

Chemistry: The flavor of life

Preparatory Problems

46th International Chemistry Olympiad (IChO - 2014)

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Sincerely yours,
Editors



Preface

We are happy to provide Preparatory Problems for the 46th International Chemistry Olympiad. These problems were prepared with reliance on fundamental topics firmly covered in high school chemistry courses along with some advanced topics for the chemistry olympiad competition. These topics are listed under “Topics of Advanced Difficulty”, and their applications are given in the problems. Solutions will be sent to Head Mentors on February 20th, 2014 and updated on www.icho2014.hus.edu.vn on May 31st, 2014. Although a lot of efforts have gone to making this Booklet, some mistakes, typos may still be there. We welcome any comments, corrections, or questions about the problems to icho2014prep@hus.edu.vn.

We hope that these problems will be motivating for students to participate in the IChO-2014 competition. We believe that IChO-2014 will not only be a chemistry competition, but also a pleasant time for you to know about Vietnamese culture. We look forward to seeing you in Hanoi and at Hanoi University of Science, Vietnam National University in Hanoi.

Hanoi, January 31st, 2014

Editor in Chief

Nguyen Tien Thao



February 18th, 2014 (Revised)



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Fields of Advanced Difficulty

Theoretical

Kinetics: Integrated first- and second-order rate equation; analysis of moderately complex reactions mechanisms using the steady state approximation, the use of the Arrhenius equation.

Thermodynamics: Electrochemical cells, the relationship between equilibrium constants, electromotive force and standard Gibbs energy, the variation of the equilibrium constant with temperature.

Quantum mechanics: Particle-in-a-box calculations, orbital-overlaps, spin-orbit coupling.

Spectroscopy: Interpretation of IR spectra and relatively simple ^1H , ^{13}C , and ^{27}Al NMR spectra: chemical shifts, multiplicities, coupling constants and integrals.

Advanced Inorganic: Trans effect; the use of simple crystal field theory to explain electronic configurations in octahedral and tetrahedral complexes; calculation of the magnetic moment using the spin-only formula, solid state structures, packing arrangement.

Advanced Organic: Stereoselective transformations; aromatic nucleophilic substitution; polycyclic aromatic compounds and heterocycles.

Practical

Basic synthesis techniques: Thin layer chromatography, Extraction, Filtration, Drying, Titration.

UV – Vis spectroscopy.

Physical Constants, Symbols and Conversion Factors

Avogadro's constant, $N_A = 6.0221 \times 10^{23} \text{ mol}^{-1}$

Boltzmann constant, $k_B = 1.3807 \times 10^{-23} \text{ J} \cdot \text{K}^{-1}$

Universal gas constant, $R = 8.3145 \text{ J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1} = 0.08205 \text{ atm}\cdot\text{L}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$

Speed of light, $c = 2.9979 \times 10^8 \text{ m}\cdot\text{s}^{-1}$

Planck's constant, $h = 6.6261 \times 10^{-34} \text{ J}\cdot\text{s}$

Faraday constant, $F = 9.64853399 \times 10^4$ C

Mass of electron, $m_e = 9.10938215 \times 10^{-31} \text{ kg} \cdot \text{mol}^{-1}$

Standard pressure, $P = 1 \text{ bar} = 10^5 \text{ Pa}$

Atmospheric pressure, $P_{\text{atm}} = 1.01325 \times 10^5 \text{ Pa} = 760 \text{ mm Hg} = 760 \text{ Torr}$

Zero of the Celsius scale, 273.15 K

$$1 \text{ picometer (pm)} = 10^{-12} \text{ m}; \quad 1 \text{ \AA} = 10^{-10} \text{ m}; \quad \text{nanometer (nm)} = 10^{-9} \text{ m}$$
$$1 \text{ eV} = 1.6 \times 10^{-19} \text{ J}$$

Periodic Table of Elements with Relative Atomic Masses

1																										18									
1 H 1.008		2																								2 He 4.003									
3 Li 6.941		4 Be 9.012												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 32.07		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 72.64		33 As 74.92		34 Se 78.96		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 95.96		43 Tc [98]		44 Ru 101.07		45 Rh 102.91		46 Pd 106.42		47 Ag 107.87		48 Cd 112.41		49 In 114.82		50 Sn 118.71		51 Sb 121.76		52 Te 127.60		53 I 126.90		54 Xe 131.29	
55 Cs 132.91		56 Ba 137.33		57 La 138.91		72 Hf 178.49		73 Ta 180.95		74 W 183.84		75 Re 186.21		76 Os 190.23		77 Ir 192.22		78 Pt 195.08		79 Au 196.97		80 Hg 200.59		81 Tl 204.38		82 Pb 207.2		83 Bi 208.98		84 Po (209)		85 At (210)		86 Rn (222)	
87 Fr (223)		88 Ra 226.0		89 Ac (227)		104 Rf (261)		105 Ha (262)																											
										58 Ce 140.12																									
										59 Pr 140.91																									
										60 Nd 144.24																									
										61 Pm (145)																									
										62 Sm 150.36																									
										63 Eu 151.96																									
										64 Gd 157.25																									
										65 Tb 158.93																									
										66 Dy 162.50																									
										67 Ho 164.93																									
										68 Er 167.26																									
										69 Tm 168.93																									
										70 Yb 173.05																									
										71 Lu 174.97																									
										90 Th 232.04																									
										91 Pa 231.04																									
										92 U 238.03																									
										93 Np 237.05																									
										94 Pu (244)																									
										95 Am (243)																									
										96 Cm (247)																									
										97 Bk (247)																									
										98 Cf (251)																									
										99 Es (254)																									
										100 Fm (257)																									
										101 Md (256)																									
										102 No (254)																									
										103 Lr (257)																									



PART 1. THEORETICAL PROBLEMS

Problem 1. Polar and non-polar molecules

In chemistry, a molecule is considered *non-polar* when its positive charge center and negative charge center coincide, i.e. the charge distribution is symmetrical in the molecule. On the other hand, when a molecule has two distinct centers for positive and negative charges, it is considered *polar*.

This charge distribution property is measured by a quantity called the *dipole moment* which is defined as the magnitude of the charge q and the distance l between the charges:

$$\vec{\mu} = q\vec{l}$$

The dipole moment is a vector pointing from the positive charge center to the negative one.



The dipole moment is often expressed in debyes (D). The relationship between debyes (D) and coulomb meters (C·m) in SI units is as follows: $1 \text{ D} = 3.33 \times 10^{-30} \text{ C} \cdot \text{m}$.

1. The dipole moment is closely related to the molecular geometry. In order to calculate the net dipole moment μ of multi-atomic molecules, we can add the dipole moment vectors for individual bonds. In this case, an individual bond is considered to have its own dipole moment called the bond moment.



For a non-linear molecule with three atoms, ABC, the net dipole moment μ can be calculated by adding vectors in which $\vec{\mu}_1$ and $\vec{\mu}_2$ are the bond moments for AB and AC bonds, and α is the bond angle. Determine the general equation for calculating the net dipole moment.

2. The directions of the individual bond moments should be considered.

2.1 The molecule of CO_2 is linear. Calculate the net dipole moment μ of the molecule.

2.2 A non-linear molecule of A_2B such as H_2S has the net dipole moment $\mu \neq 0$. Determine μ for H_2S if $\mu_{\text{SH}} = 2.61 \times 10^{-30} \text{ C}\cdot\text{m}$ and the bond angle $\alpha = 92.0^\circ$.

3. The bond angle HCH in the formaldehyde molecule is determined experimentally to be approximately 120° ; the bond moments for C-H and C-O bonds are $\mu_{\text{C-H}} = 0.4 \text{ D}$ and $\mu_{\text{C=O}} = 2.3 \text{ D}$, respectively.

3.1 Determine the orbital hybridization of C and O atoms, and plot the overlaps of orbitals in the formaldehyde molecule.

3.2 Calculate the net dipole moment (μ) of the formaldehyde (D), given the order of the electronegativity as $\chi_{\text{O}} > \chi_{\text{C}} > \chi_{\text{H}}$. (*Hints: Electronegativity is the ability of an atom in a molecule to attract shared electrons to itself*).

4. The dipole moments of water and dimethylether in gaseous state are determined as 1.84 D, and 1.29 D, respectively. The bond angle formed by two bond moments of O-H in the water molecule is 105° . The bond angle formed by two bond moments of O-C in the ether molecule is 110° .

Estimate the bond angle formed by the bond moments of O-H and C-O in the methanol molecule, given that the dipole moment of methanol molecule is 1.69 D. Assume that individual bond moments are unchanged in different molecules.



Problem 2. Calculations of lattice energy of ionic compounds

1. Lithium is the lightest metal and does not exist in pure form in nature due to its high reactivity to water, moisture, oxygen... Lithium readily forms ion with a 1+ charge when reacting with nonmetals. Write down the following chemical reactions at room temperature:

1.1 Lithium reacts with water.

1.2 Lithium reacts with halogens, e.g. Cl_2 .

1.3 Lithium reacts with dilute sulfuric acid and concentrated sulfuric acid.

2. The change in enthalpy of a particular reaction is the same whether it takes place in one step or in a series of steps (Hess's law). Use the following data:

Sublimation enthalpy of Li(s) , $\Delta_{\text{S}}H = 159 \text{ kJ}\cdot\text{mol}^{-1}$.

Ionization energy of Li(g) , $I = 5.40 \text{ eV}$.

Dissociation enthalpy of Cl_2 , $\Delta_{\text{D}}H = 242 \text{ kJ}\cdot\text{mol}^{-1}$.

Electron affinity of Cl(g) , $E = -3.84 \text{ eV}$.

Formation enthalpy of LiCl(s) , $\Delta_{\text{f}}H = -402.3 \text{ kJ}\cdot\text{mol}^{-1}$.

$r_{\text{Li}^+} = 0.62 \text{ \AA}$; $r_{\text{Cl}^-} = 1.83 \text{ \AA}$; $N_{\text{A}} = 6.02 \times 10^{23} \text{ mol}^{-1}$.

2.1 Establish the Born-Haber cycle for lithium chloride crystal.

2.2 Calculate the lattice energy U_0 ($\text{kJ}\cdot\text{mol}^{-1}$) using the Born-Haber cycle.

3. In practice, experimental data may be employed to calculate lattice energies in addition to the Born-Haber cycle. One of the semi empirical formulae to calculate the lattice energy U_0 for an ionic compound, which was proposed by Kapustinskii, is as follows:

$$U_0 = -287.2 \frac{Z_+ Z_- \sum v}{r_+ + r_-} \left(1 - \frac{0.345}{r_+ + r_-} \right)$$



where: v is the number of ions in the empirical formula of ionic compound,

r_+ and r_- are the radii of the cation and anion, respectively, in Å,

Z_+ and Z_- are cation and anion charges, respectively,

U_0 is the lattice energy, in $\text{kcal}\cdot\text{mol}^{-1}$.

Use the Kapustinskii empirical formula to calculate U_0 (in $\text{kJ}\cdot\text{mol}^{-1}$) of LiCl crystal, given that $1 \text{ cal} = 4.184 \text{ J}$.

4. Based on the results of two calculation methods in sections 2 and 3, choose the appropriate box:

According to the Born-Haber cycle and Kapustinskii empirical formula for lithium chloride crystal structure, both methods are close to the experimental value.

☐

Only the calculated result of the Born-Haber cycle is close to the experimental value.

☐

Only the calculated result of the Kapustinskii empirical formula is close to the experimental value.

☐

Data: Given the experimental value of lattice energy for LiCl is 849.04 kJ/mol .

5. In the formation of LiCl crystal, it is found out that the radius of lithium cation is smaller than that of chloride anion. Thus, the lithium ions will occupy the octahedral holes among six surrounding chloride ions. Additionally, the body edge length of LiCl cubic unit cells is 5.14 Å . Assume that Li^+ ions just fit into octahedral holes of the closest packed chloride anions.

5.1 Calculate the ionic radii for the Li^+ and Cl^- ions.



5.2 Compare the calculated (theoretical) radii with the experimental radii given below, and choose the appropriate box:

Both calculated radii of lithium and chloride ions are close to the experimental values.	☐
Only the calculated radius of lithium ion is close to the experimental value	☐
Only the calculated radius of chloride ion is close to the experimental value.	☐

The experimental radii of Li^+ and Cl^- are 0.62 Å and 1.83 Å, respectively.

Problem 3. A frog in a well

The energy levels of an electron in a one-dimensional box are given by:

$$E_n = n^2 \frac{h^2}{8mL^2} \quad n: 1, 2, 3 \dots$$

in which h is the Planck's constant, m is the mass of the electron, and L is the length of the box.

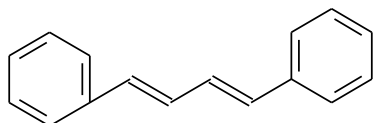
1. The π electrons in a linear conjugated neutral molecule are treated as individual particles in a one-dimensional box. Assume that the π electrons are delocalized in the molecular length with the total number of N π electrons and their arrangement is governed by the principles of quantum mechanics.

1.1 Derive the general expression for $\Delta E_{\text{LUMO} - \text{HOMO}}$ when an electron is excited from the HOMO to the LUMO.

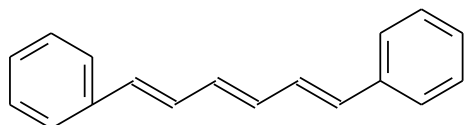
1.2 Determine the wavelength λ of the absorption from the HOMO to the LUMO.

2. Apply the model of π electrons in a one-dimensional box for three dye molecules with the following structures (see the structural formula). Assume

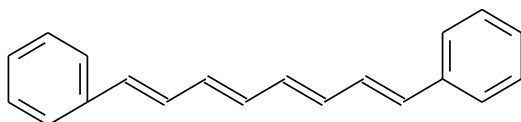
that the π electrons are delocalized in the space between the two phenyl groups with the length L is approximately equal to $(2k + 1)(0.140)$ nm, in which k is the number of the double bonds.



a) 1,4-diphenyl-1,3-butadiene
(denoted as **BD**)



b) 1,6-diphenyl-1,3,5-hexatriene
(denoted as **HT**)



c) 1,8-diphenyl-1,3,5,7-octatetraene
(denoted as **OT**)

2.1 Calculate the box length L (Å) for each of the dyes.

2.2 Determine the wavelength λ (nm) of the absorption for the molecules of the investigated dyes.

3. Recalculate the box length L (Å) for the three dye molecules, assuming that the π electrons are delocalized over the linear conjugated chain which is presented as a line plotted between the two phenyl groups (see the structural formula). The bond angle $C - C - C$ is 120° and the average length of $C - C$ bond is 0.140 nm.

4. Give the following experimental data on the wavelength λ of absorption.

Substance	BD	HT	OT
λ (nm)	328.5	350.9	586.1



4.1 Determine the box length L (Å) of the linear conjugated chain for each of the three investigated dyes.

4.2 Tabulate the values of the box length L for the dyes calculated above by the three different methods, denoted as **1**, **2**, and **3**. Choose the method which is the most fit to the experimental data.

Problem 4. Particles in 2, 3 - Dimensional Box

1. In Problem 3, the energy E of particle in one- dimensional box is calculated as:

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

where h is Planck's constant; m is the mass of the particle; L is the box length; n is the quantum number, $n = 1, 2, 3 \dots$

An electron in a 10 nm one-dimensional box is excited from the ground state to a higher energy level by absorbing a photon of the electromagnetic radiation with a wavelength of 1.374×10^{-5} m.

1.1 What is the energy gap (ΔE) of the two mentioned transitions?

1.2 Determine the final energy state for this transition.

2. The treatment of a particle in a one- dimensional box can be extended to a two-dimensional box of dimensions L_x and L_y yielding the following expression for energy:

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



The two quantum numbers independently can assume only integer values. Consider an electron confined in a two-dimensional box that is $L_x = 8.00$ nm in the x direction and $L_y = 5.00$ nm in the y direction.

2.1 What are the quantum numbers for the first three allowed energy levels? Write the first three energy, E_{xy} , in order of increasing energy?

2.2 Calculate the wavelength of light necessary to move an electron from the first excited state to the second excited one.

3. Similarly, the treatment of a particle in a one-dimensional box can be extended to a rectangular box of dimensions L_x , L_y , and L_z , yielding the following expression for energy:

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

The three quantum numbers n_x , n_y , and n_z independently can assume only integer values. An oxygen molecule is confined in a cubic box of volume 8.00 m^3 . Assume that the molecule has an energy of $6.173 \times 10^{-21} \text{ J}$; temperature $T = 298 \text{ K}$.

3.1 What is the value of $n = (n_x^2 + n_y^2 + n_z^2)^{\frac{1}{2}}$ for this molecule?

3.2 What is the energy separation between the levels n and $n + 1$?

4. In quantum mechanics, an energy level is said to be degenerate if it corresponds to two or more different measurable states of a quantum system. Consider a particle in a cubic box. What is the degeneracy of the level that has energy 21/3 times that of the lowest level?



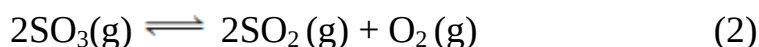
Problem 5. Tug of war

“Tug of war is a sport that directly pits two teams against each other in a test of strength. This is also a traditional game of Vietnamese people”

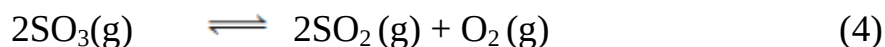
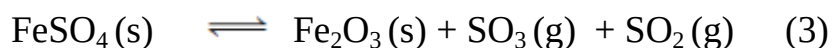
The following table gives the standard molar Gibbs energy at different temperatures for the reaction (1) below:

	$\text{SO}_3(\text{g}) \rightleftharpoons \text{SO}_2(\text{g}) + \frac{1}{2} \text{O}_2(\text{g}) \quad (1)$				
T/°C	527	552	627	680	727
$\Delta_r G^\circ / \text{kJ} \cdot \text{mol}^{-1}$	21.704	20.626	14.210	9.294	4.854

1. Use the Van Hoff's equation to estimate the $\ln K_{p1}$ at each temperature.
2. Plot $\ln K_{p1}$ against $1/T$ to determine the value of $\Delta_r H^\circ$ in $\text{kJ} \cdot \text{mol}^{-1}$ assuming that $\Delta_r H^\circ$ does not vary significantly over the given temperature range.
3. Using the best-fit line to plot a $\ln K_{p1}$ versus $1/T$, determine the K_{p2} for the following reaction (2) at 651.33 °C:



4. An amount of 15.19 g of iron (II) sulfate was heated in an evacuated 1.00 L container to 651.33 °C, in which the following reactions take place:



When the system has reached equilibrium, the partial pressure of oxygen is of 21.28 mmHg. Calculate the equilibrium pressure of the gases and the value of K_{p3} for the reaction (3) at equilibrium.

5. Calculate the percentage of FeSO_4 decomposed?

Problem 6. Radiochemistry

Zircon (ZrSiO_4) is a mineral found abundantly in placer deposits located in the central coast of Vietnam. Besides being widely utilized in the ceramic industry, zircon is also used as a raw material for the manufacture of zircaloy which is used to build fuel rods that hold the uranium dioxide (UO_2) fuel pellets in nuclear reactors. Zircon ore contains a trace amount of uranium, and it is not a viable source of uranium in practice. However, zircon crystals make a perfect storage medium to avoid the loss of uranium and lead (Pb) isotopes because of its stable crystal structure. This allows developing uranium-lead dating method.

There are 3 naturally occurring decay series:

- The thorium series begins with ^{232}Th and ends up with ^{208}Pb .
- The uranium series (also referred to as the uranium-radium series) is headed by ^{238}U . The half-life ($t_{1/2}$) of ^{238}U is 4.47×10^9 years.
- The actinium series is headed by ^{235}U with the half-life of 7.038×10^8 years.

Four stable isotopes of Pb exist in nature: ^{204}Pb , ^{206}Pb , ^{207}Pb , and ^{208}Pb . The natural abundance of each isotope is shown in the following table.

^{204}Pb	^{206}Pb	^{207}Pb	^{208}Pb
1.4	24.1	22.1	52.4

An analysis of a zircon mineral sample gives the following mass ratios of U and Pb isotopes:

$$m(^{238}\text{U}) : m(^{235}\text{U}) : m(^{206}\text{Pb}) : m(^{204}\text{Pb}) = 99.275 : 0.721 : 14.30 : 0.277$$

1. Indicate the stable isotope of Pb which is not involved in the above decay series.



2. Determine the mass ratio of ^{238}U to ^{235}U when the zircon mineral was first formed. Assume that the mineral already contained natural Pb right at the onset of its formation.
3. Production of uranium from low-grade will encounter many difficulties, notably large concentration of impurities and low concentrations of uranium in leach solutions. Various technological advances have been applied to overcome the aforementioned problems; these include fractional precipitation, liquid-liquid extraction, or ion exchange methods.

