



38th International Chemistry Olympiad

Preparatory Problems

2-11 July 2006
Gyeongsan, Korea

*"Chemistry for Life,
Chemistry for Better Life"*

Green Chemistry, Clean world!



KOREAN CHEMICAL SOCIETY



KOREA SCIENCE AND
ENGINEERING FOUNDATION

Hydrogen is the most important constituent of the universe.

Gerhard Herzberg
1971 Nobel Prize in chemistry

I remember, in the winter of our first experiments, just seven years ago, looking at snow ... around my doorstep – great heaps of protons quietly precessing in the earth's magnetic field.

Edward Purcell
1952 Nobel Prize in physics

Much of life can be understood in rational terms if expressed in the language of chemistry. It is an international language, a language without dialects, a language for all of time, and a language that explains where we came from, what we are, and where the physical world will allow us to go. Chemical language has great esthetic beauty and links the physical sciences to the biological sciences.

Arthur Kornberg
1959 Nobel Prize in physiology or medicine

An idea will not work unless you do.

Oswald Avery
discoverer of DNA as the genetic material

Problem 1: “A brief history” of life in the universe

Chemistry is the language of life. Life is based on atoms, molecules and complex chemical reactions involving atoms and molecules. It is only natural then to ask where atoms came from. According to a widely accepted model, the universe began about 15 billion years ago in a big bang and has been expanding ever since. The history of the universe as a whole can be viewed in terms of a series of condensations from elementary to complex particles as the universe cooled. Of course, life as we know it today is a special phenomenon that takes place at moderate temperatures of the Earth.

Light elements, mostly hydrogen and helium, were formed during the first several minutes after the big bang in the rapidly expanding and, therefore, rapidly cooling early universe. Stars are special objects in space, because temperature drop is reversed during star formation. Stars are important in chemistry, because heavy elements essential for life are made inside stars, where the temperature exceeds tens of millions of degrees.

The temperature of the expanding universe can be estimated simply using:

$$T = 10^{10} / t^{1/2}$$

where T is the average temperature of the universe in Kelvin (K) and t is time (age of the universe) in seconds. Answer 1-1 through 1-6 with one significant figure. Round off if you want.

- 1-1. Estimate the temperature of the universe when it was 1 second old at which time the temperature was too high for fusion of protons and neutrons into helium nuclei to occur.
- 1-2. Estimate the temperature of the universe when it was about 3 minutes old and the nuclear synthesis of helium was nearly complete.
- 1-3. Estimate the age of the universe when the temperature was about 3,000 K and the first neutral atoms were formed by the combination of hydrogen and helium nuclei with electrons.
- 1-4. The first stable molecules in the universe were possible only after the temperature of the expanding universe became sufficiently low (approximately 1,000 K) to allow

atoms in molecules to remain bonded. Estimate the age of the universe when the temperature was about 1,000 K.

1-5. Estimate the average temperature of the universe when the universe was about 300 million years old and the first stars and galaxies were born.

1-6. Estimate the temperature of the universe presently and note that it is roughly the same as the cosmic microwave background measurement (3 K).

1-7. Order the following key condensations logically, consistent with the fact that over 99% of atoms in the expanding universe are hydrogen or helium.

a - () - () - () - () - () - () - () - ()

a. quarks → proton, neutron

b. 10^{14} cells → human being

c. H, C, N, O → H₂, CH₄, NH₃, H₂O (in interstellar space)

d. proton, helium nucleus + electron → neutral H, He atoms

e. proteins, nucleic acids, membrane → first cell

f. proton, neutron → helium nucleus

g. H₂, He, CH₄, NH₃, H₂O, dust → solar system

h. H, He atoms → reionization, first generation stars and galaxies

i. proton, helium nucleus (light elements)

→ heavy elements such as C, N, O, P, S, Fe, U; supernova explosion

j. H₂, CH₄, NH₃, H₂O, etc.

→ amino acids, sugars, nucleotide bases, phospholipids on Earth

Problem 2: Hydrogen in outer space

Hydrogen is the most abundant element in the universe constituting about 75% of its elemental mass. The rest is mostly helium with small amounts of other elements. Hydrogen is not only abundant. It is the building block of all other elements.

Hydrogen is abundant in stars such as the sun. Thus the Milky Way galaxy, consisting of over 100 billion stars, is rich in hydrogen. The distance between stars is several light years on the average. Hydrogen is also the major constituent of the interstellar space. There are about 100 billion galaxies in the universe. The empty space between galaxies is vast. For example, the Milky Way galaxy is separated from its nearest neighbor, the Andromeda galaxy, by 2 million light years. Hydrogen again is the primary constituent of the intergalactic space even though the number density is much less than in the interstellar space. The average density of matter in the intergalactic space, where the current temperature is the cosmic background energy of 2.7 K, is about 1 atom/m³.

- 2-1. Calculate the average speed, $(8RT/\pi M)^{1/2}$, of a hydrogen atom in the intergalactic space.
- 2-2. Calculate the volume of a collision cylinder swept out by a hydrogen atom in one second by multiplying the cross-sectional area, πd^2 , by its speed where d is the diameter of a hydrogen atom (1×10^{-8} cm). Molecules whose centers are within the cylinder would undergo collision.
- 2-3. Calculate the number of collisions per second experienced by a hydrogen atom by multiplying the above volume by the number density. How many years does it take for a hydrogen atom to meet another atom in the intergalactic space?
- 2-4. Calculate the mean free path λ of hydrogen in the intergalactic space. λ is the average distance traveled by a particle between collisions.

Hydrogen atoms are relatively abundant in interstellar regions within a galaxy, there being about 1 atom per cm³. The estimated temperature is about 40 K.

- 2-5. Calculate the average speed of hydrogen atom in the interstellar space.

2-6. Calculate the mean free path (λ) of hydrogen in the interstellar space.

2-7. What do these results imply regarding the probability of chemical reactions in space?

Problem 3: Spectroscopy of interstellar molecules

Atoms in interstellar space seldom meet. When they do (most likely on ice surfaces), they produce radicals and molecules. These species, some of which presumably played a role in the origin of life, have been identified through the use of different spectroscopic methods. Absorption spectra of interstellar species can be observed by using the background radiation as the energy of excitation. Emission spectra from excited species have also been observed. Simple diatomic fragments such as CH and CN were identified in interstellar space over 60 years ago.

- 3-1. The background electromagnetic radiation in the interstellar space has a characteristic energy distribution related to the temperature of a blackbody source. According to Wien's law, the wavelength (λ) corresponding to the maximum light intensity emitted from a blackbody at temperature T is given by $T\lambda = 2.9 \times 10^{-3}$ m K. Let's consider a region near a star where the temperature is 100 K. What is the energy in joule of a photon corresponding to the peak emission from a blackbody at 100 K?

When molecules with non-zero dipole moments rotate, electromagnetic radiation can be absorbed or emitted. The spectroscopy related to molecular rotation is called microwave spectroscopy, because the electromagnetic radiation involved is in the microwave region. The rotational energy level of a diatomic molecule is given by $E_J = J(J+1)h^2/8\pi^2I$ where J is the rotational quantum number, h is the Planck constant, I is the moment of inertia, μR^2 . The quantum number J is an integer increasing from 0 and the reduced mass μ is given by $m_1m_2/(m_1+m_2)$ for diatomic molecules (m_1 and m_2 are masses of the two atoms of the molecule). R is the distance between the two bonded atoms (bond length).

- 3-2. Carbon monoxide is the second most abundant interstellar molecule after the hydrogen molecule. What is the rotational transition (change of J quantum number) with the minimum transition energy? What is the minimum transition energy of the $^{12}\text{C}^{16}\text{O}$ rotation in joule? The bond length of CO is 113 pm. Compare the transition energy of CO with the radiation energy in problem 3-1. What does the result imply? The distribution of molecules in different energy levels is related to the background temperature, which affects the absorption and emission spectra.

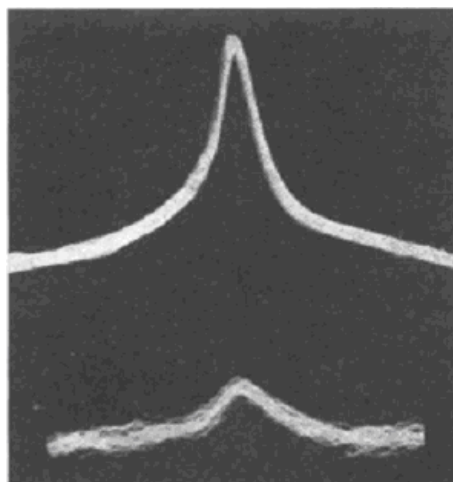


Figure 3-1. Oscillogram for the lowest rotational transition of $^{12}\text{C}^{16}\text{O}$ at 115,270 MHz. The upper curve was taken at the temperature of liquid air, the lower at the temperature of dry ice. (Reference: O. R. Gilliam, C. M. Johnson and W. Gordy. *Phys. Rev.* vol. 78 (1950) p.140.)

- 3-3. The equation for the rotational energy level is applicable to the rotation of the hydrogen molecule. However, it has no dipole moment so that the transition of $\Delta J = 1$ by radiation is not allowed. Instead a very weak radiative transition of $\Delta J = 2$ is observed. Calculate the temperature of interstellar space where the photon energy at the maximum intensity is the same as the transition energy of the hydrogen molecule ($^1\text{H}_2$) between $J = 0$ and 2. The H-H bond length is 74 pm.

Problem 4: Ideal gas law at the core of the sun

Life on Earth has been made possible by the energy from the sun. The sun is a typical star belonging to a group of hydrogen-burning (nuclear fusion, not oxidation) stars called main sequence stars. The core of the sun is 36% hydrogen (^1H) and 64% helium (^4He) by mass. Under the high temperature and pressure inside the sun, atoms lose all their electrons and the nuclear structure of a neutral atom becomes irrelevant. The vast space inside atoms that was available only for electrons in a neutral atom becomes equally available for protons, helium nuclei, and electrons. Such a state is called plasma. At the core of the sun, the estimated density is 158 g/cm^3 and pressure $2.5 \times 10^{11} \text{ atm}$.

- 4-1. Calculate the total number of moles of protons, helium nuclei, and electrons combined per cm^3 at the core of the sun.

- 4-2. Calculate the percentage of space occupied by particles in hydrogen gas at 300 K and 1 atm, in liquid hydrogen, and in the plasma at the core of the sun. The density of liquid hydrogen is 0.09 g/cm^3 . The radius of a nuclear particle can be estimated from $r = (1.4 \times 10^{-13} \text{ cm})(\text{mass number})^{1/3}$. Assume that the volume of a hydrogen molecule is twice that of a hydrogen atom, and the hydrogen atom is a sphere with the Bohr radius ($0.53 \times 10^{-8} \text{ cm}$). Estimate your answer to 1 significant figure.

- 4-3. Using the ideal gas law, estimate the temperature at the core of the sun and compare your result with the temperature required for the fusion of hydrogen into helium ($1.5 \times 10^7 \text{ K}$).

Problem 5: Atmosphere of the planets

The solar system was born about 4.6 billion years ago out of an interstellar gas cloud, which is mostly hydrogen and helium with small amounts of other gases and dust.

5-1. The age of the solar system can be estimated by determining the mass ratio between Pb-206 and U-238 in lunar rocks. Write the overall nuclear reaction for the decay of U-238 into Pb-206.

5-2. The half-life for the overall reaction is governed by the first alpha-decay of U-238



which is the slowest of all reactions involved. The half-life for this reaction is 4.51×10^9 yr. Estimate the mass ratio of Pb-206 and U-238 in lunar rocks that led to the estimation of the age of the solar system.

Elemental hydrogen and helium are rare on Earth, because they escaped from the early Earth. Escape velocity is the minimum velocity of a particle or object (e.g., a gas molecule or a rocket) needed to become free from the gravitational attraction of a planet. Escape velocity of an object with mass m from the Earth can be determined by equating the gravitational potential energy, GmM/R , to the kinetic energy, $(1/2)mv^2$, of the object. Note that the m 's on both sides cancel and, therefore, the escape velocity is independent of the mass of the object. However, it still depends on the mass of the planet.

G : the universal constant of gravitation = $6.67 \times 10^{-11} \text{ N m}^2 \text{ kg}^{-2}$

M : Earth's mass = $5.98 \times 10^{24} \text{ kg}$

R : Earth's radius = $6.37 \times 10^6 \text{ m}$

5-3. Calculate the escape velocity for the Earth.

5-4. Calculate the average speed, $(8RT/\pi M)^{1/2}$, of a hydrogen atom and a nitrogen molecule at ambient temperature. Compare these with the escape velocity for the Earth. Note that the temperature of the upper atmosphere where gases can escape into space will be somewhat different. Also note that photolysis of water vapor by ultraviolet radiation can yield hydrogen atoms. Explain why hydrogen

atoms escape more readily than nitrogen molecules even though the escape velocity is independent of the mass of the escaping object.

The chemical composition of the atmosphere of a planet depends on the temperature of the planet's atmosphere (which in turn depends on the distance from the sun, internal temperature, etc.), tectonic activity, and the existence of life.

As the sun generated heat, light, and solar wind through nuclear fusion of hydrogen to helium, the primitive inner planets (Mercury, Venus, Earth, and Mars) lost most of their gaseous matter (hydrogen, helium, methane, nitrogen, water, carbon monoxide, etc.). As the heavy elements such as iron and nickel were concentrated at the core through gravity and radioactive decay produced heat, internal temperature of the planets increased. Trapped gases, such as carbon dioxide and water, then migrated to the surface. The subsequent escape of gases from the planet with a given escape velocity into space depends on the speed distribution. The greater the proportion of gas molecules with speed exceeding the escape velocity, the more likely the gas is to escape over time.

5-5. Circle the planet name where the atmospheric pressure and composition are consistent with the given data. Explain.

Average surface temperature and radius of the planet are as follows:

Venus: 730 K; 6,052 km Earth: 288 K; 6,378 km Mars: 218 K; 3,393 km
Jupiter: 165 K; 71,400 km Pluto: 42 K; 1,160 km

	pressure (in atm)	composition (%)	planet
a.	> 100	H ₂ (82); He(17)	(Venus, Earth, Mars, Jupiter, Pluto)
b.	90	CO ₂ (96.4); N ₂ (3.4)	(Venus, Earth, Mars, Jupiter, Pluto)
c.	0.007	CO ₂ (95.7); N ₂ (2.7)	(Venus, Earth, Mars, Jupiter, Pluto)
d.	1	N ₂ (78); O ₂ (21)	(Venus, Earth, Mars, Jupiter, Pluto)
e.	10 ⁻⁵	CH ₄ (100)	(Venus, Earth, Mars, Jupiter, Pluto)

5-6. Write the Lewis structure for H₂, He, CO₂, N₂, O₂, and CH₄. Depict all valence electrons.

5-7. All of the above atmospheric components of the planets are atoms and molecules with low boiling point. Boiling point is primarily determined by the overall polarity of the molecule, which is determined by bond polarity and molecular geometry. Nonpolar molecules interact with dispersion force only and, therefore, have low boiling points. Yet there are differences in boiling points among nonpolar molecules. Arrange H_2 , He, N_2 , O_2 , and CH_4 in the order of increasing boiling point. Explain the order.

Problem 6: Discovery of the noble gases

Molecules such as H₂, N₂, O₂, CO₂, and CH₄ in Problem 5 are formed through chemical bonding of atoms. Even though valency was known in the 19th century, the underlying principle behind chemical bonding had not been understood for a long time. Ironically, the discovery of the noble gases with practically zero chemical reactivity provided a clue as to why elements other than the noble gases combine chemically.

1882, Rayleigh decided to accurately redetermine gas densities in order to test Prout's hypothesis.

6-1. What is Prout's hypothesis? What evidence did he use to support his hypothesis? (Search the Internet or other sources.)

To remove oxygen and prepare pure nitrogen, Rayleigh used a method recommended by Ramsay. Air was bubbled through liquid ammonia and was passed through a tube containing copper at red heat where the oxygen of the air was consumed by hydrogen of the ammonia. Excess ammonia was removed with sulfuric acid. Water was also removed. The copper served to increase the surface area and to act as an indicator. As long as the copper remained bright, one could tell that the ammonia had done its work.

6-2. Write a balanced equation for the consumption of oxygen in air by hydrogen from ammonia. Assume that air is 78% nitrogen, 21% oxygen, and 1% argon by volume (unknown to Rayleigh) and show nitrogen and argon from the air in your equation.

