## Problem 13: Carbocations and Aromaticity

Carbocations are reactive intermediates having a charge of +1 on the central carbon atom, with three groups attached. The carbocation center is electron deficient and lies in the same plane of the three attached atoms. Proton NMR is one of the primary instrumental methods applied to determine the structure and properties of carbocations. In a superacid media, such as SbF_5, stable carbocations can be generated and directly observed by NMR. SbF_5 is a strong Lewis acid that complexes with a weak base such as F^- to form SbF_6^-.

13-1   What is the product **A** in the following reaction?
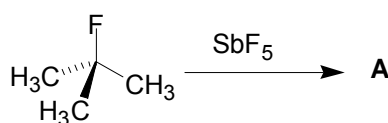
13-2   Two proton NMR spectra of $(CH_3)_3CF$ were obtained using neat $(CH_3)_3CF$ and $(CH_3)_3CF$ in SbF_5, respectively. One spectrum, denoted as spectrum I, showed a singlet at δ 4.35, and the other, spectrum II, revealed a doublet at δ 1.30 with a coupling constant J = 20 Hz. Which spectrum was obtained from $(CH_3)_3CF$ in SbF_5?

13-3   Tropylium ion **B** is one of the most stable carbocations. How many π electrons are there in the tropylium ion?


B
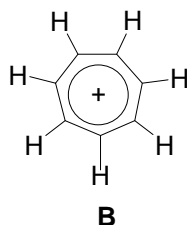
13-4   Is tropylium ion **B** an aromatic structure? Explain.

13-5   The chemical shift of benzene in the ^1H NMR spectrum is δ 7.27. What does the proton NMR spectrum of **B** look like?

(a) A singlet at δ 9.17.

(b) A singlet at δ 5.37

(c) A triplet at δ 9.17.

(d) A Triplet at δ 5.37.

13-6   4-Isopropyltropolone **C** was the first example of a non-benzenoid aromatic compound.   It
         was isolated from cypress trees in Taiwan by Professor T. Nozoe at the National Taiwan
         University in 1938.   Draw resonance structure(s) to illustrate the aromaticity of **C**.


C
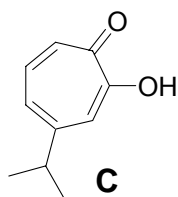
13-7   The proton of the OH group in tropolone is acidic.   Three moles of tropolone **C** can react
         with one mole of tris(2,4-pentanedionato)iron(III) (Fe(acac)$_3$) to form a red complex **D**.
         What is the structure of **D**?

## Problem 14: Photochemical Ring Closure and Opening

1,3,5-Hexatriene is known to undergo light-induced cyclization to give 1,3-cyclohexadiene.   The
photochemical reaction is reversible and stereospecific. Thus, irradiation of (2*E*,4*Z*,6*E*)-octatriene
(**A**) with UV-light gives cyclohexadiene (**B**).   The choice of the wavelength of light depends on
the absorption maximum of the compound to be irradiated, and the absorption maximum is
related to the number of conjugated double bonds in a chain.
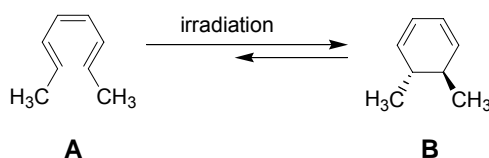
14-1   What is the chemical name of the starting triene (**C**) for the related reaction shown below?
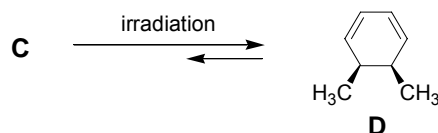
A similar reaction mechanism is involved in the synthesis of biologically active molecules.   For
example, in the presence of sunlight, 7-dehydrocholesterol (**E**) undergoes an electrocyclic ring
opening reaction to give provitamin D$_3$ (**F**), which can be further transformed through a
[1,7]-hydrogen shift to yield vitamin D$_3$ (**G**).

7-dehydrocholesterol **(E)** → sunlight → provitamin D$_3$ **(F)** → [1,7] H-shift → vitamin D$_3$ **(G)**
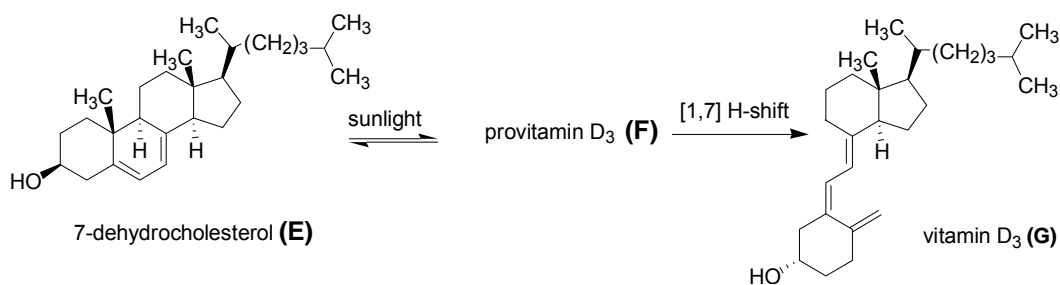
14-2   Of the two compounds 7-dehydrocholesterol (**E**) and vitamin D$_3$ (**G**), which would you expect to absorb light with the higher energy?   (**E** or **G**)

14-3   What is the chemical structure of **F**?

This principle has been elaborated to develop photochromic materials.   For example, irradiation of colorless compound **H** with UV light gives colored compound **I**.   The color change is reversed upon exposure to visible light.

