

**Chemistry for Life,
Chemistry for better Life**



Theoretical Test



**2006. 7. 7
Gyeongsan, Korea**

General Directions

- Write your name and code number on each page of the answer sheet.
- You have 5 hours to finish the task. Failure to stop after the STOP command may result in zero points for the task.
- Write answers and calculations within the designated box.
- Use only the pen and the calculator provided.
- There are 23 pages of Problems and 19 pages of Answer Sheet.
- An English-language version is available.
- You may go to the restroom with permission.
- After finishing the examination, place all sheets including Problems and Answer Sheet in the envelope and seal.
- Remain seated until instructed to leave the room.

Periodic Table of Elements

with atomic masses

1 H 1.01	<i>Periodic Table of Elements</i> <i>with atomic masses</i>																2 He 4.00
3 Li 6.94	4 Be 9.01											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
11 Na 22.99	12 Mg 24.31											13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.07	17 Cl 35.45	18 Ar 39.95
19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.88	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.39	31 Ga 69.72	32 Ge 72.61	33 As 74.92	34 Se 78.96	35 Br 79.90	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.94	43 Tc 98.91	44 Ru 101.07	45 Rh 102.91	46 Pd 106.42	47 Ag 107.87	48 Cd 112.41	49 In 114.82	50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 126.90	54 Xe 131.29
55 Cs 132.91	56 Ba 137.3	57-71	72 Hf 178.49	73 Ta 180.95	74 W 183.84	75 Re 186.21	76 Os 190.23	77 Ir 192.22	78 Pt 195.08	79 Au 196.97	80 Hg 200.59	81 Tl 204.38	82 Pb 207.19	83 Bi 208.98	84 Po 208.98	85 At 209.99	86 Rn 222.02
87 Fr 223	88 Ra 226	89-103	104 Rf 261	105 Db 262	106 Sg 263	107 Bh 264	108 Hs 265	109 Mt 268									

57 La 138.91	58 Ce 140.12	59 Pr 140.91	60 Nd 144.24	61 Pm 144.92	62 Sm 150.36	63 Eu 151.96	64 Gd 157.25	65 Tb 158.93	66 Dy 162.50	67 Ho 164.93	68 Er 167.26	69 Tm 168.93	70 Yb 173.04	71 Lu 174.97
89 Ac 227	90 Th 232	91 Pa 231	92 U 238	93 Np 237	94 Pu 244	95 Am 243	96 Cm 247	97 Bk 247	98 Cf 251	99 Es 252	100 Fm 257	101 Md 258	102 No 259	103 Lr 262

Constants and useful formulas

Gas constant $R = 8.314 \text{ J K}^{-1} \text{ mol}^{-1}$

Faraday constant $F = 96485 \text{ C mol}^{-1}$

Use as standard pressure: $p = 1.013 \cdot 10^5 \text{ Pa}$

Use as standard temperature: $T = 25^\circ\text{C} = 298.15 \text{ K}$

Avogadro's number $N_A = 6.022 \cdot 10^{23} \text{ mol}^{-1}$

Planck constant $h = 6.626 \cdot 10^{-34} \text{ J s}$

Speed of light $c = 3.00 \cdot 10^8 \text{ m s}^{-1}$

$\Delta G = \Delta H - T\Delta S$ $\Delta G = -nFE$

$\Delta G^0 = -RT \cdot \ln K$ $\Delta G = \Delta G^0 + RT \cdot \ln Q$ with $Q = \frac{\text{product of } c(\text{products})}{\text{product of } c(\text{reactands})}$

$\Delta H(T_f) = \Delta H^0 + (T_f - 298.15 \text{ K}) \cdot C_p$ ($C_p = \text{constant}$)

Arrhenius equation $k = A \cdot e^{-\frac{E_a}{RT}}$

Ideal gas law $pV = nRT$

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

Beer- Lambert Law $A = \log \frac{P_0}{P} = \epsilon c d$

$V(\text{cylinder}) = \pi r^2 h$

$A(\text{sphere}) = 4\pi r^2$

$V(\text{sphere}) = \frac{4}{3} \pi r^3$

$1 \text{ J} = 1 \text{ N m}$

$1 \text{ N} = 1 \text{ kg m s}^{-2}$

$1 \text{ Pa} = 1 \text{ N m}^{-2}$

$1 \text{ W} = 1 \text{ A V} = 1 \text{ J s}^{-1}$

$1 \text{ C} = 1 \text{ A s}$

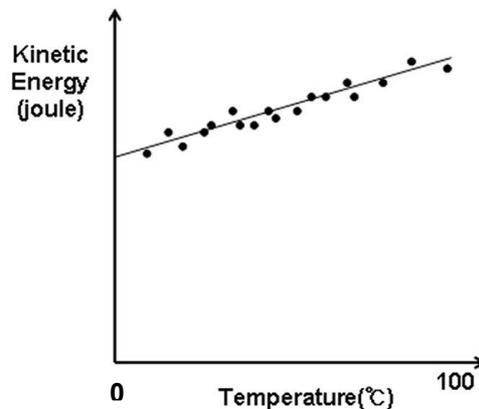
**1. Avogadro's number
pts)**

(5

Spherical water droplets are dispersed in argon gas. At 27°C, each droplet is 1.0 micrometer in diameter and undergoes collisions with argon. Assume that inter-droplet collisions do not occur. The root-mean-square speed of these droplets was determined to be 0.50 cm/s at 27°C. The density of a water droplet is 1.0 g/cm³.

1-1. Calculate the average kinetic energy ($mv^2/2$) of this droplet at 27°C. The volume of a sphere is given by $(4/3) \pi r^3$ where r is the radius.

If the temperature is changed, then droplet size and speed of the droplet will also change. The average kinetic energy of a droplet between 0°C and 100°C as a function of temperature is found to be linear. Assume that it remains linear below 0°C.



At thermal equilibrium, the average kinetic energy is the same irrespective of particle masses (equipartition theorem).

The specific heat capacity, at constant volume, of argon (atomic weight, 40) gas is 0.31 J g⁻¹ K⁻¹.

1-2. Calculate Avogadro's number without using the ideal gas law, the gas constant, Boltzmann's constant).

