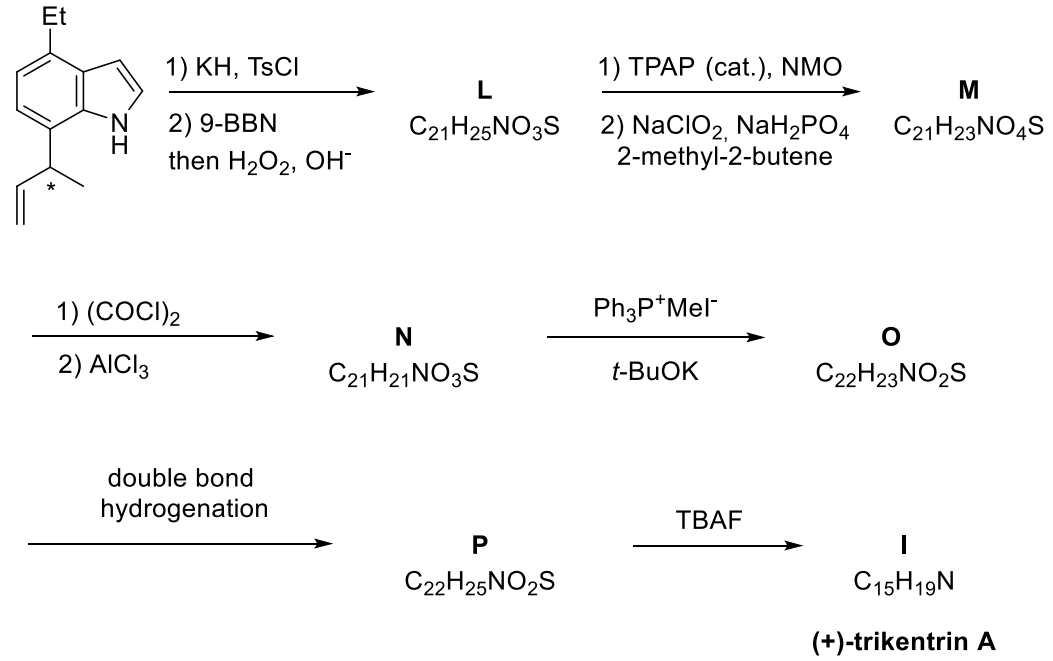
Choose the correct statement(s):

- ☐ Ligand **3** gave the best enantioselectivity.
- ☐ Ligand **4** gave a racemic mixture.
- ☐ Each of the ligands **K1**–**K4** is chiral.
- ☐ Each of the ligands **K1**–**K4** gave excellent yield (>95%) of the product.

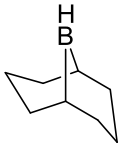
7.5. For the hydrovinylation step, **choose** the correct statement(s):

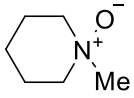
☐ $(allyl)_2Ni_2Br_2$ or $[(allyl)NiBr]_2$ is a source of vinyl.
☐ In this Ni-allyl complex, each nickel has oxidation number +2.
☐ In this Ni-allyl complex, the electron count of Ni is 18.
☐ This complex has a square planar geometry.

7.6. Draw the structures of **L**–**P**. The absolute configuration of the asymmetric center in the hydrovinylation product is *S*. **Hint:** In the ^{13}C NMR spectrum of compound **M**, one carbonyl carbon signal was observed at δ = 178.3 ppm.



TsCl = *p*-toluenesulfonyl chloride ; TPAP = $(C_3H_7)_4NRuO_4$

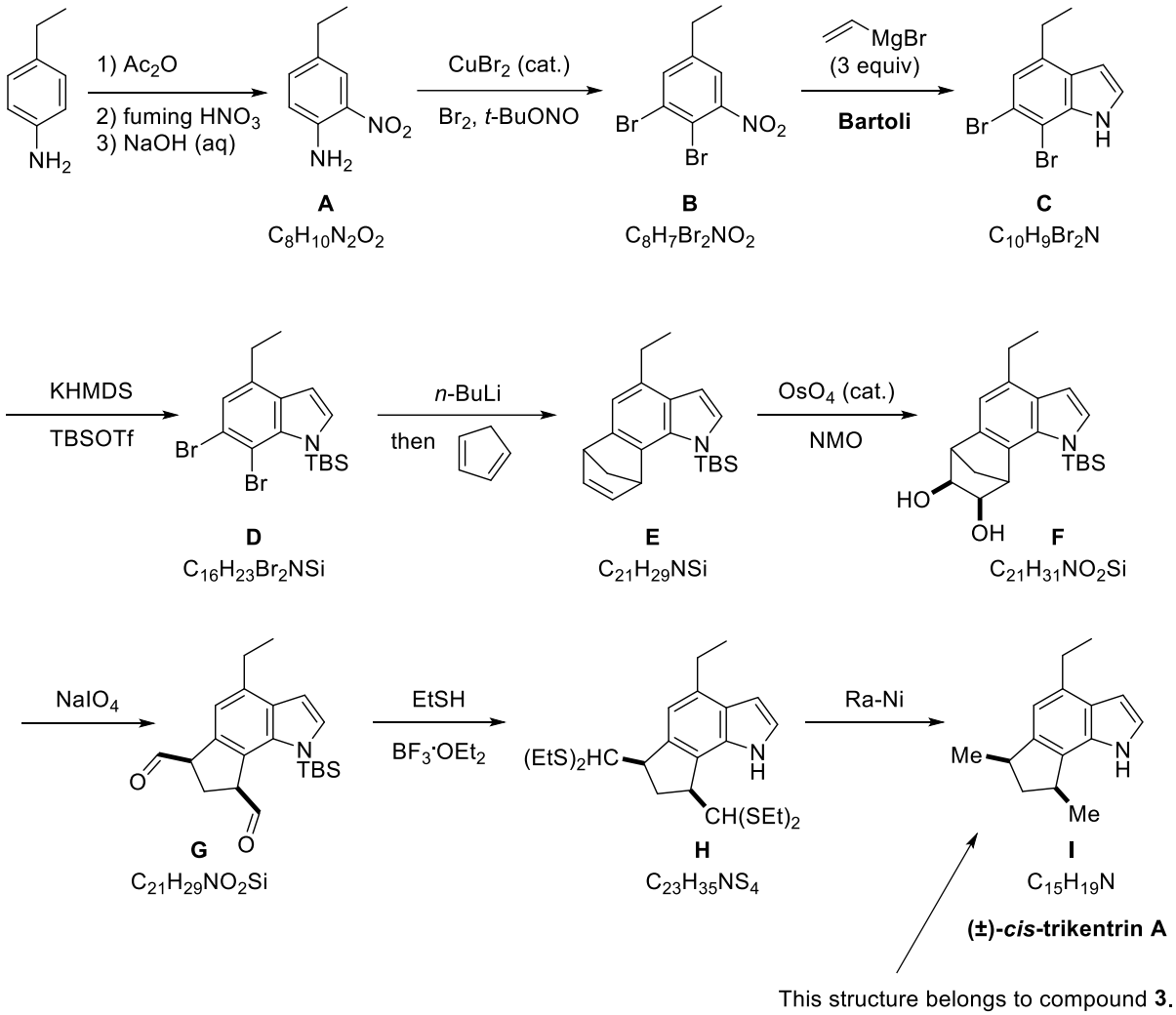
9-BBN = 

NMO = 

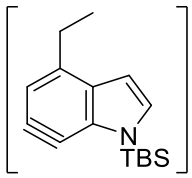
TBAF = tetra-*n*-butylammonium fluoride

Solution:

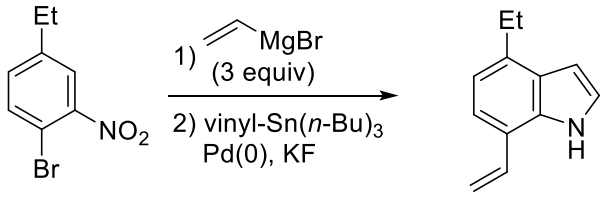
7.1.



7.2.



7.3.



First step is **Bartoli** reaction.

J

$C_{12}H_{13}N$

7.4.

☒ Ligand **3** gave the best enantioselectivity.

☒ Ligand **4** gave a racemic mixture.

☐ Each of the ligands **K1**–**K4** is chiral.

☐ Each of the ligands **K1**–**K4** gave excellent yield (>95%) of the product.

7.5.

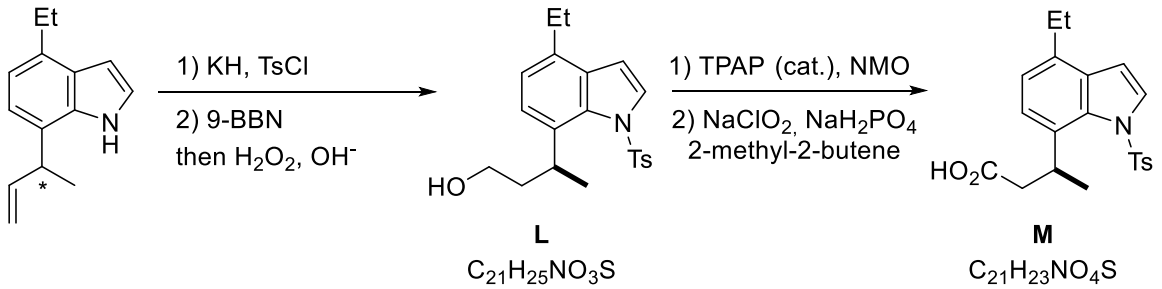
☐ $(allyl)_2Ni_2Br_2$ or $[(allyl)NiBr]_2$ is a source of vinyl.

☒ In this Ni-allyl complex, each nickel has oxidation number +2.

☐ In this Ni-allyl complex, the electron count of Ni is 18.

☒ This complex has a square planar geometry.

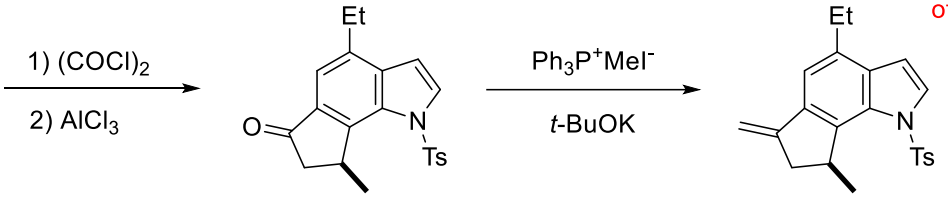
7.6.



L
$C_{21}H_{25}NO_3S$

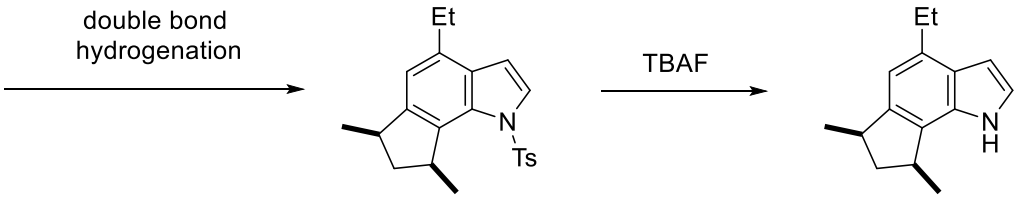
M
$C_{21}H_{23}NO_4S$

Chemical shift at δ = 178.3 ppm indicates the presence of a carboxylic acid group.



N
$C_{21}H_{21}NO_3S$

O
$C_{22}H_{23}NO_2S$

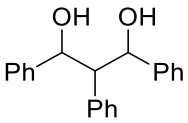


P
$C_{22}H_{25}NO_2S$

I
$C_{15}H_{19}N$

(+)-*cis*-trikentrin A

Problem 8. Stereoisomers of 1,2,3-Triphenylpropane-1,3-diol



8.1. **Draw** all possible stereoisomers of 1,2,3-triphenylpropane-1,3-diol.

8.2. **List** all the achiral compounds.

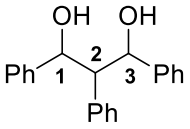
8.3. **List** all the chiral compounds.

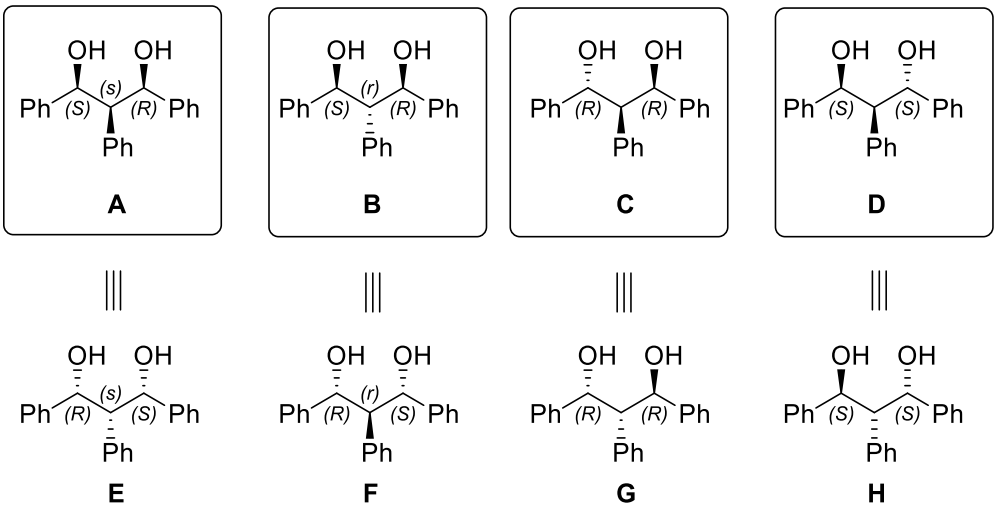
8.4. Which of the following properties or methods can be used to distinguish between the chiral compounds from question **8.3**? **Choose** all correct statements.

- ☐ boiling point
- ☐ UV spectroscopy
- ☐ refractive index
- ☐ melting point
- ☐ optical rotation
- ☐ dipole moment
- ☐ NMR spectroscopy in an achiral environment
- ☐ IR spectroscopy

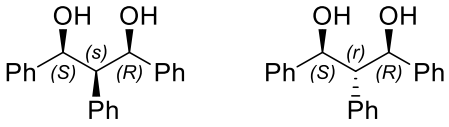
Solution:

8.1. 1,2,3-Triphenylpropane-1,3-diol has an internal plane of symmetry. Therefore, the formula for the maximum number of stereoisomers 2^n would give us 8 stereoisomers, but due to the fact that there is an internal plane of symmetry 1,2,3-triphenylpropane-1,3-diol exists as only four stereoisomers: two meso compounds and a pair of enantiomers. Carbon-2 in **A** and **B** is called a pseudo-asymmetric carbon atom. Carbon-2 in **C** and **D** is not a stereogenic center.





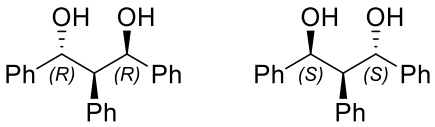
8.2.



A **B**

Meso **Meso**

8.3.



C **D**

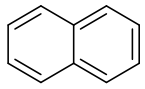
8.4.

- ☐ boiling point
- ☐ UV spectroscopy
- ☐ refractive index
- ☐ melting point
- ☒ optical rotation
- ☐ dipole moment
- ☐ NMR spectroscopy in an achiral environment
- ☐ IR spectroscopy

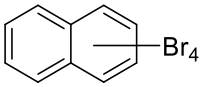
Problem 9. NMR, Symmetry, and Structural Analysis

Naphthalene halides: Key compounds for many applications

Besides benzene, naphthalene is one of the best-known aromatic hydrocarbons. Therefore, the chemistry of naphthalene (**1**) has been extensively studied and many naphthalene derivatives have been synthesized. Halogen derivatives of this kind of compound are key for many transformations. For this reason, nearly all halogenated derivatives of naphthalene are known in the literature. Both ^{1}H and ^{13}C NMR spectra of symmetric compounds are characteristic, and allow researchers to exclude possible non-symmetrical structures to analyze the correct structures. Let us consider naphthalene tetrabromide isomers **2**.



1
Naphthalene



2
Naphthalene tetrabromides

9.1. **Draw** the structures of all naphthalene tetrabromide(s) with 3 signals in ^{13}C NMR and one signal (singlet) in ^{1}H NMR spectra.

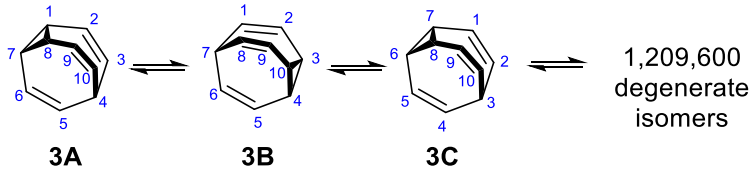
9.2. **Draw** the structures of all naphthalene tetrabromide(s) with 5 signals in ^{13}C NMR spectra.

9.3. **Draw** the structures of all naphthalene tetrabromide(s) with 6 signals in ^{13}C NMR and a doublet (J = 8–9 Hz) in ^{1}H NMR spectra.

9.4. **Draw** the structures of all naphthalene tetrabromide(s) with 6 signals in ^{13}C NMR and a doublet (J = 1.5–2.0 Hz) in ^{1}H NMR spectra.

Dynamic NMR: fast transformation between tautomeric forms and identical nuclei in NMR

Bullvalene (**3**) is very suitable for degenerate Cope rearrangements. Without counting enantiomers, the number of possible valence tautomers of a bullvalene with ten distinguishable positions is 10!/3 = 1,209,600. This arrangement enables all carbon and hydrogen atoms to appear equivalent on the NMR timescale. At sufficiently high temperature, both ^{1}H NMR and ^{13}C NMR spectra of bullvalene show only one signal, average to a rounded peak. However, at −60 °C, as Cope rearrangements do not take place, olefinic and aliphatic protons are observed separately.



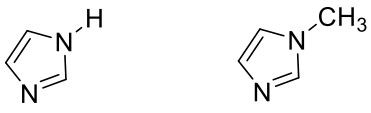
3A **3B** **3C**

Bullvalene

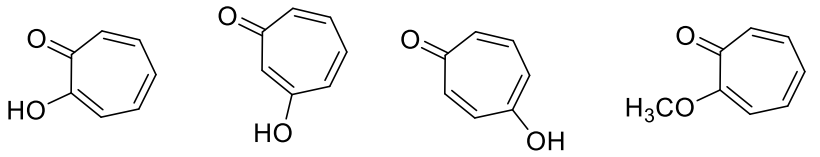
9.5. At low temperature, ignoring any Cope rearrangement, **how many** carbon signals do you expect from the ^{13}C NMR spectrum of bullvalene?

Label identical carbon atoms with letters **a**, **b**, **c**… on the molecular structure.

9.6 Owing to fast tautomerism, some molecules give clearer spectra due to apparent symmetry. In light of this information, how many signals do you expect from the ^{13}C NMR spectra of the following compounds?



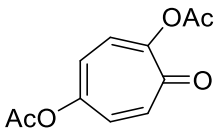
1*H*-imidazole 1-methyl-1*H*-imidazole



α-tropolone β-tropolone χ-tropolone 2-methoxtropone

9.7. In the literature, it has been shown that the tropolone diacetate derivative **4** has fewer signals than expected in ^{13}C NMR spectroscopy.

Draw reasonable resonance structure(s) and/or transformation(s) responsible for this symmetry. How many signals do you expect for this molecule in the ^{13}C NMR spectrum?

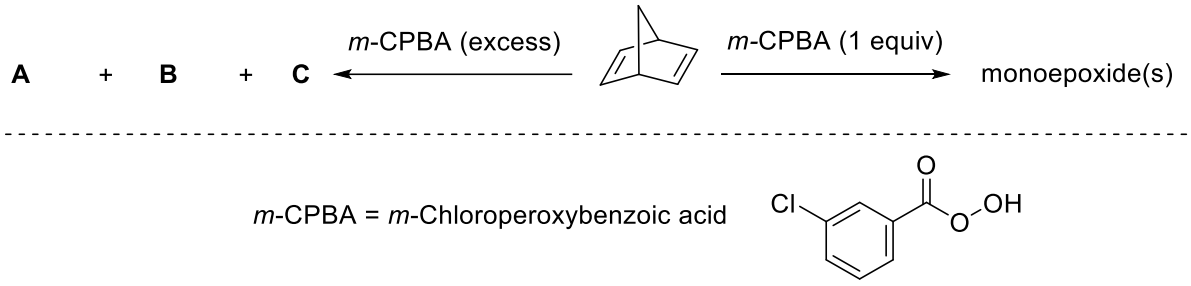


4

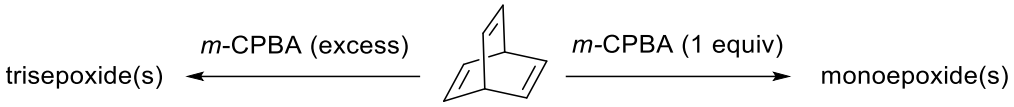
Stereochemistry of the epoxidation reaction of bicyclic alkenes.

9.8. Considering the following pieces of information, **draw** the structures of all possible stereoisomers formed under the given reaction conditions.

Hint: A and **B** are isomers with 3 signals and **C** is an isomer with 4 signals in ^{13}C NMR spectroscopy.

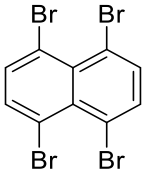


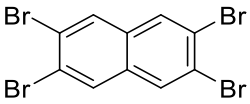
9.9. **Draw** the structures of the stereoisomer(s) formed under the given reaction conditions. How many signals do you expect for the epoxide product(s) in ^{13}C NMR spectra?



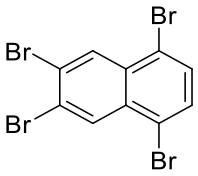
Solution:

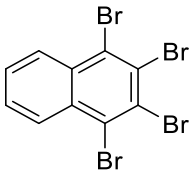
9.1.

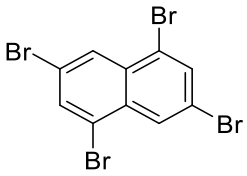


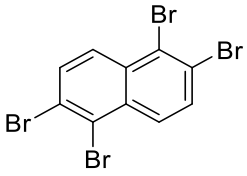


9.2.

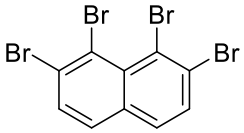




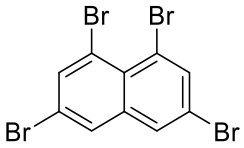




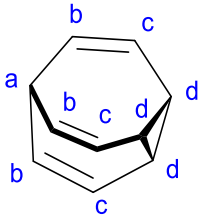
9.3.



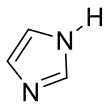
9.4.



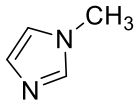
9.5. Bullvalene gives 4 signals for carbons a, b, c, and d.



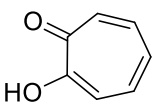
9.6.



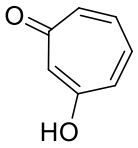
1*H*-imidazole
2 signals



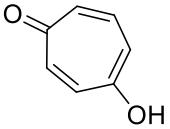
1-methyl-1*H*-imidazole
4 signals



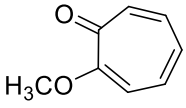
α-tropolone
4 signals



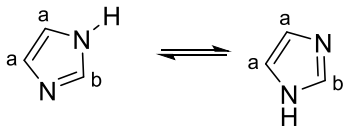
β-tropolone
4 signals



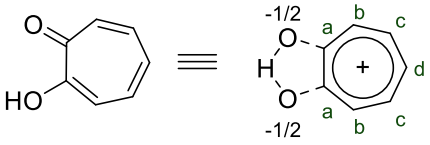
χ-tropolone
4 signals



2-methoxtropone
8 signals

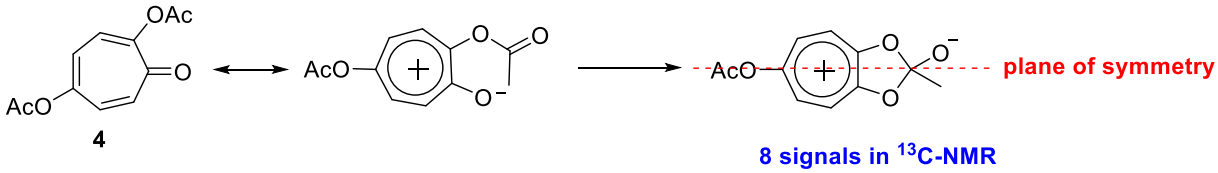


2 signals : a and b



4 signals : a, b, c and d

9.7.

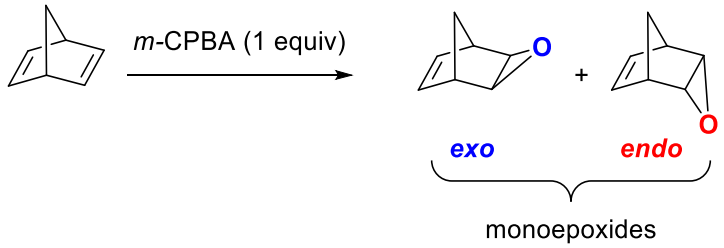


4

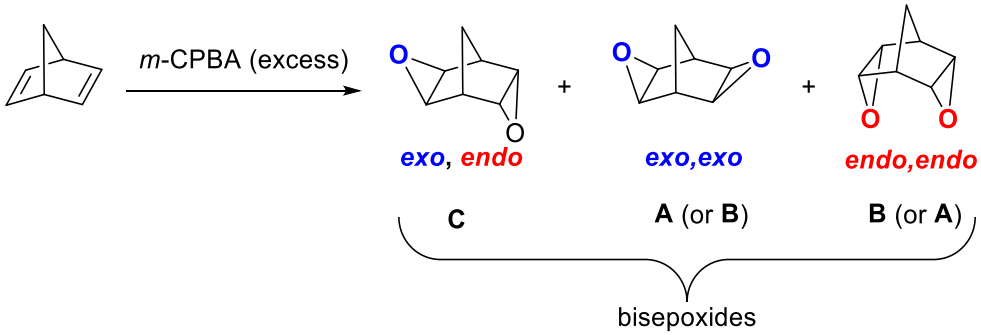
8 signals in ^{13}C-NMR

plane of symmetry

9.8.

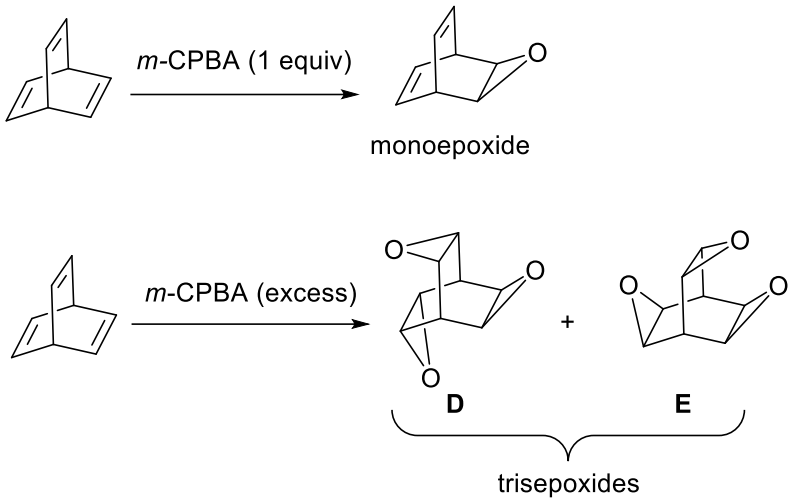


monoepoxides



bisepoxides

9.9.

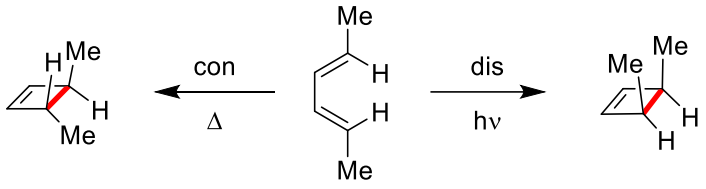


D is an isomer with 2 signals in ^{13}C NMR and **E** is an isomer with 4 signals in ^{13}C NMR.

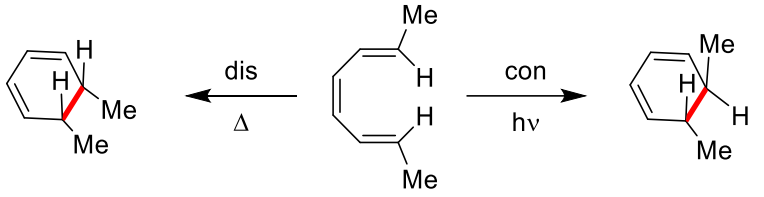
Problem 10. Woodward–Hoffmann Rules and Pericyclic Reactions

The **Woodward–Hoffmann rules** (or the **pericyclic selection rules**), developed by Robert B. Woodward and Roald Hoffmann, are used to rationalize or predict some stereochemical aspects and the activation energy of pericyclic reactions. They are for all classes of pericyclic reactions (and their reverse 'retro' processes), such as cycloadditions, sigmatropic shift, electrocyclization, ene, and cheletropic reactions.

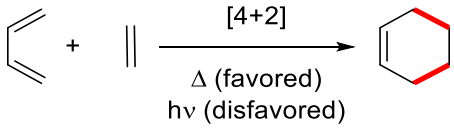
Woodward–Hoffmann rules for electrocyclic reactions		
System	**Conditions**	**Motion**
4*n*	thermal (Δ)	conrotatory (con)
	photochemical (hν)	disrotatory (dis)
4*n*+2	thermal	disrotatory
	photochemical	conrotatory

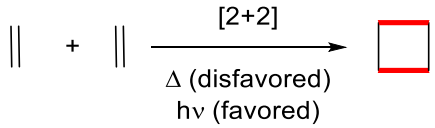


trans-isomer (2*E*,4*E*)-hexa-2,4-diene *cis*-isomer

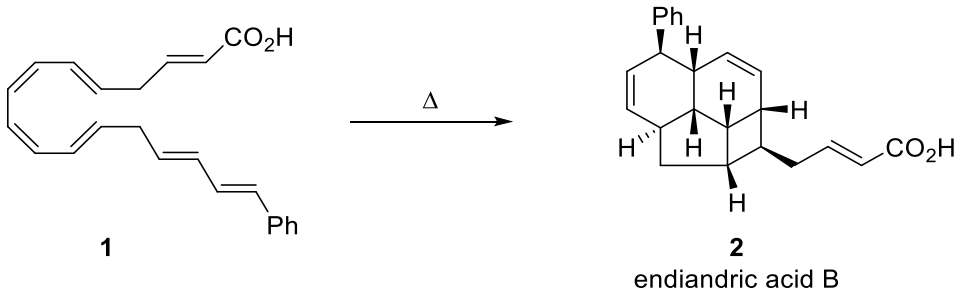


cis-isomer (2*E*,4*Z*,6*E*)-octa-2,4,6-triene *trans*-isomer





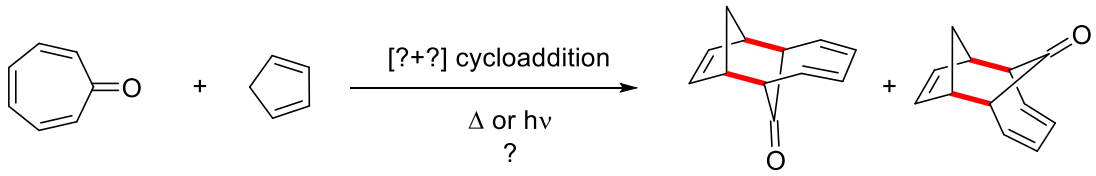
10.1. Thermal reaction of compound **1** results in the formation of endiandric acid **2** by a series of pericyclic reactions. **Show** all steps and **classify** their pericyclic processes.



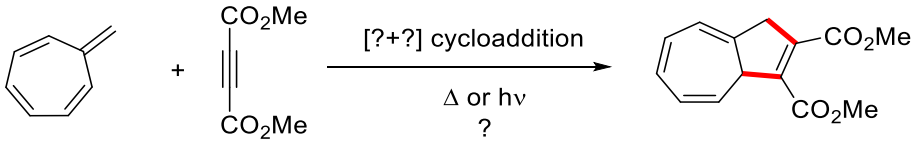
1 **2**
endiandric acid B

How many π electrons are involved in the following reactions? Are these reactions thermally or photochemically allowed according to the Woodward–Hoffmann rules?

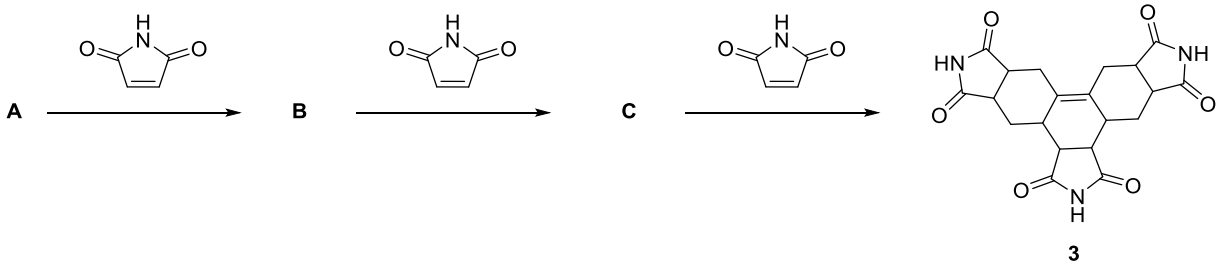
10.2.



10.3.



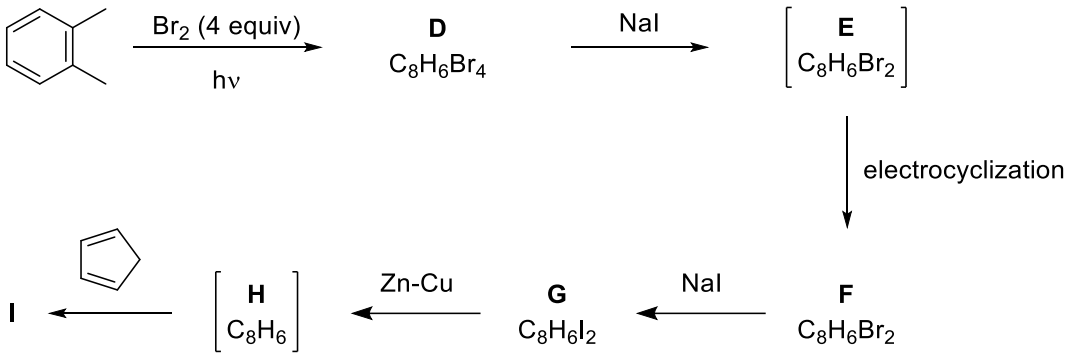
10.4. Domino Diels–Alder reaction of **A** with succinimide results in the formation of adduct **3**. **Draw** the structures of **A**–**C**.



3

10.5. The following reaction scheme illustrates the synthesis of *endo*-isomer of benzenoid tetracyclic hydrocarbon **I** starting from *o*-xylene. Br_2-elimination of tetrabromo-*o*-xylene **D**

with sodium iodide leads to a reactive intermediate which undergoes a 4π electrocyclization to yield compound **F**. **Draw** the structures of intermediates and products **D–I**.

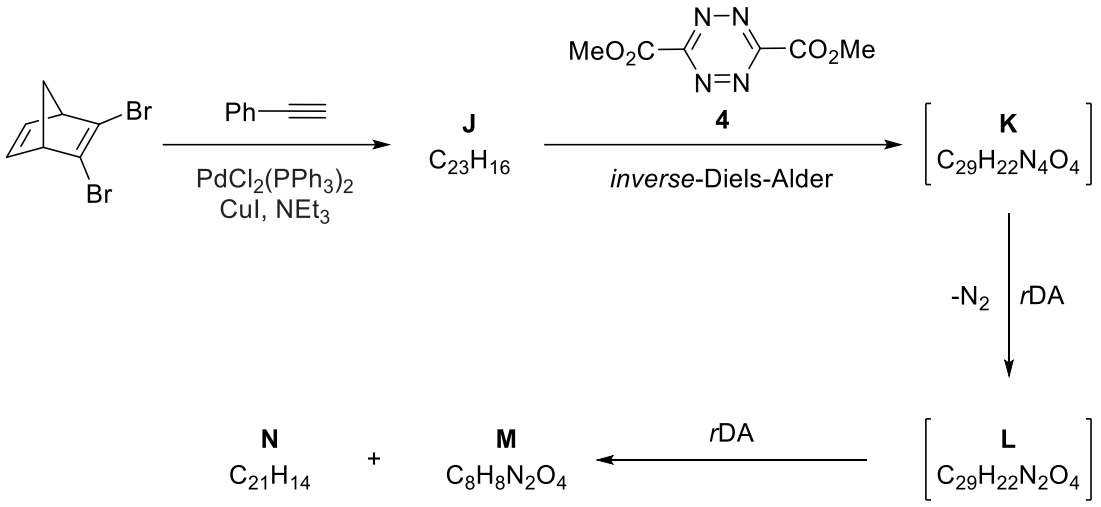


***retro*-Diels–Alder Reaction**

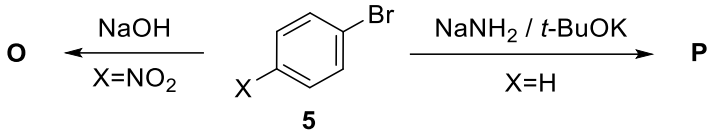
The *retro*-Diels–Alder (*r*DA) reaction is the reverse of the Diels–Alder reaction, i.e., the formation of diene and dienophile from cyclohexene. Generally, an *r*DA reaction is initiated by heating. In some cases, low temperature is sufficient for this transformation, depending on the nature of the substrate.

10.6. Cyclopentadienes are very useful synthetic intermediates in the fields of organic and coordination chemistry. Parent (unsubstituted) cyclopentadiene is obtained by the thermal decomposition of dicyclopentadiene. However, substituted cyclopentadienes are generally unstable due to the facile migration of the endocyclic double bonds. Consequently, practical and general methods for the synthesis of substituted cyclopentadienes are limited. In the following reaction scheme, the synthesis of a substituted cyclopentadiene derivative is given. Besides *r*DA, some steps also involve the *inverse*-Diels–Alder reaction, which is a cycloaddition between an electron-rich dienophile and an electron-poor diene (such as tetrazine **4**), through the interaction of the HOMO orbital of dienophile and the LUMO orbital of diene.

Draw the structures of the intermediates and products **J**–**N**.