In an experiment to extract uranium from sample of low uranium content using diluted H_2SO_4 , in the preliminary treated leach solutions, the concentration of uranyl sulfate (UO_2SO_4) is 0.01 M and the concentration of iron(III) sulfate ($\text{Fe}_2(\text{SO}_4)_3$) goes up to 0.05 M. The separation of uranium from iron and other impurities can be carried out by the fractional precipitation method.

Calculate the pH necessary to precipitate 99% of Fe^{3+} without losing uranium ions. Assume that the adsorption of uranium onto $\text{Fe}(\text{OH})_3$ is negligible. Under the experimental conditions, the solubility product values for $\text{UO}_2(\text{OH})_2$ and $\text{Fe}(\text{OH})_3$ are 1.0×10^{-22} and 3.8×10^{-38} , respectively.

4. One of the proper methods to obtain a rich uranium solution is the liquid-liquid extraction with the organic phase containing the extracted agent of tributylphosphate (TBP) diluted in kerosene. When extracting uranium in the form of uranyl nitrate ($\text{UO}_2(\text{NO}_3)_2$) under appropriate conditions, the relationship between the concentrations of uranium in water and organic phases is given by:

$$\text{Distribution coefficient: } D = \frac{C_{\text{org.}}}{C_{\text{aq}}} = 10$$

where: C_{org} and C_{aq} are the equilibrium concentrations (M) of $\text{UO}_2(\text{NO}_3)_2$ in organic and aqueous phases, respectively.



Calculate the mole percentage (in comparison with the initial concentration) of $\text{UO}_2(\text{NO}_3)_2$ remaining in the aqueous phase after extracting 1.0 L of the solution (with an initial concentration of 0.01 M) with 500 mL of organic solvent.

5. Propose a scheme to extract 96% of $\text{UO}_2(\text{NO}_3)_2$ from 1.0 L of the aqueous phase into 500 mL of the organic phase. Assume that the distribution coefficient remains constant throughout the extraction process ($D = 10$).

Problem 7. Applied thermodynamics

1. In applied thermodynamics, Gibbs free energy plays an important role and can be calculated according to the following expression:

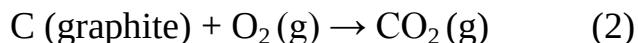
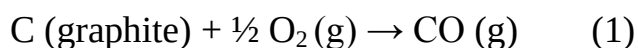
$$\Delta G^\circ_{298} = \Delta H^\circ_{298} - T\Delta S^\circ_{298}$$

ΔG°_{298} - standard free energy change

ΔH°_{298} - standard enthalpy change

ΔS°_{298} - standard entropy change

The burning of graphite is represented by two reactions:



The dependence of ΔH° , ΔS° on temperature is as follows:

$$\text{Reaction (1): } \Delta H^\circ_{\text{T}}(1) (\text{J}\cdot\text{mol}^{-1}) = -112298.8 + 5.94\text{T};$$

$$\Delta S^\circ_{\text{T}}(1) (\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}) = 54.0 + 6.21\ln\text{T}$$

$$\text{Reaction (2): } \Delta H^\circ_{\text{T}}(2) (\text{J}\cdot\text{mol}^{-1}) = -393740.1 + 0.77\text{T};$$

$$\Delta S^\circ_{\text{T}}(2) (\text{J}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}) = 1.54 - 0.77\ln\text{T}$$

Based on the above data:



1.1 Derive the expression for the Gibbs free energy as a function of temperature, $\Delta G^\circ_T = f(T)$ for each reaction.

1.2 Predict the changes of ΔG°_T with an increase in temperature.

2. Assume that at 1400 °C, during the course of reactions (1) and (2), CO gas might continue to react with O₂ to form the final product CO₂.

2.1 Write down the reaction (3) for the formation of CO₂ from CO gas.

2.2 Calculate ΔG°_T (3).

2.3 Determine the equilibrium constant K_p for reaction (3) at the given temperature.

3. In an experiment, NiO powder and CO gas were placed in a closed container which was then heated up to 1400 °C. When the system reached equilibrium, there were four species present: NiO(s), Ni(s), CO(g) and CO₂(g). The mole percentages of CO and CO₂ are 1 % and 99 %, respectively, and the pressure of the system is 1.0 bar (10⁵ Pa).

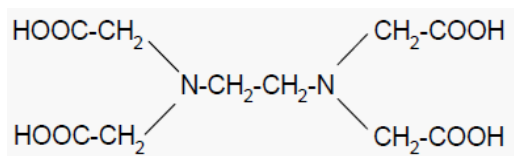
3.1 Write down the reactions in the above experiment.

3.2 Based on the experimental results and the above thermodynamic data, calculate the pressure of O₂ in the equilibrium with NiO and Ni at 1400 °C.

Problem 8. Complex compounds

Ethylenediamine tetraacetic acid (EDTA) is used as a reagent to titrate the metal ions in the complexometric titration.

EDTA is a tetraprotic acid, abbreviated as H₄Y, with the structure:



As EDTA is sparingly soluble in water, a more soluble sodium form, $\text{Na}_2\text{H}_2\text{Y}$, is usually used and H_2Y^{2-} is commonly known as EDTA. EDTA forms strong 1:1 complexes with most metal ions M^{n+} .

1. How many atoms of an EDTA molecule are capable of binding with the metal ion upon complexation?

1.1 Check in the appropriate box.

☐

2

☐

4

☐

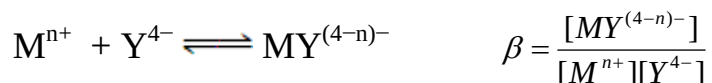
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☐

8

1.2 Draw the structure of the complex of a metal ion M^{2+} with EDTA.

2. Complexation reaction between Y^{4-} form of EDTA and metal ion M^{n+} has a large formation constant (stability constant) β :



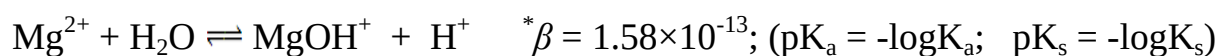
Besides complexation reaction between Y^{4-} form of EDTA and metal ion M^{n+} , other processes in the solution also develop such as formation of hydroxo complexes of the metal ion, acid-base equilibrium of H_2Y^{2-} ... To account for such processes conditional formation constant β' is used for the calculations. β' is determined from β as the following expression:

$$\beta' = \beta \cdot \alpha_{\text{M}^{n+}} \cdot \alpha_{\text{Y}^{4-}}$$



where: $\alpha_{Y^{4-}}$ and $\alpha_{M^{n+}}$ are fractions of Y^{4-} ($\alpha_{Y^{4-}} = \frac{[Y^{4-}]}{[Y]}$) and free metal ion M^{n+} ($\alpha_{M^{n+}} = \frac{[M]}{[M]}$), with $[Y]$ and $[M]$ being the total concentrations of all forms of Y^{4-} and M^{n+} , excluding $MY^{(4-n)-}$. Given that: H_4Y has $pK_{a1} = 2.00$; $pK_{a2} = 2.67$; $pK_{a3} = 6.16$; and $pK_{a4} = 10.26$ (pK_a values for H_5Y^+ and H_6Y^{2+} are ignored).

$$pK_{s(Mg(OH)_2)} = 10.95; \quad \log \beta_{MgY^{2-}} = 8.69$$



In a typical experiment, 1.00 mL of 0.10 M $MgCl_2$ solution and 1.00 mL of 0.10 M Na_2H_2Y solution are mixed together. pH of the resulting solution is adjusted to 10.26 by an NH_3/NH_4^+ buffered solution.

2.1 Calculate conditional formation constant (β') of the MgY^{2-} complex at pH = 10.26 given that acid-base equilibrium of H_2Y^{2-} and formation of mononuclear hydroxo complex of Mg^{2+} occur in the solution.

2.2 Does the $Mg(OH)_2$ precipitate in this experiment? Check in the appropriate box.

☐

Precipitation

☐

No precipitation

3. In order to titrate metal ions by EDTA, the conditional formation constant (β') of the complex metal – EDTA ($MY^{(4-n)-}$) must be large enough, usually $\beta' \geq 1.00 \times 10^8 - 1.00 \times 10^9$. To determine the concentrations of Mn^{2+} and Hg^{2+} in an analytical sample, two experiments are carried out.

Experiment 1: Add 25.00 mL of 0.040 M EDTA solution to 20.00 mL of the analytical solution. Adjust the pH of the resulting solution to 10.50. Titrate the excess EDTA with a suitable indicator and 12.00 mL of 0.025 M Mg^{2+} solution is consumed.



Experiment 2: Dissolve 1.400 gram of KCN into 20.00 mL of the analytical solution (assuming that the volume is unchanged upon dissolution) and then add 25.00 mL of 0.040 M EDTA solution. Titrate the excess EDTA in the resulting mixture at the pH of 10.50; 20.00 mL of 0.025 M Mg^{2+} solution is consumed.

3.1 Prove that: in the experiment 2, Hg^{2+} cannot be determined by titration with EDTA in the presence of KCN in solution (or Hg^{2+} is masked in the complex form of $\text{Hg}(\text{CN})_4^{2-}$).

3.2 Write down chemical equations for the reactions in the two experiments and calculate molar concentrations of Mn^{2+} and Hg^{2+} in the analytical solution.

Given that: $\log \beta_{\text{HgY}^{2-}} = 21.80$; $\log \beta_{\text{Hg}(\text{CN})_4^{2-}} = 38.97$; $pK_{a(\text{HCN})} = 9.35$

(Other processes of Hg^{2+} are ignored; the pK_a values of H_4Y are provided in question 2).

4. In the titration of polyprotic acids or bases, if the ratios of consecutive dissociation constants exceed 1.00×10^4 , multiple titrations are possible with an error less than 1%. To ensure the allowed error, only acids or bases with equilibrium constants larger than 1.00×10^{-9} can be titrated. To find the end-point, pH range of the indicator must be close to that of the equivalence point (pH_{EP}); the point at which the stoichiometric amounts of analyte and titrant has reacted. Titrate 10.00 mL of 0.25 M $\text{Na}_2\text{H}_2\text{Y}$ solution by 0.20 M NaOH solution in a typical experiment.

4.1 Write down the chemical equation for the titration reaction.

4.2 Determine the value of pH_{EP} .

4.3 Choose the most suitable indicator (check in the appropriate box) for the above titration from the following: bromothymol blue ($\text{pH} = 7.60$); phenol red ($\text{pH} = 8.20$); phenolphthalein ($\text{pH} = 9.00$).

☐

Bromothymol blue

☐

Phenol red

☐

Phenolphthalein

4.4 Titration error q defined as the difference between the titrant amount added and the titrant amount needed to reach the equivalence point is expressed as:

$$q = \frac{C_{\text{NaOH}}V_1 - C_{\text{NaOH}}V_2}{C_{\text{NaOH}}V_2} \times 100\% = \frac{V_1 - V_2}{V_2} \times 100\%$$

where C_{NaOH} is the NaOH concentration; V_1 : End-point volume of NaOH; V_2 : equivalence point volume of NaOH.

Calculate the consumed volume of NaOH solution and the titration error if the final pH is 7.60.

Problem 9. Lead compounds

1. Consider the following nuclide: $^{209}\text{Bi}(\text{I})$, $^{208}\text{Pb}(\text{II})$, $^{207}\text{Pb}(\text{III})$, $^{206}\text{Pb}(\text{IV})$. Which nuclide is the last member of the decay series for ^{238}U ? Check in the appropriate box.

☐

(I)

☐

(II)

☐

(III)

☐

(IV)

2. There are three natural decay series. They begin with Th-232(I), U-238(II), U-235(III) and end with Pb-208, Pb-206, Pb-207. In which decay chain are there 6 α decays and 4 β decays? Choose the correct answer by checking in the appropriate box.



(I)



(II)



(III)



None

3. $\text{Pb}(\text{NO}_3)_2$ solution is slowly added into 20.00 mL of a mixture consisting of 0.020 M Na_2SO_4 ; 5.0×10^{-3} M $\text{Na}_2\text{C}_2\text{O}_4$; 9.7×10^{-3} M KI; 0.05 M KCl and 0.0010 M KIO_3 . When the bright yellow precipitate of PbI_2 begins to form, 21.60 mL of $\text{Pb}(\text{NO}_3)_2$ solution is consumed.

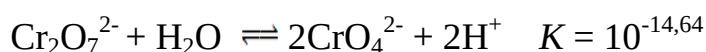
3.1 Determine the order of precipitation?

3.2 Calculate the concentration of $\text{Pb}(\text{NO}_3)_2$ solution?

Given that: $\text{p}K_{\text{s}(\text{PbSO}_4)} = 7.66$; $\text{p}K_{\text{s}(\text{Pb}(\text{IO}_3)_2)} = 12.61$; $\text{p}K_{\text{s}(\text{PbI}_2)} = 7.86$; $\text{p}K_{\text{s}(\text{PbC}_2\text{O}_4)} = 10.05$; $\text{p}K_{\text{s}(\text{PbCl}_2)} = 4.77$. (Other processes of the ions are ignored).

4. One of the common reagents to detect Pb^{2+} species is K_2CrO_4 , giving yellow precipitate PbCrO_4 , which is soluble in excess of NaOH. The solubility of PbCrO_4 depends not only on pH but also on the presence of coordinating species... Given that the solubility of PbCrO_4 in 1 M acetic acid solution is $s = 2.9 \times 10^{-5}$ M, calculate the solubility product K_{sp} of PbCrO_4 .

$$\text{p}K_{\text{a}(\text{CH}_3\text{COOH})} = 4.76; \lg \beta_{\text{Pb}(\text{CH}_3\text{COO})^+} = 2.68; \lg \beta_{\text{Pb}(\text{CH}_3\text{COO})_2} = 4.08; \text{p}K_{\text{a}(\text{HCrO}_4^-)} = 6.5$$



5. Lead-acid battery, commonly known as lead battery consists of two lead plates a positive electrode covered with a paste of lead dioxide and a negative electrode made of sponge lead. The electrodes are submersed in an electrolyte consisting of water and sulfuric acid H_2SO_4 . Write the chemical equations for processes on each electrode, overall reaction as the battery discharges and the cell diagram.



Given that: $E_{\text{Pb}^{2+}/\text{Pb}}^0 = -0.126 \text{ V}$; $E_{\text{PbO}_2/\text{Pb}^{2+}}^0 = 1.455 \text{ V}$; $pK_{a(\text{HSO}_4^-)} = 2.00$; $pK_{s(\text{PbSO}_4)} = 7.66$;

at 25 °C: $2.303 \frac{RT}{F} = 0.0592 \text{ V}$

6. Calculate:

6.1 $E_{\text{PbSO}_4/\text{Pb}}^0$; $E_{\text{PbO}_2/\text{PbSO}_4}^0$

6.2 The potential V of the lead battery if $C_{\text{H}_2\text{SO}_4} \approx 1.8 \text{ M}$.

Problem 10. Applied electrochemistry

1. Reduction-oxidation reactions have played an important role in chemistry due to their potential to be valuable sources of energy for technology and life. Write down chemical equations for the following reactions:

1.1 Oxidation of glucose ($\text{C}_6\text{H}_{12}\text{O}_6$) with KMnO_4 solution in the presence of sulfuric acid to form gaseous CO_2 .

1.2 Oxidation of FeSO_4 with KMnO_4 in an acidic medium (sulfuric acid) to form $\text{Fe}_2(\text{SO}_4)_3$.

1.3 Based on the reaction in section 1.2, determine the anodic reaction and cathodic reaction and the relevant cell diagram.

1.4 Derive the expression for electromotive force E of the cell.

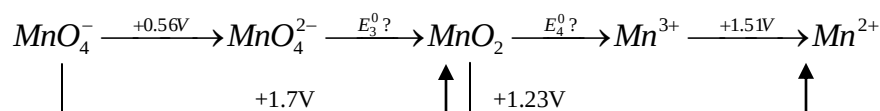
2. In the thermodynamics point of view, Gibbs free energy ΔG at constant P, T condition is closely related to electromotive force E of a redox reaction according to below expression:

$$\Delta G = -nFE \rightarrow E = -\frac{\Delta G}{nF}$$

where: n – number of electrons transferred,

F – Faraday constant.

The correlation of the standard reduction potential between Mn ions in acidic medium is:



2.1 Determine the standard reduction potential of the pair $\text{MnO}_4^{2-}/\text{MnO}_2$

2.2 Determine the standard reduction potential of the pair $\text{MnO}_2/\text{Mn}^{3+}$

3. A process is spontaneous if Gibbs free energy is negative. Based on the thermodynamic data:

3.1 Determine Gibbs free energy of the following reaction:



3.2 Is the reaction spontaneous?

3.3 Calculate K_c for the reaction.

Problem 11. Phosphoric acid

A is a solution of H_3PO_4 with pH of 1.46.

1. Calculate the molar concentrations of all species in solution **A**. Given that K_a values for H_3PO_4 are 7.5×10^{-3} ; 6.2×10^{-8} and 4.8×10^{-13} , respectively.

2. Mixing of 50 ml of solution **A** and 50 ml of 0.4 M NH_3 solution results in 100 ml of solution **B**. Calculate pH of solution **B** ($pK_{\text{NH}_4^+} = 9.24$).

3. 100 mL of solution **B** is mixed with 100 ml of 0.2 M $\text{Mg}(\text{NO}_3)_2$ solution. Determine if precipitate of NH_4MgPO_4 forms. The hydrolysis of Mg^{2+} is ignored

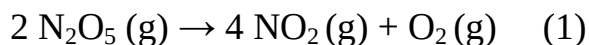
and precipitation of NH_4MgPO_4 is assumed to be the only reaction, given that $K_{\text{sp}} = 2.5 \times 10^{-13}$.

4. Calculate the solubility ($\text{mol} \cdot \text{L}^{-1}$) of $\text{Ca}_3(\text{PO}_4)_2$, given $K_{\text{sp}} = 2.22 \times 10^{-25}$.

(Hint: The hydrolysis of Ca^{2+} is ignored).

Problem 12. Chemical Kinetics

Thermal decomposition of dinitrogen pentoxide (N_2O_5) in the gas phase has time-independent stoichiometry.



A kinetic measurement for N_2O_5 at 63.3°C is shown in Figure 1 below.

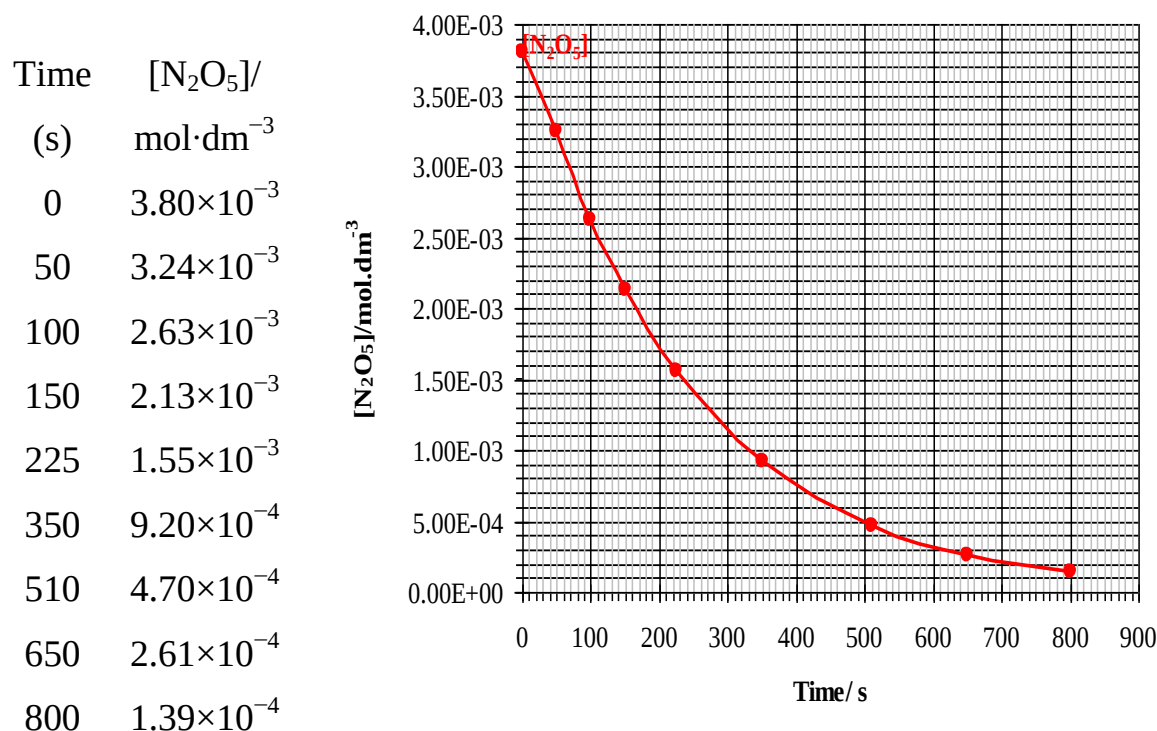


Figure 1. Concentration of N_2O_5 versus time.