6-3. Calculate the molecular weight of nitrogen one would get from the density measurement of nitrogen prepared as above. Note that argon in the sample, initially unknown to Rayleigh, did contribute to the measured density. (atomic weight: N = 14.0067, Ar = 39.948)

Rayleigh also prepared nitrogen by passing air directly over red-hot copper.

6-4. Write a balanced equation for the removal of oxygen from air by red-hot copper. Again show nitrogen and argon from the air in your equation.

- 6-5. Calculate the molecular weight of nitrogen one would get from the density measurement of the nitrogen prepared by the second method.
- 6-6. To Rayleigh's surprise, the densities obtained by the two methods differed by a thousandth part – a difference small but reproducible. Verify the difference from your answers in 6-3 and 6-5.
- 6-7. To magnify this discrepancy, Rayleigh used pure oxygen instead of air in the ammonia method. How would this change the discrepancy?
- 6-8. Nitrogen as well as oxygen in the air was removed by the reaction with heated Mg (more reactive than copper). Then a new gas occupying about 1% of air was isolated. The density of the new gas was about () times that of air.
- 6-9. A previously unseen line spectrum was observed from this new gas separated from 5 cc of air. The most remarkable feature of the gas was the ratio of its specific heats (C_p/C_v), which proved to be the highest possible, 5/3. The observation showed that the whole of the molecular motion was (). Thus, argon is a monatomic gas.
 (1) electronic (2) vibrational (3) rotational (4) translational
- 6-10. Calculate the weight of argon in a 10 m x 10 m x 10 m hall at STP.

In 1894, Rayleigh and Ramsay announced the discovery of Ar. Discovery of other noble gases (He, Ne, Kr, Xe) followed and a new group was added to the periodic table. As a result, Rayleigh and Ramsay received the Nobel Prizes in physics and in chemistry, respectively, in 1904.

- 6-11. Element names sometimes have Greek or Latin origin and provide clues as to their properties or means of discovery. Match the element name with its meaning.

helium •	• new
neon •	• stranger
argon •	• lazy
krypton •	• hidden
xenon •	• sun

Problem 7: Solubility of salts

The solubility of metals and their salts played an important role in Earth's history changing the shape of the Earth's surface. Furthermore, solubility was instrumental in changing the Earth's atmosphere. The atmosphere of the primitive Earth was rich in carbon dioxide. Surface temperature of the early Earth was maintained above the boiling point of water due to continued bombardment by asteroids. When the Earth cooled, it rained and a primitive ocean was formed. As metals and their salts dissolved the ocean became alkaline and a large amount of carbon dioxide from the air dissolved in the ocean. The CO₂ part of most carbonate minerals is derived from this primitive atmosphere.

As life arose about 3.8 billion years ago and photosynthetic bacteria evolved about 3 billion years ago, molecular oxygen was produced as a by-product of photosynthesis. As oxygen reacted with the metal ions in the ocean, metal oxides with low solubility were deposited on the ocean floor which later became dry land through plate tectonic motion. Iron and aluminum ores were, and still are, of particular importance as raw materials in human civilization.

Let's consider a solubility problem using silver halides. K_{sp} values for AgCl and AgBr are 1.8×10^{-10} and 3.3×10^{-13} , respectively.

- 7-1. Excess AgCl was added to deionized water. Calculate the concentration of Cl⁻ in equilibrium with solid AgCl. Repeat the calculation for Br⁻ assuming that AgBr was added instead of AgCl.
- 7-2. Assume that 0.100 L of 1.00×10^{-3} M Ag⁺ solution is added to a Cl⁻ solution of the same volume and concentration. What is the concentration of Cl⁻ in the solution once equilibrium has been established? What percentage of the total chloride is in solution?
- 7-3. Assume that 0.100 L of 1.00×10^{-3} M Ag⁺ solution is added to a Br⁻ solution of the same volume and concentration. What is the concentration of Br⁻ in the solution once equilibrium has been established? What percentage of the total bromide is in solution?

7-4. Experimental verification of the answers in 7-2 and 7-3 is difficult, because the exact volume and concentration of the solutions are unknown. Repeat the calculations in 7-2 and 7-3 assuming that the concentration of the Ag^+ solution is $1.01 \times 10^{-3} \text{ M}$.

Now let's assume that $1.00 \times 10^{-3} \text{ M Ag}^+$ solution is slowly added with constant stirring to a 0.100 L solution containing both Cl^- and Br^- at $1.00 \times 10^{-3} \text{ M}$ concentration.

7-5. Which silver (I) halide will precipitate first? Describe the situation when the first precipitate appears.

7-6. Determine the percentage of Br^- , Cl^- , and Ag^+ ions in solution and in the precipitate after addition of 100, 200, and 300 mL of Ag^+ solution.

V_{add}	% Br in solution	% Br in precipitate	% Cl in solution	% Cl in precipitate	% Ag in solution	% Ag in precipitate
100 mL						
200 mL						
300 mL						

Problem 8: Physical methods for determination of Avogadro's number

Avogadro's number is a fundamental constant in chemistry. However, an accurate determination of this value took a long time. Avogadro (1776-1856) himself did not know Avogadro's number as it is known today. At about the time of his death, Avogadro's number determined from gas properties, such as diffusion coefficient and viscosity, approached 5×10^{22} . Avogadro's number as we know it today (6.02×10^{23}) became available only in the early 20th century. Let's consider three separate approaches.

8-1. At thermal equilibrium, the probability of finding a molecule with a mass m at height h is proportional to the Boltzmann factor, $\exp(-E(h)/k_B T)$, where $E(h)$ is the gravitational potential energy (mgh , where g is 9.81 m/s^2) and k_B is the Boltzmann constant. Thus, the number density at h follows "barometric" distribution:

$$\frac{\rho(h)}{\rho(h_0)} = \exp\left[-\frac{mg(h-h_0)}{k_B T}\right]$$

- Spherical particles of diameter $0.5 \mu\text{m}$ and density 1.10 g/cm^3 are suspended in water (density 1.00 g/cm^3) at 20°C . Calculate the effective mass m of the particles corrected for buoyancy.
- Now the number density of the particles with effective mass will follow barometric distribution. In an experiment where a vertical distribution of such particles was measured, it was observed that the number density at h decreased to $1/e$ times the number density at h_0 over a vertical distance of $6.40 \times 10^{-3} \text{ cm}$. Calculate Boltzmann's constant.
- Calculate Avogadro's number using Boltzmann's constant and the gas constant. ($R = 8.314 \text{ J/mol}\cdot\text{K}$)

8-2. Avogadro's number can also be determined by single crystal X-ray crystallography. The density of sodium chloride crystal is 2.165 g/cm^3 . The sodium chloride lattice is shown below (Figure 8-1). The distance between the centers of adjacent Na^+ and Cl^- ions was determined to be $2.819 \times 10^{-8} \text{ cm}$. Calculate Avogadro's number.

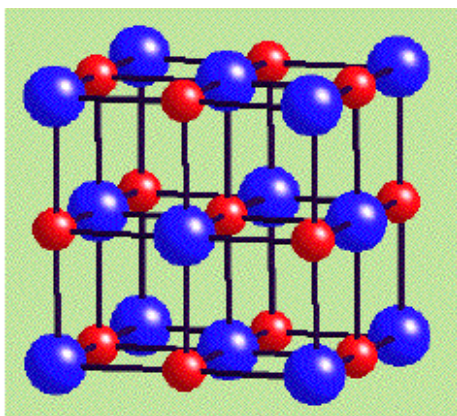


Figure 8-1. Lattice structure of sodium chloride

In the rock-salt structure one finds a face-centered cubic array of anions and the same array of cations. The two arrays interpenetrate each other. A unit cell contains 4 anions (8 centered at the apexes are each shared by 8 unit cells thus giving 1 anion, and 6 positioned at the face centers are each shared by 2 unit cells giving 3 anions). A unit cell also contains 4 cations.

8-3. In a celebrated oil drop experiment, Millikan determined in 1913 that the basic unit of electric charge is 1.593×10^{-19} coulombs. Calculate Avogadro's number from this value and Faraday, which is electric charge per equivalent (1 Faraday = 96,496 coulomb as used by Millikan).

Problem 9: An electrochemical method for determination of Avogadro's number

By definition, Avogadro's number is the number of atoms in exactly 12 g of carbon-12. Avogadro's number recommended by CODATA (Committee on Data for Science and Technology) in 2002 is $6.0221415(10) \times 10^{23} \text{ mol}^{-1}$, where the number in parenthesis represents one standard deviation in the last two digits.

Avogadro's number can be determined electrolytically. Current and time are measured in order to obtain the number of electrons passing through the electrochemical cell from $Q = I \cdot t$ (charge = current \times time). Copper electrodes were used for electrolysis of 0.5 M H_2SO_4 . During electrolysis, copper is lost from the anode as the copper atoms are converted to copper ions. The copper ions pass through the solution. At the surface of the cathode, hydrogen gas is liberated through reduction of hydrogen ions in the acidic solution. Experimental results are as follows:

decrease in anode mass: 0.3554 g

constant current: 0.601 A

time of electrolysis: 1802 s

Note that $1 \text{ A} = 1 \text{ C/s}$ or $1 \text{ A} \cdot \text{s} = 1 \text{ C}$ and the charge of one electron is $1.602 \times 10^{-19} \text{ C}$.

- 9-1. Write the reactions at both the anode and cathode.
- 9-2. Calculate the total charge that passed through the circuit.
- 9-3. Calculate the number of electrons involved in the electrolysis.
- 9-4. Calculate the mass of a copper atom.
- 9-5. Determine Avogadro's number. Atomic weight of copper is 63.546 g/mol.
- 9-6. What is the percent error in this measurement of Avogadro's number?
- 9-7. It is also possible in principle to collect the hydrogen gas evolved and use its weight to determine Avogadro's number. Calculate the weight of evolved hydrogen gas. Is this determination of Avogadro's number from the weight of evolved hydrogen practical?

Problem 10: Enthalpy, entropy, and stability

All chemical changes in living and non-living systems obey laws of thermodynamics. The equilibrium constant of a given reaction is determined by changes in Gibbs free energy, which is in turn determined by enthalpy change, entropy change, and the temperature.

10-1. Fill in the blanks (a-f) with all that apply from the following:

equilibrium constant, K_{eq}

entropy change, ΔS

enthalpy change, ΔH

free energy change, ΔG

- | | |
|--|---------|
| a. strongly temperature-dependent | () |
| b. closely related to bond strength | () |
| c. measure of change in randomness | () |
| d. related to the quantity of reactants and products | () |
| e. measure of spontaneity of a reaction | () |
| f. measure of heat released or absorbed | () |

The following equilibrium exists in the vapor phase dissociation of molecular addition compounds of donor molecules, D, and boron compounds, BX_3 .



$$K_p = [D][BX_3]/[D \cdot BX_3]$$

10-2. Dissociation constants (K_p) at 100°C of the molecular addition compounds $Me_3N \cdot BMe_3$ and $Me_3P \cdot BMe_3$ are 0.472 and 0.128 atm, respectively. Calculate the standard free energy change of dissociation at 100°C for both compounds. Which complex is more stable at this temperature?

10-3. The standard entropy change of dissociation, ΔS° , is 45.7 cal/mol·K for $Me_3N \cdot BMe_3$ and 40.0 cal/mol·K for $Me_3P \cdot BMe_3$. Calculate the standard enthalpy change of dissociation for both compounds. Which compound has the stronger central bond? Assume that ΔH and ΔS are temperature-independent.

10-4. Which is more critical in determining the overall stability of these addition compounds at 100°C, enthalpy term (ΔH) or entropy term ($T \Delta S$)?

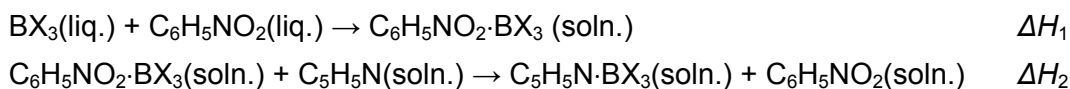
10-5. At what temperature does $\text{Me}_3\text{N} \cdot \text{BMe}_3$ become more thermodynamically stable than $\text{Me}_3\text{P} \cdot \text{BMe}_3$? Assume that ΔH and ΔS are temperature-independent.

Problem 11: Lewis acids and bases

Acids and bases are essential for life. Amino acids have both acidic and basic groups. DNA and RNA are nucleic acids that contain bases such as adenine, guanine, thymine, cytosine, and uracil. Thus, understanding acid-base chemistry is essential for understanding life. Oxygen was so named by Lavoisier because of its acid-forming nature; the acid-forming nature of oxygen is a manifestation of its high electronegativity. Lewis extended the definition of acids and bases, and electronegativity is again central in understanding Lewis acidity and basicity.

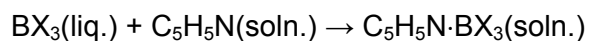
- 11-1. Describe the molecular structure of BX_3 . What is the hybridization of the boron orbitals?
- 11-2. How does this hybridization change when the boron halide forms an adduct with a base such as pyridine (C_5H_5N)? Is the structural change around boron upon adduct formation more favorable when X is F or I? List BF_3 , BCl_3 , and BBr_3 in the order of increasing Lewis acidity based on the above structural consideration.
- 11-3. Electronegativity is another important consideration in predicting Lewis acidity. List BF_3 , BCl_3 , and BBr_3 in the order of increasing Lewis acidity, based only on the electronegativity of the halogen elements (inductive effect).
- 11-4. Is adduct formation between the boron halide (Lewis acid) and pyridine (Lewis base) exothermic or endothermic? Which Lewis acid will show the greatest enthalpy change upon adduct formation?
- 11-5. Although the gaseous state would be best for computing the relative strengths of the three boron halides under consideration, the liquid state of these materials could be used as a satisfactory reference state since the boron halides are relatively non-polar liquids or gases.

The enthalpy changes when mixing liquid boron halide with nitrobenzene, ΔH_1 , and when mixing the nitrobenzene-boron halide solution with pyridine also in nitrobenzene, ΔH_2 , are given below.

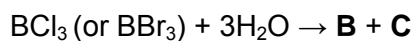
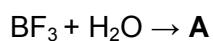


	BF ₃	BCl ₃	BBr ₃
ΔH_1 (kcal/mol)	- 6.7	- 8.7	- 12.5
ΔH_2 (kcal/mol)	- 25.0	- 30.8	- 32.0

Calculate ΔH_3 for the following reactions. Do they agree with your prediction in 11-4?



11-6. Boron halides also show very different reactivity with water. BF₃ forms stable addition compounds whereas BCl₃ and BBr₃ react violently with H₂O at temperatures below 20°C. Predict the products, **A**, **B**, and **C**, for the following reactions.



11-7. What kind of extra bond can be formed in BX₃ between the central boron and one of its halides possessing lone pair electrons in order to fulfill the 'octet rule'? Explain how this extra bond affects the Lewis acidity of BX₃.

Problem 12: Solubility equilibrium in a buffer solution

Biochemical reactions take place in buffered aqueous environments. For example, the pH of the blood is maintained around 7.4 by the buffering action of carbonate, phosphate, and proteins. Many chemical reactions in the laboratory are also carried out in buffer solutions. In this problem, let's consider the solubility equilibrium in a buffer solution.

12-1. H₂S gas occupying 440 mL at STP can be dissolved in 100 mL of water at 25°C.

Calculate the molar concentration of H₂S in water saturated with H₂S. Assume that there is no volume change in water upon dissolution of H₂S.

12-2. Assume that equilibrium is established after a 0.010 M FeCl₂ solution is saturated with H₂S by continuously bubbling H₂S into the solution.

$$K_{sp}(\text{FeS}) = [\text{Fe}^{2+}][\text{S}^{2-}] = 8.0 \times 10^{-19} \text{ at } 25^\circ\text{C} \quad (1)$$

For acid dissociation of H₂S,

$$K_1 = [\text{H}^+][\text{HS}^-]/[\text{H}_2\text{S}] = 9.5 \times 10^{-8} \quad (2)$$

$$K_2 = [\text{H}^+][\text{S}^{2-}]/[\text{HS}^-] = 1.3 \times 10^{-14} \quad (3)$$

For self ionization of water,

$$K_w = [\text{H}^+][\text{OH}^-] = 1 \times 10^{-14} \quad (4)$$

In the solution, the positive charge is balanced by the negative charge:

$$[\text{H}^+] + 2[\text{Fe}^{2+}] = [\text{Cl}^-] + [\text{OH}^-] + [\text{HS}^-] + 2[\text{S}^{2-}] \quad (5)$$

Cross out terms that are negligibly small in the charge balance equation, (5), in order to determine [H⁺] and [Fe²⁺]. Would you increase or decrease the pH of the solution to precipitate more FeS? How does the increase of 1 in pH affect the concentration of Fe²⁺ ion?