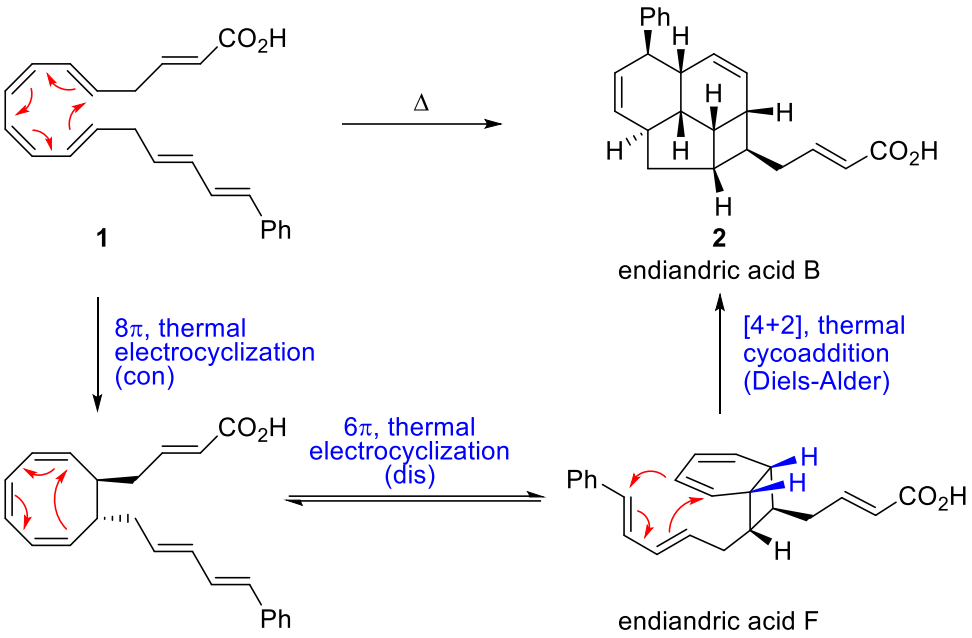


10.7. Nucleophilic aromatic substitution reactions constitute an important class of reactions in synthetic organic chemistry. In the following scheme, the reactions of aryl halide **5** proceed via two different kinds of intermediates in presence of a cyclic 1,3-diene depending on the reaction conditions and the nature of the substituent on the aromatic ring. **<u>Draw</u>** the structures of products (**O** and **P**), and **<u>discuss</u>** possible intermediates responsible for the formation of these products.

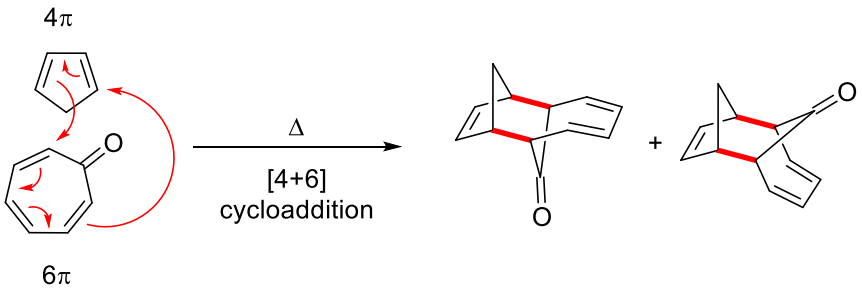


Solution:

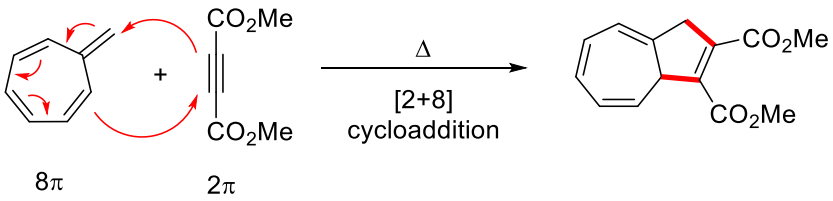
10.1.



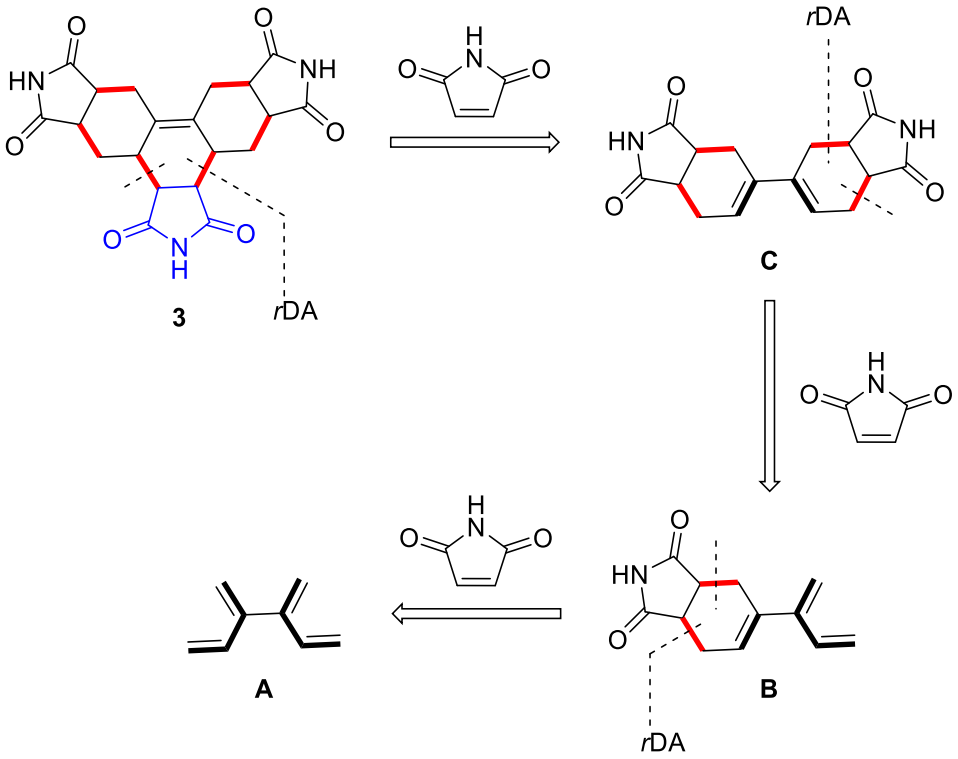
10.2.



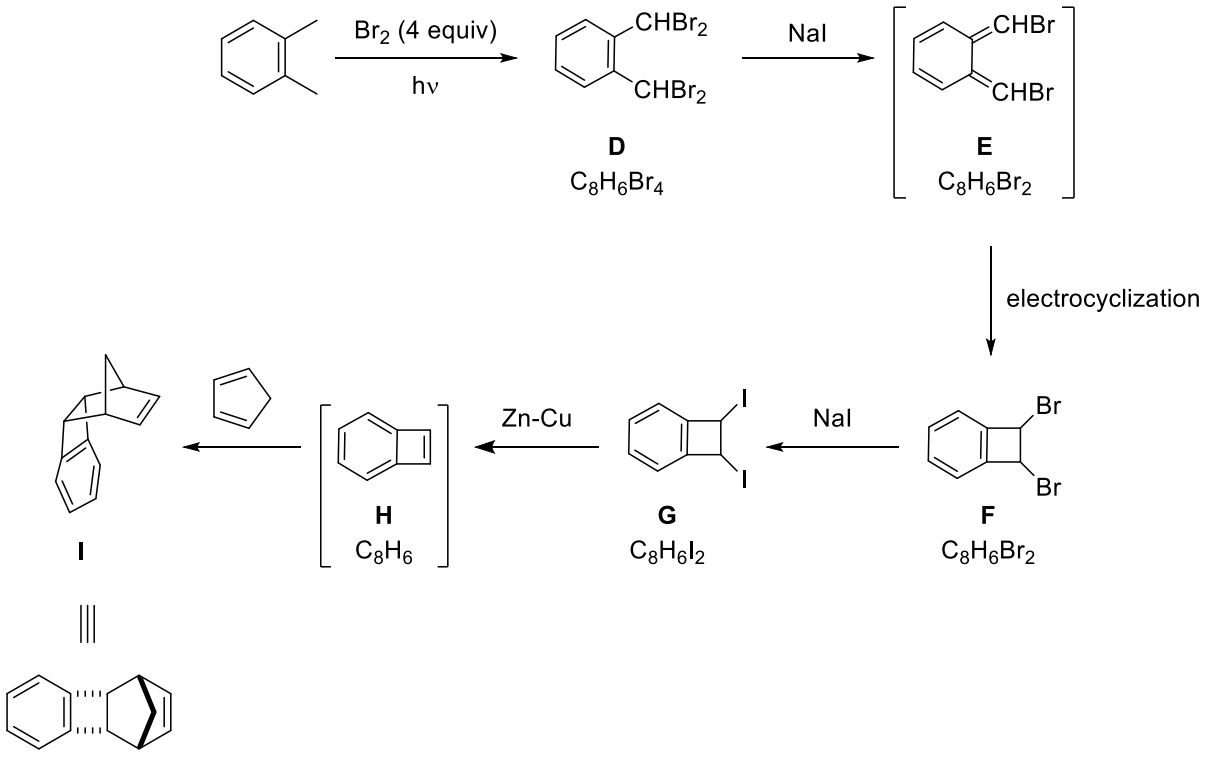
10.3.



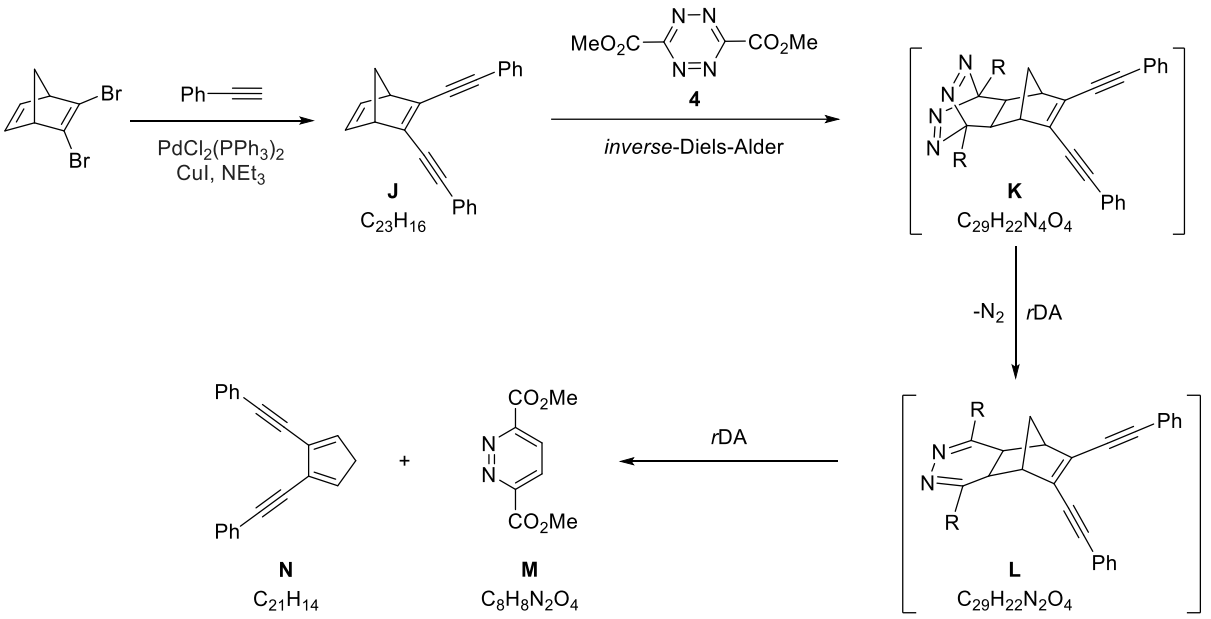
10.4.


3
rDA
C
A
B
rDA

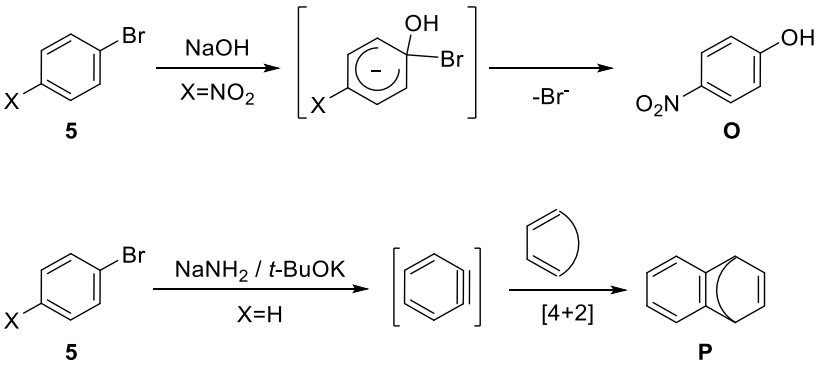
10.5.


Br2 (4 equiv)
hν
D
C8H6Br4
NaI
E
C8H6Br2
electrocyclization
F
C8H6Br2
NaI
G
C8H6I2
Zn-Cu
H
C8H6
I

10.6.



10.7. Aryl halides generally undergo nucleophilic aromatic substitution reactions via two mechanisms: 1) addition-elimination mechanism 2) elimination-addition mechanism via aryne intermediates. In general, reactions of aryl halides bearing electron-withdrawing groups with strong bases/nucleophiles proceed via addition-elimination mechanism, whereas reactions of aryl halides, which are not electron deficient, take places via elimination-addition (aryne) mechanism.

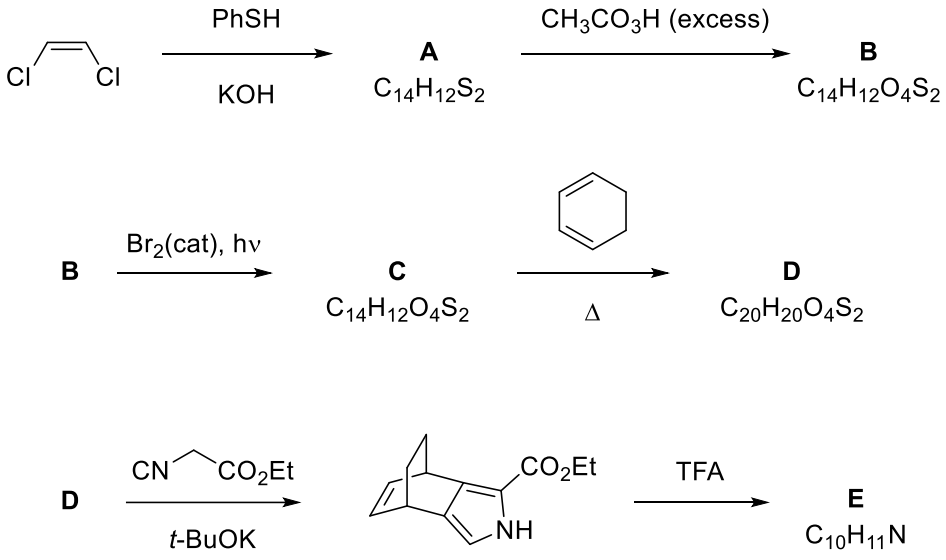


Problem 11. Benzoporphyrin

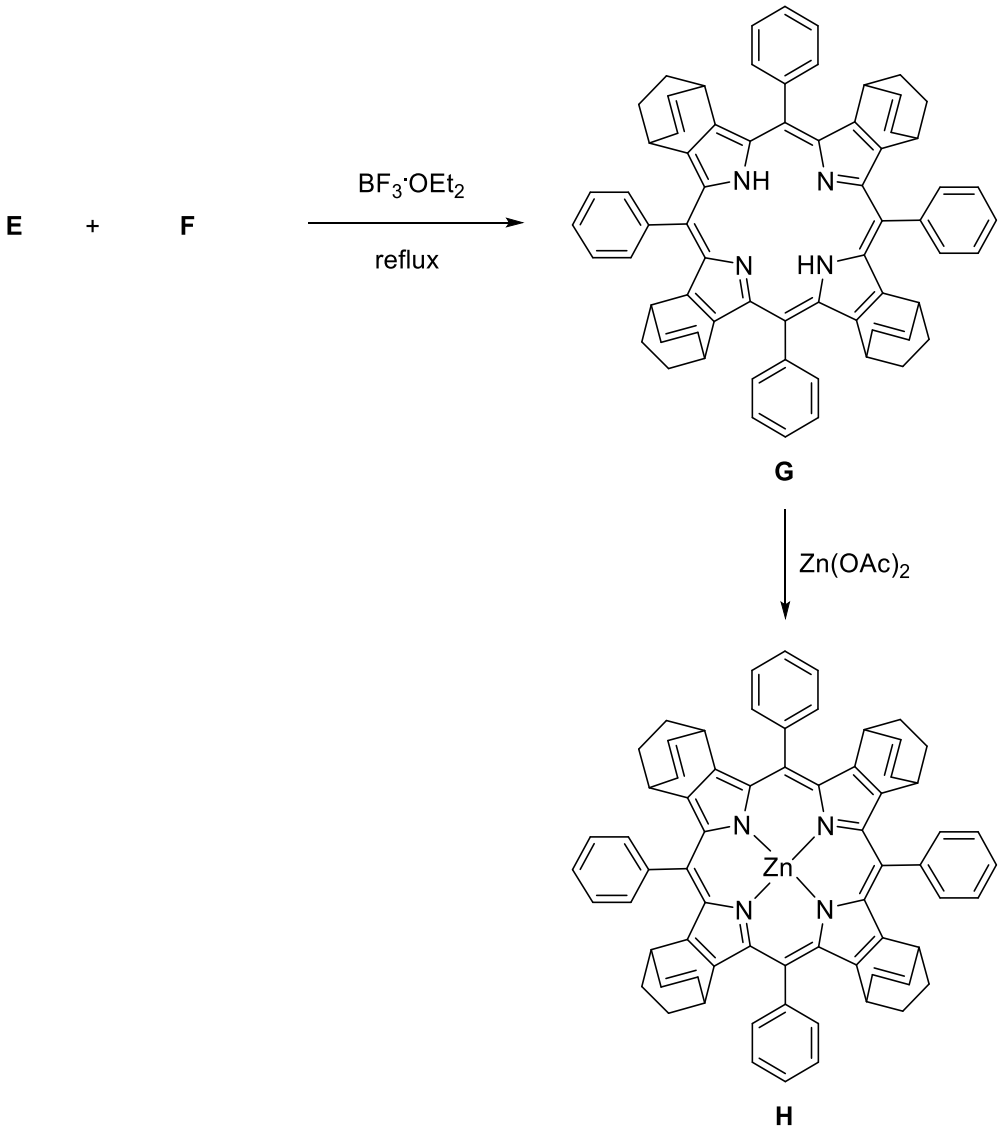
The name "porphyrin" derives from the Greek word *porphyra*, meaning purple. Porphyrins are a group of macrocycle organic compounds, composed of four modified pyrrole subunits. They have a total of 26 π-electrons, 18 of which form a planar porphyrin ring structure. They are often described as aromatic. Metal complexes derived from porphyrins occur naturally. One of the best-known families of porphyrin complexes is heme, the pigment in red blood cells. A benzoporphyrin is a porphyrin with a benzene ring fused to pyrrole unit(s).

11.1. Benzoporphyrins can be prepared starting from a masked pyrrole derivative **E**. The synthesis of **E** starts with a reaction of *cis*-1,2-dichloroethene and thiophenol to give **A**. Oxidation of **A** yields **B** having phenylsulfonyl units. The *cis*-product **B** is then converted to its *trans* isomer **C** when treated with a catalytic amount of Br_2 under UV light. The Diels–Alder reaction between **C** and 1,3-cyclohexadiene under thermal conditions gives the product **D**, which is converted to a pyrrole carboxylic acid ester when reacted with ethyl isocyanoacetate. Ester then is treated with TFA to give the pyrrole derivative **E**.

Draw the structures of compounds **A**–**E** including stereochemistry when necessary.

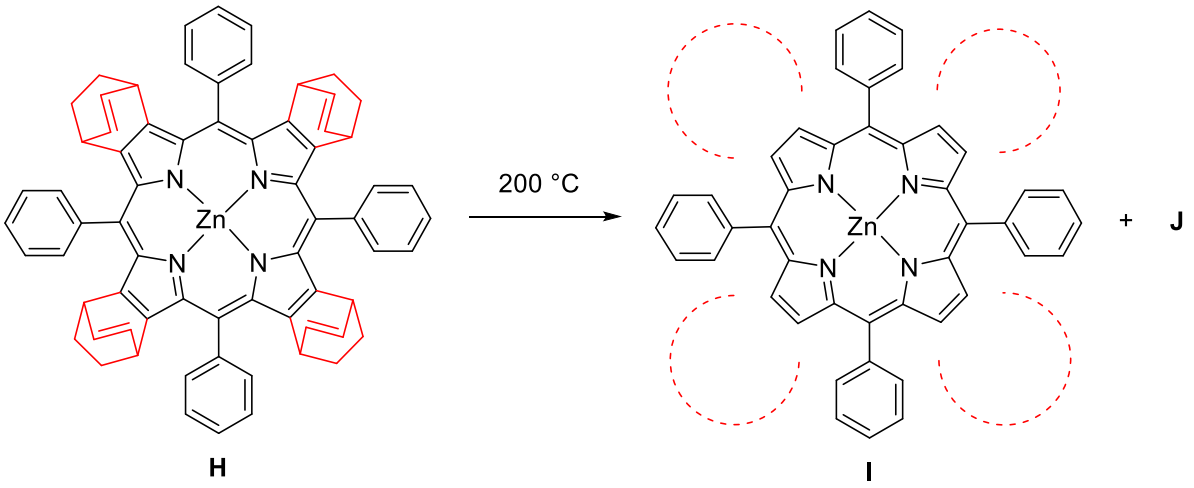


11.2. Porphyrins can easily be prepared *via* a cyclization reaction of pyrrole derivatives with aldehydes. **Draw** the structure of aldehyde **F** and **determine** the oxidation state of zinc in compound **H**.



11.3. When **H** is heated under vacuum, it can give a more conjugated product through a *retro*-Diels–Alder reaction.

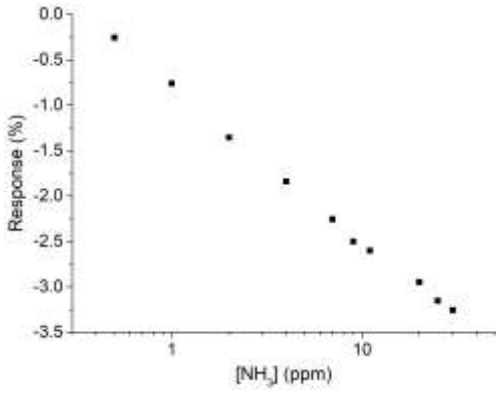
To complete the structure of **I**, **draw** the structures of the dashed circle part of **I** (all the circles are identical) and **J**.



H I

Ammonia is a major metabolic compound and the importance of its sensitive detection has been emphasized recently because of its correlation with specific diseases. In normal physiological conditions, ammonia can be expelled from slightly alkaline blood and emanated through the skin or exhaled with the breath. Dysfunction in the kidney or liver that converts ammonia to urea can result in an increase in the ammonia concentration in breath or urine. Consequently, the detection of the ammonia present in breath or urine can be used for the early diagnostics of liver or stomach diseases. The development of sensor devices for measuring ammonia with a sensitivity of 50 ppb–2 ppm and with a fast response time is highly desired.

For that purpose, **I** was used to prepare a fiber-optic ammonia gas sensor. Exposure of this sensor to ammonia changes the transmittance of the fiber-optic. By using an appropriate spectrometer, ammonia gas in different concentrations was passed through the sensor and the change in transmittance was measured. The results of these measurements are listed in the Table below.



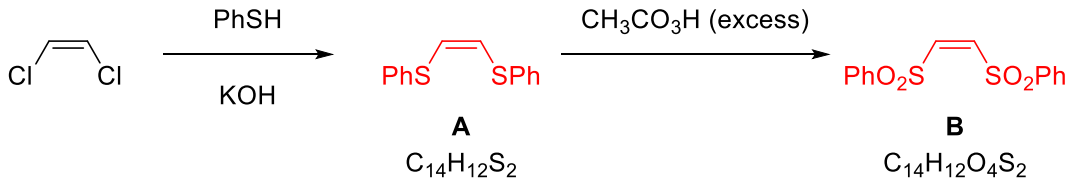
[NH_3] (ppm)	**Sensor response (%)**
0.500	–0.2540
1.00	–0.7590
2.00	–1.354
4.00	–1.838
7.00	–2.255
9.00	–2.500
11.0	–2.600
20.0	–2.947
25.0	–3.152
30.0	–3.256

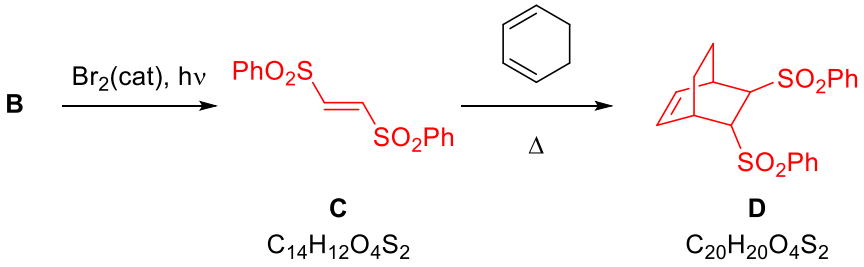
11.4. Using the linear region of sensor response data prepare a calibration curve and **find** the calibration equation as $y = a + bx$.

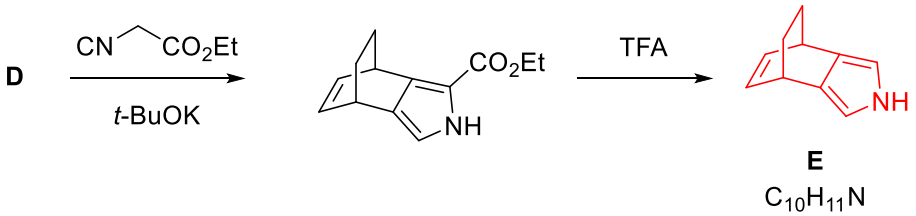
11.5. This sensor is then used for the detection of ammonia in human breath. When a kidney patient's breath was fed into the sensor, a –3.812% change in the response is observed. **Calculate** the ammonia concentration in the patient's breath.

Solution:

11.1.



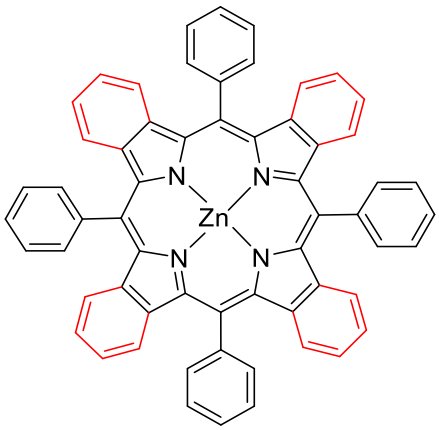




11.2.

F	**Oxidation state of Zinc in G = 2+**

11.3.



I

+ $H_2C{=}CH_2$

J

11.4.

log([NH_3])	Sensor Response (%)
–0.301	–0.2540
0.00	–0.759
0.301	–1.354
0.602	–1.838
0.845	–2.255
0.954	–2.500
1.041	–2.600
1.301	–2.947
1.398	–3.152
1.477	–3.256

$y = -0.8058 - 1.6814x$

12.5. $-3.812 = -0.8058 - 1.6814 \times \log[NH_3]$

$\log[NH_3] = 1.788$

$[NH_3] = 61.4\ ppm$

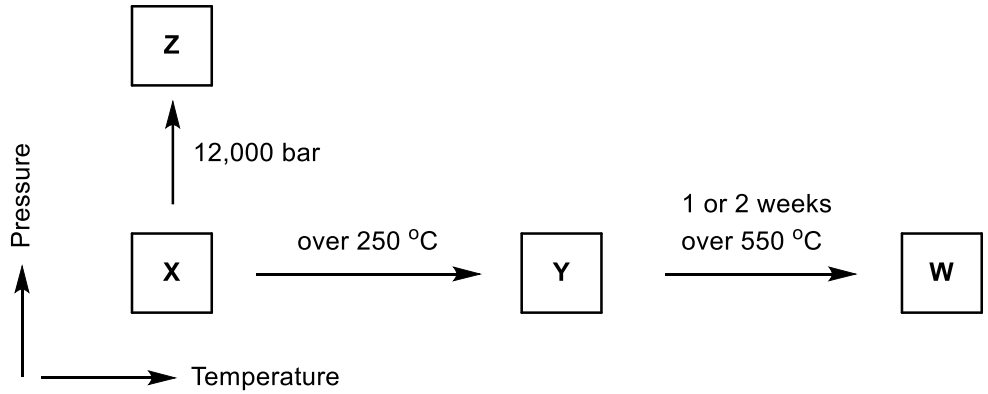
Problem 12. Blue to Green, Turquoise

The beauty of the turquoise color of Lake Salda, where blue meets white sands, fascinates those who see it. Lake Salda, in the southern province of Burdur's Yeşilova district, has been referred to as "Turkey's Maldives" in recent years for its white sandy beaches and turquoise water. In fact, turquoise is an opaque, blue to green mineral that is a hydrated phosphate of copper and aluminum with the chemical formula of $CuAl_6(PO_4)_4(OH)_8 \cdot 4H_2O$, and is known as a gemstone. The word turquoise dates back to the 17th century and is derived from the French turquois, meaning "Turkish" because the mineral was first brought to Europe through Turkey, from mines in the historical Khorasan Province of Persia. Phosphorus, which is also in the structure of turquoise, is an essential part of life. Without the phosphates in biological molecules such as ATP, ADP, and DNA, we would not survive. Phosphorus compounds can be found in the minerals in our bones and teeth. With few exceptions, minerals containing phosphorus are in the maximally oxidized state as inorganic phosphate rocks, which are partially made of apatite, and they are today the chief commercial source of this element. Phosphate products are used as fertilizers in agriculture. They are also used in animal feeds, as a leavening agent in baking powder and flour, as an additive to beverages, and in pharmaceuticals. Industrial uses include water softening, rust proofing, fire proofing, in insecticides and detergents, and for the manufacture of elemental phosphorus.

Lake Salda

There are three important allotropes of phosphorus: **X**, **Y**, and **Z**. However, another form of phosphorus, **W**, also exists (given below). **X** is a soft, waxy solid. It is exceptionally harmful

and to a great degree reactive and also displays chemiluminescence. Crystals of **X** are composed of P_4 molecules. **Y** is obtained by heating **X** to 250 °C within the sight of daylight. It is nonpoisonous and odorless. **Y** does not show chemiluminescence. It exists as a polymeric solid. **Z** is produced from **X** under inert atmosphere. **Z** is the most stable allotrope of phosphorus and has a layered structure. **W** is a form of phosphorus that can be produced by day-long annealing of **Y** above 550 °C.



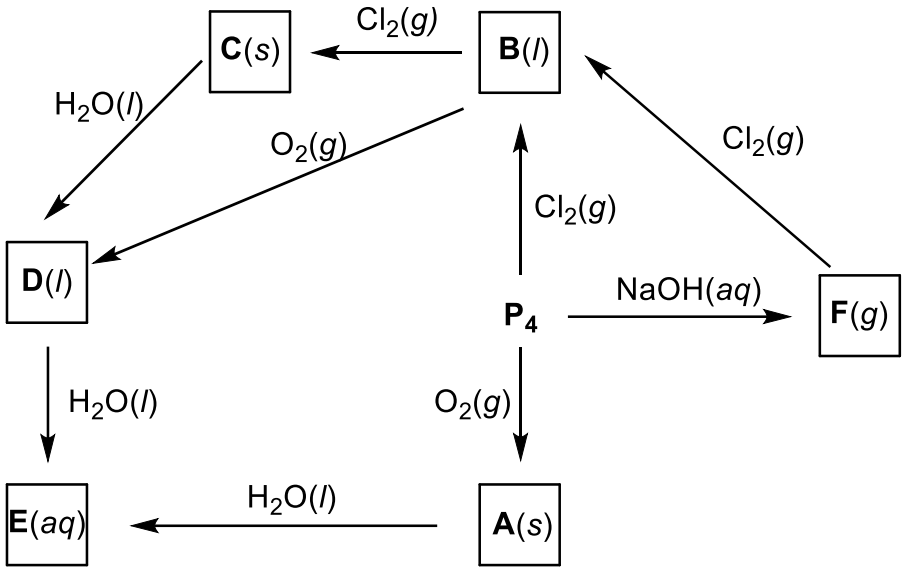
The interconvertible forms of all allotropes of phosphorus

12.1. **Identify** allotropes of phosphorus indicated by **X**, **Y**, **Z**, and **W**.

12.2. **Draw** the structure of **X**, **Y**, **Z** allotropes of phosphorus and **sketch** the geometry of **X**.

12.3. P_4 ignites suddenly in air at around 35 °C to form a phosphorus oxide derivative. Thus, it is kept under water. When P_4 reacts with different amounts of dry halogens, phosphorus trihalides (PX_3) or phosphorus pentahalides (PX_5) are obtained. PX_5 can also be obtained by the reaction of the halogens with PX_3. The phosphorus pentahalides undergo hydrolysis in two steps to form acid. The phosphoryl halides can be prepared by the hydrolysis of the appropriate pentahalides in a limited amount of water or by the reaction of the trihalides with oxygen. Dropping of the oxide derivative of phosphorus into water produces a hissing sound, heat, and acid product. The reaction of P_4 with sodium or potassium hydroxide produces phosphine gas as the major product and potassium or sodium hypophosphite as a by-product. Phosphine burns in chlorine spontaneously, forming a phosphorus trihalide (PX_3) or phosphorus pentahalide (PX_5).

Write the formulas of products **A**–**F**.



When phosphorus reacts with excess of halogens, it can form five-coordinated compounds such as PCl_5. Phosphorus mixed pentahalides like PF_2Cl_3 are prepared by the addition of one halogen to the phosphorus trihalide of a second halogen.

12.4. **Draw** the Lewis structures of PCl_5 and PF_2Cl_3 molecules.

12.5. By using VSEPR theory, **predict** the molecular geometries of PCl_5 and PF_2Cl_3.

12.6. **Estimate** the polarity of PCl_5 and PF_2Cl_3 molecules.

12.7. **Compare** the axial P–Cl bond length to the equatorial P–Cl bond length in PCl_5.

12.8. **Draw** the hybridization scheme of the PF_2Cl_3 molecule and **estimate** which hybrid orbitals are used to form the axial and equatorial bonds.

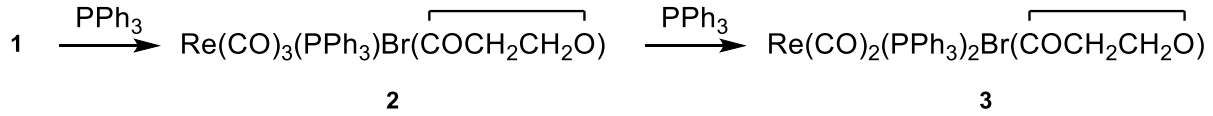
12.9. The synthesis of PH_3 from hydrogen with white phosphorus is given below. **Calculate** ΔH for the following reaction, using bond energies (single bond energies (BE) (in $kJ.mol^{-1}$) for P–P: 213, H–H: 435, P–H: 326).

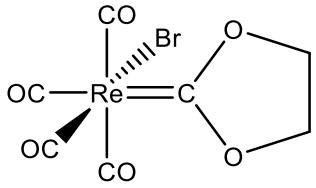
$$P_4(g) + 6H_2(g) \rightarrow 4PH_3(g)$$

Organophosphorus compounds are organic compounds containing phosphorus. Phosphorus can adopt a variety of oxidation states, and organophosphorus compounds are generally classified based on their derivatives of phosphorus(V) or phosphorus(III), which are the predominant classes of compounds. Organophosphorus compounds are widely used as nucleophiles and ligands. Two major applications are as reagents in the Wittig reaction and as supporting

phosphine ligands in homogeneous catalysis. Their nucleophilicity is evidenced by their reactions with alkyl halides to give phosphonium salts. Phosphines are nucleophilic catalysts in organic synthesis, e.g., the Rauhut–Currier reaction and Baylis–Hillman reaction.

Triphenylphosphine (PPh_3) is a common organophosphorus compound and it is widely used in the synthesis of organic and organometallic compounds. When a toluene solution of compound **1** and excess of PPh_3 are heated to reflux, first compound **2** is formed and then compound **3**.





1

Spectral data of compounds **1**–**3** are given below (for ^{1}H NMR and ^{13}C NMR data [δ values (relative area)]:

	1	**2**	**3**
^{1}H NMR	4.83 singlet	7.62–7.41 (m, 15H) 4.19 (m, 4H)	7.70–7.32 (m, 30H) 3.49 (s, 4H)
^{13}C NMR	224.3 187.2 185.3 184.0 73.3	231.0 194.9 189.9 188.9 129.0–134.7 (several peaks) 72.2	237.1 201.8 193.8 127.7–134.0 (several peaks) 68.80
IR		2038 cm^{-1} 1958 cm^{-1} 1906 cm^{-1}	1944 cm^{-1} 1860 cm^{-1}
MS (m/z)		684.5	919.7

12.10. <u>Identify</u> the structures of **2** and **3**.

*Hint: The ^{13}C NMR signal of **1** at 224.3 ppm is similar to the chemical shift observed for carbene carbons; the peaks between 184 and 202 ppm correspond to carbonyls; and the peak at δ 73.3 is typical for CH_2CH_2 bridges in dioxycarbene complexes.*

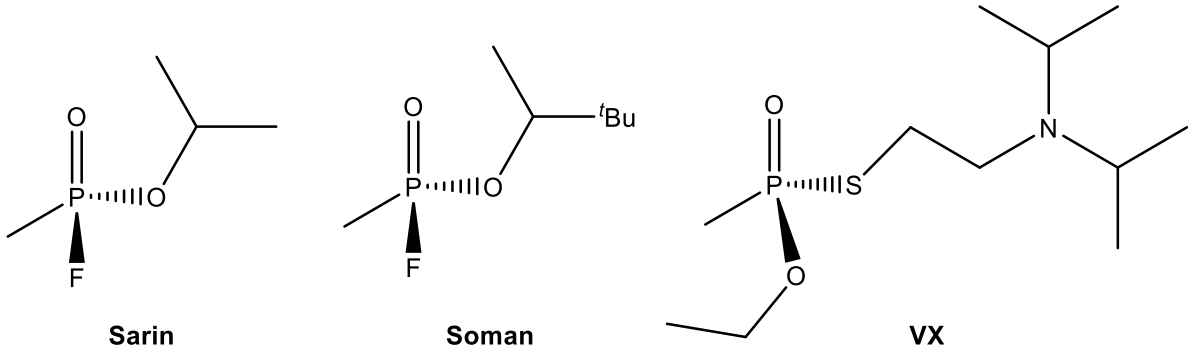
12.11. <u>Determine</u> if **2** is more likely to be the facial (*fac*) or meridional (*mer*) isomer.

