

PROBLEM SETS. QUESTIONS AND ANSWERS

Chapter 1

1.1 A famous scientist of the 20th century was Linus Pauling who received two Nobel prizes during his life. Look up a biography of Pauling and list his most notable contributions to science.

Ans. Linus Pauling (1901-1994) made many advancements in the understanding of chemical bonds and published in 1939 a classic book entitled, *The Nature of the Chemical Bond*. Pauling received his first Nobel Prize in 1954 for work on the structure of proteins. Pauling received a Nobel Peace Prize in 1962 for his opposition to testing nuclear devices in the atmosphere. Pauling was a strong advocate for taking large doses of Vitamin C to combat colds and cancer, and he wrote several books on the subject, *Vitamin C and the Common Cold* (1970), *Cancer and Vitamin C* (1979) and *How to Live Longer and Feel Better* (1986).

1.2 Section 1.2a shows the electronic configuration for the 2nd row elements. a) Show the electronic configuration for the third row elements. b) Common ions in the 3rd row are Na^{+1} , Mg^{+2} , Al^{+3} , Si^{+4} , P^{+5} , S^{-2} , Cl^{-1} . What characteristic of their electronic configurations do these ions share that accounts for their stability?

ans. a)

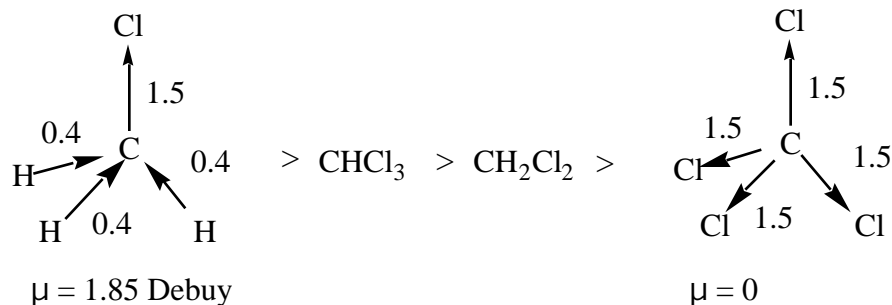
Element (atomic number)	Electron Configuration
Na (11)	$1s^2, 2s^2, 2p^6 3s^1$
Mg (12)	$1s^2, 2s^2, 2p^6 3s^2$
Al (13)	$1s^2, 2s^2, 2p^6 3s^2 3p^1$
Si (14)	$1s^2, 2s^2, 2p^6 3s^2 3p^2$
P (15)	$1s^2, 2s^2, 2p^6 3s^2 3p^3$
S (16)	$1s^2, 2s^2, 2p^6 3s^2 3p^4$
Cl (17)	$1s^2, 2s^2, 2p^6 3s^2 3p^5$
Ar (18)	$1s^2, 2s^2, 2p^6 3s^2 3p^6$

b) The ions Na^{+1} , Mg^{+2} , Al^{+3} , Si^{+4} , P^{+5} result from loss of electrons from the neutral element to give the stable electronic configuration of He, $1s^2, 2s^2, 2p^6$. Both S^{-2} and Cl^{-1} result from the neutral element accepting electrons to give the stable configuration of Ar, $1s^2, 2s^2, 2p^6 3s^2 3p^6$.

1.3 The dipole moment (μ) of a molecule is the vector sum of the dipole moments of the individual bonds. In some cases these sums cancel each other while in other

cases they enhance each other. Given the bond moments of H-C (0.4) and C-Cl (1.5), predict the dipole moment, and thus the polarity, of CH_3Cl , CH_2Cl_2 , CHCl_3 and CCl_4 .

ans.



H and Cl are additive

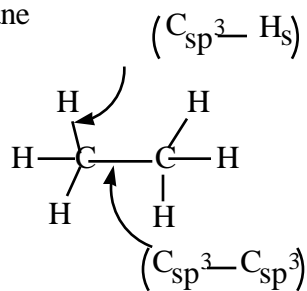
Cl's cancel each other

1.4 For the compounds below write the complete structure and designate the bonding in each bond.

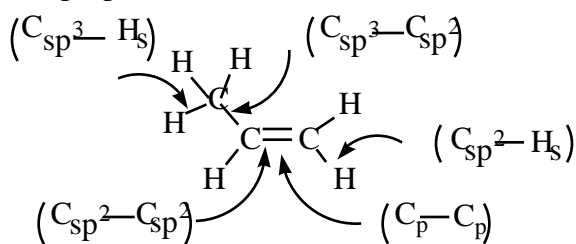
a) ethane, CH_3CH_3 b) propene, $\text{CH}_3\text{CH}=\text{CH}_2$ c) propyne, $\text{CH}_3\text{C}\equiv\text{CH}$

ans.

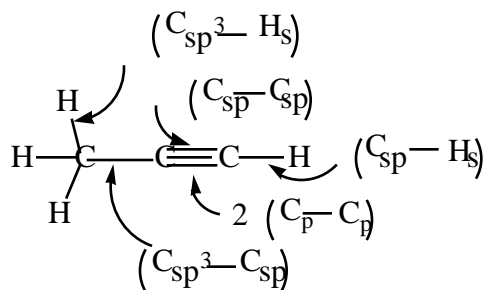
a) ethane



b) propene



c) propyne



1.5 Hydrogen bonds in alcohols and carboxylic acids have a bond strength of 8-10 kcal/mole. The energy required to break these bonds explains the higher boiling points of

hydrogen bonded substances. a) Use a chemical handbook to find the boiling points of the following compounds to see the effect of hydrogen bonding on the boiling point.

$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$ versus $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ versus $\text{CH}_3\text{CH}_2\text{COOH}$

b) What are the molecular weights for these compounds and how does the molecular weight affect the bp in them?

ans

a)

$\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$ $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ $\text{CH}_3\text{CH}_2\text{COOH}$

bp 35 °C

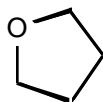
bp 114 °C

bp 141 °C

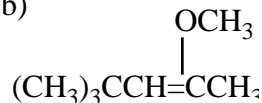
b) all have a molecular weight of 74. Thus van der Waals attractions due to size are the same. Bp differences attributed to polar attractions and hydrogen bonding.

1.6 Expand the structures below to show all atoms and unshared electron pairs.

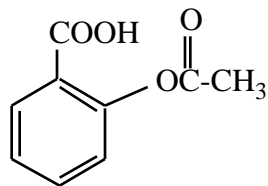
a)



b)



c)



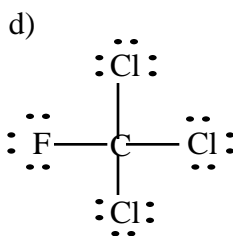
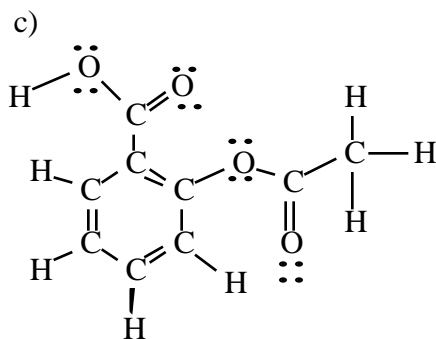
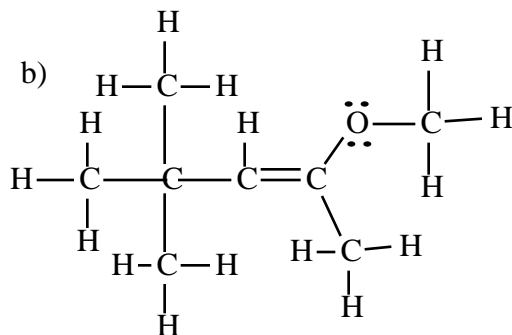
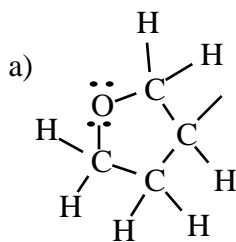
aspirin

d)

FCCl_3

Freon-11

ans

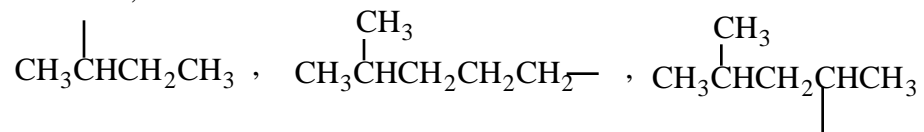


1.7

ans. Many sites are available for all areas of chemistry. Look at the home pages for the Department of Chemistry, Northern Illinois University and for the University of Florida.

Chapter 2

2.1. Write the alkyl substituent names for ethane, octane, cyclohexane and the structures,



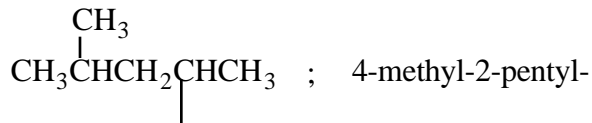
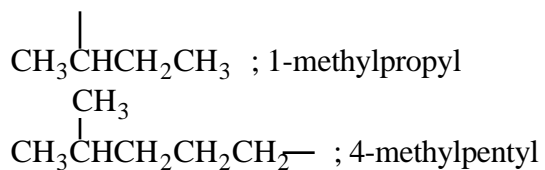
ans.

name the alkane, remove the ane, add yl

ethane; ethyl

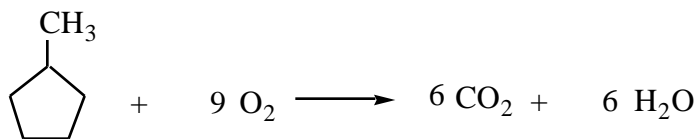
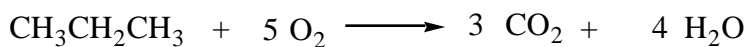
octane; octyl (there are several positions for attachment of octyl)

cyclohexane; cyclohexyl



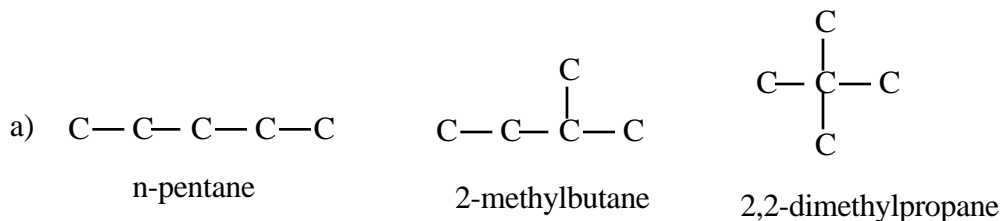
2.2. Write balanced equations for the complete combustion of propane and methylcyclopentane.

Complete combustion means oxidation to carbon dioxide and water.



2.3. Draw and name all of the structural isomers of a) pentane and b) hexane.

Ans.



(Hydrogens not shown)

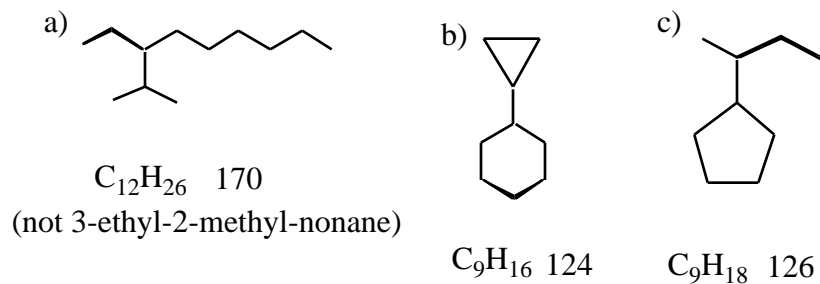
b) n-hexane, 2-methylpentane, 3-methylpentane, 2,2-dimethylbutane, 2,3-dimethylbutane

(you draw the structures, show all hydrogens)

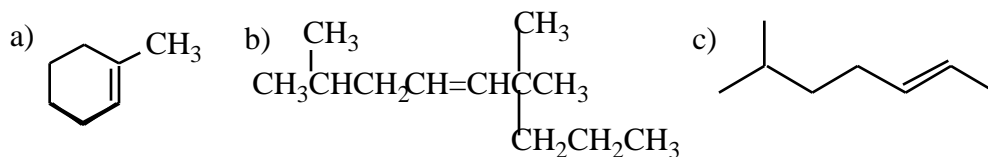
2.4. Write structures, formulas, and formula weights for the following.

a) 3-isopropylnonane b) cyclopropylcyclohexane c) sec-butylcyclopentane

ans.



2.5. Provide names for each compound below.



ans

a) 1-methylcyclohexene

b) 2,6,6-trimethyl-4-nonene

not 5-nonene

c) 6-methyl-2-heptene

2.6. Write structures that correspond to the names given.

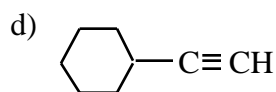
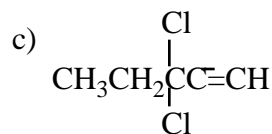
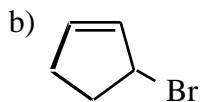
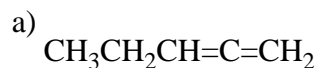
a) 1,2-pentadiene

b) 3-bromocyclopentene

c) 3,3-dichloro-1-pentyne

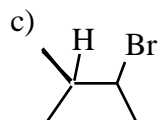
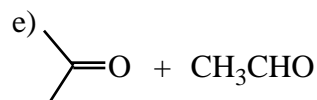
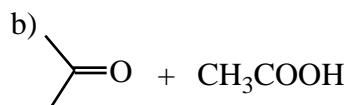
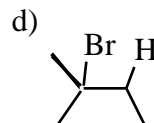
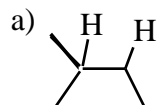
d) cyclohexylethyne

ans.



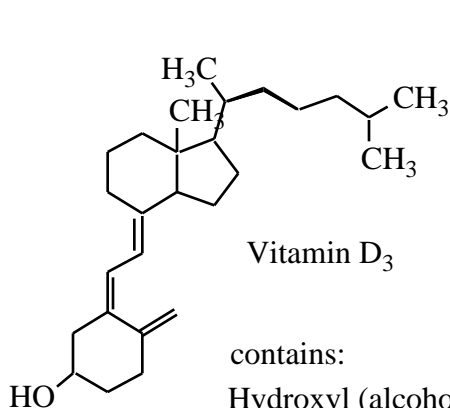
2.7. Show the products from the reaction of 2-methyl-2-butene with a) H_2 / Pt , b) hot $KMnO_4$, c) HBr -peroxide, d) HBr (no peroxide), e) Br_2 , f) O_3 / Zn

ans.

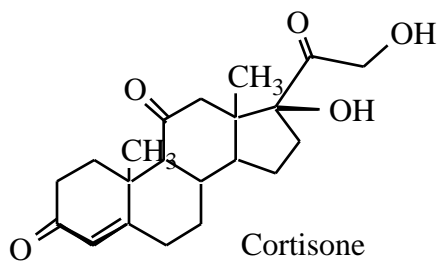


2.8. Both Vitamin D and Cortisone contain significant hydrocarbon portions of their structure. Find their structures in a reference book (Merck Index) and list the function groups present in each molecule.

ans.



contains:
Hydroxyl (alcohol)
three alkenes as a conjugated triene

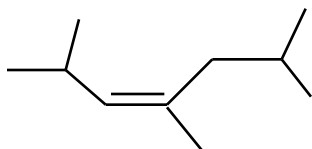


contains:
carbonyl (ketone)
alkene (conjugated)
two hydroxyl (alcohol)

Chapter 3

3.1 Name the two alkenes below and show the alkene configuration by a) cis-trans rules and b) E, Z rules.

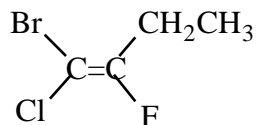
ans



cis-2,4,6-trimethyl-3-heptene

- a) longest chain is cis
 b) isopropyl and sec-butyl groups have higher priority and are on the same side Z

Z-isomer



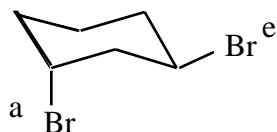
E-1-bromo-1-chloro-2-fluoropropene

- a) no good cis or trans determination
 b) Br and F have higher priorities and are opposite, E-isomer

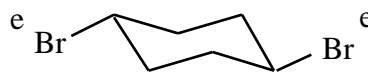
3.2 Draw structures for trans-1,3-dibromo- and trans-1,4-dibromocyclohexane and examine the axial-equatorial relationships of the bromine atoms.

ans.

trans-1,3-dibromocyclohexane



trans-1,4-dibromocyclohexane

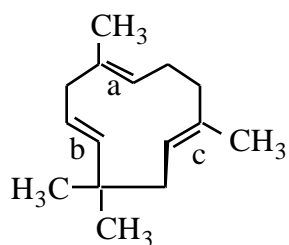


Large substituent, Br, prefers equatorial position.