2. Detection of Hydrogen

(5 pts)

Hydrogen is prevalent in the universe. Life in the universe is ultimately based on hydrogen.

2-1. There are about 10^{23} stars in the universe. Assume that they are like our sun (radius, 700,000 km; density, 1.4 g/cm^3 ; $3/4$ hydrogen and $1/4$ helium by mass). Estimate the number of stellar protons in the universe to one significant figure.

In the 1920s, Cecilia Payne discovered, by spectral analysis of starlight, that hydrogen is the most abundant element in most stars.

2-2. The electronic energy of a hydrogen atom is given by $-C/n^2$ relative to zero energy at infinite separation between the electron and the proton (n is the principle quantum number, and C is a constant). For detection of the $n=2 \rightarrow n=3$ transition (656.3 nm in the Balmer series), the electron in the ground state of the hydrogen atom needs to be excited first to the $n=2$ state. Calculate the wavelength (in nm) of the absorption line in the starlight corresponding to the $n=1 \rightarrow n=2$ transition.

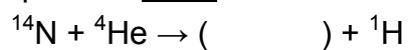
2-3. According to Wien's law, the wavelength (λ) corresponding to the maximum light intensity emitted from a blackbody at temperature T is given by $\lambda T = 2.9 \times 10^{-3} \text{ m K}$. Calculate the surface temperature of a star whose blackbody radiation has a peak intensity corresponding to the $n = 1 \rightarrow n = 2$ excitation of hydrogen.

The ground state of hydrogen is split into two hyperfine levels due to the interaction between the magnetic moment of the proton and that of the electron. In 1951, Purcell discovered a spectral line at 1420 MHz due to the hyperfine transition of hydrogen in interstellar space.

2-4. Hydrogen in interstellar space cannot be excited electronically by starlight. However, the cosmic background radiation, equivalent to 2.7K, can cause the hyperfine transition. Calculate the temperature of a

blackbody whose peak intensity corresponds to the 1420 MHz transition.

2-5. Wien generated hydrogen ions by discharge of hydrogen gas at a very low pressure and determined the e/m (charge/mass) value, which turned out to be the highest among different gases tested. In 1919, Rutherford bombarded nitrogen with alpha-particles and observed emission of a positively charged particle which turned out to be the hydrogen ion observed by Wien. Rutherford named this particle the "proton". Fill in the blank in the answer sheet.



3. Interstellar Chemistry

(5 pts)

Early interstellar chemistry is thought to have been a prelude to life on Earth. Molecules can be formed in space via heterogeneous reactions at the surface of dust particles, often called the interstellar ice grains (IIGs). Imagine the reaction between H and C atoms on the IIG surface that forms CH. The CH product can either desorb from the surface or further react, through surface migration, with adsorbed H atoms to form CH₂, CH₃, etc.

Depending on how energetically a molecule “jumps” from its anchored site, it either leaves the surface permanently (desorption) or returns to a new position at the surface (migration). The rates of desorption and migratory jump follow the Arrhenius formula, $k = A \exp(-E/RT)$, where k is the rate constant for desorption or migratory jump, A the jumping frequency, and E the activation energy for the respective event.

3-1. Desorption of CH from the IIG surface follows first-order kinetics.

Calculate the average residence time of CH on the surface at 20 K.

Assume that $A = 1 \times 10^{12} \text{ s}^{-1}$ and $E_{\text{des}} = 12 \text{ kJ mol}^{-1}$.

3-2. Consider the shortest time it would take for one CH unit to move from its initial position to the opposite side of an IIG by successive migratory jumps. Assume that the activation energy for migration (E_{mig}) is 6 kJ mol^{-1} , and the IIG is a sphere with a $0.1 \text{ }\mu\text{m}$ radius. Each migratory jump laterally advances the molecule by 0.3 nm . Show work and choose your answer from (a)-(e) below.

(a) $t \leq 1 \text{ day}$ (b) $10 \text{ day} \leq t \leq 10^2 \text{ yr}$ (c) $10^3 \text{ yr} \leq t \leq 10^6 \text{ yr}$

(d) $10^7 \text{ yr} \leq t \leq 10^{10} \text{ yr}$ (e) $t \geq 10^{11} \text{ yr}$

3-3. Consider the reaction of CO with H₂ to form H₂CO. The activation energy on a metal catalyst is 20 kJ mol^{-1} , which produces formaldehyde

at a rate of 1 molecule/s per site at 300 K. Estimate the rate of formaldehyde formation per site if the reaction takes place at 20 K.

3-4. Which is a set of all true statements? Circle one.

(a) Most CH species desorb from the IIG surface before encountering other reactants by surface migration.

(b) IIGs can assist transformation of simple molecules to more complex ones in interstellar space.

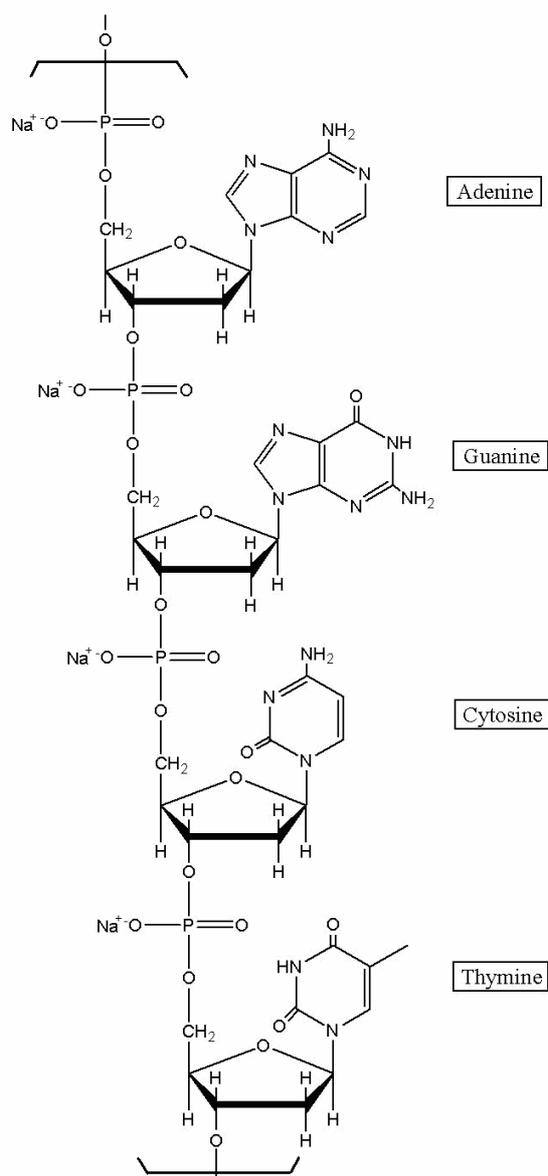
(c) For a reaction on the IIG to occur at an appreciable speed during the age of the Universe (1×10^{10} yr), the reaction energy barrier must be absent or negligible.