14-4   Give the structure of colored compound **I**.

H
colorless → UV light / visible light → **I** colored compound
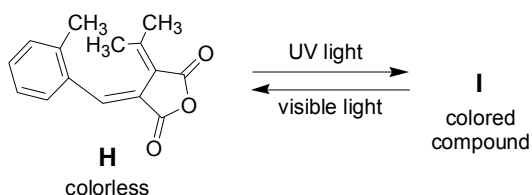
Aromatic hydrocarbons are usually highly fluorescent.   However, a neighboring amino substituent may quench the fluorescence.   This quenching mechanism is due to Photoinduced Electron Transfer (PET), which can be clearly illustrated by the molecular orbital diagrams shown below.   Upon irradiation with a light of suitable wavelength (step 1), the initial aromatic chromophore (state a) will pump an electron from the highest occupied molecular orbital (HOMO) up to the lowest unoccupied molecular orbital (LUMO) (state b).   In the presence of a neighboring amino group, one of the lone-pair electrons at the nitrogen atom moves to the HOMO of the excited chromophore (step 2), and thus blocks the normal fluorescent pathway (state c). Coordination of the amine lone-pair electrons to proton or metal ions efficiently inhibits the PET process, and retrieves the fluorescence of the aromatic chromophore (step 3).

20
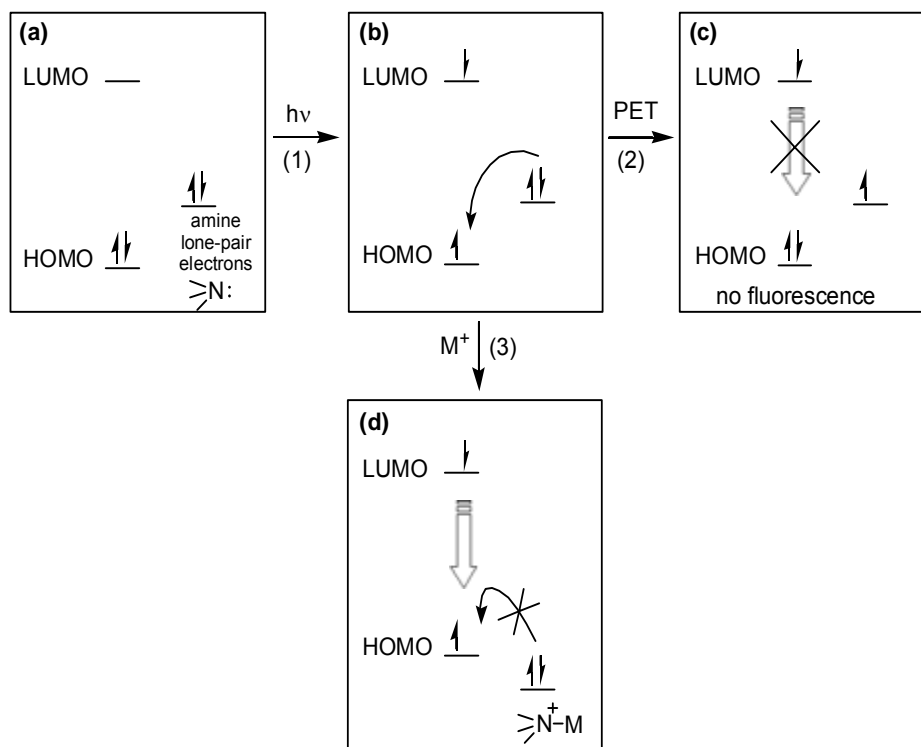
Many interesting and sensitive proton or metal ions fluorescent sensors have been developed based on the manipulation of the PET process.   For example, compound **J** is used as a pH-sensor.


J
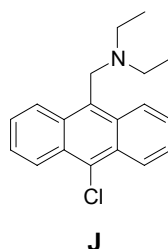
14-5   Do you expect that compound **J** is fluorescent in an alkaline solution (pH = 10.0)?

Problem 15: Stereochemistry

A simple two-dimensional representation for showing the three-dimensional arrangement of groups bonded to a carbon center is called a "*Fischer projection*".   In this molecular representation, the intersection point of two perpendicular lines represents an sp^3 center.   The horizontal lines connecting B and D to the central carbon atom represent the bonds that are out of plane relative to the observer.   The vertical lines connecting A and C to the central carbon atom

represent the bonds that are directed away from the observer into the plane of the page.
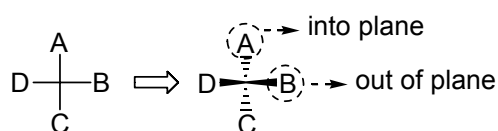

15-1 ChiraPhos was developed by Prof. Kagan and has found useful applications in asymmetric synthesis. Using the Fischer projection shown below, assign the absolute configuration of the chiral centers of ChiraPhos in terms of the *R/S* notation according to the Cahn-Ingold-Prelog sequence rule.
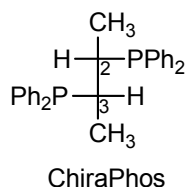
ChiraPhos

15-2 One of the stereoisomers of ChiraPhos is a *meso* compound. What are the identities of **X** and **Y** in the Fischer projection shown below?

meso-ChiraPhos
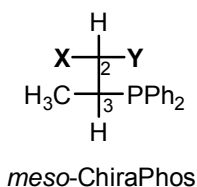
It is very useful and common to use Fischer projections for the stereo representation of carbohydrates. For example, the following Fischer projection represents the structure of D-glucose. It is interesting to note that the open-chain glucose can be interconverted with cyclic structures through the hemiacetal formation between the C_5-OH and the C_1-aldehyde group.

