COURSE GUIDE

CHM 203
ORGANIC CHEMISTRY II

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INTRODUCTION

Chemistry is the study of matter. Matter is studied under the three divisions of chemistry, viz: Physical, Inorganic and Organic chemistry. While inorganic and physical chemistry are detailed elsewhere, organic chemistry which deals with hydrocarbons, their numerous derivatives in addition to their physical and chemical properties will be studied in this text. This course is coded CHM 203. It forms the second part of organic chemistry courses you will encounter during the course of your programme in chemistry and related programmes. CHM 203 is a two credit unit course. The course content consists of 3 inter-related and interesting modules.

WHAT YOU WILL LEARN IN THIS COURSE

In this course, you will learn about the electronic concepts in organic chemistry where we discussed the various factors affecting the structure and physical properties of organic compounds, availability of electrons and stereochemistry, the relationship between the structure of organic compounds and their reactivity. Also this course describes Aromatic hydrocarbons and their derivatives in addition to their physical and chemical properties which determine their uses in the industry. You will find several **In-Text Questions** (ITQs) and **Self-Assessment Questions** (SAQs), with answers provided as well as activity exercise in each unit.

COURSE AIMS

The course aims at giving you an in-depth knowledge of the physical and chemical properties of selected, important classes of organic compounds thus giving you a solid foundation in organic compounds of industrial importance. The aim of this course can be summarized as follows:

1. Discuss the Relationship between the structure and reactivity of organic compounds.
2. Acquaint learners with Aromatic and polynuclear aromatic compounds.
3. To study the determinants of the properties and identification of selected classes of organic compounds.
4. To determine the importance of molecular architecture on physical properties of organic compounds.

COURSE OBJECTIVES

Each unit has its respective objective which you should always refer to in your course of study so that derailment from set target will be avoided. Always make a list of your attainment after each unit and compare them with the objectives listed by the course developers. Thus the overall objective of the course can be summarized as:

a) Familiarize ourselves with molecular structure of organic compounds.
b) Note the characteristics of selected groups of organic compounds.
c) Describe how compounds of the same group can be identified.
d) Describe the importance and uses of organic compounds

CONTENTS

CHM 203 Organic Chemistry II consists of three modules which have been painstakingly put together to take you through a unique, structured learning experience.

WORKING THROUGH THIS COURSE

In order to be able to successfully complete this course, you are required to carefully study each unit along with recommended textbooks and other materials that may be provided by the National Open University. You may also need to exploit other e-reading such as internet for further useful information on the course.

Each unit contains SAQs and ITQs. At certain points in the course you would be required to submit assignments for grading and recording purposes. You are also to participate in the final examination at the end of the course. It is recommended that you devote an abundant time for reading and comprehension. It is highly necessary that you avail yourselves the opportunity of attending the tutorial sessions where you will be able to compare your understanding of the course contents with your colleagues.

COURSE MATERIALS

The course materials are made up of the following sections:

COURSE GUIDE

This describes how best to study this major aspect of organic chemistry and it also spells out what constitute the course itself.

STUDY UNITS

Each study unit gives an overview of the content to be covered in this course. This is sub-divided into sub-headings as introduction, objectives; that is what to focus on, the content, conclusion, summary, references and a list of other materials to be consulted in order to augment or facilitate the student's understanding and finally the tutor-marked assignments.

Module 1 Electronic Concept and Stereochemistry

Unit 1	Factors Affecting Structure and Physical Properties of Organic Compounds
Unit 2	Factors Affecting Availability of Electrons
Unit 3	Stereochemistry

Module 2 Functional Groups and Reactivity in Organic Chemistry

Unit 1	Functional Group Chemistry of Main Class Organic Compounds
Unit 2	Alkanes, Free Radical Substitution Reactions in Alkanes and The Reactivity-Selectivity Principle
Unit 3	Various Organic Reactions
Unit 4	Nucleophilic Substitution and Elimination Reactions

Module 3 Aromatic Compounds

Unit 1	Benzene and other Aromatic Compounds
Unit 2	Reactions in Aromatic Compounds

ASSIGNMENT FILES

The files contain tutorial questions that cover the whole course. These will enable you to assess your understanding of the course by the facilitator. The marks scored for the assignments will be stored and will constitute 30% of the final score at the end of the semester examination.