(a) (b) (c) (a, b) (a, c) (b, c) (a, b, c)

4. The Chemistry of DNA
(pts)

(5

4-1. In 1944 Oswald Avery isolated a genetic material and showed, by elemental analysis, that it was a sodium salt of deoxyribonucleic acid. A segment of DNA with formula mass of 1323.72 is shown.



Assuming that equimolar amounts of the four bases are present in DNA, write the number of H atoms per P atom. Calculate, to 3 significant

figures, the theoretical weight percentage of H expected upon elemental analysis of DNA.

4-2. Chargaff extracted the separated bases and determined their concentrations by measuring UV absorbance. The Beer-Lambert law was used to obtain the molar concentration. Chargaff discovered the following molar ratio for bases in DNA:

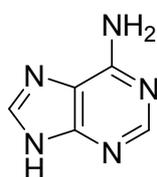
adenine to guanine = 1.43 thymine to cytosine = 1.43
adenine to thymine = 1.02 guanine to cytosine = 1.02

Chargaff's discovery suggested that the bases might exist as pairs in DNA. Watson and Crick mentioned in their celebrated 1953 paper in *Nature*: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

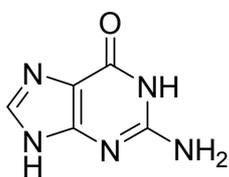
Draw structures of the specific pairing found in DNA. Indicate hydrogen bonds. Omit the sugar-phosphate backbone.

4-3. Mutation can occur through base pairings different from the above. Draw structures of any three alternative base pairs.

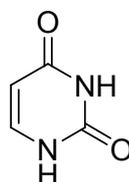
4-4. The plausibility of the formation of purine and pyrimidine bases in the prebiotic atmosphere of the Earth from HCN, NH₃, and H₂O has been demonstrated in the laboratory. Write the minimum number of HCN and H₂O molecules required for formation of the following compounds.



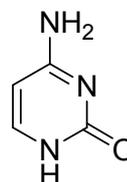
adenine



guanine



Uracil



cytosine

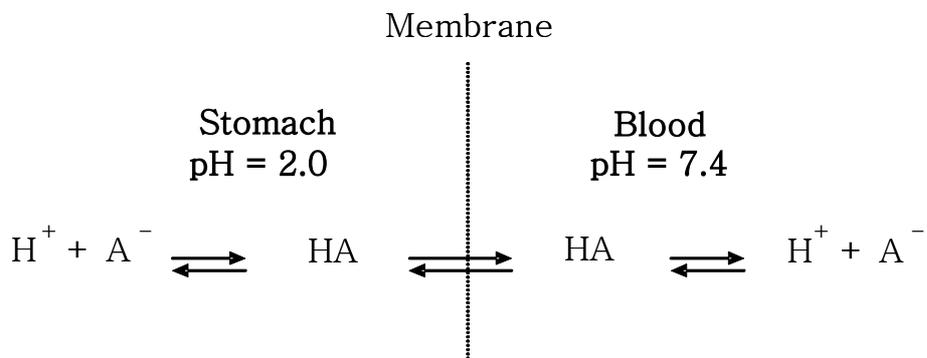
5. Acid-Base Chemistry

(5 pts)

5-1. Calculate $[H^+]$, $[OH^-]$, $[HSO_4^-]$, and $[SO_4^{2-}]$ in a 1.0×10^{-7} M solution of sulfuric acid ($K_w = 1.0 \times 10^{-14}$, $K_2 = 1.2 \times 10^{-2}$ at 25°C). In your work you may use mass- and charge-balance equations. Answer with two significant figures.

5-2. Calculate the volume of 0.80 M NaOH solution that should be added to a 250 mL aqueous solution containing 3.48 mL of concentrated phosphoric acid in order to prepare a pH 7.4 buffer. Answer with three significant figures. ($H_3PO_4(aq)$, purity = 85 % wt/wt, density = 1.69 g/mL, FW = 98.00) ($pK_1 = 2.15$, $pK_2 = 7.20$, $pK_3 = 12.44$).

5-3. The efficacy of a drug is greatly dependent on its ability to be absorbed into the blood stream. Acid-base chemistry plays an important role in drug absorption.



Assume that the ionic form (A^-) of a weakly acidic drug does not penetrate the membrane, whereas the neutral form (HA) freely crosses the membrane. Also assume that equilibrium is established so that the concentration of HA is the same on both sides. Calculate the ratio of the total concentration ($[HA] + [A^-]$) of aspirin (acetylsalicylic acid, $pK = 3.52$) in the blood to that in the stomach.

6. Electrochemistry

(5 pts)

Water is a very stable molecule, abundant on earth and essential for life. As such, water was long thought to be a chemical element. However, soon after the invention of a voltaic cell in 1800, Nicholson and Carlyle decomposed water into hydrogen and oxygen by electrolysis.

- 6-1.** Water can be thought of as hydrogen oxidized by oxygen. Thus, hydrogen can be recovered by reduction of water, using an aqueous solution of sodium sulfate, at a platinum electrode connected to the negative terminal of a battery. The solution near the electrode becomes basic. Write a balanced half-reaction for the reduction of water.
- 6-2.** Water can also be thought of as oxygen reduced by hydrogen. Thus, oxygen can be recovered by oxidation of water at the Pt electrode connected to the positive terminal. Write a balanced half-reaction for the oxidation of water.
- 6-3.** When copper is used at both electrodes, gas is generated only at one electrode during the initial stage of electrolysis. Write the half-reaction at the electrode that does not generate gas.