12-3. How would you adjust the final pH of the solution saturated with H₂S to reduce the concentration of Fe²⁺ from 0.010 M to 1.0 × 10⁻⁸ M?

12-4. You want to use acetic acid (HOAc)/sodium acetate (NaOAc) buffer to achieve 1.0×10^{-8} M concentration of Fe^{2+} as described above. Suppose that you are making the buffer by mixing acetic acid and sodium acetate in water in a volumetric flask. Enough acetic acid was added to make the initial concentration 0.10 M. Considering that the precipitation reaction produces H^+ ($\text{Fe}^{2+} + \text{H}_2\text{S} \rightarrow \text{FeS(s)} + 2\text{H}^+$), how would you adjust the initial concentration of sodium acetate to obtain 1.0×10^{-8} M Fe^{2+} after equilibrium is established? The acid dissociation constant for acetic acid at 25°C is 1.8×10^{-5} .

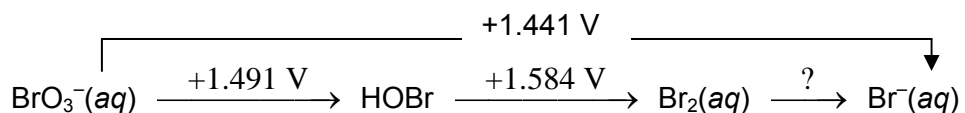
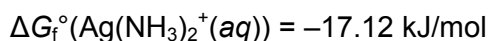
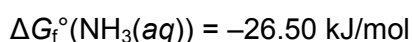
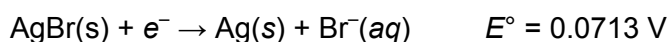
12-5. What is the pH of the buffer before H_2S is introduced and FeS is precipitated?

Problem 13: Redox potential, Gibbs free energy, and solubility

The proton, neutron, and electron are the three sub-atomic particles important in chemistry. These particles occupy two regions. Proton and neutron occupy the central place of the nucleus and electron the vast space outside the nucleus.

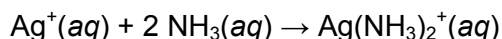
Neutron transfer does not take place in ordinary chemical reactions. Proton (hydrogen ion) transfer constitutes acid-base reactions. Electron transfer constitutes oxidation-reduction reactions. Oxidation-reduction reactions are essential for life. Photosynthesis and respiration are two prime examples. Oxidation-reduction reactions also allow key thermodynamics quantities to be measured as demonstrated in this problem.

Given the following information:



13-1. Calculate $\Delta G_f^\circ(\text{Ag}^+(\text{aq}))$.

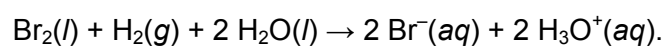
13-2. Calculate the equilibrium constant for the following reaction at 25°C.



13-3. Calculate the K_{SP} value of $\text{AgBr}(\text{s})$ at 25°C.

13-4. Calculate the solubility of AgBr in a 0.100 M aqueous solution of ammonia at 25°C.

13-5. A galvanic cell using the standard hydrogen electrode as an anode is constructed in which the overall reaction is



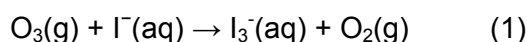
Silver ions are added until AgBr precipitates at the cathode and $[\text{Ag}^+]$ reaches 0.0600 M. The cell voltage is then measured to be 1.721 V. Calculate ΔE° for the galvanic cell.

13-6. Estimate the solubility of bromine in the form of $\text{Br}_2(aq)$ in water at 25°C.

Problem 14: Measuring the ozone level in air

Ozone both helps protect and leads to damage of life forms. As the oxygen level in the Earth's atmosphere built up significantly about 2 billions years ago during which time the, ozone level in the upper atmosphere also increased. This ozone layer effectively blocked ultraviolet radiation and made life on land possible. Today, the ozone layer appears to be depleting - developing a large hole - thus, the fate of this layer is of great concern. On the other hand, ozone is a health hazard in our immediate environment at ground level. It is a key constituent of photochemical smog.

A simple method for measuring the concentration of ozone in the ground-level atmosphere is as follows. Air is bubbled through an acidic aqueous solution containing iodide and the atmospheric ozone oxidizes iodide to triiodide via the following unbalanced reaction:



At the end of the sampling period, the triiodide concentration is determined with a UV-Vis spectrophotometer at 254 nm.

Air was bubbled for 30.0 min into 10 mL of an aqueous solution containing excess of KI under the following atmospheric conditions: pressure = 750 torr, temperature = 298 K, flow rate = 250 mL min⁻¹. The absorbance of the resulting I₃⁻ solution was measured in a 1.1-cm cell by using a spectrophotometer equipped with a photocell. The photocell resistance is inversely proportional to the light intensity. Resistance values for the blank and the sample solution were 12.1 kΩ and 19.4 kΩ, respectively. The molar absorption coefficient of the I₃⁻ solution was determined to be 2.4 × 10⁵ M⁻¹ · cm⁻¹. In various useful units, the universal gas constant is: R = 8.314472 J · K⁻¹ · mol⁻¹ = 0.08205746 L · atm · K⁻¹ · mol⁻¹ = 62.3637 L · torr · K⁻¹ · mol⁻¹ = 1.987 cal · K⁻¹ · mol⁻¹

14-1. Balance equation (1).

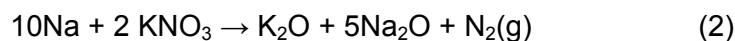
14-2. Draw the Lewis structure for ozone.

14-3. Calculate the number of moles of ozone in the sampled air.

14-4. Assuming that the gases behave ideally under the conditions used, calculate the concentration in *ppb* of ozone present in the sampled air.

Problem 15: Lifesaving chemistry of the airbag

Certain chemical reactions can protect people from serious injury or death. The following chemical reactions used to be utilized to rapidly produce large amounts of nitrogen gas inside an automobile airbag:



- 15-1. Write the Lewis structure for the azide anion and nitrogen molecule.
- 15-2. How many grams of sodium azide and potassium nitrate are needed to generate enough nitrogen to fill a 15-liter airbag at 50°C and 1.25 atm?
- 15-3. Separately, write a balanced equation for the decomposition of nitroglycerine. Finally, write a balanced equation for the decomposition of lead azide used for detonation. In what ways are the reactions for sodium azide, nitroglycerine and lead azide similar?
- 15-4. Write a balanced equation for the reaction of sodium azide with sulfuric acid to form hydrazoic acid (HN_3) and sodium sulfate.
- 15-5. When 60 g of sodium azide reacts with 100 mL of 3 M sulfuric acid, how many grams of hydrazoic acid are produced?

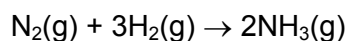
Problem 16: Catalysts for the synthesis of ammonia

The synthesis of ammonia is a prime example of how chemistry can be used to improve human life. Even though primitive living systems had been “fixing” nitrogen to make compounds of nitrogen for hundreds of millions of years, human beings learned to prepare ammonia only about 100 years ago.

Ammonia is a source of nitrogen atom required for all amino acids and is essential in the production of fertilizer. Amino groups can be easily transformed into nitro groups found commonly in explosives such as TNT. More than 100 million tons of ammonia are produced annually worldwide, second only to sulfuric acid. However, Nature produces even more ammonia than the chemical industry. Ammonia is synthesized from nitrogen and hydrogen, however, the chemical bond of the nitrogen molecule is extremely stable, keeping ammonia from being synthesized without proper conditions or use of catalyst. In the early 20th century, Haber-Bosch method was developed for ammonia synthesis using high pressure and temperature, which is still employed in today’s chemical industry. Haber (1918) and Bosch (1931) were awarded the Nobel Prize in chemistry for these contributions.

16-1. First, let us see if the reaction is feasible from a thermodynamic standpoint.

Calculate the standard entropy change of the system in the following reaction:



The standard entropy is 191.6, 130.7, and 192.5 J/(K·mol) for N₂, H₂, and NH₃, respectively. Does the entropy of the system increase or decrease? If it decreases, what must be the case for the reaction to proceed spontaneously?

16-2. To see if the reaction is likely to be exothermic, consider a similar reaction between oxygen and hydrogen to make water. Is that reaction exothermic? Match the compounds with the standard enthalpy of formation (ΔH_f°) in kJ/mol.

H ₂ O(g) •	• - 46.11
HF(g) •	• - 241.82
NH ₃ (g) •	• - 271.1

16-3. Using the value of ΔH_f° you selected above, calculate the entropy change at 25°C of the system and the surroundings combined.

16-4. Reaction rate is another important consideration. The rate determining step of the reaction, $\text{N}_2(\text{g}) + 3\text{H}_2(\text{g}) \rightarrow 2\text{NH}_3(\text{g})$ is the atomization of the nitrogen molecule. Assuming that the activation energy of the atomization is the bond energy of the nitrogen molecule (940 kJ mole^{-1}) and that the A factor of the rate determining step is 10^{13} sec^{-1} , calculate the rate constant of atomization at 800°C using the Arrhenius rate law. Calculate the rate constant at the same temperature when the activation energy is lowered by half with a catalyst.

The amount of catalyst used by the chemical industry is enormous. More than 100 tons of catalyst are used in a factory where 1000 tons of ammonia can be produced daily. In addition to the Fe catalyst that has been used since Haber and Bosch, a Ru catalyst is used in ammonia synthesis. Metal complex binding with elemental nitrogen and hydrogen is also studied as homogeneous catalyst for ammonia synthesis in solution.

16-5. Reactions between reactants and undissolved metal catalyst can occur at the metal surface so that the catalyst surface area affects the catalysis rate. Calculate the mole number of nitrogen molecules adsorbed on 1 kg of Fe catalyst. Assume that the catalyst is composed of $1 \mu\text{m}^3$ cube (very fine powder) and that all six faces of the cube are available for nitrogen adsorption. The density of Fe is 7.86 g/cm^3 and the adsorption area for a nitrogen molecule is 0.16 nm^2 .

16-6. If a soluble, homogeneous catalyst with MW of 500 g/mole is synthesized for nitrogen molecule binding, how many nitrogen molecules bind to 1 kg of catalyst? Assume one catalyst molecule binds one nitrogen molecule. Compare the result with the number of nitrogen molecules adsorbed on the Fe surface in Problem 16-2.

16-7. While ammonia is synthesized under high pressure and temperature in the chemical industry, natural ammonia is synthesized from atmospheric nitrogen, $\sim 0.8 \text{ atm}$. Enzymes for ammonia synthesis in nature called nitrogenases are proteins with cofactors that contain Fe or Mo. The ammonia synthesis reaction by nitrogenases is an electron transfer reaction: $\text{N}_2(\text{g}) + 8\text{H}^+ + 8\text{e}^- \rightarrow 2\text{NH}_3(\text{g}) + \text{H}_2(\text{g})$. 16 ATP molecules are consumed in the reaction. ATP molecule decomposes into

ADP and inorganic phosphate, and releases an energy of 30.5 kJ/mole. Calculate the energy required to synthesize 1 mole of ammonia using nitrogenase. At least 400 kJ of energy is used for the synthesis of 1 mole of ammonia in the chemical industry these days.

Problem 17: From sand to semiconductors

Chemistry enables life. Chemistry also enriches life. For thousands of years, human beings have been putting sand to good use. Glass was made from sand. Lenses were made from glass and were used to make telescopes, microscopes, eyeglasses, and glassware for chemical experiments.

More recently, sand became a starting material for semiconductors. One of the most abundant elements in the Earth's crust is silicon, which is found in compounds containing Si-O bonds. Silica (SiO₂) is present in abundance at the earth's surface.

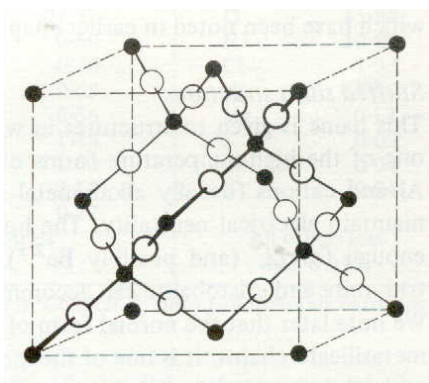
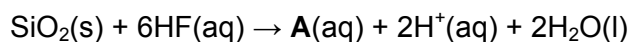


Figure 17-1. β -cristobalite, one structure of silica.

17-1. How many Si and O atoms exist in the unit cell of β -cristobalite?

17-2. Suggest the hybridized orbital of Si for this structure and guess the bond angle of O-Si-O.

SiO₂ is very unreactive, yet it reacts with HF. The reaction with HF may be used to etch glass or in semiconductor manufacturing:



17-3. Draw the molecular structure of **A**.

Silicon can be obtained by heating silica and coke (a form of carbon) at 3000°C in an electric arc furnace.

17-4. Write a balanced equation for the reaction of SiO_2 with carbon. In this case, assume that only one kind of gas is formed whose Lewis structure should show formal charges.

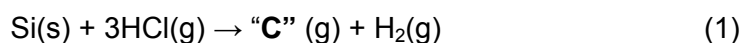
17-5. Sketch the molecular orbitals of the gas formed from the reaction above.

To obtain ultrapure silicon, crude silicon is treated either with Cl_2 gas to give "B" or with HCl gas to give "C".

17-6. Write a balanced equation for the reaction of Si with Cl_2 .

17-7. Predict the molecular structure of "B".

17-8. Is the product "C" from the following reaction (1) polar or not? Draw the 3-dimensional structure of C and sketch the direction of its dipole moment, if any:



The reverse reaction of (1) is spontaneous at 1000°C , depositing ultrapure silicon. The final purification of the silicon takes place by a melting process called zone refining. This process depends on the fact that the impurities are more soluble in the liquid phase than in the solid phase (Figure 17-2). The zone refining procedure can be repeated until the desired level of purity (less than 0.1 ppb impurity) is obtained.

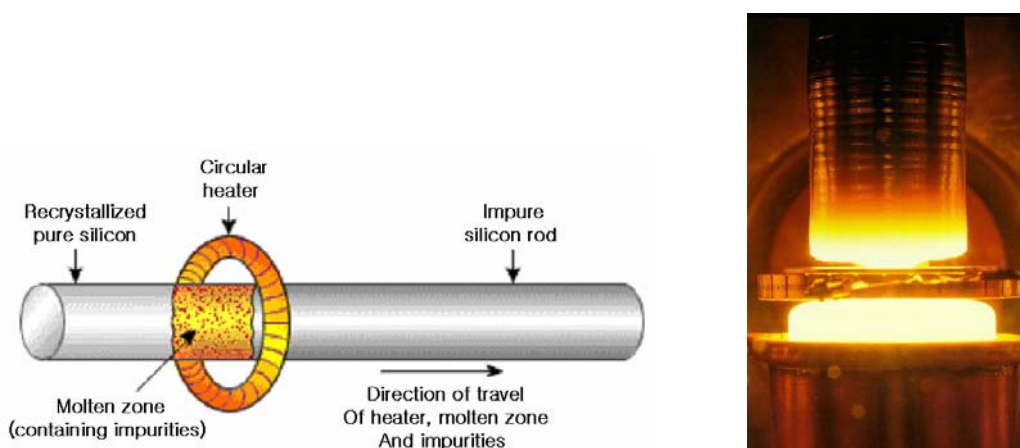


Figure 17-2. Zone refining of silicon

17-9. How many atoms per gram in the silicon wafer have been replaced by impurity atoms when the impurity level is 0.1 ppb?

Like all semiconductors, high-purity silicon fails to conduct electrical current until a minimum electrical voltage is applied, but at higher voltages it conducts moderately well. Semiconducting properties of silicon can be improved significantly by doping. Doping is the addition of a minor amount of a different element.