D-glucose   α-anomer   β-anomer

(open chain)   (cyclic structures)
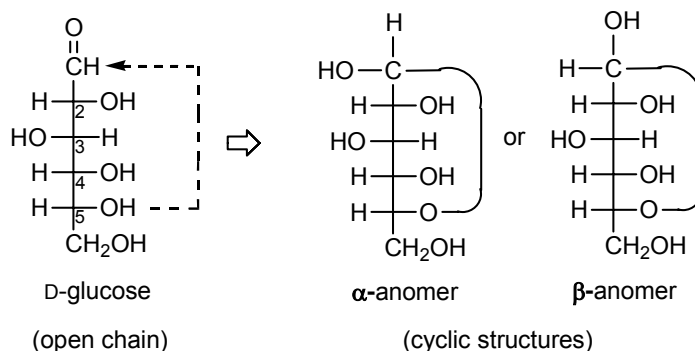
The hemiacetal formation generates two stereoisomers, which are called *"anomers"*. The pure α-anomer of D-glucose has a specific rotation of +112.2°, whereas the pure β-anomer has a specific rotation of +18.7°. In water, either one of the two anomers gives an equilibrium mixture with a specific rotation of +52.6°.

15-3 Calculate percentage of α-anomer in the equilibrium mixture of D-glucose in water.

15-4   Which is the more stable anomer in water? (α or β)

15-5   Draw the chair conformation of the β-anomer.

15-6   What is the common intermediate for the interconvertion between the α- and β-anomers?

The addition reaction of HCN to an aldehyde generates a cyanohydrin, which can be further reduced to form an α-hydroxyaldehyde.


cyanohydrin
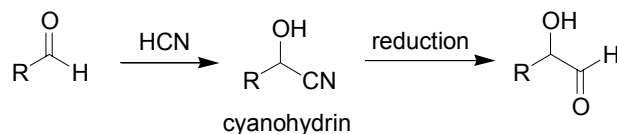
High homologs of carbohydrates, such as D-talose, can be synthesized from D-glyceraldehyde by repeating the same reaction conditions three times as shown below.
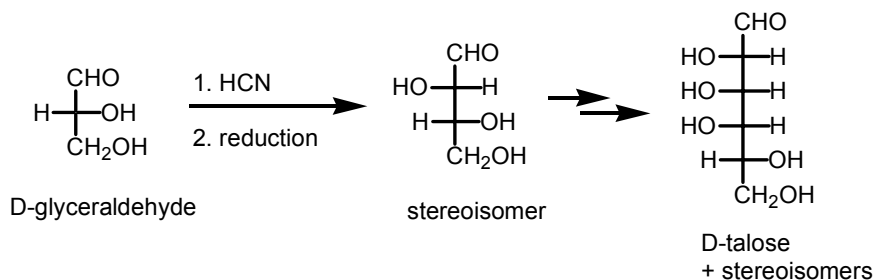
15-7   How many pairs of enantiomers will appear in the final product mixture?

Enzymes are remarkable biological catalysts that control the pattern of chemical transformations in living organisms.   Because of their striking catalytic power and specificity, applying enzymes in organic synthesis has become one of the fastest growing areas for the development of new synthetic methodology.   Following are the data for the yeast-mediated kinetic resolution of racemic 2-substituted cyclohexanone via Baeyer Villiger reactions (Table 1).

Table 1. Yeast-mediated kinetic resolution of racemic 2-substituted cyclohexanone via Baeyer Villiger reactions
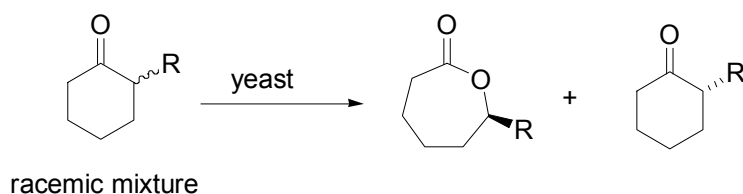
| Entry	R	Yield (%)	ee%	Yield (%)	ee%
1	Et	79	95	69	98
2	*n*-Pr	54	97	66	92
3	Allyl	59	98	58	98

ee: enantiomeric excess

15-8   What is the ratio of (*R*)/(*S*) isomers of 6-allylcaprolactone in entry 3?

15-9   MCPBA (*meta*-chloroperbenzoic acid) is a common oxidizing agent for Baeyer Villiger reactions.   Using MCPBA as an oxidizing agent, instead of yeast, for the above reaction, what will be the ee% of the caprolactone product?

Problem 16: Organic Synthesis

One of the primary demands for the development of organic light emitting diodes (OLEDs) is the search for highly efficient luminescent materials which can be either small molecules or polymers. For example, fluorene, a methylene-bridged biphenyl, exhibits a higher quantum yield of fluorescence than biphenyl.