Another species in solution that can be reduced is sodium ion. The reduction of sodium ion to metallic sodium does not occur in aqueous solution, because water is reduced first. However, as Humphrey Davy discovered in 1807, sodium can be made by electrolysis of fused sodium chloride.

- 6-4.** Based on these observations, connect the half-reactions with the standard reduction potential (in volts).

Reduction of copper ion (Cu^{2+})	· ----- ·	+0.340
Reduction of oxygen	· ·	-2.710
Reduction of water	· ·	-0.830
Reduction of sodium ion (Na^+)	· ·	0.000
Reduction of hydrogen ion	· ·	+1.230

The electrode potential is affected by other reactions taking place around the electrode. The potential of the Cu^{2+}/Cu electrode in a 0.100 M Cu^{2+} solution changes as $\text{Cu}(\text{OH})_2$ precipitates. Answer with 3 significant figures for the following problems. The temperature is 25°C . Note that $K_w = 1.00 \times 10^{-14}$ at 25°C .

6-5. Precipitation of $\text{Cu}(\text{OH})_2$ begins at $\text{pH} = 4.84$. Determine the solubility product of $\text{Cu}(\text{OH})_2$.

6-6. Calculate the standard reduction potential for $\text{Cu}(\text{OH})_2(\text{s}) + 2\text{e}^- \rightarrow \text{Cu}(\text{s}) + 2\text{OH}^-$.

6-7. Calculate the electrode potential at $\text{pH} = 1.00$.

Lithium cobalt oxide and specialty carbon are active ingredients for the positive and negative electrodes, respectively, of a rechargeable lithium battery. During the charge/recharge cycles, the following reversible half-reactions occur.



The total amount of energy a battery can store is rated in mAh. A battery rated at 1500 mAh can power a device drawing 100 milliamps for 15 hours.

6-8. Graphite has lithium intercalation sites between its layers. Assuming a maximum 6:1 carbon-to-lithium intercalation stoichiometry, calculate the theoretical charge capacity of 1.00 gram of graphite to intercalate lithium. Answer in mAh/g with 3 significant figures.

7. Hydrogen Economy

(4 pts)

Hydrogen is more energy-dense than carbon, by mass. Thus, historically there has been a move toward fuel with higher hydrogen content: coal → oil → natural gas → hydrogen. Cost-effective production and safe storage of hydrogen are two major hurdles to the successful inauguration of a hydrogen economy.

7-1. Consider hydrogen in a cylinder of 80 MPa at 25 °C. Using the ideal gas law, estimate the density of hydrogen in the cylinder in kg/m³.

7-2. Calculate the ratio between heat generated when hydrogen is burned and heat generated when the same weight of carbon is burned. The difference comes to a large extent from the fact that the most abundant isotope of hydrogen has no neutron and hydrogen has no inner electron shell. $\Delta H_f^\circ [\text{H}_2\text{O}(\text{l})] = -286 \text{ kJ/mol}$, $\Delta H_f^\circ [\text{CO}_2(\text{g})] = -394 \text{ kJ/mol}$.

7-3. Calculate the theoretical maximum work produced by the combustion of 1 kg hydrogen (a) from the electric motor using hydrogen fuel cell and (b) from the heat engine working between 25 °C and 300 °C. The efficiency (work done/heat absorbed) of an ideal heat engine working between T_{cold} and T_{hot} is given by $[1 - T_{\text{cold}}/T_{\text{hot}}]$.

$$S_{298}^\circ[\text{H}_2(\text{g})] = 131 \text{ J/(K mol)}$$

$$S_{298}^\circ[\text{O}_2(\text{g})] = 205 \text{ J/(K mol)}$$

$$S_{298}^\circ[\text{H}_2\text{O}(\text{l})] = 70 \text{ J/(K mol)}$$

If the fuel cell is working at 1 W and the standard potential difference, how long will the electric motor run at what current?

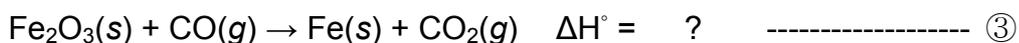
8. Chemistry of Iron Oxides

(5

pts)

The nucleus of iron is the most stable among all elements and, therefore, iron accumulates at the core of massive red giant stars where nucleosynthesis of many elements essential for life (such as C, N, O, P, S, etc.) takes place. As a result, among heavy elements iron is quite abundant in the universe. Iron is also abundant on Earth.

8-1. Development of a technology for reducing iron oxide to iron was a key step in human civilization. Key reactions taking place in the blast furnace are summarized below.



8-1-1. Indicate the reducing agent in each reaction.

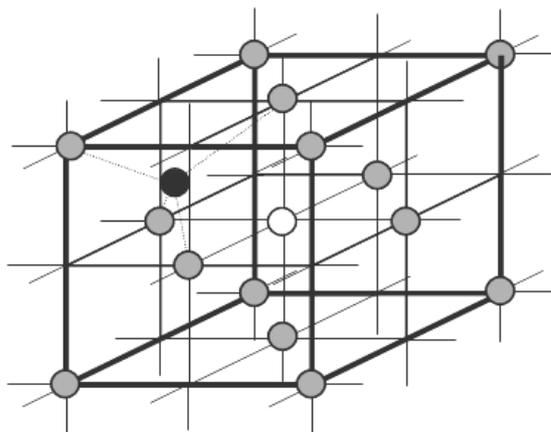
8-1-2. Balance reaction $\textcircled{3}$ and calculate the equilibrium constant of reaction $\textcircled{3}$ at 1200 °C. ($\Delta H_f^\circ(\text{Fe}_2\text{O}_3(s)) = -824.2 \text{ kJ/mol}$, $S^\circ(\text{J/mol/K})$: $\text{Fe}(s) = 27.28$, $\text{Fe}_2\text{O}_3(s) = 87.40$, $\text{C}(s) = 5.74$, $\text{CO}(g) = 197.674$, $\text{CO}_2(g) = 213.74$)

8-2. In the manufacture of celadon pottery, Fe_2O_3 is partially reduced in a charcoal kiln to mixed oxides of Fe_3O_4 and FeO . The amount of the different oxides seems to be related to the “mystic” color of celadon ceramics.