*Hint: The three v(CO) bands with equal intensities are observed in the IR spectrum of compound **2**. Protons of the carbene ligand occur as a multiplet in the ^{1}H NMR spectrum.*

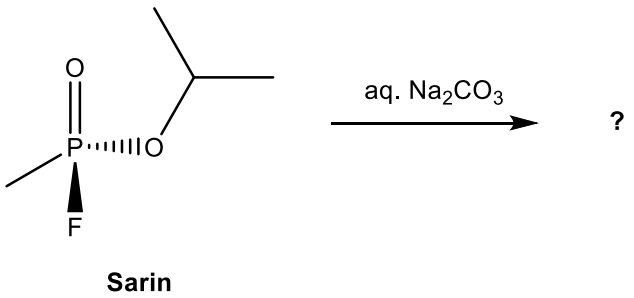
12.12. <u>Determine</u> if **3** is more likely to be *cis* or *trans* isomer.

*Hint: The two v(CO) bands are of approximately equal intensity at 1944 and 1860 cm^{-1} in the IR spectrum of compound **3**. The ^{31}P NMR spectrum shows a single resonance signal.*

Some organophosphorus compounds such as **sarin**, **soman**, and **VX** are often referred as "nerve gases" despite the fact that they are liquids at room temperature. Each country signing the 1997 Chemical Weapons Convention agreed to ban the development of chemical weapons and to destroy chemical weapons and associated production facilities by 2012. Sarin can be destroyed by room temperature hydrolysis using aqueous Na_2CO_3 to give NaF and the sodium salt of an organophosphate. The hydrolysis of nerve agent VX is more difficult. It reacts slowly with aqueous NaOH at room temperature, and the reaction has to be carried out at 360 K over several hours.



12.13. <u>Determine</u> the organophosphorus salt formed in the following hydrolysis reaction.



Two chromium complexes containing the ligands CO, PF_3, and PCl_3 in octahedral geometry are given below. In an octahedral complex, the molecular orbitals created by coordination can be seen as resulting from the donation of two electrons by each of six σ-donor ligands to the d-

orbitals on the metal, called σ-bonding. π-bonding (Pi bonding) in octahedral complexes is also possible when the ligand has *p*, *d* or π^* molecular orbitals available. Ligands such as CO, CN^- and phosphines (of formula PR_3) are π acceptor, with empty orbitals that can interact with metal d orbitals in a π fashion. In most cases, the net back π bonding predominates, and electron density is transferred from the metal to the ligand. π-bonding can affect metal-ligand bond energy and bond length in carbonyl and phosphine complexes.

Answer the following questions considering the π interaction.

12.14. In which complex is the C–O bond **shorter**, $Cr(CO)_5(PF_3)$ or $Cr(CO)_5(PCl_3)$?

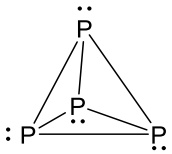
12.15. In the infrared spectrum of which complex do the C–O stretching bands have **higher energy**, $Cr(CO)_5(PF_3)$ or $Cr(CO)_5(PCl_3)$?

Solution:

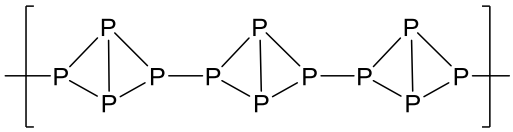
12.1.

Allotrope	**White**	**Red**	**Black**	**Violet**
Compound	X	Y	Z	W

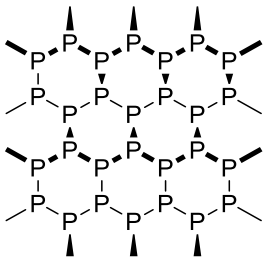
12.2. Structures of allotropes:



white phosphorus



red phosphorus



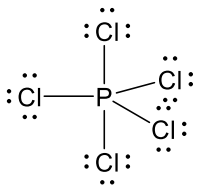
black phosphorus

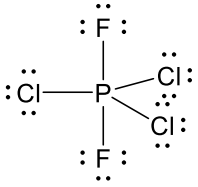
Geometry of **X**: **Tetrahedral**

12.3.

Compound	**A**	**B**	**C**	**D**	**E**	**F**
Formula	**P_4O_{10}** or **P_2O_5**	**PCl_3**	**PCl_5**	**$POCl_3$**	**H_3PO_4**	**PH_3**

12.4.





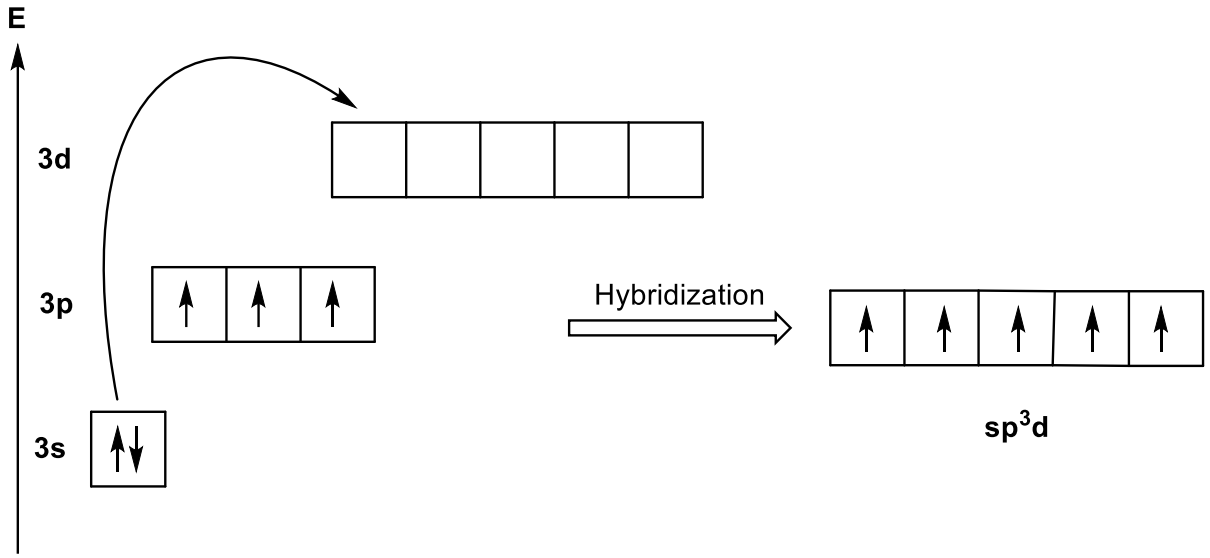
12.5. Molecular geometries: **Trigonal bipyramidal**

12.6. The molecular geometry of PCl_5 and PF_2Cl_3 is trigonal bipyramidal with symmetric charge distribution around the central atom. Therefore, these molecules are **nonpolar**.

12.7. Axial P–Cl bonds are longer than equatorial P–Cl bonds because of the bond pair–bond pair repulsion.

There are two P–Cl bonding environments in this molecule. Each equatorial P–Cl bond makes two 90° and two 120° bond angles with the other bonds in the molecule. Each axial P–Cl bond makes three 90° and one 180° bond angles with the other bonds in the molecule.

12.8.



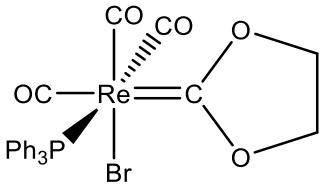
Axial bonds consist of ***d–p*** and equatorial bonds consist of ***sp²*** hybrid orbitals

12.9.

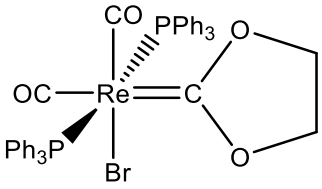
$$\Delta H_{rxn} = \sum BE_{reactants} - \sum BE_{products} = 6BE(P-P) + 6BE(H-H) - 12BE(P-H)$$

$$\Delta H_{rxn} = (6 \times 213) + (6 \times 435) - (12 \times 326) = \boldsymbol{-24kj.mol^{-1}}$$

12.10.



2



3

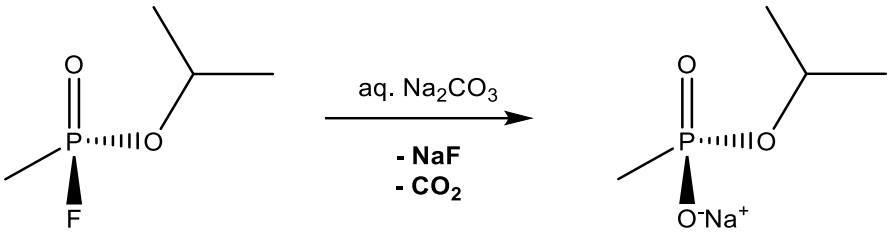
Both **2** and **3** have peaks with similar chemical shifts to the peak at 224.3 ppm for **1**, suggesting that the carbene ligand is retained in the reaction. Similarly, **2** and **3** have peaks near 73.3 ppm,

a further indication that the carbene ligand remains. According to ^{13}C NMR data both **2** and **3** have new peaks in the range 129 to 135 ppm. The most likely explanation is that the reaction involves replacement of carbonyl with PPh_3 and that the new peaks in the 129 to 135 range are due to the phenyl carbons of the phosphine. In both **2** and **3**, integration of the $–CH_2CH_2–$ peaks (4.19, 3.39 ppm, respectively) and the phenyl peaks (7.32 to 7.70 ppm) gives the expected ratios for replacement of one or two COs (in ^1H NMR).

12.11. Compound **2** is a ***fac* isomer**. The three peaks due to v(CO) absorptions in **2** are characteristic of facial (*fac*) tricarbonyl complexes. Due to the presence of the asymmetric center, the protons in the carbene ligand occur as a multiplet at 4.19.

12.12. Compound **3** is a ***trans* isomer**. The presence of two v(CO) bands of approximately equal intensity at 1944 and 1860 cm^{-1} indicates that the CO ligands are *cis* to each other. The ^{31}P NMR spectrum shows a single resonance, and the ^1H NMR spectrum shows a singlet at 3.39 ppm. According to these data, PPh_3 groups are *trans* to each other and compound **3** is a *trans* isomer.

12.13.



Sarin

12.14. $Cr(CO)_5(PF_3)$

As the back bonding (π-bonding) between the metal and the ligand is strengthened, the metal–carbon bond strengthens and the C–O bond weakens. Because PF_3 is a better π-acceptor than PCl_3 due to higher electronegativity of F, compared to Cl. Therefore, PF_3 reduces the electron density over the metal center more than PCl_3 and the π-electron donation from metal to π* antibonding orbitals of CO is reduced, as a result the CO bond is stronger and shorter in the PF_3 substituted complex.

12.15. $Cr(CO)_5(PF_3)$

Problem 13. Spinel Oxides

The simple d-block oxides such as Fe_3O_4 and Co_3O_4 and many related mixed metal compounds have important properties. They have structures related to the mineral spinel, $MgAl_2O_4$, and may be given a general formula of AB_2O_4.

Stoichiometric amounts of two aqua complexes of transition metal (**A** and **B**) nitrate salts are thermally reacted to form a spinel AB_2O_4 crystalline solid that has a face-centered cubic (*fcc)* structure with a unit cell composition of 8 AB_2O_4. Depending on the location of these two cations (A and B), the spinel structures are divided into two categories as normal and inverse spinels. In a normal spinel, the A^{2+} ions occupy the tetrahedral holes and the B^{3+} ions occupy the octahedral holes, but in the inverse spinel structures, the 2+ ions are replaced by half of the 3+ ions in the structure.

Crystalline solid has an ordered structure in which the unit cell repeats along all 3 principal axes of a three-dimensional matter. The smallest group of atoms in the material that constitute this repeating pattern is the unit cell of the structure. The unit cell completely reflects the geometry and structure of the entire crystal, which is built up by repetitive translation of the unit cell along the principal axes. Face centered cubic (*fcc*) is one of a common structure type of crystalline solid. Anions (X) are in the corners and faces of a cube (1/8 from each corners and ½ from each faces, because the corners and faces are shared by 8 and 2 unit cells, respectively) in the simplest *fcc* structure. The cations (M) occupy the holes among the anions. There are 8 tetrahedral (corners) and 4 octahedral holes (1 at the middle and 3 on the edges, each edge has ¼ octahedral hole) in a *fcc* structure. Therefore, the unit cell composition is M_4X_4 with an empirical formula of MX. However, the unit cell of a spinel structure is constructed by 8 of these *fcc* units.

29.746 g salt of **A** was mixed with 58.202 g salt of **B** in a thermal process to produce 24.724 g pure product, AB_2O_4. In the spinel formation process, the metal ion of salt A keeps its oxidation state but the metal ion **B** undergoes oxidation. Both salts contain the same number of the water

molecule(s), metal ion, and nitrate ion(s). Elemental analysis of the spinel provided the following data: 6.538 g metal A and 11.786 g metal B. Assume the end product is a diamagnetic solid matter. Considering the information provided above. Answer the following questions.

13.1. Suggest formulas for the salts of **A** and **B**.

13.2. Draw the structure of one of the complex ions i) without and ii) with one of the nitrates being in the coordination sphere as a bidentate ligand and **identify** if the inversion center is present in the complexes. Inversion is a symmetry operation that translates every atom through the center to the opposite side.

13.3. Place the metal ions in an appropriate location in the crystal structure and **suggest** if it is a normal or inverse spinel.

The x-ray diffraction data of AB_2O_4 provides a unit cell parameter of 8.085 Å, which is constructed from 8 *fcc* units and corresponds to a length of the edges of the cube.

13.4. Sketch one of the *fcc* units of AB_2O_4 and **place** the atoms in the unit.

13.5 What is the density of AB_2O_4? (hint: 1 Å is 1.0×10^{-10} m)

Reacting this spinel with other transition metals (M) produces M doped AB_2O_4, where M has a choice of occupying the place of either A or B-sides. The side product is **AO (mono-oxide of A)**.

13.6. M is Mn^{2+} in compound **C** and Ni^{2+} in compound **D**, **suggest** the location of Mn^{2+} and Ni^{2+} ions in the structure of **C** and **D**, respectively. Assume splitting energy in Ni^{2+} and B^{3+} are 11500 cm^{-1} and 20800 cm^{-1} in the octahedral field, respectively, and the pairing energy is 19500 cm^{-1}.

If the doping is in a small quantity or in some cases the doped metal ion behaves like a free ion in the lattice (it means, electrons of M only feel the surrounding atoms and localized to M and its 1 shell of atoms in the structure). Assume Mn^{2+} is behaving like a free ion in the lattice and creating its own localized electronic energy levels.

13.7. Draw the d-orbital splitting and identify if the Mn^{2+} species are paramagnetic or diamagnetic.

Magnetic susceptibility could be calculated from the spin only formula:

$$\mu(spin\ only) = (n(n+2)^{1/2},$$

where n is a number of unpaired electrons. However, some other electronic couplings affect the magnetic moment such that a correction term is needed. The correction term α is related to ground state (where α = 4 for a non-degenerate and 2 for a degenerate ground state, degeneracy of a ground state can be determined from the electron configurations, such as completely filled and half-filled set of orbitals creates a non-degenerate and a partially filled set of orbitals create degenerate states) and λ = 88 cm^{-1} for Mn^{2+} and -315 cm^{-1} for Ni^{2+}), and splitting energy (Δ is 5000 cm^{-1} for Mn^{2+} and 11500 cm^{-1} for Ni^{2+}) and the magnetic moment is:

$$\mu_{eff} = \mu(spin\ only)\left(1 - \frac{a\lambda}{\Delta}\right).$$

The magnetic susceptibility can be experimentally determined and it is interrelated with the magnetic moment (if we ignore the diamagnetic contributions) with the following formula:

$$\mu_{eff} = \sqrt{\frac{3kX_mT}{L\mu_0 x{\mu_B}^2}} = 0.7977\sqrt{X_mT} \text{ and } 1\mu_B = \frac{eh}{4\pi m_e} = 9.27\ \times 10^{-24}\ JT^{-1}$$

Where k = Boltzmann constant; L = Avogadro number; μ_0 = vacuum permeability; T = temperature in Kelvin and X_m(molar magnetic susceptibility)$is\ in\ cm^3\ mol^{-1}$.

13.8. **<u>What is</u>** the magnetic susceptibility of the products at 25 °C, if the samples C and D weigh 25.433 and 25.471 g, respectively (each obtained from 24.724 g AB_2O_4)?

13.9. **<u>Place</u>** all the metal ions (A, B, Mn^{2+}, and Ni^{2+}) into their appropriate locations in the lattice and **<u>fill up</u>** the following table. Use t_{2g} for d_{xy}, d_{xz}, and d_{yz} and e_g for d_{x2-y2}, d_{z2} orbitals in octahedral (O_h) and t_2 and e orbitals in tetrahedral (T_d) cases. If there is distortion, **<u>predict</u>** the type of distortion(s) and **<u>show</u>** the d-orbital splitting.

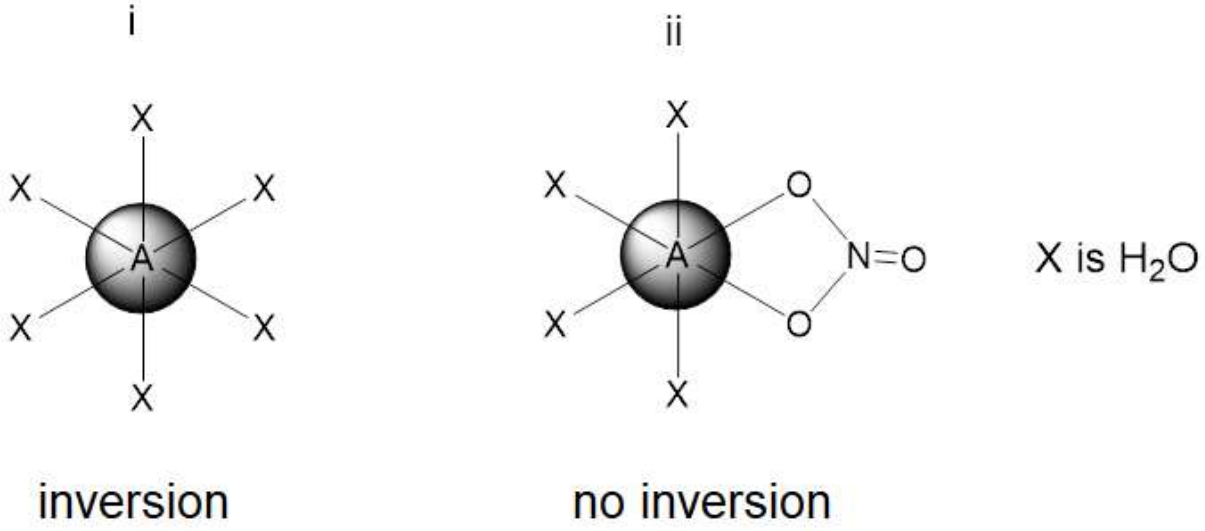
Hint: d_{xz}, d_{xy}, d_{yz} orbitals are represented by t_{2g} and t_2 in octahedral and tetrahedral geometries, respectively. Similarly, d_{x2-y2} and d_{z2} are represented as e_g and e in octahedral and tetrahedral geometries, respectively.

M	**Local geometry**	**Electron configuration**	**Degeneracy**	**Type of distortion**

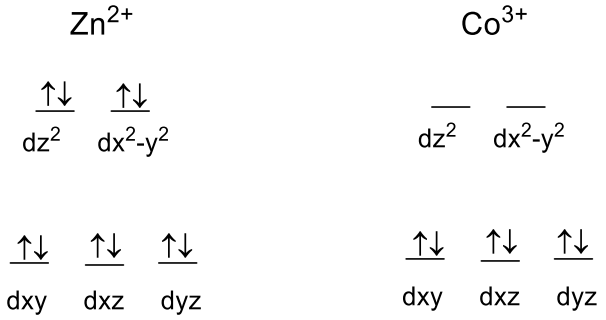
Solution:

13.1. Weight of AB_2O_4 is 24.724 g and 6.538 g **A** and 11.786 g **B** and remaining is oxygen
Amount of oxygen = 24.724 – 6.538 – 11.786 = 6.400 g
1 mol product has 64 g of oxygen (= 4 × 16); therefore, we have 0.1 mol AB_2O_4 product
1 mol salt **A** must be 29.746 × 10 = 297.46 g/mol
10 × 6.538 g is **A**
rest is water molecules and nitrate ions.
297.46 – 65.38 = 232.06 g = (n × MWt_{H2O}) + (2 × MWt_{NO3-}),
n = 6
The atomic weight of **A** is 65.38 g/mol; therefore, **A** is Zn and **B** is 58.93 g/mol and Co.
Formulas of the salts are: **$[Zn(H_2O)_6](NO_3)_2$** and **$[Co(H_2O)_6](NO_3)_2$**

13.2.

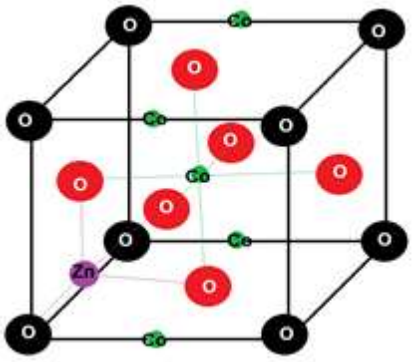


13.3. Zn is d^{10} no crystal field stabilization; therefore, Zn^{2+} is in tetrahedral and Co^{3+} ions are in octahedral holes. It is a normal spinel.



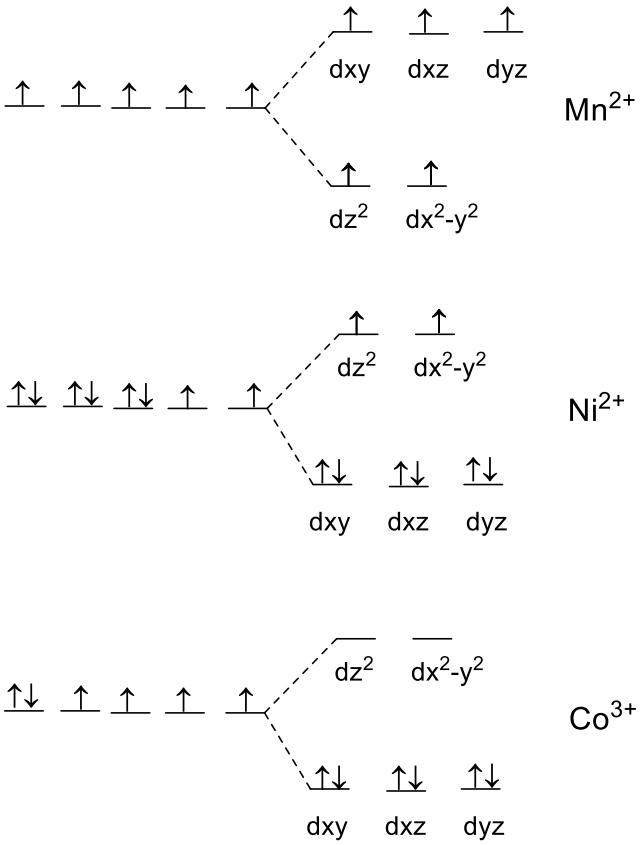
$CFSE = 0.0$ $CFSE = 6(-0.4\Delta) + 2PE = -2.4\Delta + 2PE$

13.4.



13.5. $Volume\ of\ the\ unit\ cell = (8.085A^{\circ})^3 = 528.5\ A^{\circ 3}$ but the volume of one unit (1/8 of the unit cell) is $V = (4.0425 \times 10^{-8}cm)^3 = 6.606 \times 10^{-23}cm^3$
$Weight\ of\ one\ unit = (247.54\ g/mol)/6.0221 \times 10^{23} = 4.1105 \times 10^{-22}\ g/unit$
$\boldsymbol{Density} = 4.1105 \times 10^{-22}g/6.606 \times 10^{-23}cm^3 = \mathbf{6.224\ g/cm^3}$

13.6.



$CFSE\ (Mn^{2+}) = 0.0$
$CFSE\ (Ni^{2+}) = 6 \times (-0.4\Delta) + 2(0.6\Delta) = -1.2\Delta\ for\ Ni^{2+} = -1.2 \times 11500$
$= -13{,}800 cm^{-1}$

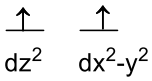
$CFSE\ (Co^{3+}) = 6 \times (-0.4\Delta) + 2PE = -2.4\Delta + 2PE\ for\ Co^{3+}$
$= -2.4 \times 20{,}800 + 2 \times 19{,}500 = -10{,}920 cm^{-1}$

Both Mn^{2+} and Ni^{2+} ions will replace Zn^{2+} ions (charge balance), but there will be an exchange between Ni^{2+} and Co^{3+}, because CFSE of Ni^{2+} is lower than that of Co^{3+}.

Therefore,
Mn^{2+} - tetrahedral site in $(Zn_{1-x}Mn_x)_{tet.}(Co_2)_{oct.}O_4$
Ni^{2+} - octahedral site in $(Zn_{1-x}Co_x)_{tet.}(Co_{2-x}Ni_x)_{oct.}O_4$

13.7.

Mn^{2+}



paramagnetic

13.8. n = 5 in Mn^{2+} and 2 in Ni^{2+} cases and α = 4 for both. Mn^{2+} electron configuration is $(d_{x2-y2}, d_{z2})^2 (d_{xy}, d_{xz}, d_{yz})^3$, a half-filled system and Ni^{2+} electron configuration is $(d_{xy}, d_{xz}, d_{yz})^6 (d_{x2-y2}, d_{z2})^2$), ground state is also nondegenerate.

$\mu_{eff} = \mu(spin\ only)(1 - a\,\lambda/\Delta) = (n(n+2))^{1/2}(1 - a\,\lambda/\Delta)$
$= (5(5+2)^{1/2}(1 - 4 \times 88/5000) = 5.500\ \mu B\ in\ Mn^{2+}$
$= (2(2+2)^{1/2}(1 - 4 \times (-315)/11{,}500) = 3.138\ \mu B\ in\ Ni^{2+}$

Weight increase:
$25.433 - 24.724 = 0.709\ g\ in\ Mn^{2+}(0.01\ mol\ MnO)$
$25.471 - 24.754 = 0.747\ g\ in\ Ni^{2+}(0.01\ mol\ NiO)$

Molar susceptibility:
$X_m = (5.500/0.7977)^2/298.15 = 0.159\ {}^{cm^3}/_{mol}\ for\ Mn^{2+}$

$X_m = (3.138/0.7977)^2/298.15 = 0.052\ {}^{cm^3}/_{mol}\ for\ Ni^{2+}$

Magnetic susceptibility of 0.01 mol doped samples:

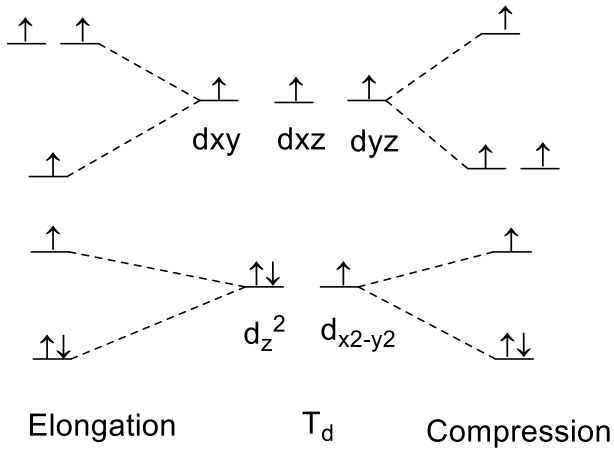
$\mathbf{1.59 \times 10^{-3}}\ cm^3\ \boldsymbol{for\ Mn^{2+}}$

$\mathbf{5.20 \times 10^{-4}} cm^3 \boldsymbol{for\ Ni^{2+}}$

13.9.

M	Local geometry	Electron configuration	Degeneracy	Type of distortion
Zn^{2+}	T_d	$(e)^4(t_2)^6$	non	no
Co^{3+}	O_h	$(t_{2g})^6$	non	no
Mn^{2+}	T_d	$(e)^2(t_2)^3$	non	no
Ni^{2+}	O_h	$(t_{2g})^6(e_g)^2$	non	no
Co^{3+}	T_d	$(e)^3(t_2)^3$	yes	yes

The Co^{3+} in tetrahedral side is high spin with an $(e)^3(t_2)^3$ electron configuration and subject to distortion.



Distortion on the bond angle is also possible, where the d-orbitals will split similar to elongation and compression cases.

Problem 14. Platinum Complexes as Anticancer Drugs

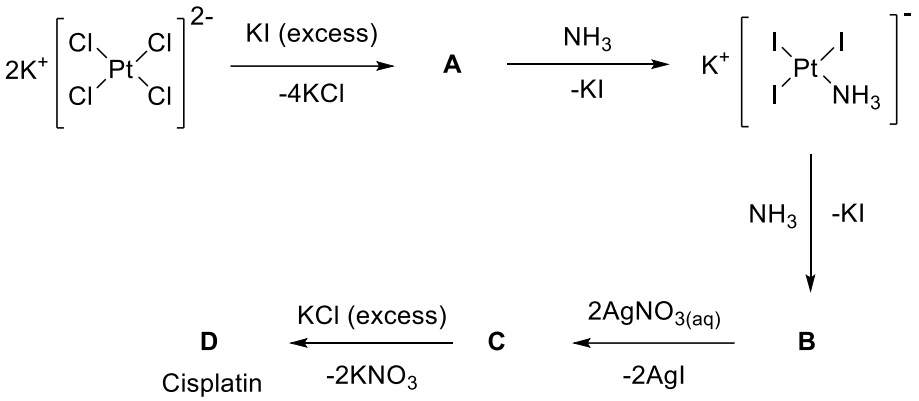
Medicinal inorganic chemistry based on metal-based drugs is broadly defined as the area of research related to metal ions and metal complexes and their clinical applications. It is a new research area that developed from the discovery of the anticancer agent cisplatin. Cisplatin, *cis*-diamminedichloroplatinum(II), is a yellow powder and an anticancer drug widely used in the treatment of a variety of tumors, especially those of the testes, ovaries, head, and neck.

The synthesis of cisplatin starts with $K_2[PtCl_4]$, but has undergone several improvements since it was published more than 100 years ago. The main problem is the occurrence of impurities and the formation of the by-product *trans*-platin. Nowadays, the synthetic routes are mostly based on a method published in the 1970s by Dhara. In the initial step, $K_2[PtCl_4]$ is reacted with excess KI, and the platinum complex is converted into the iodo analogue (**A**). Subsequently, NH_3 is added to the compound **A** and compound **B** is formed by ligand exchange in which two NH_3 ligands are exchanged with two iodo ligands. **B** is a yellow solid that is filtered, dried, and mixed with the aqueous solution of $AgNO_3$. The insoluble AgI can be filtered off and *cis*-diamminediaquaplatinum(II) nitrate (**C**) is formed; then excess KCl is added to the solution of **C** to yield cisplatin (**D**).

The success of the synthesis relies on the strong *trans* effect of the iodo ligands. The spectator ligands T that are *trans* to the leaving group in square-planar complexes influence the rate of substitution. This phenomenon is called the *trans* effect. Key point is that a strong σ-donor ligand or π-acceptor ligand greatly accelerates substitution of a ligand situating in the trans position. *Trans* effects follow the order given below.

For a T σ -donor: $OH^- < NH_3 < Cl^- < Br^- < CN^-, CH_3^- < I^- < \mathbf{S}CN^- < PR_3, H^-$

For a T π-acceptor: $Br^- < I^- < \mathbf{N}CS^- < NO_2^- < CN^- < CO, C_2H_4$



14.1. **Write** the formulas of **A**–**D**.

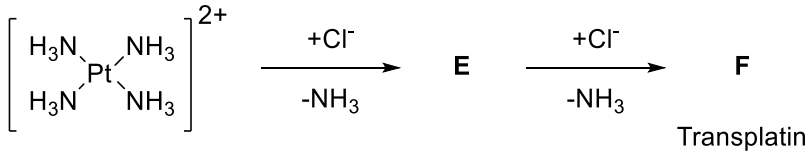
14.2. **Draw** molecular structures of **A**–**D**.

14.3. Is the complex **D** polar?

14.4. **Sketch** the d-orbital splitting of cisplatin complex **D** in view of Crystal Field Theory and show the electron distribution diagram.

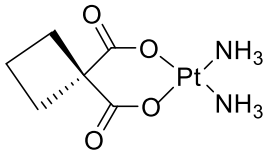
14.5. **Determine** magnetic nature of complex **A**.

The platinum complex binds to DNA and causes cross-linking, which triggers the programmed cell death (apoptosis). However, the other geometrical isomer of the square planar structure transplatin, *trans*-diamminedichloroplatinum(II) (**F**), is not effective for the treatment of cancer. Transplatin is synthesized starting from $[Pt(NH_3)_4]^{2+}$ to which the first and second Cl^- ligands are added to form transplatin (**F**) as represented in the scheme below.

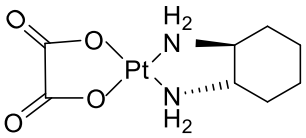


14.6. **Draw** the molecular structures of **E** and **F**.

The most important classes of antitumor agents, cisplatin, carboplatin, and oxaliplatin as platinum(II) diamines are widely used in chemotherapy to treat a wide variety of cancers.

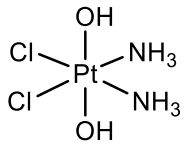


Carboplatin

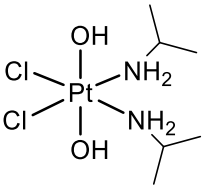


Oxaliplatin

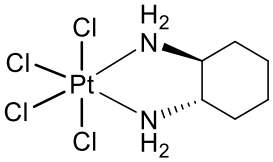
However, the therapeutic index of these agents is relatively narrow; their use is often plagued with severe toxicity and the development of resistance, which leads to disease progression. Recently, oxoplatin, iproplatin, ormaplatin and satraplatin are Pt complexes that have been used clinically (oxoplatin) or in clinical trials.



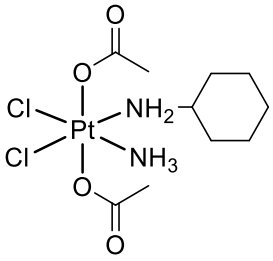
Oxoplatin



Iproplatin



Ormaplatin



Satraplatin

14.7. All complexes have the same geometry and oxidation number for the Pt central atom.

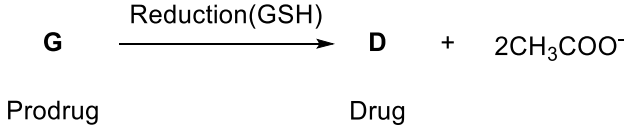
Write the oxidation state of Pt and geometry of the complexes.

14.8. Which Pt complex, cisplatin or satraplatin, is kinetically more inert for substitution reactions?

14.9 Oxaplatin is an isomer of $[Pt(NH_3)_2Cl_2(OH)_2]$ complex. **Draw** all stereoisomers and **indicate** the chiral one(s).

Platinum complexes (oxoplatin, iproplatin, ormaplatin, and satraplatin) can be considered prodrugs that are primarily intracellularly activated by biological reducing agents such as thiols, ascorbic acid, and glutathione (GSH) to kill cancer cells.

In a study, for example, the reduction of *cis,trans,cis*-$[PtCl_2(OCOCH_3)_2(NH_3)_2]$ (**G**, prodrug), which has a similar structure to satraplatin, by aqueous extract of cancer cells (A2780, A2780cisR, and HT-29) yields cisplatin (**D**, drug) and free acetate ion as given below.



14.10. **Draw** the molecular structure of **G**.

14.11. **Sketch** the d-orbital splitting of the metal ion in **G** and **write** the electronic configuration.

14.12. **Decide** whether **G** is paramagnetic or diamagnetic.

14.13. The complex **G** crystallizes into a monoclinic crystal system of parameters: the lengths of the unit cell: a = 14.9973, b = 8.57220, c = 11.1352 Å, the β angle in the unit cell = 126.7690°, the number of the molecules in the unit cell (Z) = 4, M = 436.16 g/mol (the complex has one water molecule in the crystal structure).

Calculate the density (ρ) of the complex.

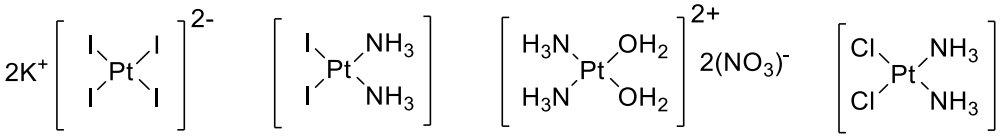
Hint: the volume of a monoclinic crystal unit cell is $V = a \times b \times c \times \sin\beta$

Solution:

14.1.

A	B	C	D
$K_2[PtI_4]$	*cis*-$[Pt(NH_3)_2I_2]$	*cis*-$[Pt(H_2O)_2(NH_3)_2](NO_3)_2$	*cis*-$[Pt(NH_3)_2Cl_2]$

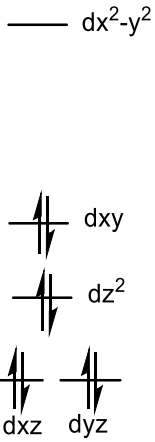
14.2.



A **B** **C** **D**

14.3. The complex **D** is polar.

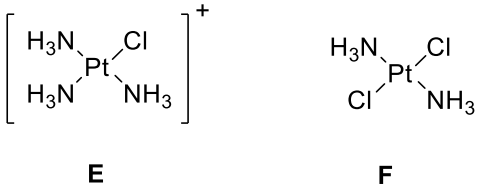
14.4. The complex has a square planar structure.



$\mathbf{Pt^{2+} = [Xe]4f^{14}5d^8}$

14.5. The complex has a diamagnetic nature.

14.6.



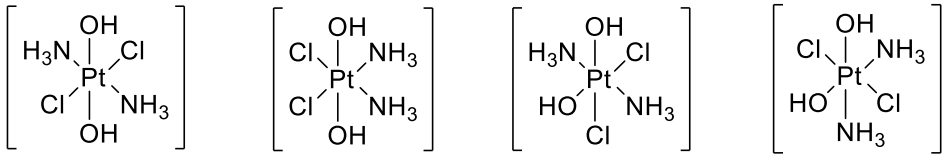
E **F**

14.7. The oxidation state of platinum: **4+**

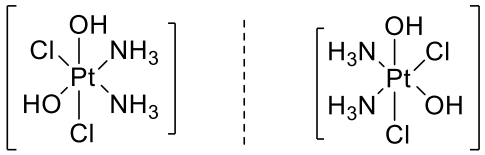
The geometry of the complexes: **octahedral**

14.8. Satraplatin, because it has octahedral geometry.

14.9.