Fluorene   **Biphenyl**
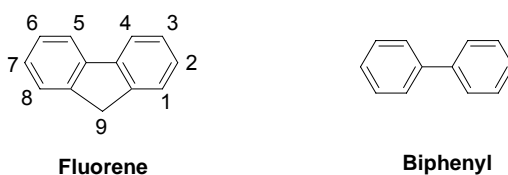
Many fluorene derivatives have been developed that have subsequently found promising applications in flat-panel-display technology.   In order to avoid intermolecular interactions, bulky substituents have been introduced at the C9 position of fluorene.   One example of this is compound **C**, an interesting and useful building block in the development of a highly efficient blue light emitting material, the synthesis of which is shown in the following scheme.
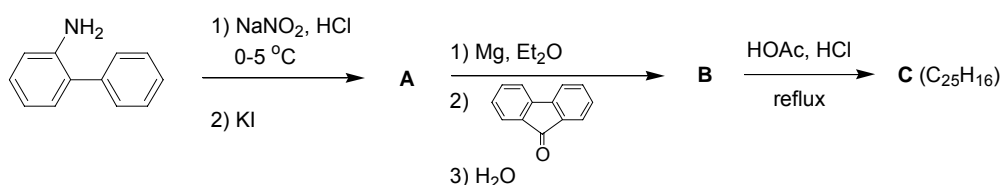
16-1   Draw the structures of **A**, **B**, and **C**.

Liquid crystals have become a part of our daily life, from wristwatches, pocket calculators, to full color flat-panel displays.   Liquid crystal molecules usually contain a rigid core with a flexible terminal alkyl chain as shown in the example below.

Flexible
terminal
alkyl chain   Rigid core
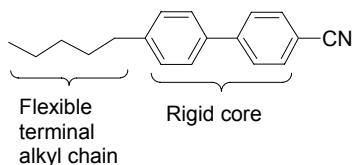
Biphenyl and terphenyl are common basic skeletons for the rigid core of liquid crystals.   This kind of structure can be effectively synthesized through palladium catalyzed coupling of an aryl bromide or iodide with arylboronic acid, known as the Suzuki coupling reaction.

Terphenyl
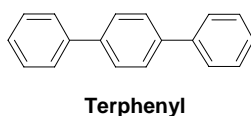
A typical example of a Suzuki coupling reaction is shown below.   Bromobenzene reacts with phenylboronic acid in the presence of a palladium catalyst to give biphenyl.
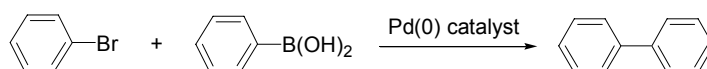
The following is a synthetic scheme for the preparation of two liquid crystal molecules, 4-cyano-4'-pentylbiphenyl and **G**.
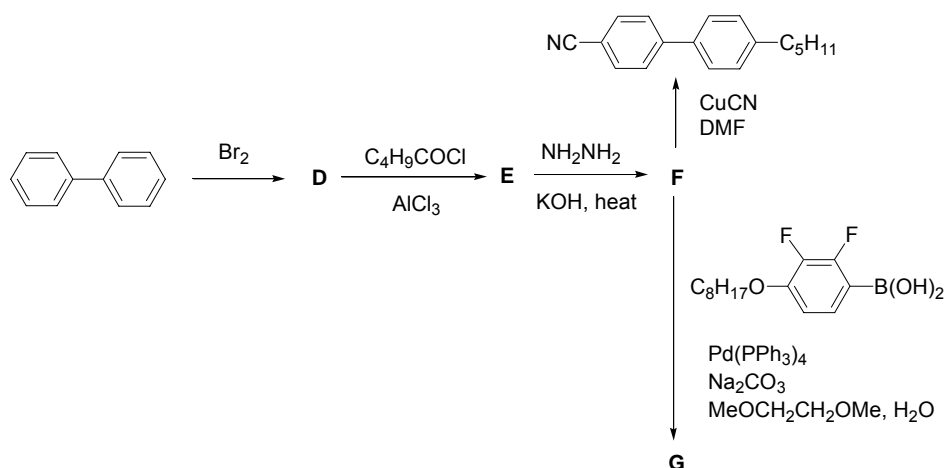
16-2   What are the structures of **D**, **E**, **F**, and **G**?

Problem 17: Spectroscopy and Polymer Chemistry

Organic polymers have had a great impact on our daily lives. Millions of tons of different kinds of polymers are produced every year. Synthetic organic polymers have a variety of uses, from textiles to computer chips, and to the life saving artificial heart valve. They are widely used as plastics, adhesives, engineering materials, biodegradable plastics, and paints. Poly(vinyl alcohol) (**PVA**) is an important example of a water-soluble polymer. One synthetic route to PVA is summarized in Scheme 1.
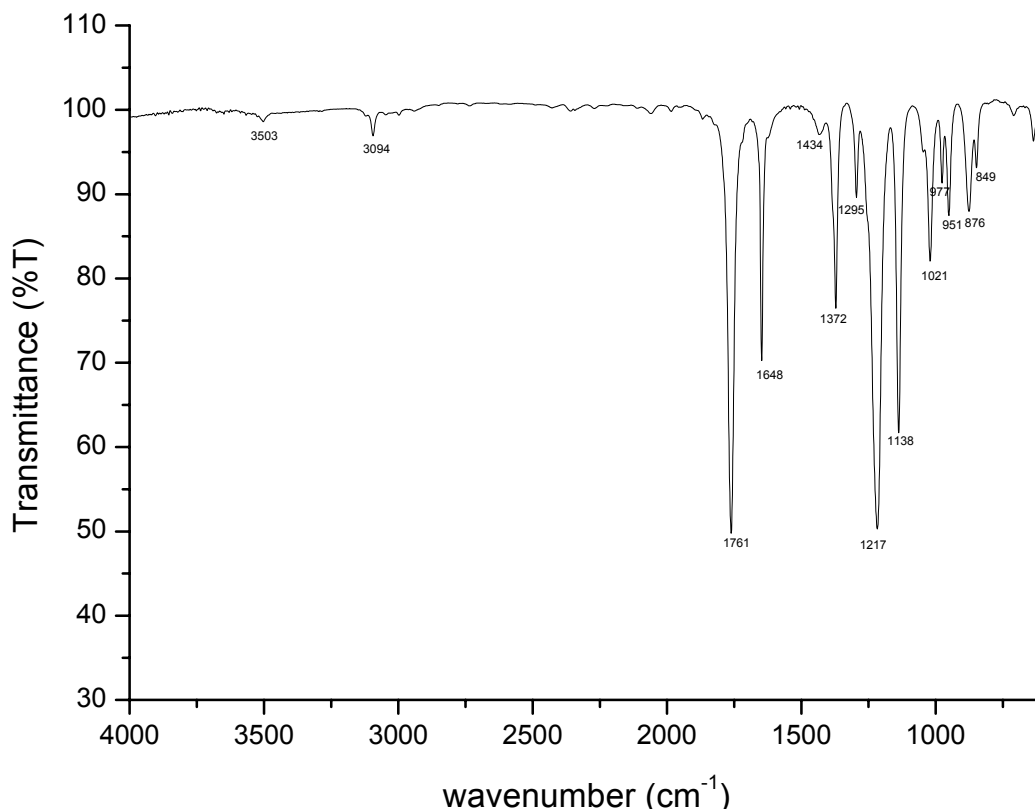
Scheme 1