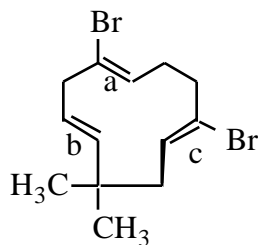
3.3 Humulene is a triene found in hops. Label bonds a, b, and c by both cis-trans and E-Z rules. If two methyl groups are replaced by Br atoms then the compound on the right occurs. Label the a, b, and c bonds in the dibromo compound also by cis-trans and EZ rules. How did the Br affect the nomenclature?

ans.

humulene



- a - trans or E
 b - trans or E
 c - trans or E



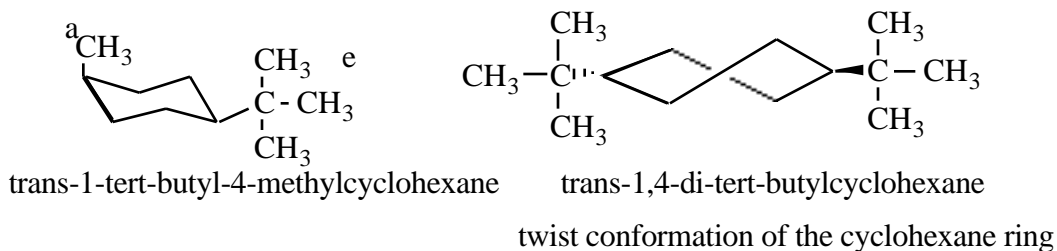
- a - trans for hydrocarbon, but Z isomer Br has higher priority than C
 b - trans or E
 c - trans for hydrocarbon, but Z isomer.

The Br atoms changed the priority in the nomenclature for a and c.

3.4 Tertiary butyl groups are so large that they will not occupy an axial position in a cyclohexane ring. Draw structures for a) cis-1-tert-butyl-4-methylcyclohexane and b) cis-1,4-di-tert-butylcyclohexane and determine the structural changes.

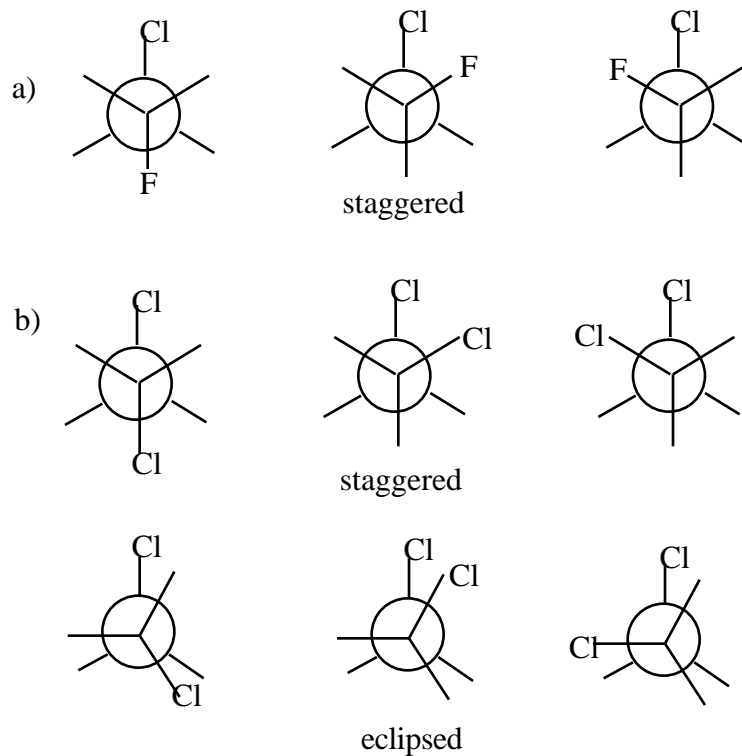
ans.

In a the tert-butyl group occupies an equatorial position and the methyl occupies an axial position. But in b one tert-butyl group would be required to occupy an axial position which is just energetically too high. Thus the ring changes from a chair conformation to a twist conformation to accommodate the two tert-butyl groups.



3.5 a) Draw Newman projections for the staggered conformations of 1-fluoro-2-chloroethane. b) Draw Newman projections for all of the conformations of 1,2-dichloroethane.

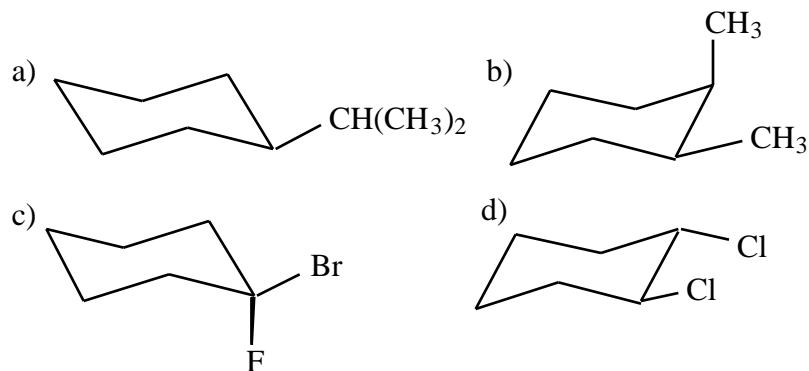
ans.



3.6 Draw the structure for the more stable conformation of

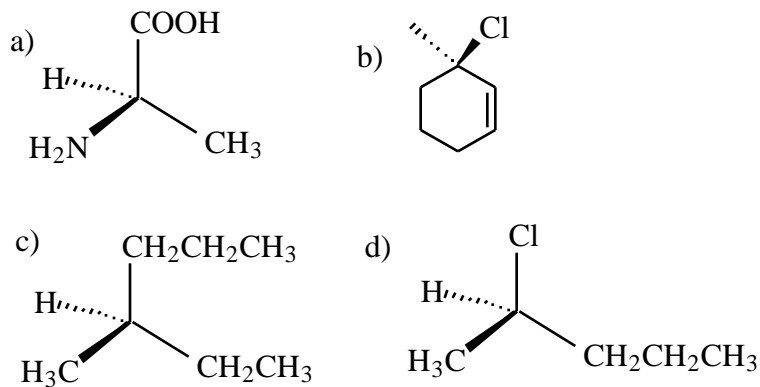
- a) isopropylcyclohexane b) cis-1,2-dimethylcyclohexane
 c) 1-fluoro-1-bromocyclohexane d) trans-1,2-dichlorocyclohexane

ans.



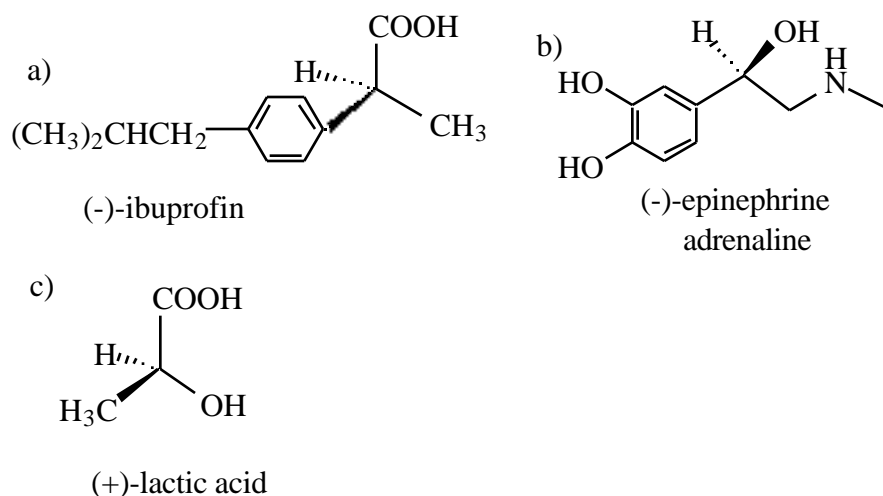
3.7 Identify the stereogenic center in each compound below and draw with a dotted-line wedge structure the R isomer.

ans.



3.8 The compounds below are all well-known compounds with important biological activity. The S enantiomer is the active substance in each case. Draw the S isomer for each compound.

ans.



Chapter 4

4.1 Many primary sources contain a historical background on Kekule. Write a brief biography about him.

ans. Taken from *Britannica*

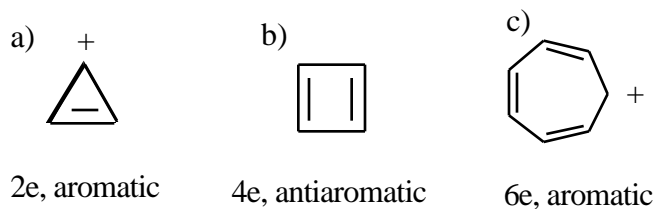
Kekule von Stradonitz, August (1829 - 1896) born in Darmstadt, Germany is described as a chemist who laid the groundwork for the modern structural theory in organic chemistry. In 1858 he showed that carbon is tetravalent and could form long chains. "One night in 1865 Kekule dreamed of the benzene molecule as a snake biting its tail while in whirling motion. From that vision his concept of the six-carbon benzene ring was born".

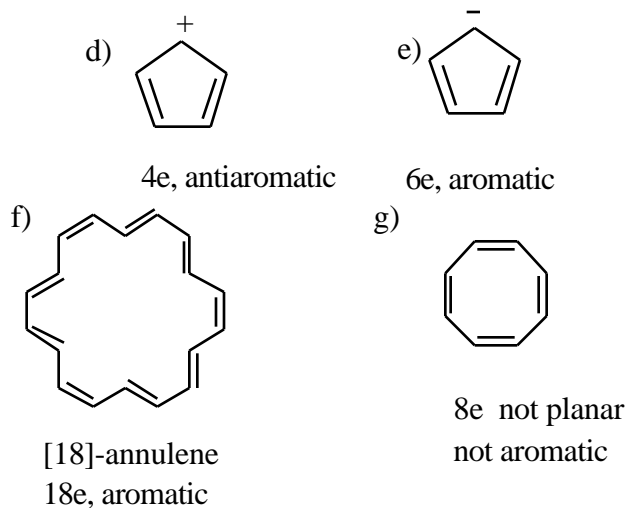
Factual dream or not, Kekule started much of the early theory of organic chemistry.

4.2. Determine, according to Huckel's rule, which compounds below are aromatic.

ans.

Aromatic compound must be cyclic, planar and contain $4n + 2$ electrons
 Compounds that are cyclic, planar and contain $4n$ electrons are called antiaromatic, a particularly unstable system.

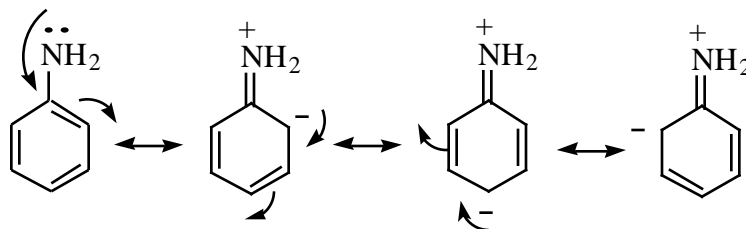




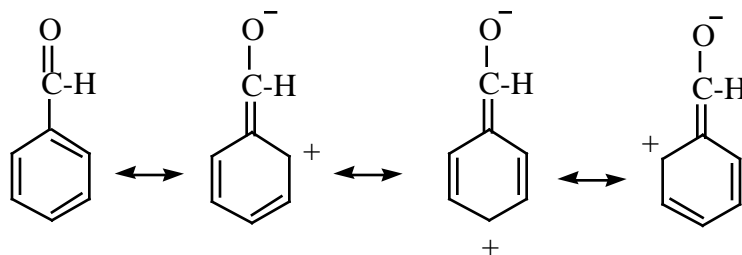
4.3 Draw the ground state resonance structures for a) aniline, and b) benzaldehyde. What is the purpose of writing these resonance structures?

ans.

a) aniline



b) benzaldehyde

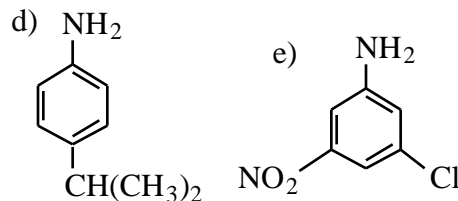
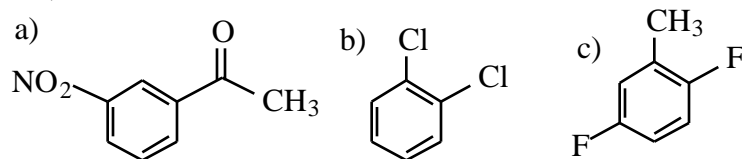


The purpose of writing resonance structures is to get a better understanding of the true electronic structure of a compound when one structure alone is inadequate. Resonance shows that the ring in aniline contains some negative charge and would thus react readily with electrophiles at the ortho and para positions. Resonance in benzaldehyde shows that the ring is deficient in electrons and thus would not readily react with electrophiles.

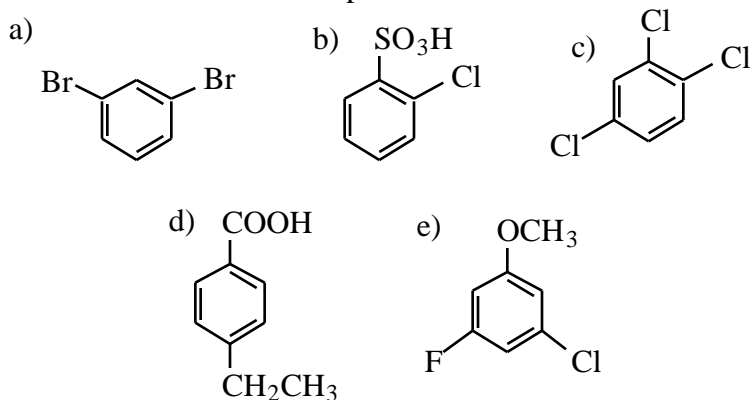
4.4 Draw structures that correspond to each name below.

- a) meta-nitroacetophenone b) o-dichlorobenzene c) 2,5-difluorotoluene
 c) p-isopropylaniline e) 3-chloro-5-nitrophenol

ans,



4.5 Give systematic names for the compounds below.



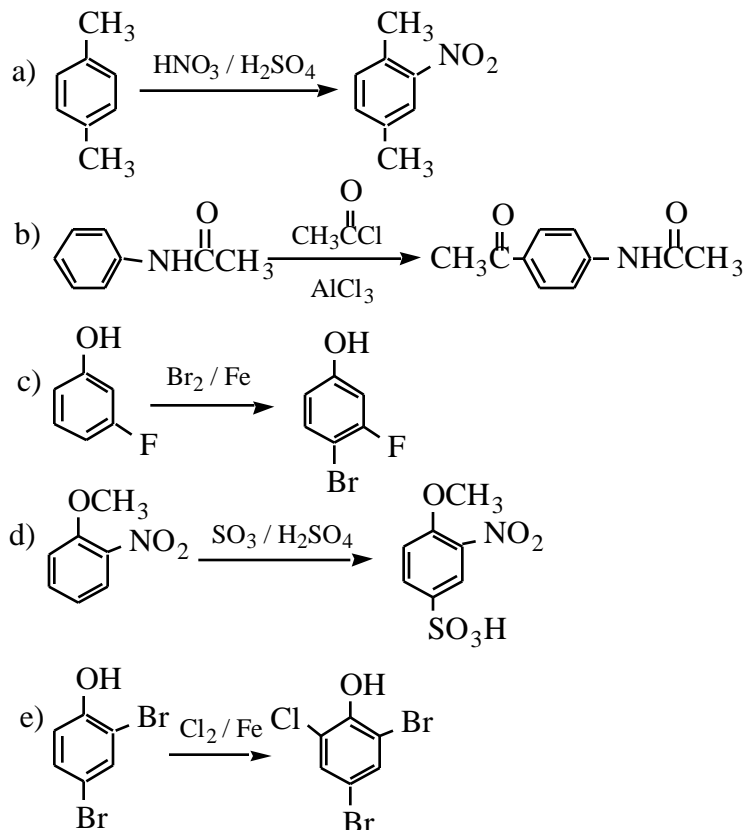
ans.