PRESENTATION SCHEDULE

The method of operation, that is, self-tutored and face to face facilitation with respect to the course will be available at the information desk at different study centres nearest to you.

You are welcome to the study of CHM 203 - Organic Chemistry II, one of the tripods on which the study of chemistry stands.

MAIN COURSE

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MODULE 1 ELECTRONIC CONCEPT AND STEREOCHEMISTRY

INTRODUCTION

The study of organic chemistry involves the reactions and interactions of molecules. Since molecules are composed of atoms, it is necessary to study the structure of atoms and how they contribute to the properties of molecules. In this module we will study the factors that affect the structures and physical properties of organic compounds. This knowledge will make learning about organic molecules a little easier. Because organic chemistry is a study of compounds that contain carbon and to have a better understanding of the properties of organic molecules, one has to study their three-dimensional (3D) structure. Why is this important? Our perception of smell and taste depends, in many instances, on the 3D structure of molecules. Enzymes are very selective in the 3D structure of the molecules they interact with. The effectiveness of drugs is highly dependent on their 3D structure. Organic chemists need to be able to determine the 3D structures (stereochemistry) of new and existing molecules to relate 3D structure to reactivity. Hence, the following units will be discussed in this module:

Unit 1	Effect of molecular architecture on physical properties of organic compounds
Unit 2	Factors affecting availability of electrons in organic compounds
Unit 3	Stereochemistry

UNIT 1 EFFECT OF MOLECULAR ARCHITECTURE ON PHYSICAL PROPERTIES OF ORGANIC COMPOUNDS

CONTENTS

6.0 Tutor Mark Assignment
7.0 References/Further Readings

1.0 INTRODUCTION

In our previous knowledge in organic chemistry, we have learnt some of the important aspects of bonding and the structures of organic molecules in detail. But have you thought about how we establish the identity and structure of a molecule? One answer to this question could be comparing its physical and chemical properties with those of the known compounds. Earlier methods of identification involved the determination of physical properties such as melting point, boiling point, solubility and refractive index. The chemical methods used for identification involved, however, either the degradation of the molecule to simple compounds of known structure or its synthesis from the simple compounds of known structure. The structure and properties of organic compounds are considerably influenced by the conditions under which they are formed most especially bond type and temperature. In this unit, we will discuss the relationship between molecular structure and physical properties. The study of physical properties is also important in the purification of organic compounds.

2.0 OBJECTIVES

By the end of this unit you should be able to:

- identify organic molecules using their physical properties such as melting and boiling points, solubility and refractive index
- determine the relationship between molecular structure and physical properties of organic compounds.

3.0 MAIN CONTENT

3.1 Molecular Architecture and Factors Affecting Physical Properties of Compound

The bonding and structural features of a compound are manifested in its physical properties. Thus, physical properties of a compound such as melting point, boiling point, solubility, etc., often give valuable clues about its structure. Conversely, if the structure of a compound is known, its physical properties can be predicted.

The physical properties of a compound depend upon the number and nature of atoms constituting its structural units and also on the nature of forces holding these units together. You know that in case of ionic compounds, the positive and negative ions are held together by strong electrostatic forces. Contrary to this, in covalent compounds, the molecules are held together by intermolecular forces. Let us now study briefly what these intermolecular forces are. Then, you will learn how these intermolecular forces affect the physical properties of the compounds.

3.1.1 Intermolecular Forces

Forces between molecules are responsible for the magnitude of the melting and boiling temperatures and for solubility characteristics of molecules. The greater the attraction between molecules of a specific compound, the higher the melting and boiling points are likely to be. Solubility characteristics use the classic saying, like dissolves like. Polar molecules are most soluble in polar solvents and nonpolar molecules are most soluble in nonpolar solvents. The three important intermolecular forces are: (i) dipole-dipole interactions, (ii) London forces and (iii) hydrogen bonding. Let us now consider these intermolecular forces one by one.