1. What is the half-life ($t_{1/2}$) for the decomposition of N_2O_5 at 63.3 °C?
2. The reaction order for the reaction (1) can be determined by plotting of $\ln [\text{N}_2\text{O}_5]_0/[\text{N}_2\text{O}_5]_t$ versus time or $\{[\text{N}_2\text{O}_5]_0/[\text{N}_2\text{O}_5]_t - 1\}$ versus time.
 - 2.1 Plot the graphs into the two figures below to determine the reaction order?
 - 2.2 Write down the rate law and integrated rate equation.

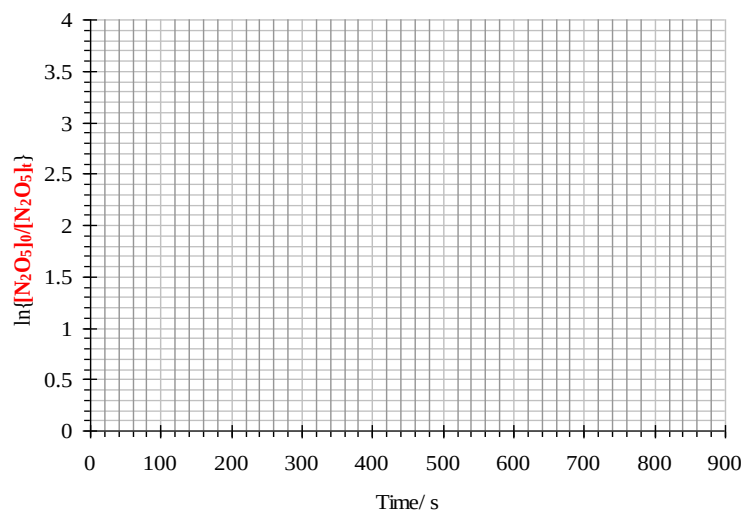


Figure 2. A re-plot of the data in Figure 1 as function of $\ln \{[\text{N}_2\text{O}_5]_0/[\text{N}_2\text{O}_5]_t\}$ versus time

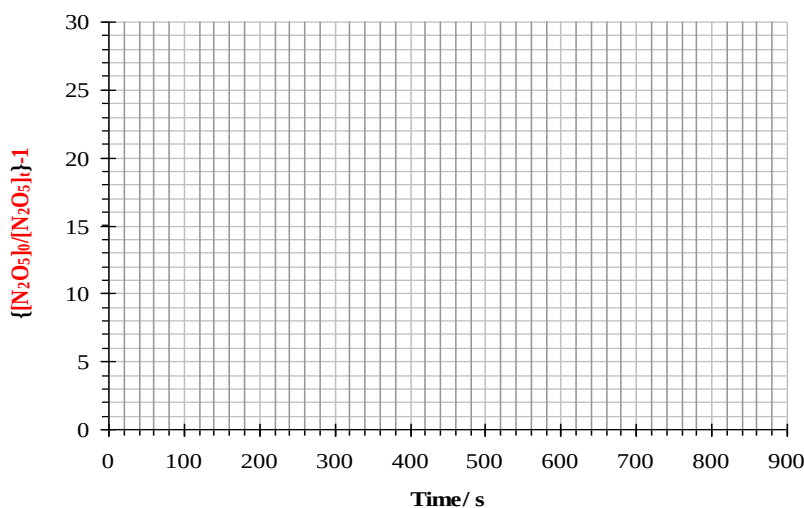


Figure 3. A re-plot of the data in Figure 1 as function of $\{[\text{N}_2\text{O}_5]_0/[\text{N}_2\text{O}_5]_t - 1\}$ versus time



3. Determine the rate constant for the reaction (1).
4. The rate constant k for (1) at 45 °C is of $5.02 \times 10^{-4} \text{ s}^{-1}$. Calculate the activation energy (E_a) and pre-exponential factor (A) for the reaction (1) assuming that the activation energy and pre-exponential factor are temperature independent.
5. The following mechanism is proposed for the reaction (1):



Using this mechanism, derive the rate law for $-d[\text{N}_2\text{O}_5]/dt$ assuming that the intermediate concentrations can be treated by the steady-state approximation.

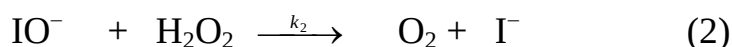
Problem 13. Kinetics of the decomposition of hydrogen peroxide

In order to decompose hydrogen peroxide (H_2O_2) with iodide ion as catalyst in neutral solution, the 3 % H_2O_2 solution (which approximately corresponds to 30 g of H_2O_2 in 1 L of solution) is mixed with 0.1 M KI solution and water at different volumetric ratios; and the volume of the oxygen gas released $V_{\text{O}_2}(\text{mL})$ is measured.

Experiment	$V_{\text{H}_2\text{O}_2}(\text{mL})$	$V_{\text{KI}}(\text{mL})$	$V_{\text{H}_2\text{O}}(\text{mL})$	$V_{\text{O}_2}(\text{mL/min})$
at 298 K and 1 atm				
1	25	50	75	4.4
2	50	50	50	8.5
3	100	50	0	17.5
4	50	25	75	4.25
5	50	100	0	16.5



1. Determine the reaction order with respect to H_2O_2 , and I^- , respectively.
2. Write down the chemical reaction, and determine the rate law.
3. Calculate the molarity of H_2O_2 at the beginning of the experiment #4 and after 4 min.
4. The reaction mechanism involves a series of the following steps:



Do the two above steps have the same rate or different rates? Which step determines the overall rate of the oxygen release? Justify your answer.

Problem 14. Magnetism of transition metal complexes

A transition metal complex containing diamagnetic ligands can be overall *diamagnetic* (all electrons are paired) or *paramagnetic* (having unpaired electron(s)) depending on the electronic configuration of the central metal ion, the nature of the ligand, and geometry of the ligand sphere. The magnitude of paramagnetism of a metal complex is commonly reported in terms of the effective magnetic moment (μ_{eff}) which can be obtained from the experimental measurement of molar magnetic susceptibility (χ_{m}) and is commonly expressed in Bohr magneton (BM).

Theoretically, the magnetic moment is contributed by two components, the spin angular momentum and the orbital angular momentum. For many complexes of first row d-block metal ions, however, the contribution of the second component can be ignored. Thus, the so-called spin only magnetic moment can be determined by the number of unpaired electrons, n :

$$\mu (\text{spin only}) = \sqrt{n(n+2)} \text{ (BM)}$$

1. The observed effective magnetic moment of two octahedral complexes, $\text{K}_4[\text{Mn}(\text{CN})_6] \cdot 3\text{H}_2\text{O}$ and $\text{K}_4[\text{Mn}(\text{SCN})_6]$ are 2.18 BM and 6.06 BM, respectively.

1.1 Calculate number of unpaired electrons in each complex. Which complex is low spin? Which complex is high spin?

1.2 Rationalize your answers by applying crystal field theory.

2. Calculate the μ (spin only) of complex $[\text{Ni}(\text{H}_2\text{O})_6]\text{Cl}_2$.

3. In practice, the experimentally observed μ_{eff} value of $[\text{Ni}(\text{H}_2\text{O})_6]\text{Cl}_2$ is 3.25 BM. This is not surprising due to the fact that magnetic moment of octahedral complexes of Ni^{2+} (d^8) usually does not obey the spin only formula. In these cases, the contribution of orbital angular momentum should be taken into account. The simplification of spin-orbit coupling model can be applied to calculate their magnetic moment:

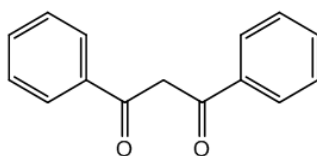
$$\mu_{\text{eff}} = \mu(\text{spin only}) \times \left(1 - \frac{4\lambda}{\Delta_{\text{oct}}}\right)$$

where λ is spin-orbit coupling constant of Ni^{2+} and has the value of 315 cm^{-1}

Δ_{oct} is the crystal-field splitting parameter

Calculate the effective magnetic moment of $[\text{Ni}(\text{H}_2\text{O})_6]\text{Cl}_2$ taking into account spin-orbit coupling. Δ_{oct} of $[\text{Ni}(\text{H}_2\text{O})_6]^{2+}$ is 8500 cm^{-1} .

4. Dibenzoylmethane (DBM) is a well known chelating $\kappa\text{-O,O}$ -ligand which can form stable complexes with many transition metal ions.



DBM

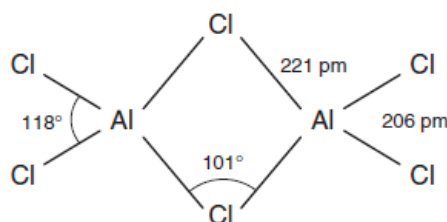


Reaction of $\text{Ni}(\text{CH}_3\text{COO})_2 \cdot 4\text{H}_2\text{O}$ with DBM in EtOH - H_2O solution gives light green crystalline complex **A** which loses 6.8 % of mass on heating at 210 °C in the air to form green solid **B**. The substance **B** is quantitatively converted to brown prismatic crystals **C** by re-crystallization in dry toluene. **B** and **C** are two polymorphic forms and their inter-conversion is reversible. The X-ray single crystal structure of **C** shows a square planar geometry with the chemical composition of $[\text{Ni}(\text{DBM})_2]$. While **B** is paramagnetic with effective magnetic moment of 3.27 BM, the complex **C** is diamagnetic. When **B** and **C** are kept in the air, they slowly convert to **A**. This happens much faster in the presence of some organic solvents (*Inorg. Chem.*, 2001, 40, 1626-1636).

- 4.1 Draw the splitting diagram of the d orbitals of Ni^{2+} in **C** and confirm its diamagnetic property.
- 4.2 What is the molecular formula of **A**? Assume that **A** is a mononuclear complex.
- 4.3 The effective magnetic moment of **A** is 3.11 BM (*Synth. React. Inorg. Met. Org. Chem.*, 2009, 39, 694-703). What is the most suitable molecular geometry of **A**? (Assuming that If **A** is an octahedral complexes, Δ_{oct} of **A** is similar to that of $[\text{Ni}(\text{H}_2\text{O})_6]^{2+}$).
- 4.4 Draw all possible isomers of **A**.
- 4.5 What do you expect for the molecular geometry of **B**?

Problem 15. Structure and synthesis of Al-Keggin ion

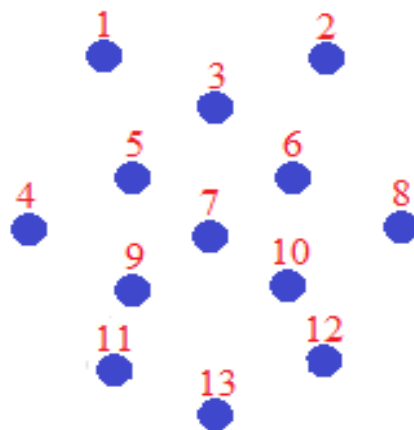
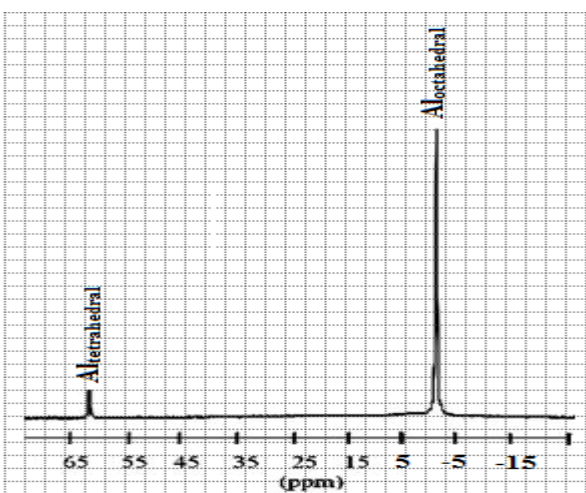
1. A molecular dimer of aluminum chloride in gas phase has the structure:



1.1 What is the hybridization of the Al atoms in a dimer?

1.2 Determine the distance between two Al atoms.

2. Aluminum chloride dissociates in basic solution yielding several Al-polycations. A typical Al-Keggin ion with the molecular formula of $[\text{Al}_{13}\text{O}_{28}\text{H}_{24}.12\text{H}_2\text{O}]\text{Cl}_n$ was formed at a hydrolysis ratio $[\text{OH}^-]/[\text{Al}^{3+}]$ of 1.5 to 2.5. It is only composed of tetrahedral and octahedral Al cations. The ^{27}Al NMR spectrum of an Al_{13} ion is shown below. The sharp signal at 64 ppm is due to the very symmetrical environment of the corresponding Al atom(s) in the Keggin cation.



2.1 Determine the absolute value of (n) in the Al_{13} Keggin ion.



2.2 Assign ^{27}Al NMR signals in the spectrum to the appropriate Al cation(s) in the right figure.

2.3 In an Al_{13} -Keggin ion, Al tetrahedron(s) is(are) only linked with other Al atoms by the oxygen bridge. Propose the structural formula for the Al_{13} -Keggin ion.

2.4 Determine the number of oxygen atoms bridging adjacent octahedra.

2.5 Write down the overall equation to prepare Al-Keggin ions from the reaction between NaOH and AlCl_3 solution.

3. Al_{13} -Keggin ions have recently been prepared by solid - solid interaction referred to as mechanochemical synthesis [*J. Catal.* 245 (2007) 346; *Inorg. Chem. Commun.* 11 (2008) 1125]. A mixture of $(\text{NH}_4)_2\text{CO}_3/[\text{Al}(\text{H}_2\text{O})_6]\text{Cl}_3$ was blended together in a silicon carbide crucible (with the inner volume of 17 cm^3) in the presence of three hardened silicon carbide balls (with the radius of 0.542 cm) in atmospheric condition ($25\text{ }^\circ\text{C}$, 1 atm). The milling was kept for a period of time at $25\text{ }^\circ\text{C}$ until the pressure gauge remains at constant value of 2.50 atm (*Hint: The volume of solids is negligible*).

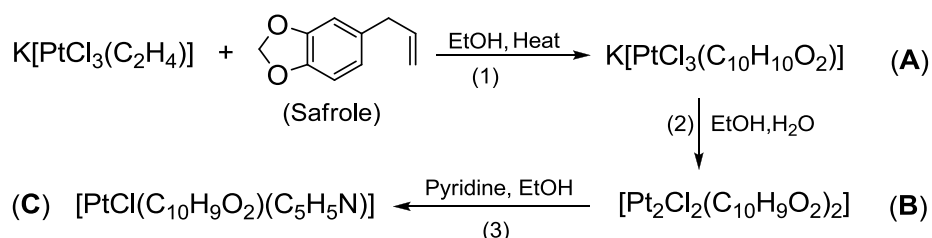
3.1 Write down the overall reaction between aluminum hexahydrate chloride and ammonium carbonate to yield the Al_{13} -Keggin ions.

3.2 Determine the number of molecular Al_{13} -Keggin cations in the crucible.

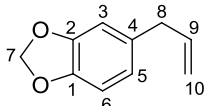
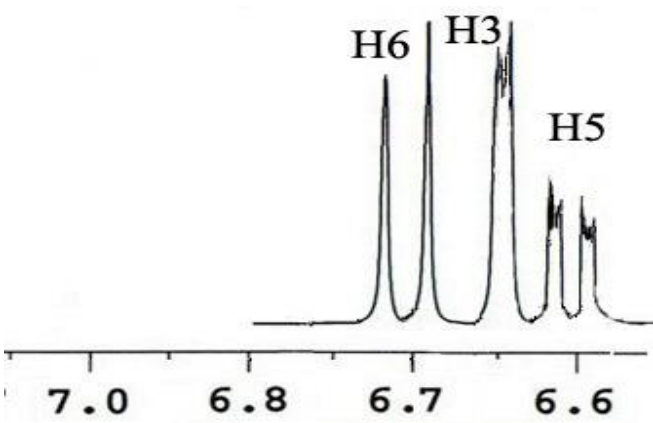
Problem 16. Safrole

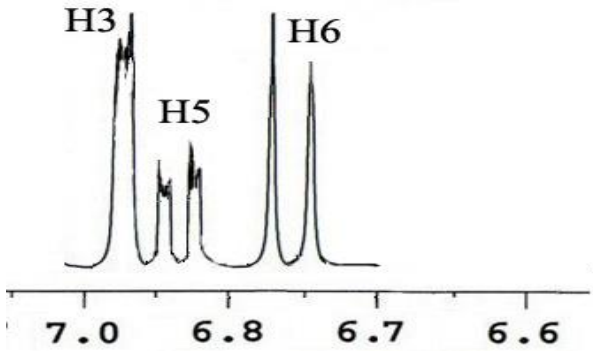
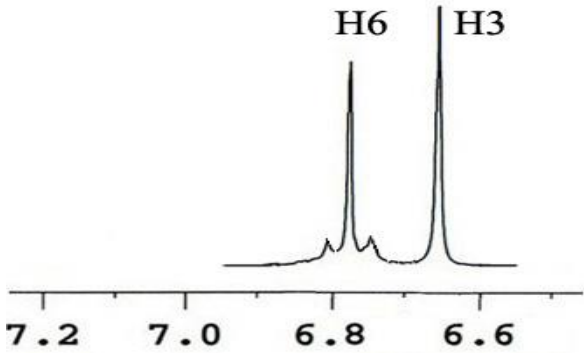
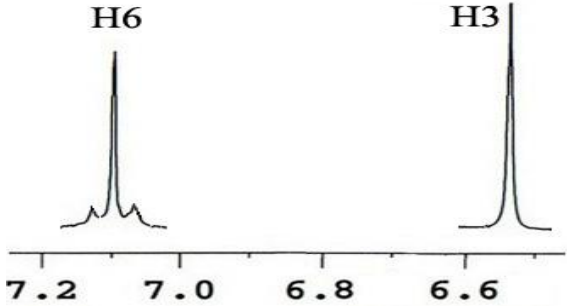
Safrole (4-allyl-1,2-methylenedioxybenzene) is obtained from oil extracted from sassafras, an evergreen tree growing in the central and northern regions of Vietnam. Safrole has interesting functionality and chemical reactivity suggesting its use as an efficient and versatile natural synthon in the synthesis of numerous

biologically active compounds. [PtCl(Safrole-1H)(Pyridine)] is a complex with a similar activity to the anticancer drug Cisplatin. [PtCl(Safrole-1H)(Pyridine)] has been synthesized for the first time by chemists at the Department of Chemistry, Hanoi National University of Education. The reaction scheme is given below.



Some spectral signals of uncoordinated safrole and coordinated safrole in **A**, **B** and **C** are given below.

	IR absorption, $\nu_{\text{C9-C10}}, \text{cm}^{-1}$	¹ H NMR signals of aromatic protons, δ (ppm)
Uncoordinated	1630	

Coordinated in A	1510	
Coordinated in B	1495	
Coordinated in C	1500	

1. Write balanced equations for the three reactions in the above scheme.
2. What information about the coordination of safrole with Pt in **A**, **B** and **C** can be obtained from the IR and ¹H NMR data?
3. Draw the structures of **A**, **B** and **C**, given that in **C** pyridine is in the *cis*-position with respect to the allyl group of safrole.
4. What is the driving force of each of the reactions (1), (2) and (3)?
5. Why does reaction 3 not seem to obey the *trans* effect?

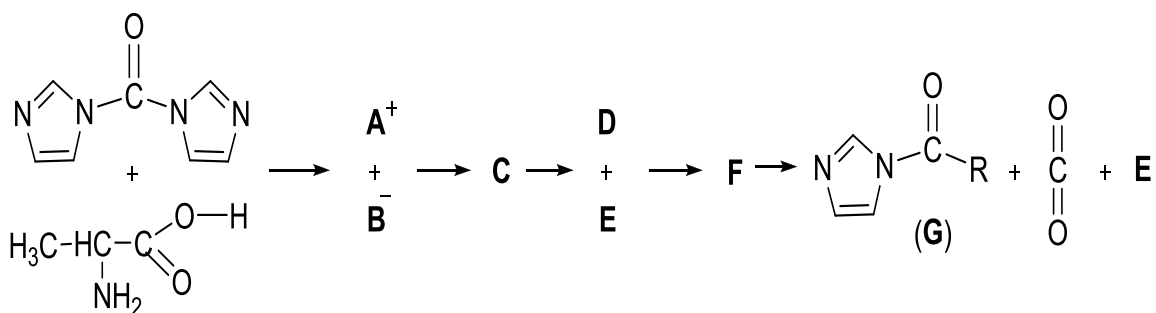


Problem 17. Imidazole

Heterocyclic chemistry is one of the most important fields of organic chemistry and biochemistry. Approximately 55% of publications in organic chemistry are related to the field, and the number of heterocyclic compounds recently found is far more than that of homocyclic compounds. The five-membered ring compounds with two heteroatoms are often present in many substances that are important for life. For example, imidazole ring is present in the essential amino acid, histidine, and its decarboxylation product, histamine. Histidine residues are found at the active sites of ribonuclease and of several other enzymes and play a vital part in the structure and binding functions of hemoglobin. Several drugs are based on the imidazole ring such as nitroimidazole, cimetidine, azomicin, metronidazole, medazolam.