- a) m-dibromobenzene
 b) o-chlorobenzenesulfonic acid
 c) 1,2,4-trichlorobenzene
 d) p-ethylbenzoic acid
 e) 3-chloro-5-fluoroanisole

4.6 Complete the following reactions.

- a) nitration of p-dimethylbenzene (called p-xylene)
 b) acylation of acetanilide
 c) bromination of 3-fluorophenol
 d) sulfonation of o-nitroanisole
 e) chlorination of 2,4-dibromophenol

ans.



4.7 Draw structures for the substituents below and label them as ring activators or ring deactivators, and show their directing influence.

a) nitro b) acetyl c) hydroxy d) amino e) sulfonic acid f) formyl g) carboxy h) methyl i) phenyl j) halogen

ans.

Activator
o / p directors

CH₃ (methyl)NH₂ (amino)

OH (hydroxy)

Deactivators
m directors

$$\begin{array}{c} \text{O} \\ || \\ \text{CH} \end{array}$$
 (formyl)
SO₃H (sulfonic acid)

COOH (carboxy)

$$\begin{array}{c} \text{O} \\ || \\ \text{CH}_3\text{C} \end{array}$$
 (acetyl)
NO₂ (nitro)

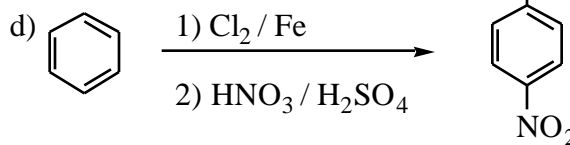
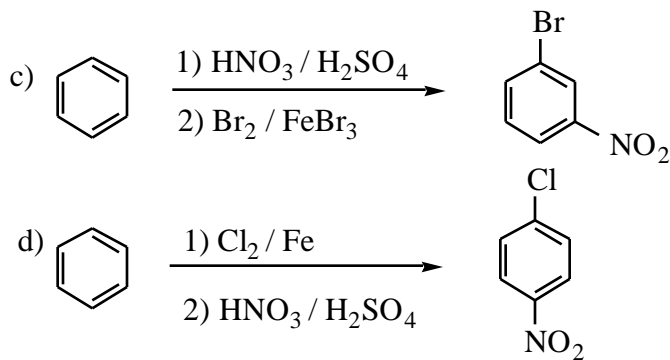
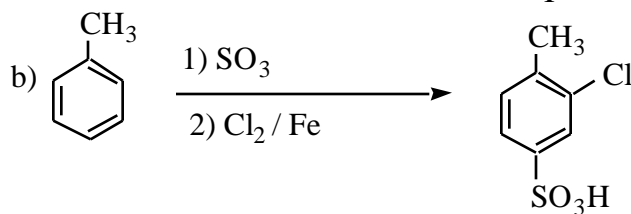
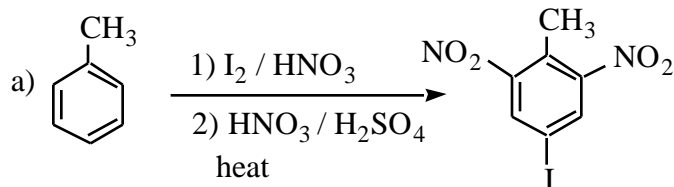
F, Cl, Br, I (halogen)

o/p directors

Note that halogens are deactivators, but are o/p directors

4.8 The reactions below require more than one step. Show how you would complete the sequences.

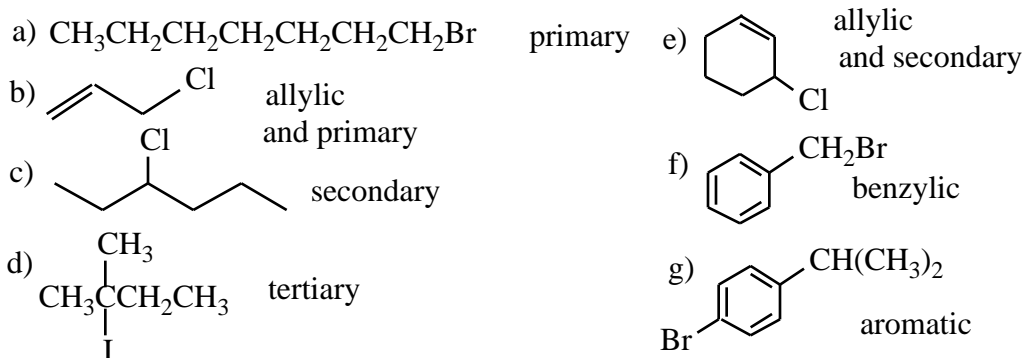
ans.



Chapter 5

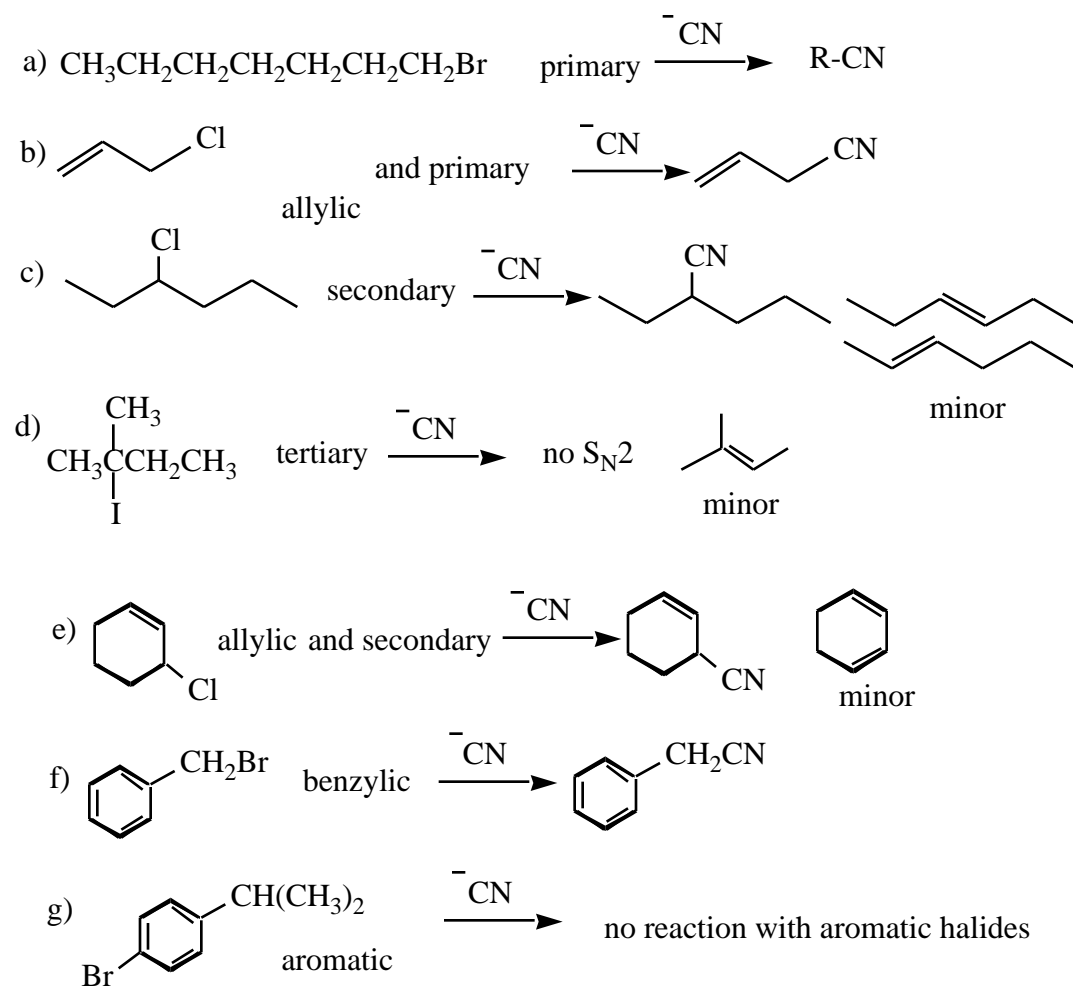
a) 1-bromoheptane b) allyl chloride c) 3-chlorohexane d) 2-iodo-2-methylbutane f) 3-chlorocyclohexene e) benzyl bromide (bromomethylbenzene) f) 1-bromo-4-isopropylbenzene.

ans.



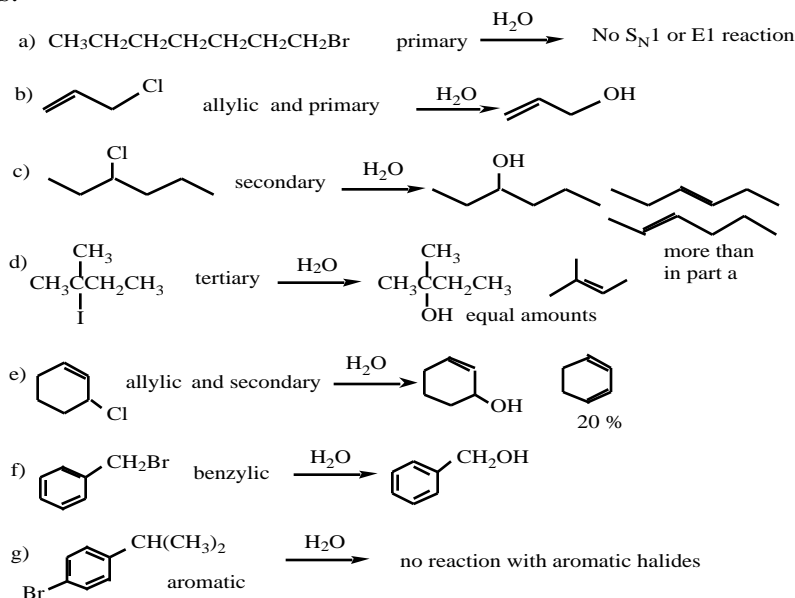
5.2 Use compounds a-g above in the two reactions reaction with cyanide ion ($\text{S}_{\text{N}}2$ conditions).

ans.



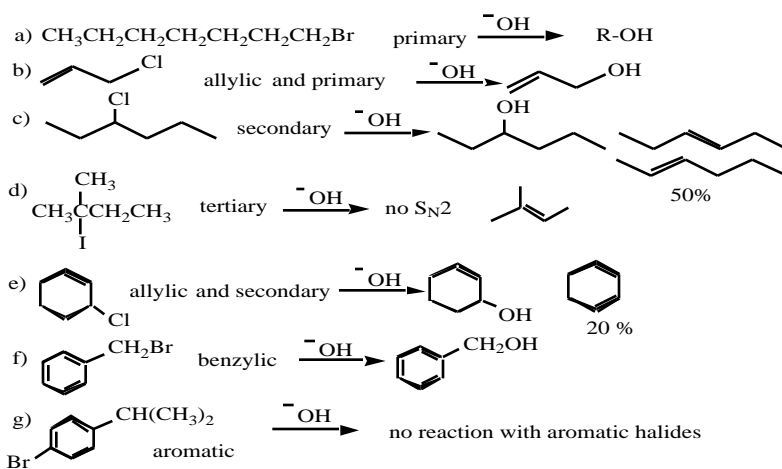
5.3 Use the compounds from a-g above in reactions with acetone and water solution (S_N1 and E1 conditions).

ans.



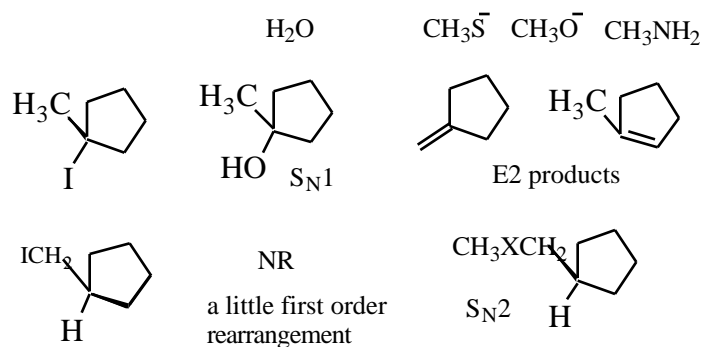
5.4 Use the compounds from a-g above in reactions with conc hydroxide (S_N2 and E2 conditions).

ans.

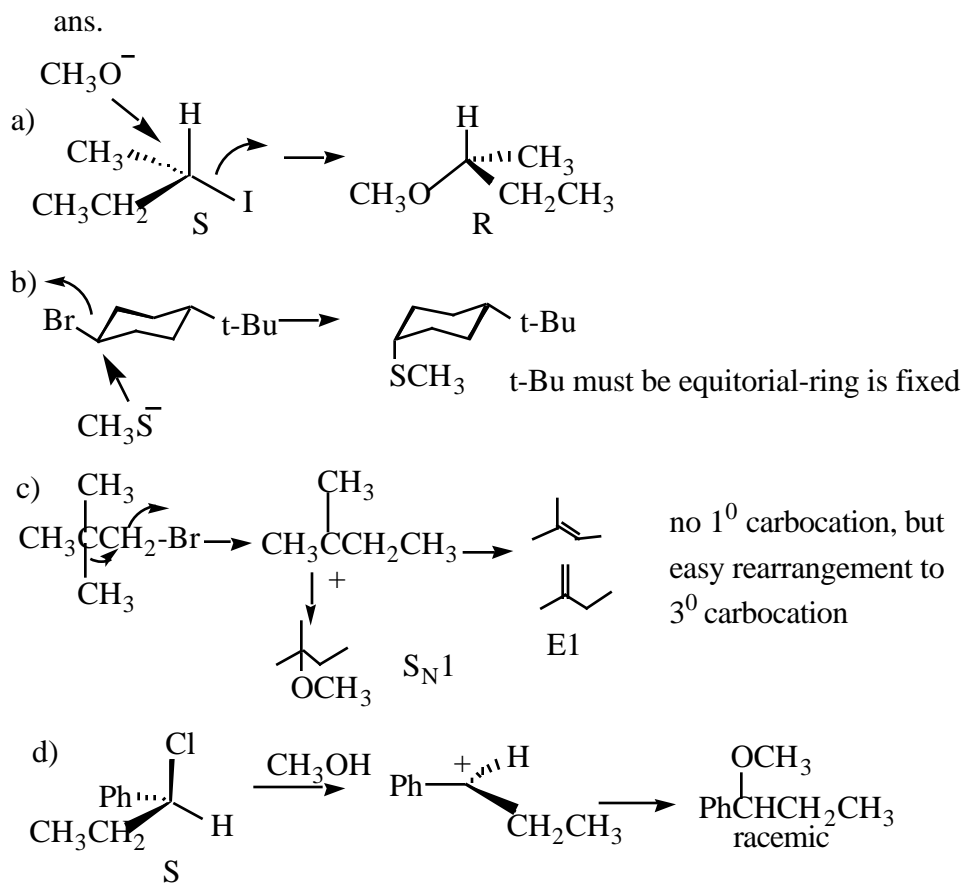


5.5 What would happen with the substrate below on reaction with 1) CH₃S⁻, b) methoxide, and c) water, and d) CH₃NH₂ ?

ans.

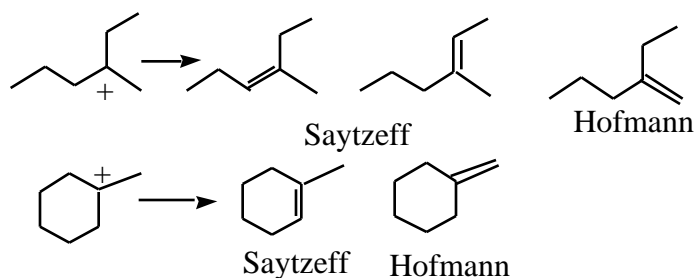


5.6 Complete each reaction below as required.



5.7 Show and label the Hofmann and Saytzeff E1 products from the carbocations below.

ans.