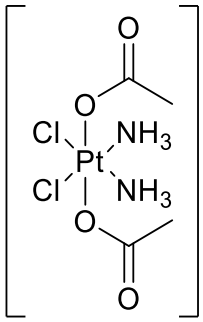
oxaplatin



enantiomers

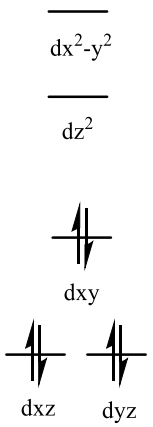
Chiral

14.10.



G

14.11. The complex has a distorted octahedral structure and low spin complex.



$\mathbf{Pt^{4+} = [Xe]4f^{14}5d^{6}}$

14.12. The complex having t_2g^6 electronic distribution has a diamagnetic nature.

14.13.

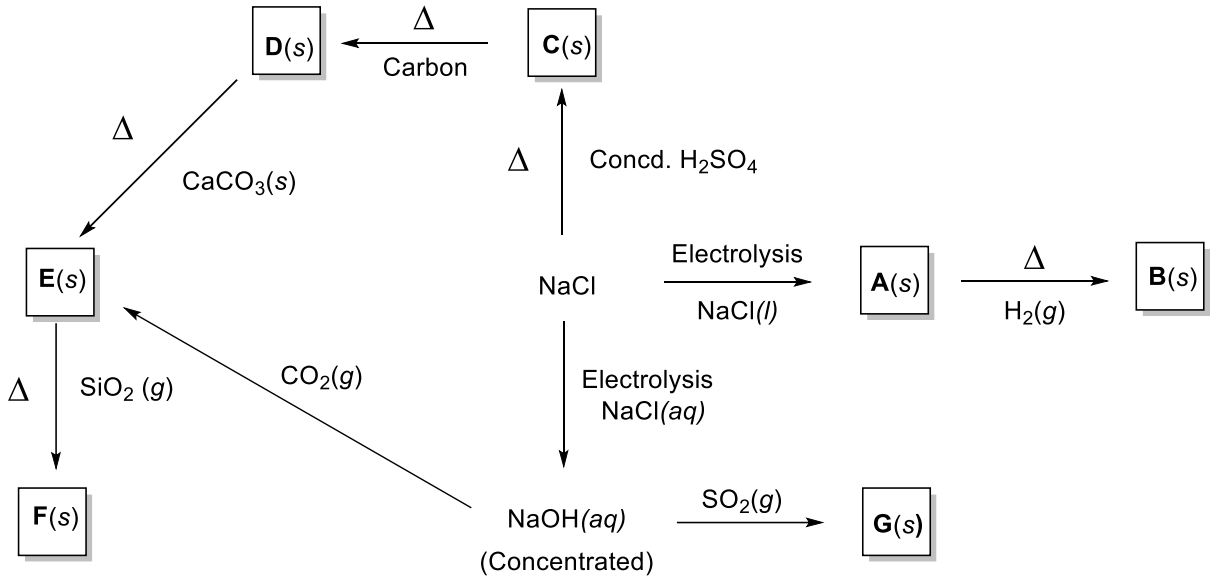
$V = a \times b \times c \times \sin\beta$
$V = 14.9973 \times 8.57220 \times 11.1352 \times \sin 126.7690^{o}$
$V = 1146.74\ Å^3$
$V = 1146.74\ Å^3 = 1146.74 \times 10^{-24} cm^3$
$p = Z \times M/N_A \times 1/V$
$= 4 \times 436.16\ g.mol^{-1}/6.0221 \times 10^{23}\ mol^{-1} \times 1/1146.74 \times 10^{-24} cm^3 = \mathbf{2.52\ g/cm^3}$

Problem 15. Sodium Compounds from Salt

The Salt Lake basin in Turkey is of great importance for the conservation of biological diversity and is classed as a wetland according to international criteria. It is also one of Turkey's richest lakes for the presence of birds. There are 85 bird species, 129 insect species (4 of which are endemic), 15 mammal species, and 38 endemic plant species. Some 40% of Turkey's salt needs (as table salt) are supplied from this lake. Salt in the Salt Lake is formed by meteorological waters draining underground and melting the previously formed salt domes and carrying them along the tectonic lines. Salt production in the Salt Lake is done by evaporation of lake water under the sun. A pooling system is used in the salt production with solar energy.

Salt Lake

Table salt is one of the most common household chemicals. It is 97% to 99% sodium chloride, which is an ionic compound with the chemical formula NaCl, representing a 1:1 ratio of sodium and chloride ions. NaCl is the compound most responsible for the salinity of seawater and of the extracellular fluid of many multicellular organisms. In its edible form of table salt, it is commonly used as a condiment and food preservative. A second major application of sodium chloride is de-icing of roadways in subfreezing weather. Large quantities of sodium chloride are also used in many industrial processes such as the chloro-alkaline industry and soda-ash industry as well as in miscellaneous industrial uses: water softening, medicine, agriculture, firefighting, and cleanser. NaCl is used, directly or indirectly, in the production of many sodium compounds, which consume most of the world's production. The scheme below shows the preparation of some sodium compounds starting from NaCl.



Preparation of some sodium compounds starting from NaCl.

15.1. **Write** the formulas of products **A**–**G**.

Sodium carbonate (Na_2CO_3, soda ash) is used primarily in the manufacture of glass, which is produced mostly from natural sources, such as the mineral trona, $Na_2CO_3{\cdot}NaHCO_3{\cdot}nH_2O$. It can be also manufactured mostly from NaCl, $CaCO_3$, and NH_3 using a process introduced by the Belgian chemist Ernest Solvay in 1863. The key step involves the reaction of NH_3(g) and CO_2(g) in saturated NaCl(aq). Of the possible ionic compounds that could precipitate from such a mixture (NaCl, NH_4Cl, $NaHCO_3$, and NH_4HCO_3), the least soluble is *sodium hydrogen carbonate* (sodium bicarbonate, $NaHCO_3$). It is isolated from solution by filtration and then converted to sodium carbonate (Na_2CO_3) by heating. According to this explanation,

15.2. **Balance** the reactions given below.

$$NaCl(aq) + CO_2(g) + NH_3(g) + H_2O(I) \rightarrow$$

$$2NaHCO_3(s) \xrightarrow{\Delta}$$

15.3. Using $CaCO_3$ (limestone), **how can you produce** the CO_2 gas you need to prepare $NaHCO_3$?

15.4. **Write** the Lewis structure of $CaCO_3$ with all resonances and **show** formal charges for each atom in the structure.

15.5. **Describe** the molecular geometry and **propose** a plausible hybridization scheme for the central atom in the ion CO_3^{2-}.

15.6. **Compare** the bond lengths of CO_3^{-2}, CO, and CO_2 in increasing order.

NaCl crystallizes in a face-centered cubic (fcc) structure. The density of NaCl is 2180 kg/m^3 and the ionic radius of Na^+ is 99 pm.

15.7. **How many** atoms are there in the unit cell? **Which atoms** occupy octahedral holes?

15.8. **Calculate** the length of the unit cell of NaCl and the ionic radius of the Cl^- ion (as pm).

15.9. The alkali metals react rapidly with oxygen to produce several different ionic oxides. Under appropriate conditions, generally by carefully controlling the supply of oxygen, the oxide M_2O can be prepared for each of the alkali metals. Lithium reacts with excess oxygen to give ……(**A**)…. and a small amount of ……(**B**)……. Sodium reacts with excess oxygen to give mostly ….**(C)**…… and a small amount of ……(**D**)……..Potassium, rubidium, and cesium react with excess oxygen to form …….(**E**)….., ……(**F**)….., and ……(**G**)…..

Fill in the blanks above (for **A**–**G**) with convenient formulas of metal oxides.

15.10. **Draw** the Lewis structures of oxide, peroxide, and superoxide ions.

15.11. **Draw** the molecule orbital energy level diagram of peroxide and superoxide ions and **compare** their bond lengths and energies.

When $LiClO_4$, $NaClO_4$, and $KClO_4$ crystallize from an aqueous solution that may or may not contain water molecules called water of crystallization as part of the solid structures, although no simple rule exists for predicting with certainty whether the ions will retain all or part of their hydration spheres in the solid state, cations with high charge densities tend to retain all or part of their hydration spheres in the solid state. When the cations have low charge densities, the cations tend to lose their hydration spheres; thus, they tend to form anhydrous salts. The ionic radius of Li^+, Na^+, and K^+ is 76 pm, 102 pm, and 138 pm, respectively.

15.12. **Calculate** the charge densities of the ions in C mm^{-3}.

15.13. **Which perchlorate salt** is most susceptible to form an anhydrous compound?

Solution:

15.1.

A	B	C	D	E	F	G
Na	NaH	Na_2SO_4	Na_2S	Na_2CO_3	Na_2SiO_3	Na_2SO_3

15.2.

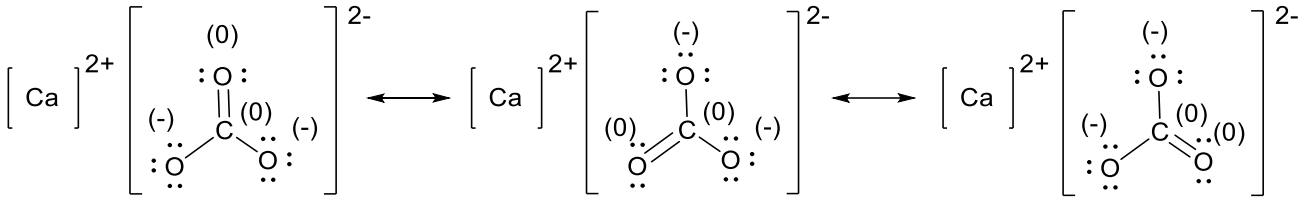
$$NaCl(aq) + CO_2(g) + NH_3(g) + H_2O(I) \rightarrow NaHCO_3(s) + NH_4Cl(aq)$$

$$2NaHCO_3(s) \xrightarrow{\Delta} Na_2CO_3(s) + H_2O(g) + CO_2(g)$$

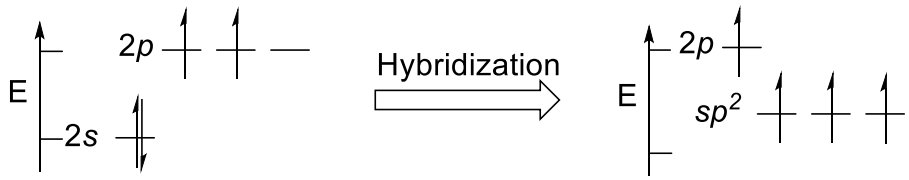
15.3.

$$CaCO_3(s) \xrightarrow{\Delta} CaO(s) + CO_2(g)$$

15.4.



15.5. Molecular geometry: trigonal planar



15.6. $CO < CO_2 < CO_3^{-2}$

15.7. 4 Cl^- atoms + 4 Na^+ atoms. Na^+ ions occupy octahedral hole.

15.8.

$$\rho = \frac{The\ mass\ of\ the\ unit\ cell\ (g)}{The\ volume\ of\ the\ unit\ cell\ (cm^3)} = \frac{m}{(I)^3}$$

$$(I)^3 = \frac{4\ atom\ NaCl \times \dfrac{58.44\ g/1\ mol\ NaCl}{6.0221 \times 10^{23} atom/1\ mol\ NaCl}}{2180\ kg \times \dfrac{1000\ g}{1\ kg}/1m^3 \times \dfrac{10^6 cm^3}{1m^3}}$$

$$I = 5.625 \times 10^{-8} cm = 5.625 \times 10^{-10} m = 562.5\ pm$$

$$2r(Cl^-) + 2r(Na^+) = 562.5\ pm$$

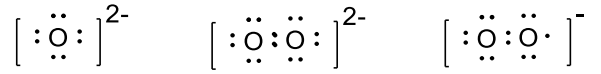
$$2r(Cl^-) + (2 \times 99) = 562.5$$

$$r(Cl^-) = 182.3\ pm$$

15.9.

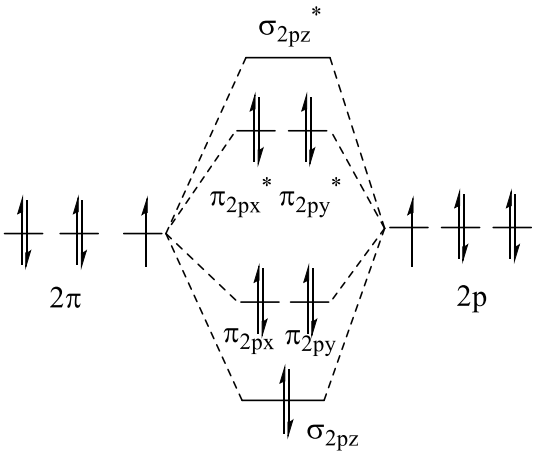
A	B	C	D	E	F	G
Li_2O	Li_2O_2	Na_2O_2	Na_2O	KO_2	RbO_2	CsO_2

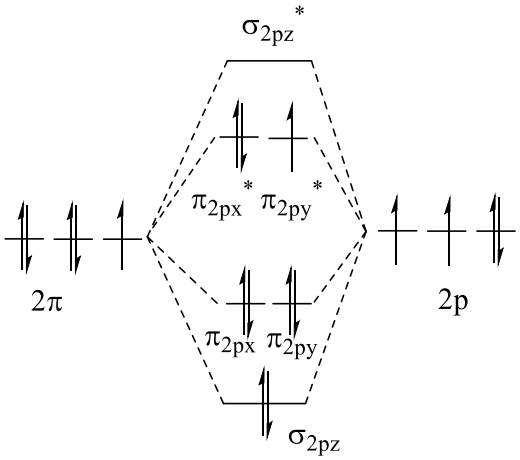
15.10.

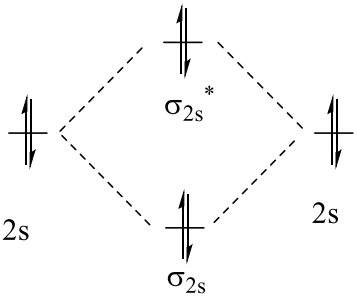


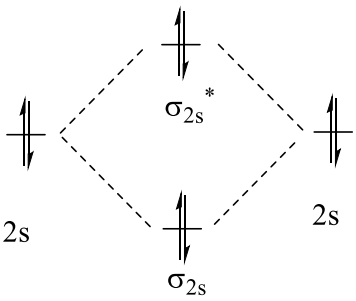
oxide ion peroxide ion superoxide ion

15.11.









O O

O_2^{2-} O_2^-

$Bond\ order = \frac{8-6}{2} = 1$ $Bond\ order = \frac{8-5}{2} = 1.5$

$Bond\ length\ of\ O_2^{2-} > bond\ length\ of\ O_2^-$

$Bond\ energy\ of\ O_2^- > bond\ energy\ of\ O_2^{2-}$

15.12.

$$\rho = \frac{(1.60 \times 10^{-19} C)(z)}{4/3\,\pi r^3}$$

$$\rho(Li^+) = \frac{(1.60 \times 10^{-19} C)(1)}{4/3\pi(76 \times 10^{-9} mm)^3} = 87\ C\ mm^{-3}$$

$$\rho(Na^+) = \frac{(1.60 \times 10^{-19} C)(1)}{4/3\pi(102 \times 10^{-9} mm)^3} = 36\ C\ mm^{-3}$$

$$\rho(K^+) = \frac{(1.60 \times 10^{-19} C)(1)}{4/3\pi(138 \times 10^{-9} mm)^3} = 15\ C\ mm^{-3}$$

15.13. $KClO_4$

Problem 16. Thermal Springs of Turkey and Sulfur Chemistry

Turkey is one of the 7 countries in the world in terms of thermal source richness with almost 1300 thermal springs throughout Anatolia. There are thermal hotels in many cities such as Ankara, Bursa, Balıkesir, Yalova, Erzurum, Sivas and Afyonkarahisar. Afyonkarahisar, located in the Aegean region, is the most famous city in Turkey for its thermal springs. The thermal waters of Afyonkarahisar contain over 42 different minerals and many trace elements. The most concentrated ones are sulfur, calcium, chloride, sodium, and carbonates. Among these minerals, sulfur is important as "nature's beauty mineral" because the human body needs it to manufacture collagen, which keeps human skin elastic, beautiful, and young looking. Moreover, sulfur is used to minimize the symptoms of many skin diseases including dermatitis, eczema, dandruff, and warts. People with arthritis may obtain pain relief from taking a soothing bath in thermal sulfur springs. Mineral water containing sulfur compounds is also shown to decrease cholesterol and blood pressure. Therefore, sulfur chemistry is an important topic. In this question, you will explore sulfur chemistry by studying its different reactions and compounds.

Hot spring

Sulfur is extracted as the element from underground deposits. It has many allotropes and its allotropy is complicated, but the most common sulfur allotrope is the puckered rings of S_8 (orthorhombic sulfur, α-form).

16.1. **Sketch** the molecular structure of S_8 and **indicate** whether the molecule has a horizontal mirror plane or not.

Upon the burning of S_8 with oxygen, compound **A** is produced. Further catalytic oxidation of compound **A** yields compound **B**. The reaction of **A** and **B** with water (hydrolysis) yields **C** and **D.** Compound **D** is an oxoacid and a central substance of the chemical industry worldwide.

16.2. Write the formulas of compounds **A**–**D**.

16.3. Draw molecular shape of the compounds by giving the name of geometries.

16.4. Write the oxidation state of the sulfur atoms in **C** and **D**.

16.5. Give balanced chemical equations for the synthesis of **A**–**D**.

Compound **A** can also be obtained by heating alkaline or alkaline earth sulfide minerals like CaS in an excess of air.

16.6. Write the balanced chemical equation for the synthesis of **A** from CaS.

Upon the reaction of **D** and **B**, compound **E** which is a dense and corrosive liquid that is used as a basic chemical for sulfonation processes is produced.

16.7. Give a balanced chemical equation for the synthesis of **E** from **D**.

16.8. Write molecular formula and **draw** the molecular shape of **E**.

16.9. Determine the oxidation state of the sulfur atoms in **E.**

The reaction of S_8 with a stoichiometric amount of chlorine gas yields compound **F** and the further reaction of **F** with excess chlorine gas results in the formation of **G**, which is used as a precursor for the synthesis of sulfur dyes and synthetic rubber. The reaction of **G** with **B** yields the compounds **H** and **A**. **H** is a toxic compound used as the chlorinating agent in organic synthesis.

16.10. Write molecular formulas and draw the molecular shapes of **F**, **G**, and **H**.

16.11. Give balanced chemical equations for the synthesis of compounds **F**, **G**, and **H**.

One of the most common naturally occurring sulfur minerals is pyrite (FeS_2: iron(II) disulfide), called fool's gold because it is a brass-yellow mineral and thus most people suppose that it is gold ore. The treatment of pyrite with hydrochloric acid results in the formation of a colorless, flammable, water-soluble gas with a "rotten egg" odor, compound **I**. Compound **I** is dissolved

in thermal waters for spa applications since it is reported that the therapeutic effects of thermal water are directly correlated to its sulfur concentration. Compound **I** is slightly heavier than air and can be detected by lead(II) acetate paper strip test in which a reaction occurs between lead(II) acetate and **I**, producing compound **J**. Moreover, upon the oxidation of **I**, compound **A** can be yielded.

16.12. Write the molecular formulas of **I** and **J**.

16.13. Draw the molecular shape of **I** and **write** the name of the shape.

16.14. Give balanced chemical equations for the synthesis of **I** and **J.**

The sulfur oxoacids are chemical compounds that contain sulfur, oxygen, and hydrogen atoms. Sulfur has several oxoacids; one of them is thiosulfuric acid, with the molecular formula $\mathbf{H_2S_2O_3}$, which can be synthesized by the reaction of sulfite with **I**. On the other hand, the controlled oxidation of sulfur trioxide by MnO_2 in acidic solution yields another sulfur oxoacid, called dithionic acid, $\mathbf{H_2S_2O_6}$.

16.15. Give balanced chemical equations for the synthesis of $H_2S_2O_3$ and $H_2S_2O_6$.

16.16. Draw the molecular shapes of $H_2S_2O_3$ and $H_2S_2O_6$.

On the other hand, the thiosulfate ion ($S_2O_3^{2-}$) is a very good complexing agent for Ag^+ and thus it is used in photography for removing unchanged AgBr from exposed photographic film. Upon the reaction of sodium thiosulfate ion with AgBr, sodium salt of a coordination compound with coordination number 2 is yielded.

16.17. Give a balanced chemical equation for the reaction of AgBr with $Na_2S_2O_3$.

16.18. Draw the molecular structure of the yielded coordination complex considering its geometry.

16.19. Write the electron configuration of the silver ion in the coordination compound.

The determination of H_2S content in thermal waters is important for spa applications. An iodometric titration method can be utilized for this purpose. In a typical experiment, 500 mL of sample is collected from a thermal water source and purged with $N_2(g)$ to ensure the transfer of all H_2S gas into 50 mL of 0.010 M NaOH solution in a closed system. After adjusting pH of the solution to 6.0, 12.5 mL of 0.300 M I_2 solution and 1.0 g of KI are added to this solution and the resultant solution is stored in the dark for 15 minutes after sealing it with parafilm. After

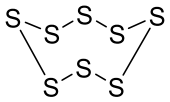
adding 1.0 mL of 20 mg/mL starch solution, the resultant solution is titrated with 0.0500 M $Na_2S_2O_3$ until the end-point and consumed $Na_2S_2O_3$ volume is recorded as 95.62 mL.

16.20. Write all balanced equations of this experiment.

16.21. Calculate H_2S concentration in the thermal water source in ppm by assuming that there is no interfering species in the water source and all H_2S content of thermal water is swept into the NaOH solution.

Solution:

16.1.



Horizontal mirror plane: NO

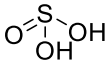
16.2.

A	B	C	D
SO_2	SO_3	H_2SO_3	H_2SO_4

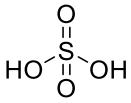
16.3.

Bent

Trigonal planar



Trigonal pyramidal



Tetrahedral

16.4.

C	D
S^{4+}	S^{6+}

16.5.

$^1/_8 S_8 + O_2 \rightarrow SO_2$ (***A***)

$SO_2 + {}^1/_2\, O_2 \rightarrow SO_3$ (***B***)

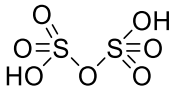
$SO_2 + H_2O \rightarrow H_2SO_3$ (***C***)

$SO_3 + H_2O \rightarrow H_2SO_4$ (***D***)

16.6. $CaS(s) + {}^3/_2\, O_2(g) \rightarrow SO_2(g) + CaO(s)$

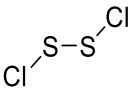
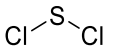
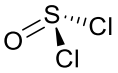
16.7. $H_2SO_4 + SO_3 \rightarrow H_2S_2O_7$ (***E***)

16.8. E = $H_2S_2O_7$



16.9. The oxidation state of sulfur atoms in **E** is 6+.

16.10.

F = S_2Cl_2	**G** = SCl_2	**H** = $SOCl_2$
	 angular	 trigonal pyramidal

16.11.

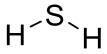
$S_8 + 4Cl_2 \rightarrow 4S_2Cl_2(\boldsymbol{F})$

$S_2Cl_2 + Cl_2 \rightarrow 2SCl_2(\boldsymbol{G})$

$SCl_2 + SO_3 \rightarrow SOCl_2(\boldsymbol{H}) + SO_2$

16.12. I = H_2S **; J** = PbS

16.13.


angular

16.14.

$FeS_2 + 2HCl \rightarrow H_2S(\boldsymbol{I}) + S + FeCl_2$

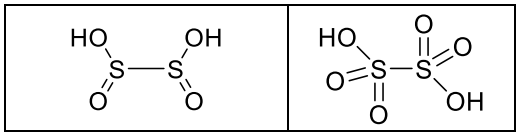
$Pb(CH_3COO)_2 + H_2S \rightarrow PbS\ (\boldsymbol{J}) + 2CH_3COOH$

16.15.

$SO_3 + H_2S \rightarrow H_2S_2O_3$

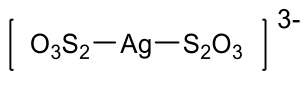
$MnO_2 + 2SO_3^{2-} + 4H^+ \rightarrow Mn^{2+} + S_2O_6^{2-} + 2H_2O$

16.16.



16.17. $AgBr + 2Na_2S_2O_3 \rightarrow Na_3[Ag(S_2O_3)_2] + NaBr$

16.18.



16.19.

$_{47}$Ag: [Kr]$5s^1 4d^{10}$

$_{47}Ag^+$: [Kr]$4d^{10}$

16.20.

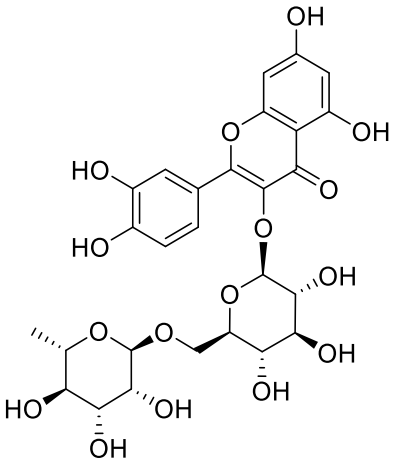
$H_2S + 2OH^- \rightarrow S^{2-} + 2H_2O$
$S^{2-} + H^+ \rightarrow HS^-$
$I_2 + I^- \rightarrow I_3^-$
$I_3^- + HS^- \rightarrow S^o + H^+ + 3I^-$
$I_3^- + 2S_2O_3^{2-} \rightarrow 3I^- + S_4O_6^{2-}$

16.21.

$$\left[\left(\frac{0.300\ mol\ I_2}{1\ L\ solution} \times 0.0125\ L\ solution \times \frac{1\ mol\ I_3^-}{1\ mol\ I_2}\right) - \left(\frac{0.0500\ \text{mol}\ S_2O_3^{2-}}{1\ L\ solution}\right.\right.$$
$$\left.\left. \times 0.09562\ L\ solution \times \frac{1\ mol\ I_3^-}{2\ \text{mol}\ S_2O_3^{2-}}\right)\right] \times \frac{1\ mol\ H_2S}{1\ mol\ I_3^-} \times \frac{34000\ mg}{1\ mol\ H_2S}$$
$$\times \frac{1}{0.5\ L\ sample\ solution} = 92.45\ ppm$$

Problem 17. Electrochemical Determination of Rutin

Flavonoids are a group of natural products with some phenolic groups that are present in many fruits and vegetables. Flavonoids are commonly used in our daily life due to their antioxidant and anticarcinogenic properties. Rutin is a flavonoid class substance composed of the flavonol quercetin and disaccharide rutinose.



Chemical structure of rutin.

It is of very low toxicity for human health and it is known that rutin can supply electrons to reactive free radicals to produce more stable and healthy structures. Rutin is also known as vitamin P, in which P is due to its *permeability*. Rutin is an electrochemically active material and many researchers have extensively studied its electrochemical behavior using different electrochemical techniques.

Cyclic voltammetry is a useful technique for electrochemical measurement of an analyte, which is dissolved in a useful electrolyte solution. There are three electrodes in an electrochemical cell solution; working, counter, and reference electrodes. The potential of working electrode is scanned versus reference electrode because reference electrode has a constant potential value. Reverse electrochemical reactions of the working electrode occur at the counter electrode. Therefore, current flows between working and counter electrodes. Reference electrode is used to adjust the potential of the working electrode at a known value. This technique is applied based on potentiodynamic application. Potential of the working electrode is scanned versus reference electrode between two potential values depending on time. Cyclic voltammetry application results in a graphic (voltammogram) of current versus scanned potential. There are two important parameters to evaluate a voltammogram; peak potential and peak current. The

peak potential and peak current are calculated using x-axis and y-axis of a voltammogram at the peak maximum, respectively.

The cyclic voltammetry (CV) behavior of rutin at 25 °C has been tested using a glassy carbon electrode, a saturated calomel electrode (SCE), and a Pt wire as working, reference, and counter electrodes, respectively. In this study, CV data for 1.0×10^{-4} mol/dm^3 rutin solutions at different pH values have been obtained by scanning the potential between 0.00 and 0.80 V at a scan rate of 100 mV/s. Anodic peak potential (Ep_a), cathodic peak potential (Ep_c), anodic peak current (Ip_a), and cathodic peak current (Ip_c) values supplied from related CVs depending on the pH are presented in the following Table.

Table. Some CV parameters depending on the pH of a solution containing 1.0×10^{-4} mol/ dm^3 rutin.

pH	Ep_a/mV	Ep_c/mV	Ip_a/μA	Ip_c/μA
1.5	643	614	0.105	–0.104
2.0	609	578	0.118	–0.119
3.0	544	514	0.116	–0.117
4.0	499	470	0.104	–0.104
5.0	441	410	0.093	–0.092
6.0	372	344	0.099	–0.100

17.1. In a three-electrode system, electrochemical oxidation or reduction of an analyte in the electrochemical cell occurs on the _____ because its potential is adjusted against the _____.

Which of the following words fit into the blanks in the above sentence?

a) working electrode / reference electrode
b) counter electrode / working electrode
c) reference electrode / working electrode
d) working electrode / counter electrode

17.2. Both anodic and cathodic peak potentials shift to negative potential values by increasing the pH because the electrochemical reaction of rutin includes _____.

Which of the following words fits into the blank in the above sentence?

a) Na^+
b) K^+

c) H^+
d) I^-

17.3. Electrochemical oxidation of rutin is _____ because of the fact that Ip_a/Ip_c is about 1 and ΔEp is almost 0.0592/n V.

Which of the following words fits into the blank in the above sentence?

a) irreversible
b) reversible
c) quasi-reversible
d) catalyzed

17.4. How long does it take to obtain each CV value?

17.5. **Calculate** the number of transferred electrons for the electrochemical reaction of rutin including 2 H^+.

17.6. **Propose** an electrochemical redox mechanism for rutin.

17.7. The SCE reaction is $Hg_2Cl_2(s) + 2e^- \rightarrow 2Hg(l) + 2Cl^-$ and the SCE contains saturated KCl solution prepared by dissolving 342 g of KCl in 1.0 L of aqueous solution. How does the potential of the SCE change (*decrease or increase*) in the case of 1.0 M KCl?

In order to determine the amount of rutin in a vitamin P tablet, the following procedures have been used:

i) A 500 mg vitamin P tablet is dissolved in deionized water, pH is adjusted to 2.0, and total volume is completed to 500 mL in a volumetric flask. A 10 mL part of this solution is placed in a three-electrode cell. CV is obtained with an anodic peak current (Ip_a) of 2.26 μA.

ii) A solution in the absence of rutin has been prepared at pH 2.0. After placing all electrodes into this solution, CV has been recorded three times by cleaning the electrode with deionized water for each measurement. Then Ip_a values have been read as 0.16, 0.11, and 0.18 μA, respectively.

iii) The standard rutin solutions of 1.0, 5.0, 10.0, 20.0, 30.0, and 50.0 mM have been prepared and Ip_a values of these solutions have been obtained from related CVs as demonstrated in the following Table.

Table. Ip_a values for various rutin standard solutions.

C_{rutin}/mM	Ip_a/μA
1.0	1.11
5.0	6.43
10.0	12.62
20.0	24.73
30.0	36.20
50.0	58.55

Note that all of the CVs have been obtained by using same working electrode beyond this experiment.

17.8. Draw a calibration curve for the rutin determination method.

17.9. Write a mathematical equation for the calibration curve.

17.10. Calculate the rutin amount in the vitamin P tablet as wt %.

17.11. Calculate the calibration sensitivity and limit of detection (LOD) of this method for a signal to noise ratio (S/N) of 3.0.

Note: Limit of detection: $LOD = \frac{k \times s_{blank}}{m}$

Solution:

17.1. a) working electrode / reference electrode

17.2. c) H^+

17.3. b) reversible

17.4. Because the totally scanned potential window is $0.80\,V - 0.00\,V = 0.80\,V \times 2 = 1.60\,V = 1600\,mV$ and the scan rate is $100\,mV/s$, the scanning time of each CV is calculated as $1600\,mV/100\,mV/s = 16\,s$.

17.5. Transferred electron number of the following possible electrochemical reaction of rutin can be found depending on the Nernst equation:

$$Rutin + 2H^+ + ne^- \rightarrow RutinH_2^{(2-n)}$$

$$E = E^o - \frac{0.0592}{n} log \frac{\left[RutinH_2^{(2-n)}\right]}{[Rutin][H^+]^2}$$

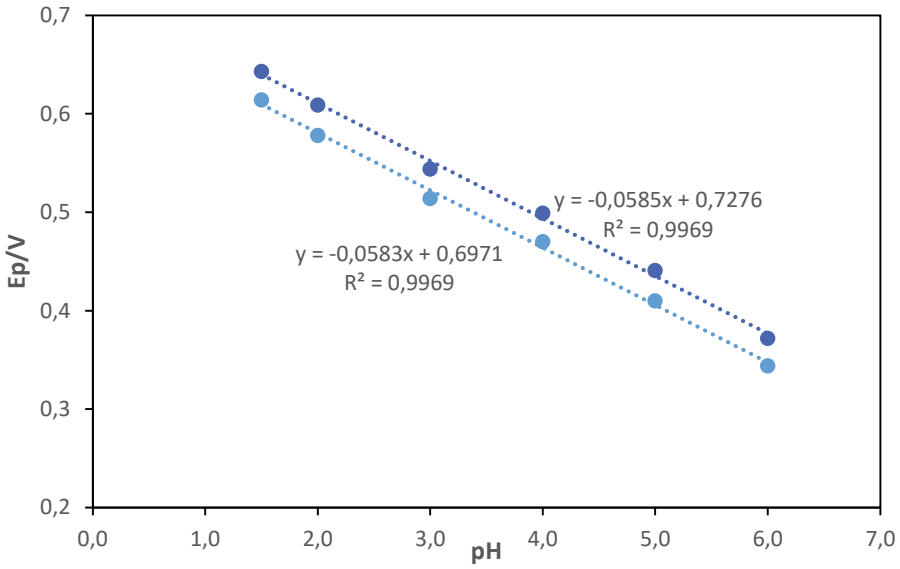
$$E = E^o - \frac{0.0592}{n}\left(log \frac{\left[RutinH_2^{(2-n)}\right]}{[Rutin]} + \log[H^+]^{-2} \right)$$

$$E = E^o - \frac{0.0592}{n} log \frac{\left[RutinH_2^{(2-n)}\right]}{[Rutin]} - \frac{0.0592}{n}\log[H^+]^{-2}$$

Because $\frac{\left[RutinH_2^{(2-n)}\right]}{[Rutin]}$ is constant, we can assume that

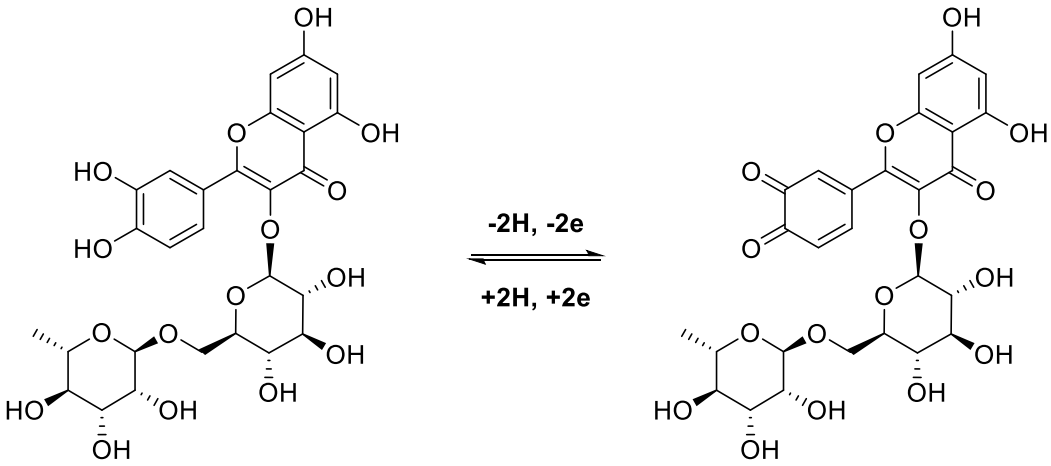
$E^o - \frac{0.0592}{n} log \frac{\left[RutinH_2^{(2-n)}\right]}{[Rutin]}$= a

$$E = a - \frac{0.0592 \times 2}{n}\text{pH}$$



When graphs are drawn for both p_a and Ep_c vs. pH, we obtain equations of $Ep_a(V) = -0.0585$ pH + 0.7276 and $Ep_c(V) = -0.0583$ pH + 0.6971, respectively. The slopes are 0.0585 and 0.0583. These values are very close to the theoretical value of $0.0592x2/n$ for the electron number of 2.

17.6.



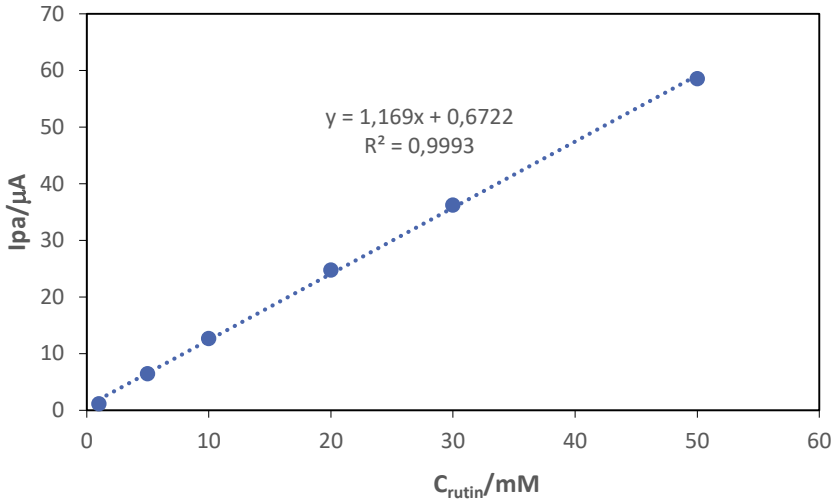
17.7. SCE reaction: $Hg_2Cl_2(s) + 2e^- \rightarrow 2Hg(l) + 2Cl^-$
The Nernst equation of this reaction at 25 °C is

$$E = E^o - \frac{0.0592}{2}\log[Cl^-]^2$$

$$[Cl^-] = \frac{\frac{342\ g}{74.5\ g/mol}}{1\ L\ solution} = 4.59\ M$$

Because potential of the SCE depends on the chloride concentration, its potential increases by decreasing Cl^- concentration. Therefore, its potential shifts to lower values (*decreases*), if the KCl concentration is changed from 4.59 M to 1.0 M KCl.

17.8.