1. Draw the structures of 1,3-diazole (imidazole, $C_3H_4N_2$), imidazol-1-ide anion, imidazolium cation, 1,3-oxazole (oxazole, C_3H_3NO) and 1,3-thiazole (thiazole, C_3H_3NS). Which structure(s) can be considered aromatic?
2. Arrange imidazole, 1,3-oxazole and 1,3-thiazole in decreasing order of melting and boiling points and justify your order.
3. Using structural formulae, write down equations for the ionization of imidazole, oxazole, and thiazole in water. Arrange the substances in decreasing order of base strength and justify your answer.
4. Propose a reaction mechanism showing the catalytic behavior of imidazole in hydrolyzing $RCOOR'$ without a participation of OH^- . Justify this behavior based on the structure of imidazole.
5. Propose a reaction mechanism for the formation of 1,1'-carbonyldiimidazole ($C_7H_6N_4O$, CDI) from imidazole and phosgen ($COCl_2$).

6. Explain why the C=O stretching frequency in 1,1'-carbonyldiimidazole is 100 cm^{-1} higher than that of 1,1'-carbonyldipyrrolidine ($\text{CO}(\text{C}_4\text{H}_8\text{N})_2$).
7. Write down reaction equations for the preparation of CDI (a) using a mixture of 4 mol imidazole and 1 mol phosgene and (b) using a mixture of 2 mol imidazole, 1 mol phosgene, and 2 mol NaOH. Explain why reaction (a) is preferable.
8. CDI is often used for the activation of carbonyl group for the coupling of amino acids in peptide synthesis.
- 8.1 Use curly arrow mechanisms to complete the scheme below, showing the formation of the active compound **G** from CDI and Alanine.



- 8.2 Propose a reaction mechanism for the formation of dipeptide Ala-Gly from **G** and Glycine.

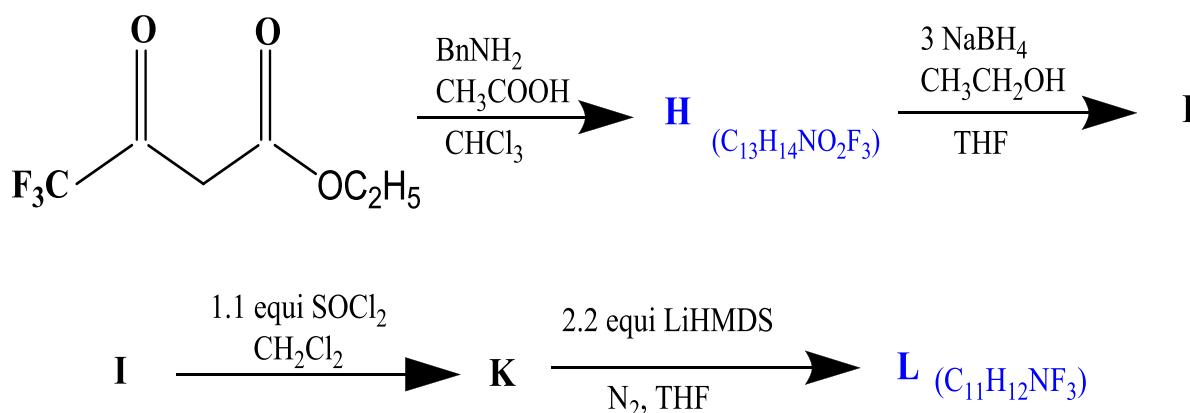
Problem 18. Small heterocycles

Heterocyclic compounds containing the CF_3 group are interesting targets of advanced researches to generate biologically active compounds. It is quite difficult to bring the trifluoromethyl group into saturated heterocyclic structures, especially heterocycles containing nitrogen. However, these heterocycles bearing CF_3 groups

have several promising applications. Therefore, studies of such compounds have been carried out by many chemists.

Trifluoroacetaldehyde (**A**) was treated with ethanol and then refluxed with benzylamine in toluene to afford compound **B** ($C_9H_8NF_3$). The reaction of compound **B** with ethyl diazoacetate in diethyl ether with borontrifluoride etherate ($BF_3 \cdot Et_2O$) as a catalyst at $-78^\circ C$ for 4 hours provided compound **C** ($C_{13}H_{14}NO_2F_3$). The reduction of compound **C** by $LiAlH_4$ in THF at room temperature for 2 hours formed compound **D**. Then, **D** reacts with hydrogen in the presence of $Pd(OH)_2$ as a catalyst in CH_2Cl_2 at room temperature for 60 hours to obtain **E** ($C_4H_6NOF_3$). Compound **E** was then allowed to react with 2 equivalents of tosyl chloride (TsCl) in dicloethane with the catalytic Et_3N and amount of 4-dimethylaminopyridine (DMAP). The reaction was carried out at room temperature for 2 hours, then 3 hours of reflux, to furnish compound **F**. **F** reacted with 1.2 equivalents of phenol in the presence of K_2CO_3 in DMF to form compound **G** ($C_{17}H_{16}NSO_3F_3$).

A derivative of **G** can be synthesized according to the following diagram:





1. Complete synthetic schemes from **B** to **L**.
2. Write reaction mechanisms from **B** to **C**.
3. Write reaction mechanisms from **F** to **G**.

Note:

BnNH₂: benzylamine, C₆H₅NH₂;

Bn: Benzyl, C₆H₅CH₂-, THF: tetrahydrofuran

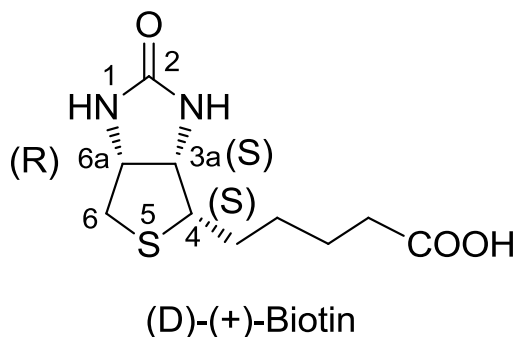
LiHMDS: Lithium bis(trimethylsilyl)amide, Et: C₂H₅-;

Equi: equimolarity

Problem 19. Vitamin H

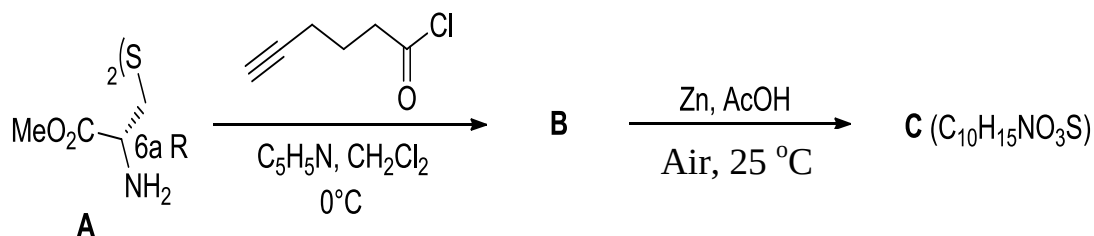
Vitamin H or biotin is a highly effective growth promoter which plays an important role in many organisms, for instance baker's yeast (*Saccharomyces cerevisiae*). Human beings have different demand in biotin depending on age. Lack of biotin can lead to diseases such as dermatitis, absence of appetite, fatigue, muscular pain and nerve perturbation.

Biotin was first found in 1901 by Wildiers as a growth-promoting vitamin of yeasts. Thereafter, it was found in egg yolk (by Kögl, 1936) and in liver (by Szent-Györgyi, 1936). The absolute configurations of chiral carbons of biotin were established by Trotter and Hamilton in 1966 by the single-crystal X-Ray diffraction. The molecule of biotin has three chiral carbons. Hence, there are theoretically eight diastereomers. Only the (3*aS*, 4*S*, 6*aR*)-(D)-(+)-biotin, however, shows the high bioactivity.



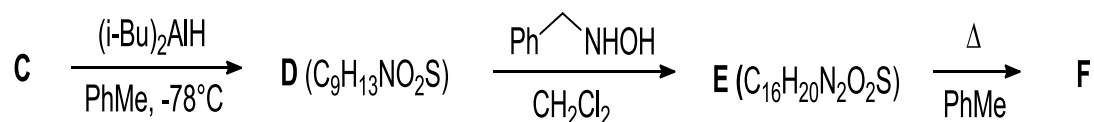
In 1982, researchers from Hoffmann-La Roche published an elegant synthesis procedure for (D)-(+)-Biotin from the methyl ester of the amino acid L-Cysteine with the following steps.

1. The thiol group of the methyl ester of L-cysteine was transformed into a disulfide S-S bond (compound **A**) in an oxidation reaction. **A** was then treated with hex-5-ynyl chloride to give compound **B** which was subsequently reduced by Zn/CH₃COOH to afford a thiol. This compound was cyclized by the addition of the –SH group to the terminal alkyne under atmospheric condition, resulting in the formation of **C** with a ten-membered ring containing a (Z) C=C double bond. Write down the structural formulae of **A**, **B** and **C** in the hereunder scheme.

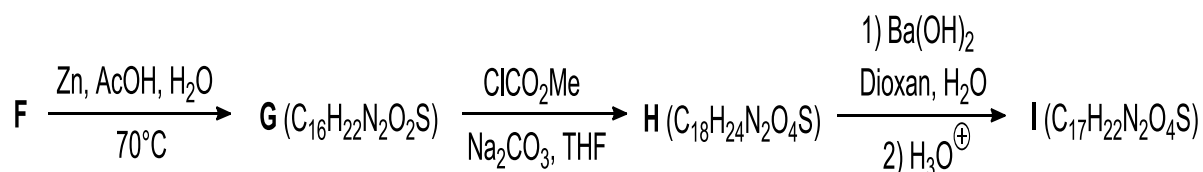


2. The reduction of **C** by diisobutylaluminium hydride ((i-Bu)₂AlH, DIBAL) resulted in the formation of (**D**). The condensation reaction between **D** and benzylhydroxylamine in dichloromethane produced nitron **E** (a nitron is an organic compound which contains a > C=N⁺-O⁻ group). **E** underwent a 1,3-dipolar

intramolecular cyclization reaction to afford polycyclic compound **F** of which the two heterocycles, isoxazolidine (1,2-oxazolidine) and tetrahydrothiophene, shared a common bond. The cyclization reaction resulted in the (*S*) configurations of the two carbons at the common bond and the (*R*) configuration of the carbon connected to the oxygen. Write down the structural formulae of **D**, **E** and **F**.



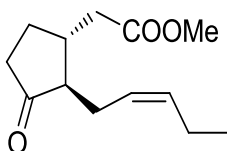
3. When **F** was reduced with Zn powder in acetic acid, the N-O bond of the heterocycle isoxazolidine was broken to give compound **G**. The reaction between **G** and chloroformate in the presence of Na_2CO_3 in THF resulted in the formation of compound **H**. The treatment of **H** in a hot solution of $\text{Ba}(\text{OH})_2$ in dioxane, followed by an acidic work-up yielded the bicyclic δ -hydroxy acid **I** containing all the chiral centers of (*D*)-(+)-Biotin but with an “excessive” -OH group. Draw the structures of **G**, **H** and **I** and explain the formation of **I** from **H**.



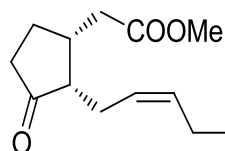
4. **I** was treated with SOCl_2 to yield the corresponding chloride acid **K**, given that the configuration of the carbon attached to the “excessive” -OH is maintained in **K**. Ester **L** was formed when **K** was reacted with methanol. **L** was reduced with NaBH_4 in dimethylformamide at 80°C to give ester **M** which was hydrolyzed in aqueous acidic solution of HBr to give optically pure (*D*)-(+)-Biotin. Draw the structures of **I**, **K**, **L** and **M** and the intermediates to explain the influence of the sulfur atom on the stereochemical outcome of **K**.

Problem 20. No perfume without jasmine

The Spanish jasmine originated from the valleys of Himalaya. This so called *Jasminum grandiflorum* L., which was grafted on the wild *Jasminum officinale* L., has the possibility to resist against the cold of the mountain climate. In 1962, E. Demole and E. Lederer successfully isolated and clearly determined the structures of the important flavor component of the essential oil of jasmine. It was actually a mixture of two diastereomers (Z)-(3*R*,7*R*) methyl jasmonate and (Z)-(3*R*,7*S*) methyl jasmonate with the structures shown below.



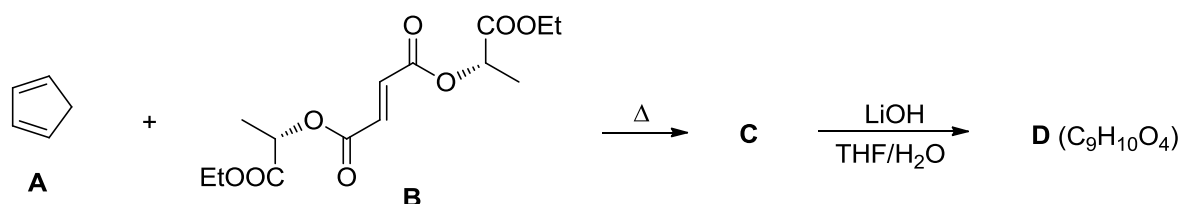
(Z)-(3*R*,7*R*) methyl jasmonate



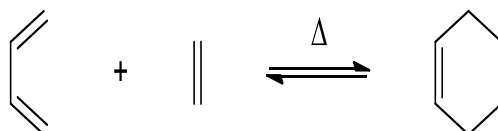
(Z)-(3*R*,7*S*) methyl jasmonate

Due to its important role in perfume industry as well as its limited natural resource, the synthesis of jasmonates has attracted interest of many chemists. The first synthesis of optically pure (Z)-(3*R*,7*S*)-methyl jasmonate was carried out in 1990 by Helmchen with the following steps:

1. The first step in the synthesis is a Diels-Alder reaction between cyclopentadiene **A** and ester **B** of fumaric acid with (S)-ethyl lactate to yield **C**.

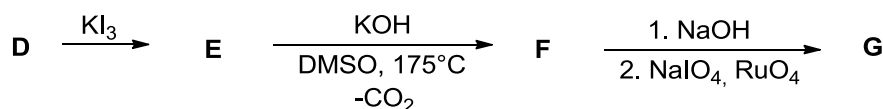


A cyclo-addition reaction, a kind of pericyclic reaction, involves bonding between the termini of two π systems to produce a new ring (scheme below). The product has two more σ bonds and two less π bonds than the reactants. The Diels-Alder reaction, or so called [4+2], is a common thermally activated cycloaddition whose stereoselectivity is *syn* addition. In this concerted *syn* addition, the stereochemical relationships among the substituents are retained in the product(s).



The hydrolysis of **C** in basic solution followed by an acidification step resulted in the formation of **D**. Draw the structures of **C** and **D**.

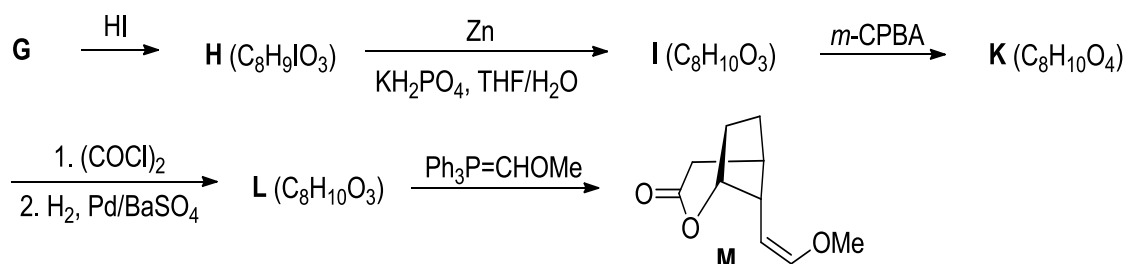
2. The reaction between **D** and I_2 in KI solution gave rise to the formation of the δ -iodolacton of the *endo* $-\text{COOH}$ group. When heated under basic condition, **E** underwent a decarboxylation-cyclization reaction to produce compound **F**. The hydrolysis in basic medium followed by oxidation with $\text{NaIO}_4/\text{RuO}_4$ transformed **F** into γ -keto acid **G**. Write down the structures of **E** to **G**.



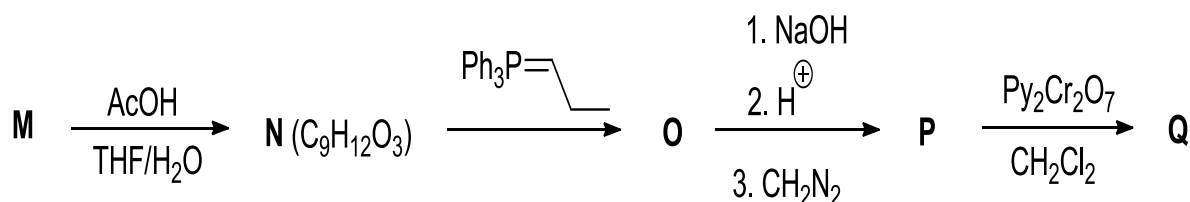
3. **G** was reacted with HI to yield compound **H** containing only five-membered rings. When **H** was reduced by $\text{Zn}/\text{KH}_2\text{PO}_4$ in tetrahydrofuran, it transformed into carboxylic acid **I** which was then oxidized in a Bayer-Villiger rearrangement with



meta-chloroperoxybenzoic acid (*m*-CPBA) to give the major product **K**. **K** was treated with oxaloyl chloride, followed by a Pd/BaSO₄ catalyzed reduction with H₂ (Rosenmund reduction) to give **L**. Compound **M** was separated from the Wittig reaction mixture between **L** and the yield Ph₃P=CHOCH₃. Draw the structures of the compounds from **G** to **L**.



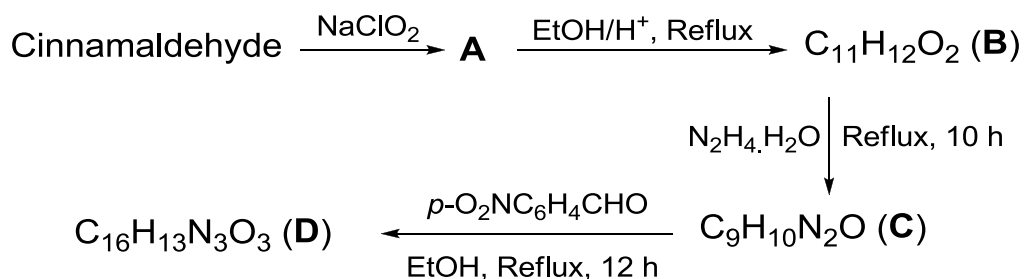
4. Hydrolysis of **M** in THF/H₂O solution of acetic acid produced **N** which underwent a Wittig reaction with the ylide Ph₃P=CHCH₂CH₃ to form **O**. The hydrolysis of **O** in basic solution, followed by a neutralization step and then treatment with diazomethane resulted in the formation of **P**. In the last step, the target molecule, (*Z*)-(3*R*,7*S*)-methyl jasmonate **Q**, was obtained in the oxidation reaction of **P** with pyridinium dichromate. Draw the structures of compounds from **N** to **P**.