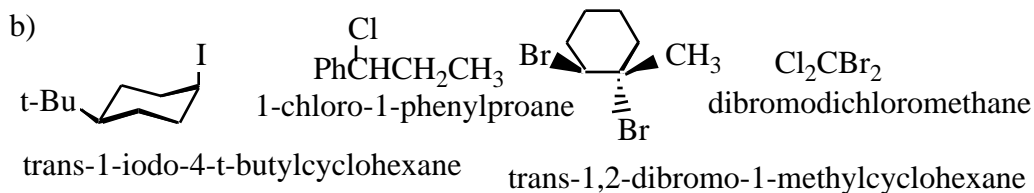
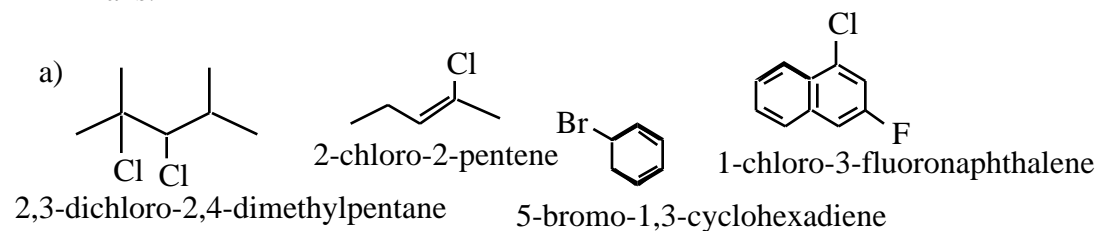
Chapter 6

6.1 a) Provide structures for the names given, and b) provide names for the structures given.

a) names: 2,3-dichloro-2,4-dimethylpentane; 2-chloro-2-pentene; 1-chloro-3-fluoronaphthalene; 5-bromo-1,3-cyclohexadiene.

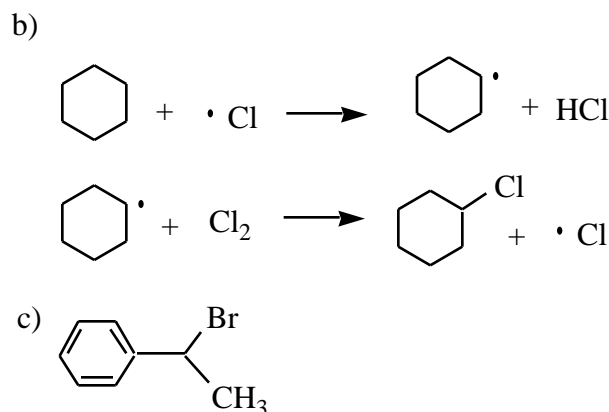
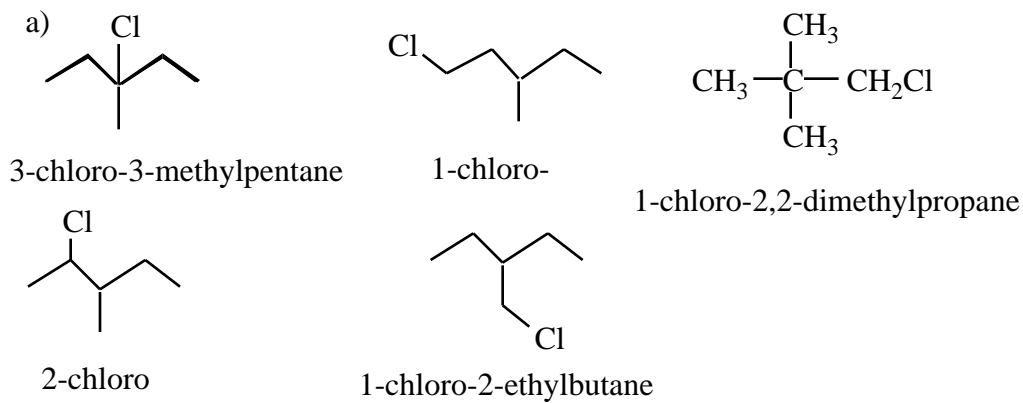
b) structures.

ans.



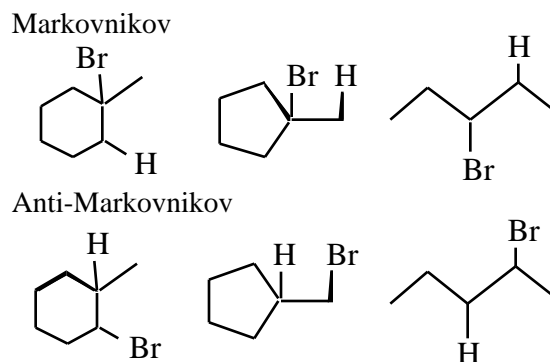
6.2 a) Show and provide names for all of the free radical monochlorination products with 3-methylpentane, and 2,2-dimethylpropane. b) Show the propagation step for the monochlorination of cyclohexane. c) Show the major product from the reaction of ethyl benzene with NBS and peroxide.

ans.



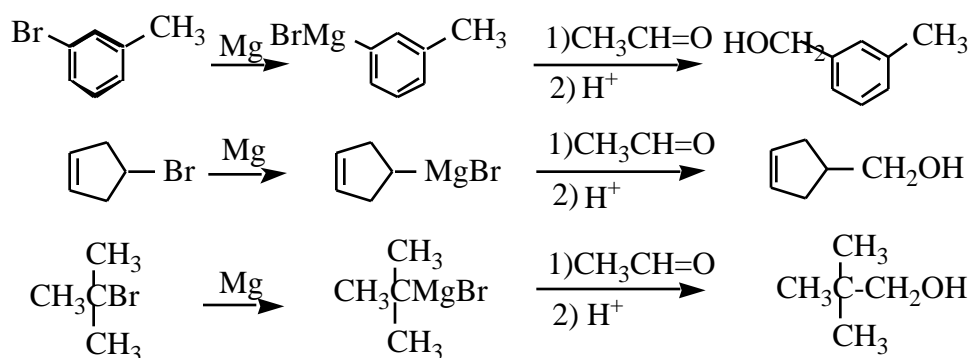
6.3 Show the a) Markovnikov addition and b) the anti-Markovnikov products for addition to the alkenes below.

ans.



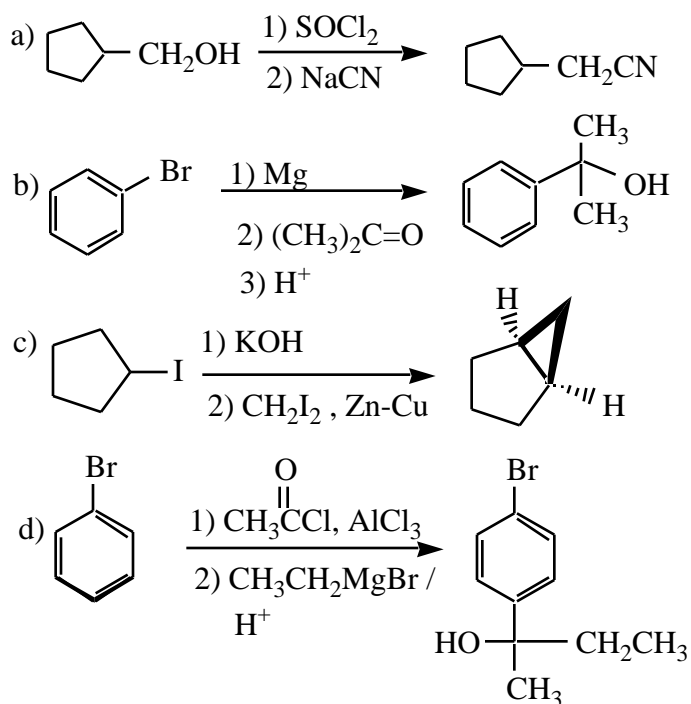
6.4 Give the structures of the Grignard reagents obtained from reaction of each halide with Mg in ether, and show the reaction product for reaction of the Grignard reagent with acetaldehyde ($\text{CH}_3\text{CH}=\text{O}$) and acid.

ans.



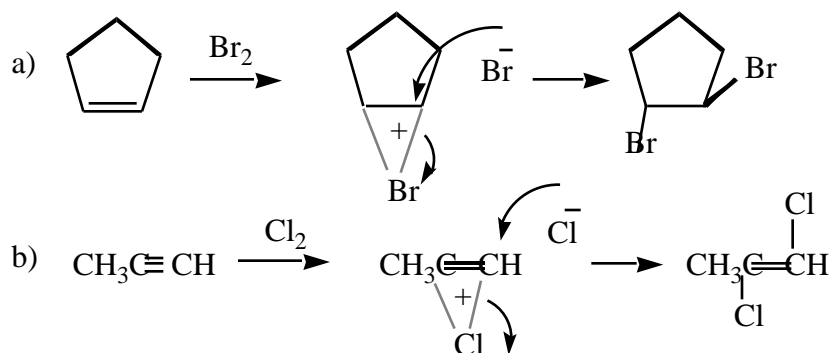
6.5 Give the final product for each sequence below.

ans.



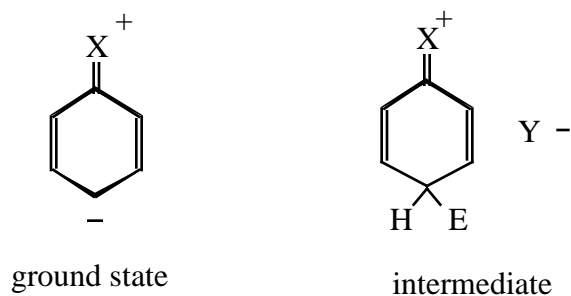
6.6 Show the product and mechanism for the reactions below. Include the stereochemistry.

ans.



6.7 Show the most important resonance structure for each compound below that accounts for the orientation in electrophilic substitution. How does the relative reactivity of these compounds compare with benzene.

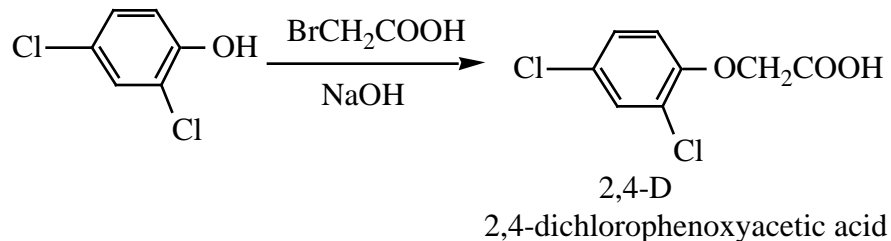
ans.



Halogen deactivates the ring, thus lower reactivity than benzene.
Halogen directs to the ortho and para positions.

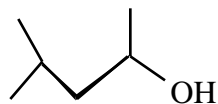
6.8 2,4-D is an important insecticide. Find its structure from any source and suggest a synthesis of it from a phenolic compound (chapter 7) in the S_N2 process.

ans.

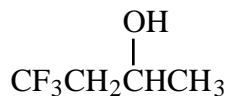


Chapter 7

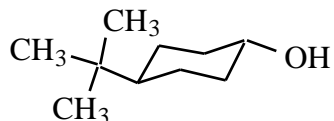
7.1 Provide IUPAC names for the structures a - d, and provide structures for e - h.
ans.



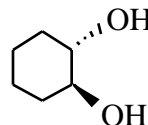
a) 4-methyl-2-pentanol



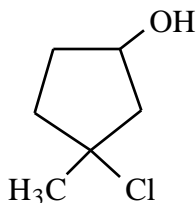
b) 4,4,4-trifluoro-2-butanol



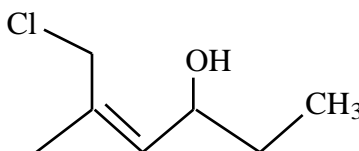
c) trans-4-tert-butylcyclohexanol



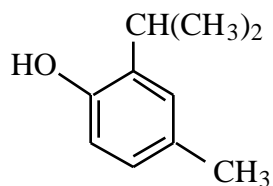
d) trans-1,2-cyclohexandiol



e) 3-chloro-3-methylcyclopentanol

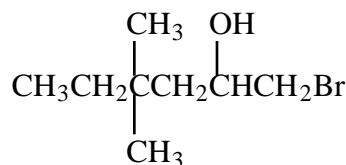


f) 6-chloro-5-methyl-4-hexen-3-ol



g) 2-isopropyl-5-methylphenol

(also known as thymol
from oil of thyme)



h) 1-bromo-4,4-dimethyl-2-hexanol

7.2 Classify the alcohols in problem 7.1 as primary, secondary, tertiary, allylic, phenolic.

ans. All of the alcohols are secondary alcohols except g which is phenolic.

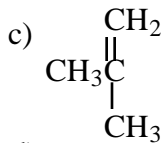
Compound f is secondary and allylic.

7.3 Show the product for the reactions of a - f with hydroxide.

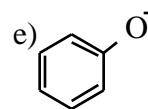
ans.

a) NR

b) $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$



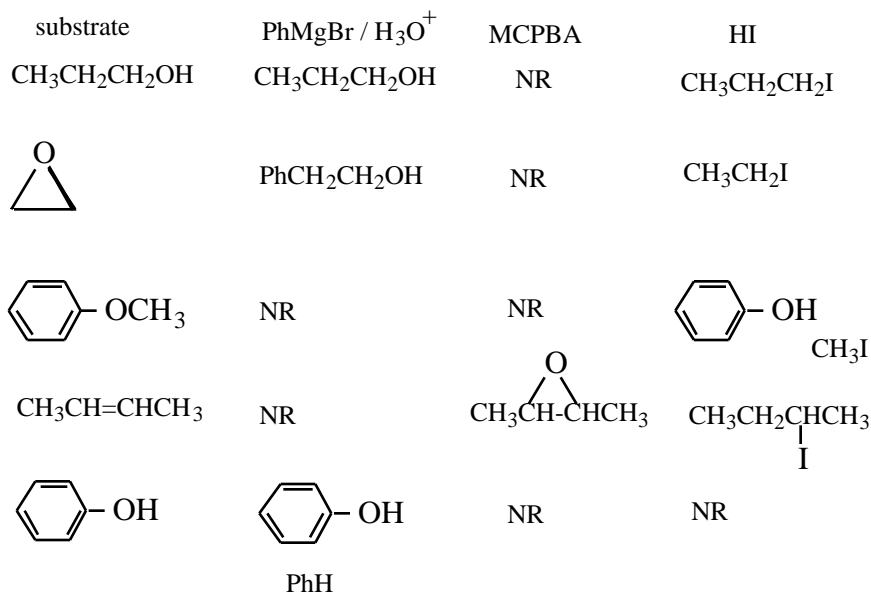
d) NR



f) NR

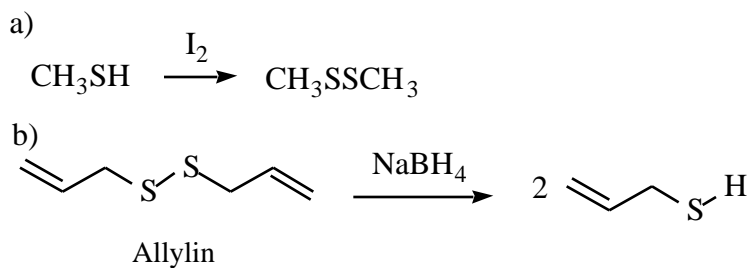
7.4 Give the products for the reactions of each substrate below with PhMgBr / H_3O^+ , meta-chloroperoxybenzoic acid (MCPBA), and HI.

ans.



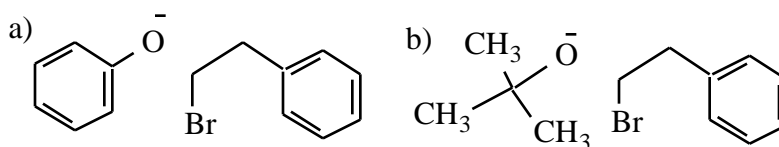
7.5 a) Reaction of methane thiol with iodine gives a new compound, C₂H₆S₂, that is a hamster sex attractant. What is the structure? b) Allylin, sect 7.4g, reacts with NaBH₄, to give a thiol. What is the thiol?

ans.



7.6 Use an alkoxide and an alkyl halide to prepare the ethers below.

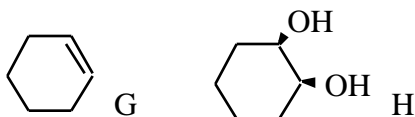
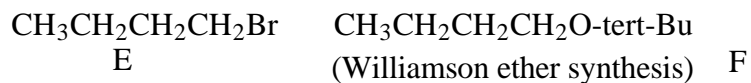
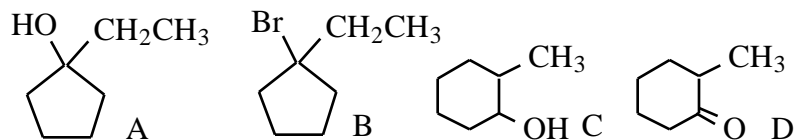
ans.