(i) **Dipole-Dipole Interactions:** are defined as the interactions between the different molecules of a compound having permanent dipoles. Dipoles result from unequal sharing of electrons in bonds. If molecules are close to each other, the negative pole of one molecule is attracted to the positive pole of another molecule. Consider the example of chloromethane which has a permanent dipole. The molecule of chloromethane orient themselves in such a way that the positive end of one dipole points towards, and is thus attracted by, the negative end of the other dipole. These interactions, called dipole-dipole interaction are depicted in Fig 1.1.

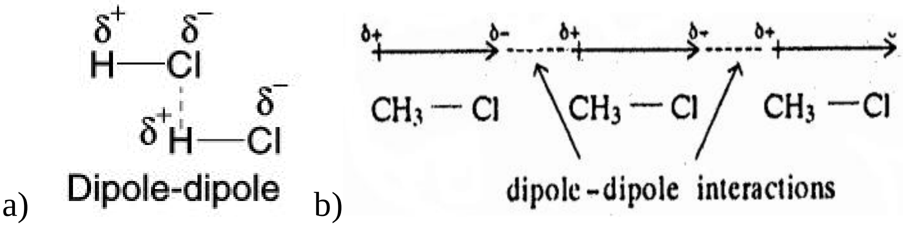


Fig. 1.1: Intermolecular forces (“- - - - -” indicates interaction). a) A polar hydrogen chloride molecule interacting with another hydrogen chloride molecule b) Arrangement of chloromethane molecules showing positive and negative poles of one molecule and the Dipole-dipole interactions between chloromethane molecules.

The dipole-dipole interactions are weak interactions and are of the order of 4 to 12 kJ mol^{-1} whereas the bond energy for an ordinary covalent bond ranges from 125 to 420 kJ mol^{-1}.

In-Text Question 1

When the positive end of a molecule attracts the negative end of another molecule, the electrostatic forces that arise is named ________

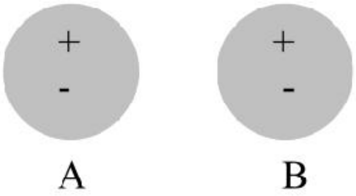
A. Electrovalent bond B. Dipole-dipole forces C. Weak forces D. Gaseous forces

In-Text Answer 1

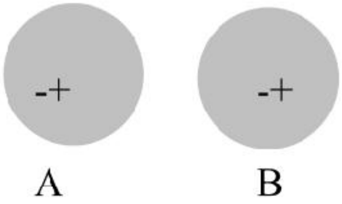
Option B

(ii) **London Forces:** The intermolecular interactions exist between non polar molecules also. At any given instant, the electrons surrounding an atom or molecule are not uniformly distributed; that is, one side of the atom may have a greater electron density than the other side. This results in a momentary dipole within the atom. The dipole on one atom may induce a dipole on another atom. The net result is an attraction between atoms.

Consider two nonpolar molecules A and B in which the centre of positive charge coincides with that of the negative charge.



When the molecules A and B approach each other, there is a distortion in the distribution of the charge resulting in a small and momentary dipole in one molecule. This small dipole can then create another dipole in the second molecule which is called **induced dipole**. Thus, if the momentary dipole of molecule A and B is as shown below;



Such a distribution of charge leads to mutual attraction between the molecules. These induced dipole – induced dipole interaction are also known as **London forces** (illustrated with … in Figure 1.2).

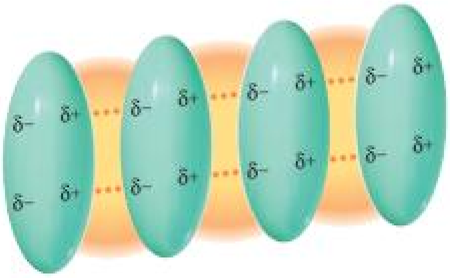


Fig. 1.2: London forces are induced-dipole–induced-dipole interactions.