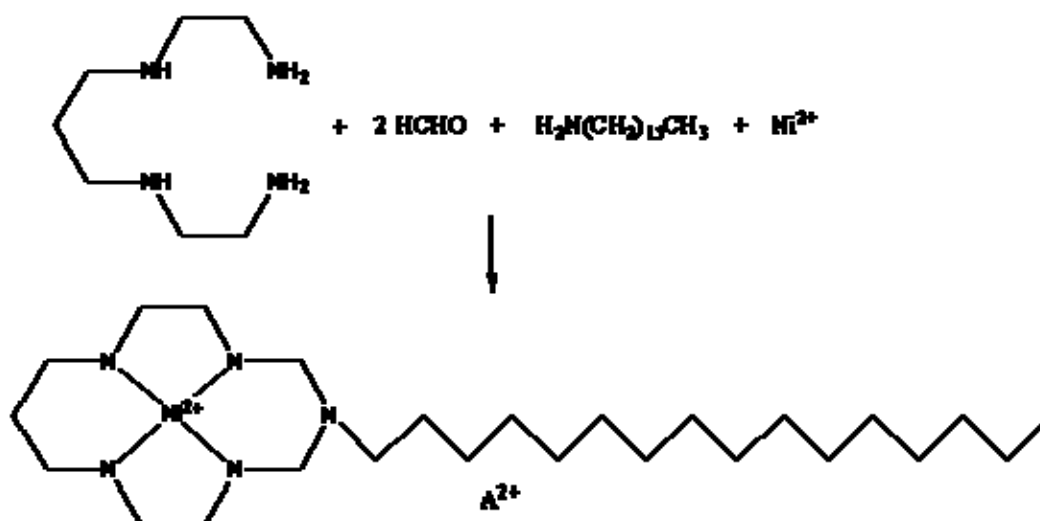
17-10. When a small number of boron atoms replace silicon atoms in solid silicon, what is the charge carrier? What is the name for this type of doped-semiconductor?

17-11. Draw a band diagram that can explain conductivity improvement upon replacement of some silicon atoms with boron atoms. Show in your drawing the band gap change after doping.

Problem 18: Self-assembly

Useful and essential structures can be made by self-assembly. In fact, life-forms were first made possible by the self-assembly of cell membranes about 4 billion years ago. Self-assembly is a fundamental principle that generates structural organization on all scales from molecules to galaxies. Self-assembly is defined as reversible processes in which pre-existing parts or disordered components of a pre-existing system form stable structures of well-defined patterns.

Some transition metal complexes can participate in the self-assembly. For example, a Ni complex with a long alkyl chain can be formed from many separate parts in the following reaction.



18-1. Predict the structure around the Ni(II) cation.

18-2. Determine whether A^{2+} is paramagnetic or not, using the d-orbital splitting pattern of Ni(II) in this structure.

18-3. Indicate the hydrophobic portion in A^{2+} .

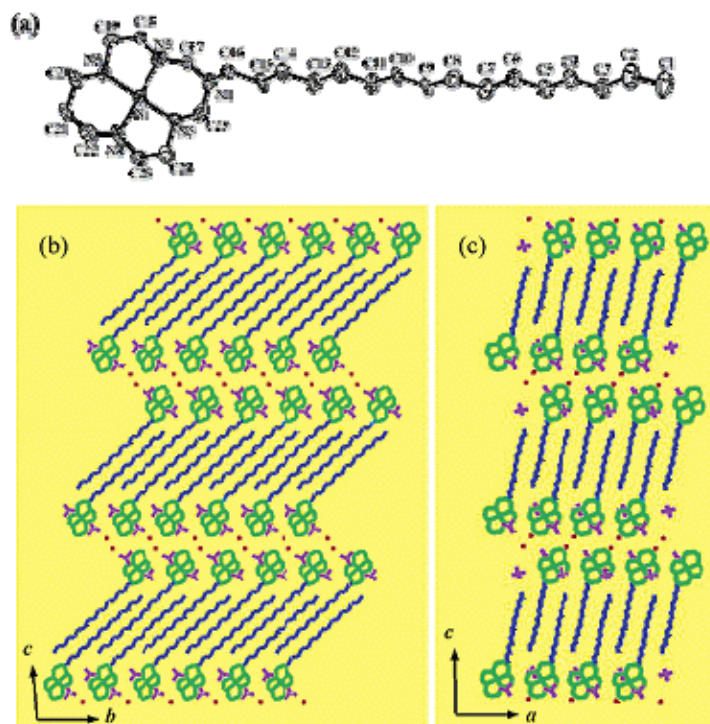
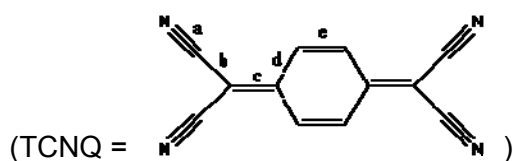


Figure 18-1. The molecular structure for A^{2+} and the packing structure of $A(ClO_4)_2 \cdot H_2O$.

18-4. What is the driving force for such assembly? (Hint: Its ionic compound, $A(ClO_4)_2 \cdot H_2O$, is found to float on the surface of water although its density is greater than 1.0.)

Metal complexes of TCNQ (7,7,8,8-tetracyano-p-quinodimethane) have been studied due to magnetic and electric conducting properties.



The infrared spectrum is diagnostic for the formal oxidation state and the coordinative status of the TCNQ molecules.

18-5. For TCNQ as pictured, which bond (among a-e) has the highest vibrational frequency?

18-6. Point out the bond(s) (among a-e) which might be shortened when TCNQ is reduced to form the radical anion.

The TCNQ derivative of A^{2+} ($[A^{2+}(TCNQ)_2](TCNQ \cdot CH_3COCH_3)$) also shows an interesting structural feature as shown in Figure 18-2.

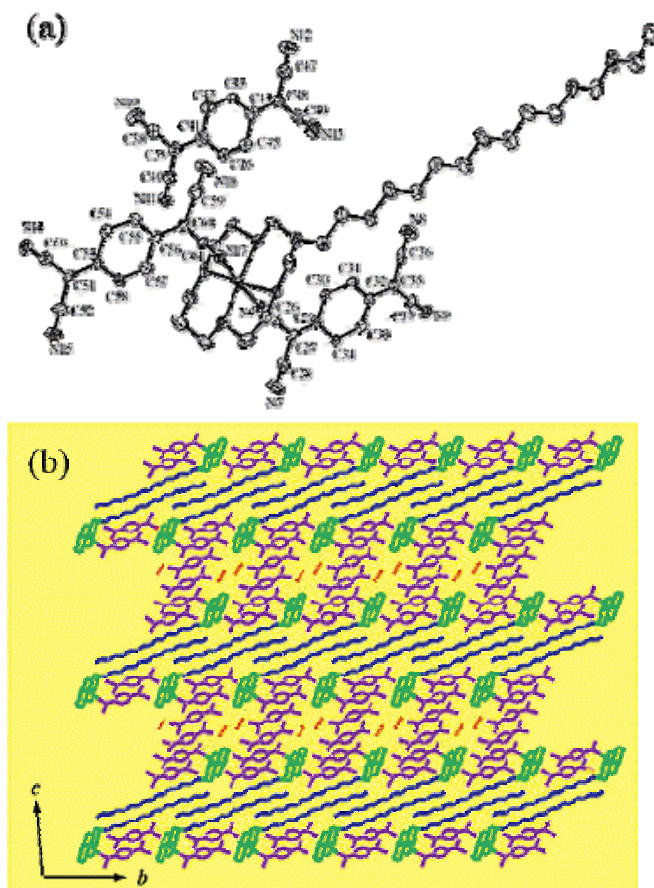


Figure 18-2. The molecular structure for A^{2+} and the packing structure of $[A^{2+}(TCNQ)_2](TCNQ \cdot CH_3COCH_3)$

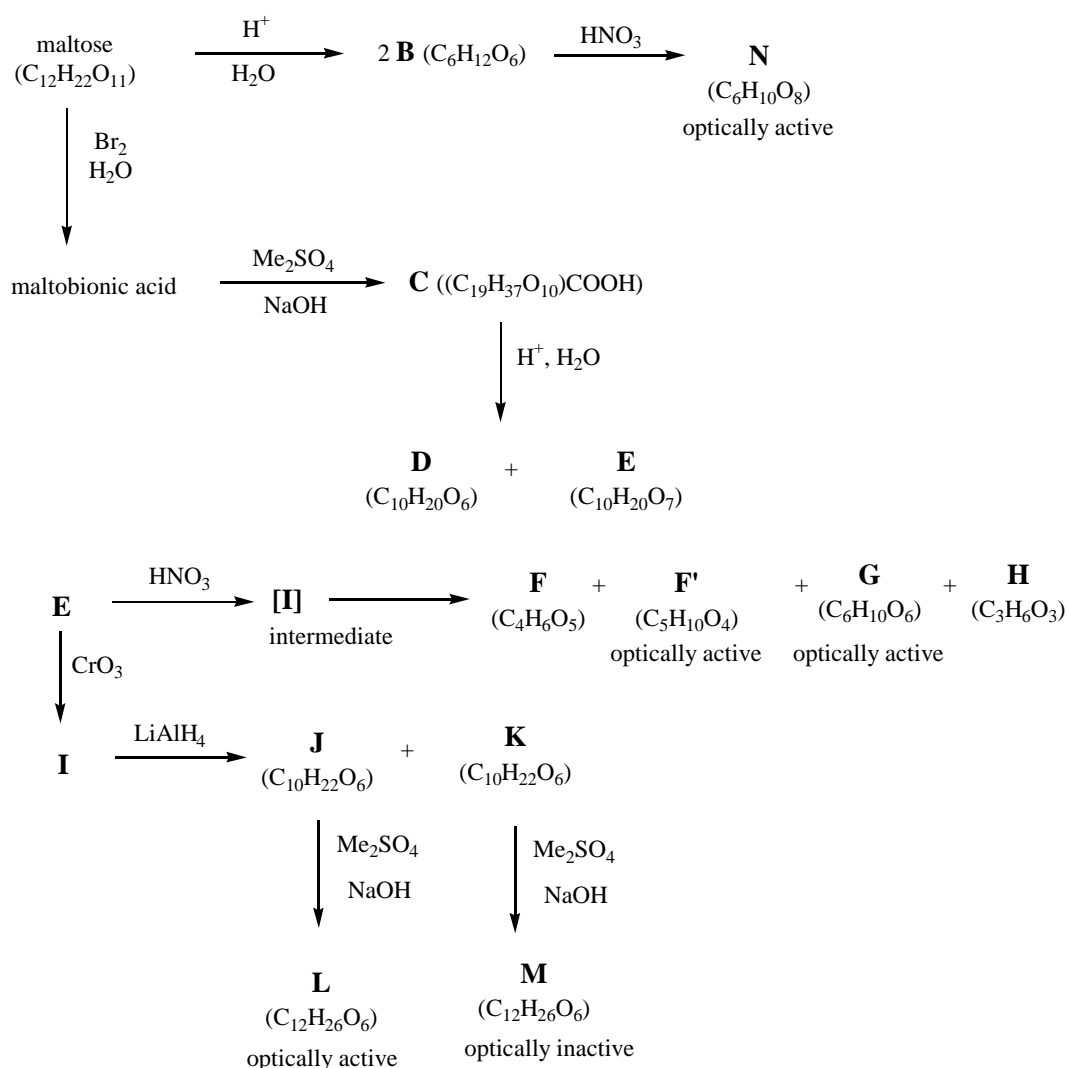
18-7. What is the coordination number for Ni in the TCNQ derivative of A^{2+} ?

18-8. In this structure, TCNQ molecules overlap one another. What is the driving force for such organization?

Problem 19: Stereochemistry (Organic synthesis – 1)

The fermentation of starch with malt produces ethyl alcohol. During this process, the hydrolysis of starch is catalyzed by the enzyme diastase present in malt to produce maltose, a disaccharide.

Maltose ($C_{12}H_{22}O_{11}$) reduces Tollens' and Fehling's reagents and it is oxidized by bromine in water to maltobionic acid ($(C_{11}H_{21}O_{10})COOH$), a mono carboxylic acid. In order to deduce its structure, maltose was subjected to series of reactions:

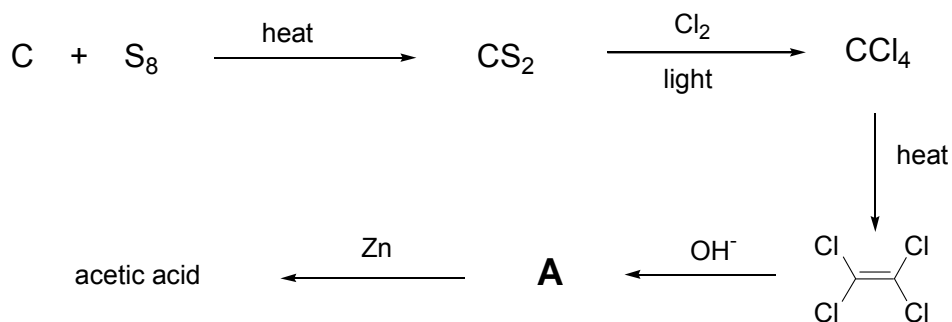


19-1. Draw structures **B**, **D-N** in a Fisher projection.

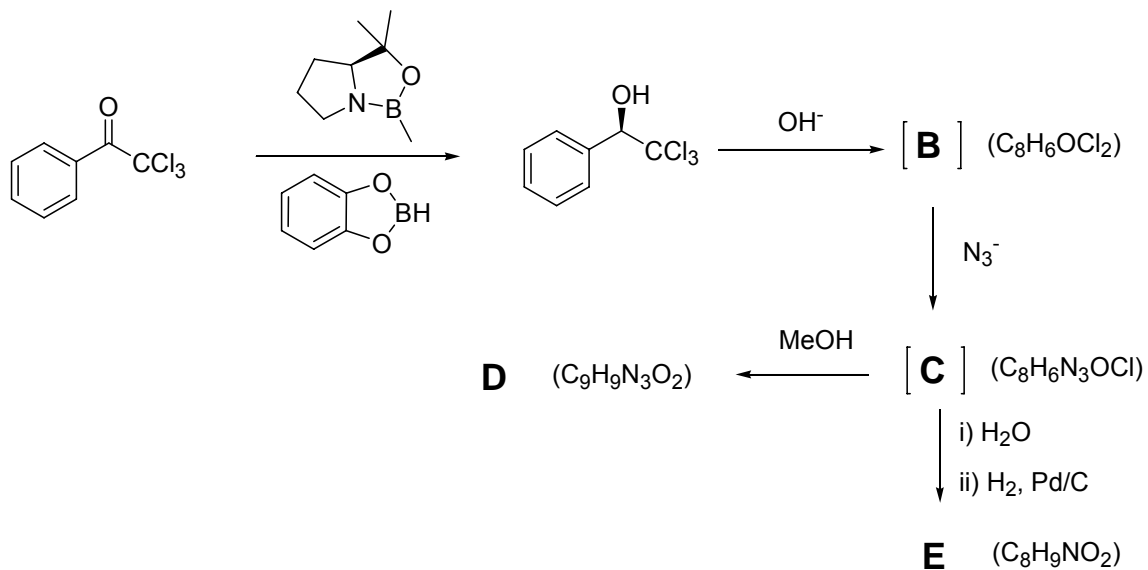
19-2. Draw structures for maltose, maltobionic acid and **C** in a Haworth projection.

Problem 20: Total synthesis (Organic synthesis – 2)

The first total synthesis of an organic compound was accomplished in the 19th century by Kolbe starting from carbon and sulfur as depicted in the following scheme.



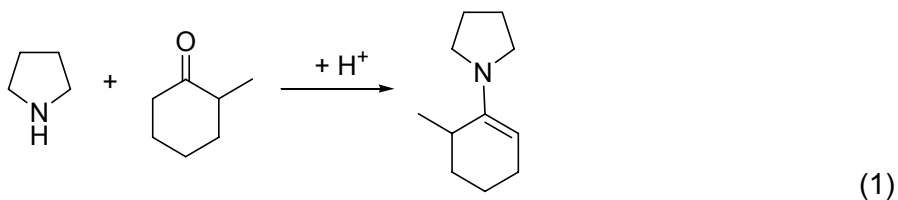
Even in modern organic synthesis, a similar synthetic strategy has been applied in the synthesis of amino acids.



Draw the structures of **A-E** and designate the *absolute* stereochemistry of **D** and **E** using the R/S convention.

Problem 21: Enamine chemistry (Organic synthesis – 3)

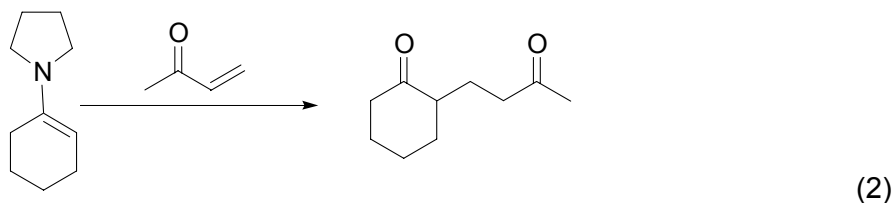
Enamine is formed between ketone and secondary amine in the presence of acid catalyst.