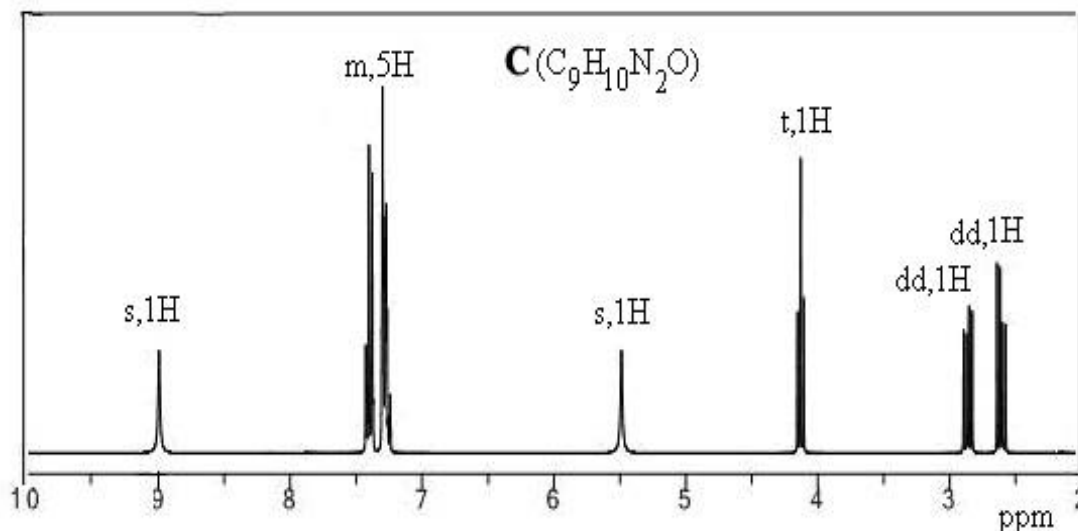
Problem 21. Vietnamese cinnamon

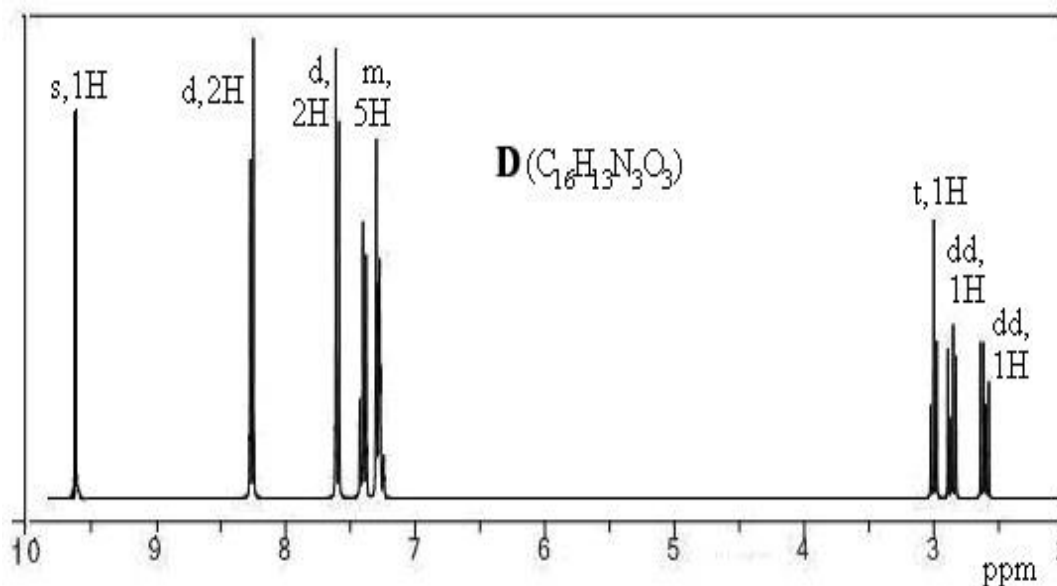
Cinnamomum loureiroi, also known as Vietnamese cinnamon, is an evergreen tree grown in the central and northern regions of Vietnam. Aromatic bark of the tree has medicinal and culinary value. Essential oil of the bark contains cinnamaldehyde ((2*E*)-3-phenylprop-2-enal) as the main component.

Mild oxidation of cinnamaldehyde with NaClO₂ affords an acid **A**. **A** undergoes subsequent esterification with ethanol to form ethyl cinnamate (**B**). Refluxing ethyl cinnamate and 80% hydrazine hydrate solution for 10 h gives **C** (C₉H₁₀N₂O). Refluxing **C** and *p*-nitrobenzaldehyde in ethanol for 12 h affords **D** (C₁₆H₁₃N₃O₃).

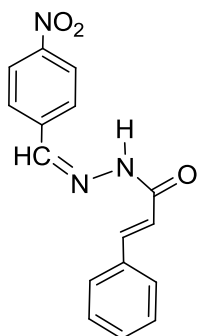


¹H NMR spectra of **C** and **D** are given below (the multiplicity and relative intensity is shown for each signal).

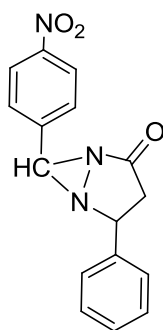




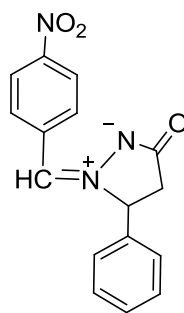
1. Give the structures for **A**, **B**, **C**.
2. Assign 1H NMR signals in the first spectrum to appropriate proton groups of **C**.
3. Propose a reaction mechanism for the formation of **C** from **B**.
4. Among four given below structures, select one for **D** and give the reasons for your selection.



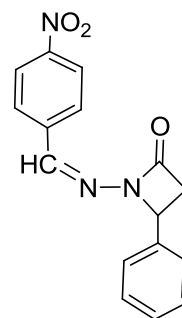
(D1)



(D2)



(D3)



(D4)

5. Assign 1H NMR signals in the second spectrum to appropriate proton groups of **D**.



Problem 22. Cinnamic acid

1. Ultraviolet irradiation of *trans*-cinnamic acid ((*E*)-3-phenylprop-2-enoic acid) in solution yielded a mixture of *cis*-cinnamic and *trans*-cinnamic acids. *trans*-Cinnamic acid can be crystallized in two forms: α -form or β -form. Ultraviolet irradiation of crystalline *trans*-cinnamic acid in the α -form yielded α -truxillic acid (2,4-diphenylcyclobutane-1,3-dicarboxylic acid). Ultraviolet irradiation of crystalline *trans*-cinnamic acid in the β -form yielded β -truxinic acid (2,3-diphenylcyclobutane-1,4-dicarboxylic acid). α -Truxillic acid possesses a symmetric center. In β -truxinic acid, the two phenyl groups are on the same side of the cyclobutane ring, and the two carboxyl groups are on the opposite sides.

1.1 Propose a reaction mechanism for the isomerization of *trans*-cinnamic acid.

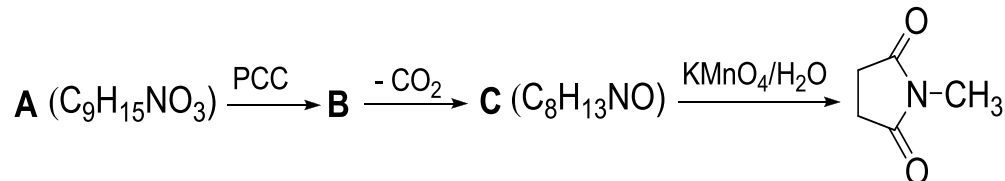
1.2 Draw the structure of α -truxillic acid and all its diastereoisomers.

1.3 Draw the structure of β -truxinic acid and all its diastereoisomers. Show the structures which have enantiomers.

1.4 Suggest how the different packing arrangements of *trans*-cinnamic acid in the α - and β - crystal forms leads to the different structures of α -truxillic and β -truxinic acid.

1.5 Why does cinnamic acid not dimerize in solution upon ultraviolet irradiation?

2. Hydrolysis of α -truxilline ($C_{38}H_{46}N_2O_8$, an alkaloid obtained from *Truxillo coca*) gives α -truxillic acid, methanol and an acid **A** ($C_9H_{15}NO_3$). Oxidation of **A** with pyridinium chlorochromate (PCC) leads to **B**, which is readily decarboxylated to form optically inactive ketone **C** ($C_8H_{13}NO$). Oxidation of **C** with potassium permanganate gives N-methylsuccinimide.



2.1 Propose the structures of **A**, **B**, **C**. Are **A**, **B** optically active or not? Explain.

Why **C** is optically inactive?

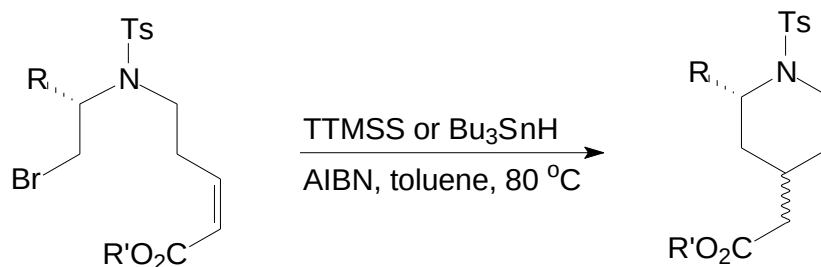
2.2 Propose the structure of α -truxillone. Is α -truxillone optically active or not? Explain.

Problem 23. Tris(trimethylsilyl)silane and azobisisobutyronitrile

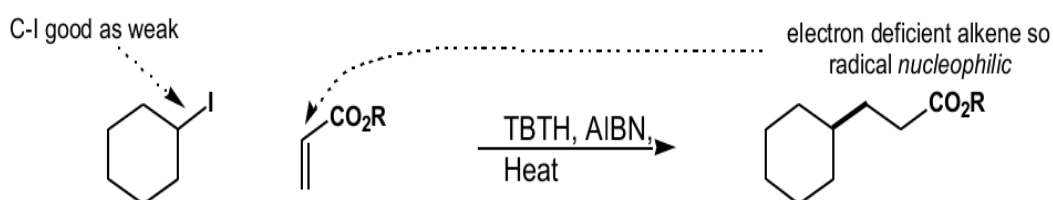
In the late eighties, Chatgililoglu and coworkers introduced tris(trimethylsilyl)silane, (TTMSS or $(\text{TMS})_3\text{SiH}$) as a radical-based reducing agent for functional group modifications and a mediator for sequential radical reactions. The use of $(\text{TMS})_3\text{SiH}$ allows reactions to be carried out under mild conditions with excellent yields of products and remarkable chemo-, regio-, and stereoselectivity. $(\text{TMS})_3\text{SiH}$ is an effective reducing agent for the removal of a variety of functional groups. Examples of dehalogenation (Cl, Br and I) and reductive removal of chalcogen groups (SR and SeR) are well known. The most popular thermal initiator is azobisisobutyronitrile, {AIBN, $[(\text{CH}_3)_2\text{C}(\text{CN})]_2\text{N}_2$ } under heating conditions in toluene.

1. Reactions using TTMSS and AIBN are given in the hereunder examples.

1.1 Radical cyclisation was studied using two different reducing agents: tributyltin hydride (TBTH, Bu_3SnH) and tris(trimethylsilyl)silane (TTMSS).

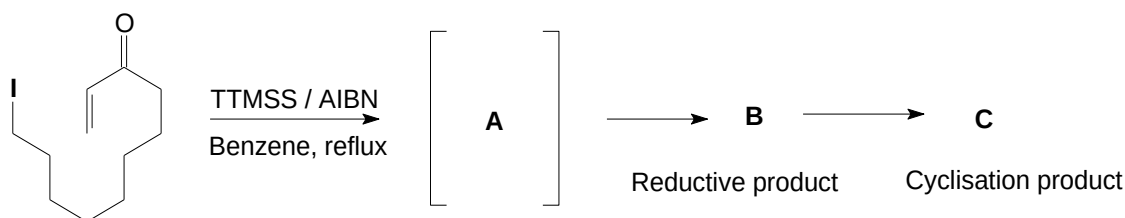


1.2 Radical introduction of a side chain (alkylation)

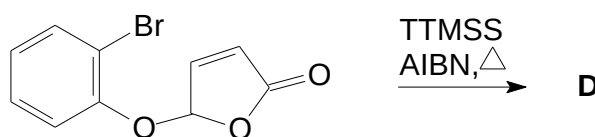


2. TTMSS has found multiple applications in the organic synthesis described in the below reactions:

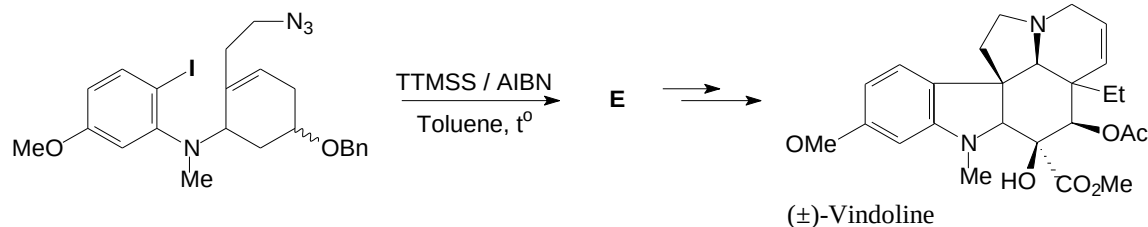
2.1 The compound (**I**) was converted to **B** and **C** via the radical intermediate **A**.



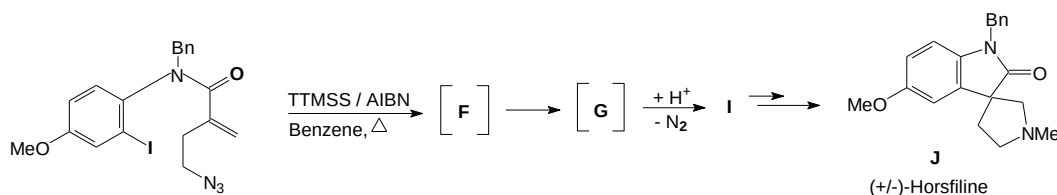
2.2 The compound (**II**) was converted to **D**.



2.3 The compound (**III**) was converted to **E**, and then through several steps to afford (±) - vindoline



2.4 Horsfiline (**J**) is an oxindole alkaloid found in the plant *Horsfieldia superba*, which has analgesic effects. The method for horsfiline synthesis from the compound (**IV**) was described below:



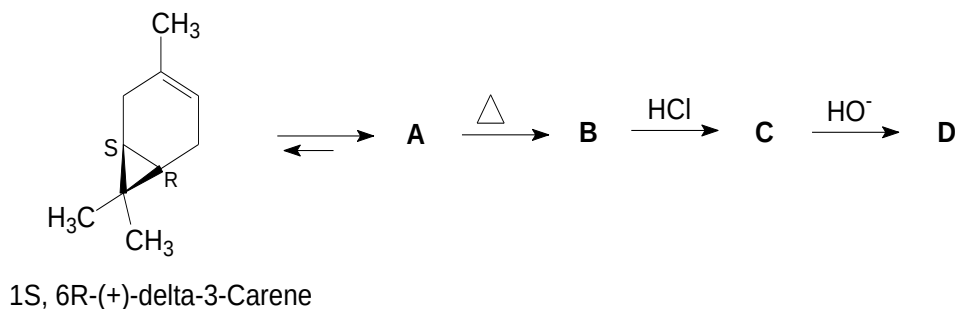
Write down the structural formulae of all compounds **A** to **I** given in the above reactions.

Problem 24. (–)-Menthol from (+)-δ-3-Carene

Carene, or δ-3-carene, is a bicyclic monoterpene which occurs naturally as a constituent of turpentine. (+)-δ-3-Carene has the required structural features to serve as a starting material for (–)-menthol.

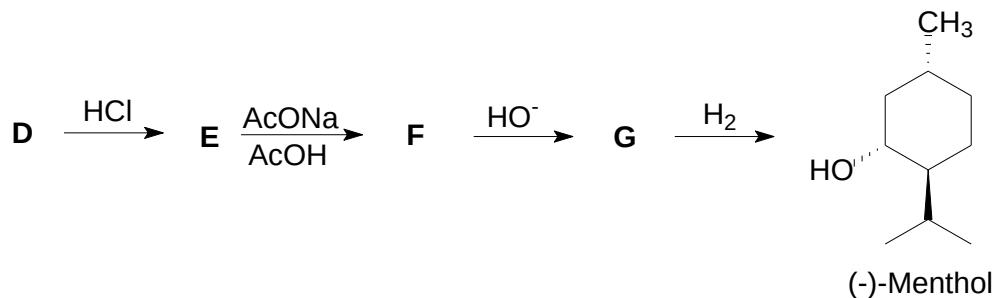
The procedure of preparation of (–)-menthol from (+)-δ-3-carene was described as follows. Catalytic isomerization of δ-3-carene provides the needed (+)-δ-2-carene (**A**) which then was pyrolysed to cleave the cyclopropane ring. The resultant 2,8-menthaldien (**B**) had the right stereochemistry at C1 and C4 of (–)-menthol.

Treatment of the unconjugated diene **B** with 1 equivalent mole of HCl gives **C** and then, dehydrochlorination leads to a conjugated diene (**D**).



Treatment of **D** with hydrogen chloride affords 8-chloro-3-*p*-menthene (**E**) which then reacted with sodium acetate and acetic acid to give mixed (*cis/trans*) pulegol esters (**F**) via allylic displacements. Hydrolysis of **F** affords (-)-*cis* and (+)-*trans*-pulegol (**G**).

Because the absolute configuration of C-1 is fixed in this system, reduction of either pulegol isomer provides menthol isomers which can be readily equilibrated to predominantly (-)-menthol.

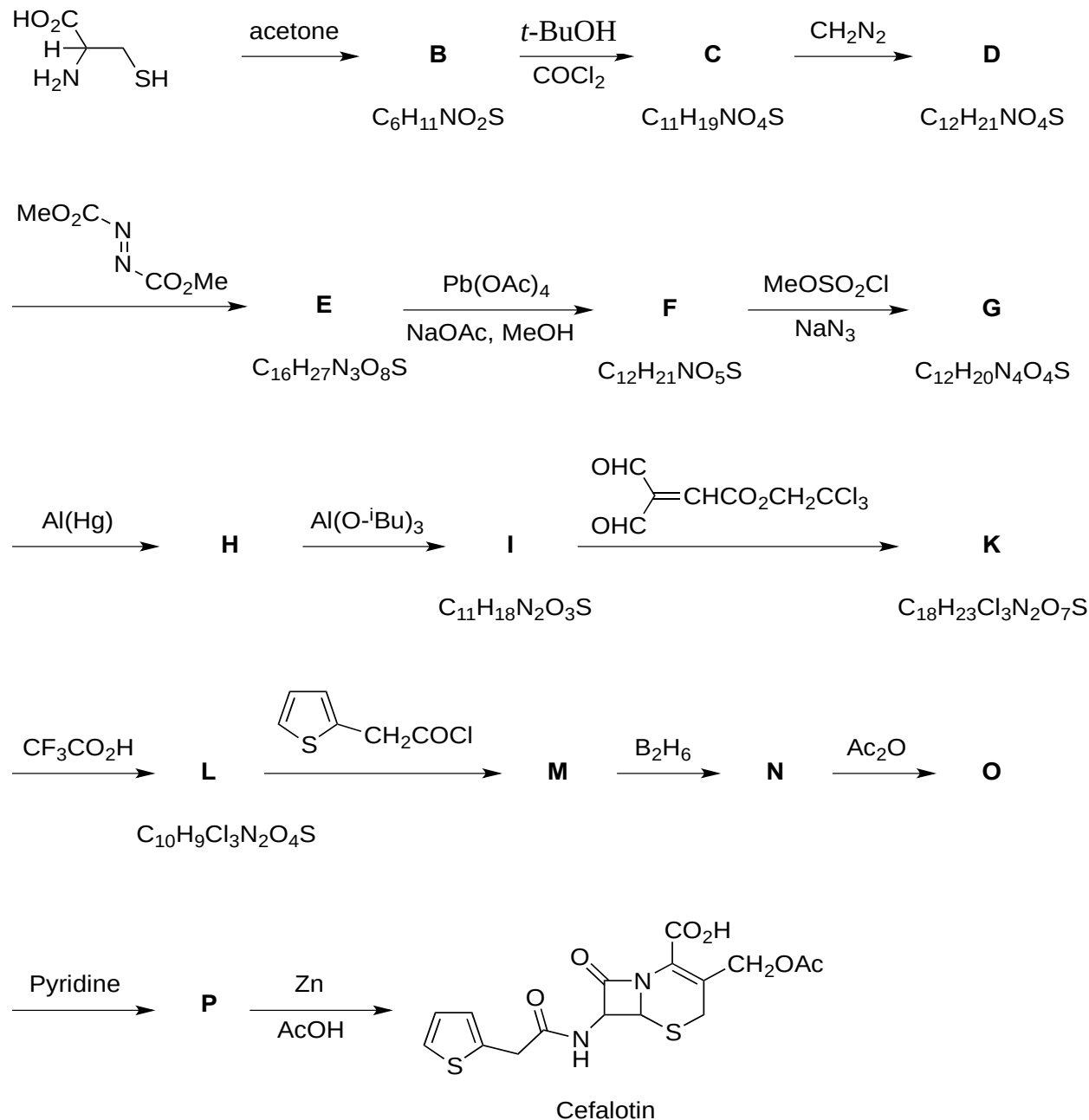


Write down the structural formulae of the compounds **A** to **G**.

Problem 25. Cefalotin

Cefalosporin is a β -lactam group antibiotic. Cefalotin, a derivative of cefalosporin, has stronger activities on gram (-) and gram (+) bacteria, but lower

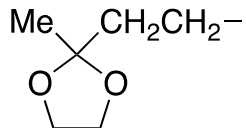
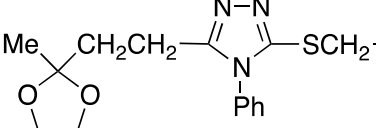
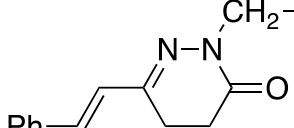
toxicity. Therefore, it has been studied and applied into medical treatment. Cefalotin has been synthesized from L-cistein according to the following diagram:



1. Complete the above synthetic scheme.
2. Write down a reaction mechanism from **K** to **L**.
3. How many optical isomers of cefalotin should be expected?

Problem 26. A heterocyclic compound

Recently, several transformations of levulic acid (4-oxopentanoic acid) have been reported in the Journal of Chemistry (Vietnam). One of them is the synthesis of three hydrazides (RCONHNH₂) from levulic acid in which R is one of the followings:

 Compound A	 Compound B	 Compound C
--	--	--

Assuming that you have: inorganic chemicals, levulic acid, other acyclic organic compounds, benzene derivatives (PhCHO, PhNCS, 3-NO₂C₆H₄SO₃Na), catalysts (piperidine, TsOH), and solvents.