London forces are the only forces of attraction possible between nonpolar molecules. These interactions are weaker than the dipole-dipole interactions and are of the order of 4 kJ mol^{-1}. These forces vary with the distance between the molecules. If '*r*' is the distance between the two molecules, then the London forces are proportional to $1/r^6$. This explains the interaction between helium atoms (Fig. 1.3), that are nonpolar, yet they must have attraction for each other since they form liquids when cooled sufficiently. All molecules exhibit dispersion forces.

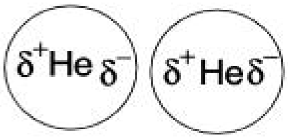


Fig 1.3: London dispersion forces in two helium atoms

In-Text Question 2

1. Classify the following statement as **true** or **false**: London forces are the only forces operating between polar molecules.
2. At 25°C, chlorine (Cl_2) is a gas whereas bromine (Br_2) is a liquid. Why?

(iii) **Hydrogen Bonding:** This is a special type of dipole-dipole interaction. It does not refer to an actual bond, but a strong interaction between a covalently bonded hydrogen atom and a molecule containing an atom with nonbonding electrons, such as oxygen, nitrogen, and the halogens. The hydrogen atom undergoing hydrogen bonding must be covalently bonded to an oxygen, a nitrogen, or a fluorine atom, resulting in a highly polar covalent bond. This puts a large partial positive charge (δ^+) on the covalently bonded hydrogen atom and it seeks an electron pair on another atom. Hydrogen bonds are stronger than most dipole-dipole interactions but weaker than a covalent bond. An example is shown for water in Fig 1.4.

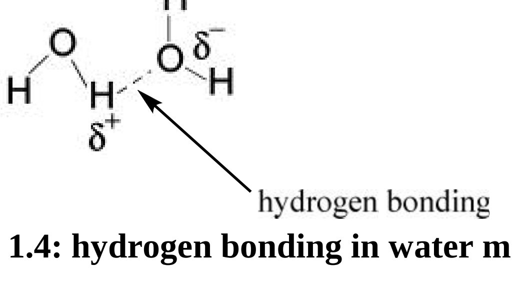


Fig. 1.4: hydrogen bonding in water molecules

The strength of a hydrogen bond ranges from 10 to 40 kJ mol^{-1}. Hydrogen bonding has an important influence on physical properties such as melting point, boiling point and solubility of substances. This will be illustrated using examples in the following subsections.

The dipole-dipole, induced dipole-induced dipole etc. interactions are collectively known as **van der Waals forces**. Some authors prefer to give the name van der Waals forces only for London forces. Having understood the intermolecular forces, let us now study how the variation in molecular structure affects these intermolecular forces which in turn is reflected in the physical properties of the molecules.

In-Text Question 3
Which response includes only those compounds that can exhibit hydrogen bonding?

(a) AsH_3, H_2Te
(b) AsH_3, CH_3NH_2
(c) CH_4, AsH_3, H_2Te
(d) CH_3NH_2, HF
(e) HF, H_2Te

3.1.2 Melting Point

The melting point (mp) is the temperature at which a solid is converted into a liquid.

Pure crystalline solids have sharp melting points. Thus, melting point is used as an important physical property both for the identification of organic compounds and for making the general assessment of the purity of these compounds. Pure crystalline solids have **sharp** melting points and they melt over a temperature range of 1° or less. In contrast to this, impure crystalline solids melt over wider ranges of temperatures. In a crystalline solid, the constituent ions or molecules are arranged in an orderly and rigid fashion. When such as solid is heated, the thermal energy of the molecules increases. This finally leads to the disintegration of the crystal structure and at the melting point a disorderly and random arrangement of particles, characteristic of a liquid, is obtained. Since the electrostatic forces holding the ions are very strong, they can be overcome only at high temperatures. Therefore, the ionic compounds generally have high melting points. For example, the melting point of sodium chloride is 1074 K and that of sodium ethanoate is 595 K. But, the intermolecular forces are very weak as compared to the interionic forces and hence, these can be overcome at lower temperatures leading to lower melting points for covalent compounds. The melting point of methane, a covalent compound, is only 90 K and the melting point of methanol, another covalent compound, is 179 K.