21-1. Propose a mechanism for enamine formation in the presence of acid catalyst (equation 1).

21-2. This process exhibits a bell-shaped pH dependence in the presence of acid catalyst. The maximum rate of formation occurs at pH 3-4. Propose a plausible reason why this dependence occurs.

21-3. Enamine reacts with conjugated enones such as methylvinylketone to form a 1,5-dicarbonyl compound after the hydrolysis of enamine (equation 2).

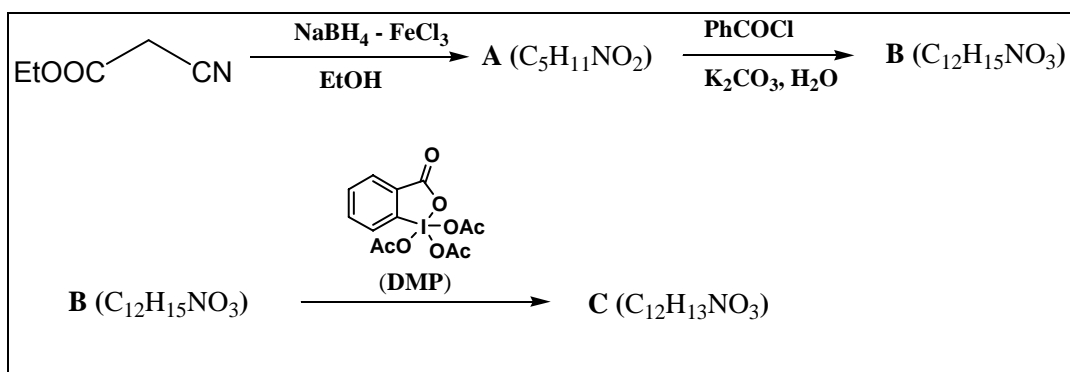


The product of this reaction now has one chiral center. Suggest conditions of special amine to make stereospecific product as shown in equation 2.

Problem 22: Oxidation and reduction in organic synthesis

In the manipulation of organic compounds, oxidation reaction and reduction reaction are the most important reactions. Especially, a chemo-selective, region-selective or stereo-selective reduction/oxidation is very important in designing an efficient organic synthesis of a target molecule. While nature achieves such selectivity through specific design of active sites of enzymes, chemical transformation mostly relies on subtle difference in reactivity by changing the nature of reagents.

The following scheme is a good example of chemo-selective reduction and oxidation reactions starting from ethyl cyanoacetate.

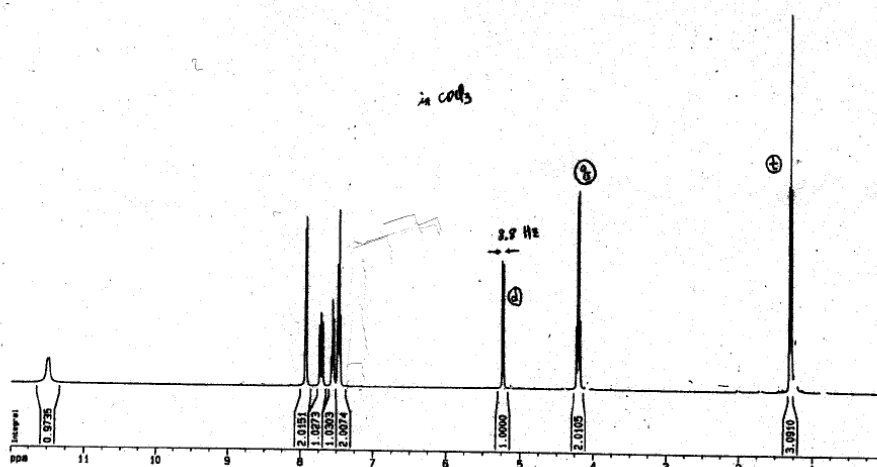


22-1. When ethyl cyanoacetate was treated with a reducing agent NaBH_4 in presence of FeCl_3 , a selective reduction of a functional group was observed. When the product A was reacted with benzoyl chloride, 1 equivalent of benzoyl chloride was consumed to form B. What are the structures of A and B?

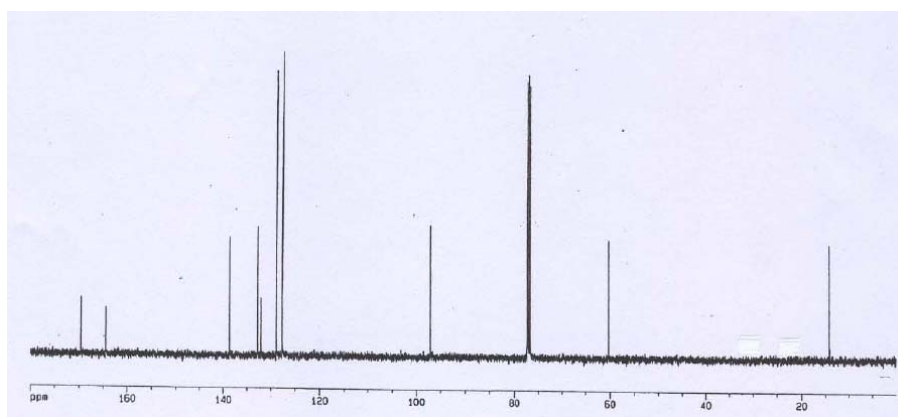
22-2. Dess-Martin Periodinane (DMP) is a strong but mild oxidizing agent, and can oxidize various functional groups in a selective manner. When B was oxidized with DMP a clean oxidation occurred to form C. $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, IR and mass spectra were obtained. These spectra showed that a clean transformation occurred to form a single product. In the $^1\text{H-NMR}$ a doublet between 5~6 ppm shows the coupling constant $J=8.8$ Hz. Draw the structure of C.

22-3. In the $^1\text{H-NMR}$, the chemical shift of one peak showed up near $\delta = 11.5$ ppm. Assign the proton in the structure C for this chemical shift. What is the reason for the chemical shift for the assigned proton that does not appear in the region ($\delta \approx 8$ ppm) for ordinary protons of that functional group?

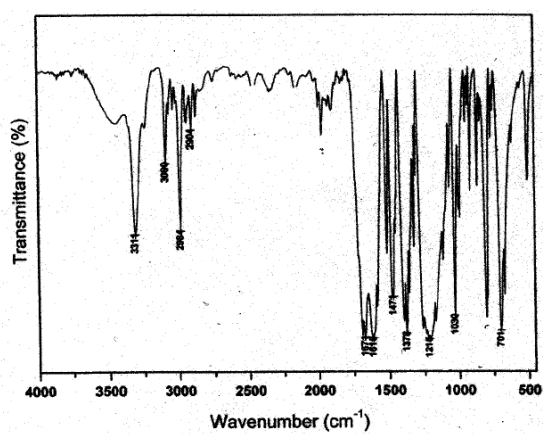
1H-NMR of C



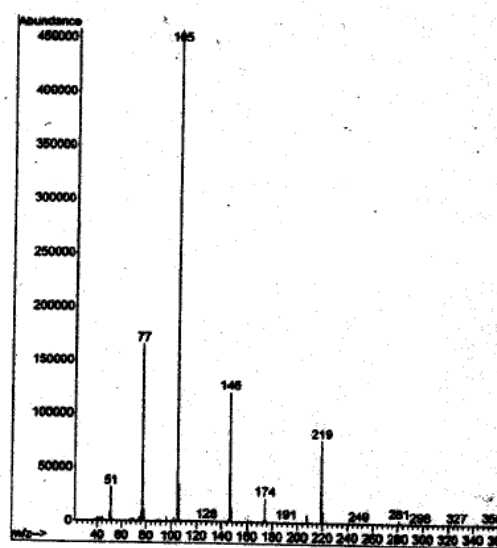
13C-NMR of C



IR of C



Mass spectrum of C



Problem 23: Antifreeze proteins

The temperature below 0°C occurs commonly on earth. How can organisms survive in conditions where water freezes? For many insects exposed to prolonged subfreezing conditions, cryoprotectant synthesis begins in their bodies during early autumn, and these substances are cleared in early spring. Figure 1 shows the seasonal content of glycerol in a freeze-avoiding insect.

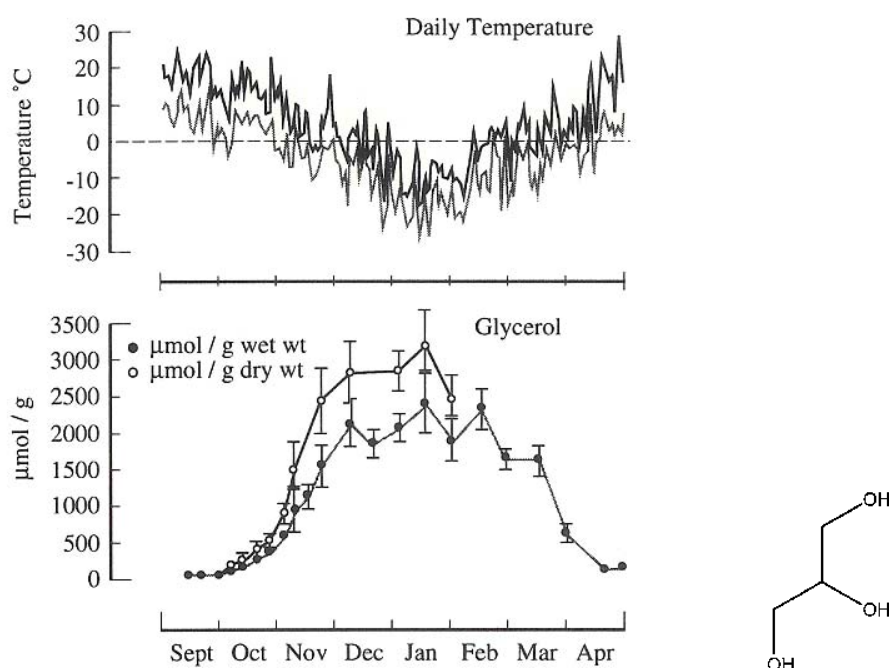
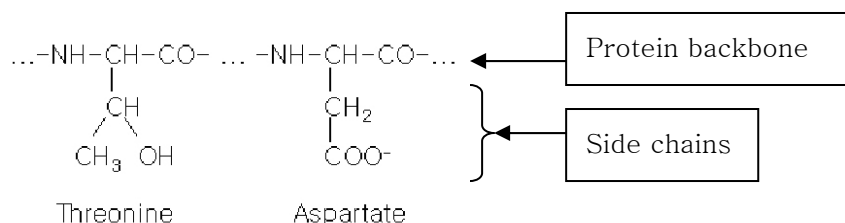


Figure 23-1. Daily maximum and minimum temperatures and glycerol content in the freeze-avoiding larvae of the goldenrod gall moth. The structure of glycerol is given on the right. (Reference: K.B. Storey and J.M. Storey 1988 *Physiol. Rev.* 68:27)

23-1. What is the weight percent of glycerol in the insect if it could avoid freezing at –20°C due to glycerol concentration alone? Assume the insect behaves as an ideal solution. What would be the osmotic pressure at this glycerol concentration? Comment on the resulting values. The freezing point depression constant for water is $K_f = 1.86^\circ\text{C}/(\text{mol}/\text{kg})$.

23-2. What is the actual fraction of glycerol in the insect's wet weight in January?
 What would be the freezing point of water in the insect in January considering the amount of glycerol alone?

23-3. In addition to freezing point depressants, "antifreeze proteins" are known to act to avoid freezing in animals including cold-water fish and many insects. The colligative freezing point depression due to antifreeze proteins is quite small. Experiments suggest that antifreeze proteins inhibit the growth of small ice particles. If some threonine or aspartate side chains composing the protein are chemically modified, the antifreeze activity disappears. What kind of interactions between antifreeze proteins and ice particles are probably responsible for the antifreeze activity?



Problem 24: The human body

The human body consists of cells, which in turn consist of atoms. About two thirds of body weight is water, which means that about two thirds of cell mass is water.

24-1. A human body weighing 60 kg consists of about 10^{27} atoms. Consider the average atomic weight of the three atoms in a water molecule. For your own information, consider the average atomic weight of atoms in other molecules such as proteins, fats, and carbohydrates.

24-2. A human body consists of about 100 trillion (10^{14}) cells. Assume that all human cells are cubic and identical in size. Estimate the size of an average human cell (length of the edge of the cube) in one significant figure.

24-3. Assume that all atoms in a cell are uniformly distributed. Estimate the distance between two atomic nuclei in a cell.

24-4. Estimate the distance between the centers of mass of two water molecules in pure water.

24-5. Estimate the average distance between atomic nuclei in pure water. Compare your result with answers in 24-3 and 24-4.

Problem 25: Hemoglobin

Another important class of compounds in the human body is proteins. Many proteins carry out catalytic functions. Hemoglobin, on the other hand, transports oxygen from the lung to remote parts of the body.

25-1. The molecular weight of hemoglobin is about 67,000 g/mol. The average amount of hemoglobin in erythrocytes in 100 mL of blood is 15 grams. The concentration of hemoglobin in blood is () M.

25-2. Estimate the average distance between two oxygen molecules in the air we breathe. Assume frigid air at 0°C in which 21% of air is oxygen.

25-3. Henry's law is written

$$\text{solubility} = k_{\text{H}} \times \text{partial pressure} \quad (k_{\text{H}}: \text{Henry's constant})$$

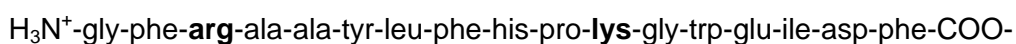
Henry's constant for oxygen is $1.3 \times 10^{-3} \text{ mol L}^{-1} \text{ atm}^{-1}$. Estimate the average distance between two oxygen molecules in water in equilibrium with air.

25-4. A hemoglobin molecule can bind up to four oxygen molecules. Estimate the average distance between two oxygen molecules in blood when all of the hemoglobin is saturated with oxygen. Compare your result with answers in 25-2 and 25-3 and note how efficiently hemoglobin concentrates and transports oxygen to tissues where the partial pressure of oxygen is low.

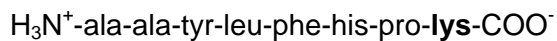
25-5. There are about () amino acids in hemoglobin. Estimate using average molecular weight of amino acids and check against literature values.

25-6. There are about () different kinds of amino acids in hemoglobin.

25-7. Trypsin hydrolyzes peptide bonds at the carboxyl group of arginine and lysine. Consider, for example, the following peptide.



Upon complete hydrolysis by trypsin, the following set of peptides will result.



Upon complete hydrolysis of hemoglobin after reduction of the disulfide bonds and alkylation, you expect to find on the average about () amino acids in a tryptic peptide (peptide resulting from hydrolysis by trypsin).

25-8. The average molecular weight of the tryptic peptides is about ().

Problem 26: Mass spectrometry of hemoglobin

26-1. If you lived in the 19th century, what method would you use to determine the molecular weight of hemoglobin? Explain.

Breakthroughs in molecular weight determinations of biopolymers such as proteins were recognized with the 2002 Nobel Prize in chemistry awarded to Fenn for developing electrospray ionization mass spectrometry (ESI MS) and to Tanaka for pioneering work leading to matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). In MALDI-TOF MS, proteins are embedded in a crystal of UV-absorbing matrix molecules and desorbed/ionized upon irradiation with a UV laser pulse. Singly charged protonated protein ion, $[M+H]^+$, is produced as a major species from a protein with mass M .

26-2. Consider hemoglobin with a 67,434 Da molecular weight. After desorption/ionization, the $[M+H]^+$ ion is accelerated by 20.000 kV. Calculate the energy of the protein ion in joule. (coulomb x volt = joule) ($e = 1.60218 \times 10^{-19}$ coulomb)

26-3. The accelerated protein ion is then allowed to travel 1.0000 m in an evacuated flight tube to a detector. All electrical energy is converted to kinetic energy ($mv^2/2$). If the flight time of the protein ion was determined to be 1.3219×10^{-4} s, what is the molecular weight of hemoglobin calculated from the flight time measurement? What is the mass accuracy in ppm?