1. Provide the synthetic scheme to obtain **A**. What is the purpose of 1,3-dioxolane formation? Write down the reaction equation to prepare TsOH from toluene.
2. Provide the synthetic scheme to obtain **B**. What is the reaction mechanism using PhNCS? Write down the reaction equation to synthesize PhNCS from alinine?
3. Provide the synthetic scheme to obtain **C**. What is the role of 3-O₂NC₆H₄SO₃Na? Write down the reaction equation to prepare 3-O₂NC₆H₄SO₃Na from benzene. Using signals from proton nuclear magnetic resonance spectroscopy to prove that the reaction with 3-O₂NC₆H₄SO₃Na has occurred?
4. The three hydrazines (**A**, **B**, and **C**) are reacted with PhCHO to generate corresponding products (**E**, **F**, and **G**). Draw a common reaction mechanism for these transformations. If 4-NO₂C₆H₄CHO or 4-Me₂NC₆H₄CHO was used instead of PhCHO, should the reactions proceed more difficult or easier?

Problem 27. Lotus

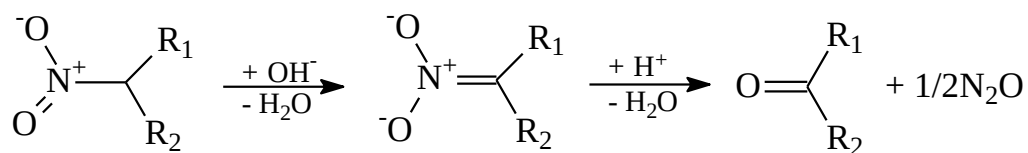
Lotus is known as the scientific name of *Nelumbo nucifera*. Recently, Vietnamese researchers collaborating with Canadian scientists discovered the ability to promote the production of insulin in β cells of nuciferine, which may be used to treat the **Hypoglycemia**. (K. Hoa Nguyen, H.Dien Pham, B.L. Gregoire Nyomba et al. *J. of Ethnopharmacology*, 2012, 142, 488-495). There are some ways to synthesize nuciferine from different



reactants, but the synthetic procedures are almost very complicated and the reaction yield is very low. Chia-Fu Chang et al. at Changhua National University (Taiwan) reported a procedure to synthesize the nuciferine through 3 steps using a benzaldehyde derivative in Nef reaction, Pictet-Spengler reaction and radical cyclization (*Synth. Commun.*, 2010, 40, 3452-3466,).

- Nef's reaction (John Ulric Nef, 1894):
$$R_2CHNO_2 \xrightarrow[2.H_2SO_4]{1.NaOH} R_2CO + 1/2N_2O$$

The mechanism of Nef's reaction:

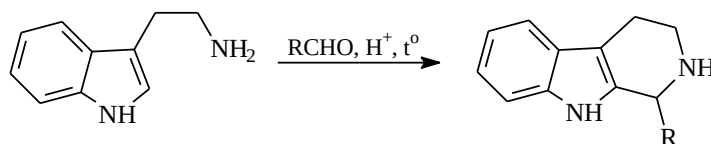


Example:
$$CH_3CH_2NO_2 \xrightarrow[2.H_2SO_4]{1.NaOH} CH_3CHO + 1/2 N_2O$$



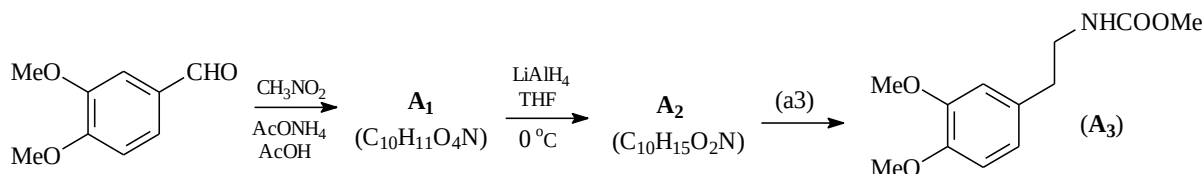
Radical initiator: AIBN [azobisisobutyronitrile, $\text{Me}_2\text{C}(\text{CN})\text{N}=\text{NC}(\text{CN})\text{Me}_2$]

The Pictet-Spengler addition-cyclization (Amé Pictet, Theodor Spengler, 1911): is the condensation reaction and then cyclization between β -arylethylamine and aldehyde or ketone in the presence of acid catalyst with heating. Example:

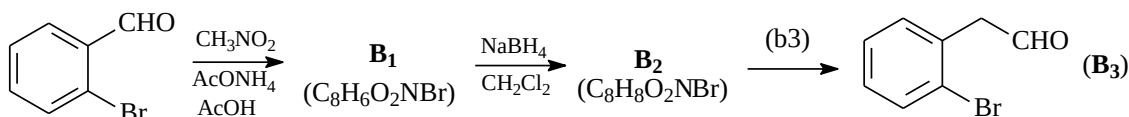


The reaction scheme for the synthesis of nuciferine is:

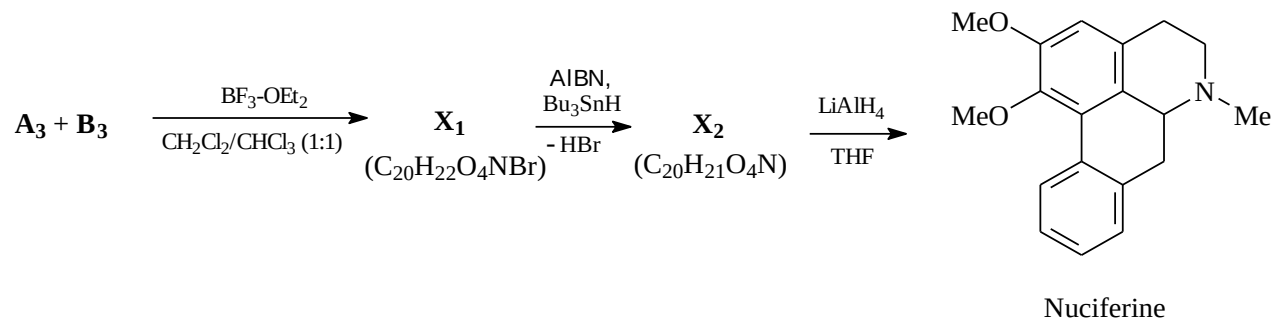
Step 1: Synthesis of *N*-methoxycarbonyl amine.



Step 2: Synthesis of arylacetaldehyde.



Step 3: Synthesis of nuciferine

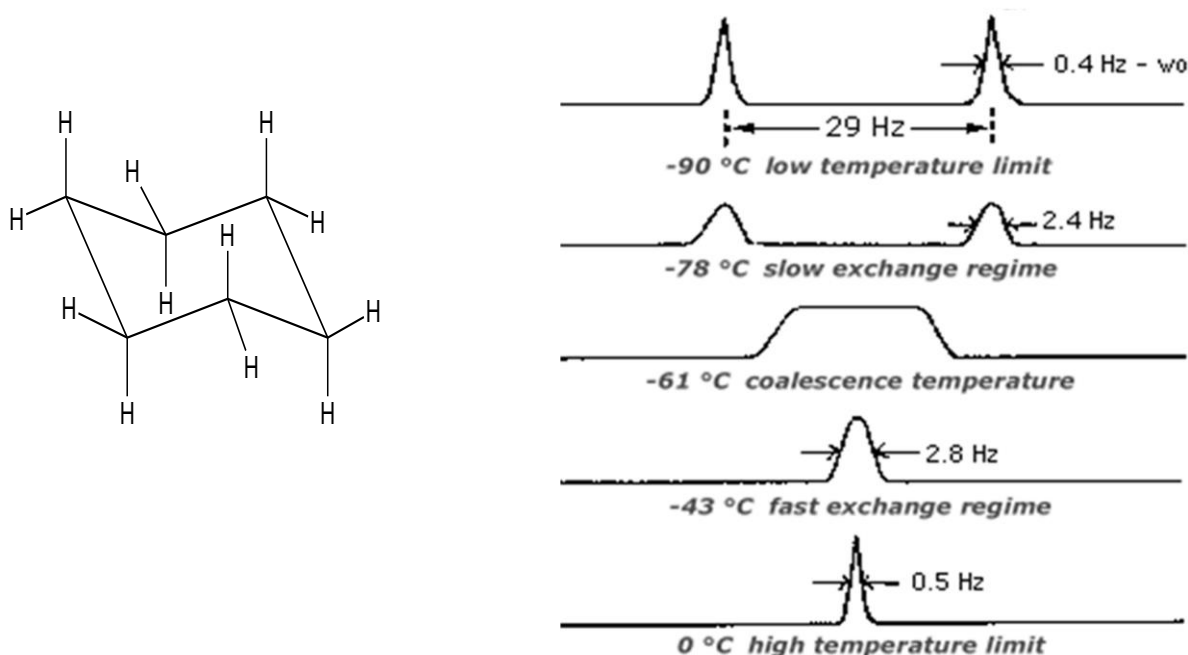


1. Determine the structural formulae for **A₁**, **A₂**, **B₁**, **B₂**, **X₁**, **X₂**, reaction conditions for (a3), (b3) and complete the above reaction scheme.
2. Indicate the reaction mechanism for the formation of **A₁** from 3,4-dimethoxybenzaldehyde (step 1); **X₁** from **A₃** + **B₃** (step 3).
3. Determine the structural formulae for two isomers of **Y_{1a}**, **Y_{1b}** and compound **Y₂** based on the schematic conversion below:



Problem 28. NMR Spectra

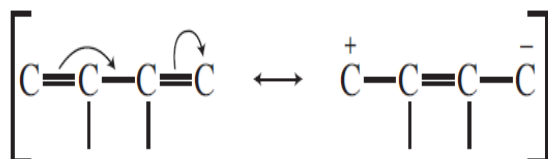
1. At room temperature, the NMR spectrum of cyclohexane shows only a single resonance peak. As the temperature of the sample is lowered, the sharp single peak broadens until at $-61.0\text{ }^{\circ}\text{C}$ it begins to split into two broaden peaks. As the temperature is lowered further to $-90\text{ }^{\circ}\text{C}$, each of the two bands begins to give a splitting pattern of its own. Explain the origin of these two families of bands.



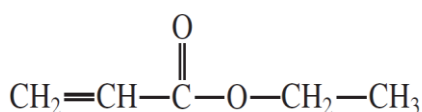
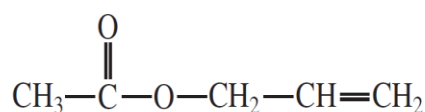
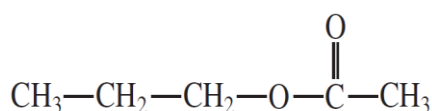
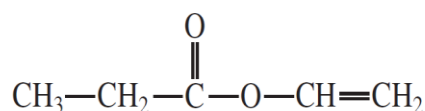
2. In *cis*-1-bromo-4-*tert*-butylcyclohexane, the proton on carbon-4 is found to give resonance at 4.33 ppm . In the *trans* isomer, the resonance of the C_4 hydrogen is at 3.63 ppm . Why do these compounds have different chemical shift values for the C_4 hydrogen? Justify why this difference cannot be observed in the 4-bromomethylcyclohexanes except at very low temperatures.

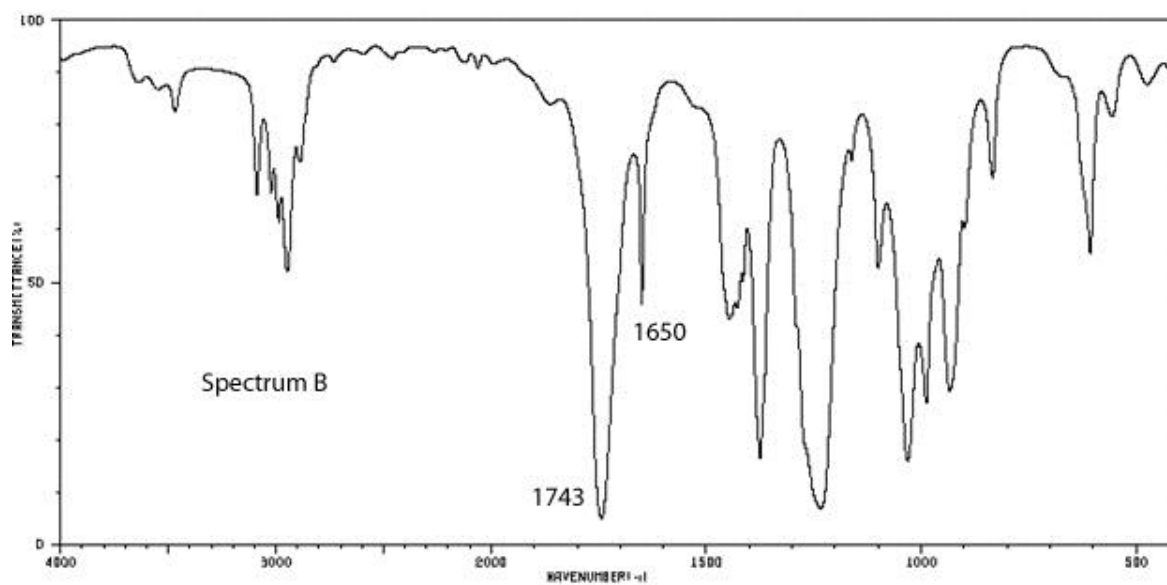
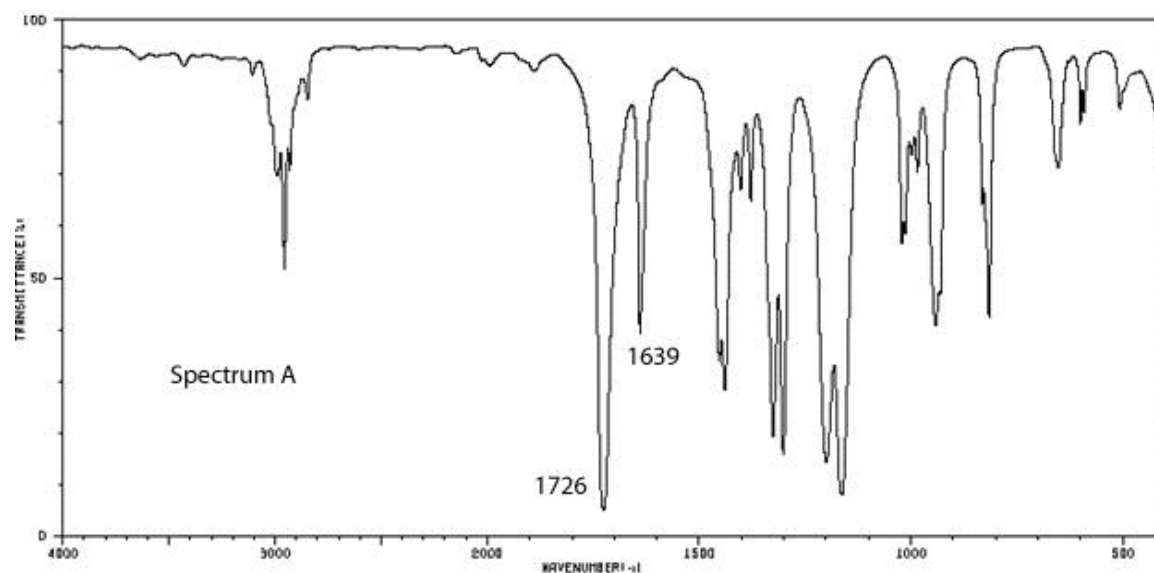
Problem 29. IR spectra

1. Substitution of an amino group on the *para* position of acetophenone shifts the C=O frequency from about 1685 to 1652 cm⁻¹, whereas a nitro group attached to the *para* position yields a C=O frequency of 1693 cm⁻¹. Explain the shift for each substituent from the 1685 cm⁻¹ base value for acetophenone.
2. Conjugation of a C=C double bond with either a carbonyl group or another double bond provides the multiple bond with more single-bond character (through resonance, as the following example shows), a lower force constant K , and thus a lower frequency of vibration. For example, the vinyl double bond in styrene gives an absorption band at 1630 cm⁻¹. Esters show a very strong band for the C=O group that appears in the range of 1750–1735 cm⁻¹ for simple aliphatic esters. The C=O band is shifted to lower frequencies when it is conjugated to a C=C or phenyl group (Hint: $\bar{\nu} = \frac{1}{2\pi c} \sqrt{\frac{K}{\mu}}$, μ , reduced mass; c , speed of light).



Assign a structure to each of the spectra shown. Choose from the following 5-carbon esters.







Part 2. PRACTICAL PROBLEMS

THE SAFETY RULES AND REGULATIONS

Regulations of the International Chemistry Olympiad (ICHO)

Safety

(1) During the experimental part, the competitors must wear laboratory coats and eye protection. The competitors are expected to bring their own laboratory coats. Other means of protection for laboratory work are provided by the organizer.

(2) When handling liquids, each student must be provided with a pipette ball or filler. Pipetting by mouth is strictly forbidden.

(3) The use of acutely toxic substances (GHS hazard statement H300, H310, H330) is strictly forbidden. The use of toxic substances is not recommended, but may be allowed if special precautions are taken. Substances with GHS hazard statements H340, H350, H360 (proven mutagens, carcinogens, and teratogens) must not be used under any circumstances (see Appendix B for definitions of these categories).

(4) Detailed recommendations involving students' safety and the handling and disposal of chemicals can be found in Appendices A 1, A 2, and B.

a) Appendix A 1: Safety Rules for Students in the laboratory.

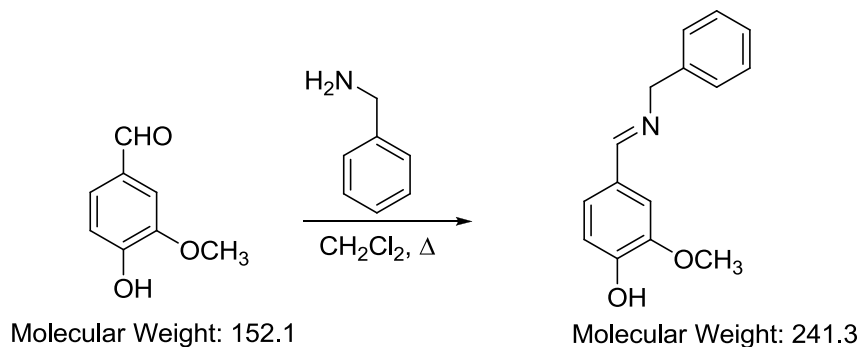
b) Appendix A 2: Safety Rules and Recommendations for the Host Country of the IChO.

c) Appendix B contains a reference to the hazard symbols and statements of the Globally Harmonized System of Classification of Chemicals (GHS), the use of which is expected in labeling and classifying materials used at the IChO.

Problem 30. Condensation between vanillin and benzylamine

1. Introduction

Vanillin is a phenolic aldehyde with the molecular formula $C_8H_8O_3$. Thus, it has three types of functional groups including aldehyde, ether, and phenol. This compound is often used as a flavoring agent in foods, beverages, and pharmaceuticals. Vanillin is the primary component of the extract of the *Vanilla planifolia*. It is known that the aldehyde functional group in vanillin can be easily converted into enamine derivatives or imides through the condensation reaction between vanillin and amines. The products are synthones which are widely applied in the synthetic organic chemistry and pharmaceuticals.



2. Chemicals and Reagents

- Vanillin: 1-2 g
- Benzylamine,
- Dichloromethane: 20 mL,
- Sodium sulfate, Na_2SO_4

3. Equipment and Glassware

- Erlenmeyer flasks, 250 mL
- Graduated cylinders, 10, 25, 50 mL
- Beral pipets,



- Beakers, 50 mL,
- Hot plate,
- Spatulas,
- Büchner funnel with filter flask and filter paper, separating funnel.
- Melting point apparatus and capillary tubes,
- Small vials with caps,
- Vials with caps, 20 mL
- Thin layered chromatography (TLC) spotters,
- TLC plates (silica with fluorescent indicator A254),
- Chamber for TLC development,
- Magnetic stirrer,
- Ice water bath.

4. Experimental procedure

1. Add 1.0 g of vanillin into a dry 50-mL flask then add 10 mL of dichloromethane solvent into the flask. The mixture is stirred for 10 min at room temperature, and then 0.7 g of benzylamine and 2.0 g of Na_2SO_4 are simultaneously added into the flask.
2. The reaction mixture is further stirred at reflux condition (65-67 °C) for 90 min. Cool the flask to room temperature.
3. Dilute the resultant mixture with 40 mL and swirl the flask.
4. Transfer the mixture into a separating funnel and then extract with 30 mL of dichloromethane. Extract the organic phase 2 times more with 30 mL of dichloromethane.
5. Dry the extracting organic fraction with MgSO_4 . Filter the organic fraction through a Buchner funnel. Discard the solid and collect the filtrate.