Can not use aryl halide nor tertiary halide

7.7 Provide structures for the reaction products A - H below.

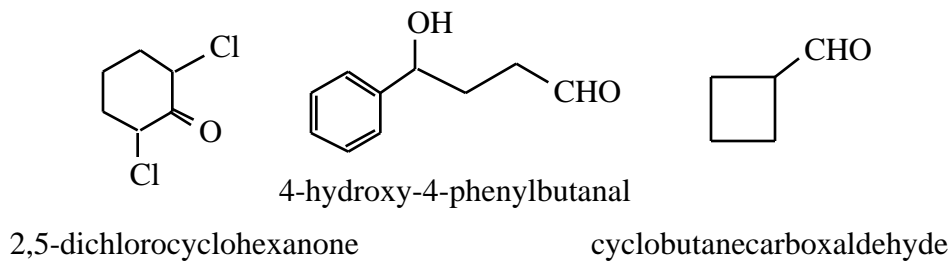
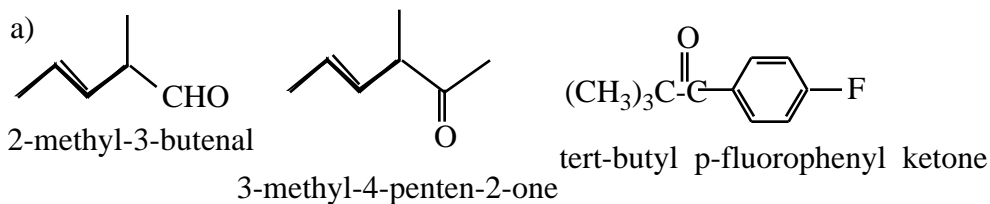
ans.

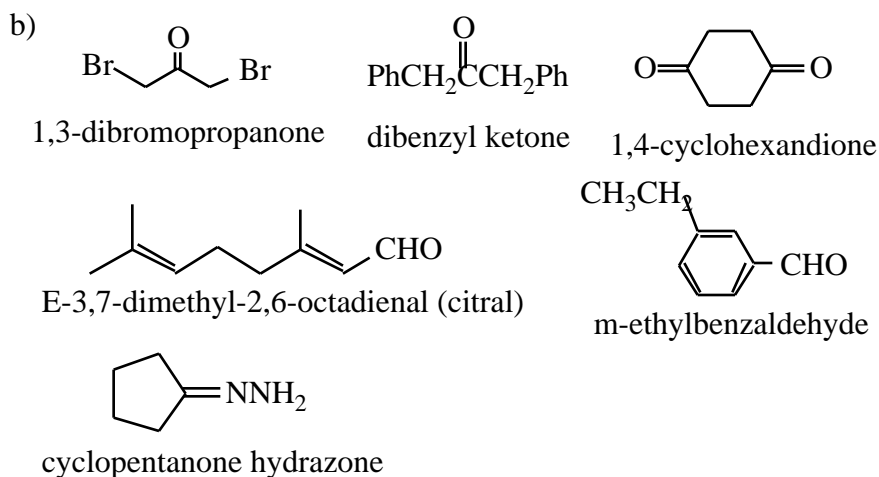


Chapter 8

8.1 Provide the IUPAC names of the compounds in part (a), and provide the structures for the compounds in part (b).

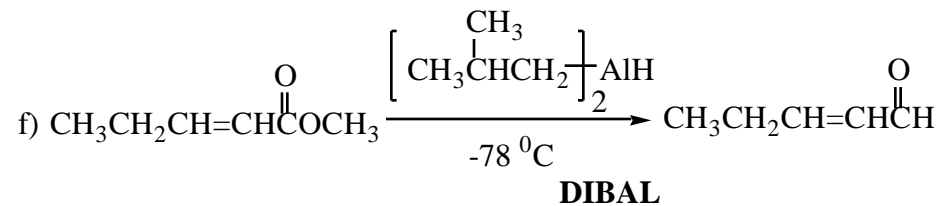
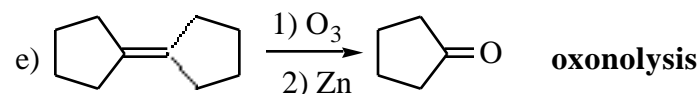
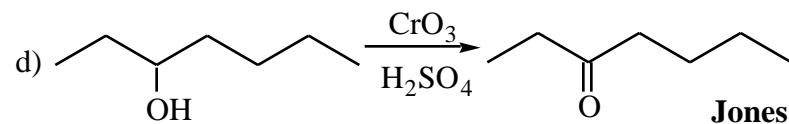
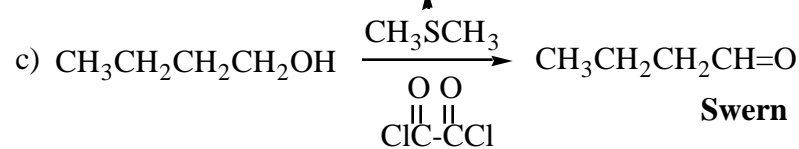
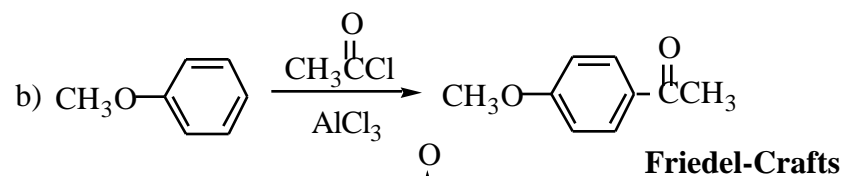
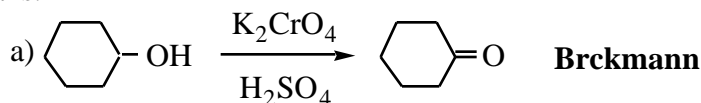
ans.





8.2 Complete each preparation.

ans.

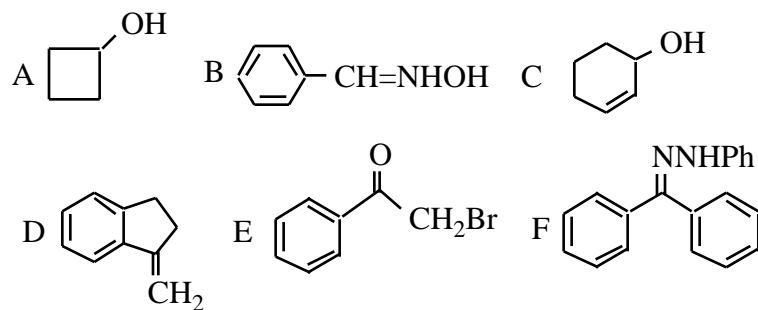


8.3 Complete each reaction.

ans.

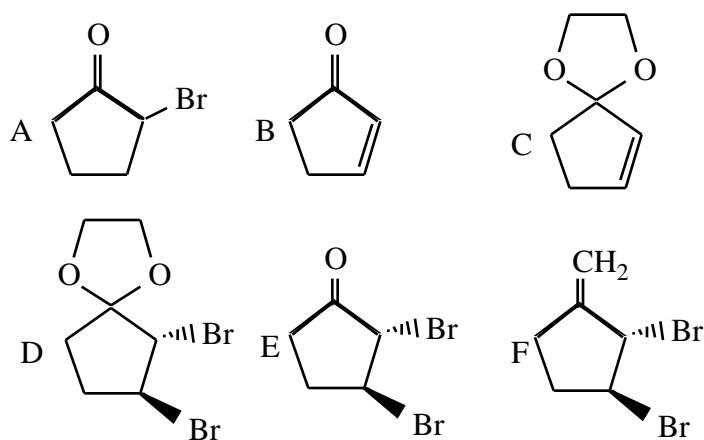
8.6 Show the structures for products A - F.

ans.



8.7 Give the structure for A - F in the sequence below.

ans.

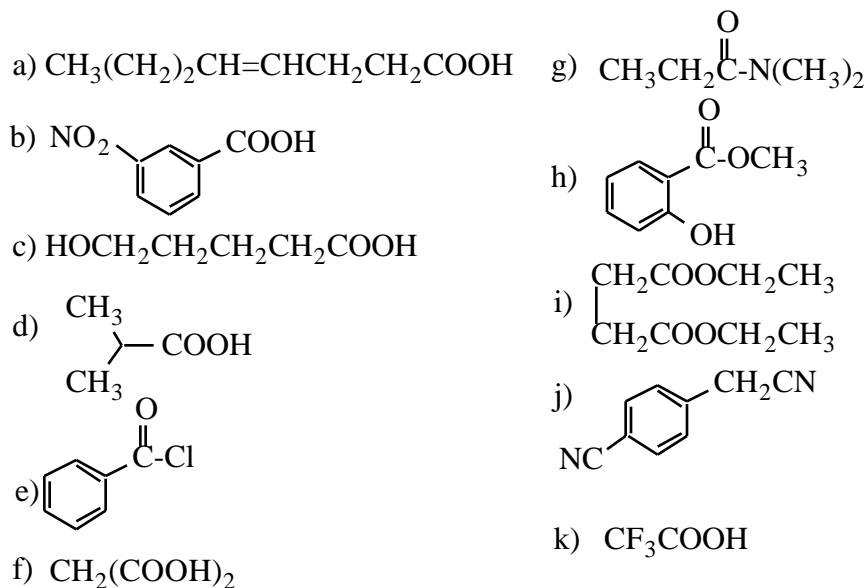


Chapter 9

9.1 Draw the correct structure corresponding to the names given below.

- a) 4-octenoic acid b) m-nitrobenzoic acid c) 5-hydroxypentanoic acid
 d) isobutyric acid e) benzoyl chloride f) malonic acid
 g) N,N-dimethylpropanamide h) methyl salicylate
 i) diethyl succinate j) 4-cyanophenylacetonitrile k) trifluoroacetic acid

ans.

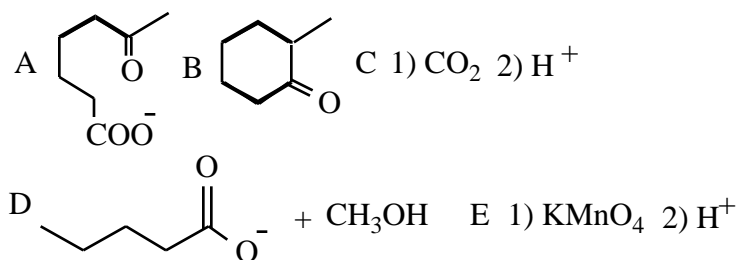


9.2 Give correct IUPAC names for the compounds below.

- a) 4,5-dibromoheptanoic acid b) 1,2-benzenedicarboxylic acid
 phthalic acid
 c) 2-chloropropanoic acid d) N,N-dimethylcyclopentanecarboxamide
 e) succinic anhydride f) 6-fluoro-1-naphthoic acid

9.3 Provide structures for the reagents or products A - D.

ans.

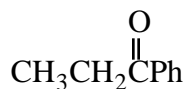
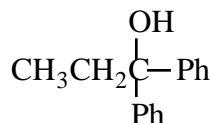
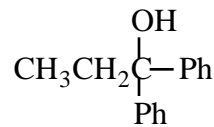
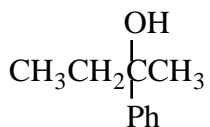


9.4 Give the product for each substrate with the reagents shown.

ans.

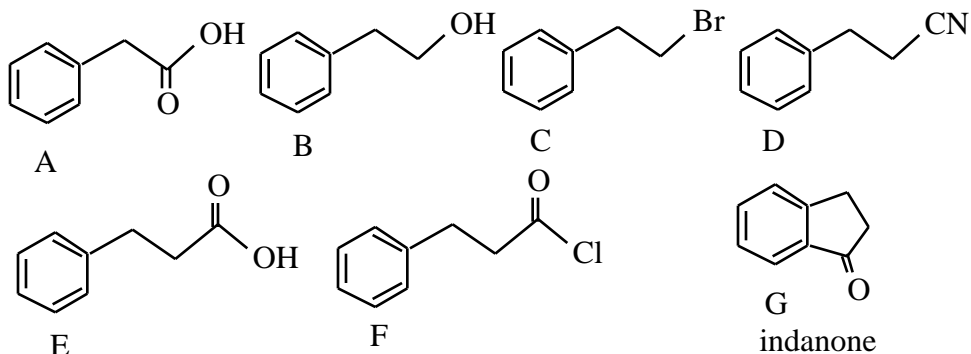
9.6 Give the reaction product obtained from the reaction of $\text{PhMgBr} / \text{H}^+$ (excess if needed) with each compound below.

ans.



9.7 Provide the structures of A - G in the synthesis below. What is the name of the final compound?

ans.



9.8 Give the IUPAC names for A-F above.

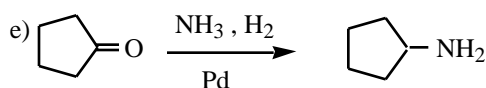
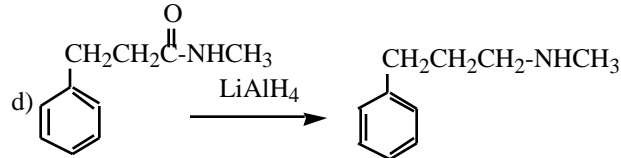
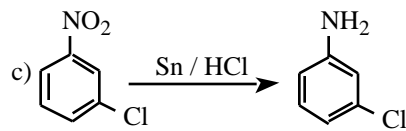
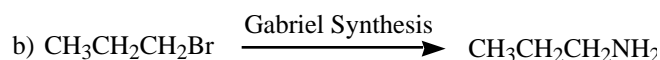
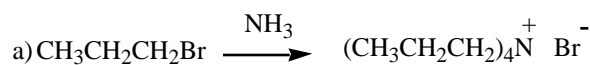
ans.

- A) 2-phenylethanoic acid B) 2-phenylethanol
 C) 1-bromo-2-phenylethane D) 3-phenylpropanonitrile
 E) 3-phenylpropanoic acid F) 3-phenylpropanoyl chloride G) indanone
 starting material name is 1-phenyl-2-propanone

CHAPTER 10

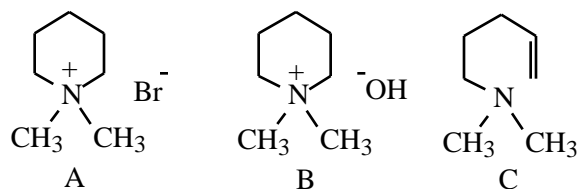
10.1 Provide both the common and IUPAC names for the compounds below.

ans.



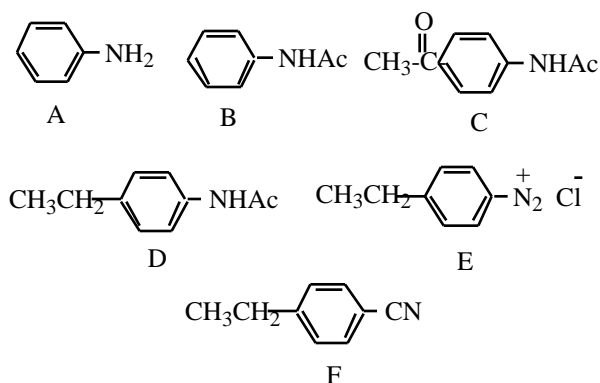
10.4 Provide correct structures for A, B, C below.

ans.



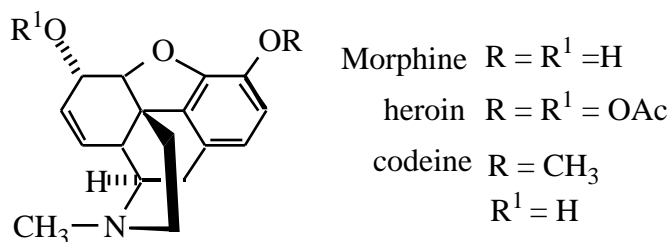
10.5 Give the correct structures for A - F.

ans.



10.6 Three opium derived highly addictive pain-relieving drugs are morphine, heroin and cocaine. The general structure is shown below. Find from any organic source book the structures of the R and R¹ groups to determine the similarities of the compounds.