26-4. The flight tube is maintained under a high vacuum at 25°C. What is the residual pressure in the flight tube at which the mean free path of air molecules is the same as the length of the flight tube? See Problem 2 for definition of mean free path. Assume that all air molecules are spheres with a diameter of 2 angstroms.

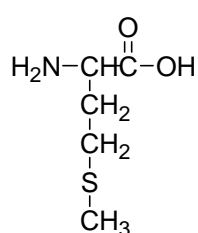
Problem 27: Post-translational modification

Nature uses 20 amino acids to make diverse proteins. However, since the diversity from 20 amino acids sometimes is not enough, chemical modifications are carried out mostly at the side chains of amino acids to generate more diverse functional groups by many natural enzymes. Many types of these post-translational modifications are important in recognition of protein-protein, protein-DNA, protein-RNA molecules. These modifications are used as turn-on (off) switches, transferring messages, known as signal transduction in living cells.

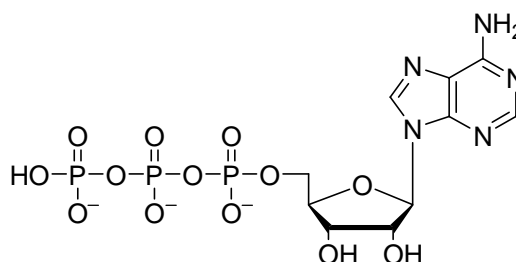
Recently, methylation was found to be as important as other known post-translational modifications, such as phosphorylation and glycosylation. Like other modifications, there is a reverse reaction, demethylation. The two processes work oppositely, turning signals on and off (off and on), like phosphorylation and glycosylation. However, processes of methylation and demethylation in nature are quite different. In other words, the mechanisms of the two facilitating enzymes are not the reverse of each other.

27-1. Considering the functional groups of side chains existing in 20 amino acids, what kind of functionality is suitable for generating more diversity owing to methylation and demethylation? Name two amino acids.

27-2. In methylation of an amino acid side chain, S-adenosylmethionine (SAM) is used as a cofactor. SAM is made from methionine and ATP. Deduce the structure of SAM.



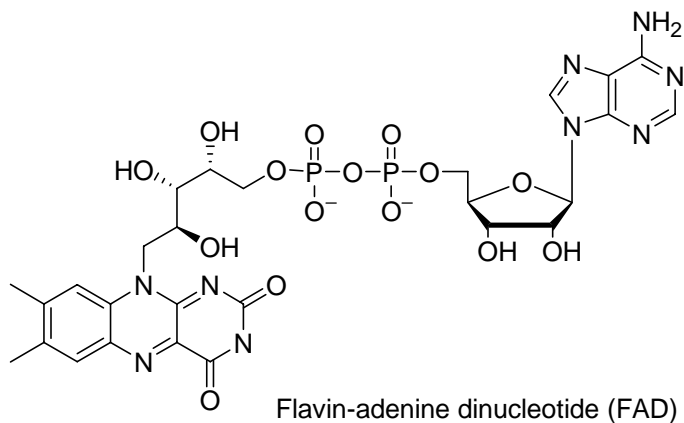
Methionine (Met)



Adenosine triphosphate (ATP)

27-3. Propose a mechanism of amino acid methylation with SAM.

27-4. Two steps make up the proposed mechanism for demethylation. The enzyme uses FAD as a cofactor for the first step. Propose plausible mechanisms for demethylation.



Problem 28: Transition state in enzymatic reactions

Enzymes are catalysts for living organisms. They have evolved to enable specific chemical reactions necessary for life to thrive more efficiently. In the active site of an enzyme, amino acid residues including side chains have evolved to provide space for the transition state (TS) of the chemical transformation to exist with conformational and electrostatic match. Thus, the binding affinity of this TS to the enzyme is expected to be very high (if one can calculate), stabilizing the energy of the transition state through an enzyme-TS complex. This lowers the activation energy of the reaction and creates rate acceleration. If one can calculate the binding constant owing to the complex formation, one could readily deduce how efficient the enzyme is by calculating $k_{\text{cat}}/k_{\text{uncat}}$.

Man-made enzymes are holy grails for some chemists, because they can give insight about the behavior of natural enzymes and can be used as useful synthetic and therapeutic tools. Catalytic antibodies can be one of these kinds of artificial enzymes. Antibodies have antigen-binding sites, in which the target antigen binds with high affinity ($K_D = 10^{-9}$ - 10^{-11} M) and with great specificity. These properties can be exploited as active sites in artificial enzymes. Antigen-binding sites may serve to specifically recognize substrates and perform certain chemical reactions.

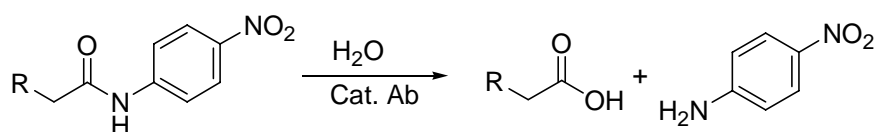
Since these catalytic antibodies need to accommodate transition state (TS) structures in chemical transformations, an antigen that triggers the production of the catalytic antibody must be designed and synthesized just like the TS structure. However, chemists cannot prepare a transition state structure because it is transient. Instead, one can synthesize a stable compound that resembles the structure of the transition state. This newly designed compound is called a transition state analogue (TSA). Once a TSA is made, it can be injected into mice to generate antibodies. The half-life of the TSA should be longer than 2 weeks at physiological conditions to obtain an adequate immune response. After generating as many antibodies as possible, the most tightly binding and specific antibodies are selected as candidates for antibody catalysts.

28-1. If one of the selected antibodies has $K_D = 10^{-13}$ M against the TSA, comparing with normal antibody ($K_D = 10^{-6}$ M) how much stabilization energy can the TSA gain from the binding to this specific antibody?

28-2. Let us assume that the TSA can be considered as the real transition state (TS). Then, how much rate enhancement will be obtained when we will use this catalytic

antibody for the intended chemical transformation? Describe this enhancement by $k_{\text{cat}}/k_{\text{uncat}}$.

Most scientists are interested in the specific hydrolysis of the pathogenic proteins or peptides such as β -amyloid as the intended chemical reaction by catalytic antibodies. Assuming that the following reaction is the intended reaction by catalytic antibody, TS of the hydrolysis of the amide bond should be considered to make a plausible TSA.



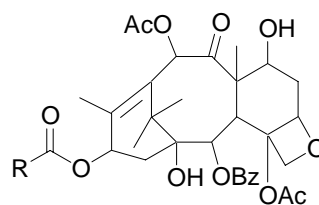
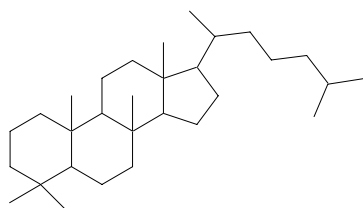
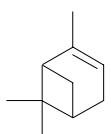
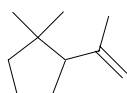
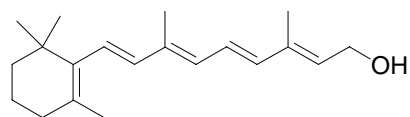
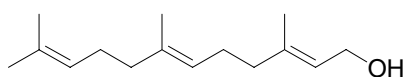
28-3. What is the transition state or reactive intermediate of the above amide bond hydrolysis?

28-4. Design a stable TSA suitable for replacing the TS. Remember that the TSA should be stable and structurally close to the TS.

Problem 29: Nature's building blocks

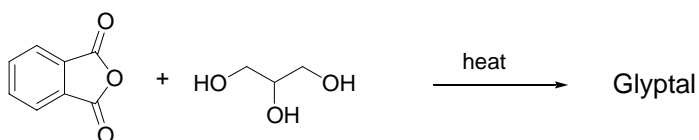
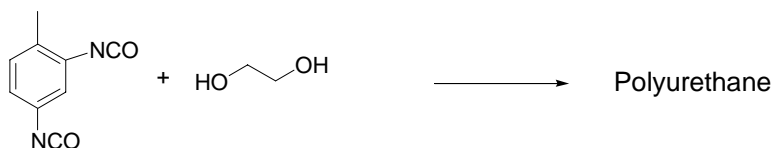
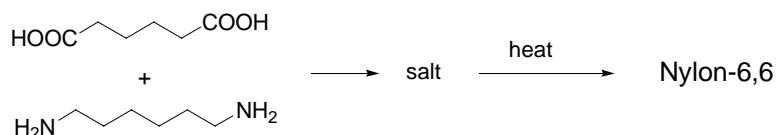
Natural rubber is a polymer composed of isoprene, the conjugated diene 2-methyl-1,3-butadiene. Isoprene can be found not only in rubber but in a wide range of natural products called terpenes, most of which have carbon skeletons made up of isoprene units joined head-to-tail. Recognition of this fact - the isoprene rule - has been great help in working out structures and determining the biosynthetic origin of terpenes.

29-1. Find the isoprene units in the following terpenoid natural products.



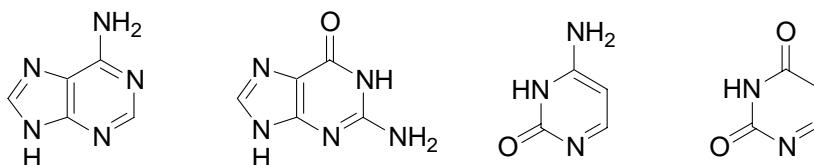
In polymer chemistry, the repeating unit is called a monomer and the repeating units are joined together through chain reaction polymerization or step-reaction polymerization. A few examples of step-reaction polymerization are provided below.

29-2. Draw the repeating unit in each polymer product.



Nature also was suspected to have used basic building blocks such as HCN, NH₃ and water that are observed in interstellar space to produce adenine, guanine, cytosine and uracil in the “prebiotic system” as Oro has demonstrated in 1960.

29-3. Identify the origin of each carbon and nitrogen atoms of these bases from HCN, NH₃ and H₂O



Problem 30: True or false

- 30-1. Hydrogen is the most abundant element at the core of the sun.
- 30-2. Hydrogen is the only element in the periodic table that can exist without a neutron. This suggests that a neutron is essential for binding positively charged protons in the nucleus.
- 30-3. The number of neutrons for heavy nuclei exceeds the number of protons, because the electrostatic repulsion between protons is long-range whereas the strong nuclear force among the protons and the neutrons is short-range.
- 30-4. Helium is the second-most abundant element in the universe. The molar ratio between hydrogen nuclei (proton) and helium nuclei (α -particle) is about 3 to 1.
- 30-5. Helium was first made in the interior of the first star in the history of the universe.
- 30-6. The mass of an α -particle = 2 x (proton mass + neutron mass).
- 30-7. Neutral atoms were first made before the birth of the first star in the history of the universe.
- 30-8. The discovery of argon precedes the discovery of the octet rule.
- 30-9. Mendeleev's periodic table precedes the discovery of argon.
- 30-10. The discovery of proton precedes the discovery of electron.
- 30-11. The ionization energy of hydrogen is greater than the bond energy of the hydrogen molecule.
- 30-12. The enthalpy of formation of $\text{CO}_2(\text{g})$ is about the same as twice the enthalpy of formation of $\text{H}_2\text{O}(\text{g})$, because there are two electronegative oxygen atoms in CO_2 whereas there is only one in H_2O .

Problem 31: Molecular weight determination of carbon dioxide from density measurements

Introduction

Avogadro's principle (1811) is fundamental. For example, molecular weight determinations from gas densities are based on this principle. Cannizzaro showed in 1858 that molecular weights determined from gas density measurements can be used to determine atomic weight. For example, the molecular weight of nitric oxide, nitrous oxide, and nitrogen dioxide relative to that of hydrogen gas, which Cannizzaro defined to be 2, is 30, 44, and 46, respectively. From a large body of such data, one could deduce the atomic weight of different elements.

Gas density measurements led to another major breakthrough in the 19th century. Rayleigh and Ramsay discovered argon while determining the density of nitrogen gas (see Problem 6). Soon a new group was added to help complete the periodic table. Avogadro's principle is exemplified in the following experiment which involves determining the molecular weight of carbon dioxide from density measurements. This experiment also uses the ideal gas law.

Materials

dry ice, water

Apparatus

Balance with at least 0.01 g accuracy, two 500 mL flasks with sidearm, rubber tubing, rubber stopper, aluminum foil, cylinder, thermometer, barometer

Experimental Design

- 31-1. Devise two separate procedures for determining the density of carbon dioxide at room temperature and atmospheric pressure using dry ice as the source of carbon dioxide.
- 31-2. Indicate possible sources of error and suggest ways to minimize these errors.
- 31-3. Calculate the molecular weight of carbon dioxide (i) from its density relative to that of air and (ii) using the ideal gas law.

Procedure A

1. Record the ambient temperature (T) and atmospheric pressure (p).
2. Weigh a flask. Record W_1 .

$$W_1 = W(\text{flask}) + W(\text{air}) \quad (1)$$
3. Place crushed dry ice at the bottom of the flask and allow time for sublimation to occur. After a while, make sure that there is no solid dry ice remaining and measure the temperature inside the flask. Wait until temperature is equalized with the openings loosely covered with aluminum foil to let carbon dioxide at room temperature and atmospheric pressure fill the flask, wipe out condensed water on the outer surface of the flask, and weigh. Record W_2 .

$$W_2 = W(\text{flask}) + W(\text{CO}_2) \quad (2)$$

4. Seal the opening of the side arm with a rubber stopper. Fill the flask to the rim with water and measure volume of the water with a graduated cylinder. This is the volume of carbon dioxide in the flask (V). Calculate the weight of air, $W(\text{air})$, occupying this volume under the experimental conditions. Assume that 78% of air is nitrogen, 21% oxygen, and 1% argon. A mole of air weighs 29.0 g. Calculate $W(\text{flask})$ from (1) and $W(\text{air})$. Then calculate $W(\text{CO}_2)$ from (2) and $W(\text{flask})$.
5. Determine the molecular weight of carbon dioxide from $W(\text{CO}_2)$ and $W(\text{air})$.
6. Also determine the molecular weight of carbon dioxide using the ideal gas law.

$$MW(\text{CO}_2) = (29.0)[W(\text{CO}_2)/W(\text{air})]$$

$$pV = [W(\text{CO}_2)/MW(\text{CO}_2)]RT$$

Procedure B

1. Connect two flasks through their side arm with one piece of rubber tube. Elevate one flask and place a sufficient amount of crushed dry ice at the bottom of this flask. Seal the opening of this elevated flask with a rubber stopper and let carbon dioxide gas overflow through its side arm, and fill the receiving (lower) flask.
2. Once a sufficient amount of carbon dioxide has overflowed, weigh the receiving flask filled with carbon dioxide after covering its openings with aluminum foil. The advantage of this procedure is that carbon dioxide in the receiving flask is at room temperature and atmospheric pressure.
3. Determine the volume, V , and weight of the flask as in Procedure A.
4. Repeat until consistent weight of carbon dioxide in the flask is obtained.
5. Determine the molecular weight of carbon dioxide as above.

Problem 32: Determination of molecular weight by freezing point depression

Introduction

Accurate measurement of gas density was used for the determination of molecular weight of gaseous compounds in the 19th century. For liquid and solid compounds, however, colligative properties had to be used. Here, freezing point depression will be used to demonstrate how 19th century chemists estimated the molecular weight of an unknown compound and determined the molecular formula from a given empirical formula. Freezing point depression also can be used to test Arrhenius's theory of electrolytic dissociation.