17.9. $Ip_a(\mu A) = 1.169 C_{rutin}(mM) + 0.6722$

17.10. Ip_a of 10 mL sample is 2.26 μA.

$$2.26\ \mu A = 1.169 C_{rutin}(mM) + 0.6722$$
$$C_{rutin} = 1.36\ mM$$
$$\frac{1.36\ mmol\ rutin}{1\ L\ solution} \times 0.010\ L\ solution \times \frac{0.500\ L\ solution}{0.010\ L\ solution} \times \frac{610\ mg\ rutin}{1\ mmol\ rutin} \times \frac{100}{500\ mg\ vitamin\ P} = 82.96\%$$

17.11. The calibration sensitivity is the slope of this calibration graph (m): 1.169 µA/mM

$$LOD = \frac{k \times s_{blank}}{m}$$

where k is 3 for S/N of 3 and s_{blank} is the standard deviation of the signal of blank solution. There are three signals of blank solution: 0.16, 0.11, and 0.18 µA.

$\bar{x} = 0.15$

$$s = \sqrt{\frac{\sum_{x=1}^{N}(x_i - \bar{x})^2}{N-1}} = \sqrt{\frac{0.01^2 + 0.04^2 + 0.03^2}{2}} = 0.036\ \mu A$$

s_{blank} is 0.036

$$LOD = \frac{3 \times 0.036\ \mu\text{A}}{1.169\ \mu\text{A/mM}} = 0.09\ mM$$

Problem 18. Particle in a Box Problem: Free Electron Model

The particle in an one-dimensional box model is a crude approximation for conjugated molecules. In this model, π electrons are assumed to move freely over the carbon framework of conjugated bonds. Therefore, this model is also called the free electron model (FEM). The length of the box may be approximated via $L = n_C \times 1.40$ Å, where L is the box length and n_C is the number of carbons. Furthermore, the Pauli principle is applied when electrons are filled to the energy levels. The energy of a particle in an one-dimensional box can be written as follows:

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

where m is the mass of the particle, h is the Planck constant, and n is a positive integer.

For the 1,3,5,7-octatetraene molecule assuming FME:

18.1. **Draw** an energy diagram, fill the electrons, and calculate orbital energies.

18.2. **Calculate** the total π energy of the molecule.

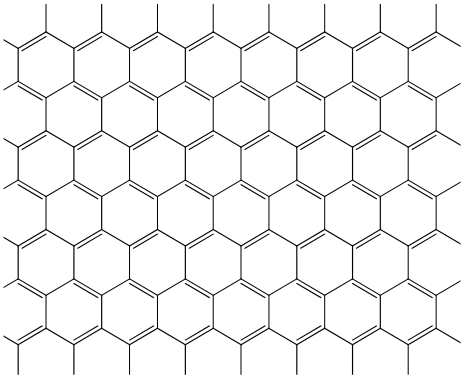
18.3. **Determine** the wave length of the light (in nm) that require to excite an electron from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO).

For two-dimensional conjugated systems, we may use the particle in a two-dimensional box model. In this case, the energy can be written as follows:

$$E_{n_1,n_2} = \frac{h^2}{8m}\left(\frac{n_1^2}{L_1^2} + \frac{n_2^2}{L_2^2}\right)$$

where L_1 and L_2 are the lengths and n_1 and n_2 are the quantum numbers of the first and second dimensions, respectively.

Graphene is a sheet of carbon atoms in the form of a two-dimensional hexagonal lattice in which one atom forms each vertex.



For a square shaped graphene sheet with $L_1 = L_2 = 11$ Å:

18.4. The distance between two adjacent carbons in the hexagonal 6-carbon unit is approximately 1.4 Å. **Calculate** the number of electrons in a (11 Å × 11 Å) sheet of graphene. For this problem you may ignore edge electrons. (Area of a regular hexagon with a side of *L* is $A = \frac{3\sqrt{3}}{2} L^2$).

18.5. Calculate the energy of the HOMO.

18.6. Calculate the energy of the LUMO.

18.7. The difference between energies of the LUMO and HOMO is called the band gap (E_g). **Calculate** the band gap.

The models for a particle in a one- and two-dimensional box can be extended to a three-dimensional rectangular box of dimensions L_1, L_2, and L_3, yielding the following expression for the allowed energy levels:

$$E_{n_1,n_2,n_3} = \frac{h^2}{8m}\left(\frac{n_1^2}{L_1^2} + \frac{n_2^2}{L_2^2} + \frac{n_3^2}{L_3^2}\right),$$

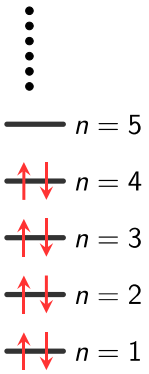
where n_1, n_2, and n_3 are the quantum numbers of the first, second, and third dimensions, respectively. For a particle in a cubic box of length L:

18.8. Give the expressions for the five different lowest energies.

18.9. Draw a diagram showing all the five energy levels. **Indicate** degeneracy of each level.

Solution:

18.1. The MO diagram:



$$E_1 = \frac{h^2}{8mL^2} = 4.8029 \times 10^{-20}\ J$$

$$E_2 = \frac{4h^2}{8mL^2} = 1.9211 \times 10^{-19}\ J$$

$$E_3 = \frac{9h^2}{8mL^2} = 4.3226 \times 10^{-19}\ J$$

$$E_4 = \frac{16h^2}{8mL^2} = 7.6846 \times 10^{-19}\ J$$

$$E_5 = \frac{25h^2}{8mL^2} = 1.2007 \times 10^{-18}\ J$$

18.2. $E_T = 2 * (E_1 + E_2 + E_3 + E_4) = 2.8817 \times 10^{-18}\ J$

18.3.

$$\lambda = \frac{hc}{(E_5 - E_4)} = 459.55\ nm$$

18.4. Area of a hexagon:

$$A_h = \frac{3\sqrt{3}}{2}\,(1.4\times 10^{-10})^2 = 5.0922\times 10^{-20}\,m^2$$

Number of hexagon units:

$$N_h = \frac{Total\ area}{area\ of\ a\ hexagon} = \frac{(11\times 10^{-10})^2}{5.0922\times 10^{-20}} = 23.762 \approx 24$$

Since each carbon atom in a graphene sheet is shared by 3 hexagonal units, each unit contains 6/3=2 carbon atoms contributing 2 π-electrons total. Therefore, the total number of electrons is 48.

18.5. Since there are 48 π-electrons, the state numbers for the HOMO and LUMO are 24 and 25, respectively. The corresponding quantum numbers are $n_H = (6,1)$ and $n_L = (6,2)$. Hence,

$$E_H = 1.8423\times 10^{-18}\,J$$

18.6. The energy of the LUMO: $E_L = 1.9916\times 10^{-18}\,J$

18.7. The band gap: $E_g = E_L - E_H = 1.4937\times 10^{-19}\,J$

18.8. For a cubic box the energy expression becomes:

$$E_{n_1,n_2,n_3} = \frac{h^2}{8mL^2}\,(n_1^2+n_2^2+n_3^2)$$

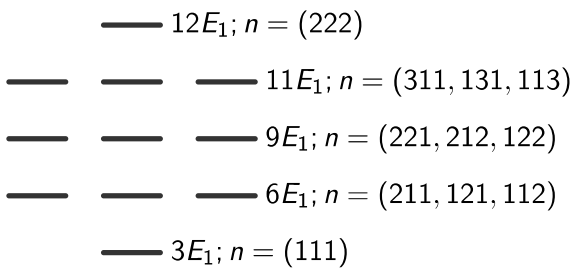
and let us define:

$$E_1 = \frac{h^2}{8mL^2}$$

Hence, the five lowest energies are corresponding to quantum number triplets of:

Level-1: (1,1,1)	$3E_1$
Level-2: (2,1,1); (1,2,1); (1,1,2)	$6E_1$
Level-3: (2,2,1); (2,1,2); (1,2,2)	$9E_1$
Level-4: (3,1,1); (1,3,1); (1,1,3)	$11E_1$
Level-5: (2,2,2)	$12E_1$

18.9.


12E1; n = (222)
11E1; n = (311, 131, 113)
9E1; n = (221, 212, 122)
6E1; n = (211, 121, 112)
3E1; n = (111)

Problem 19. Harmonic Oscillator and Rigid Rotor Models

Vibration of a diatomic molecule is reminiscent of two masses on a spring with a potential energy that is a function of the displacement from equilibrium. Hence, the harmonic oscillator model is utilized to compute vibrational frequencies. These frequencies are called harmonic vibrational frequencies. The energy of a harmonic oscillator can be written as follows:

$$E_n = h\,\nu\left(n + \frac{1}{2}\right)$$

where ν is the harmonic vibrational frequency, h is the Planck constant, and n is a nonnegative integer. The harmonic vibrational frequency can be calculated as follows:

$$\nu = \frac{1}{2\pi}\sqrt{\frac{k}{\mu}}$$

where k is the force constant and μ is the reduced mass:

$$\mu = \frac{m_1 m_2}{m_1 + m_2}$$

where m_1 and m_2 are the masses of the first and the second atoms, respectively.

For the $^{12}C^{16}O$ molecule the value of the force constant is 1902.4 N/m. For this problem, the atomic masses of isotopes can be approximated by their mass numbers.

19.1. **Calculate** the harmonic vibrational frequency of the $^{12}C^{16}O$ molecule in Hz.

19.2. **Express** the harmonic vibrational frequency of the $^{12}C^{16}O$ molecule in cm^{-1}.

19.3. **Calculate** the zero-point vibrational energy (ZPVE) of the $^{12}C^{16}O$ molecule in kcal/mol.

19.4. **Calculate** the harmonic vibrational frequency of the $^{13}C^{16}O$ molecule in cm^{-1}.

19.5. **Calculate** the harmonic vibrational frequency of the $^{12}C^{17}O$ molecule in cm^{-1}.

The harmonic oscillator model can readily be extended to polyatomic molecules. In this case, the total vibrational energy of a molecule with n_{freq} vibrational frequencies can be written as follows:

$$E_{n_1 n_2 \ldots n_{n_{freq}}} = h \sum_{i=1}^{n_{freq}} \nu_i \, (n_i + \frac{1}{2})$$

where ν_i are the harmonic vibrational frequencies, h is the Planck constant, and n_i are nonnegative integers.

For the water molecule the harmonic vibrational frequencies are 1649, 3832, and 3943 cm^{-1}. Using the harmonic oscillator model, for the water molecule:

19.6. <u>Calculate</u> the ZPVE value (in J and cm^{-1} units).

19.7. <u>Calculate</u> the first 5 energy levels (in cm^{-1}).

To describe the rotational motion of a diatomic molecule, the rigid rotor model is used. In this model the bond length (R) of the diatomic molecule is kept constant during the rotational motion. Using the rigid rotor model, the rotational energy of a diatomic molecule can be written as follows:

$$E_l = \frac{h^2}{8\,\pi^2 I}\; l(l+1)$$

where I is the moment of inertia and l is a nonnegative integer. The moment of inertia can be written as follows:

$$I = \mu\, R^2$$

where μ is the reduced mass and R is the bond length of the diatomic molecule.

In the microwave spectrum of the $^{12}C^{16}O$ molecule the value of frequency for the lowest energy transition is 115.270 GHz.

19.8. <u>Calculate</u> the bond length of the $^{12}C^{16}O$ molecule in Å.

19.9. For the $^{12}C^{16}O$ molecule **<u>predict</u>** the frequency of the next two absorptions (selection rule is $\Delta l = \pm 1$).

19.10. For the $^{12}C^{17}O$ molecule, **<u>calculate</u>** the frequency of the lowest energy absorption.

Solution:

19.1.

$$\mu = \frac{12 \times 16}{12 + 16} = 6.8571\ amu$$

$$\nu = \frac{1}{2\pi}\sqrt{\frac{k}{\mu}} = 6.5054 \times 10^{13}\ Hz$$

19.2.

$$\omega = \frac{\upsilon}{c} = 2170.0\ cm^{-1}$$

19.3.

$$E = \frac{1}{2}\ h\nu = 2.1553 \times 10^{-20}\ J$$

$$E = 3.1021\ kcal/mol$$

19.4.

$$\mu = \frac{13 \times 16}{13 + 16} = 7.1724\ amu$$

$$\nu = \frac{1}{2\pi}\sqrt{\frac{k}{\mu}} = 6.3608 \times 10^{13}\ Hz$$

$$\omega = \frac{\upsilon}{c} = 2121.8\ cm^{-1}$$

19.5.

$$\mu = \frac{12 \times 17}{12 + 17} = 7.0345\ amu$$

$$\nu = \frac{1}{2\pi}\sqrt{\frac{k}{\mu}} = 6.4229 \times 10^{13}\ Hz$$

$\omega = \frac{v}{c} = 2142.5\ cm^{-1}$

19.6. For a polyatomic molecule

$$E_{zpve} = \frac{1}{2}\ h \sum_{i=1}^{n_{freq}} \nu_i$$

Hence, $E_{zpve} = 9.3601 \times 10^{-20}\ J$; in cm^{-1} units $E_{zpve} = 4712\ cm^{-1}$

19.7. Vibrational energy of a polyatomic molecule can be rearranged to:

$$E_{n_1 n_2 \ldots n_{n_{freq}}} = E_{zpve} + h \sum_{i=1}^{n_{freq}} n_i\ \nu_i$$

Since ZPVE is a constant value, we may disregard it for a moment when expressing energy levels. Then for the water molecule we may write:

$E(n_1, n_2, n_3) = h\ (n_1\nu_1 + n_2\nu_2 + n_3\nu_3)$

Further, in cm^{-1} we may express the energy as follows:

$\tilde{E}(n_1, n_2, n_3) = (n_1\omega_1 + n_2\omega_2 + n_3\omega_3)$,

where ω_1, ω_2, and ω_3 are harmonic vibrational frequencies in cm^{-1}. Hence,

$\tilde{E}(n_1, n_2, n_3) = (1649\ n_1 + 3832\ n_2 + 3943\ n_3)$

Please note that the first energy level is always the ZPVE level. Hence,

Level-1: (0,0,0)	$E_1 = E_{zpve} = 4712\ cm^{-1}$
Level-2: (1,0,0)	$E_2 = E_{zpve} + 1649\ cm^{-1} = 6361\ cm^{-1}$
Level-3: (2,0,0)	$E_3 = E_{zpve} + 3298\ cm^{-1} = 8010\ cm^{-1}$
Level-4: (0,1,0)	$E_4 = E_{zpve} + 3832\ \text{cm}^{-1} = 8544\ cm^{-1}$
Level-5: (0,0,1)	$E_5 = E_{zpve} + 3943\ \text{cm}^{-1} = 8655\ cm^{-1}$

19.8. When the given equations are rearranged we obtain the following formula for bond length:

$$R = \frac{1}{2\pi}\left(\frac{h}{\mu\nu}\right)^{\frac{1}{2}}$$

$R = 1.1308$ Å

19.9. For the frequency of adjacent transitions, we can write:

$$\Delta E = E_{l+1} - E_l = \frac{h^2}{4\pi^2 I}(l+1) = h\nu$$

$$\nu = \frac{h}{4\pi^2 I}(l+1)$$

$$\nu_1 = 230.54\ GHz$$

and

$$\nu_2 = 345.81\ GHz$$

19.10. For isotopes, bond lengths are the same; hence $\nu = \frac{h}{4\pi^2 I} = 112.36\ GHz$

Problem 20. Journey to Different Earth-Like Planets

In the future, humankind will most likely consume all resources that are necessary for life on earth and will have to relocate to an earth-like planet. Assume that you have started to live on a new planet where standard pressure condition is 2 bar, standard concentration is 1 mol dm^{-3}, and all types of gases behave as an ideal gas. On this planet, you are asked to determine equilibrium conditions for the reaction below:

$$XY_4(g) \rightleftharpoons X(s) + 2Y_2(g)$$

$$\Delta_r S° = 80\ JK^{-1}mol^{-1} \text{ at } 298\ K$$

20.1. **Calculate** the change in standard enthalpy of the reaction at 298 K by using the following information:

$X_4Y_8(s) \rightarrow 4X(s) + 4Y_2(g)$	$\Delta_r H_1^\circ = 123.34\ kJ\ mol^{-1}$
$Y_2(g) + X_4Y_6(l) \rightarrow X_4Y_8(s)$	$\Delta_r H_2^\circ = -48.48\ kJ\ mol^{-1}$
$X_4Y_6(l) \rightarrow 2X_2Y_3(g)$	$\Delta_r H_3^\circ = 32.84\ kJ\ mol^{-1}$
$X_2Y_3(g) + {}^1/_2\, Y_2(g) \rightarrow X(s) + XY_4(g)$	$\Delta_r H_4^\circ = -53.84\ kJ\ mol^{-1}$

20.2. **Calculate** $\Delta_r G°$ of the reaction at 298 K.

20.3. **Calculate** K° of the reaction at 298 K.

20.4. Assume that $\Delta_r H°$ of the reaction does not depend on temperature. **Find** K of the reaction at 50 °C**.**

20.5. **Calculate** the percent degree of dissociation for XY_4 at 298 K where total pressure is 0.2 bar.

20.6. In order to increase the amounts of products, which one do you choose to **increase** (if you choose both, put a cross next to both of them):

☐	pressure
☐	temperature of the reaction vessel

Moreover, in this future, the Earth will have a very unstable climate. The surface temperature could increase or decrease all of a sudden. Suppose that you travelled through time to the era in which the Earth's climate is extremely unstable. Your task in this era is to observe the thermodynamics of phase transitions of water, the most precious substance where all life has originated. Suppose that the temperature suddenly decreased to −20 °C.

One mole of water becomes supercooled liquid water at −20 °C and 1 bar pressure and then turns into ice at the same temperature (note that the temperature of the surroundings is constant at −20 °C).

By using the following data for water:

The heat of fusion ($\Delta_m H°$) of ice at 0 °C and 1 bar is 6020 J mol^{-1}

$C_{p,m}(H_2O(s)) = 37.7 J\ mol^{-1}K^{-1}$
$C_{p,m}(H_2O(l)) = 75.3\ J\ mol^{-1}K^{-1}$

During the conversion of supercooled liquid water to ice at −20 °C:

20.7. **Calculate** the total entropy change in the system.

20.8. **Calculate** the total entropy change in the surroundings.

20.9. **Calculate** the total entropy change in the universe.

$\Delta S = C_p ln \frac{T_{final}}{T_{initial}}$ and $\Delta S = -\frac{q_{transition}}{T}$

Solution:

20.1. $2\Delta_rH° = \Delta H_1 + \Delta H_2 + (-\Delta H_3) + (-2\,\Delta H_4) = 149.70$ kj mol^{-1}. $\Delta_rH° =$ **74.85 kJ mol^{-1}**

20.2. $\Delta_rG° = \Delta_rH° - T\Delta_rS°$

$= 74850$ J/mol – (298K) × (80 J mol^{-1} K^{-1})

$\Delta_rG° =$ **5.10×10^4 J mol^{-1}**

20.3. $\Delta_rG° = -$ RTlnK

$K = e^{-\Delta_rG/RT}$

$K =$ **1.14×10^{-9}**

20.4.

$$ln\frac{K_f}{K_i} = -\frac{\Delta_rH}{R}\left(\frac{1}{T_f} - \frac{1}{T_i}\right)$$

K at 50 °C = **1.20×10^{-8}**

20.5. $XY_4(g) \rightleftharpoons X(s) + 2Y_2(g)$

	XY_4 (g)	X (s)	Y_2 (g)
Initial amount	n	–	–
Amount of change	−αn		2αn
Final amount	n − αn = n (1−α)		2αn
Mole Fraction	$\frac{1-\alpha}{1+\alpha}$		$\frac{2\alpha}{1+\alpha}$
Partial Pressures	$\frac{1-\alpha}{1+\alpha}P_{Total}$		$\frac{2\alpha}{1+\alpha}P_{Total}$

$$K = \frac{(P(Y_2)/P°)^2}{(P(XY_4)/P°)} = \frac{4\alpha^2}{1-\alpha^2} \times \frac{P}{P°}$$

$1 - \alpha^2 = 1$ ($\alpha << 1$)

$1.14\times10^{-9} = 4\alpha^2\times0.1$

$\alpha = 5.35 \times 10^{-5}$, percent degree of dissociation $(\alpha\%) = \mathbf{5.35 \times 10^{-3}\%}$

20.6. As the temperature increases, the degree of dissociation increases. As the pressure increases, the degree of dissociation decreases.

20.7. Supercooled water at −20 °C (1) → Water at 0 °C (2) → Ice at 0 °C (3) → Ice at −20 °C

$\Delta S_1 = \int_{T_i}^{T_f} \frac{dq_{reversible}}{T} = \int_{T_i}^{T_f} \frac{C_{p,m}dT}{T} = \int_{253.15}^{273.15} \frac{75.3\ dT}{T} = 75.3ln\frac{273.15}{253.15} = 5.73\ \text{J}\ mol^{-1}K^{-1} =$

$\Delta S_2 = -\frac{q_{freezing}}{T} = -\frac{6020}{273.15} = -22.04\ \text{J}\ mol^{-1}K^{-1}$

$\Delta S_3 = \int_{T_i}^{T_f} \frac{dq_{reversible}}{T} = \int_{T_i}^{T_f} \frac{C_{p,m}dT}{T} = \int_{273.15}^{253.15} \frac{37.7\ dT}{T} = 37.7ln\frac{253.15}{273.15} = -2.87\ \text{J}\ mol^{-1}K^{-1}$

$\Delta_{sys}S = \Delta S_1 + \Delta S_2 + \Delta S_3 = \mathbf{-19.18\ J\ mol^{-1}\ K^{-1}}$

20.8. The total change in entropy in the surroundings should be found by total heat given off to the surroundings

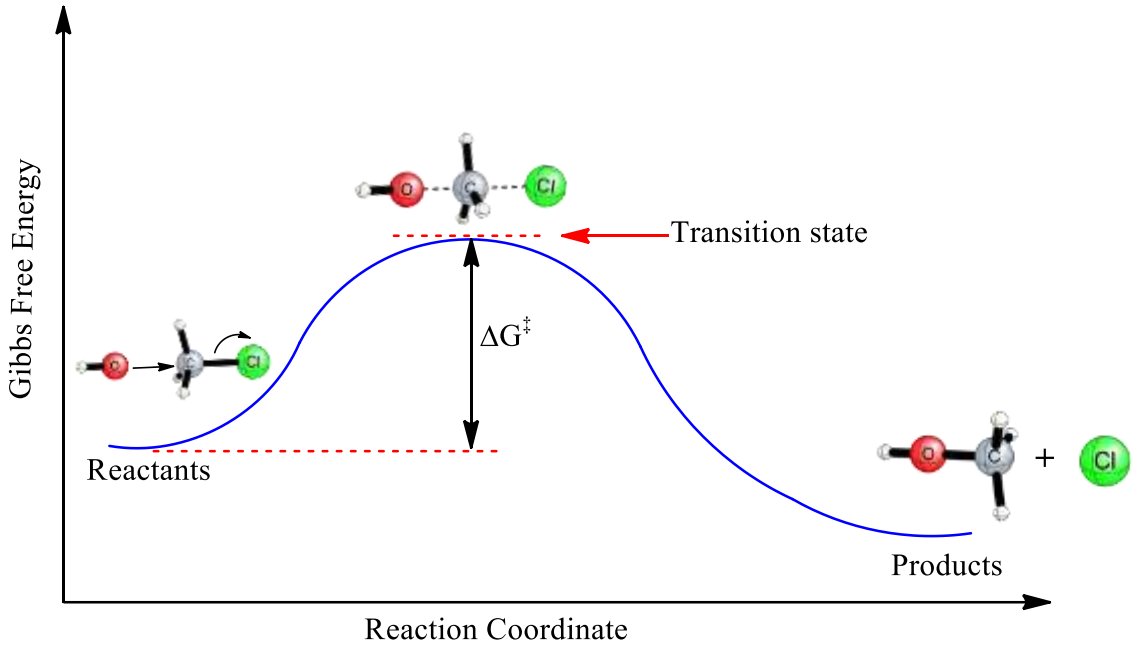
$q = -(20\text{K} \times 75.3\ \text{J mol}^{-1}\ \text{K}^{-1}) + 6020\ \text{J mol}^{-1} + (20\ \text{K} \times 37.7\ \text{J mol}^{-1}\ \text{K}^{-1}) = 5268\ \text{J mol}^{-1}$

$\Delta_{sur}S\ \frac{q_{sur}}{T} = \frac{5268}{253.15} = \mathbf{20.81\ J\ mol^{-1}\ K^{-1}}$

20.9. $\Delta_{universe}S = \Delta_{sys}S + \Delta_{sur}S = \mathbf{1.63\ J\ mol^{-1}\ K^{-1}}$

Problem 21. Rate Constant Models and Kinetic Isotope Effect

Transition state theory (TST) is a very helpful model to explain the reaction rates of elementary chemical reactions. The TST assumes a quasi-equilibrium between reactants and transition state.



Reaction: $HO^- + CH_3Cl \longrightarrow [HO\text{----}CH_3\text{----}Cl]^{\ddagger} \longrightarrow CH_3OH + Cl^-$

Similar to the Arrhenius model, the TST proposes the following temperature-dependent rate constant expression:

$$k_{TST} = \frac{k_B T}{h} \exp\left[-\frac{\Delta G^{\ddagger}}{RT}\right]$$

where, k_B is the Boltzmann constant, h is the Planck constant, and $\Delta G^{\ddagger}$ is the activation free energy.

The TST rate constant introduces a simple temperature-dependent factor instead of Arrhenius factor A. Further, the TST model allows us to better understand the activation energy concept and build a bridge between the theory and experiment. Moreover, the TST activation free energy is a temperature dependent parameter instead of Arrhenius temperature independent E_a.

For the decomposition of an organic compound obeying first-order reaction kinetics, the following rate constant values are obtained at given temperatures:

t (°C)	10	30	50	70
k/10^{-4} (s^{-1})	1.1408	17.2075	185.5042	1515.7157

21.1. Using the Arrhenius model, **calculate** the activation energy.

21.2. Calculate the Arrhenius factor A.

21.3. Calculate the half-life of the organic compound at 75 °C.

21.4. Assume that the rate constants provided obey the TST model, instead of the Arrhenius model. Then, **calculate** activation free energy at 30 °C.

21.5. Assume that the rate constant obtained from both Arrhenius and TST models are equal to each other. Then, **derive** expressions for activation enthalpy and entropy in terms of the activation energy and the Arrhenius factor. It is assumed that entropy is constant.

21.6. Using the expressions obtained, **calculate** the activation enthalpy at 80 °C.

The kinetic isotope effect (KIE) is the change in the reaction rate of a chemical reaction when one of the atoms in the reactants, generally hydrogen, is replaced by one of its isotopes, generally deuterium. KIE is generally utilized in organic chemistry in a procedure called as "deuterium labelling" by changing one or more hydrogen(s) with deuterium(s).

In one of the common theoretical approaches to explain KIE, it is assumed that the change in reaction rate is a quantum chemical effect that primarily results from heavier isotopes having lower vibrational frequencies compared to their lighter counterparts. Hence, one may assume that the TST model is valid, and the change in the activation free energy arises solely from the change in the zero-point vibrational energies (ZPVEs). Therefore, we may write the following equation:

$$\frac{k_H}{k_D} = \frac{\exp[(ZPVE(R,H) - ZPVE(TS,H))/RT]}{\exp[(ZPVE(R,D) - ZPVE(TS,D))/RT]}$$

where k_H and k_D are the rate constants of reactions including hydrogen and deuterium, respectively, $ZPVE(R,H)$ and $ZPVE(R,D)$ are the ZPVE values of the reactants including hydrogen and deuterium, respectively, and $ZPVE(TS,H)$ and $ZPVE(TS,D)$ are the ZPVE values of TSs including hydrogen and deuterium, respectively.

For a thermal decomposition of an organic compound, the difference between ZPVE values of deuterium including TS (TS-D) and hydrogen including TS (TS-H) is -2.3 kJ/mol. Further, the ZPVE value of hydrogen including reactant (R-H) is 3.0 kJ/mol higher than that of deuterium including reactant (R-D).

21.7. **Calculate** the $\frac{k_H}{k_D}$ value at 298.15 K.

21.8. **Calculate** the $\frac{k_H}{k_D}$ value at 330.0 K.

21.9. If the rate constant k_H is 2.5×10^2 and k_D is 2.0×10^2 , then what is the temperature?

Solution:

21.1. From the slope of $lnk - 1/T$ plot: $E_a = 96.83$ kJ/mol.

21.2. From the intercept of $lnk - 1/T$ plot: $= 8.33 \times 10^{13}$.

21.3. From the $lnk - 1/T$ plot we obtain

$$\ln k = -\frac{11646.4569}{T} + 32.0531$$

From this equation,

$k(348.15\ K) = 0.2468$, hence $t_{1/2} = 2.81$s.

21.4. From the TST rate constant expression:

$$\frac{\Delta G^{\ddagger}}{RT} = ln\left(\frac{k_B T}{h}\right) - lnk$$

Hence, $\Delta G^{\ddagger}(303.15\ K) = 90.33$ kJ/mol.

21.5.

$$\frac{k_B T}{h} \exp\left[-\frac{\Delta G^{\ddagger}}{RT}\right] = A \exp\left[-\frac{E_a}{RT}\right]$$

$$ln\left(\frac{k_B}{h}\right) + lnT - \frac{\Delta G^{\ddagger}}{RT} = lnA - \frac{E_a}{RT}$$

$$ln\left(\frac{k_B}{h}\right) + lnT - \frac{\Delta H^{\ddagger}}{RT} + \frac{\Delta S^{\ddagger}}{R} = lnA - \frac{E_a}{RT}$$

Then, the temperature including and non-including terms should be equal to each other:

$$lnT - \frac{\Delta H^{\ddagger}}{RT} = -\frac{E_a}{RT}$$

and,

$$ln\left(\frac{k_B}{h}\right) + \frac{\Delta S^{\ddagger}}{R} = lnA$$

Hence:

$$\Delta H^{\ddagger} = E_a + RT\ lnT$$

$$\Delta S^{\ddagger} = R\ lnA - R\ ln\left(\frac{k_B}{h}\right)$$

21.6. $\Delta H^{\ddagger} =$ 114.06 kJ/mol.

21.7.

$$\frac{k_H}{k_D} = \exp\left(\frac{700}{298.15R}\right) = 1.33$$

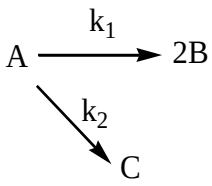
21.8.

$$\frac{k_H}{k_D} = \exp\left(\frac{700}{330\ R}\right) = 1.29$$

21.9. From the given equation $T =$ 377.29 K.

Problem 22. Parallel Reaction Kinetics

The reaction in which a reactant undergoes two or more independent reactions concurrently is called a parallel or competing reaction. Dehydration of ethanol, nitration of phenol, and nitration of benzene are examples of parallel reactions. The reaction given below is an example of a parallel first-order reaction.



22.1. For the parallel first-order reactions of **A** given above, **<u>find</u>** the concentrations of **B** and **C** as an equation depending on initial **A** concentration at time *t* after the start of the reaction. **<u>Find</u>** the ratio of **B** concentration to **C** concentration.

$$Hint: \int e^{ax}\,dx = \frac{1}{a}\,e^{ax} + c$$

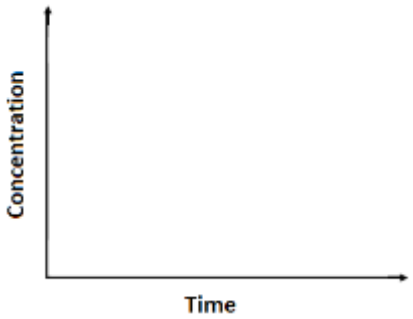
22.2. The effective rate constant (k_{eff}) for the decomposition of **A** can be defined as (k_1+k_2). Assume that the effective rate constant satisfies the Arrhenius equation. **<u>Write</u>** the expression for the effective activation energy ($E_{A,eff}$) in terms of k_1, k_2, $E_{a,1}$, and $E_{a,2}$ and **<u>estimate</u>** the $E_{A,eff}$ for the given values (k_1=6.2 min^{-1}, k_2=3.2 min^{-1}, $E_{a,1}$=35 kJ mol^{-1}, and $E_{a,2}$=60 kJ mol^{-1}).

$$Hint: \frac{d}{dx}\,e^{ax} = a.e^{ax}$$

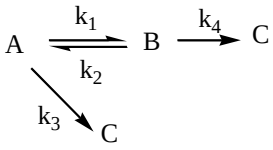
<u>Calculate</u> the half-life for the effective rate constant ($t_{1/2}\,(eff)$).

22.3. If k_1 and k_2 values of the given parallel first-order reactions of **A** are 6.2 and 3.2 min^{-1}, respectively, at 278 K, **<u>find</u>** the temperature for the production of equimolar concentrations of **B** and **C**. (E_a energies for the formation of **B** and **C** are 35 and 60 kJ mol^{-1}, respectively).

22.4. **<u>Draw</u>** symbolic concentration change curves for [A], [B], and [C] if $k_1 > k_2$.



22.5. The reaction given below is an example of parallel-consecutive first-order reactions with a reversible step.



The following data are given for this reaction:

k_1 = 0.109 min^{-1}, k_2 =0.0752 min^{-1}, k_3 = 0.0351 min^{-1}, k_4 =0.0310 min^{-1}.

Time (min)	$\theta_{A,t}$ (min)	$\theta_{B,t}$ (min)
12.9	6.89	3.79

$$\theta_{A,t} = \int_0^t \frac{[A]}{[A]_0} dt \qquad \theta_{B,t} = \int_0^t \frac{[B]}{[A]_0} dt$$

Find the [A], [B], [C] concentrations after 12.9 minutes if $[A]_0$= 5 mol dm^{-3}.

Solution:

22.1.

$$-\frac{d[\mathrm{A}]}{dt} = k_1[\mathrm{A}] + k_2[A]$$

$$-\frac{d[\mathrm{A}]}{dt} = (k_1 + k_2)[A]$$

$$[A] = [A]_0\, e^{-(k_1+k_2)t}$$

$$\frac{d[B]}{dt} = 2k_1[A] = 2k_1[A]_0\, e^{-(k_1+k_2)t}$$

$$[B] = \frac{2k_1[\mathrm{A}]_0}{(k_1+k_2)}\left[1 - e^{-(k_1+k_2)t}\right]$$

$$\frac{d[C]}{dt} = k_2[\mathrm{A}] = k_2[A]_0\, e^{-(k_1+k_2)t}$$

$$[C] = \frac{k_2[A]_0}{(k_1+k_2)}\left[1 - e^{-(k_1+k_2)t}\right]$$

$$\frac{[B]}{[C]} = \frac{2k_1}{k_2}$$

22.2. $k_{eff} = k_1 + k_2$

$$A_{eff}.e^{-\frac{E_{a,eff}}{RT}} = A_1.e^{-\frac{E_{a,1}}{RT}} + A_2.e^{-\frac{E_{a,2}}{RT}}$$

Differentiate the equation

$$A_{eff}.e^{-\frac{E_{a,eff}}{RT}}\left(\frac{E_{a,eff}}{RT^2}\right) = A_1.e^{-\frac{E_{a,1}}{RT}}\left(\frac{E_{a,1}}{RT^2}\right) + A_2.e^{-\frac{E_{a,2}}{RT}}\left(\frac{E_{a,2}}{RT^2}\right)$$

$$k_{eff}.E_{a,eff} = k_1E_{a,1} + k_2E_{a,2}$$

$$E_{a,eff} = \frac{k_1 E_{a,1} + k_2 E_{a,2}}{k_1 + k_2}$$

$$E_{a,eff} = 43.5 \ kJmol^{-1}$$

$$t_{1/2(eff)} = 0.074 \ min$$

22.3.

Equation (1): $\ln \frac{k_1'}{k_1} = \frac{E_{a,1}}{R}\left[\frac{1}{T_1} - \frac{1}{T_2}\right]$

Equation (2): $\ln \frac{k_2'}{k_2} = \frac{E_{a,2}}{R}\left[\frac{1}{T_1} - \frac{1}{T_2}\right]$

Equation (2) - Equation (1)

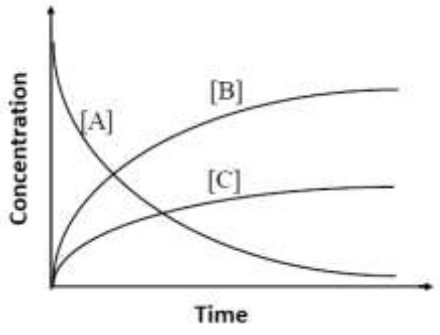
$$\ln \frac{k_2'}{k_2} - \ln \frac{k_1'}{k_1} = \left[\frac{E_{a,2} - E_{a,1}}{R}\right]\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

$$\ln \frac{k_1}{k_2} - \ln \frac{1}{2} = \left[\frac{E_{a,2} - E_{a,1}}{R}\right]\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

For equimolar production of B and C, $k_2' = 2k_1'$

$T_2 = 317.8 \ K$

22.4.



22.5.

$$-\frac{d[A]}{dt} = (k_1 + k_3)[A] - k_2[B]$$

$$\frac{d[B]}{dt} = (k_1)[A] - (k_2 + k_4)[B]$$

$$\frac{d[C]}{dt} = (k_3)[A] + (k_4)[B]$$

$$-\int_{[A]_0}^{[A]} d[A] = (k_1 + k_3)\int_0^t [A]\,dt - k_2\int_0^t [B]dt$$

$$\int_{[B]_0}^{[B]} d[B] = (k_1)\int_0^t [A]\,dt - (k_2 + k_4)\int_0^t [B]dt$$

$$\int_{[C]_0}^{[C]} d[C] = (k_3)\int_0^t [A]\,dt + (k_4)\int_0^t [B]dt$$

$$\frac{[A]_0 - [A]}{[A]_0} = (k_1 + k_3)\theta_{A,t} - k_2\,\theta_{B,t}$$

$$\frac{[B]}{[A]_0} = (k_1)\theta_{A,t} - (k_2 + k_4)\theta_{B,t}$$

$$\frac{[C]}{[A]_0} = (k_3)\theta_{A,t} + (k_4)\theta_{B,t}$$

$[A] = 1.46\ mol\ dm^{-3}$, $[B] = 1.74\ mol\ dm^{-3}$, $[C] = 1.80\ mol\ dm^{-3}$

Problem 23. Reaction Kinetics with Absorbance Measurement

It is often experimentally convenient to use an analytical method that provides an instrumental signal that is proportional to concentration, rather than providing an absolute concentration. Absorbance, fluorescence intensity, and conductance are examples of this type of instrument response. The requirements are that the reactants and products both give a signal that is directly proportional to their concentrations and there is an experimentally usable change in the observed property as the reactants are transformed into the products. In this experiment, absorption spectroscopy and Beer's law can be used.