Fe_3O_4 (magnetite) itself is a mixed oxide containing Fe^{2+} and Fe^{3+} ions and belongs to a group of compounds with a general formula of AB_2O_4 . The oxide ions form a face-centered cubic array. The figure shows the array of oxygens (gray circles) and representative sites for divalent A and trivalent B cations. The

dark circle represents a tetrahedral site and the white circle an octahedral site.



8-2-1. How many available octahedral sites for iron ions are there in one AB_2O_4 unit? Certain sites are shared by neighboring units.

AB_2O_4 can adopt a normal- or an inverse-spinel structure. In normal-spinel structure, two B ions occupy two of the octahedral sites and one A occupies one of the tetrahedral sites. In an inverse-spinel structure, one of the two B ions occupies a tetrahedral site. The other B ion and the one A ion occupy octahedral sites.

8-2-2. What percentage of available tetrahedral sites is occupied by either Fe^{2+} or Fe^{3+} ion in Fe_3O_4 ?

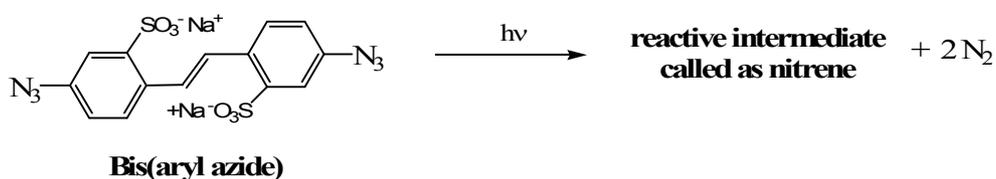
8-2-3 Fe_3O_4 has an inverse-spinel structure. Draw the crystal field splitting pattern of Fe^{2+} and fill out the electrons. The electron pairing energy is greater than the octahedral field splitting.

9. Photolithographic process

(5 pts)

Photolithography is a process used in semiconductor device fabrication to transfer a pattern from a photomask to the surface of a substrate. In a typical photolithography process, light is projected, through a mask that defines a particular circuitry, onto a silicon wafer coated with a thin layer of photoresist.

- 9-1. The earliest photoresists were based on the photochemistry that generates a reactive intermediates from bis(aryl azide). Patterning becomes possible through the cross-linking reaction of the nitrenes generated from the azides.

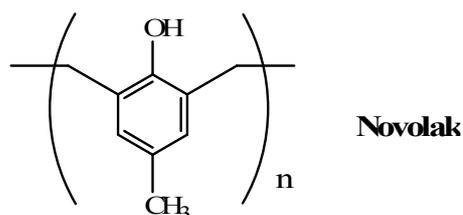


- 9-1-1. Draw two possible Lewis structures of $\text{CH}_3\text{-N}_3$, the simplest compound having the same active functional group of bis(aryl azide). Assign formal charges.

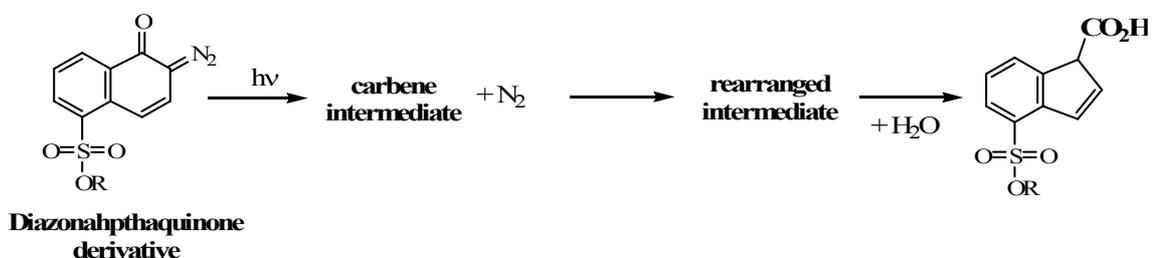
- 9-1-2. Draw the Lewis structure of nitrene expected from $\text{CH}_3\text{-N}_3$.

- 9-1-3. Draw the structures for two possible products, when this nitrene from $\text{CH}_3\text{-N}_3$ reacts with ethylene gas (CH_2CH_2).

- 9-2. Photoresists consisting of Novolak polymers, utilizes acid to change their solubility. The acid component can be produced photochemically from diazonaphthaquinone. In fact, "Novolaks" have been the representative "positive" photoresists of the modern microelectronic revolution.



When irradiated, diazonaphthaquinone undergoes photochemical decomposition followed by rearrangement eventually producing a carboxylic acid.

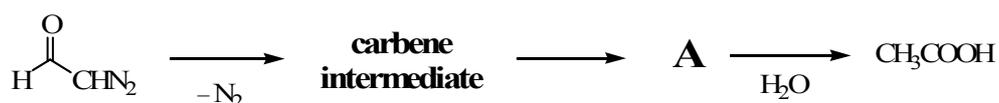


9-2-1. Draw three Lewis structures of diazoacetaldehyde (see below), the simplest compound having the same active functional group of diazonaphthaquinone. Indicate formal charges.

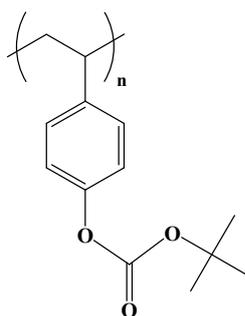


diazoacetaldehyde

9-2-2. Draw a Lewis structure of the rearranged intermediate, A (see below), generated from diazoacetaldehyde after losing N_2 . A satisfies Lewis' octet rule and reacts with water to form acetic acid, $\text{CH}_3\text{CO}_2\text{H}$.