Materials

ice, sodium chloride, unknown compound A (glucose), unknown compound B (sucrose)

Apparatus

thermometer or digital temperature sensor (0.1°C accuracy), beaker, test tube, wire

Procedure

1. Mix enough sodium chloride with ice and water in a beaker to bring the temperature of the ice water down to about $-8 \sim -10^{\circ}\text{C}$. Add more ice and salt as necessary to maintain this temperature range.
2. Add several milliliters of water to the test tube (2~3 cm in diameter). Place a thermometer or digital temperature sensor and a wire bent at one end to form a ring to facilitate mixing. Then immerse the lower half of the test tube assembly into the ice bath and monitor the temperature change for about 10 min while vigorously agitating the water with the wire. The temperature will drop sharply to a point of super-cooling and increase slightly to the freezing point, where the temperature will remain steady. Calibrate the thermometer or the temperature sensor to 0°C at the freezing point of water.
3. Prepare 1.00 and 2.00 molal solution of sodium chloride in water. Determine the freezing point of these solutions following the procedure above. Using the three data points (origin from zero point calibration, 1.00 and 2.00 molal concentration), construct a curve showing freezing point vs. molal concentration. Determine

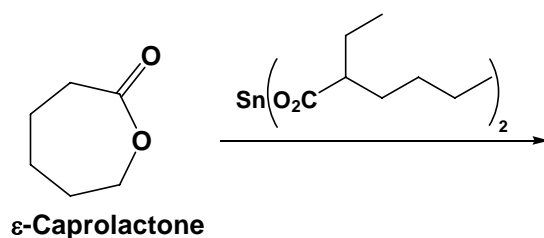
freezing point constant, K_f , of water from the slope and the van't Hoff i factor for sodium chloride.

$$-\Delta T_f = K_f m i$$

4. Dissolve 20 g of unknown compound in 80 g of water. Also dissolve 20 g of unknown compound B in 80 g of water. Determine the freezing point depression of these solutions and calculate molality.
5. From the calculated molality and the number of grams of the compound in 1,000 g of solvent, calculate the molecular weight of both compounds.
6. Elemental analysis showed that the compounds are simple carbohydrates. The weight percentages of C, H, and O (by difference) for both compounds were similar within experimental error (C: 40~42%, H: 6~7%, O: 51~54%). Suggest molecular formulas for compounds A and B.

Problem 33: Molecular weight determination of polymer by titration**Introduction**

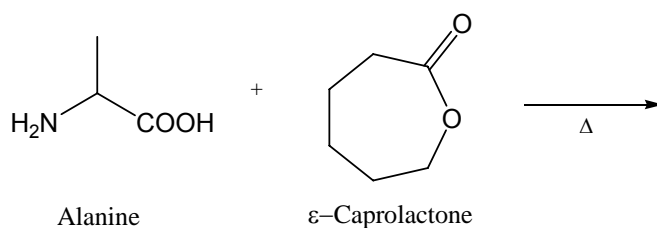
Polycaprolactone (PCL) is a biodegradable polyester with a low melting point ($\sim 60^\circ\text{C}$) typically prepared by ring opening polymerization (ROP) of ϵ -caprolactone (ϵ -CL) using a catalyst such as tin(II) 2-ethylhexanoate (stannous octanoate).



PCL is fully biodegradable. Furthermore its low melting point makes PCL a useful component of a composite biodegradable material. For example, PCL mixed with starch is used to make cheap biodegradable trash bags.

PCL is degraded by hydrolysis of its ester linkages under physiological conditions and, therefore, has also received a great deal of attention for use as an implantable biomaterial. PCL has been approved in certain countries for use in the human body, and may be potentially used in drug delivery, sutures, adhesion barriers and scaffolds for tissue repair. So far, a variety of drugs have been encapsulated within PCL beads for controlled release and targeted drug delivery.

Recently, it has been reported that the ROP of ϵ -CL can proceed with a heat in the presence of natural amino acids. Therefore, the biocompatibility and in vivo safety of PCL thus-obtained could be satisfying for medical and pharmaceutical purposes.



In this experiment, four ROP reactions will be carried out for different time intervals to prepare polymer samples with varying molecular weights. Since the degree of polymerization (DP) of these samples is relatively low and each polymer molecule

contains an end-group suitable for simple acid-base titration, the average molecular weight of the polymers can be determined by end-group analysis. A main problem in such an approach for molecular weight determination is finding a solvent for the polymer that is compatible with the titration. Fortunately, an appropriate solvent system is available for PCL. PCL can be titrated with KOH in isopropyl alcohol/1,4-dioxane solvent ($v/v=1/4$) using 1% phenolphthalein solution in pyridine as an indicator. The average molecular weight, M_n , of the polymer can be calculated as follows from the sample weight and the number of moles of the end group:

$$M_n = \text{weight of polymer sample in g} / \text{number of moles from end group analysis}$$

The degree of polymerization at specific reaction time can be obtained from M_n for each polymer sample.

$$DP = M_t/M_0,$$

M_t ; molecular weight at time t

M_0 ; molecular weight of one monomeric unit

Materials

(R and S codes refer to risk and safety phrases for the chemicals.)

L-alanine,

ϵ -caprolactone (S 23-24/25),

KOH (R 22-35, S 26-36/37/39-45),

Tetrahydrofuran (THF, R 11-19-36/37, S 16-29-33),

methanol (R 11-23/24/25-39/23/24/25, S 7-16-36/37-45),

isopropyl alcohol (R 11-36-67, S 7-16-24/25-26),

1,4-dioxane (R 11-19-36/37-40-66, S 9-16-36/37-46),

1% phenolphthalein solution in pyridine (R 11-20/21/22, S 26-28)

Apparatus

Balance with at least 0.01 g accuracy, four 50 mL flask, four 250 mL beaker, test tubes, 50 mL burette, Pasteur pipette, oil bath, and hot plate stirrer, vacuum oven, mg-scale balance

Procedure 1: Neat ring-opening polymerization

1. In each of four 50 mL 1-neck round bottom flasks (RBF), mix 0.13g L-alanine (1.5 mmol) and 5.13 g ϵ -caprolactone (45 mmol) and stir the mixture at 160°C in an oil bath. Connect the flasks to nitrogen line to release any pressure developed during the heating.
2. After 1, 5, 12, and 24 h, remove one of the flasks from the bath and cool it down to room temperature. Dissolve the mixture in 5 mL tetrahydrofuran (THF) and precipitate the polymer product by pouring the solution into 80 mL methanol/H₂O (v/v=4/1) solution.
3. Filter the precipitated polymer products and dry in a vacuum oven for several hours. Measure the weight of dried polymer products.

Procedure 2: Titration with KOH

1. Prepare a standardized solution of KOH (about 0.008 M) in isopropyl alcohol/1,4-dioxane (v/v=1/4).
2. Dissolve each polymer sample obtained above in 5.0 mL of isopropyl alcohol/1,4-dioxane (v/v=1/4). Add 4 drops of 1% phenolphthalein/pyridine solution to 1.0 mL aliquot of each polymer solution and titrate with the standardized KOH solution. Repeat this titration.
3. Calculate the average experimental molecular weight value (g/mol) from the average volume of the titrant.
4. Repeat steps 2 and 3 for other polymer samples.

Questions

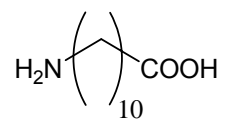
Assume that 100% conversion of monomer is obtained after 24 h, and all the amino acid (alanine) is incorporated into the polymer.

- 33-1. What is the structure of the resulting compound if alanine attacks the caprolactone? And explain the meaning of titration with KOH.
- 33-2. At times of 1, 5, 12, and 24 h, calculate yields, mol of KOH used in titration, the number of polymer chain, average experimental molecular weight value (g/mol) of polymer (M_n), and degree of polymerization.

	1 h sample	2 h sample	5 h sample	24 h sample
Polymer yield (g)				
volume of KOH solution (ml)				
amount of KOH (mmol)				
amount of polymer (mmol)				
M_n (g/mol)				
degree of polymerization				

33-3. Draw each polymeric product from the 1, 5, 12, and 24 h trials. The repeat unit in polymer chain can be expressed as an example showed below.

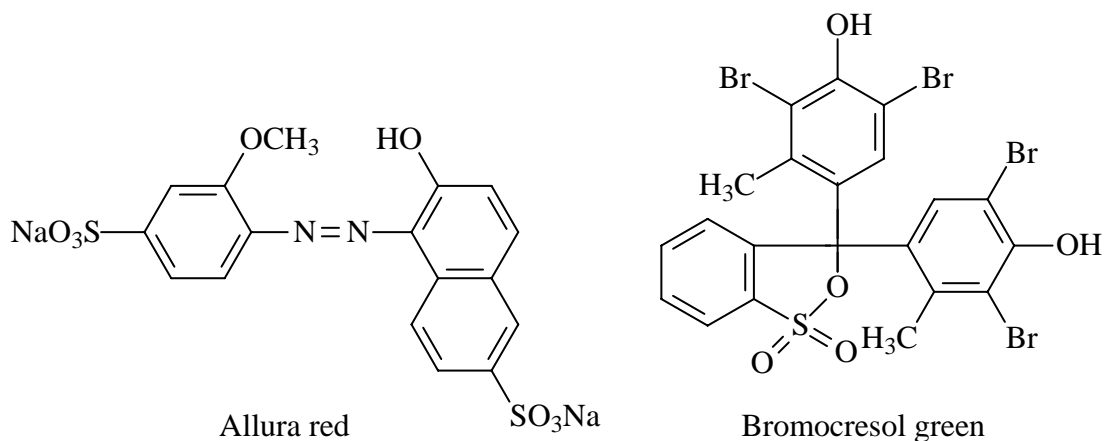
Example) 11-aminoundecanoic acid



Problem 34: Separation and quantitative determination of dyes by column chromatography and spectrophotometry

Introduction

In this experiment, students receive small volumes of unknown liquid which is a mixture of allura red ($C_{17}H_{12}N_2O_8S_2Na_2$, *abbrev.* AR) and bromocresol green ($C_{21}H_{14}Br_4O_5S$, *abbrev.* BCG) in their basic forms. An aliquot is placed on a small silica gel column, which students prepare by filling silica gel in a Pasteur pipet. The students separate the dyes by *stepwise* elution with the solvents listed in Table 1. The students choose two eluents that are expected to give the best separation of the dyes. The samples are then diluted to a known volume and quantified by visible spectrophotometry. The components of the entire experiment – column preparation, separation, calibration curves, and analysis of the unknown – can be undertaken easily if students know how to perform quantitative serial dilution, operate a spectrophotometer, and know how to select the analytical wavelengths for the dyes.



Materials

Reagent	Concentration	R phrases	S phrases
allura red	solid		
bromocresol green	solid		22-24/25
hydrochloric acid	w(HCl) 35%	23-34-37	26-45
triethylamine		11-20/21/2-35	3-16-26-29-36/37/39-45
methanol		11-23/24/25-39/23/24/25	7-16-36/37-45
ethyl acetate		11-36-66-67	16-26-33
silica gel	solid		22-24/25

Apparatus

visible spectrophotometer; analytical balance; sample cell (10-mm pathlength); twelve 10-mL and two 50-mL volumetric flasks; two 50-mL beakers; three 2-mL Pasteur pipets; one 100- μ L micropipette, pipet filler

Procedure 1: Preparation of stock solutions of dyes

These dye solutions tend to decompose over extended periods of time, so they should be prepared just prior to the experiment.

1. Bromocresol green. An accurately weighed sample (300 mg) is dissolved in ethyl acetate in a 50-mL volumetric flask, to which sufficient triethylamine is added to produce the purple basic form.
2. Allura red. An accurately weighed sample (about 100 mg) is dissolved in about 30 mL of methanol in a 50-mL volumetric flask, to which triethylamine is added dropwise until the dye is completely dissolved. Methanol is then added to the mark to dilute the mixture. *Note:* Allura red should be pre-purified as follows: Dissolve the sodium salt of AR in methanol and then filter. To this solution, add an excess of concentrated HCl. After about 30 min, the resulting crystals of the protonated form can be filtered off.

Procedure 2: Preparation of standard solutions of dyes

Prepare five standard solutions for each dye by diluting the stock solution in the same solvents used for the preparation of the stock solutions in 10-mL volumetric flasks. To the AR standard solutions 3-4 drops of concentrated HCl are added to have the dye in its acidic form. The concentration of the standard solutions should be in the range of one tenth to nine tenths of the original concentration of the stock solution.

Procedure 3: Preparation of calibration curves of dyes

Prepare a calibration curve for each dye using its absorbances at respective peak maximum vs. concentration in ppm.

Procedure 4: Preparation of a chromatographic column

Prepare a chromatographic column by placing a small plug of glass wool (or cotton) at the constriction of a 2-mL Pasteur pipet. Silica gel (45/70 mesh) slurried in ethyl acetate is added to the pipet to produce 4-5 cm of packed gel in the column.

Procedure 5: Column chromatography and quantitation

1. Transfer a 40- μ L aliquot of unknown liquid to the column.
2. Rinse the walls of the column with a few drops of an eluent selected from Table 1, pass the eluent through the column and collect the eluate in a 10-mL volumetric flask containing 2-3 drops of triethylamine.
3. Pass a second eluent through the column selected from Table 1, and collect the eluate in a separate 10-mL volumetric flask containing 3-4 drops of concentrated HCl. A small band of impurity may be left behind at the top of the column.
4. Dilute the first fraction in its purple, basic form to volume with the first eluent.
5. Dilute the second fraction in its acidic, red form to volume with the second eluent.
6. Find the concentration of each sample, and thus the amount (mg) of each dye in the unknown from the calibration curve for each dye.

Table 34-1. Possible eluent systems

Eluent No.	Eluent Set I	Eluent Set II
1	ethyl acetate	methanol
2	methanol	ethyl acetate
3	ethyl acetate-HCl ^a (200:1 v/v)	methanol-HCl (200:1 v/v)
4	ethyl acetate-TEA (200:1 v/v)	methanol-TEA (200:1 v/v)
5	methanol-HCl (200:1 v/v)	ethyl acetate-HCl (200:1 v/v)
6	methanol-TEA (200:1 v/v)	ethyl acetate-TEA (200:1 v/v)

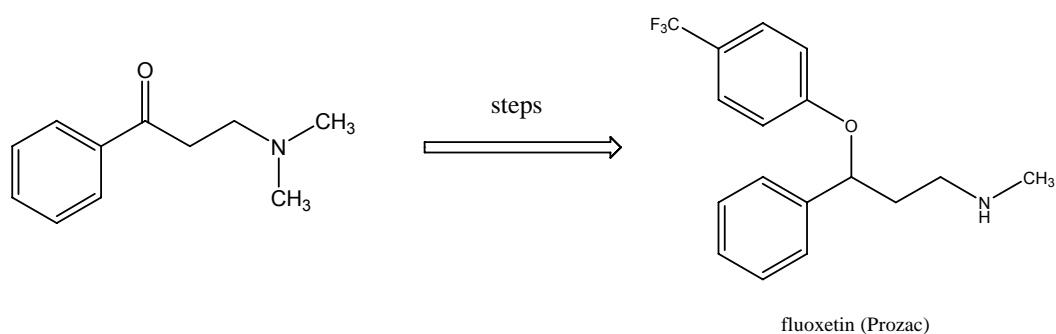
a. concentrated hydrochloric acid.

Questions

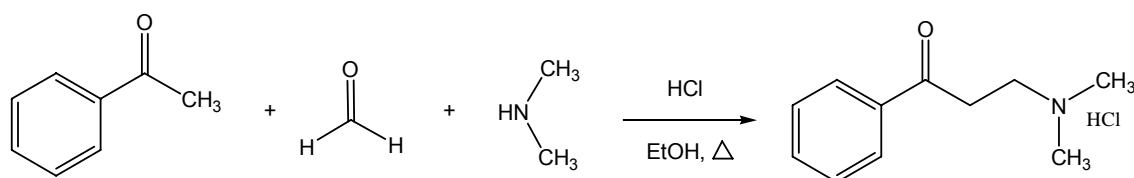
- 34-1. What are the concentrations in ppm of AR and BCG in your sample?
- 34-2. Note that separation is performed in the normal phase LC mode. Considering the structures of the dyes, which dye would you want to elute first for best results? Which eluent would you use for eluting the first-eluting dye? Explain.
- 34-3. Which dye would be eluted second? Which eluent would you use for eluting the second dye? Explain.

Problem 35: Synthesis of β -dimethylaminopropiophenone hydrochloride**Introduction**

Prozac is a famous antidepressant, also known as the “happy drug” as it can help alleviate depression. The active ingredient in Prozac is fluoxetine. Fluoxetine is prepared from β -dimethylaminopropiophenone in a four step sequence.



The target molecule can be obtained through a one-pot reaction involving three or more starting compounds, also known as a multicomponent reaction (MCR). Among MCRs classic name-reactions have developed into popular organic-chemical reactions in the pharmaceutical industry for the preparation of compound libraries of low molecular drug-like compounds. For example, the Mannich reaction is a “one pot” combination reaction of three synthetic fragments to make a single product. This multicomponent reaction can be applied to the synthesis of β -dimethylaminopropiophenone, as paraformaldehyde and dimethylamine hydrochloride are combined in the presence of acetophenone to produce directly β -dimethylaminopropiophenone.