A is the reactant and **B** is the only product (**A** → **B**) and both give an absorbance at selected wavelength that is directly proportional to their concentrations. In this experiment, $\varepsilon_A \neq \varepsilon_B$, where ε is the molar absorptivity.

For the hydrolysis of **A** to **B** in aqueous solution, the absorbance-time data are given in the Table below. The experimental conditions: pH of the medium is 7.0 and temperature is 25 °C. The initial **A** concentration is 4.0×10^{-6} M and measurements are recorded at 400 nm in a 5-cm cell.

t/s	A_t
0	0.0840
20	0.1090
60	0.1515
120	0.2010
160	0.2255
200	0.2440
∞	0.3170

23.1. **Calculate** the molar absorptivities of **A** and **B** under these conditions.

23.2. **Find** the rate constant.

23.3. **Find** the half-life ($t_{1/2}$).

23.4. After **how many** seconds [A] is equal to 1.0×10^{-6} M?

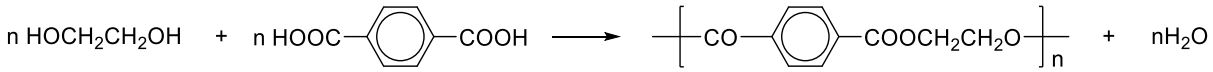
23.5. If k is equal to 0.01029 s^{-1} at 30 °C, **calculate** E_a.

23.6. Assuming that the transition state rate constant is equal to one obtained from the experimental data, **calculate** activation free energy.

$$k_{TST} = \frac{k_B T}{h} e^{-\Delta G^{\ddagger}/RT}$$

where k_B is the Boltzmann constant, h is Planck's constant, and R is the universal gas constant.

The condensation reaction of acid catalyzed ethylene glycol and terephthalic acid is monitored as a function of extent of the reaction (p: ratio of condensed [A] to $[A]_0$) and the reaction obeys second-order kinetics. The concentration of each monomer is equal to each other and it is $[A]_0$=4.8 mol dm^{-3}.



Ethylene glycol Terephthalic acid Polyethylene terephthalate

Time (h)	Extent of Reaction
0	0
0.5	0.636
1.5	0.839
2.5	0.897

23.7. **Find** the rate constant.

23.8. **Find** the half-life of the reaction.

23.9. **What** will the monomer concentration be after one hour?

Solution:

23.1.

At $(t = 0)$, we set $[A] = [A]_0$ and $[B] = 0$. (Eq. 1)
At $(t = \infty)$, $[A] = 0$ and $[B] = [A]_0$ (Eq. 2)

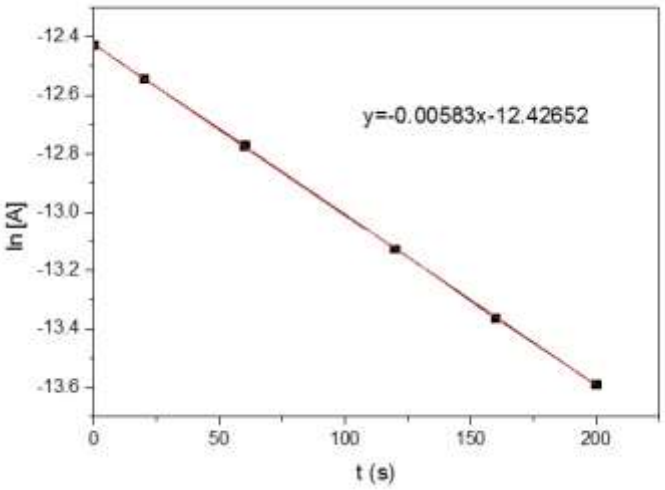
$A = \varepsilon bC$ $\quad 0.084 = \varepsilon_A . 5. (4 \times 10^{-6})$ $\quad \varepsilon_A = 4200\ dm^3.mol^{-1}.cm^{-1}$
$\quad 0.317 = \varepsilon_B . 5. (4 \times 10^{-6})$ $\quad \varepsilon_B = 15850\ dm^3.mol^{-1}.cm^{-1}$

23.2. Applying Beer's law gives

$A_0 = \varepsilon_A\ b\ [A]_0$ (Eq. 2)
$A_\infty = \varepsilon_B\ b\ [B]$ (Eq. 3)
$A_t = \varepsilon_A b\ [A]_t + \varepsilon_B b\ [B]_t$ (Eq. 4)

t/s	$[A]$	$ln[A]$
0	4×10^{-6}	–12.4292
20	3.5708×10^{-6}	–12.5427
60	2.8412×10^{-6}	–12.7713
120	1.9914×10^{-6}	–13.1266
160	1.5708×10^{-6}	–13.3639
200	1.2532×10^{-6}	–13.5898

Evidently the reaction shown in the Figure plotted by using values written in the Table is first-order over the period of time.



ln[A] versus t $\rightarrow y = -0.00583x - 12.42652$

$$ln\frac{[A]}{[A]_0} = -kt$$

$$ln[A] = ln[A]_0 - kt$$

Rate constant $k = 0.00583\ s^{-1}$

23.3. $t_{1/2} = ln2/k = 118.89\ s$

23.4. $ln[A] = ln[A]_0 - kt$

$t = 237.8\ s$

23.5.

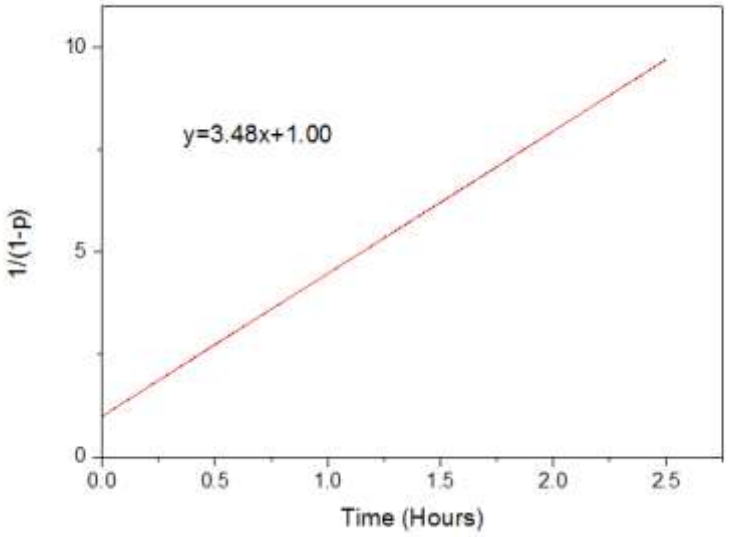
$$\ln\frac{k_2}{k_1} = \left(\frac{E_a}{R}\right)\left[\frac{1}{T_1} - \frac{1}{T_2}\right]$$

$$\ln\frac{0.01029\ s^{-1}}{0.00583\ s^{-1}} = \left(\frac{E_a}{8.3145\ J\ mol^{-1}\ K^{-1}}\right)\left[\frac{1}{298.15\ K} - \frac{1}{303.15\ K}\right]$$

$E_a = 85.4\ kJ\ mol^{-1}$

23.6. $\Delta G^{\ddagger} = 85.7\ kJ\ mol^{-1}$

23.7. $\frac{1}{[A]} - \frac{1}{[A]_0} = k't \qquad p = \frac{[A]_0 - [A]}{[A]_0}$



Slope $= 3.481\ h^{-1} = k'[A]_0 \qquad k' = 0.73\ dm^3 mol^{-1}\ h^{-1}$

23.8. $t_{1/2} = \frac{1}{k'[A]_0} \qquad t_{1/2} = 0.287\ h^{-1}$

23.9. $\frac{1}{[A]} - \frac{1}{[A]_0} = k't \qquad [A] = 1.07\ mol\ dm^{-3}$

Problem 24. Acridine Orange / DNA Binding Interactions

Acridine orange (AO) is a fluorescent dye that binds to DNA via an intercalative mode of binding. AO can insert itself into the DNA base pairs. Interactions of intercalating agents such as AO with DNA have been widely studied, and complexation can be followed with spectrometric titrations by varying the DNA-to-dye ratio. Stock solutions of DNA can be standardized spectrophotometrically (ε = 13,200 mol dm^{-3} cm^{-1} at 260 nm for a molar DNA concentration, C_{DNA}, expressed in base pairs.)

24.1. **Give** an expression to calculate the pure DNA concentration from an absorbance reading at 260 nm from a UV spectrum of solution containing DNA (quartz cuvette length: 1.0 cm).

The interaction between DNA and AO to form the AO–DNA complex can be expressed by the following reaction:

$$AO + DNA \rightleftharpoons AO - DNA,$$

whose equilibrium constant is

$$K = \frac{[AO-DNA]}{[AO][DNA]} \qquad (1)$$

Where [DNA], [AO] and [AO-DNA] are equilibrium concentrations.

24.2. **Provide** a mass balance expression for the overall AO concentration (C_{AO}) at equilibrium conditions.

Binding of AO to DNA can be followed by recording fluorescence intensity (F). Both AO and AO–DNA complex display a maximum emission intensity at λ_{em} = 520 nm. In dilute solutions, concentration is proportional to F. Therefore, quantitative estimation of complexation can be determined by using F.

$$F = \varphi_i \times C_i$$

where φ_i is the fluorescence constant and C_i is the concentration for species i.

24.3. **Provide** an expression for the overall F in terms of φ and concentrations of AO and of DNA at equilibrium.

Consider that initially there is only AO in the measuring cell displaying an emission at λ_{em} = 520 nm, and finally at equilibrium both AO and AO–DNA complex have emission at the same wavelength. $F - \varphi_{AO}\, C_{AO} = \Delta F$, and $\varphi_{AO-DNA} - \varphi_{AO} = \Delta\varphi$ is given.

24.4. <u>Show that</u> $\Delta F = [AO - DNA]\Delta\varphi$.

The binding equilibrium constant for AO intercalation to DNA (ignore AO self-aggregation and dimerization) can be determined from the equation:

$$\frac{C_{AO}}{\Delta F} = \frac{1}{\Delta\varphi} + \frac{1}{\Delta\varphi K}\frac{1}{[DNA]} \qquad (2)$$

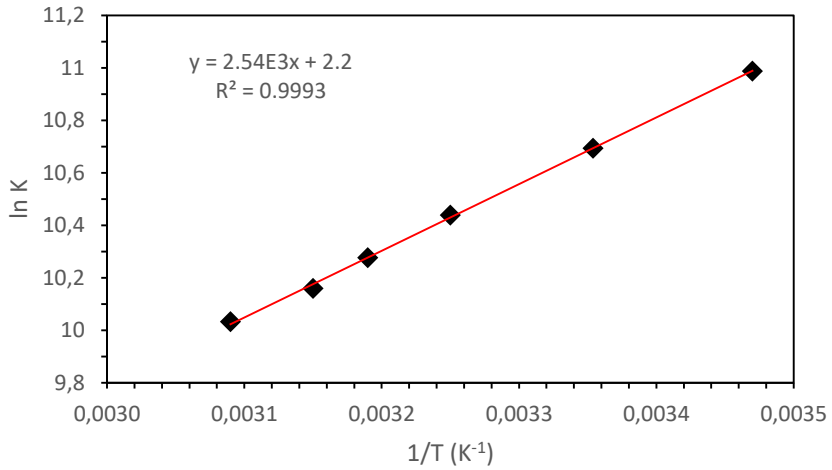
24.5. <u>Derive</u> equation (2) starting from equation (1).

Spectrofluorometric titration is performed by adding increasing amounts of the DNA directly into the cell containing the AO. Each time DNA is added, the fluorescence intensity at λ_{em} = 520 nm, where only free and bound AO have emission, is recorded.

C_{AO} (mol dm^{-3})	C_{DNA} (mol dm^{-3})	F_{520} (a.u.)*
1.857×10^{-7}	6.535×10^{-6}	162
1.832×10^{-7}	1.032×10^{-5}	188
1.800×10^{-7}	1.521×10^{-5}	210
1.725×10^{-7}	2.671×10^{-5}	240
1.604×10^{-7}	4.516×10^{-5}	260

* a.u. is arbitrary unit

24.6. <u>Calculate</u> the equilibrium binding constant for AO–DNA using the data given in the Table above. Assume that there is no AO self-aggregation or dimerization. Take $\varphi_{AO} = 5.00 \times 10^8$ mol dm^{-3}, and [DNA] ≅ C_{DNA}.



24.7. Given that $K = e^{-\frac{\Delta G^\circ}{RT}}$ and the plot above, **calculate** the values of ΔrH°, ΔrS°, and ΔrG° for the complexation of AO with DNA at 25 °C. (Assume that ΔrH° and ΔrS° do not change with the temperature.)

AO can undergo some self-aggregation (dimerization) at higher concentrations. The quantitative analysis of the dimerization can be expressed as follows:

$$2D \underset{k_d}{\overset{k_f}{\rightleftharpoons}} D_2$$

Here *D* represents AO monomer while D_2 represents dimeric AO, and k_f and k_d are the rate constants for dimer formation and dimer dissociation, respectively. According to that reaction, AO concentration dependence of the relaxation time, τ, which represents the time passed for a system to reach the new equilibrium when a sudden change is applied, is expressed by the relationship:

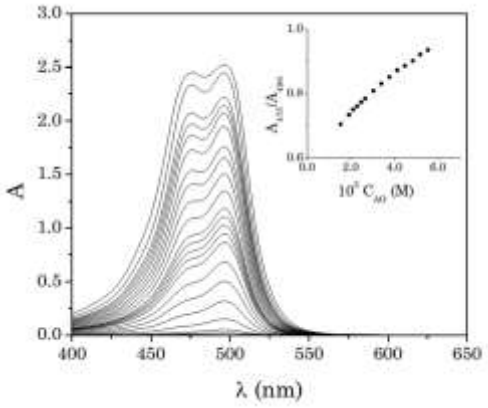
$$\frac{1}{\tau} = k_d + 4k_f C_{AO}$$

Data for dimerization of AO at 25 °C are given in the Table below.

10^6 C_{AO} (mol dm^{-3})	10^5 Relaxation time, τ (s)
2.50	2.32
4.50	2.27
8.00	2.18
11.0	2.11

24.8. **Calculate** the values of k_d and k_f.

The absorbance spectra of AO derivative at various concentrations (0 to 7.3×10^{-5} mol dm^{-3}) in water are shown in the Figure below. The spectra indicate that two absorbance peaks exist: one at 496 nm and the other at 475 nm. The inset gives the ratio of absorbance peaks (A_{475}/A_{496}) as a function of AO concentration.



24.9. **Choose** correct statement(s) according to the absorbance spectra of the AO derivative.

- ☐ The band observed at 496 nm is attributed to the monomeric form.
- ☐ If there were only the monomeric form, the ratio of absorbance peaks (A_{475}/A_{496}) would remain constant.
- ☐ To reduce dimerization, the concentration of AO should be reduced.

24.10. If the initial concentration of AO is 1.0×10^{-5} mol dm^{-3}, then **calculate** the dimer fraction at equilibrium.

$$2D \underset{k_d}{\overset{k_f}{\rightleftharpoons}} D_2$$

Solution:

24.1.

$$C_{\mathrm{DNA}} = \frac{A_{260}}{13{,}200\ \mathrm{mol\ dm^{-3}cm^{-1}}\ 1.0\ cm}$$

24.2. $C_{\mathrm{AO}} = [\mathrm{AO}] + [\mathrm{AO-DNA}]$

24.3. $F = \varphi_{AO}\,[AO] + \varphi_{AO-DNA}\,[AO-DNA]$

24.4.

$F = \varphi_{AO}\,[AO] + \varphi_{AO-DNA}\,[AO-DNA]$

$F = \varphi_{AO}\,(C_{AO} - [AO-DNA]) + \varphi_{AO-DNA}\,[AO-DNA]$

$F = \varphi_{AO}\,C_{AO} - \varphi_{AO}\,[AO-DNA] + \varphi_{AO-DNA}\,[AO-DNA]$

$F - \varphi_{AO}\,C_{AO} = [AO-DNA](\varphi_{AO-DNA} - \varphi_{AO})$

$\Delta F = [AO-DNA]\,\Delta\varphi$

24.5.

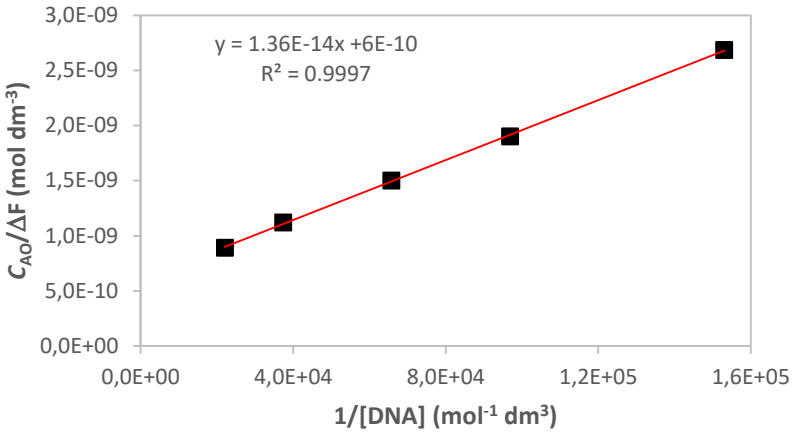
$$\frac{1}{\mathrm{K}} = \frac{(C_{\mathrm{AO}} - [\mathrm{AO-DNA}])[\mathrm{DNA}]}{[\mathrm{AO-DNA}]}$$

$$\frac{C_{\mathrm{AO}}}{[AO-DNA]} = 1 + \frac{1}{K[DNA]}$$

$$[\mathrm{AO-DNA}] = \frac{\Delta \mathrm{F}}{\Delta\varphi}$$

$$\frac{C_{\mathrm{AO}}}{\Delta \mathrm{F}} = \frac{1}{\Delta\varphi} + \frac{1}{\Delta\varphi K}\frac{1}{[DNA]}$$

24.6. A plot of $C_{AO}/\Delta F$ vs. 1/[DNA] is a straight line whose slope and intercept are equal to $1/\Delta\varphi K$ and $1/\Delta\varphi$, respectively. Therefore, K is obtained as the intercept/slope ratio, whereas $\Delta\varphi$ is the intercept reciprocal.



$K = intercept\ /\ slope = 4.41 \times 10^4\ mol^{-1}dm^3$

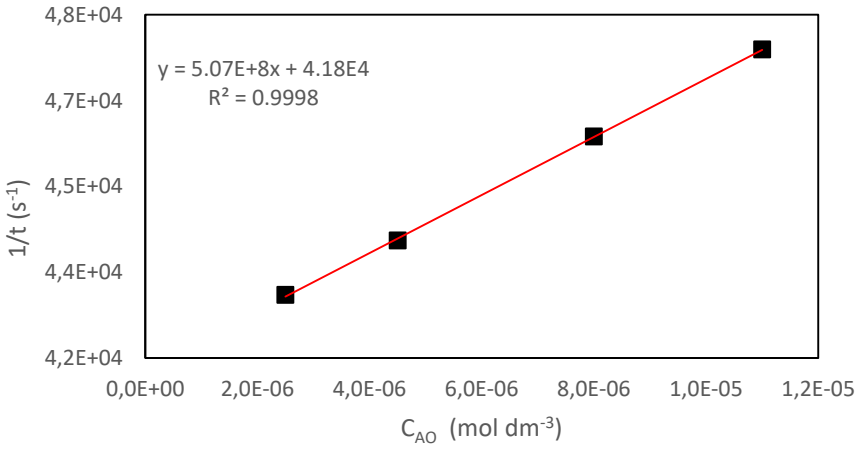
24.7. $\Delta rG° = -RTlnK \Rightarrow \Delta rG° = -8.3145 \times 298.15\ ln\ 4.41 \times 10^4 = -26.6\ kJ\ mol^{-1}$

$\ln K = (-\frac{\Delta rH°}{R})\ \frac{1}{T} + \frac{\Delta rS°}{R}$ where,

$Slope\ of\ the\ plot = -\Delta rH°/R \Rightarrow \Delta rH° = -21.1\ kJ\ mol^{-1}$

$Intercept\ of\ the\ plot = \Delta rS°/R \Rightarrow \Delta rS° = 18.3\ J\ K^{-1}mol^{-1}$

24.8. If the plot of $1/\tau$ versus C_{AO} is obtained, then the slope of the plot is equal to $4k_f$ and the intercept of the plot is equal to k_d.



$Slope\ of\ the\ plot = 4k_f \rightarrow k_f = 1.27 \times 10^8\ mol^{-1}\ dm^3\ s^{-1}$
$Intercept\ of\ the\ plot = k_d = 4.18 \times 10^4\ s^{-1}$

24.9.

☒ The band observed at 496 nm is attributed to the monomeric form.
☒ If there were only the monomeric form, the ratio of absorbance peaks (A_{475}/A_{496}) would remain constant.
☒ To reduce dimerization, the concentration of AO should be reduced.

24.10. The equilibrium constant for dimerization, K_D, can be expressed as

$$K_D = \frac{[\mathrm{D_2}]}{[\mathrm{D}]^2} = \frac{k_f}{k_d} = \frac{1.27 \times 10^8 \ \mathrm{mol^{-1}\ dm^3\ s^{-1}}}{4.18 \times 10^4 \ \mathrm{s^{-1}}} = 3.03 \times 10^3 \ \mathrm{mol^{-1}\ dm^3}$$

	$2D \rightleftharpoons D_2$	
Initially:	1.0×10^{-5}	---
Reaction:	$-x$	$+\frac{x}{2}$
At equilibrium:	$(1.0 \times 10^{-5} - x)$	$+\frac{x}{2}$

$$K_D = \frac{[\mathrm{D_2}]}{[\mathrm{D}]^2} = \frac{\frac{x}{2}}{(1.0 \times 10^{-5} - x)^2} = 3.03 \times 10^3 \ \mathrm{mol^{-1} dm^3}$$

$$x = \ 5.42 \times 10^{-7} \ \mathrm{mol\ dm^{-3}}$$

$$[\mathrm{D_2}] = \frac{x}{2} = 2.71 \times 10^{-7} \ \mathrm{mol\ dm^{-3}}$$

The fraction of the dimeric form at equilibrium can be determined as:

$$\frac{2.71 \times 10^{-7}}{9.73 \times 10^{-6}} \times 100\% = 2.8\%$$

Problem 25. Spectrophotometric Determination of an Antihistaminic Drug

Spectrophotometric procedures are simple, rapid, and accurate methods that can be utilized for the determination of drug molecules. The method is based on formation of a complex between two reagents. Many complexes are colored and absorb in the visible region; thus they can be determined spectrophotometrically.

An antihistaminic drug, *D*, acts as an electron donor group and complexes with a π-acceptor, *S*. Absorbance of the resulting complexes recorded at relevant maxima (460 nm) with respect to drug concentration shows a linear tendency with good correlation coefficients.

$$D + S \rightleftharpoons DS$$

$$K = \frac{[DS]}{[D][S]}$$

where [DS], [D], and [S] represent the equilibrium concentrations of the *DS* complex, *D*, and *S*, respectively.

$$C_D = [D] + [DS]$$

where C_D is the overall concentration of the drug.

At a wavelength where only the formed *DS* complex absorbs light, the following expression holds:

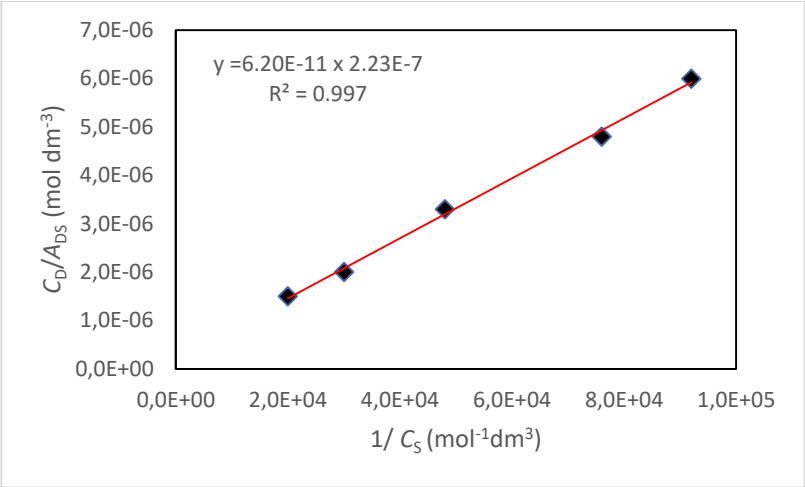
$$A = \varepsilon_{DS} l [DS]$$

where *l* is the length of the measuring cuvette.

The binding equilibrium constant of the complexation can be calculated using the Benesi–Hildebrand equation, which depends on the experimental conditions where one of the component species should be present in large excess so that its concentration is not altered on formation of complex.

$$\frac{C_D}{A_{DS}} = \frac{1}{\varepsilon_{DS}} + \frac{1}{\varepsilon_{DS}\, K} \times \frac{1}{C_S}$$

where C_S and C_D are total concentrations of *S* and *D*. A_{DS} is the absorbance of the complex, ε_{DS} is the molar absorptivity of the complex, and *K* is the equilibrium constant.



25.1. Considering the Benesi–Hildebrand plot recorded at 25 °C, **find** the equilibrium constant for the complex formation and molar absorptivity of the complex.

25.2. The initial equal concentration of *D* and *S* is 9×10^{-5} mol dm^{-3}. **Calculate** the fraction of the complex formed when equilibrium is reached. Consider there is a 1:1 molar ratio between *D* and *S* in the complexation.

25.3. **Calculate** the ΔrG° in kJ mol^{-1} at 25 °C.

The kinetics of complexation of *D* with *S* is studied by varying temperature (25, 45, and 60 °C). The Table gives the rate constant of complexation at different temperatures.

T (°C)	k (sec^{-1})
25	0.0200
45	0.0504
60	0.0944

25.4. **Calculate** the activation energy, E_a.

25.5. Given that $k_{TST} = \frac{k_B T}{h} e^{-\frac{\Delta G^{\ddagger}}{RT}}$, **calculate** the activation enthalpy ($\Delta H^{\ddagger}$), activation entropy ($\Delta S^{\ddagger}$), and free activation enthalpy ($\Delta G^{\ddagger}$) of the reaction for 25 °C.

Solution:

25.1. The Benesi–Hildebrand plot is a straight line whose slope and intercept are equal to $1/\varepsilon_{DS}K$ and $1/\varepsilon_{DS}$, respectively. Therefore, *K* is obtained as the intercept/slope ratio, whereas ε_{DS} is the intercept reciprocal.

$$Intercept = 1/\varepsilon_{DS} = 2.23 \times 10^{-7}$$

$$\varepsilon_{DS} = 4.49 \times 10^{6}\ mol^{-1}dm^{3}\ cm^{-1}$$

$$Slope = \frac{1}{K\varepsilon_{DS}} = 6.20 \times 10^{-11}$$

$$K = \frac{2.23 \times 10^{-7}}{6.20 \times 10^{-11}} = 3.60 \times 10^{3}\ mol^{-1}dm^{3}$$

25.2.

	D +	S ⇌	DS
Initially:	9×10^{-5}	9×10^{-5}	---
Reaction:	$-x$	$-x$	$+x$
At equilibrium:	$(9 \times 10^{-5} - x)$	$(9 \times 10^{-5} - x)$	$+x$

$$K_D = \frac{[DS]}{[D][S]} = \frac{x}{(9 \times 10^{-5} - x)^2} = 3.60 \times 10^{3}\ mol^{-1}\ dm^{3}$$

$$x = 1.84 \times 10^{-5}\ mol\ dm^{-3}$$

$$Fraction\ of\ [DS]\ at\ equilibrium = \frac{1.84 \times 10^{-5}}{(2 \times 7.16 \times 10^{-5}) + 1.8410^{-5}} \times 100\% = 11.4\%$$

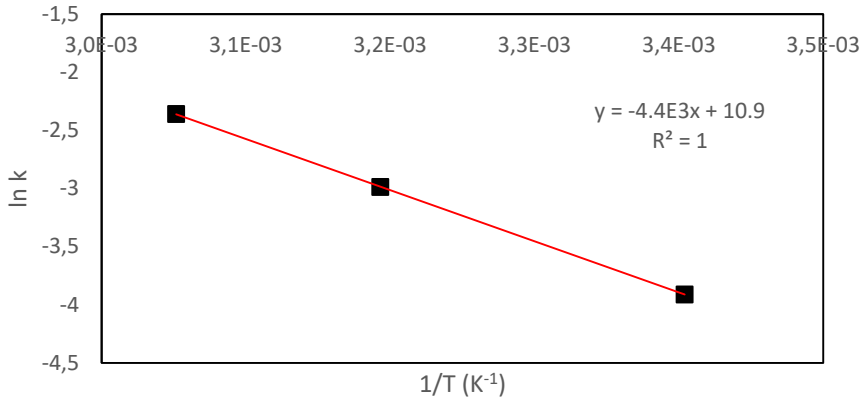
25.3. $\Delta rG° = -RTln\ K = -8.3145 \times 298.15 \times ln3.59 \times 10^{3} = -20.3\ kJ\ mol^{-1}$

25.4. The relationship between the temperature and rate of reaction can be determined from the Arrhenius equation, $k = Ae^{-E_a/RT}$

The equation can be expressed as

$$ln\ k\ =\ -E_a/RT + ln\ A$$

A plot of *ln* k versus 1/T is a straight line whose slope and intercept are equal to $-E_a/R$, and ln *A*, respectively.

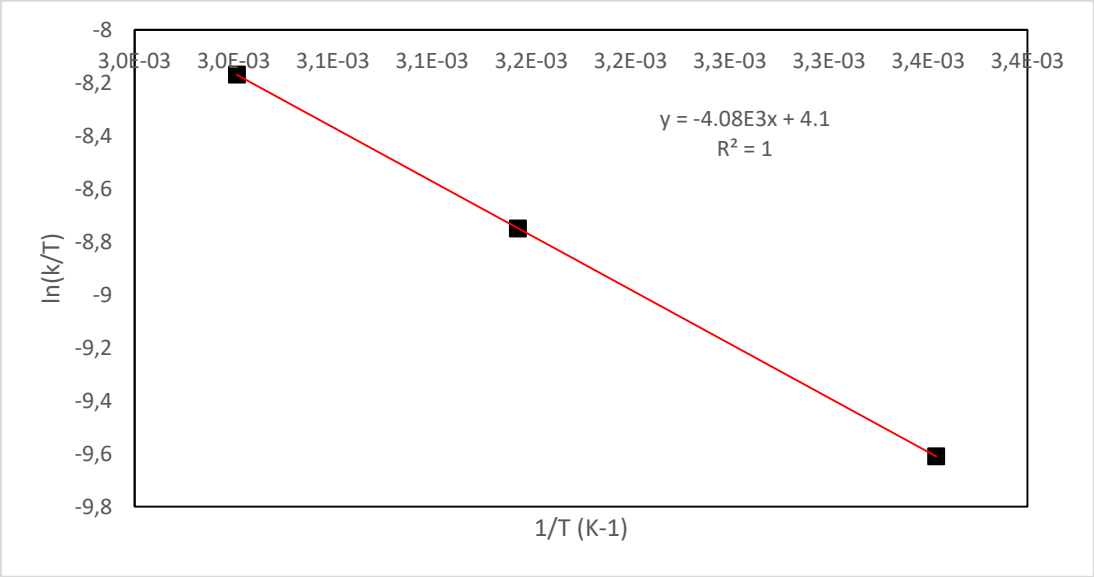


$$Slope = -Ea\ /R\ \Rightarrow\ Ea = -\left(-\ 4400 \times 8.3145\ J\ K^{-1}\ mol^{-1}\right)\ =\ 36.6\ kJ\ mol^{-1}$$

25.5. The equation can be rearranged in such a way that

$$\ln\left(\frac{k}{T}\right) = -\frac{\Delta H^{\ddagger}}{R}\frac{1}{T} + \ln\left(\frac{k_B}{h}\right) + \frac{\Delta S^{\ddagger}}{R}$$

The plot of *ln*(k/T) versus 1/T produces a straight line whose slope and intercept are equal to $-\Delta H^{\ddagger}/R$ and $ln(k_B/h) + \Delta S^{\ddagger}/R$, respectively.



$Slope = -4080 = -\Delta H^{\ddagger}/R => \Delta H^{\ddagger} = 33.9\ kJ\ mol^{-1}$

$Intercept = 4.1 = ln(k_B/h) + \Delta S^{\ddagger}/R \ => \ \Delta S^{\ddagger} = -\ 163.7\ J\ K^{-1}\ mol^{-1}$

$\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$

$\Delta G^{\ddagger} = \ 33{,}900\ J\ mol^{-1} - \ 298.15\ K \times (-\ 163.7\ J\ K^{-1}\ mol^{-1}\ ) = \ 82.7\ kJ\ mol^{-1}$

Part II: Practical Problems

Safety

Participants in the Olympiad must be prepared to work in a chemical laboratory and be aware of all relevant rules and safety procedures. The organizers will strictly enforce the safety rules given in *Appendix A* of the IChO Regulations during the Olympiad.

The Preparatory Problems are designed to be carried out in properly equipped chemical laboratories under competent supervision **only**. For each chemical, the GHS hazard and precautionary numbers are reported. We did not include specific and detailed safety and disposal instructions as regulations are different in each country. Mentors must carefully adapt the problems accordingly.

A Material Safety Data Sheet (MSDS)

A Material Safety Data Sheet (MSDS) is a technical document that contains detailed and comprehensive information about the hazards of a chemical and how to work safely with the chemical product. You have to know about the hazards with the chemicals in experiments.

Dress code

During the examination, the students will be required to wear:

- pants covering their whole legs;
- closed and flat shoes;
- a lab coat with long sleeves;
- if applicable, long hair tied back.

Safety glasses will be supplied and must be carried during the whole examination, even if the student wears prescription glasses. Contact lenses are prohibited.

Any student that fails to respect these rules will not be allowed to enter the lab.

The GHS hazard statements (H-phrases) associated with the materials used are indicated in the problems. Their meanings are as follows.

Definition of GHS hazard statements:

Physical hazards

H224 Extremely flammable liquid and vapour.
H225 Highly flammable liquid and vapour.

H226 Flammable liquid and vapour.
H272 May intensify fire; oxidizer.
H290 May be corrosive to metals.
H290 May be corrosive to metals.

Health hazards

H301 Toxic if swallowed.
H302 Harmful if swallowed.
H302 + H312 + H332 Harmful if swallowed, in contact with skin or if inhaled.
H304 May be fatal if swallowed and enters airways.
H311 Toxic in contact with skin.
H312 Harmful in contact with skin.
H312 + H332 Harmful in contact with skin or if inhaled.
H314 Causes severe skin burns and eye damage.
H315 Causes skin irritation.
H317 May cause an allergic skin reaction.
H318 Causes serious eye damage.
H319 Causes serious eye irritation.
H330 Fatal if inhaled.
H334 May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H335 May cause respiratory irritation.
H336 May cause drowsiness or dizziness.
H340 May cause genetic defects.
H350 May cause cancer.
H360FD May damage fertility. May damage the unborn child.
H372 Causes damage to organs through prolonged or repeated exposure.

Environmental hazards

H400 Very toxic to aquatic life.
H410 Very toxic to aquatic life with long lasting effects.
H411 Toxic to aquatic life with long lasting effects.
H412 Harmful to aquatic life with long lasting effects.

Precautionary Statements

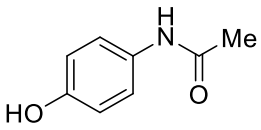
P201 Obtain special instructions before use.
P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
P221 Take any precaution to avoid mixing with combustibles, heavy-metal compounds, acids and alkalis.
P260 Do not breathe dust or mist.

P261 Avoid breathing dust/ fume/ gas/ mist/ vapours/ spray.
P264 Wash skin thoroughly after handling.
P273 Avoid release to the environment.
P280 Wear protective gloves.
P280 "Wear protective gloves/ protective clothing/ eye protection/ face protection."
P301 + P310 + P331 IF SWALLOWED: Immediately call a POISON CENTER/doctor. Do NOT induce vomiting.
P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER/doctor if you feel unwell. Rinse mouth.
P301 + P330 + P331 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P302 + P352 IF ON SKIN: Wash with plenty of water.
P302 + P352 + P312 "IF ON SKIN: Wash with plenty of water. Call a POISON CENTER/doctor if you feel unwell."
P303 + P361 + P353 "IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water."
P304 + P340 IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
P304 + P340 + P310 "IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor."
P304 + P340 + P312 "IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER/doctor if you feel unwell."
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/doctor.
P308 + P310 IF exposed or concerned: immediately call a POISON CENTER or doctor/ physician.
P314 Get medical advice/ attention if you feel unwell.
P337 + P313 If eye irritation persists: Get medical advice/ attention.
P370 + P378 "In case of fire: Use dry sand, dry chemical or alcohol-resistant foam to extinguish."
P403 + P233 Store in a well-ventilated place. Keep container tightly closed.
P403 + P235 Store in a well-ventilated place. Keep cool.

Risk and Safety Statements

R 51/53 Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
S 61 Avoid release to the environment. Refer to special instructions/ Safety data sheets.

Problem P1. Drug Delivery from a Polymeric Hydrogel System



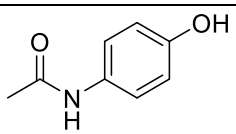
Chemical structure of paracetamol.

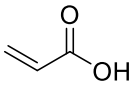
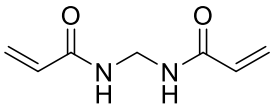
Nowadays, studies in the field of medicine aim to reduce the drug dose to a minimum, extend the dose range, and improve the quality of life by ensuring that the patient is not affected by the side effects of the drug. "Controlled release systems" provide the best response to this goal. Controlled release is a system that can be prepared in membrane or matrix form. Controlled release of a drug from systems such as a hydrogel film or sphere allows the drug to be more effectively introduced into the body.

Paracetamol is a drug active substance with analgesic and antipyretic properties. It is one of the most common drugs used to reduce moderate/mild pain and fever.

In this problem, you will examine the controlled release of paracetamol active substance from a hydrogel polymer system.