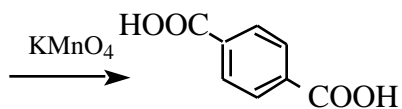
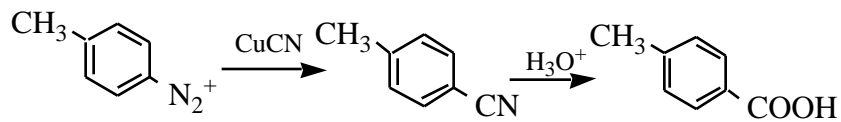
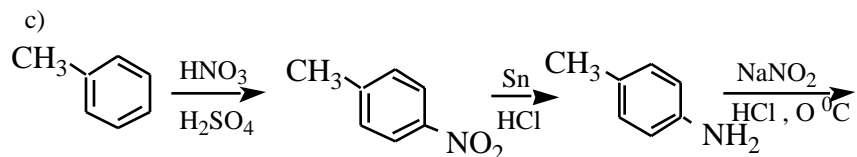
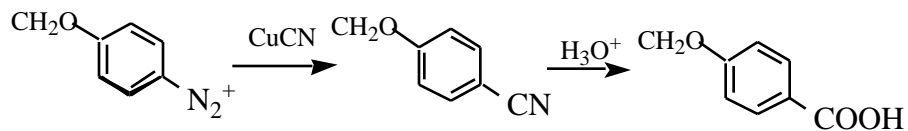
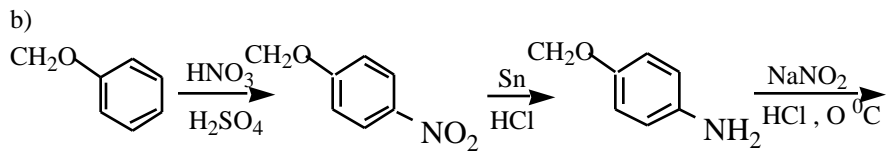
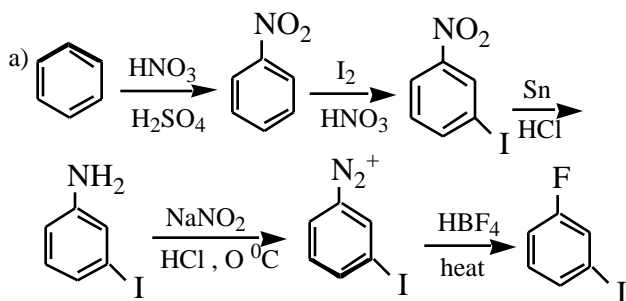
ans.



all three compounds have very similar structures

10.7 Complete the following synthetic procedures by using aromatic diazonium salt intermediates.

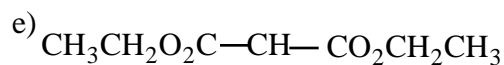
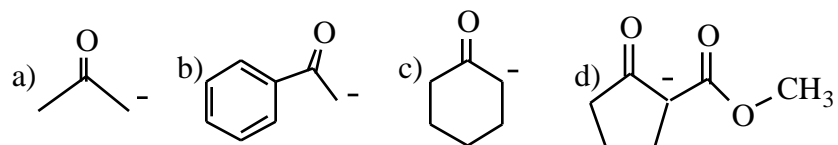
ans.



Chapter 11

11.1 Show the enolates obtained from a) acetone, b) acetophenone, c) cyclohexanone, d) methyl 2-cyclopentanonecarboxylate, e) diethyl malonate

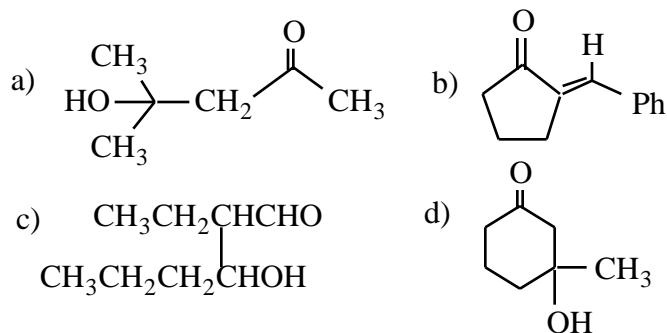
ans.



enolate anions are anions alpha to a carbonyl function

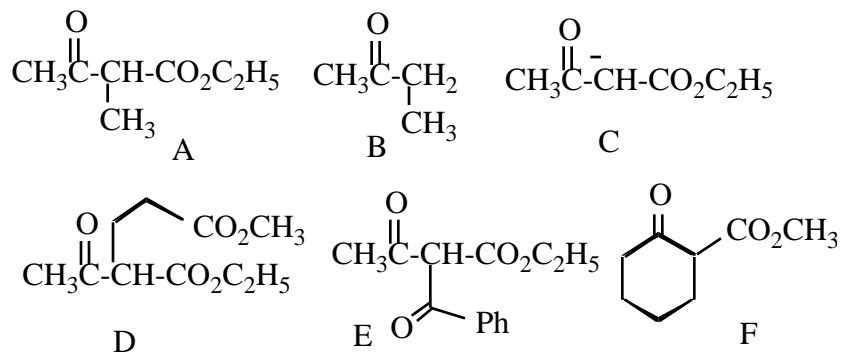
11.2 Show the aldol or crossed-aldol product in each reaction.

ans.



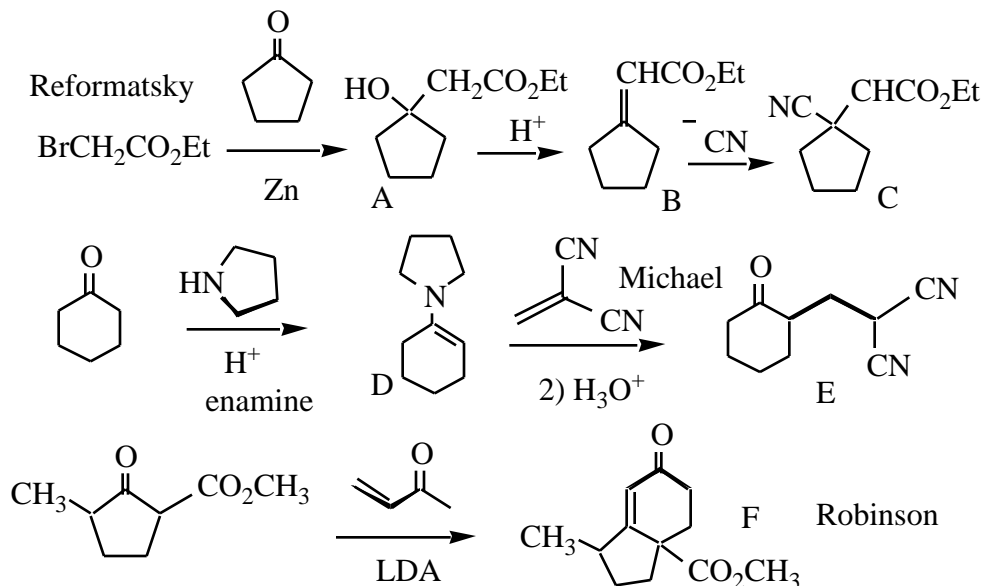
11.3 Show the correct structures for the products A - F.

ans.



11.4 Complete the structures for A - F below. Label the names of the processes.

ans.



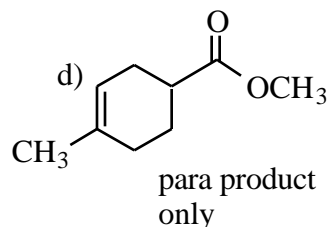
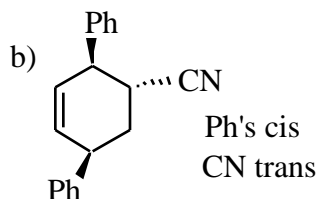
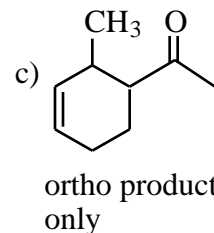
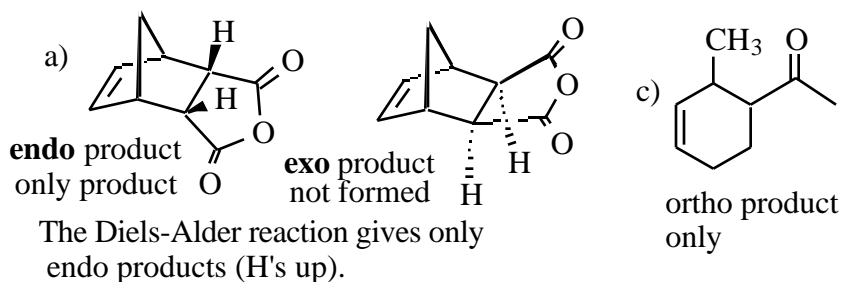
11.5 Make a list of the carbon-carbon bond forming reactions found a) in this chapter, and b) in all of the previous chapters. You should also give an example of each reaction.

ans.

a) This chapter: Aldol and crossed aldol condensations, Claisen and crossed Claisen condensations, Dieckmann reaction, Robinson reaction, Reformatsky reaction, Enamine alkylation, Michael Reaction, Diels-Alder reaction, enolate alkylation (ethyl acetoacetate and diethyl malonate). b) Other chapters: Grignard (organometallic) reactions with carbonyl and carbon dioxide, Friedel-Crafts acylation and alkylation, Vilsmeier reaction, Wittig reaction, S_N2 reactions with acetylide and cyanide nucleophiles, addition of HCN to carbonyl, carbocation rearrangement. There are also many other carbon-carbon bond forming reactions not given in this book. Examples are not listed here, that is the student's job. Most of the other reactions found so far are functional groups modification reactions. The combination of carbon-carbon bond forming reactions and functional group modifications are the backbone of organic synthesis once a good synthetic plan is achieved.

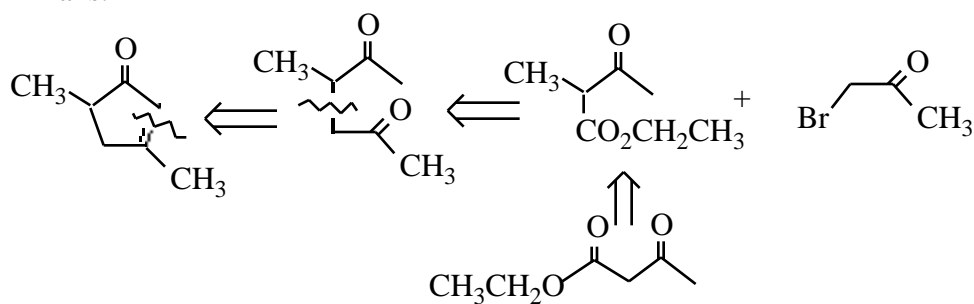
11.6 Complete the Diels-Alder reactions with complete regio and stereoselectivity.

ans.



11.7 Analyze the synthesis of the compound below.

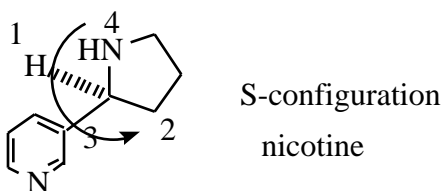
ans.



Chapter 12

12.1 What is the configuration of the stereogenic center in nicotine. Show the priorities.

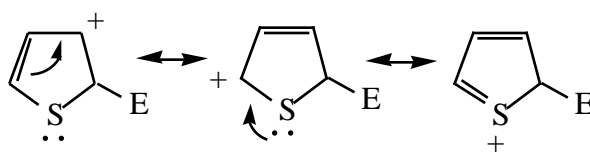
ans.



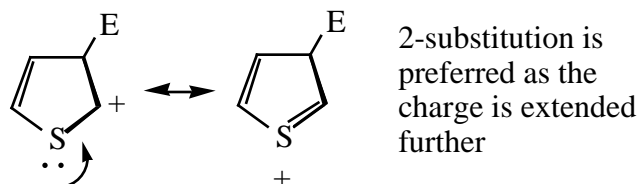
12.2 Draw resonance structures to show the electrophilic substitution at the 2 and 3-positions of thiophene. Explain why thiophene undergoes electrophilic substitution in the 2-position.

ans.

2-substitution



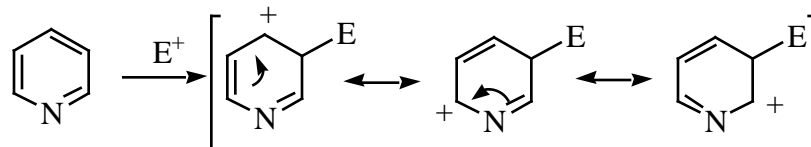
3-substitution



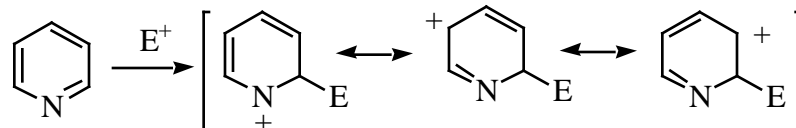
12.3 Show resonance structures for electrophilic substitution in pyridine in the 3-position. Compare with substitution in the 2-position.

ans.

3-position substitution

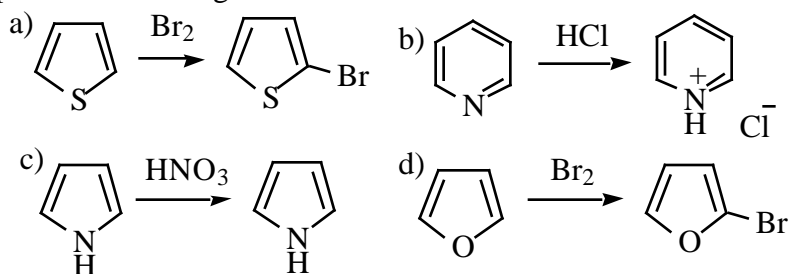


2-position substitution



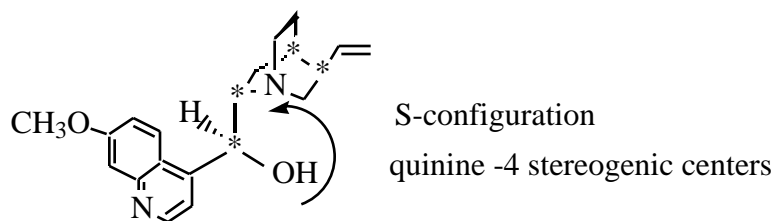
3-substitution does not put a positive charge on a divalent nitrogen atom, but 2 substitution does. Pyridine is deactivated and gives electrophilic substitution with extreme conditions.

12.4 Complete the following reactions.



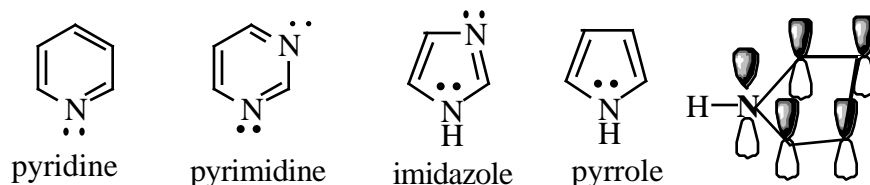
12.5 How many stereogenic centers in quinine? What is the configuration of the alcohol carbon atom?

ans.



12.6 The nitrogen heterocycles pyridine, imidazole and pyrimidine all react at the nitrogen atom with acid to form a quaternary salt, but pyrrole does not. Explain.

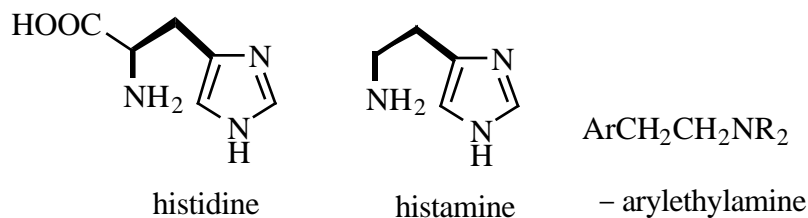
ans.



All of these heterocycles are 6 electron aromatic systems, but only pyrrole needs its nitrogen electrons to have 6 electrons. Thus pyrrole has no non-bonding electrons available for reaction with acid. Pyrrole is not basic, but the others are.

12.7 Histidine and histamine contain a structural unit found in many compounds that affect the central nervous system. Identify that unit.

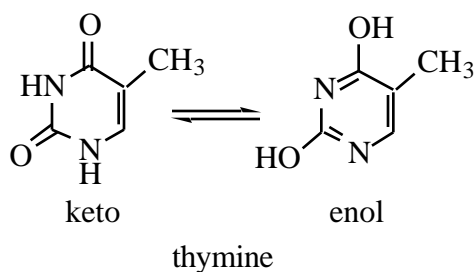
ans.



The unit is the -aryl ethyl amine unit. The aromatic ring can heterocyclic or hydrocarbon. Morphine, quinine and many other compounds also contains the unit.

12.8 The pyrimidine components found in nucleosides have important keto-enol equilibrium. Show the equilibrium with thymine.

ans.