Monomer **A** $\xrightarrow{\text{polymerization}}$ Polymer **B** $\longrightarrow$ Poly(vinyl alcohol) (**PVA**)

Polymer **B** shown above is also a major component in chewing gum. Elemental analysis of **A** suggests a ratio of C:H:O = 56:7:37. In addition, elemental analysis of **B** gives an almost identical composition of C, H, and O. The following IR and ^{1}H NMR spectra were recorded for Monomer **A**.
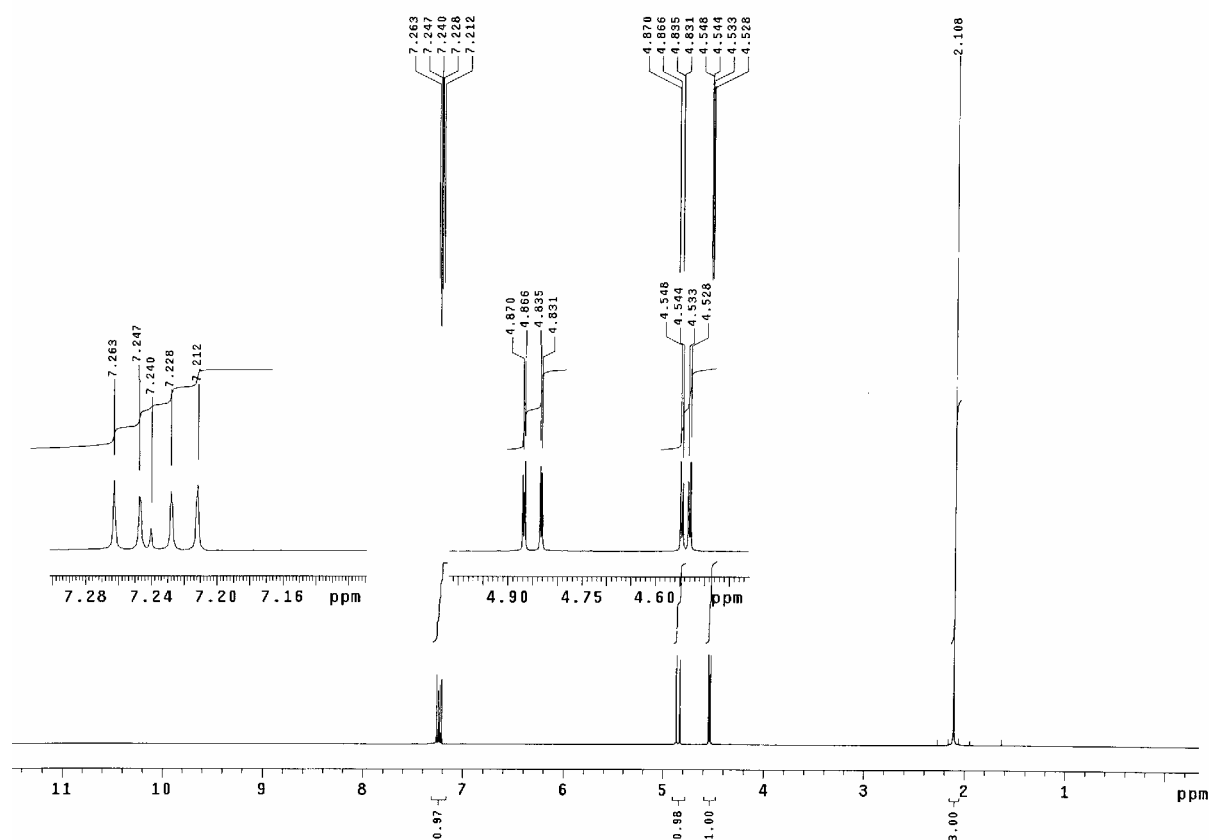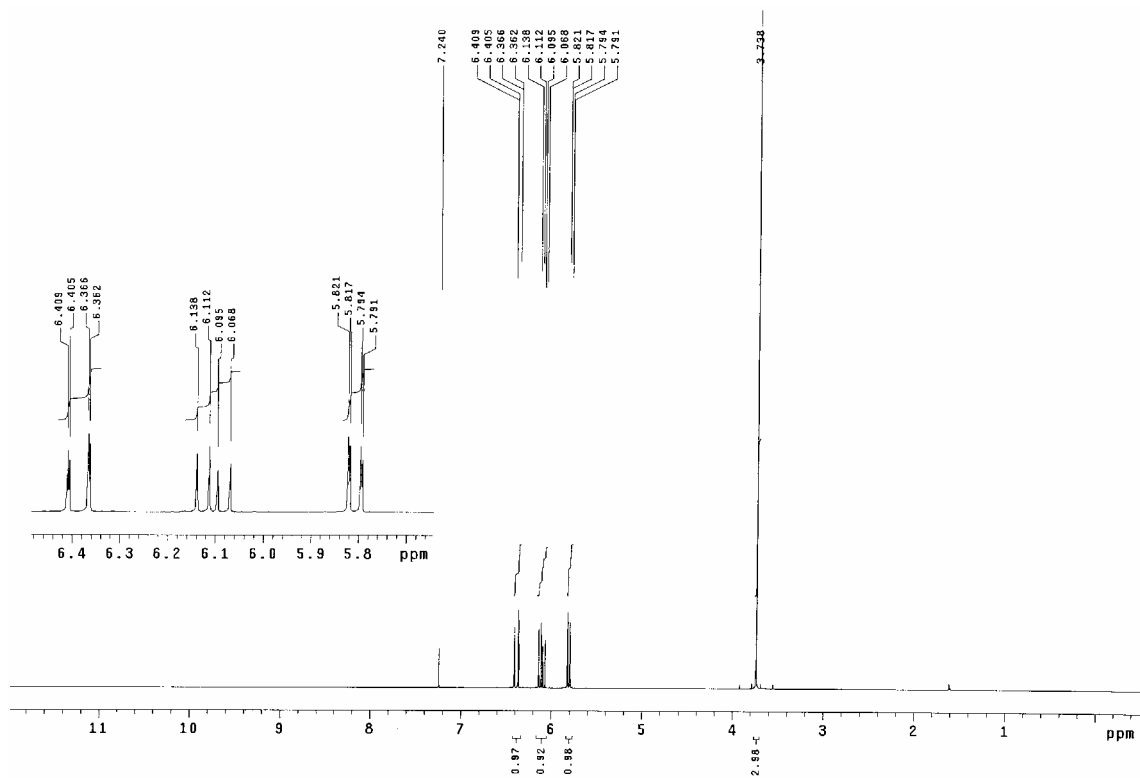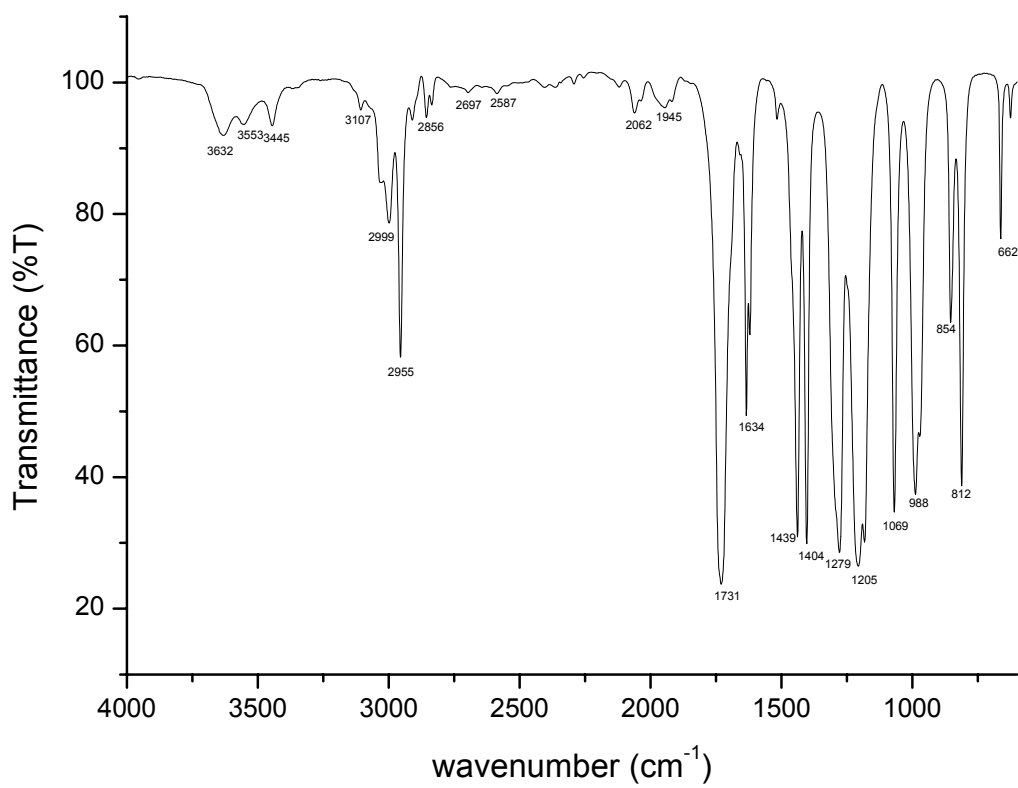

^{1}H NMR spectrum of Monomer **A**

IR Spectrum of Monomer **A**

17-1   What is the molecular formula of **A**?

17-2   Which functional group would give an IR absorption band at 1761 cm^{-1}?

17-3   What is the chemical structure of **A**?

17-4   Draw a portion of polymer **B**.   Show at least three repeat units.

17-5   Provide a method for the transformation of **B** to **PVA**.

17-6   How many pairs of enantiomers would be obtained from polymer **B** with a molecular weight of 8600, assuming that the polymer is terminated by hydrogen abstraction and the mass of the terminal groups can be ignored?