6. Remove the solvent in the filtrate by rotary evaporation to obtain the product(s).
7. Determine the purity of the crude product by thin layer chromatography method. Use precoated silica gel plates (Silica Gel PF-254) and visualize the spots by UV-light. Use ethyl acetate: heptane 15:85 mixture as an eluent.

Note: It is recommended to carry out the experiment under a hood.

5. Questions and Data analysis:

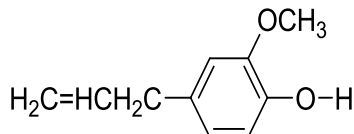
1. Weight the obtained product.
2. Draw the mechanism of imine formation.
3. What is the role of Na_2SO_4 in the present experiment?

Problem 31. Synthesis of eugenoxo acetic acid

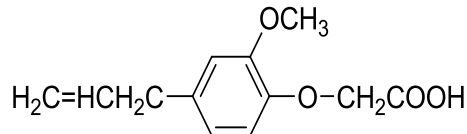
1. Introduction

Eugenoxoacetic acid (IUPAC name: 2-methoxy-4-(2-propenyl)phenoxyacetic) is an odorless, colorless and non-cytotoxic compound. It has shown anti-viral and anti-bacteria properties and is therefore used as antioxidant food preservative in food industry. Recently, eugenoxoacetic acid and its ester derivatives such as methyl and ethyl esters have been found to be the ability to inhibit lipid increasing which leads to their potential application in the treatment of human hyperlipidaemia. In addition, eugenoxoacetic acid acts as a promising plant growth promoter due to their auxin (aryloxyacetic) structural characteristics.

The nature and living organism friendly properties of eugenoxoacetic are the result of the combination of acetic moiety which is present in vinegar and eugenol moiety which is the main constituent of the essential oil obtained from clove oil.



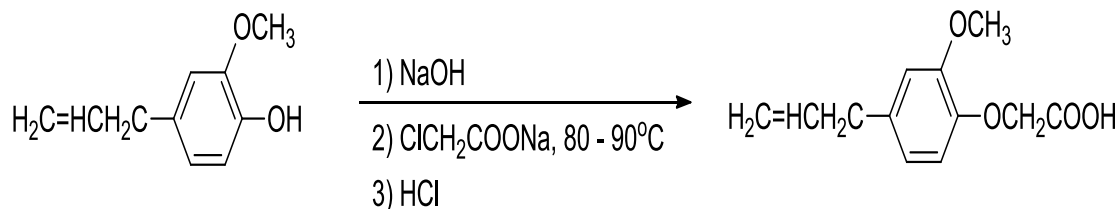
Eugenol



Eugenoxyacetic acid

Clove is an aromatic plant in the family Lamiaceae which is native to tropical areas and widespread as a cultivated plant. In Vietnam, there are two species of clove, *Ocimum sanctum* L. and *Ocimum gratissimum* L., which have been used in many traditional medicinal purposes without adverse effects.

In this practical problem, eugenoxyacetic acid will be synthesized from eugenol as shown in the scheme below:



2. Chemicals and apparatus

- Clove essential oil,
- Monochloroacetic acid,
- NaOH,
- Na₂CO₃
- Aqueous HCl solution,
- Distilled water.

3. Apparatus and glassware

- Erlenmeyer flask: 50 mL,
- Magnetic stirrer with heater,
- Magnetic bar,
- Beaker: 100 mL,



- Beaker: 250 mL,
- Glass filter: 25 mL,
- Glass filter: 50 mL,
- Vacuum filter set (vacuum pump, Filter flask),
- Dropping funnel,
- Spatula,
- Glass rod,

4. Experimental procedure:

Step 1

1. Dissolve 0.6 g NaOH in 3.0 ml distilled water in a 50 mL-Erlenmayer flask and then add 2.0 mL clove essential oil. Keep the flask in the water bath at 80-90 °C while stirring with the magnetic stirrer.
2. Dissolve carefully 1.0 g monochloroacetic acid in 5.0 mL distilled water in a 25 mL beaker; stir the solution with the spatula. Add Na₂CO₃ slowly just to the alkaline reaction (Solution **A**).

Step 2

1. Add slowly the solution **A** to an Erlenmayer flask and keep stirring the mixture at 90-95 °C for 60 min. Cool the reaction mixture with water to room temperature, and then acidify with HCl 1:1 to the acidic reaction (*test by litmus paper*) (Solution **B**).
2. Add a small amount of crushed ice (5-10 g) to the solution B and stir until the yellow oil turns to the solid. Isolate the solid by filtration with suction in to a sintered glass crucible. Wash the solid with water to obtain the crude product as pale yellow solid.

Step 3

1. Purify the product as follows: transfer the crude product to a 250 mL beaker, add 80-100 mL hot water (about 90 °C) to the beaker and continue boiling for 5-10 min. Cool the solution with water and ice-cold water.



2. Isolate the product by filtering with suction into a sintered glass crucible and wash the solid several times to obtain white needles. Dry the solid in the drying oven for 60 min. Weigh the dried product.

5. Questions and data analysis:

1. Write down the reactions occurring in step 1a, 1b and 2.
2. Calculate the reaction yield.
3. Propose a mechanism for the reaction in step 2.
4. Explain why the reaction must be conducted in alkaline medium? Should an excess amount of alkaline be used in the reaction?
5. Compare the possibilities of the chlorine atom in monochloroacetic acid and those in alkyl chlorides to be substituted.
6. If the pure product obtained in the experiment above (mp. 72 °C) is re-crystallized in benzene, its mp. Will rise to 100.5 °C. Suggest an explanation for this observation and propose method to test your explanation.
7. When eugenoxycetic acid is refluxed in KOH solution, and acidified with HCl (1:1) solution, an isomer of eugenoxycetic acid, isoeugenoxycetic acid can be obtained in the form of two stereoisomers. Determine the structures of these two isomers and explain the formation of isoeugenoxycetic acid with a suitable reaction mechanism.

Problem 32. Complexometric titration of iron, aluminum, and magnetism in the aqueous solution

1. Introduction

Complexometric titration is one of the most common methods of volumetric analysis in chemical laboratories. In this method, the most widely used complexing

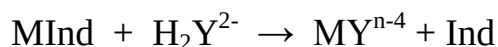
agent is disodium salt of ethylenediaminetetraacetic acid (EDTA). EDTA is a polyprotic acid (H_4Y). The solution Na_2H_2Y is used as a standard solution for titration of metal ions (M^{n+}):



The formation constant (K_f) of MY^{n-4} depends on the nature of metal ions. For example:

Metal ions	K_f	Titrated at pH
Fe^{3+}	$10^{25.1}$	2.0
Al^{3+} , Pb^{2+} , Zn^{2+}	$10^{16.13}$	4.0 – 5.0
Mg^{2+}	$10^{8.69}$	9.0 – 10.0

Metal ions can be titrated separately due to the formation of MY^{n-4} complex with conditional formation constant at a suitable pH condition. In practical, the metallochromic indicators are usually used for the detection of the end point. These indicators are the color complexing agents for the metal ions. The color of the indicator differs from that of the metal-ion-complex and metal indicator complex (Mind) is much less stable than metal-EDTA-complex. Therefore, the titration of a metal ion solution is carried out with a given indicator at suitable pH of the solution:



This task is to help participants to use techniques of the volumetric analysis for the determination of metal cations.

2. Chemicals and reagents

- Standard solutions of 0.050 M EDTA (from $Na_2H_2Y \cdot 2H_2O$),
- 0.050 M $Zn(NO_3)_2$,
- Buffer solutions of 1M CH_3COOH and 1 M $NaCH_3COO$ (pH = 4.7),
- Solution of 2 M NH_3 + 2 M NH_4Cl (pH = 9.2),
- Solution of 1M HCl,
- Solution of 1M NaOH,



- Distilled water,
- Indicators: xylenol orange (1% in KCl),
- Eriochrome black T (ET – 00) (1% in KCl); The congo red (pH indicator); universal pH indicator paper; 5% solution of sulfosalicylic acid.

3. Apparatus and glassware

- Burette: 50 mL,
- Volumetric pipette: 25 mL,
- Erlenmeyer flask: 250 mL,
- Graduated cylinder: 10 mL,
- Glass beaker: 250 ml,
- Funnels and filter papers (the red tape),
- Droppers,
- Hot plate.

4. Experimental procedure

Step 1. Sample preparation

Prepare a sample solution containing three ions of Fe^{3+} , Al^{3+} , and Mg^{2+} within concentration range of 0.01 M to 0.1 M.

Step 2. Titration of iron, aluminum, and magnesium ions

1. Titration of Fe^{3+}

Add 5.00 mL of the sample solution into an Erlenmeyer flask. Adjust the pH of the solution to 2 using NaOH or HCl solution with the Congo red paper. Heat the solution to 80 - 90 °C on a hot plate and then add 0.5 mL of sulfosalicylic acid as indicator. The solution is titrated with EDTA solution to a colorless to yellow end point. Record the volume of the standard solution (V_1 mL).



2. Titration of the total amount of Fe^{3+} and Al^{3+}

Add 25.00 mL of the sample solution into an Elenmeyer flask. Add 50 mL of EDTA standard solution into the flask. Heat the solution to 80 - 90 °C and add 10 - 15 mL of the buffer solution $CH_3COOH/NaCH_3COO$ and a small amount of xylenol orange. Titrate the remaining amount of EDTA with the Zn^{2+} standard solution until the solution changes from red to yellow at the end-point. Record the volume of the standard solution (V_2 mL).

3. Titration of Mg^{2+}

Take 25.00 mL of the sample solution to a glass beaker. Add slowly the $NH_3 + NH_4Cl$ buffer solution while stirring the mixture. After the precipitation reaction is complete, add 5 mL of buffer solution and swirl the mixture. Filter the solution to an Elenmeyer flask through filter paper with a funnel. Wash the precipitate (3-4 times) with warm water. Finally, titrate Mg^{2+} with standard EDTA solution using ET - 00 until the solution changes from white red to blue. Record the volume of the standard solution (V_3 mL).

5. Questions and Data analysis

1. Write down the chemical reactions in each individual step of the titration.
2. Derive the formulae for calculating the concentrations of Fe^{3+} , Al^{3+} and Mg^{2+} in the sample solution.
3. Calculate the concentrations of each ion in the sample solution.

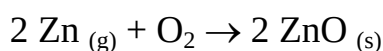
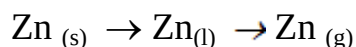


Problem 33. Determination of zinc and lead in zinc oxide powder

1. Introduction

Zinc oxide ZnO, a soft, white or faintly yellowish-white is used in the vulcanization of rubber, ceramics, paints, and many other products.

Zinc oxide is produced by burning zinc metal in air as follows:



Purity of the given zinc has an influence on the quality of zinc oxide powder. There is a very wide range of commercial grades of zinc oxide depending on content of impurities. For example, zinc oxide powder -Grade 2 (having greater than 60 wt.% of Zn) produced by electro-thermal process contains less than 4% Ca; 0.4% Fe; 8% Pb.

This task is to determine the percentage of zinc and lead in commercial zinc oxide powder by EDTA and dichromate solution.

2. Materials and Reagents

- Zinc oxide powder,
- Sulfuric acid solution, H_2SO_4 (aq), 4 M,
- Nitric acid solution, HNO_3 (aq), 6 M
- 0.025 M EDTA standard solution (from $\text{Na}_2\text{H}_2\text{Y} \cdot 2\text{H}_2\text{O}$),
- Sodium thiosulfate: 0.02 M solution (from $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$),
- Ferrous sulfate: 0.025 M solution (from $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$),
- Mixture of HCl and NaCl: Dissolve 320 g of NaCl in 200 mL of distilled water, add 100 mL of concentrated HCl 37 wt.% and dilute to 1.0 L with distilled water,
- Solution of 5% (w/v) $\text{K}_2\text{Cr}_2\text{O}_7$ (aq),



- Mixture of potassium iodide and thiocyanate, KI+ KSCN, 10% w/v,
- Mixture of CH_3COOH 2 M and $\text{NH}_4\text{CH}_3\text{COO}$ 1M,
- Ammonia solution NH_3 6 M,
- 200 mL of pH 10 buffer solution of $\text{NH}_3/\text{NH}_4\text{Cl}$,
- Eriochrome Black T (ET-00) indicator, 1% (w/w) in NaCl(s),
- Diphenylamine sulfonate indicator, 0.2% (w/w) in water,
- Starch indicator, 1% in water. This solution is prepared daily by mixing 0.5 g soluble starch with 2-3 mL distilled water and then pouring the starch into 50 mL boiling distilled water with stirring. Continue heating the solution until the solution is nearly transparent. Cool solution to room temperature before use.

3. Apparatus and glassware

- Analytical balance (± 0.0001 g)
- Hotplate
- Erlenmeyer flask, 250 mL
- Volumetric flask, 100 mL
- Volumetric pipette, 10.00 mL
- Burette 25 mL
- Glass beaker 250 mL
- Whatman Filter paper, Grade 2V, 110 mm.

4. Experimental procedure

Step 1

1. Place 0.50 g of a powder sample in a 100 mL glass beaker. Add 10 mL of 4 M H_2SO_4 into the beaker. Place the beaker on a hot plate and begin heating the mixture in the hood. Set the hot plate at medium heat. As a portion of solid



dissolves, the yellowish residues still remains in the beaker. Add slowly 3 mL of HNO_3 solution into the beaker and keep heating the solution until white precipitate appears. Evaporate the solution in the beaker until white fumes of SO_3 forms, and then stop heating. Cool the solution to the room temperature (*Hint: in hood*).

Filter the cooled solution by using filter paper to a 100 mL volumetric flask; rinse the beaker and filter paper with 1 % H_2SO_4 several times; make up the filtrate to the mark with distilled water and shake well (solution **A**).

2. Place the funnel together with the filter paper on a 250 mL Erlenmeyer flask. Pour slowly a hot mixture of 20 mL of $\text{CH}_3\text{COOH} + \text{NH}_4\text{CH}_3\text{COO}$ through the white precipitate on the filter paper until it is dissolved. Wash the filter paper with distilled water to get solution **B**.

Step 2

1. Add 10.00 mL of solution (**A**) and 5 mL of NH_3 solution into a 250 mL Erlenmeyer flask using pipettes and swirl to mix. Then, add 10 mL of $\text{NH}_3/\text{NH}_4\text{Cl}$ buffer solution (pH = 10) to the mixture.

Add ET-00 indicator and about 10 mL of deionized water. Titrate carefully with the EDTA standard solution until the color changes from wine red to blue. Record the volume of EDTA used for this titration.

(*Hint: Adjust the size of the aliquot on Zn^{2+} as necessary to stay within titration range*).

2. Add the solution **B** and 5 mL of 10 % NaCH_3COO into a 250 mL beaker. Heat the mixture slowly (taking at least 10 minutes) to 90 °C and then add gently 10 mL of $\text{K}_2\text{Cr}_2\text{O}_7$ solution. Cool the mixture to room temperature and keep further at this condition for 1 hour. Filter the precipitate through a Whatman filter paper. Wash the precipitate with warm distilled water until the filtrate is almost colorless.



Transport the funnel with filter paper to a 250 mL Erlenmeyer flask. Dissolve the yellow precipitate with 15 mL of warm mixture HCl + NaCl. Rinse the filter paper with distilled water to get the solution **C**.

Add about 5 mL of 4 M H₂SO₄, 5 mL of 4 M H₃PO₄, and 10 mL of distilled water to the solution **C**. Drop 8 droplets of diphenylamine sulfonate indicator in the solution **C**. Titrate carefully with the standard ferrous solution until the color changes from violet to green. Record the volume of ferrous solution used.

(Hint: Solution C can also be titrated using the iodometric titration).

5. Questions and Data Analysis

1. Give balanced chemical equations for the reactions when:

1.1 The zinc oxide powder dissolves in sulfuric acid and nitric acid to form a white solid.

1.2 The white precipitate is dissolved in a mixture of CH₃COOH 2 M- NH₄CH₃COO 1 M to form a complex product **X**.

1.3 The product **X** reacts with K₂Cr₂O₇(aq) to form a yellow precipitate.

1.4 The yellow precipitate dissolves in the mixture of HCl and NaCl.

1.5 The solution **C** is titrated with Fe²⁺ and/or iodometric titration.

2. Calculate the mass percentage of Zn and Pb in the powder.

3. In iodometric titration, S₂O₃²⁻ is used to titrate I₂ produced in the reduction of H₂Cr₂O₇ by I⁻. Why do we not use S₂O₃²⁻ for titration of the H₂Cr₂O₇?

4. PbCrO₄ is completely precipitated in the medium with pH of at least 5 (acetic acid- acetate buffer).

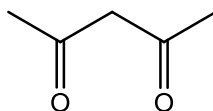
4.1 Does the addition of 100 mL of 1.0×10⁻⁴ M Pb(OAc)₂ to 20 mL of 1.0×10⁻³ M K₂CrO₄ lead to a precipitate formation, given that K_{sp} for PbCrO₄ is 1.8×10⁻¹⁴?

4.2 Find the equilibrium concentration of Pb²⁺ remaining in solution after the PbCrO₄ precipitates.

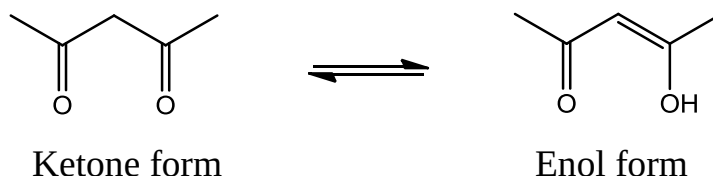
Problem 34. Preparation of copper(II) acetylacetonate

1. Introduction

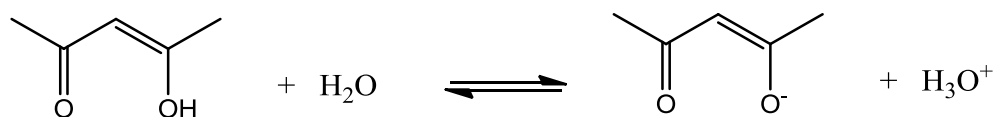
Acetylacetone (Hacac) is the simplest of the beta-diketones.



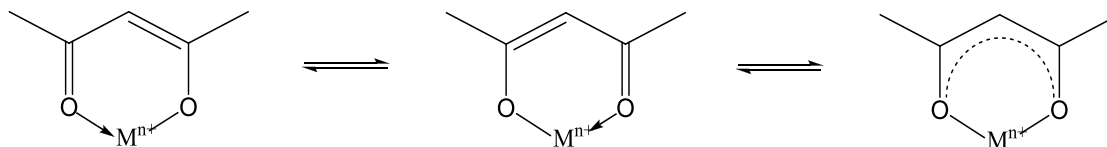
Hacac commonly exists in two tautomeric forms, ketone and enol, which can rapidly interconvert in solution as well as in the gas phase.



In aqueous solutions, Hacac is in equilibrium with hydrogen ions (H^+) and with acetylacetonate (enolate) ions (acac^-). The dissociation constant K_a is 1.51×10^{-9} .



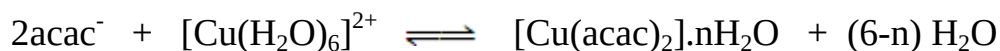
Acetylacetone can form stable complexes with many transition metal ions. In most of the structurally characterized complexes, Hacac that is singly deprotonated acts as a bidentate ligand, and binds to the metal via both two oxygen donor atoms to form six-membered chelate ring.



Acetylacetone is known to form neutral complexes with about 60 metals and is among the most versatile and most used chelating ligand in coordination chemistry.



Copper (II) acetylacetonate can be synthesized in a ligand exchange reaction:



2. Chemicals and Reagents

- Acetylacetone
- 0.2 M CuSO₄ aqueous solution
- 25% NH₃ solution
- Diluted HCl solution
- Diluted NH₃ solution
- Universal indicator papers
- Chemicals for determination of Cu content.

3. Apparatuses and Glassware:

- Glass beakers: 100 mL, 50 mL,
- Pipette: 5 mL,
- Graduated cylinder: 50 mL,
- Rubber bulb,
- Watch glass,
- Glass rod,
- Magnetic stirrer,
- Sintered glass funnel,
- Vacuum pump,
- Wash bottle,
- Analytical balance with readability of 0.001 g.



4. Experimental procedure:

Step 1. Preparation of copper (II) acetylacetonate:

1. Use 25 mL of 0.2 M CuSO_4 aqueous solution to calculate the quantities of chemicals required for synthesis of the complex.
2. Prepare the ammonium acetylacetonate (NH_4acac) solution: Add slowly 25% NH_3 aqueous solution ($d = 0.90 \text{ g.cm}^{-3}$) into liquid acetylacetone in a 50 mL glass beaker with a molar ratio $\text{Hacac} : \text{NH}_3$ of 1.0 : 0.9. A white solid appears for seconds and then dissolves completely to obtain a clear solution.
3. Prepare the copper (II) acetylacetonate: Add the freshly prepared NH_4acac solution (with a 50% excess) into a 100 mL glass beaker in which 25 mL of 0.2 M CuSO_4 aqueous solution and a stirring bar are placed. Start stirring the solution on a magnetic stirrer and adjust the pH of the mixture to 3-4 by the addition of dilute solutions of HCl and NH_3 . The pale blue solid of copper (II) acetylacetonate is precipitated. The reaction mixture is stirred for additional 30 min to complete the precipitation. The formed solids are collected on sintered glass funnel by a vacuum filtration, washed 3 times with small portions of distilled water and then transported to a watch glass and dried at 120°C for 30 min. Weigh the product on the analytical balance with the readability of 0.001 g.