Chapter 13

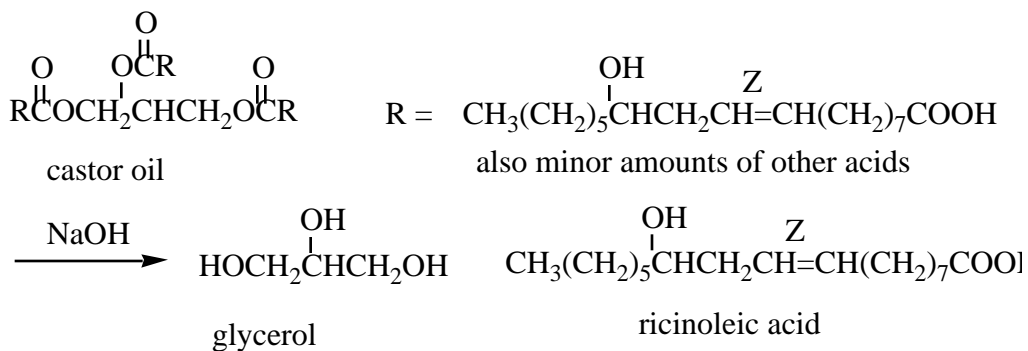
13.1 Write the structure of a fat, soap, steroid, terpene and prostaglandin.

ans.

All of these structures can be found throughout the chapter.

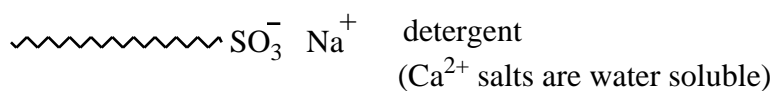
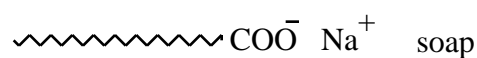
13.2 Show the saponification products of castor oil, but first find the structure of castor from another book.

ans.



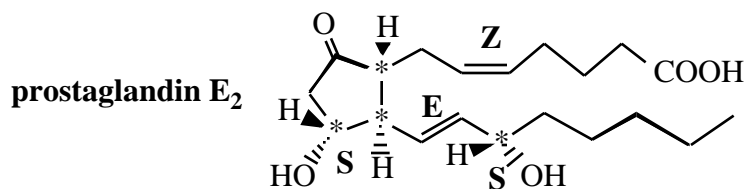
13.3 Show the major components of a soap and a detergent.

ans.



13.4 Write the structure of prostaglandin E₂. How many stereogenic centers are present? What are the configurations of the two alkene units? What are the absolute configurations of the alcohol carbons?

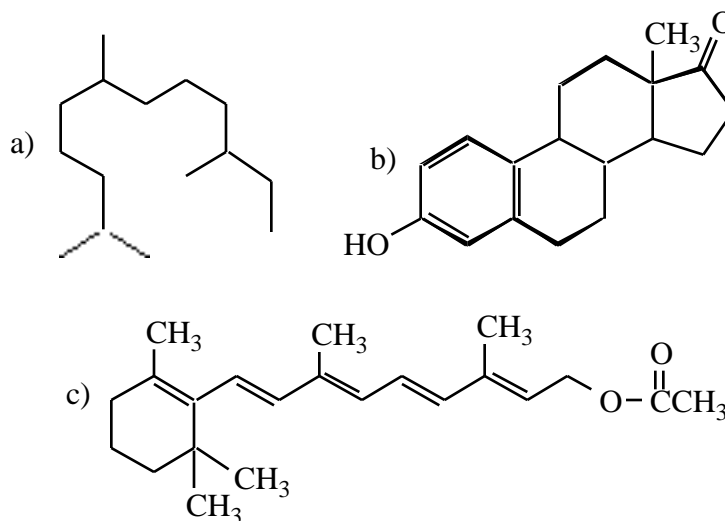
ans.



Four stereogenic centers. 5-ene is Z; 12-ene is E.
10-hydroxy is S; 14-hydroxy is S

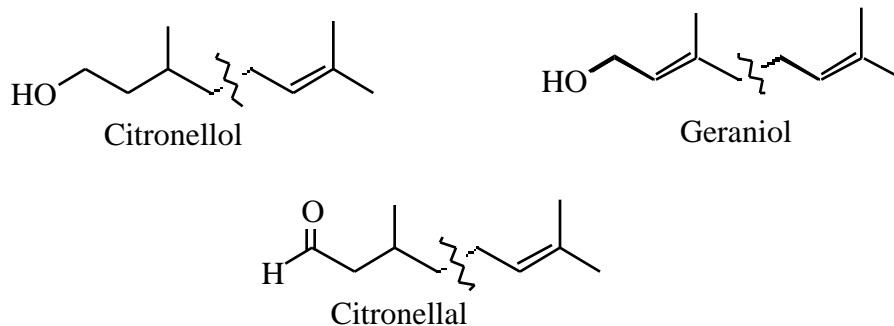
13.5 Predict products of the following reactions.

ans.



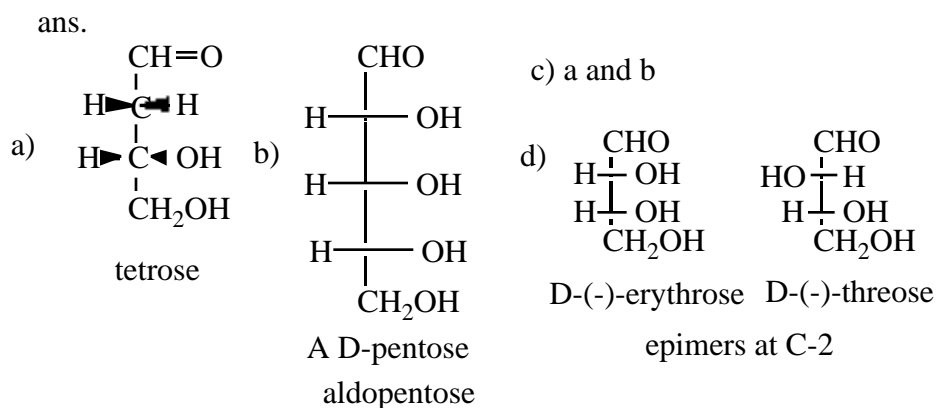
13.6 Identify the isoprene units in citronellal (Ch. 8), citrenellol (Ch. 7), and geraniol (Ch. 7)

ans.

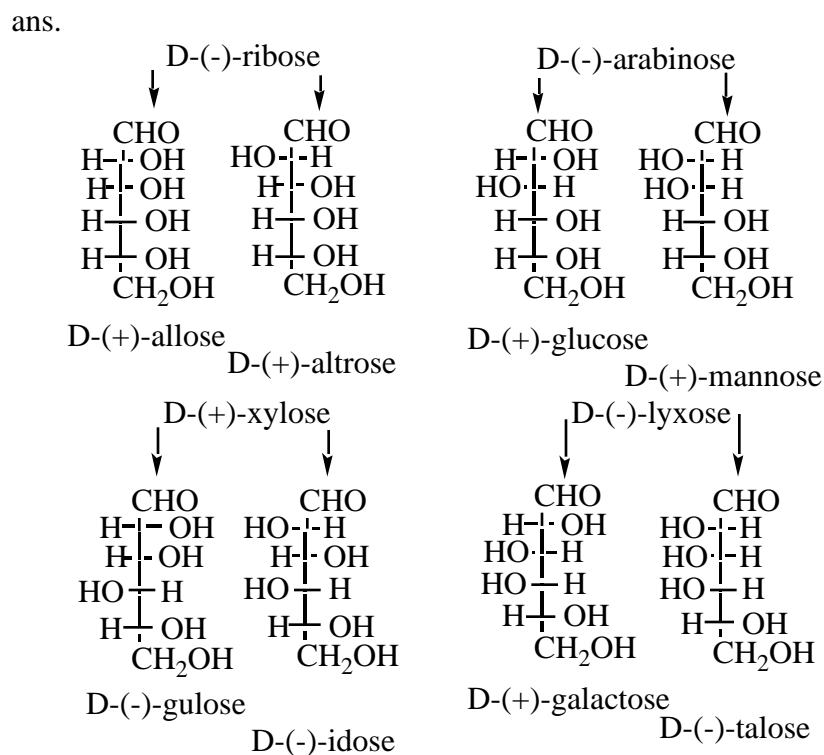


Chapter 14

14.1 Give an example of a) a tetrose b) an aldopentose c) a D-sugar d) epimers.



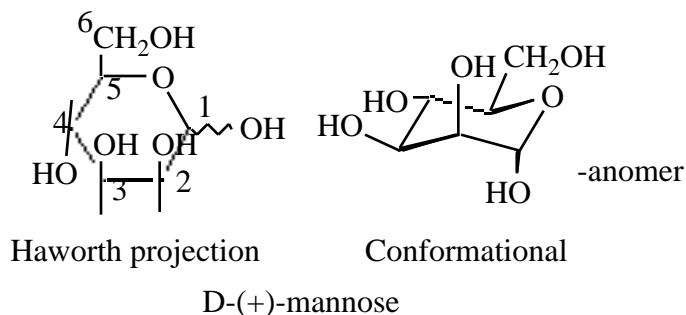
14.2 Show the carbohydrates derived by one carbon extension through the Killiani-Fischer synthesis from: a) D-(-)-ribose, b) D-(-)-arabinose, c) D-(+)-xylose, and c) D-(-)-lyxose.



14.3 What is the relationship between D-glucose and D-mannose? Draw Haworth and conformational structures of D-mannose (found in problem 14.2 answer).

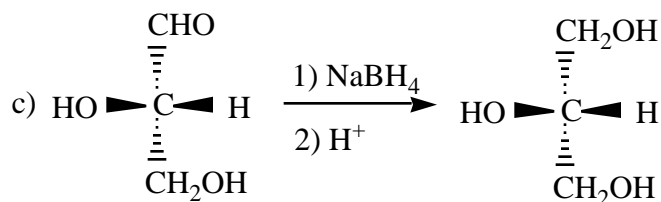
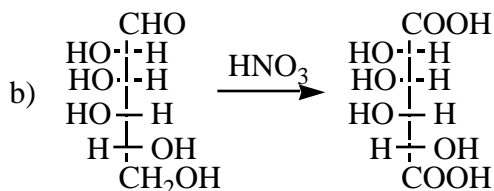
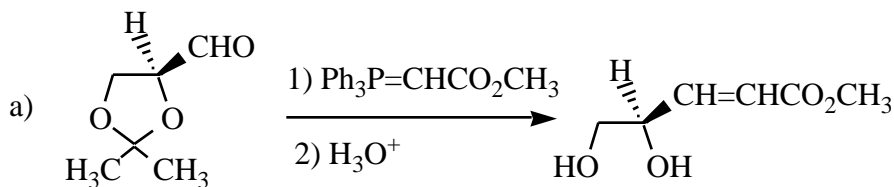
ans.

glucose and mannose are epimers at C-2



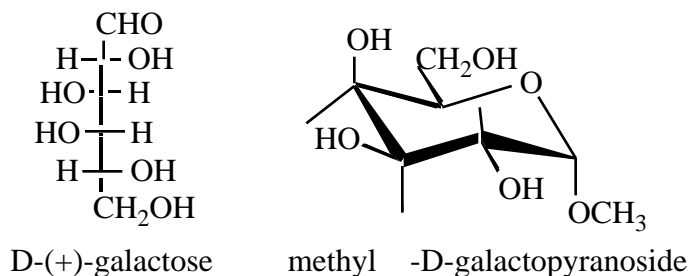
14.4 Complete the reactions below.

ans.



14.5 Show the conformational structure for the methyl α -D-galactopyranoside from D-galactose (problem 14.2)

ans.



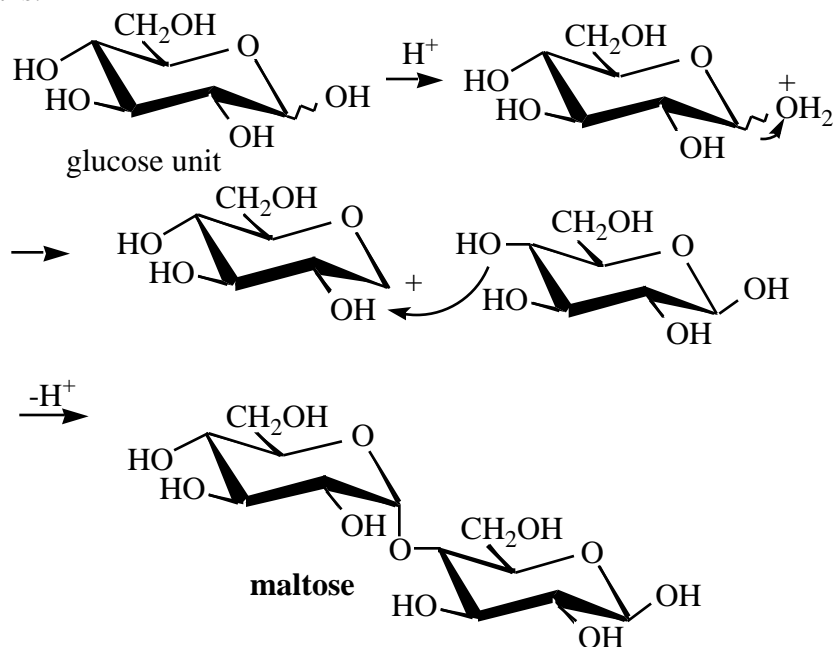
14.6 What is the configuration of the glycoside bond in a) maltose, b) lactose, c) cellobiose and d) sucrose.

ans.

a) alpha, b) beta, c) beta, d) alpha and beta

14.7 Write a mechanism for the conversion of glucose to maltose.

ans.

**14.8** Which polysaccharide would you expect makes up the grasshopper's skin?

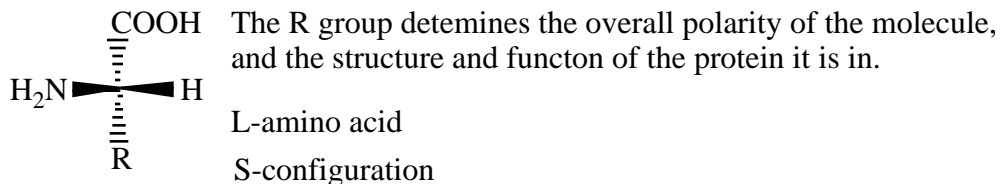
ans.

Chitin

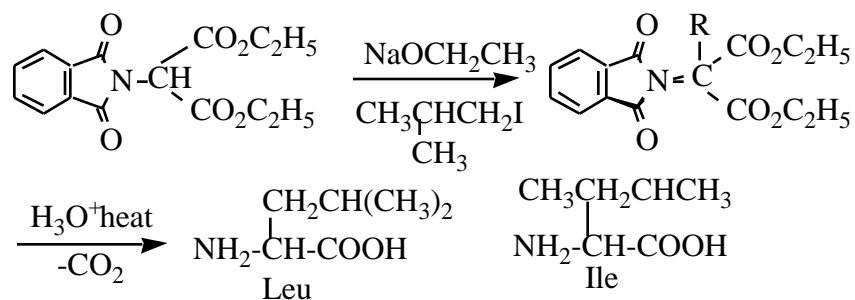
Chapter 15

15.1 What are the distinguishing features of the natural amino acids?

ans.

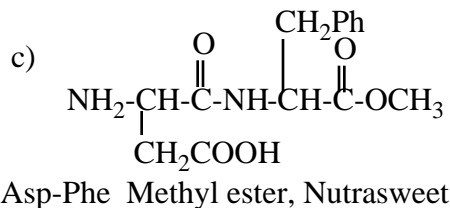
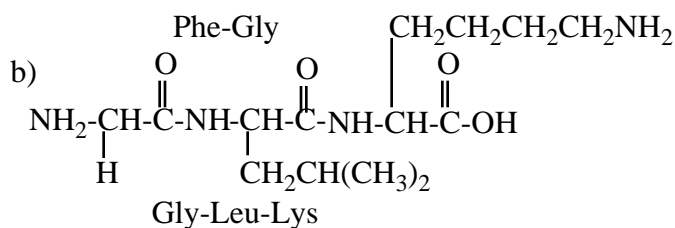
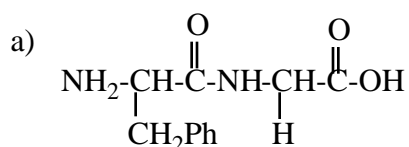
**15.2** Show a synthesis of leucine by using the Gabriel method. What are some of the shortcomings of the method? Would the Gabriel be suitable to prepare Ile?

ans.

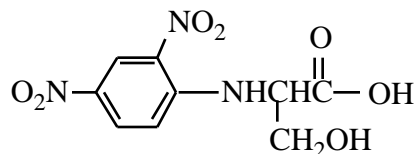


The Gabriel method involves $\text{S}_{\text{N}}2$ substitution and therefore is subject to steric effects. Ile attempts would give much $\text{E}2$ reaction. Also, a racemic mixture would be produced.