Chemicals

Substance	**Name**	**State**	**GHS Hazard Statements**
	Paracetamol	Solid	H302, H315, H317, H319, P280, P301 + P312 + P330, P305 + P351 + P338

Phosphate buffered-saline (PBS)	Phosphate buffered-saline (PBS) solution (pH: 7.4)	Solution	H319, P305 + P351 + P338
	Acrylic acid	Liquid	H226-H302 + H312 + H332-H314-H335-H400, P210, P261, P273, P280, P303 + P361 + P353, P305 + P351 + P338
	*N,N′*-Methylenebisacrylamide	Solid	H302, P301 + P312 + P330
$(NH_4)_2S_2O_8$	Ammonium persulfate	Solid	H272, H302, H315, H317, H319, H334, H335, P210, P280, P301 + P312 + P330, P302 + P352, P305 + P351 + P338
Distilled water	Deionized water	Liquid	Not Hazardous

Glassware and Equipment

- 1 Beaker, 100 mL
- 1 Graduated cylinder, 100 mL
- 1 Volumetric pipette, 5 mL
- 1 Volumetrik flask with stopper, 250 mL
- 5 Volumetric flasks with stoppers, 10 mL
- 1 Pipette filler bulb
- 1 Spatula (small)
- 6 Test tubes with plastic caps
- 1 Weighing dish
- 1 Petri dish
- 1 Glass rod
- 1 Wash bottle
- 1 Magnetic hotplate stirrer
- 1 Stopwatch
- 15 Disposable plastic pipette, 3 mL
- 2 Sheets of millimetric paper

- 1 Ruler
- 1 Felt-tip pen for glassware
- 1 Photometer
- 2 UV-vis quartz (or quality plastic, <200 nm) absorption cuvettes
- 1 Balance
- 1 stirring bar
- 1 marker
- 1 thermometer
- 1 Vortex
- 1 Hot air gun
- Vials
- Water bath
- Syringe
- Plastic Straws

Preparation of pH: 7.4 PBS: Prepare 150 mL of distilled water in a 250 mL flask. Add 1.6 g NaCl, 0.4 g KCl, 288 mg Na_2HPO_4, and 48 mg NaH_2PO_4. Add distilled water until volume is 250 mL and mix to dissolve all salts in the solution.

Preparation of Hydrogel

1. Weigh different amounts of AA monomer (5 mL, 72.9 mmol), MBAA (0.026 g, 0.17 mmol) as crosslinker, paracetamol (known amount), APS (0.1 g, 0.44 mmol) as initiator in a vial (20 mL), add deionized water (5.0 mL).
2. Use a vortex or magnetic stirrer to help dissolve the mixture in the vial.
3. Fill into pipettes with the aid of a syringe (the bottom of the paper pipettes is previously closed with a hot air gun).
4. Place in a hot water bath at 60 ^oC for polymerization of these mixtures in pipettes.
5. Remove the polymerized gels from the paper pipettes, and divide them into equal pieces.

Part A. Plotting the Calibration Curve

In this section, you are asked to prepare the standard solutions of paracetamol as seen in Table 1. After reading the absorbance (A) values of each solution by using a UV-Vis spectrophotometer, fill in the blanks in Table 1.

Table 1. Data of paracetamol standards.

$C_{paracetamol}$ (mg/L)	Absorbance at 243 nm
2	
4	
6	
8	
10	

Procedure

1. Go to the millimetric paper page.
2. Write the standard paracetamol concentrations on the x-axis and the corresponding absorbance values on the y-axis. Write the units of the axes.
3. Pass a straight line over the points and **determine** the equation of this calibration graph. If you have any problem to obtain the linearity between absorbance and concentration, you can repeat the experiment till you obtain a linear line.
4. Find the calibration equation.

Part B. Release of Paracetamol from the Polymeric Hydrogel System

Procedure

1. Turn on the magnetic hotplate stirrer and put a 250 mL beaker on it. **Add** 100 mL of PBS solution into beaker and adjust temperature of the solution to 37 °C using a thermometer.
2. Stir the solution at 250 rpm.
2. Place the hydrogel sample provided to you into the beaker. Using a glass rod, **allow** hydrogel to be in the solution (release solution) using a glass rod.
4. At different time intervals (0, 10, 20, 30, 40, and 50 min), **place** 2 mL of the release solution into different test tubes, seal each tube with a plastic cap, and **add** 2 mL of PBS solution to the release solution in each case.
5. Read the absorbance at 243 nm for all solutions you collected. **Use** PBS solution as blank.
6. Fill in the following Table 2.

Table 2. Data for the release of paracetamol from the hydrogel system depending on time.

Time (min)	Absorbance (A)
0	
10	
20	
30	
40	
50	

Calculations & Analysis

In this section, the release behavior of paracetamol from the hydrogel system will be examined. Use the absorbance values in Table 2 and the calibration equation.

P1.1. <u>Calculate</u> the cumulative drug release using the following equation:

$$\text{Cumulative drug release ratio} = \frac{v_1 \, X \, c_i + v_2 \sum (c_{i-1})}{m} \times 100\%$$

In this equation:
v_1: total volume of PBS solution (100 mL),
c_i: concentration in the release medium,
v_2: volume of the measured sample (2 mL),
m: mass of paracetamol in the hydrogel.

Table 3. Experimental data.

Time (min)	Paracetamol concentration	Cumulative drug release (%)
0		
10		
20		
30		
40		
50		

P1.2. Using another sheet of millimetric paper, record the release times (t=0, 10, 20, 30, 40, 50 min) on the x-axis and the cumulative drug release values on the y-axis. **<u>Pass</u>** a straight line through the points.

P1.3. <u>Calculate</u> the time (in minutes) required to take 20% of paracetamol from this hydrogel system for an individual person suffering from pain using the graphic of Table 3.

Solution:

Part A. Preparation of Paracetamol Calibration Curve

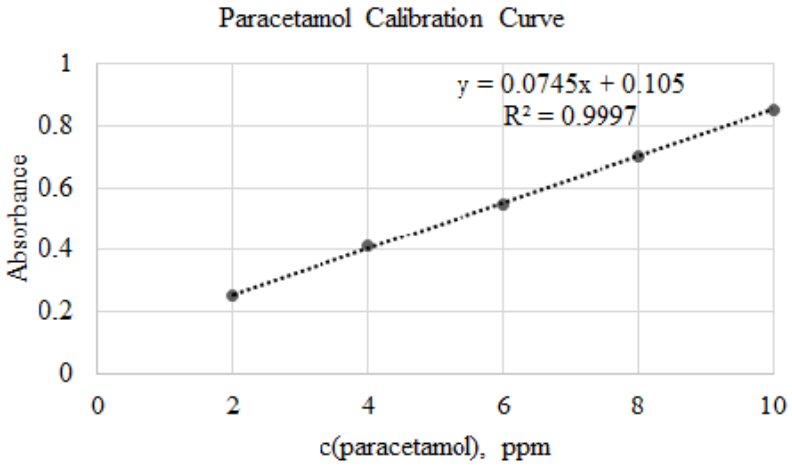
In this section, absorbance values of standard paracetamol solutions are recorded.

Table 1. Absorbance data of standard paracetamol solutions.

$V_{paracetamol}$ (mL)	$C_{paracetamol}$ (ppm)	Absorbance
1	2	0.25
2	4	0.40
3	6	0.55
4	8	0.70
5	10	0.85

Calibration Curve

The paracetamol calibration curve is drawn using the data from Table P1 by means of millimetric paper.



The calibration equation is recorded:

Calibration equation	A = 0.0745 C (ppm) + 0.105

Part B. Release of Paracetamol from the Polymeric Hydrogel System

In this section, at different time intervals (0, 10, 20, 30, 40, and 50 min), absorbance of the release solution is recorded in Table 2.

The paracetamol calibration equation has been found as $y = 0.0745\,x + 0.105$ in Part A. In this equation, the absorbance values in Table 1 are written as y and x values found. x values are the concentration of paracetamol that is released from the PBS solution. The concentration values are recorded in Table 3.

Table 2. Data for the release of paracetamol from the hydrogel system depending on time.

Time (min)	Absorbance (A)
0	0.15
10	0.35
20	0.50
30	0.65
40	0.80
50	0.95

P1.1. Cumulative drug delivery is calculated using the equation below:

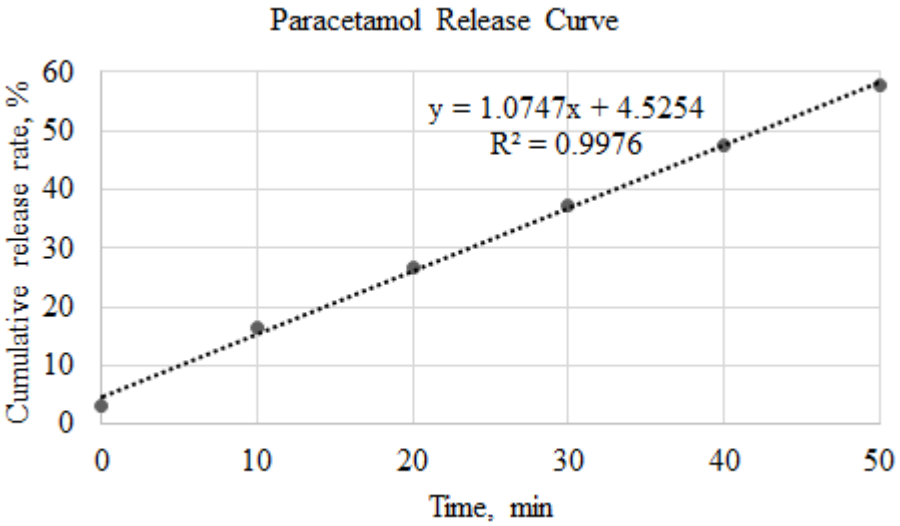
Cumulative drug release ratio = $\frac{v_1\, x\, c_i + v_2 \sum (c_{i-1})}{m} \times 100\%$

In this equation:
v_1: total volume of PBS solution (100 mL),
c_i: concentration in the release medium,
v_2: volume of the measured sample (2 mL),
m: the amount of paracetamol loaded into the hydrogel system initially (2 mg)

Table 3. Experimental data.

Time (min)	Paracetamol concentration	Cumulative drug release (%)
0	0.60	3.02
10	3.29	16.50
20	5.30	26.84
30	7.32	37.11
40	9.33	47.38
50	11.34	57.64

P1.2. Cumulative drug release curve is constructed.



A straight line is passed through the points.

P1.3. The time (in minutes) required to take 20% of paracetamol from this hydrogel system for an individual person suffering from pain is calculated.

The equation of the drug delivery curve is found as $Release\ (\%) = 1.0747\ time(\text{min}) + 4.5254$. According to this equation, if y is 20, x is calculated as 14 min. The answer is thus 14 min.

Problem P2. Determination of the Total Carbon Content of Oltu Stone (Black Amber) Samples

Erzurum is a city in the northeastern part of Anatolia and is called the peak of Turkey due to its high altitude of 1900 m. Erzurum has a unique black stone (Oltu stone, black amber). This stone has been carved since the 18th century to produce jewelry and different souvenirs. Different products of Oltu stone such as rings, earrings, necklaces, bracelets, tie pins, smoking pipes, cigarette holders, and prayer beads are produced by polishing and are sold in Taşhan (**Rustem Pasha Caravanserai**) Bazaar in Erzurum, which was established in 1561.

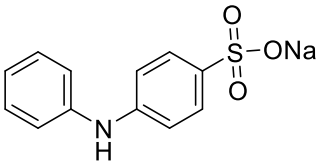
There are around 600 active quarries mining Oltu stone. The beds are about 80 cm in thickness and form by diastrophism and folding of fossilized trees. Oltu stone is soft when excavated but begins to harden when it is exposed to the air. It is generally black but can be dark brown, gray, or greenish too. Oltu stone is an important material for the electric and electronics industries because its graphite-like carbon black nature. Therefore, Oltu stone contains plenty of the element carbon.

This task aims to quantitatively determine the amount of carbon in Oltu stone samples thanks to back titration, using dichromate solution. Carbon element in the sample is first oxidized to $CO_2(g)$ with dichromate and then excess dichromate is back titrated with a standard iron(II) sulfate solution.

Note: This experiment can also be performed using another carbon-rich material such as coal or pencil graphite instead of Oltu stone.

Caution: Potassium dichromate ($K_2Cr_2O_7$) is a very strong oxidizer and corrosive. Its contact with other materials may cause a fire. Therefore, this experiment must be performed in a fume hood by using glassware, laboratory coat, and glove. After you complete the experiment, waste solutions and/chemicals should be placed in the waste container.

Chemicals

Substance	Name	State	GHS Hazard Statement
$K_2Cr_2O_7$	Potassium dichromate	Solid	H340, H350, H360FD, H272, H301, H312, H314, H317, H330, H334, H335, H372, H410, P201, P221, P273, P280, P301 + P330 + P331, P302 + P352, P304 + P340, P305 + P351 + P338, P308 + P310
H_2SO_4	Sulfuric acid	Liquid	H290, H314, P280, P301 + P330 + P331, P303 + P361 + P353, P305 + P351 + P338 + P310
H_3PO_4	Phosphoric acid	Liquid	H290, H302, H314, P260, P280, P301 + P312 + P330, P301 + P330 + P331, P303 + P361 + P353, P305 + P351 + P338 + P310
$FeSO_4$	Iron(II) sulfate	Solid	H302, H315, H319; P302 + P352, P305 + P351 + P338, P301 + P312 + P330
	Diphenylamine sodium sulfonate	Solid	H315, H319, H335

Glassware and equipment

- 2 Volumetric flasks (with stoppers), 1000 mL
- 1 Volumetric flask (with stopper), 250 mL
- 2 Volumetric flasks (with stoppers), 100 mL
- 1 Volumetric flask (with stopper), 10 mL
- 1 Measuring cylinder, 100 mL
- 1 Measuring cylinder, 50 mL
- 1 Erlenmeyer flask, 250 mL
- 1 Burette, 50 mL
- 1 two-necked digestion flask
- 1 Weighing dish
- 1 Spatula
- 1 Transfer funnel
- 1 Laboratory stand with burette clamp

- 1 Weighing balance (0.1 mg)
- 1 Magnetic hotplate stirrer
- 1 Magnetic bar
- 1 Ice-bath or water-bath
- 1 Thermometer
- 1 Stopwatch
- Beakers (for transfers)
- Bossheads and clamps
- Water-ice bath
- Pasteur pipettes

Reagent and Standard Solutions

Potassium dichromate solution: Potassium dichromate (8.825 g), previously oven dried at about 140 °C for 1 hour, is transferred into a 100 mL flask, dissolved in about 90 mL of deionized water, and then diluted to the volume with deionized water (0.3 M $K_2Cr_2O_7$).

Phosphoric acid-sulfuric acid solution: 1.5 mL of concentrated H_2SO_4 is added slowly to 5 mL of deionized water under stirring in a 10 mL flask. 1.5 mL of 85% phosphoric acid is also added to this flask, cooled at room temperature, and diluted to exact volume with deionized water. Note: Be careful during this step because the process of adding acid to water is exothermic.

Iron(II) sulfate standard solution: Iron(II) sulfate (3.038 g) is transferred into a 100 mL flask and dissolved in about 80 mL of deionized water. Then 2 mL of concentrated H_2SO_4 is added to this $FeSO_4$ solution slowly under stirring. The mixture is cooled to room temperature and diluted to exact volume (0.2 M $FeSO_4$).

Diphenylamine sodium sulfonate indicator solution: 20 mg of 4-diphenylamine sodium sulfonate is dissolved in concentrated H_2SO_4 in a 10 mL flask.

Procedure

1. Weigh about 10 mg of Oltu stone sample using a weighing balance and **write down** the exact weight of the sample.

2. Place this Oltu stone sample into a digestion flask over a magnetic hotplate stirrer and then add 5 mL of 0.3 M $K_2Cr_2O_7$ in a fume hood.

3. Add slowly 20 mL of concentrated H_2SO_4 while cooling the flask in a water-ice bath. Put a magnetic bar and stir at 200 rpm.

4. Attach a thermometer to the stopper and heat rapidly until a temperature of 160 °C is reached.

5. Maintain the temperature at 160 ± 2 °C for 10 min.

6. Transfer the solution to a 250 mL Erlenmeyer flask and **cool** to room temperature with tap water.

7. Add 8 drops of the phosphoric acid/sulfuric acid mixture and 4 drops of 4-diphenylamine sodium sulfonate indicator to the solution.

8. Fill the burette with standard 0.2 M $FeSO_4$ solution until the volume line.

9. Titrate the excess $K_2Cr_2O_7$ with a 0.2 M $FeSO_4$ solution. The color change is from violet to dirty gray (end point) and finally green.

10. Repeat steps 1–9 with another Oltu stone sample as necessary.

11. Perform the same experiment using a blank (in the absence of Oltu stone sample) solution.

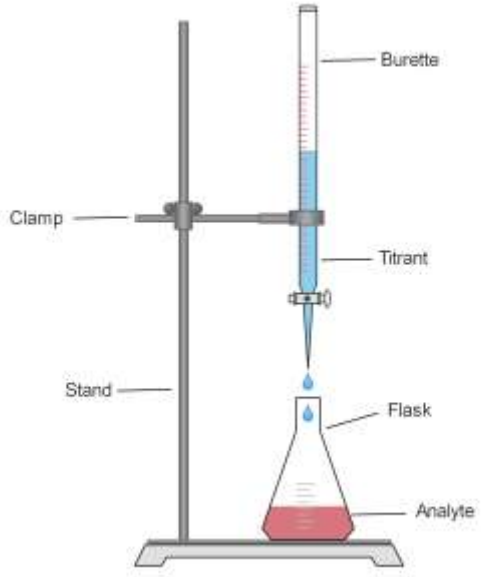


Figure P2-1. A titration setup

Calculations & Analysis

P2.1. Write all balanced equations during this experiment.

P2.2. Calculate the mean total carbon content of the Oltu stone sample as weight %.

Solution:

- Let us take a 10.2 mg Oltu stone sample for total carbon analysis.
- Consumed volume of $FeSO_4$ solution at the end point is 30.4 mL
- We have also applied another two experiments and the results are as follows:
  For 9.9 mg sample, volume of $FeSO_4$ solution at the end point is 30.8 mL.
  For 10.4 mg sample, volume of $FeSO_4$ solution at the end point is 30.1 mL.
- Result of a blank solution is 0.5 mL.

P2.1.

$$3C^o + 2Cr_2O_7^{2-} + 16H^+ \rightarrow 4Cr^{3+} + 3CO_2(g) + 8H_2O$$

$$K_2Cr_2O_7 + 6FeSO_4 + 7H_2SO_4 \rightarrow Cr_2(SO_4)_3 + 3Fe_2(SO_4)_3 + K_2SO_4 + 7H_2O$$

P2.2.

Sample number	Volume of $FeSO_4$ solution, mL	Sample weight, mg
1	30.4–0.5=29.9	10.2
2	30.8–0.5=30.3	9.9
3	30.1–0.5=29.6	10.4

Let us calculate total carbon % for sample 1:

$$\left[\frac{0.3\ mmol\ Cr_2O_7^{2-}}{mL\ Cr_2O_7^{2-}} \times 5\ mL\ Cr_2O_7^{2-} - \left(\frac{0.2\ mmol\ FeSO_4}{mL\ FeSO_4} \times 29.9\ mL\ FeSO_4 \times \frac{1\ mmol\ Cr_2O_7^{2-}}{6\ mmol\ FeSO_4}\right)\right] \times \frac{3\ mmol\ C}{2\ mmol\ Cr_2O_7^{2-}} \times \frac{12\ mg\ C}{1\ mmol\ C} \times \frac{100}{10.2\ mg\ sample} = 88.82\%$$

By the same way, we obtain the following results for all samples.

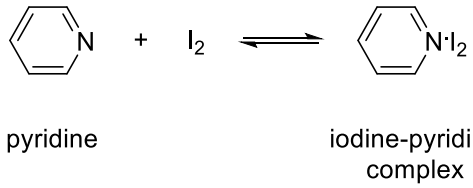
Sample number	Carbon%
1	88.82
2	89.01
3	88.85

Mean value; $\bar{x} = \frac{88.82+89.01+88.85}{3} = 88.89\%$

Standard deviation; $s = \sqrt{\frac{(88.82-88.89)^2+(89.01-88.89)^2+(88.85-88.89)^2}{2}} = \sqrt{\frac{0.0049+0.0144+0.0016}{2}} =$ 0.10%

Problem P3. Spectrophotometric Determination of the Equilibrium Constant for the Formation of a Complex

In this task, the complexation reaction between I_2 and pyridine (pyr) will be followed by spectrophotometry to determine the equilibrium constant (K) of this complexation reaction. I_2 and I_2·pyr complex can absorb visible region of electromagnetic radiation but pyr cannot because it is colorless. Analysis of the spectral changes with variation in pyr concentration and with constant total iodine concentration provides the determination of K of the complexation reaction.



Caution: All operations should be carried out in a fume hood except for spectrophotometric measurements. After you complete the experiment, waste solutions and/or chemicals should be placed in the waste container.

Chemicals

Substance	Name	State	GHS Hazard Statement
C_5H_5N	Pyridine	Liquid	H225, H302 + H312 + H332, H315, H319; P210, P280, P301 + P312 + P330, P302 + P352 + P312, P304 + P340 + P312, P305 + P351 + P338
C_6H_{12}	Cyclohexane	Liquid	H225, H304, H315, H336, H410, P210, P273, P301 + P310 + P331, P302 + P352
I_2	Iodine	Solid	H312 + H332, H315, H319, H335, H372, H400, P273, P280, P302 + P352 + P312, P304 + P340 + P312, P305 + P351 + P338, P314

Glassware and equipment

- Spectrophotometer
- 2 UV-vis glass, quartz or plastic absorption cuvettes
- 1 Volumetric flask (with stopper), 50 mL
- 6 Volumetric flasks (with stoppers), 25 mL
- 1 Pipette, 1 mL

- 1 Pipette, 10 mL
- 1 Pipetting bulb

Reagent and Standard Solutions

1. 0.050 M pyr in cyclohexane (50 mL for each student, concentrations must be known accurately).
2. 0.010 M I_2 in cyclohexane (25 mL for each student, concentrations must be known accurately).

Procedure

1. Pipette the following volumes of stock solutions into six 25-mL volumetric flasks labeled as F-0, F-1, F-2, F-3, F-4, and F-5; dilute to the mark with cyclohexane; and mix them well.

Flask	Volume of pyr stock solution/mL	Volume of I_2 stock solution/mL
F-0	0.0	1.0
F-1	1.0	1.0
F-2	2.0	1.0
F-3	3.0	1.0
F-4	4.0	1.0
F-5	5.0	1.0

2. Use two glass absorption cells with solvent in both the sample and the reference cells and **scan** the wavelength between 350 and 800 nm to record a baseline.

3. Record all spectra for the samples using this background.

4. Measure the absorbance values at the wavelengths of the two maxima in each spectrum by subtracting the absorbance of the blank from each.

Depending on the complexation reaction,

$$K = \frac{[I_2.pyr]}{[I_2][pyr]}$$

Consider a series of solutions in which increments of pyr are added to a constant amount of I_2. Letting $I_{2(0)}$ be the total concentration of I_2 (in the forms I_2 and I_2·pyr), we can write

$$[I_2] = [I_{2(0)}] - [I_2.pyr]$$

K expression can be rearranged as follows:

$$\frac{[I_2.pyr]}{[pyr]} = K[I_2]$$

$$\frac{[I_2.pyr]}{[pyr]} = K\left([I_{2(0)}] - [I_2.pyr]\right)$$

Based on the last equation, a graph of $\frac{[I_2.pyr]}{[pyr]}$ vs. $[I_2.pyr]$ has a slope of *–K*.

If we know$[I_2.pyr]$, we can find $[pyr]$ with the mass balance

$$pyr_0 = [total\ pyr] = [I_2.pyr] + [pyr]$$

To measure$[I_2.pyr]$, we use absorbance values. Suppose that I_2 and $I_2.pyr$ each has some absorbance at wavelength λ, but pyr has no absorbance at this wavelength. Let us assume that we measure absorbance values at a path length of 1 cm so that we can omit it when writing Beer's law. The absorbance at every wavelengths is the sum of absorbances of I_2 and $I_2.pyr$

$$A = \varepsilon_{I_2.pyr}[I_2.pyr] + \varepsilon_{I_2}[I_2]$$

Substituting $[I_2] = [I_{2(0)}] - [I_2.pyr]$, we can write

$$A = \varepsilon_{I_2.pyr}[I_2.pyr] + \varepsilon_{I_2}\left[I_{2(0)}\right] - \varepsilon_{I_2}[I_2.pyr]$$

In the last equation $\varepsilon_{I_2}\left[I_{2(0)}\right]$ is A_0, the initial absorbance before any pyr is added. Therefore,

$$A = [I_2.pyr]\left(\varepsilon_{I_2.pyr} - \varepsilon_{I_2}\right) + A_0 \quad \text{and} \quad [I_2.pyr] = \frac{\Delta A}{\Delta \varepsilon}$$

where $\Delta\varepsilon = \varepsilon_{I_2.pyr} - \varepsilon_{I_2}$ and $\Delta A = A - A_0$ is the observed absorbance after each addition of pyr minus the initial absorbance.

Substituting $[I_2.pyr]$ from $A = \frac{\Delta A}{\Delta \varepsilon}\left(\varepsilon_{I_2.pyr} - \varepsilon_{I_2}\right) + A_0$ and writing it in $\frac{[I_2.pyr]}{[pyr]} = K\left([I_{2(0)}] - [I_2.pyr]\right)$ gives the following equation:

$$\frac{\Delta A}{[pyr]} = K\Delta\varepsilon[I_{2(0)}] - K\Delta A$$

This equation is known as the *Scatchard equation.*

Calculations & Analysis

P3.1. **Draw** a graph of $\frac{\Delta A}{[free\ pyr]}$ vs. ΔA (*Scatchard plot*).

P3.2. **Determine** the K value of this complexation reaction from the slope.

P3.3. **Determine** the $\Delta\varepsilon$ value using the intercept.

P3.4. **Determine** the ε_{I_2} value using the absorption band of I_2.

P3.5. **Calculate** the $\varepsilon_{I_2.pyr}$ value.

P3.6. **Observe** if there is an isosbestic point in this experiment.

P3.7. If yes, **explain** why an isosbestic point is observed.

Solution:

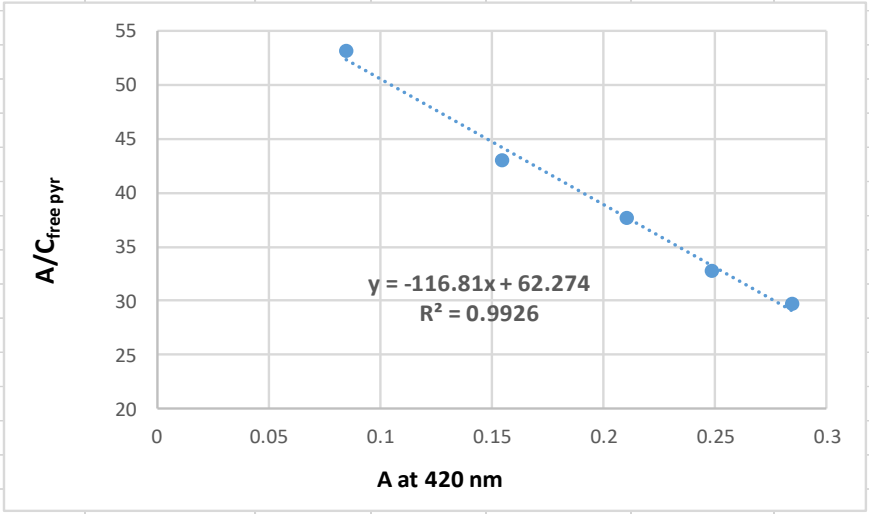
- Solutions used:
  0.050 M pyr in cyclohexane
  0.010 M I_2 in cyclohexane
- Path length (l): 1 cm
- Total volume is 25 mL

Flask	Volume of pyr stock solution/mL	Volume of I_2 stock solution/mL	[pyr], M	[I_2], M
F-0	0.0	1.0	0	4.0×10^{-4}
F-1	1.0	1.0	2.0×10^{-3}	4.0×10^{-4}
F-2	2.0	1.0	4.0×10^{-3}	4.0×10^{-4}
F-3	3.0	1.0	6.0×10^{-3}	4.0×10^{-4}
F-4	4.0	1.0	8.0×10^{-3}	4.0×10^{-4}
F-5	5.0	1.0	1.0×10^{-2}	4.0×10^{-4}

I_2 shows a band at 520 nm. A band at 420 nm arises by the formation of I_2.pyr complex, while absorbance of the band at 520 nm decreases with the addition of pyr. Depending on the Scatchard equation, the following Scatchard plot has been obtained.

P3.1. $\frac{\Delta A}{[free\ pyr]} = K\Delta\varepsilon I_{2(0)} - K\Delta A$

A at 420 nm	Cpyr/M	C_{iodine}	$C_{free\ pyr}$/M	$A/C_{free\ pyr}$
0.085	0.002	0.0004	0.0016	53.13
0.155	0.004	0.0004	0.0036	43.06
0.211	0.006	0.0004	0.0056	37.68
0.249	0.008	0.0004	0.0076	32.76
0.285	0.010	0.0004	0.0096	29.69



P3.2. Slope of the Scatchard plot presents a K value of 166.81.

P3.3. Intercept of this plot is 62.27. Thus,
$K\Delta\varepsilon I_{2(0)} = 62.274$
$166.81 \times \Delta\varepsilon \times 4.0 \times 10^{-4} = 62.27$
$\Delta\varepsilon$ =933.2 $L\ mol^{-1}cm^{-1}$

P3.4. A at 520 nm for pure I_2 (4.0×10^{-4} M) is 0.46.
$A = \varepsilon_{I_2} l c_{I_2}$
$0.46 = \varepsilon_{I_2} 4.0 \times 10^{-4}$
$\varepsilon_{I_2} = 1150\ L\ mol^{-1}cm^{-1}$

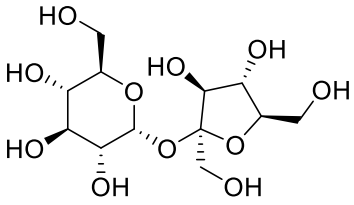
P3.5. $\Delta\varepsilon = \varepsilon_{I_2.pyr} - \varepsilon_{I_2}$
$933.2 = \varepsilon_{I_2.pyr} - 1150$
$\varepsilon_{I_2.pyr} = 2083.3 L\ mol^{-1}cm^{-1}$

P3.6. Yes, there is an isosbestic point in this experiment.

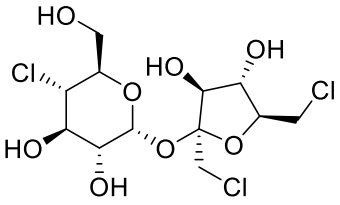
P3.7. The isosbestic point indicates a single equilibrium, which confirms a 1:1 stoichiometry for the formation of pyridine–iodine complex.

Problem P4. 1-Bromobutane

Nucleophilic substitution reactions are the most fundamental reactions among the organic functional group transformations. In these reactions, an electronegative atom or electron-withdrawing group is replaced by another atom or group. Replacement of the hydroxyl group is subject to special interest since it has a vital role in carbohydrate chemistry. For instance, sucrose is commonly used in our everyday life since many carbohydrates taste sweet. When we consume sucrose, excess calories are stored as fat in our bodies. To avoid the storage of fat because of excessive sucrose consumption, sucrose can be converted to synthetic sweetener, sucralose, through substitution reactions. On the other hand, sucralose is known diet friendly and it is much sweeter than sucrose.

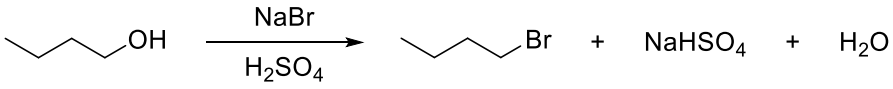


Sucrose



Sucralose

Considering the impact of substitution reactions in our everyday life, in this task, you are asked to synthesize 1-bromobutane starting from 1-butanol by an S_N2 reaction. Among several routes, an aqueous solution of sodium bromide and excess sulfuric acid method is preferred.



Chemicals

Substance	Name	State	GHS Hazard Statement
C_4H_9OH	1-Butanol	Liquid	H226, H302, H315, H318, H335, H336, P210, P280, P301 + P312 + P330, P302 + P352, P305 + P351 + P338 + P310
H_2SO_4	Sulfuric acid	Aqueous solution	H290, H314, P280, P301 + P330 + P331, P303 + P361 + P353, P305 + P351 + P338 + P310
NaBr	Sodium bromide	Solid	Not hazardous

NaOH	Sodium hydroxide	Aqueous solution	H290, H314, P280, P301 + P330 + P331, P303 + P361 + P353, P305 + P351 + P338 + P310
$CaCl_2$	Calcium chloride	Solid	H319, P264, P280, P305 + P351 + P338, P337 + P313

Glassware and equipment

- 1 Graduated cylinder, 10 mL
- 1 Graduated cylinder, 50 mL
- 1 Weighing dish
- 1 Weighing balance (0.01 g)
- 1 Spatula
- 2 Laboratory stands
- 1 Thermometer
- 1 Magnetic stirrer
- Bossheads and clamps
- 1 Condenser
- 1 Reflux condenser
- 1 Round-bottom flask, 100 mL
- 1 Dropping funnel
- 1 Distillation head
- 1 Distillation adapter
- 1 Erlenmeyer flask, 50 mL
- 1 Separatory funnel, 100 mL
- Ice-water bath

Procedure

1. Add 13.3 g of sodium bromide, 15 mL of water, and 10 mL of 1-butanol to a 100 mL round-bottom flask.

2. Cool the mixture in an ice-water bath.

3. Slowly **add** 11.5 mL of concentrated sulfuric acid while stirring and cooling the reaction mixture. (Warning: Be careful in handling concentrated sulfuric acid.)

4. Place the flask on a hot plate, clamp it securely, and fit it with a short reflux condenser. Heat the resulting mixture to boiling point. Adjust the heat for brisk and steady refluxing.

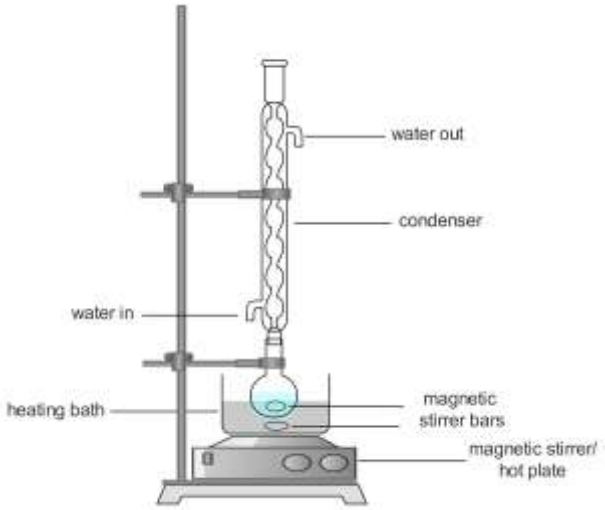


Figure P4-1. Refluxing apparatus

5. Reflux for 45 minutes, remove the heater, and let the condenser drain for a few minutes.

6. Remove the condenser, mount the distillation head to the flask, and set up the condenser for simple distillation through the distillation adapter into the 50 mL Erlenmeyer flask. Clamp joints of the glassware securely.

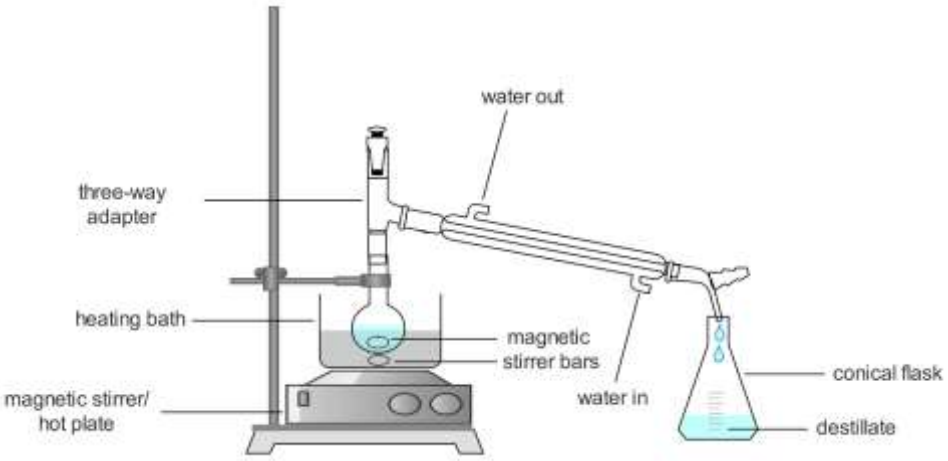


Figure P4-2. Distillation apparatus

7. Distill the mixture until clear water droplets appear.

8. Pour the distillate into a separatory funnel, shake with about 10 mL of water, and **note** that *n*-butyl bromide (1-bromobutane) now forms the lower layer. Pink coloration in this layer can be discharged by adding a little bit of sodium bisulfite and shaking the separatory funnel again (See P5.5 for detailed explanation about using separatory funnel and extraction process).

9. Drain the lower layer of 1-bromobutane into a clean flask, clean and dry the separatory funnel, and return the 1-bromobutane to the cleaned separatory funnel.

10. Then **add** 10 mL of precooled concentrated sulfuric acid to the separatory funnel, **shake** the funnel, and wait 5 minutes for separation of the layers. (Warning: Be careful in handling concentrated sulfuric acid.)

11. Separate the layers. Then **wash** 1-bromobutane with 10 mL of 3 M sodium hydroxide solution to remove traces of acid.

12. Dry the cloudy 1-bromobutane by adding anhydrous calcium chloride pellets (about 1 g) while stirring until the liquid becomes clear.

13. After 5 minutes, **decant** or **filter** the dried liquid into a 25 mL flask.

14. Distill and **collect** the product boiling in the range of 99–103 °C using a simple distillation apparatus.

Question

P4.1. In step 8, the organic layer is treated with a little bit of sodium bisulfite. **Explain** the reason.

P4.2. Explain the roles of NaBr and H_2SO_4 in the reaction.

P4.3. Is this reaction **possible** in the absence of a strong acid?

P4.4. Compare the ^1H NMR spectra of 1-butanol and 1-bromobutane in $CDCl_3$ in terms of number of peaks and multiplicities.

P4.5. Would you expect other by-products to be formed in this reaction? **What is it**?

Solution:

P4.1. Sodium bisulfite is used to remove remaining bromine in the organic layer.

P4.2. NaBr in this reaction is the source of bromide ion (Br^-) as a nucleophile, occurring a substitution reaction. H_2SO_4 protonates the hydroxyl group of 1-butanol to give $-OH_2^+$, which is an easy leaving group.

P4.3. The –OH group of 1-butanol needs to be converted to an easy leaving group by means of protonation. As a result, in the absence of an acid, 1-bromobutane is not likely to be obtained through an S_N2 reaction mechanism.