Step 2. Determination of the Cu content in the complex

1. Students propose an appropriate procedure to determine the Cu content in the product. (*Hints: The Cu^{2+} concentrations can be determined by iodometric titration, complexometric titration with EDTA...*).

5. Questions and Data analysis

1. Calculate the copper content in the complex. Suggest an appropriate molecular formula of copper (II) acetylacetonate and then calculate the percentage yield of

the synthesis of the complex.

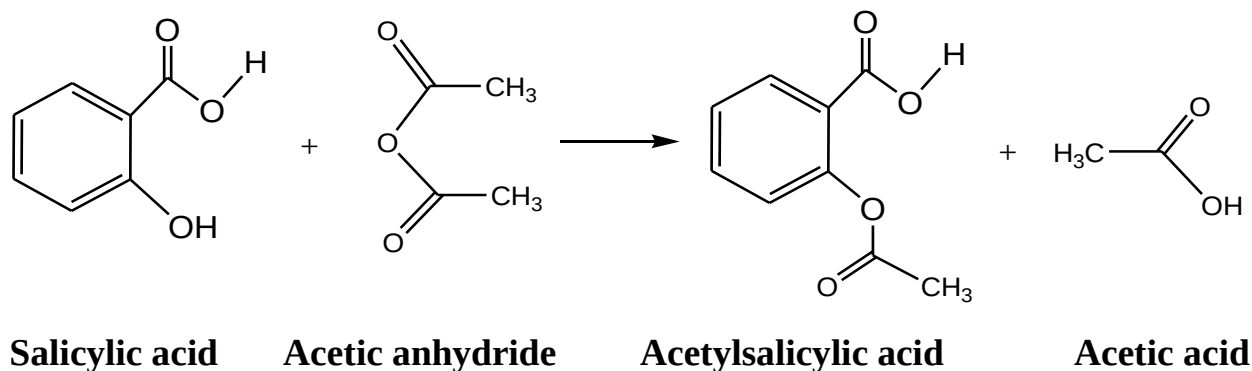
2. In the Step 1(3), why is the excess of NH_4acac used? Why does the pH need to be adjusted to 3-4?
3. Propose the molecular structure of copper (II) acetylacetonate.

Problem 35. Kinetic analysis of the hydrolysis of aspirin

1. Introduction

Aspirin (acetylsalicylic acid) is an ester of salicylic acid. It has been widely used in medicinal treatment. It is an effective analgesic (pain killer) that can reduce the mild pain of headache, toothache, neuralgia (nerve pain), muscle pain and joint pain (from arthritis and rheumatism). Aspirin behaves as an antipyretic drug (it reduces fever), and an anti-inflammatory agent capable of reducing the swelling and redness associated with inflammation. It is an effective agent in preventing strokes and heart attacks due to its ability to act as an anti-coagulant.

Aspirin can be easily synthesized in laboratory by the esterification reaction between salicylic acid and acetic anhydride as shown in the reaction below:





In acidic or basic media, aspirin is hydrolyzed to give its active form – salicylic acid. The hydrolysis reaction of aspirin, however, takes place in basic condition much faster than in acidic condition. This illustrates a very important principle: the stability of drugs and their mechanisms strongly depend on the pH condition of the body.

In general, the hydrolysis of esters may be catalyzed by either acid or base. The detailed mechanism of hydrolysis reactions has been the subject of an enormous research effort, since they are of such fundamental importance. The generally accepted mechanism of acid-base-catalyzed hydrolysis is known; however many researchers particularly in biotechnology are applying this fundamental knowledge in new and more complicated systems.

This experiment deals with both the synthesis of aspirin and kinetic study of the hydrolysis of aspirin under a basic condition. Working with synthesis of aspirin, the preparative method uses acetic anhydride and an acid catalyst, concentrated sulfuric acid, to speed up the reaction with salicylic acid. Then the hydrolysis of aspirin will be studied under pseudo-order conditions. This will allow the order with respect to aspirin concentration to be determined. The order with respect to the concentration of hydroxide ions will be given and from this data you will be asked to draw conclusions about the mechanism.

2. Chemicals and Reagents

- Pure salicylic acid $\text{CH}_3\text{CO}_2\text{C}_6\text{H}_4\text{CO}_2\text{H}$
- Acetic anhydride $\text{CH}_3\text{C}_2\text{O}_3\text{CH}_3$
- Concentrated sulfuric acid H_2SO_4
- Absolute ethanol $\text{C}_2\text{H}_5\text{OH}$,
- Standard NaOH solution.



3. Apparatus and glassware

- UV-Vis Spectrophotometer
- Thermostat
- Stirrer hotplate
- Analytical balance (± 0.0001 g)
- Beaker glass, 100 mL
- Erlenmeyer flask, 100 mL
- Pipette, 5 mL
- Büchner flask (Filter flask)
- Büchner filter
- Filter paper
- Glass rod
- Stopwatch

4. Experimental procedure

Step 1. Synthesis of acetyl salicylic acid

1. Prepare a bath using a 400 mL beaker filled about half-way with water. Heat to boil.
2. Weigh 2.0 g salicylic acid using an analytical balance and place it in a 100 mL Erlenmeyer flask. Use this quantity of salicylic acid to calculate the theoretical or expected yield of aspirin.
3. Carefully add 5.0 mL of acetic anhydride by pipette to the Erlenmeyer flask containing the acid.
4. Add about 5-6 drops of concentrated sulfuric acid as catalyst.

Caution! *Acetic anhydride could irritate your eyes. Sulfuric acid could cause burns to the skin. Handle both chemicals with care.*



5. Mix the reagents and then place the Erlenmeyer flask in boiling water bath. Heat for 15 min. The solid will completely dissolve. Swirl the solution occasionally.
6. Add 10.0 mL water to the Erlenmeyer flask, shake the flask thoroughly, and then place it in an ice bath for 10-15 min to crystallize out the entire product, acetylsalicylic acid. Collect the crystals by filtration under vacuum. If the crystallization takes place slowly, scratch gently inside the flask with a glass rod.
7. Re-crystallize the crude product as follow: Dissolve the crude product in 10.0 mL ethanol, then pour the ethanol solution into 60.0 mL warm water and place the obtained solution in the ice water for 10-15 min. Filter off the product.
8. Dry the product in an oven at 100 °C for 30 min. Weigh the dried product.

Step 2. Hydrolysis of acetylsalicylic acid

1. Prepare 50.0 mL of a 5×10^{-3} M solution of salicylic acid in 20% ethanol and approx. NaOH 5×10^{-3} M solution as follows:
 - i) Weigh out the required amount of salicylic acid ($M = 138.1 \text{ g mol}^{-1}$) in small beaker on an analytical balance.
 - ii) Dissolve the weighed acid in 10.0 mL ethanol.
 - iii) Transfer this quantitatively into a 50 mL volumetric flask already containing 5.0 mL 5×10^{-2} M NaOH, wash the vial several times and add water to the mark.
2. Prepare 50.0 mL of a 5×10^{-4} M solution of salicylic acid as follows:
 - i) Place 10.0 mL ethanol in a 50 mL volumetric flask, add by pipette to this flask 5 mL solution prepared in step 1.
 - ii) Add a required amount of 5×10^{-3} M NaOH solution to fill up to the mark. Place the flask in a heated bath at 37 °C.
3. Measure the absorbance at 295 nm. This will be the A_{∞} in the subsequent calculation (*Note:* Before measuring the absorbance of salicylic acid, the UV-Vis

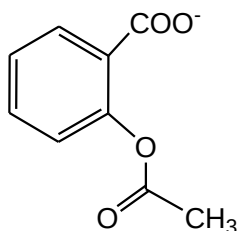
spectrophotometer should be zeroed with standard sample. Standard sample is a 5×10^{-3} M NaOH solution containing 20% ethanol).

4. Prepare 50 mL of a 5×10^{-4} M solution of acetylsalicylic acid (2- $\text{CH}_3\text{CO}_2\text{C}_6\text{H}_4\text{CO}_2\text{H}$) as described in parts 1 and 2 above.
5. Place the reaction bottle in a thermostated bath at 37 °C. Start counting the reaction time as soon as the solution is placed in the bath.
6. Five minutes after the start of the reaction, transfer a sufficient amount of the reaction solution into 1 cm UV-Vis absorption cuvette and measure the absorbance at 295 nm. Continue recording the absorbance every 5 min until the reaction time reaches 60 min. Write down the obtained experimental data in the table

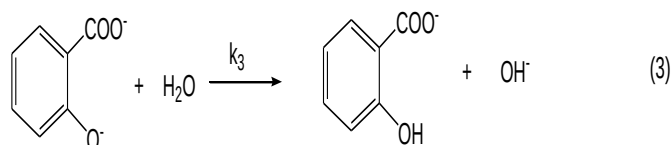
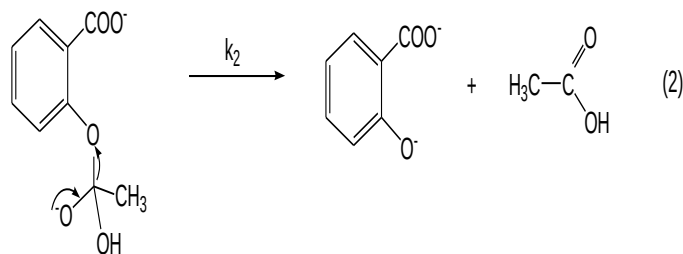
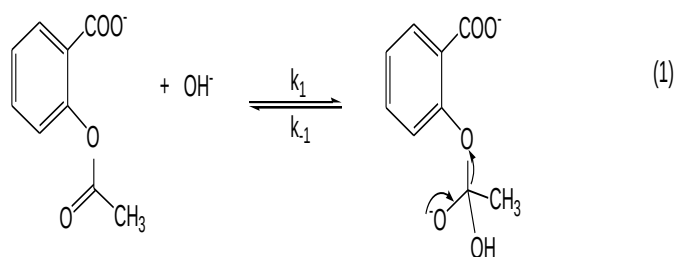
Time/min	5	10	20	30	40	50	60	∞
Absorbance A								

5. Question and data analysis:

1. Calculate the yield of the reaction.
2. Aspirin can irritate the stomach. What is usually done in the formulation of the drug that reduces this side effect?
3. Calculate the concentration of NaOH in 5×10^{-4} M solution of aspirin.
4. Plot $(A_\infty - A)$ vs. t, $\ln(A_\infty - A)$ vs. t, and $\left(\frac{1}{A_\infty - A} - \frac{1}{A_\infty}\right)$ vs. t on three separate charts. From these plots determine the order with respect to acetylsalicylic acid.
5. Determine the value of the pseudo-order rate constant, k_{obs} . Calculate the half-life of the hydrolysis under the reaction condition used. For how many half-lives was the reaction allowed to run?
6. In basic solution, acetylsalicylic acid exists as an anion.



The following mechanism has been proposed to account for the base catalyzed hydrolysis of aspirin. Based on the order with respect to aspirin, and given the order with respect to $[\text{OH}^-] = 1$, derive the rate law and indicate which of the following reactions is the rate - determining step.



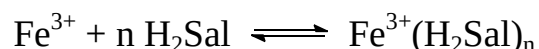


Problem 36. Complex formation of ferric ion and salicylic acid

1. Introduction

In this simple experiment we will study the complex formation of Fe^{3+} and salicylic acid in the aqueous solution. The empirical formula of the complex will be determined and also its stability constant can be estimated.

Several stable complexes between ferric ion and salicylic acid H_2Sal have been known. Their structures and compositions are much dependent on pH. In acidic solution, a violet complex is formed. At neutral pH, a different dark-red complex forms, and in basic solution the complex that forms is orange. This experiment will be carried out at pH of about 2. Under this condition, the hydrolysis of ferric ion is largely suppressed. To simplify the calculations, we will not consider to the dissociation of H_2Sal during the complex formation. Thus, regardless of the structure of the complex, we can present the complex formation equilibrium as:



Thus, the stability constant K_f is defined as

$$K_f = \frac{[\text{Fe}^{3+}(\text{H}_2\text{Sal})_n]}{[\text{Fe}^{3+}][\text{H}_2\text{Sal}]^n} \quad (1)$$

where the $[\text{Fe}^{3+}]$ and $[\text{H}_2\text{Sal}]$ refer to the concentrations of the free species.

The complex $\text{Fe}^{3+}(\text{H}_2\text{Sal})_n$ absorbs most strongly at 528 nm (and neither Fe^{3+} nor H_2Sal absorb at this wavelength). Its concentration is related to the optical absorbance through Beer's law, which is:

$$A = \epsilon \times l \times [\text{Fe}^{3+}(\text{H}_2\text{Sal})_n]$$

where ϵ is the molar extinction coefficient for the complex and l is the optical path length.



Job's method can be used to find the empirical formula of the complex. Following this method, equimolar solutions of Fe^{3+} and H_2Sal are prepared, and then mixed in ratios of 1:9; 2:8 ... 9:1. The total reagent concentrations therefore are the same in each solution. Maximum amount of equilibrium complex will be formed when the proportions of reagents employed correspond to the empirical formula of the complex and can be deduced through the measurement of optical absorbance.

2. Chemicals and Reagents:

- A solution of 0.0025 M Fe^{3+} made by dissolving the appropriate amount of ferric ammonium sulfate in 500 mL of 0.0025 M sulfuric acid.
- A solution of 0.0025 M salicylic acid made by dissolving the appropriate amount of salicylic acid in 500 mL 0.0025 M sulfuric acid.
- Saturated solution of salicylic acid (about 50 mL) in 0.0025 M sulfuric acid.

3. Apparatuses and Glassware:

- Glass beaker: 100 mL, 50 mL
- Burette: 25 mL,
- Volumetric flask: 500 mL,
- Wash bottle,
- Electronic balance with readability of 0.0001 g,
- UV-vis spectrophotometer,
- Glass cuvettes.

4. Experimental procedure



Step 1. Determine the empirical formula of the complex by Job's-method

1. Prepare in 100 mL beakers (should be **dry** and **clean**) a series of nine mixtures of the 0.0025 M iron(III) and the 0.0025 M salicylic acid solutions, plus 10.0 mL 0.0025 M:

Mixture	1	2	3	4	5	6	7	8	9
V _{mL} Iron(III)	1.00	2.00	3.00	4.00	5.00	6.00	7.00	8.00	9.00
V _{mL} salicylic acid	9.00	8.00	7.00	6.00	5.00	4.00	3.0	2.00	1.0
V _{mL} 0.0025 M HCl	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00

(Note: Use burette to take volumes of the solution)

2. Measure the absorbance of each mixture.
3. Plot absorbance *versus* volume of Fe³⁺. Absorbance should be highest for the stoichiometric mixture.

Step 2. Determine the molar extinction coefficient ϵ of the complex

1. Pipette out 1.00, 2.00, 3.00, 4.00, 5.00, 6.00 mL of 0.0025 M iron(III) solution into 5 beakers (100 mL). To each beaker add 10.00 mL of saturated salicylic acid solution and enough 0.0025 M HCl solution to bring the total volume to 20.00 mL.
2. Measure the absorbance of each solution.
3. Plot absorbance *versus* [Fe³⁺] (Because the salicylic acid is in excess, it is assumed that the concentration of iron equals the concentration of the complex).
4. Calculate ϵ from the linear plot.

Step 3. Determine the stability constant K_f



1. Prepare (in 100mL beakers) three mixtures of the same volumes of 0.0025 M Iron(III) and the 0.0025 M salicylic acid solutions and plus 0.0025 M HCl solution to total volume of 20 mL:

Mixture	1	2	3
V _{mL} 0.0025 M Iron(III)	5.00	4.00	3.00
V _{mL} 0.0025 M salicylic acid	5.00	4.00	3.00
V _{mL} 0.0025 M HCl	10.00	12.00	14.00

2. Measure the absorbance of each solution.
3. Calculate the initial concentration of Fe(III) and H₂Sal in each solution.
4. From the measured absorbance and observed ε value determined in step 2(4)). Calculate the concentration of the complex in each solution.
5. Calculate the equilibrium concentration of Fe(III) and H₂Sal. Assume that:
$$[\text{Fe}^{3+}]_{\text{equilibrium}} = [\text{Fe}^{3+}]_{\text{initial}} - [\text{Fe}^{3+}(\text{H}_2\text{Sal})_n]$$
$$[\text{H}_2\text{Sal}]_{\text{equilibrium}} = [\text{H}_2\text{Sal}]_{\text{initial}} - n \times [\text{Fe}^{3+}(\text{H}_2\text{Sal})_n]$$
6. Calculate the equilibrium constants K_{eq} for each solution (using equation 1) and determine an average value.

5. Questions and Analysis

1. What is the empirical formula of the complex?
2. The above complex is normally reported as $[\text{Fe}(\text{Sal})]^+$ in which the salicylic ligand is doubly deprotonated.
 - 2.1 Write the chemical equation in the ionic form to the formation of $[\text{Fe}(\text{Sal})]^+$.
 - 2.2 Let formulate the stability constant of the ion complex $[\text{Fe}(\text{Sal})]^+$ from observed K_{eq} , $[\text{H}^+]$, K_{a1} and K_{a2} of H₂Sal.

2.3 pK_{a1} and pK_{a2} values of H_2Sal are 2.98 and 13.60, respectively (*CRC Handbook of Chemistry and Physics*, CRC Press, 2003, pp. 1247). Calculate the stability constant (K_f) of the ion complex $[Fe(Sal)]^+$ for each solution (in section 2.3) and determine an average value. Assume that the dissociation of H_2Sal can be ignored. (Hint: $[H^+]_{eq} = 0.0025 + 2 \times n \times [Fe^{3+}(H_2Sal)_n]$).

2.4. Comment on your K_f value and explain the probable errors?

----- END -----



APPENDICES

APPENDIX A

A 1: SAFETY RULES FOR STUDENTS IN THE LABORATORY

All students of chemistry must recognize that hazardous materials cannot be completely avoided. Chemists must learn to handle all materials in an appropriate fashion. While it is not expected that all students participating in the International



Chemistry Olympiad know the hazards of every chemical, the organizers of the competition will assume that all participating students know the basic safety procedures. For example, the organizers will assume that students know that eating, drinking or smoking in the laboratory or tasting a chemical is strictly forbidden.

In addition to the common-sense safety considerations to which students should have been previously exposed, some specific rules, listed below, must also be followed during the Olympiad. If any question arises concerning safety procedures during the practical exam, the student should not hesitate to ask the nearest supervisor for direction.

Rules regarding personal protection

1. Eye protection must be worn in the laboratories at all times. If the student wears contact lenses, full protection goggles must also be worn. Eye protection will be provided by the host country.
2. A laboratory coat is required. Each student will supply this item for himself/herself.
3. Long pants and closed-toed shoes are recommended for individual safety. Long hair and loose clothing should be confined.
4. Pipetting by mouth is strictly forbidden. Each student must be provided with pipette bulb or pipette filler.

Rules for Handling Materials

1. Specific instructions for handling hazardous materials will be included by the host country in the procedures of the practical exam. All potentially dangerous materials will be labeled using the GHS symbols. Each student is responsible for recognizing these symbols and knowing their meaning (see Appendix B).
2. Do not indiscriminately dispose chemicals in the sink. Follow all disposal rules provided by the host country.



A 2: SAFETY RULES AND RECOMMENDATIONS FOR THE HOST COUNTRY OF THE INTERNATIONAL CHEMISTRY OLYMPIAD

Certainly it can be assumed that all students participating in the IChO have at least modest experience with safety laboratory procedures. However, it is the responsibility of the International Jury and the organizing country to be sure that the welfare of the students is carefully considered. Reference to the Safety Rules for Students in the Laboratory will show that the students carry some of the burden for their own safety. Other safety matters will vary from year to year, depending on practical tasks. The organizers of these tasks for the host country are therefore assigned responsibility in the areas listed below. The organizers are advised to carefully test the practical tasks in advance to ensure the safety of the experiments. This can best be accomplished by having students of ability similar to that of IChO participants carry out the testing.

APPENDIX B

HAZARD WARNING SYMBOLS AND HAZARD DESIGNATIONS

Chemicals used in the IChO laboratory experiments need to be labeled according to the Globally Harmonized System of Labelling of Chemicals (GHS) standard developed by the United Nations. The organizing country should use the locally legislated GHS system (pictograms, hazard statements, etc.) if it exists. If such rules do not exist, the original GHS directives (http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html) and the GHS compliant documentation by the chemical providers should be used.