Materials

acetophenone (R 22-36, S 26), concentrated HCl (R 23-34-37, S 26-45),
dimethylamine hydrochloride (R 22-36/37/38, S 26-36/37),
paraformaldehyde (R 20/22-37/38-40-41-43, S 26-36/37/39-45),
ethanol (R 11, S 7-16), ethyl ether (R 12-19-22-66-67, S 9-16-29-33),
hexane (R 11-38-48/20-51/53-62-65-67, S 9-16-29-33-36/37-61-62),
methanol (R 11-23/24/25-39/23/24/25, S 7-16-36/37-45),
ethyl acetate (R 11-36-66-67, S 16-26-33), NaHCO₃, acetone

KMnO₄ (R 8-22-50/53, S 60-61), ZnCl₂ (R 22-34-50/53, S 26-36/37/39-45-60-61)
FeCl₃ (R 22-38-41, S 26-39), AgNO₃ (R 34-50/53, S 26-45-60-61)
NaOH (R 35, S 26-37/39-45), NH₃ (R 34-50, S 26-36/37/39-45-61)
2,4-dinitrophenylhydrazine (R 1-11-22, S 35), conc. sulfuric acid (R 35, S 26-30-45)

Apparatus

25-mL round-bottomed flask, 50 mL Erlenmeyer flask, stirrer, temperature controller, heating mantle, sand, support stand, clamp, clamp holder, melting point apparatus, capillary tubes, magnetic bar, reflux condenser, hose, Büchner funnel, suction flask, glass rod, filter paper, 100 mL-beaker, TLC plate (silica gel 60 F₂₅₄, layer thickness: 250 μm, on glass support), micro-syringe, developing chamber with a lid, UV lamp

Procedure

Inside a fume hood, add 2 mL of acetophenone, 0.65 g of dimethylamine hydrochloride and 1.76 g of paraformaldehyde into a 25 mL round-bottomed flask. To the flask, add 4 mL of 95% ethanol followed by 40 μL of concentrated HCl. Add your magnetic bar and equip the flask with a reflux condenser. Reflux the mixture for 2 hours by placing the flask in a sand bath preheated to 120°C. Allow the reaction mixture to cool slightly (to 50~80°C) and transfer it to a small Erlenmeyer flask (pour, do not pipette or the material will freeze in the pipette). Add 16 mL of acetone and allow the flask to cool to room temperature. Mix thoroughly with a glass stirring rod. Cool the mixture in an ice-bath to complete the crystallization. Filter by suction using a Büchner funnel with a filter flask and wash the solids with 4 mL of acetone. (You can use 1 mL acetone to help transfer the last of the solid in the flask.) Let the product dry for at least 20 minutes on the funnel. Weigh the products and determine their melting point.

Extract a free amine into the organic solvent with aqueous NaHCO_3 solution for developing TLC. Dissolve about 0.1 g of the product with distilled water and then transfer the solution into a small separatory funnel. Add ethyl ether as an organic solvent. Neutralize the water layer with aqueous NaHCO_3 solution. Use a pH paper. Obtain the organic layer for TLC. Develop a TLC plate in ethyl acetate: hexane (2:1, v/v) or ethyl acetate: methanol (2:1, v/v).

Qualitative Tests

Perform the following tests with the product and report the observation.

1) The Baeyer Test (Potassium permanganate); ALKENES AND ALKYNES

(* This test is useful for indicating the presence of most olefinic or acetylenic functional groups.)

Dissolve 30 mg of the product in 2 mL of water. Add 0.1 M KMnO_4 aqueous solution dropwise, report the results.

2) Lucas test; ALCOHOLS

(* This test is useful for distinguishing among lower-molecular-weight primary, secondary, and tertiary alcohols.)

Prepare Lucas's reagent by dissolving 136 g of zinc chloride in 89 mL of conc. HCl with cooling in ice bath. Add 2 mL of Lucas's reagent to 30 mg of the product in a test tube. Note the time required to form the insoluble alkyl chloride, which appears as a layer or emulsion.

3) Ferric chloride test; PHENOLS

(* This test is useful for the recognition of phenols.)

Dissolve 30 mg of the product in 2 mL of water or a mixture of ethanol and water, and add up to 3 drops of the 2.5% aqueous ferric chloride solution. Most phenols produce red, blue, purple, or green coloration; enols give red, violet, or tan coloration.

4) Tollen's reagent (silver-Ammonia complex ion); ALDEHYDES

(* This test is useful for distinguishing aldehydes from ketones and other carbonyl compounds.)

To a clean test tube, add 2 mL of the 5% silver nitrate solution and 1 drop of the 10% sodium hydroxide solution. Add 2 M ammonium hydroxide solution drop by drop with good shaking until the dark precipitated silver oxide just dissolves. Add 1 drop of the liquid or 30 mg of the product to be tested, shake the tube to mix, and allow it to stand at room temperature for 20 minutes. If nothing happens, heat the tube in a beaker of water at 35 °C for five minutes.

5) 2,4-dinitrophenylhydrazine Test ; ALDEHYDES AND KETONES

(* This test is useful for identifying aldehydes and ketones.)

Prepare 2,4-dinitrophenylhydrazine reagent by dissolving 3 g of 2,4-dinitrophenylhydrazine in 15 mL of conc. sulfuric acid and adding this solution, with good stirring, to a mixture of 20 mL of water and 70 mL of 95% ethanol. Dissolve 100 mg of a solid product in 2 mL of 95% ethanol, and add this solution to 2 mL of the 2,4-dinitrophenylhydrazine reagent. Shake the mixture vigorously; if a precipitate does not form immediately, let the solution stand for 15 min.

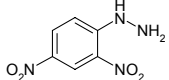
Results

- **Reagents & Products** (Show calculations)

Reagents (compound names)	M.W. (g/mol)	grams (or mL) used	mmole used	equivalent	physical properties
Product: [M.W. = _____ g/mol] Weight: _____ g Yield: _____ %					

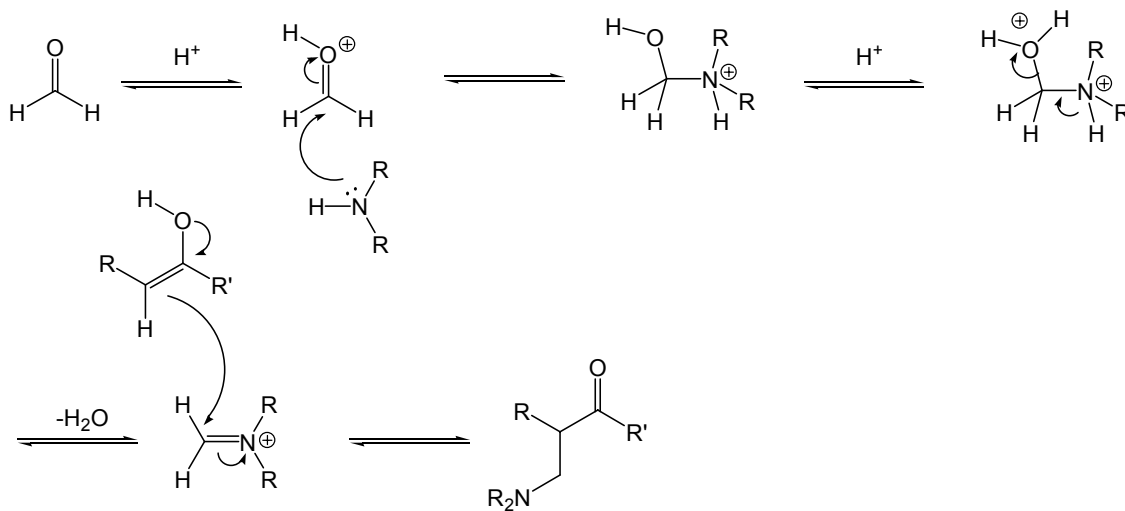
- **Melting Point:** _____ °C (Observed)
 _____ °C (Reported in the literature)

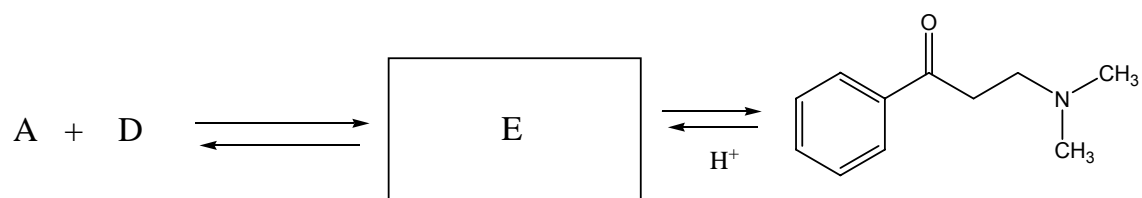
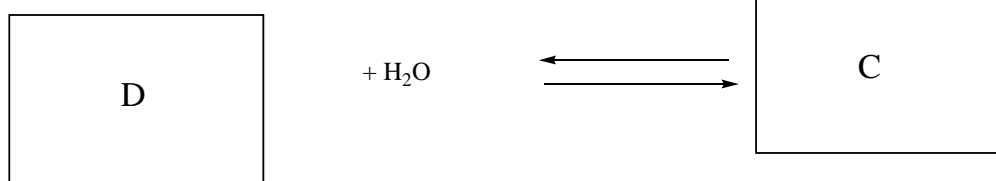
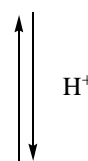
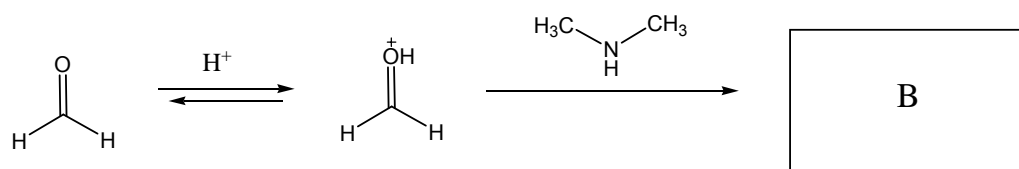
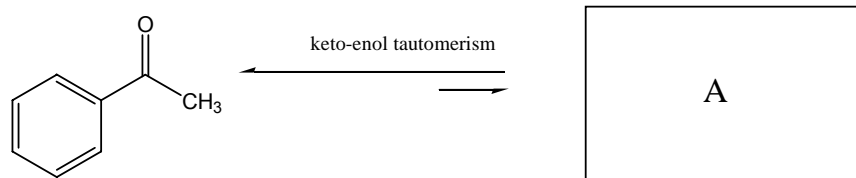
- **R_f values** (Record the R_f values and the size and shape of each spots):
 (Show calculations)

Test Reagent	Test result	
	Observed	expected
1) KMnO_4 (Baeyer's test)		
2) HCl , ZnCl_2 (Lucas's test)		
3) FeCl_3 (Ferric chloride solution)		
4) $\text{AgNO}_3/\text{NaOH}/\text{NH}_3$ (Tollen's reagent)		
5) 2,4-dinitrophenylhydrazine 		

Question

The general mechanism for a Mannich reaction is given below for an illustrative example. Account for the overall reaction in a stepwise fashion. Try depicting the mechanism (i.e., electron "pushing") for the reaction carried out in the test.





Problem 36: Enzyme kinetics by catalase

Introduction

Catalysis is a central concept in chemistry and biology, essential in life and industrial processes. Enzymes are catalysts for biochemical reactions. In this experiment, the Michaelis-Menten kinetics of hydrogen peroxide decomposition ($2\text{H}_2\text{O}_2 \rightarrow 2\text{H}_2\text{O} + \text{O}_2$) by catalase in potato juice will be investigated. Catalase is well known for its extremely high reaction rate. One catalase molecule can decompose 40 million hydrogen peroxide molecules in one second. Such a high rate is needed to scavenge reactive oxygen species and protect cellular components in the oxidative environment. The figure below shows a 3-dimensional structure of catalase from *E. coli* determined by X-ray crystallography.



The number of moles of the evolved oxygen gas can be determined from its volume measured using a buret or from the pressure change in an enclosed reaction vessel. Reaction rate can be expressed as the number of moles of oxygen per unit time. An enzyme (E) combines with a substrate (S) and produces an enzyme-substrate complex (ES) with a rate constant k_1 . ES could be decomposed back to E and S with a rate constant k_2 or concerted to a product (P) with a rate constant k_3 . The steady state condition for ES can be determined by equating the following rate equations.

$$d[\text{ES}]/dt = k_1([\text{E}]_{\text{tot}} - [\text{ES}])[S], \quad \text{where } [\text{E}]_{\text{tot}} = [\text{E}] + [\text{ES}]$$

$$-d[\text{ES}]/dt = k_2[\text{ES}] + k_3[\text{ES}]$$

$$[S]([\text{E}]_{\text{tot}} - [\text{ES}])/[\text{ES}] = (k_2 + k_3)/k_1$$

$(k_2 + k_3)/k_1$ is defined as the Michaelis-Menten constant, K_M .

Solving the last equation for [ES] one gives $[\text{ES}] = [\text{E}][S]/(K_M + [S])$.

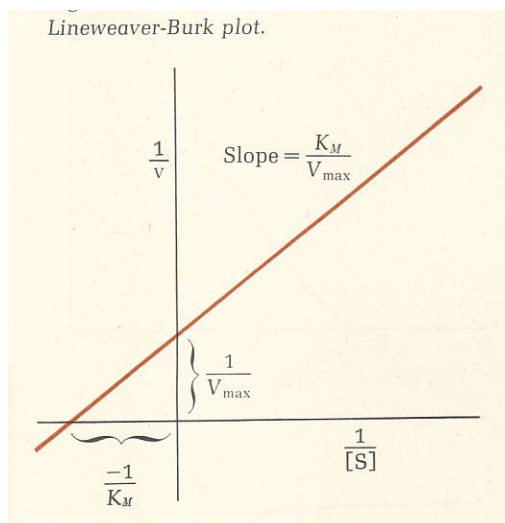
Let v be the initial rate for the evolution of oxygen: $v = k_3[\text{ES}]$

If the enzyme is present only as ES, v will approach a maximum value, $V_{\max} = k_3[E]_{\text{tot}}$
 From these relations, one gets the Michaelis-Menten equation.

$$v = V_{\max}[S]/(K_M + [S])$$

Obviously, K_M is the value of $[S]$ when $v = V_{\max}/2$. Taking the inverse of the Michaelis-Menten equation one gets the celebrated Lineweaver-Burk equation (see Figure), which is one of the most frequently used equations in chemistry.

$$1/v = (K_M/V_{\max})(1/[S]) + 1/V_{\max}$$

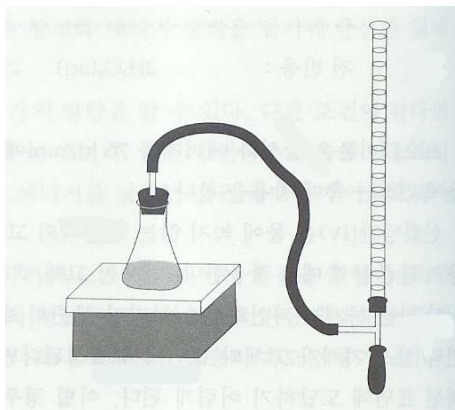


Materials

hydrogen peroxide (R 34, S 28-36/39-45), fresh potato, catalase

Apparatus

blender, ice bath, boiling water bath



Procedure

1. Prepare 0.5, 1, 2, 3, 4, 6% solution of hydrogen peroxide by diluting the given 30% hydrogen peroxide with deionized water.
2. Make potato juice by blending pieces of potato with approximately equal weight of water. Squeeze the juice with cheesecloth. Keep the juice in an ice bath.
3. Add 2 mL of the juice to 30 mL of the diluted hydrogen peroxide solutions and shake. As a control, use 30 mL of deionized water.
4. Measure the volume of oxygen produced using a set-up shown below. Make a soap bubble with the rubber bulb and measure time needed to produce a certain volume (20 mL for example) of oxygen gas at room temperature.
5. Repeat with 6% hydrogen peroxide using the juice heated in boiling water bath for 10 min to denature the enzyme.
6. If pure catalase is available, repeat the whole experiment using catalase at a known concentration (1 micromolar, for example).

Questions

- 36-1. Calculate the molar concentration of hydrogen peroxide, [S].
- 36-2. Calculate the number of moles of oxygen produced in a given time for each [S].
- 36-3. Calculate v for each [S].
- 36-4. Plot v against [S] and see if it approaches a maximum value.
- 36-5. Develop a Lineweaver-Burk plot to determine K_M and V_{max} .
- 36-6. If $[E]_{tot}$ is known, calculate k_3 from $V_{max} = k_3 [E]_{tot}$. What is the turn-over number of catalase per second?