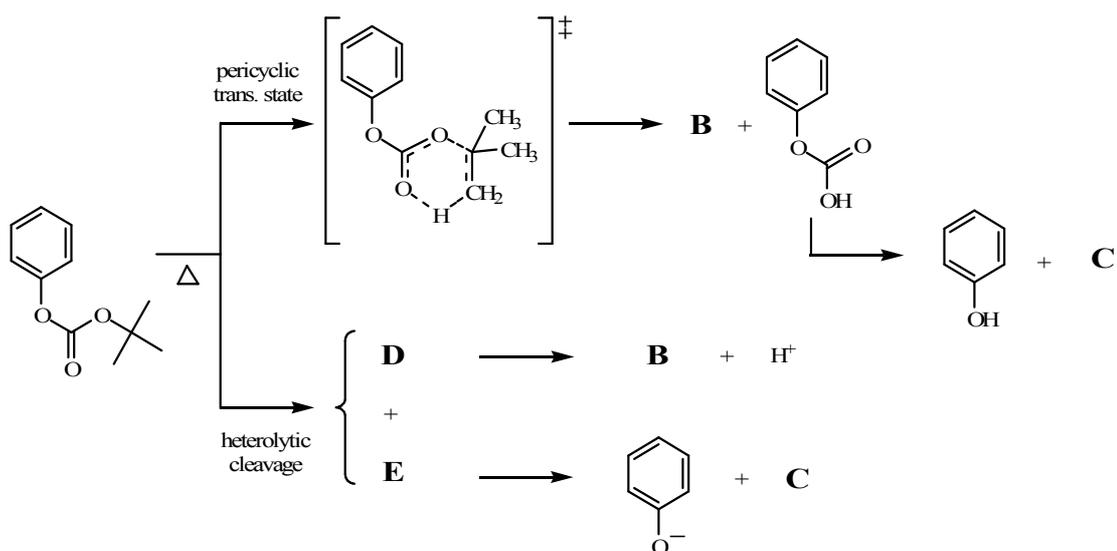


9-3. Advanced photoresists were invented in 1982 based on chemical amplification. The most popular chemical amplification for positive-tone involves the acid catalyzed deprotection of poly(*p*-hydroxystyrene) resin protected by various acid-sensitive protecting groups such as *t*-butyloxycarbonyl (*t*-BOC).

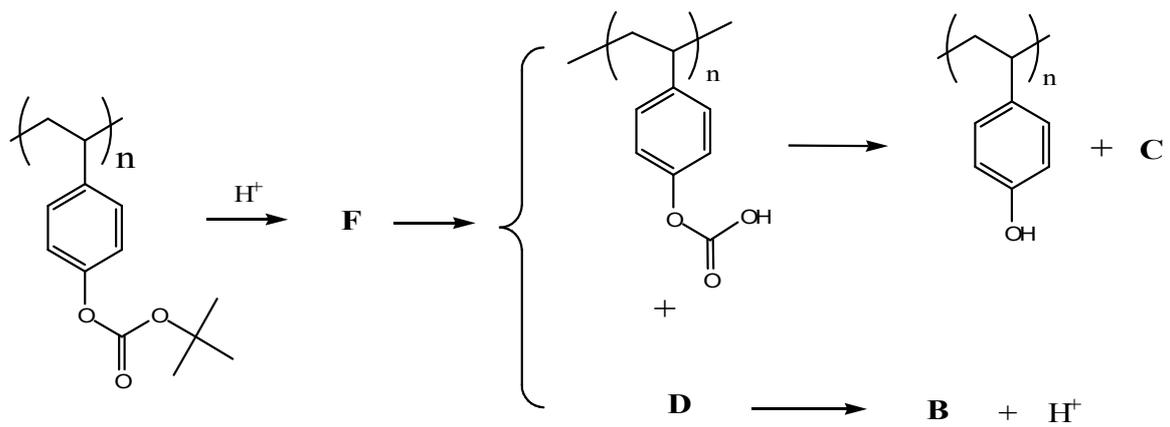


The thermal decomposition of carbonate ester itself normally occurs well above 150°C .

9-3-1. Two plausible mechanisms have been suggested for this decomposition reaction having relatively high activation energy. Draw expected intermediates and products from this reaction.

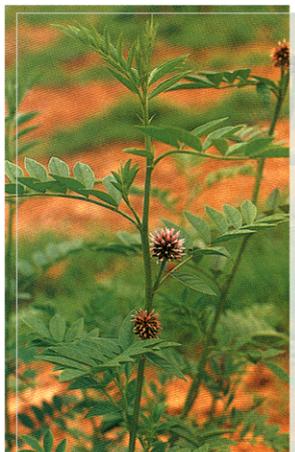


9-3-2. In the presence of a trace amount of acid, the reaction temperature can be reduced to below 100°C . Draw expected intermediate **F** from the following chemical amplification process based on using *t*-BOC.



10. Natural Products – Structural Analysis

(9 pts)



Licorice (*Glycyrrhiza. Uralensis*)



Licorice Root

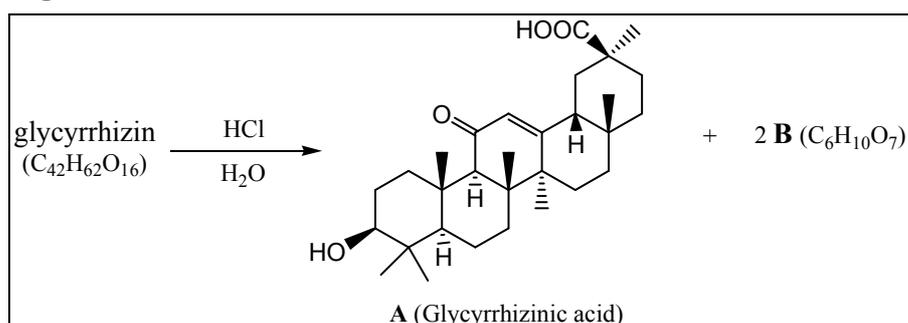
The flavor extracted from the licorice root is 50 – 150 times sweeter than table sugar.

The most important and abundant compound responsible for the sweetness and medicinal effects of licorice is *glycyrrhizin* ($C_{42}H_{62}O_{16}$).

Glycyrrhizin requires three equivalents of NaOH to effect neutralization.

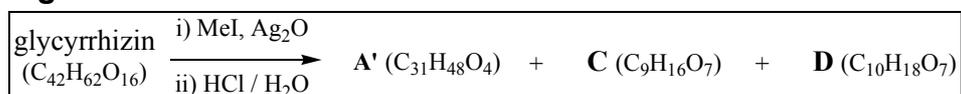
When *glycyrrhizin* was subjected to acid hydrolysis, *Glycyrrhizinic acid* (**A**) ($C_{30}H_{46}O_4$) and **B** ($C_6H_{10}O_7$) were obtained in a 1:2 molar ratio (figure 1).