17-7   Compound **C**, an isomer of **A**, is also an important monomer for the synthesis of polymers. On the basis of its ^{1}H NMR and IR spectra provided below, deduce the chemical structure of **C**.
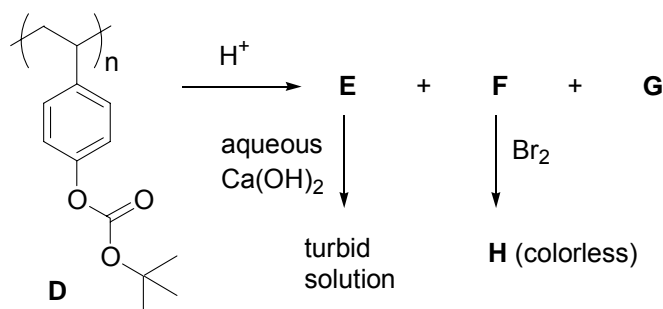
^{1}H NMR spectrum of Monomer **C**

IR Spectrum of Monomer **C**

Polymer **D** is an acid sensitive macromolecule. On treatment of **D** with a protic acid, gases **E** and **F** are released, and a new polymer **G** is formed. Gas **E** turns an aqueous solution of $Ca(OH)_2$ into a turbid solution while gas **F** reacts with bromine to give a colorless solution of **H**.

17-8 Draw the chemical structures of **E**, **F**, **G** and **H**?

Polymer **D** has been used to formulate a photo-imaging material by mixing it with a photo acid-generator (PAG). After being coated onto a substrate and exposed to light, protons are generated from the PAG, catalyzing a chemical reaction within the polymer matrix. Sometimes baking after exposure is necessary to accelerate the acid catalyzed reaction. If light is applied through a mask (Figure 1), a latent image of the mask is formed in the polymer matrix. After baking and using an aqueous basic developer to wash away the acidic materials, a patterned substrate **I** is obtained.
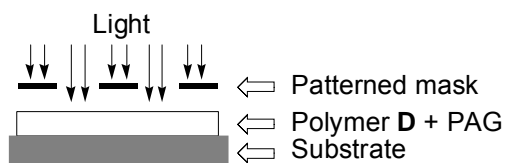

Figure 1

17-9 Which of the following diagrams best illustrates the patterned structure of substrate **I**?

(a)   (b)   (c)   (d)

The dark areas represent a polymeric coating that is structurally different from the original one.

Problem 18: Crown Ether and Molecular Recognition

The discovery of crown ethers was made by Charles Pederson in 1967. He was rewarded with a share of the 1987 Nobel Prize for chemistry with Jean-Marie Lehn and Donald Cram for their contributions to supramolecular chemistry.

The following schematic diagram shows a synthetic route to the linear diol **A**. However, because of the presence of catechol in the starting material, the resulting product was a mixture of **A** and the minor product **B**.
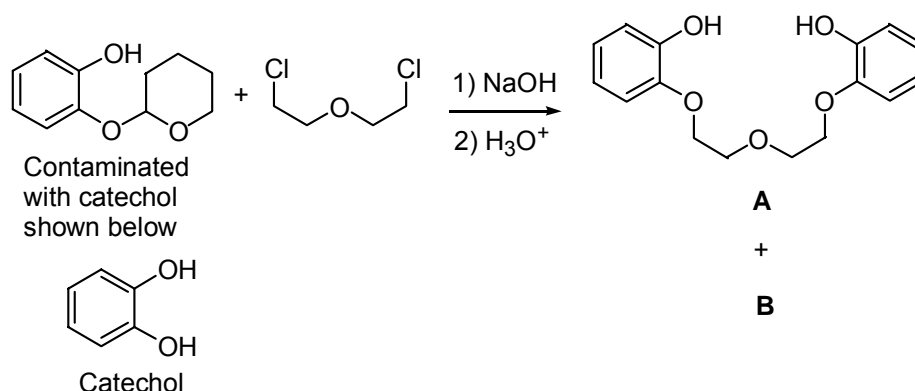

The molecular weight of **B** was found to be 360.1 and it had an elemental composition of C:H:O = 66.5:6.7:26.6. The ^{1}H NMR spectrum of **B** showed four sets of proton signals. Two of which were observed at δ 7.0-7.5 and the other two at δ 3.7-4.2. The integration ratio of the four sets of signals was 1:1:2:2. Compound **B** strongly binds with the potassium ion. A striking example is the use of **B** to assist the dissolution of $KMnO_4$ in benzene to give a purple coloration.

18-1   What is the chemical structure of **B**?

18-2   What is the major function of H_3O^+ in the above reaction?

(a) To activate $ClCH_2CH_2OCH_2CH_2Cl$.

(b) To neutralize NaOH.

(c) To remove the tetrahydropyran group.

(d) To act as a buffer to control the pH of the solution.