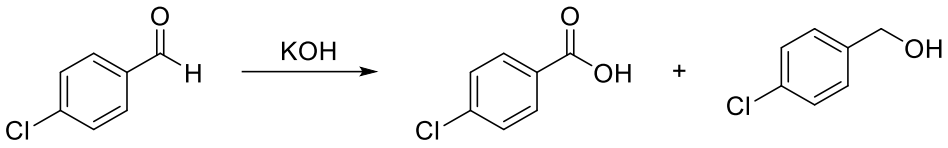
P4.4.

- 1-Butanol has 5 resonance peaks in its ^1H NMR spectrum: 1 broad singlet, 2 triplets, 1 quintet, and 1 sextet. Additionally, the singlet triplet peak can be exchanged by deuterium when 1-butanol is treated with D_2O.
- 1-Bromobutane has 4 resonance peaks in its ^1H NMR spectrum: 2 triplets, 1 quintet, and 1 sextet.

P4.5. Since the reaction is carried out at boiling temperature, etherification and elimination reactions are also possible in strong acidic medium.

Problem P5. Cannizzaro Reaction

Aldehydes are widespread in nature. Most of them are known for their sweet odors. For instance, vanillin exists in vanilla with its distinct odor. Aldehyde functional group-containing molecules are often used in perfumes because of their pleasant fragrance. Benzaldehyde provides the distinctive smell of almonds. Stanislao Cannizzaro discovered in 1853 that benzaldehyde on treatment with a base gave equimolar quantities of benzoic acid and benzyl alcohol. In this task, you are asked to prepare *p*-chlorobenzoic acid and *p*-chlorobenzyl alcohol through a Cannizzaro reaction of *p*-chlorobenzaldehyde.



Cannizzaro is a disproportionation reaction in which an internal oxidation/reduction reaction occurs. The reaction of an aldehyde with a strong base takes place only if the aldehyde has no alpha hydrogen atoms. The mechanism of the Cannizzaro reaction involves hydride ion (H^-) transfer, which takes place only in the presence of a strong nucleophile.

Chemicals

Substance	Name	State	GHS Hazard Statement
ClC_6H_5CHO	*p*-Chlorobenzaldehyde	Solid	H302, H315, H317, H319, H411, P273, P280, P302 + P352, P305 + P351 + P338
KOH	Potassium hydroxide	Solid	H290, H302, H314, P260, P280, P301 + P312 + P330, P301 + P330 + P331, P303 + P361 + P353, P305 + P351 + P338 + P310
$(C_2H_5)_2O$	Diethyl ether	Liquid	H224, H302, H336, H412, P210, P273, P301 + P312 + P330, P403 + P233
HCl	Hydrochloric acid	Aqueous solution	H290, H314, H335, P260, P280, P303 + P361 + P353, P304 + P340 + P310, P305 + P351 + P338 + P310
$NaHSO_3$	Sodium bisulfite	Aqueous solution	H302, P301 + P312 + P330

$NaHCO_3$	Sodium bicarbonate	Aqueous solution	Not a hazardous substance or mixture according to Regulation (EC) No. 1272/2008.
Na_2SO_4	Sodium sulfate	Solid	Not hazardous
C_2H_5OH	Ethanol	Liquid	H225, H319, P210, P305 + P351 + P338
CH_3OH	Methanol	Liquid	H225, H301 + H311 + H331, H370
CH_2Cl_2	Methylene chloride	Liquid	H315, H319, H336, H351
CH_3COCH_3	Acetone	Liquid	H225, H319, H336
	Petroleum ether	Liquid	H225, H304, H315, H336, H411

Glassware and equipment

- 1 Two-neck round bottom flask, 50 mL
- 1 Magnetic stirrer
- 1 Graduated cylinder, 50 mL
- 1 Condenser
- 1 Separatory funnel, 100 mL
- 1 Büchner funnel, 250 mL
- 1 Büchner flask
- 1 Filter paper
- 2 Erlenmeyer flasks
- 1 Funnel
- 1 TLC development tank
- TLC sheets
- 1 UV lamp
- 1 Hot plate

Procedure

1. <u>Dissolve</u> 2 g of *p*-chlorobenzaldehyde in 6 mL of ethanol in a 50 mL two-neck round bottom flask while stirring with a magnetic rod.

2. <u>Add</u> 6 mL of water to the above solution followed by the addition of 3.2 g of KOH in portions.

3. <u>Mount</u> a condenser above the reaction flask and heat the reaction mixture to 60–70 °C.

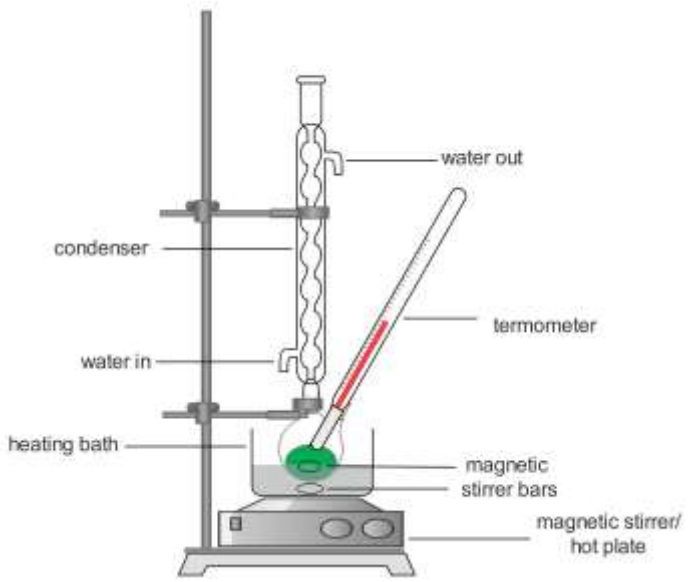


Figure P5-1. The reaction apparatus with two-neck round bottom flask.

4. After 45 minutes, **remove** the flask from the water bath, **allow** the reaction mixture cool down to room temperature, **transfer** into a separatory funnel, and **add** 30 mL of water.

5. Perform extraction with 7 mL of methylene chloride three times. To do the extraction:

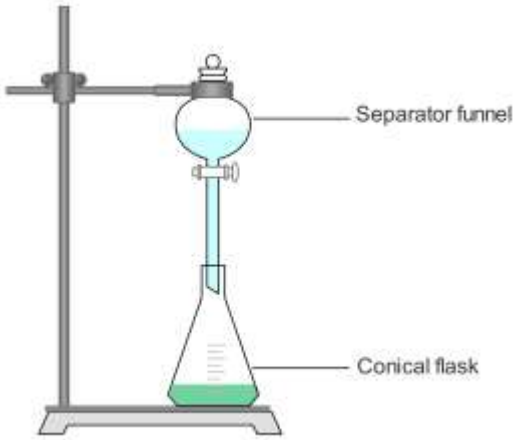


Figure P5-2. Extraction apparatus.

- Before adding methylene chloride to the separatory funnel, check the stopcock.
- To have sufficient room for extraction, fill the separatory funnel no more than three-fourths full.

- When the stoppered funnel is shaken to distribute the components between methylene chloride and water, pressure always develops through volatilization of methylene chloride from the heat of the hands can increase the pressure.
- The funnel is grasped so that the stopper is held in place by one hand and the stopcock by the other. After a brief shake or two, the funnel is held in the inverted position, and the stopcock is opened cautiously to release pressure. This process is repeated with pressure released as necessary.
- When equilibration is judged to be complete, the layers are allowed to separate.
- *p*-chlorobenzyl alcohol is distributed wholly or largely into the bottom methylene chloride layer, whereas *p*-chlorobenzoic acid sodium salt, inorganic salts, acids or bases pass into the upper water layer.
- Separate the methylene chloride and aqueous layers by drowning off the bottom methylene chloride layer.
- This process is repeated three times and organic layers are collected in to an Erlenmeyer.
- Aqueous layer is drawn of in to another Erlenmeyer.

6. **Acidify** the aqueous basic solution with concentrated HCl until the solution is acidic (Acidity of solution can be inspected by Litmus paper). This will cause *p*-chlorobenzoic acid to precipitate as a white solid.

7. After cooling down the solution, **filter** the white solid under vacuum using a Büchner funnel.

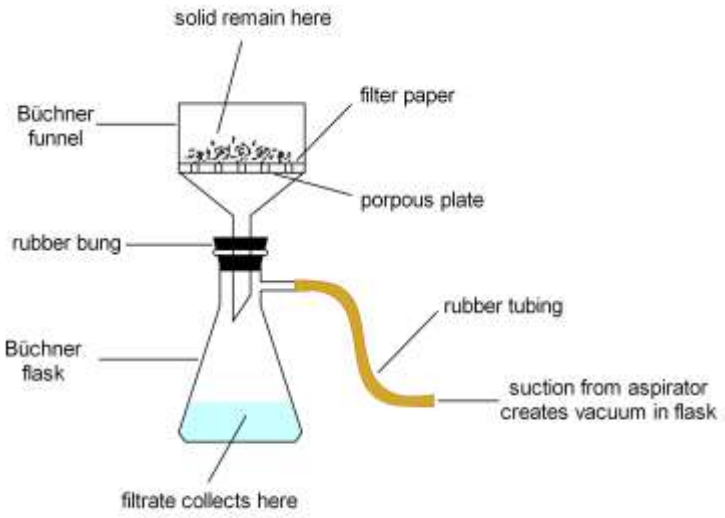


Figure P5-3. Vacuum filtration with Büchner funnel and flask.

8. **Recrystallize** the obtained *p*-chlorobenzoic acid from ethanol. After air drying, **weigh** the product, and **calculate** the percent yield.To recrystallize *p*-chlorobenzoic acid from ethanol: Place the *p*-chlorobenzoic acid in an Erlenmeyer flask (never use a beaker), add enough ethanol to cover the crystals, and then heat the flask on a steam. Add ethanol gradually, keeping it at the

boiling point, until all of the solute dissolves (Be sure no flames are nearby when working with ethanol). Once it has been ascertained that the hot solution is saturated with the *p*-chlorobenzoic acid just below the boiling point of ethanol, allow the solution to cool down to room temperature slowly. With slow cooling, recrystallization should begin immediately. If not, add a seed crystal or scratch the inside of the Erlenmeyer with a glass rod. Once recrystallization is complete, *p*-chlorobenzoic acid crystals must be filtered using Büchner funnel-Büchner flusk and washed with ice-cold ethanol.

9. Organic phases from step 5 are gathered together in a separatory funnel and **shaken** with 15 mL of 40% bisulfite solution. The mixture is then washed with saturated sodium bicarbonate until a neutral solution is obtained.**10. Drying** the organic phase with sodium sulfate followed by filtration from filter paper and removal of solvent *via* simple distillation will afford crude *p*-chlorobenzyl alcohol.

11. *p*-Chlorobenzyl alcohol is recrystallized from acetone/petroleum ether (1:9).

12. Perform TLC analysis for *p*-chlorobenzoic acid, *p*-chlorobenzyl alcohol and starting material *p*-chlorobenzaldehyde using CH_2Cl_2/MeOH (9/1) as the eluent. Report the R_f values. TCL analysis can be performed as follow:

- Transfer the TLC eluent (CH_2Cl_2/MeOH: 4/1, approximately 1 mL) in to the TLC development tank using a Pasteur pipette.
- Insert the TLC plate using tweezers, cover the tank with its cap and let the eluent reach approximately 0.5 cm bellow the top edge of the plate.
- Using tweezers, take the TLC plate out, draw the eluent front line and let the plate air-dry.
- Place the TLC plate under the UV lamp in a hood. With a pencil, circle all the visualized spots and calculate the R_f values of p-chlorobenzaldehyde and products designated as spots A, B, and C on Figure P5-3.

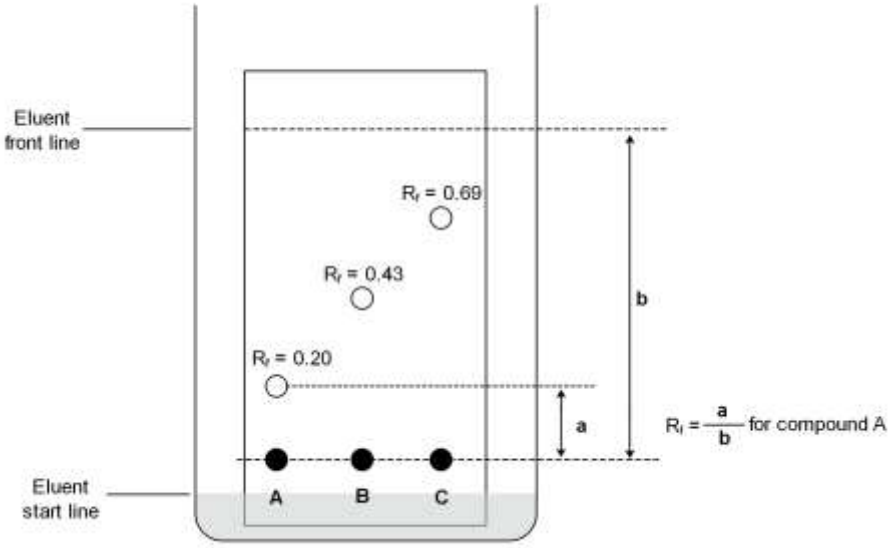


Figure P5-4. Sample TLC plate and representative R_f values.

13. **Measure** the melting points of the products and **report** their purity based on TLC results and melting points.

Question

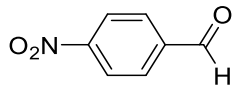
P5.1. If the aldehyde in this reaction has an α-hydrogen what kind of a reaction do you **expect**?

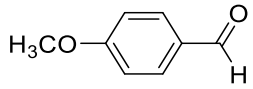
P5.2. **Write** the products if butanal or pivalaldehyde is used as reactant in this reaction.

P5.3. **Tick** the bases that can be used instead of KOH in this reaction.

- ☐ K_2CO_3
- ☐ NaOH
- ☐ $NaHCO_3$
- ☐ Et_3N

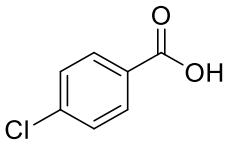
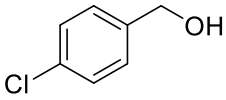
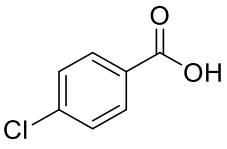
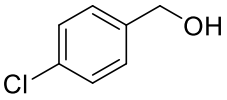
P5.4. **Which reacts faster** in the Cannizzaro reaction if the initial nucleophilic attack is the rate determining step?

☐ 

☐ 

P5.5. **What is the intermediate state** in this reaction?

P5.6. **Tick** the oxidation and reduction products of this reaction.

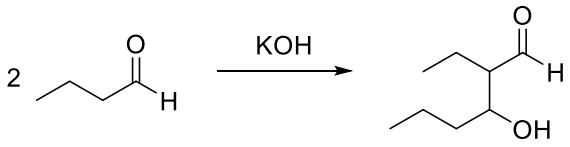
Oxidation product		Reduction product	
☐	☐	☐	☐
			

Solution:

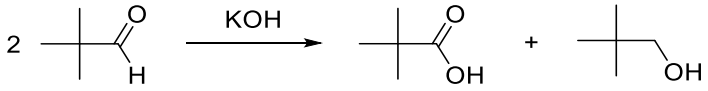
P5.1. If the aldehyde has an α-hydrogen an aldol reaction will take place through deprotonation of α-carbon.

P5.2.

- With butanal an aldol reaction occurs and the product is



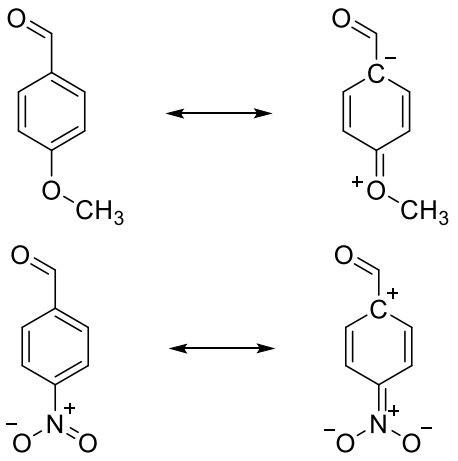
- With pivalaldehyde a Cannizzaro reaction occurs and the products are



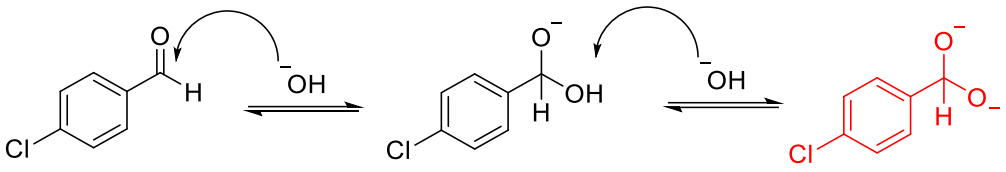
P5.3.

☒ K_2CO_3
☒ NaOH
☐ $NaHCO_3$
☐ Et_3N

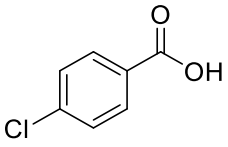
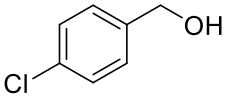
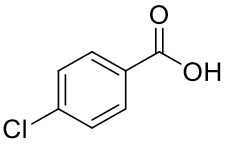
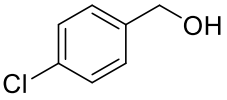
P5.4. Since $–NO_2$ is an electron-withdrawing group it will make carbonyl carbon more electropositive compared to the $–OCH_3$ group. Therefore, *p*-nitrobenzaldehyde reacts faster in the Cannizzaro reaction.



P5.5.



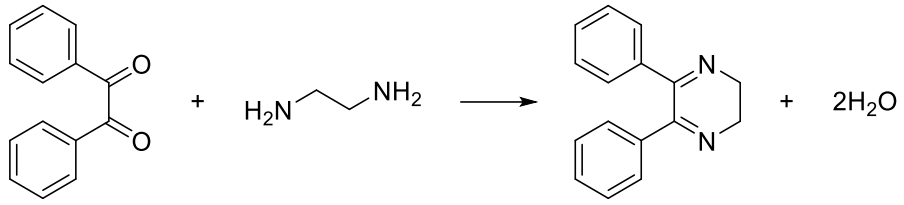
P5.6. Tick the oxidation and reduction products of this reaction.

Oxidation product		Reduction product	
☒	☐	☐	☒
			

Problem P6. 2,3-Dihydro-5,6-diphenylpyrazine

An imine is a functional group or chemical compound containing a carbon–nitrogen double bond. Some imine compounds can sometimes be referred to as Schiff bases. Imines may find utility in a wide range of contexts, including the development antimicrobial, antiviral and anticancer agents. Imines are also common intermediates in enzymatic reactions and are used as common ligands in coordination chemistry. They are also used in nanotechnology for water treatment, encapsulation and functionalized magnetic nanoparticle production.

In this experiment you are asked to synthesize 2,3-dihydro-5,6-diphenylpyrazine (DPP) through an imine formation reaction, starting from benzil and ethylenediamine.



DPP

Chemicals

Substance	Name	State	GHS Hazard Statement
$C_{14}H_{10}O_2$	Benzil	Solid	H315, H319, P302 + P352, P305 + P351 + P338
$H_2NCH_2CH_2NH_2$	Ethylenediamine	Liquid	H226, H302 + H332, H311, H314, H317, H334, H412, P210, P273, P280, P301 + P330 + P331, P302 + P352, P304 + P340, P305 + P351 + P338, P308 + P310
C_2H_5OH	Ethanol	Liquid	H225, H319, P210, P305 + P351 + P338

Glassware and equipment

- 1 Round-bottom flask, 250 mL
- 1 Stirring bar
- 1 Pipette, 10 mL
- 1 Reflux condenser
- 1 Beaker, 100 mL
- 1 Crystallization dish, 500 mL

- 1 Büchner funnel
- 1 Büchner flask
- 1 Filter paper
- 1 TLC development tank
- 1 TLC sheets
- 1 UV lamp
- 1 Magnetic stirrer with a hot plate
- 1 Ice-water bath

Procedure

1. **Dissolve** 10 g of benzil in 30 mL of ethanol (95%) by heating in a 250 mL round bottom flask. **Add** 4.5 mL of 68% ethylenediamine (or an equivalent quantity of ethylenediamine in different concentrations).

2. While stirring, **heat** the mixture in a water bath under a reflux condenser for 45 minutes (See Figure P4.1 for reflux condenser apparatus).

3. If crystals have not formed in the flask, immediately **transfer** the hot supersaturated solution into a 100- or 150-mL beaker. The difficulty of removing the crystals from the flask is thus avoided.

4. Often crystallization occurs at once when the solution is poured into the beaker, and sufficient heat is evolved to cause the alcohol to boil. **Cool** to room temperature. Finally, **place** in an ice-bath (For detailed recrystallization see P5.8).

5. The loss due to solubility in cold alcohol is negligible. **Filter** the crystals, and **wash** them with a little alcohol. **Dry** the product using a suction filter (For vacuum filtration apparatus see P5.7).

6. **Weigh** the dried product and **calculate** the percent yield.

7. **Determine** melting point (highly purified DPP melts at 161.5–162.5 °C), and **reserve** a little amount of product for TLC analysis.

8. **Perform** TLC analysis using the recrystallized product and reference benzil (See P5.12 for a sample procedure of TLC analysis).

9. **Report** the Rf values of each compound and check the purity of the recrystallized DPP.

Question

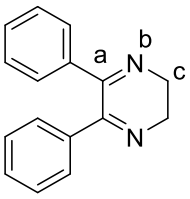
P6.1. **What is the product** when DPP is oxidized?

P6.2. Is the oxidation product of the DPP **aromatic**?

P6.3. **Which** of the following reactants or methods could be used for the oxidation of DPP?

- ☐ 2,3-Dichloro-5,6-dicyanobenzoquinone (DDQ)
- ☐ Heating in air
- ☐ Et_3N
- ☐ Na_2CO_3
- ☐ Slight heating under vacuum

P6.4. **What are the hybridizations** of nitrogen (**b**) and carbons (**a** and **c**) in DPP?

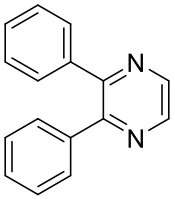


DPP

P6.5. **Draw** the structures of the products when 1,3-propanediamine and 1,4-butanediamine were used instead of ethylenediamine.

Solution:

P6.1. The oxidation product of DPP is 2,3-diphenylpyrazine.



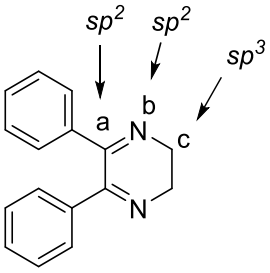
P6.2. The oxidation product 2,3-diphenylpyrazine is an aromatic compound since:

- all the atoms of the pyrazine ring are sp^2 hybridized and
- the pyrazine ring obeys Hückel's rule.

P6.3. The following marked reactants or conditions could be used for the oxidation of DPP.

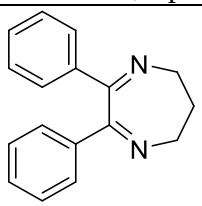
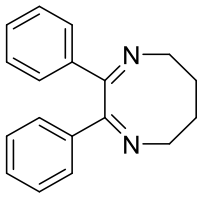
- ☒ 2,3-Dichloro-5,6-dicyanobenzoquinone (DDQ)
- ☒ Heating in air
- ☐ Et_3N
- ☐ Na_2CO_3
- ☐ Slight heating under vacuum

P6.4.



DPP

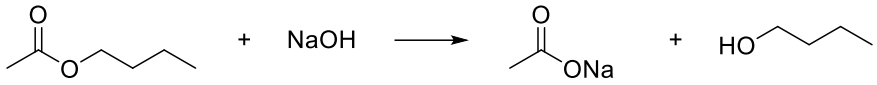
P6.5.

Products with 1,3-propanediamine and 1,4-butanediamine	
	

Problem P7. Determination of Rate Constants for *n*-Butyl Acetate Hydrolysis

Hydrolysis, in other words splitting with water, is one of the most important reaction types that an ester can undergo. The hydrolysis of ester can be catalyzed either by acids or by bases and when the catalyst is a base, the reaction yields a carboxylate salt and an alcohol.

In this experiment, you are asked to determine rate constants of the alkaline hydrolysis of *n*-butyl acetate using sodium hydroxide, which is a typical second-order reaction.



The rate of the reaction can be calculated by the following equation:

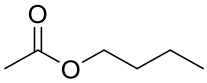
$$\text{Reaction rate} = k[CH_3COOC_4H_9][OH^-]$$

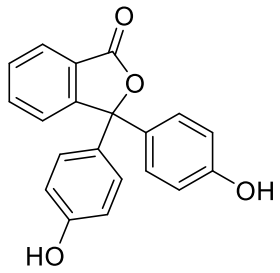
Then

$$\frac{1}{[A]} - \frac{1}{[A]_0} = k \times t,$$

where [A] is the concentration of reactant at time t ([A]= [B]), $[A]_0$ is the initial concentration and k is the second-order constant, which has dimension of concentration^{-1} time^{-1} (**L mol^{-1} s^{-1}**). In this case, a characteristic plot that will produce a linear function is 1/ [A] vs. time t, with a slope of k.

Chemicals

Substance	Name	State	GHS Hazard Statement
	*n*-Butyl acetate	Aqueous solution	H226, H336, P210
NaOH	Sodium hydroxide	Aqueous solution	H290, H314, P280, P301 + P330 + P331, P303 + P361 + P353, P305 + P351 + P338 + P310
HCl	Hydrochloric acid	Aqueous solution	H290, H314, H335, P260, P280, P303 + P361 + P353, P304 + P340 + P310, P305 + P351 + P338 + P310

	Phenolphthalein	Solution	H226, H319, P210, P280, P303 + P361 + P353, P337 + P313, P370 + P378, P403 + P235

Glassware and equipment

- 1 Laboratory stand with burette clamp
- 5 Volumetric pipettes, 20 mL
- 5 Pipette pump
- 5 Titration flasks, 250 mL
- 10 Volumetric flasks, 250 mL
- 1 Burette, 50 mL
- Stop watch

Procedure

1. Fill the burette with the solution of hydrochloric acid (HCl) (0.02 M).

2. Transfer 60 mL of the solution of *n*-butyl acetate (0.02 M) into the volumetric flask and 60 mL of the solution of sodium hydroxide (0.02 M) into another volumetric flask at room temperature. **Mix** the two solutions in titration flask.

3. Five minutes after mixing, **pipette** 20 mL of reaction mixture into a titration flask. **Add** 4 drops of phenolphthalein indicator to the solution.

4. Titrate the sample solution with HCl (0.02 M) until the solution become as colorless. **Record** the amount of HCl used. *Hint: you can add 6 ml of HCl solution immediately and then carry out the rest of titration with more care*.

5. Repeat steps 3 and 4 for 10, 15, 20, and 25 minutes from the moment of mixing. **Fill** in the table below.

Hint: You can repeat each step several times to increase the accuracy of data.

Calculations & Analysis:

Fill in the blanks in the following table with the data measured during the experiment.

Time (min)	**V_{HCl} (mL)**
5	
10	
15	
20	
25	

P7.1. **Calculate** the concentration of $[OH^-]$ at each time.

P7.2. **Plot** $\frac{1}{[OH^-]}$ vs. time .

P7.3. **Calculate** the rate constant.

P7.4. **Calculate** the reaction rate.

P7.5. **Calculate** the initial half-life for the reaction with initial conditions.

Solution:

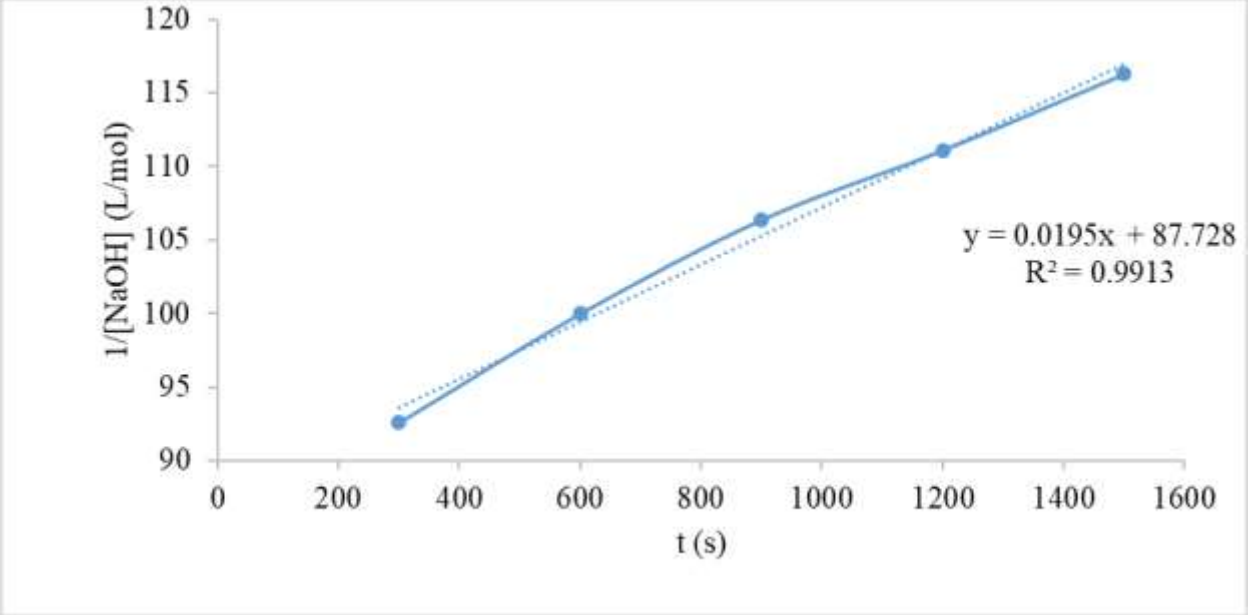
Filled table with the measured data in the experiment.

Time (min)	V_{HCl} (mL)
5	**10.8**
10	**10**
15	**9.4**
20	**9**
25	**8.6**

P7.1.

t (minutes)	t (s)	Remaining NaOH (mol)	Remaining [NaOH] (mol/L)	1/[NaOH]
5	300	0.000216	0.0108	92.5925926
10	600	0.0002	0.01	100
20	1200	0.000188	0.0094	106.382979
15	900	0.00018	0.009	111.111111
25	1500	0.000172	0.0086	116.27907

P7.2.



P7.3.

$$\frac{1}{[A]} - \frac{1}{[A]_0} = k.t,$$

k = 0.0195 L mol^{-1} s^{-1}

P7.4.

Reaction rate = k[$CH_3COOC_4H_9$][NaOH]
Reaction rate = 0.0195
$L\ mol^{-1}s^{-1} \times 0.01\ mol\ L^{-1} \times 0.01\ mol\ L^{-1} = \mathbf{1.95 \times 10^{-6}\ mol\ L^{-1}s^{-1}}$

P7.5. The half-life ($t_{1/2}$) equation for a second-order reaction is given by:

$$t_{1/2} = \frac{1}{k \times [A]_o}$$

$$t_{1/2} = \frac{1}{0.0195\ L\ mol^{-1}s^{-1} \times 0.01\ mol\ L^{-1}}$$

$$\boldsymbol{t_{1/2} = 5128\ seconds}$$

Problem P8. Activation Energy of Bromide / Bromate Reaction

Activation energy is the minimum amount of energy which is required for a chemical reaction to occur. Activation energy can be defined also as the energy difference between the reactants and the activated complexes.

In this experiment, you are asked to calculate the activation energy of the following reaction:

$$KBrO_3 + 5KBr + 3H_2SO_4 \rightarrow 3K_2SO_4 + 3Br_2 + 3H_2O$$

In this reaction, the reaction order for $KBrO_3$ and KBr is the same and is observed to be one. By using Arrhenius equation:

$$k = A \cdot e^{-\frac{E_a}{RT}} \text{ or } ln\, k = ln\, A - \frac{E_a}{RT}$$

For a first rate reaction where $A \xrightarrow{k} products$;

$$-\frac{d[A]}{dt} = k[A]$$
$$-\int_{A_0}^{A} \frac{d[A]}{[A]} = k\int_0^t dt$$
$$ln\frac{[A]_0}{[A]} = k \times t = p$$

$p = k \times t$ and it is a constant. Logarithm of this equation:

$$\ln p = \ln k + \ln t$$
$$\ln k = \ln p - \ln t$$

If we use $\ln k = \ln p - \ln t$ for Arrhenius equation then;

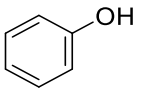
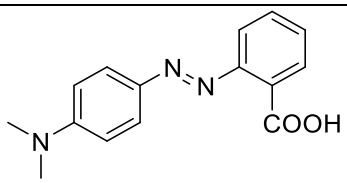
$$\ln p - \ln t = \ln A - \frac{E_a}{RT}$$
$$-\ln t = (\ln A - \ln p) - \frac{E_a}{RT}$$

Consider, $\ln A - \ln k = K$ then;

$$\ln t = \frac{E_a}{RT} - K$$

Completion of the reaction will be observed by following the decoloration of the solution. The reaction yields Br_2, which gives a very rapid reaction with phenol yielding tribromophenol. When all the phenol is used, the remaining Br_2 will decolorate the indicator.

Chemicals

Substance	**Name**	**State**	**GHS Hazard Statement**
	Phenol	Solution	H301 + H311 + H331, H314, H341, H373, P201, P260, P280, P301 + P310 + P330, P303 + P361 + P353, P305 + P351 + P338 + P310
KBr	Potassium bromide	Solid	H319, P280, P305 + P351 + P338, P337 + P313
$KBrO_3$	Potassium bromate	Solid	H271, H301, H350, P201, P210, P301 + P310 + P330
H_2SO_4	Sulfuric acid	Aqueous solution	H290, H314, P280, P301 + P330 + P331, P303 + P361 + P353, P305 + P351 + P338 + P310
	Methyl red	Solution	R 51/53 , S 61

Glassware and equipment

- 3 Glass volumetric pipettes, 10 mL
- 10 Glass test tubes, 15 mL
- Wash bottle
- 2 Laboratory stands with appropriate clamps
- Thermostated water bath
- Stop watch

Procedure

1. Prepare the following solutions in two separate test tubes:

Solution I: 5 mL of 0.01 M phenol, 5 mL of KBr–$KBrO_3$ solution (dissolve 50 mg of KBr and 14 mg of $KBrO_3$ in 5 mL of deionized water), a few drops of methyl red indicator

Solution II: 2.5 mL of 0.5 M H_2SO_4

2. Place them into a thermostated circulating water bath.

3. When the temperature reaches 25 °C, **mix** the two solutions together, **start** your timer, and **stop** the timer when the red color completely disappears. **Record** the time.

4. Repeat steps 1–3 for 35 °C, 45 °C, 55 °C, 65 °C.

If you do not have a thermostat, instead of different temperatures, perform the experiment in an ice bath (or cold water) and at room temperature, then measure the temperature, redesign the tables in step 8.2 and 8.3 accordingly.

Calculations & Analysis

P8.1. Calculate final concentrations of H_2SO_4, KBr, and $KBrO_3$.

P8.2. Fill in the following table.

T (°C)	25	35	45	55	65
t (seconds)					

P8.3. Calculate $ln\ t$ and $1/T$ for each step and fill in the table below.

ln t					
1/T (K^{-1})					

P8.4. Plot $ln\ t$ vs. $1/T$ and **determine** the slope of the plot.

P8.5. Calculate E_a.

Solution:

Filled in the blanks in the following table with the measured data in the experiment.

P8.1.

Final concentrations:

For H_2SO_4:

$$Initial\ concentration \times Initial\ volume = Final\ concentration \times Final\ volume$$
$$0.5\ M \times 2.5\ mL = Final\ concentration \times 12.5\ mL$$

$[H_2SO_4]$ = **0.1 M**

For KBr:

$$[KBr] = \frac{Amount\ of\ KBr\ in\ moles}{Final\ volume} = \frac{\frac{50\ mg}{119\ mg\ mmol^{-1}}}{12.5\ mL} = \mathbf{0.0033\ M}$$

For $KBrO_3$:

$$Concentration\ of\ KBrO_3 = \frac{Amount\ of\ KBrO_3\ in\ moles}{Final\ volume} = \frac{\frac{14\ mg}{167\ mg\ mmol^{-1}}}{12.5\ mL}$$
$$= \mathbf{6.70 \times 10^{-3}\ M}$$

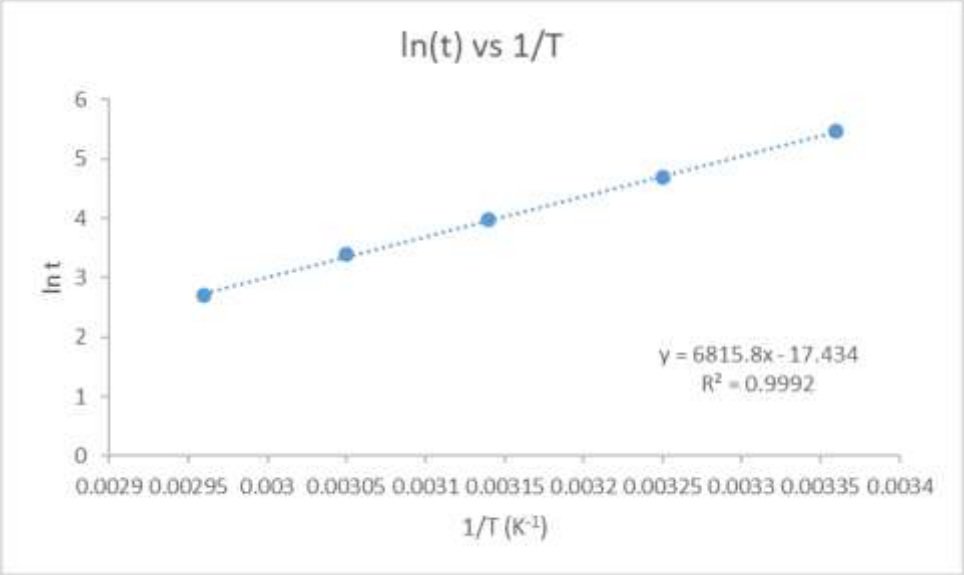
P8.2. Filled table with the data measured during the experiment.

T (°C)	25	35	45	55	65
t (seconds)	237	110	53	30	15

P8.3. Calculated lnt and 1/T for each step.

ln t	5.47	4.46	3.97	3.40	2.70
1/T (K^{-1})	0.00336	0.00325	0.00314	0.00305	0.00296

P8.4. Plot ln t vs. 1/T and determine the slope of the plot.



P8.5. Slope of ln t vs. 1/T yields $\frac{Activation\ Energy\ (E_a)}{8.314\ J\ mol^{-1}\ K^{-1}}$

Slope: 6815.8

$$\boldsymbol{Ea = 56666\ J\ mol^{-1}}$$

The End