Figure 1.



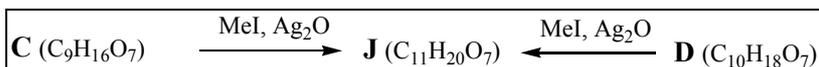
When *glycyrrhizin* was methylated with methyl iodide (MeI) at every possible site before hydrolysis, hydrolysis produced **A'** (methyl glycyrrhizinate), **C** and **D** (figure 2). B, C and D exist as mixtures of anomers.

Figure 2.



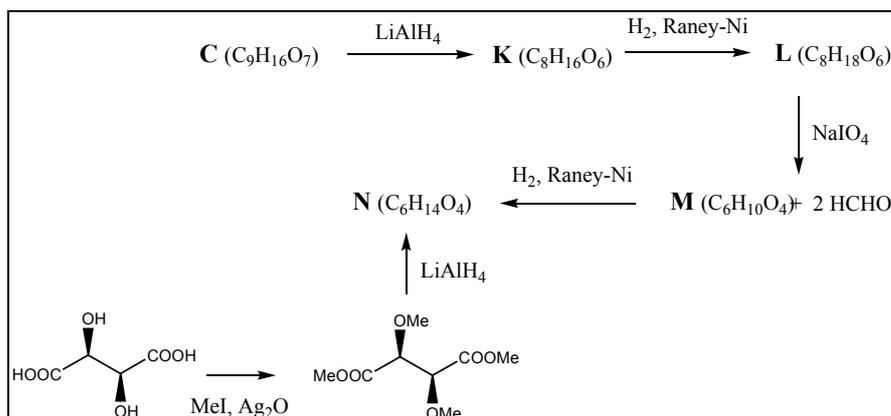
Methylation of **C** and **D** with MeI produced the same isomeric mixture of compounds, **J** (figure 3.)

Figure 3.



C was reduced with LiAlH₄ to give **K**, and **L** was produced by the reduction of **K**. Oxidative cleavage of vicinal diol of **L** with NaIO₄ produced **M** and two equivalents of formaldehyde. Reduction of **M** produced **N**. The structure and stereochemistry of **N** was confirmed by the synthesis of **N** from D-(-)-tartaric acid through methylation followed by reduction (figure 4). A ¹H-NMR spectrum of **L** showed two distinct peaks for methyl groups. (There is no symmetry in L)

Figure 4.



10-1. Complete structures for **L**, **M**, and **N** in the answer sheet.

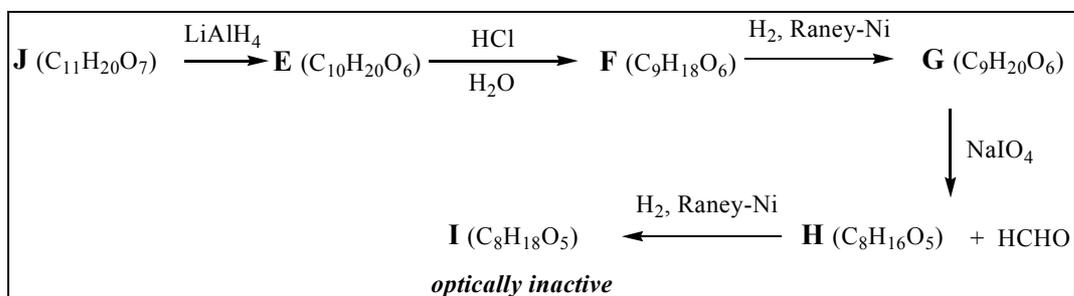
10-2. How many structures for **C** are possible? **Complete** possible structures for **C**.

To determine the correct structure of **C**, following set of reactions were performed.

J was reduced to **E**, and acid hydrolysis of **E** produced **F**. Reduction of **F** generated **G**, and **G** was oxidized with NaIO₄ to **H** with formation of one equivalent of formaldehyde. **I** was obtained from **H** through reduction. Among all

compounds from **A** to **I**, only **I** was optically inactive (figure 5).

Figure 5



10-3. Complete structures for **G** and **I**.

10-4. Which one is the correct structure for **C** among ones you have drawn in **10-2**?

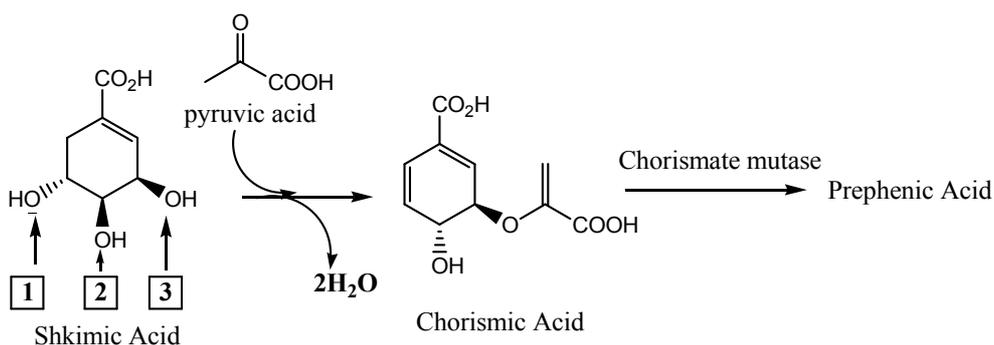
10-5. Complete structures for **B**, **D**, and **J**.

10-6. Complete the structure for Glycyrrhizin.

11. Enzyme Reaction

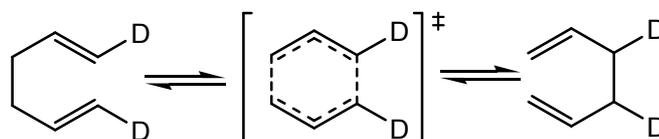
(7 pts)

Shikimic acid biosynthesis is an important pathway for amino acids, alkaloids and heterocyclic natural product production. Nature converts shikimic acid to chorismic acid through a cascade of enzymatic reactions. Then chorismate mutase catalyzes the conversion of chorismic acid to prephenic acid at the branch point for the biosynthesis of aromatic amino acids such as tyrosine and phenylalanine.