The following is the synthetic route to [2.2.2]cryptand:
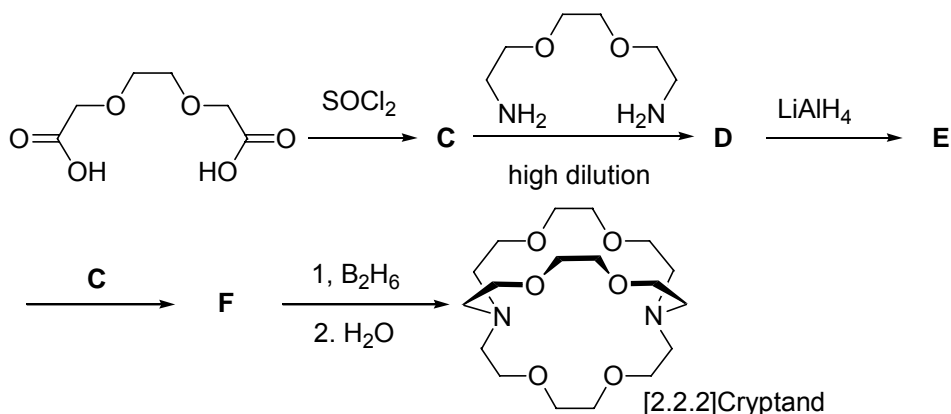
18-3 Draw the structures of **C**-**F**.

18-4 Why are high dilution conditions required in the synthesis of **D** from **C**?

(a) Since the reaction between **C** and the diamine is highly exothermic, a high dilution condition is used to dissipate the heat released from the reaction.

(b) A high dilution condition is employed in order to inhibit oligomer or polymer formation.

(c) Thermal equilibrium is favored to give **D** in higher yield under high dilution conditions.

(d) The solubility of the starting material is low.

The affinity of a metal cation is controlled by several factors such as size matching between the host cavity of the crown ether and the guest cation, and the number of donor atoms of the host. Table 1 shows the radii of different alkali metal cations and the diameters of the cavities of several crown ethers.
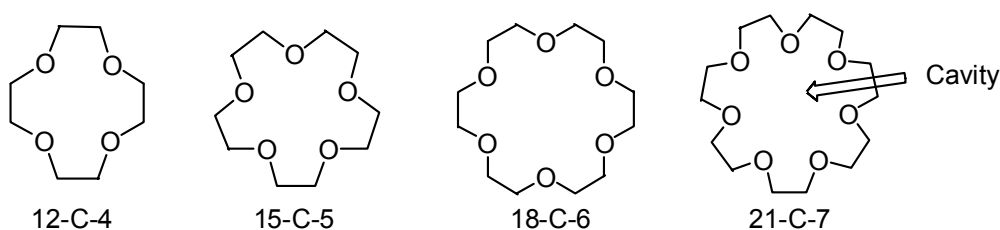

12-C-4   15-C-5   18-C-6   21-C-7

Table 1. Radii of different alkali metal cations and diameters of the cavities of crown ethers.

Cation (radius, pm)	Cavity of the crown ether (diameter, pm)
Li$^+$ (68)	12-C-4 (120-150)
Na$^+$ (98)	15-C-5 (170-220)
K$^+$ (133)	18-C-6 (260-320)
Cs$^+$ (165)	21-C-7 (340-430)

18-5 On the basis of the above data, match the experimental curves **I**-**III** in Figure 1 with appropriate cyclohexyl crown ethers **G**-**I** .
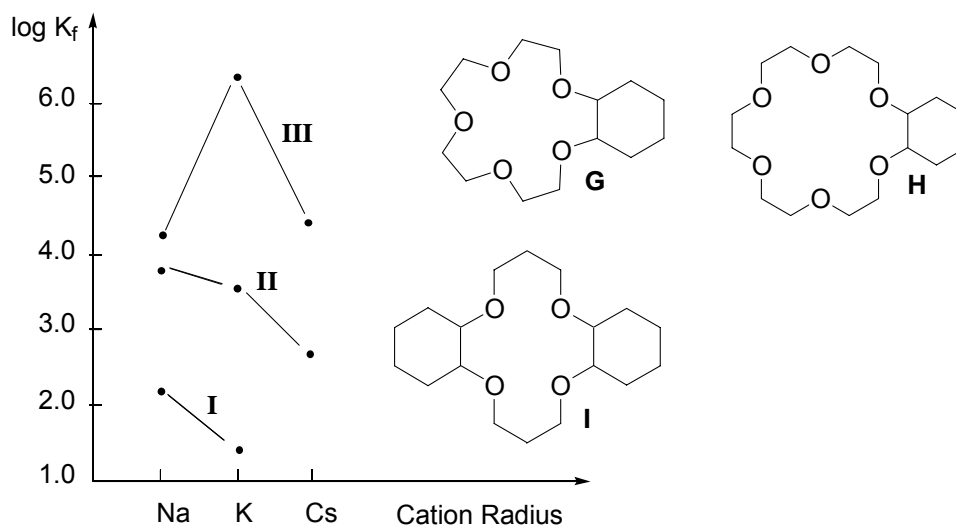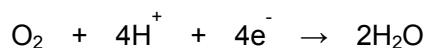
31

Figure 1. Complexation of Crown Ethers with Cations in Methanol

Problem 19: Enzyme Catalysis

In biological systems, oxidases catalyze the following reaction

$$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O$$

The reaction is the key to respiration in living systems.   The electrons come from Cytchrome c, which contains an iron center.   The half reaction is

$$Fe^{II}cyt\ c \rightarrow Fe^{III}cyt\ c + e^-$$

The extinction coefficients of Fe^{II}cyt c and Fe^{III}cyt c at 550 nm are 27.7 and 9.2 mM cm^{-1}; respectively.

The absorbance of cyt c at 550 nm was observed to decrease at a rate of 0.1 A/sec in a 5 mL solution containing 2.7×10^{-9} M oxidase, and sufficient cyt c and oxygen.

19-1   How many moles of cyt c were oxidized each second?

19-2   How many moles of oxygen were consumed each second?

19-3   What is the turnover number for oxidase?   (Turnover number: the number of product produced by one catalyst per second)