15.3 Write structures for a) Phe-Gly, b) Gly-Leu-Lys, c) Nutrasweet.
ans.



15.4 If the N-terminal end of a protein contained Ser, what would be the structure obtained by analysis with Sanger's reagent?
ans.



15.5 A peptide gave the following peptide fragments on partial hydrolysis. What is the structure of the original peptide? Trp-Gly, Val-Ala, Pro-Leu-Val, Gly-Pro-Leu

ans.

Trp-Gly

Gly-Pro-Leu

Pro-Leu-Val

Val-Ala

Trp-Gly-Pro-Leu-Val-Ala

15.6 What are the three classifications of proteins, and what are their characteristics?

ans

Fibrous proteins--insoluble proteins found in collagens (tissue), elastins (tendons) and keratins (hair)

Globular proteins--soluble proteins such as albumins (egg white), globulin (blood), histines (tissue) and protamines (in nucleic acids).

conjugated proteins--combined with other molecules such as glycoproteins (bound with carbohydrates) and lipoproteins (bound with lipids).

15.7 What is meant in protein chemistry by a) primary structure, b) secondary structure, c) tertiary structure, and d) quaternary structure?

ans.

a) primary structure refers to the sequence of amino acids.

b) secondary structure refers to the shape of the sequence such as α -helix or β -pleated sheet.

c)tertiary structure refers to folding of the protein.

d) quaternary structure refers to interactions between two or more proteins.

15.7 What are the basic components of the mechanism of enzyme catalysis?

ans.

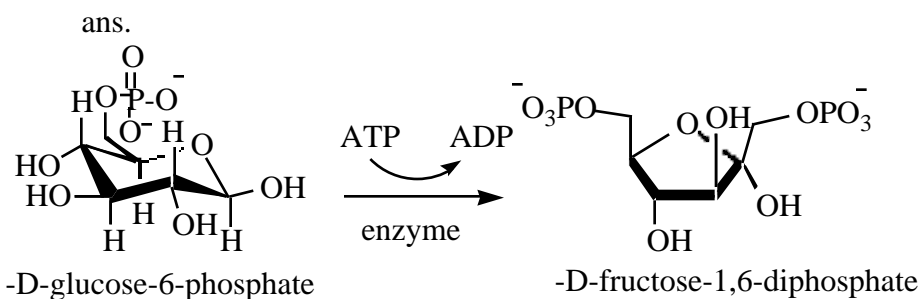
Enzymes use molecular recognition for very specific reactions with substrates. Thus the substrate recognizes (or the enzyme recognizes) the particularly fit and interaction with a substrate. The two components form a complex called the enzyme-substrate complex. A reaction takes place in the complex at an extremely fast rate to produce the products and the free enzyme. The enzyme is available to catalyze more reactions with the same substrate. Coenzymes fit with certain enzymes by molecular recognition and the pair is required to catalyze reactions with their particular substrate.

15.8 Find from another source the reason for insulin not functioning properly with cells in type-2 diabetics?

ans. Once you find out, propose a solution Many diabetic people would appreciate your cure.

16.6 Problem Set

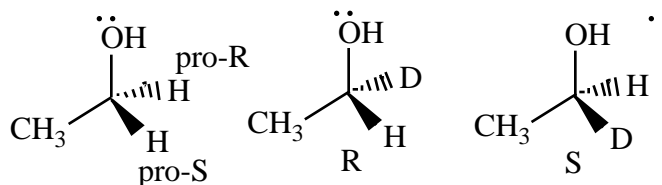
16.1 The first step in the metabolism of glucose (glycolysis) involves the formation of the glucose 6-phosphate shown in this chapter. The next step is the conversion of glucose-6-phosphate by an enzyme and ATP to fructose 1,6-diphosphate. Show the structure of fructose 1,6-diphosphate.



16.2 The oxidation of ethanol by NAD^+ is stereospecific. Only the pro-R hydrogen atom is removed. Which hydrogen atom is the pro-R hydrogen?

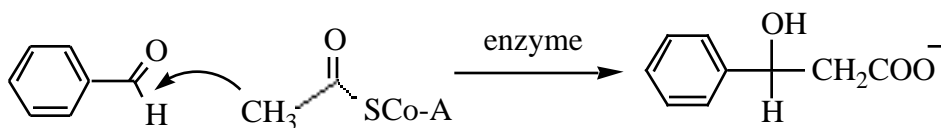
ans.

Ethanol has two hydrogen atoms and thus has no stereogenic center. If you were to replace a hydrogen with deuterium then a stereogenic center would be present. You replace a hydrogen with a deuterium and determine the absolute configuration. If the configuration of the stereogenic center is R, then the H that was replaced is pro-R.



16.3 Show a crossed Claisen reaction between benzaldehyde and acetyl-CoA. Do you expect this to be a significant biological reaction?

ans.



Not very significant. No benzaldehyde in biological systems, and if it were there an enzyme specific for the reaction would be necessary.

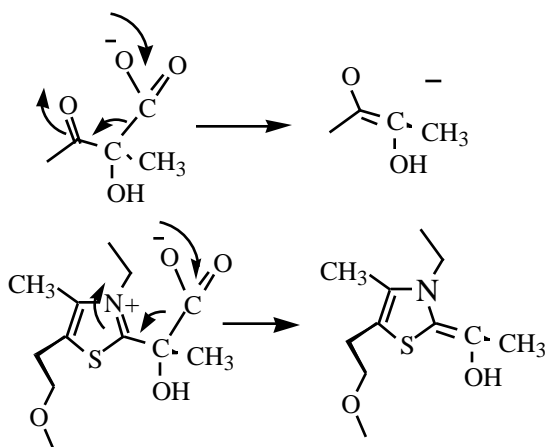
16.4 The decarboxylation of acetoacetic acid produces acetone and carbon dioxide is lost. The decarboxylation of biotin does not release carbon dioxide but instead uses the carbon dioxide in a synthetic step to produce oxaloacetate. Have you seen any organic reactions that use the carbon dioxide lost from acetoacetic acid (or malonic acid) use in a coupled synthetic step?

ans.

There appears to be no similar organic reactions. The CO_2 produced from acetoacetic acid decarboxylation could be bubbled into a Grignard reagent, but dry-ice is a better source of carbon dioxide.

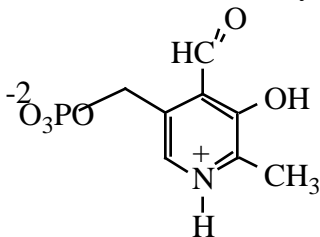
16.5 Show the analogous mechanism between decarboxylation of a α -ketoacid and the thiamine decarboxylation of pyruvate.

ans



16.6 Another biological reagent is vitamin B₆ which displays activity through pyridoxal phosphate as shown in chapter 15. Show the structure of pyridoxal phosphate and explain its function.

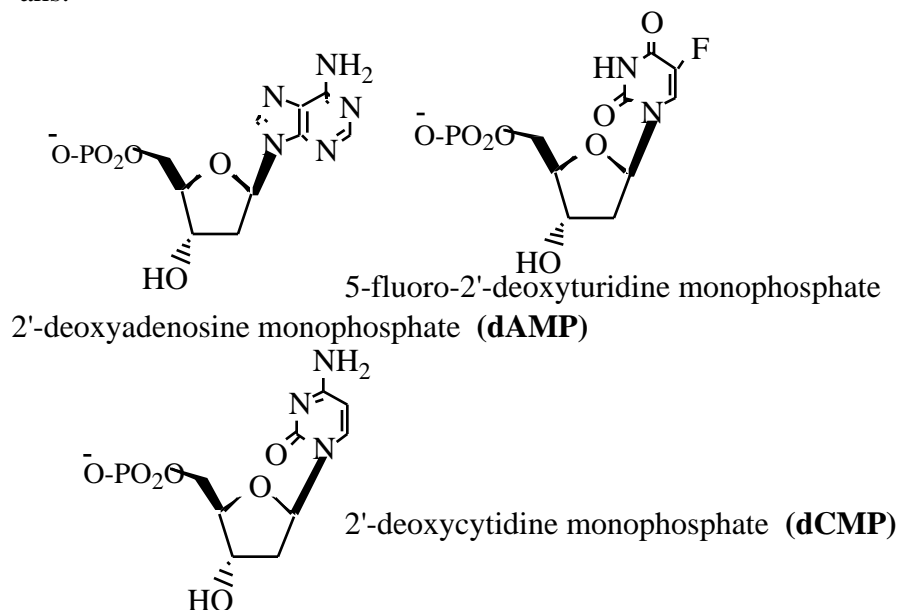
Pyridoxal phosphate functions to accept the amino group of amino acids in the metabolic conversion of the amine to a carbonyl group.



Chapter 17

17.1 Show structures of the deoxynucleosides and nucleotides derived from A, C, and 5FU.

ans.



Nucleotides. Nucleosides are without the PO_3^-

17.2 If a RNA strand contained repeating units of AUA, what would be the structure of the protein synthesized?

ans.

Ile-Ile-Ile----- (poly-Ile)

17.3 Consider the sequence of bases in a DNA segment. (5 end) A-C-C-G-T-A-C-G-G-T-A-T (3 end). What would be the base sequence in a new RNA strand, and what would be the protein that the new RNA would produce?

ans.

5-ACCGTACGGTAT-3 DNA
 3-UGCCAUGCCAUA-5 RNA 3 TO 5
 5-AUACCGUACCGU-3 RNA 5 TO 3
 Ile-Pro-Tyr-Gly protein

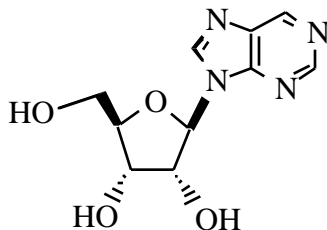
17.4 Classify the bases, A, T, U, C, G as pyrimidine or purine type.

ans.

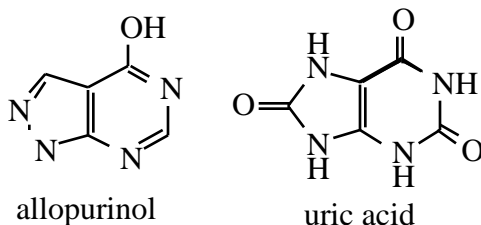
A-purine, T-pyrimidine, U-pyrimidine, C-purine, G-purine

17.5 9-β-D-ribofuranosylpurine is found in mushrooms. What is its structure?

ans.



17.6 Allopurinol is a drug used to reduce the formation of uric acid, a metabolic product from purine bases, and prevent a disease called gout. Suggest a mechanism for the action of allopurinol.



ans.

The N-N bond of allopurinol cannot be converted to a carbonyl group and thus inhibits the enzyme responsible for conversion of purines into uric acid.

Chapter 18

18.1 Find in another book source or on the internet a short biography of Paul Ehrlich.

ans.

Paul Ehrlich was born in Prussia in 1854 (d1915 German). He had little formal training in his early years, but earned a degree in Medicine from the University of Leipzig. He served as a professor at the University of Berlin. He discovered an effective drug for the treatment of syphilis and made many contributions to the field of immunology. He received a Nobel Prize in Medicine jointly with Dr. I. I. Mechnikov in 1908.

18.2 Many different chemical compounds are effective antibacterial agents. How can such a diverse range of structures accomplish this?

ans.

Bacterial cells are much simpler than human cells and often must synthesize many of its own required ingredients. Antibacterials of various structures can work to inhibit the enzyme catalyzed processes for the preparation of the ingredients.

Other agents work by breaking down the fragile bacterial cell wall or by disrupting the cell membrane. Inhibition of protein and nucleic acid synthesis are other modes of actions for antibacterial substances. Thus many paths are available for killing bacterial cells and many chemical structures can participate as antibacterial agents.

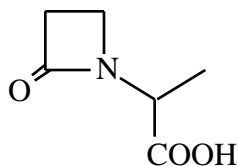
18.3 What are prodrugs?

ans.

Chemicals that are taken as treatments of disease but are not the active agent responsible for the desired effects. Biochemical transformations convert the prodrugs into the active drug. Aspirin, o-acetylbenzoic acid, is a prodrug as it is enzymatically converted into the active drug, salicylic acid.

18.4 What structural unit is found in penicillin and cephalosporin antibiotics?

ans.

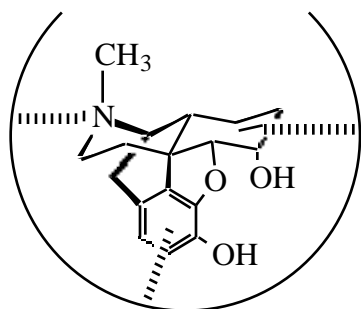


The β -lactam ring system, and the free acid function.

18.5 In addition to the β -phenethyl amine unit found in the opiates, what other structural features affect the potency of opium drugs?

ans.

In the theory of drug-protein interactions, the opiate receptor has three binding sites. The amine binding site, the phenol binding site, and the site for the other side of the molecule. The beta-phenethyl amine structure shapes the molecules for optimal binding of the three structural units.



Morphine

18.6 The accidental finding of drug activity is very important in drug therapy. How could nitroglycerine be found to be a heart stimulant.

ans.

Nitroglycerine as discovered by the workers in the explosives industry who experienced severe headaches on exposure to nitroglycerin. Studies found that

nitroglycerin dilated blood vessels in the heart. Isoamyl nitrite and other organic nitrites have similar heart stimulating effects, being discovered by workers handling the chemicals.

18.7 What is a common structural feature of anti-viral drugs?

ans.

Very few effective anti-viral drugs are known, but most have purine or pyrimidine ring systems that are capable of forming nucleosides and incorporating into the DNA or RNA of a virus.

18.8 If possible search the internet for molecular modeling. Or obtain use of a chemistry modeling program such as Chem D. Draw structures of the drugs in section 18.6 and observe their 3D shapes. Try to model a protein and show its interaction with a drug.

ans.

No particular answer, this involve computer experimentation.

18.9 What structural unit is found in many hormones, anti-inflammatory agents, and reproductive drugs.

ans.

The steroid nucleus. This could indicate that the protein receptors for the three agents are similar in structure.

Chapter 19

19.1 List the types of radiation, infrared, ultraviolet, and radio in order of increasing energy. (most energetic last). Which frequency is associated with NMR spectroscopy.

ans.

radio < infrared < ultraviolet Radio frequencies are used in NMR spectroscopy.

19.2 If the frequency difference between an observed NMR peak versus TMS is 200 MHz, what is the chemical shift in ___ppm on a spectrometer operating at 100 MHz. What is TMS and its purpose? What kind of peak is likely being observed if it occurs as a singlet?

ans.

The chemical shift = $200/100 = 2$ ppm. TMS stands for tetramethylsilane, $(\text{CH}_3)_4\text{Si}$, and its frequency is set by the operator of the spectrometer at 0 MHz. All other peaks are referenced to the TMS peak, which occurs at higher field than most other peaks.

The peak being observed is in the alkane region and as a singlet is likely to be a methyl.

19.3 Predict the chemical shifts and spin-spin coupling spectrum for $(\text{CH}_3)_2\text{CHOCH}_2\text{CH}_3$.

ans.

The methyls of the isopropyl would occur around 1.5 ppm and be observed as a doublet because of splitting from the neighboring CH. The CH of the isopropyl would be observed around 3 ppm and would be split into a septet (seven peaks) because of the 6 neighboring methyl protons. The methyl of the ethyl group would occur around 1.5 ppm and would be seen as a triplet because of splitting with the neighboring CH_2 . The CH_2 of the ethyl would occur around 2 ppm and be observed as a quartet because of the neighboring methyl group.

19.4 A compound, $\text{C}_5\text{H}_{10}\text{O}$, gives the Ir and NMR spectra shown below. What is the structure of the compound?

ans.

The compound is 2-pentanone. The ir shows a strong $\text{C}=\text{O}$, and the NMR show a methyl singlet and three separate multiplets for the propyl side of the ketone.

19.5 The mass spectrum of aspirin is shown below. Identify the origins of the peaks listed.

ans.

180 is the molecular ion (molecular mass); 139 is the molecular ion minus a radical C_2HO from the ester group; 120 is the loss of the elements of CO_2 and CH_4 .

19.6 The ^{13}C NMR and Ir spectra of $\text{C}_2\text{H}_3\text{N}$ are shown below. What is this simple compound. What is the large Ir peak?

ans.

The compound is acetonitrile, CH_3CN . The Ir shows the CN peak at 2100 cm^{-1} , and the CN and CH_3 groups as singlets in the carbon NMR spectrum.