11-1. During the transformation of shikimic acid to chorismic acid, dehydration is occurring. Choose the hydroxyl group in shikimic acid that is lost through above dehydration among all possible reactions.

11-2. Chorismate mutase rearranges chorismic acid into prephenic acid without changing the molecular formula. Chorismic acid becomes prephenic acid through the Claisen rearrangement, a concerted pericyclic process like the Cope rearrangement as shown below:

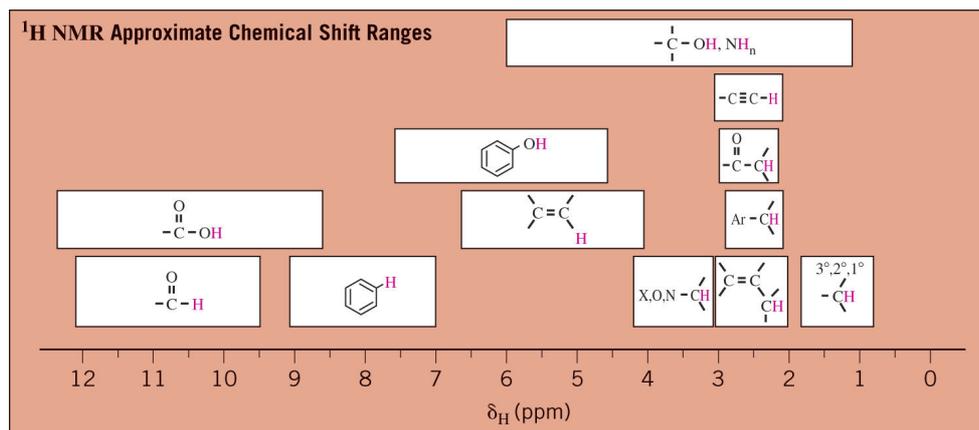


Based on the following spectral data, propose the structure of prephenic acid.

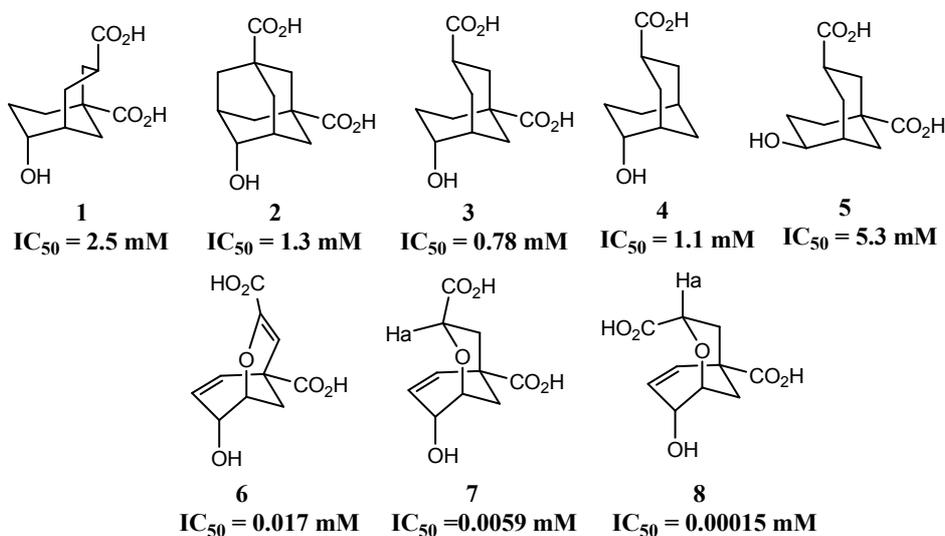
¹H-NMR (D₂O, 250 MHz): δ 6.01 (2H, d, J = 10.4 Hz), 5.92 (2H, dd J = 10.4, 3.1 Hz), 4.50 (1H, t, J = 3.1 Hz), 3.12 (2H, s). Note that there are three protons, which have been exchanged by D₂O very fast, and two protons at δ 3.12, which are exchanged slowly in prephenic acid. ¹³C-NMR (D₂O, 75

MHz): δ 203, 178, 173, 132 (for two identical carbons), 127 (for two identical carbons), 65, 49, 48.

δ , chemical shift; H, integrals; d, doublet; dd, doublet of doublet; J, coupling constant; t, triplet; s, singlet



Chorismate mutase is believed to stabilize the transition state of Claisen rearrangement. Thus it is an interesting target for inhibitor design. Inhibitors, called transition state analog (TSA)s that resemble the transition state (TS, e.g., the species in brackets “[]” above) of the reaction are designed to occupy the active site. Several inhibitors were designed and synthesized, and among them eight turned out to be potent inhibitors of the enzyme. The lower the IC₅₀ (inhibitor concentration of 50% of the enzymatic activity) value, the better the inhibitor.



11-3. Choose all correct statements based on the structures and IC_{50} values of above inhibitors. Increase of factor 5 is considered to be important.

- (a) Configuration of the hydroxyl group plays an important role in the TS and inhibitor design.
- (b) The presence of both carboxylic groups is important in the TS and inhibitor design.
- (c) Transition state of the reaction contains two six-membered rings with one chair and one twist-boat conformation.
- (d) **7** and **8** can be distinguished on the basis of the 1H -NMR of H_a .

11-4. Draw the transition state of the transformation of chorismic acid to prephenic acid based on the TSA structures and their IC_{50} values.

11-5. Compared with the uncatalyzed thermal conversion, chorismate mutase accelerates conversion of chorismic acid to prephenic acid 1.0×10^6 fold at $25^\circ C$ by lowering the activation energy of the reaction. Calculate the decrease in activation energy of chorismate mutase at $25^\circ C$.

$\Delta H^\ddagger_{\text{uncat}}$ is 86,900 J/mol for the thermal conversion of chorismic acid to prephenic acid. At what temperature will the rate of the *uncatalyzed* thermal conversion be the same as that of the *enzyme-catalyzed* conversion at $25^\circ C$, assuming that $E_a = \Delta H^\ddagger$.