Let us now study the effect of molecular weight on the melting point. If you examine the melting points of the alkanes in Table 1.1, you will see that the melting points increase (with a few exceptions) in a homologous series as the molecular weight increases. The increase in melting point is less regular than the increase in boiling point because **packing** influences the melting point of a compound. Packing is a property that determines how well the individual molecules in a solid fit together in a crystal lattice. The tighter the fit, the more energy is required to break the lattice and melt the compound.

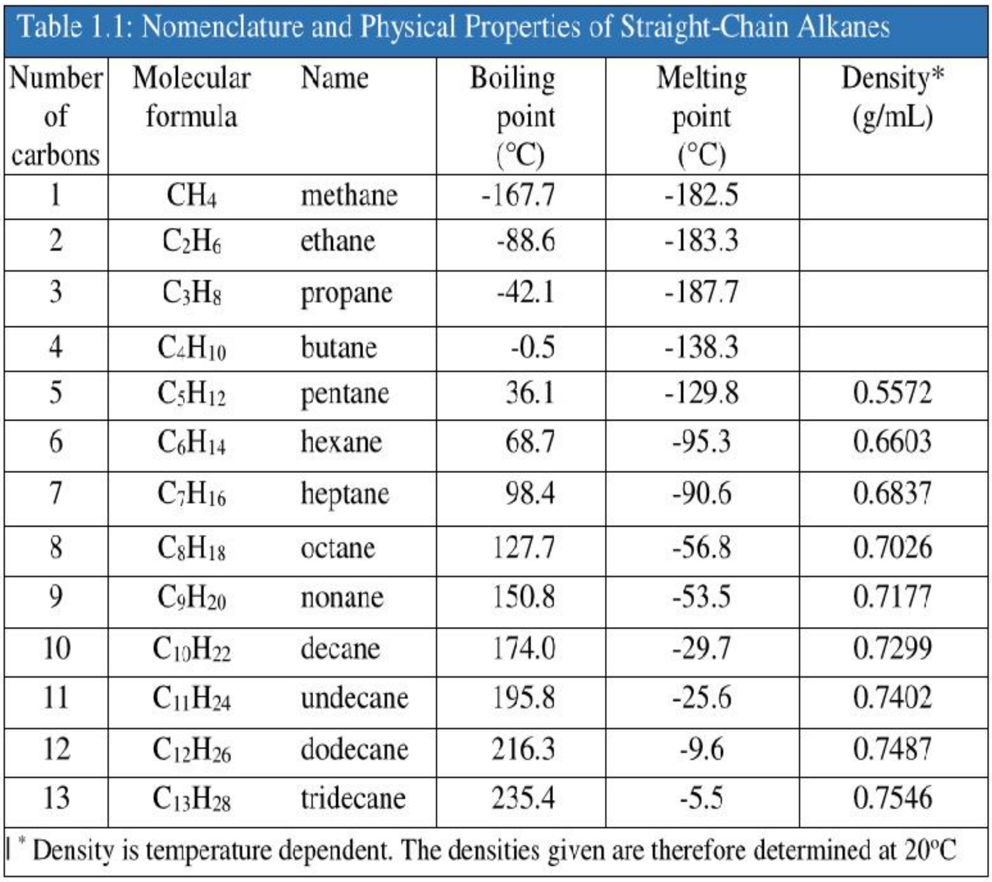


Table 1.1: Nomenclature and Physical Properties of Straight-Chain Alkanes

Number of carbons	Molecular formula	Name	Boiling point (°C)	Melting point (°C)	Density* (g/mL)
1	CH_4	methane	-167.7	-182.5	
2	C_2H_6	ethane	-88.6	-183.3	
3	C_3H_8	propane	-42.1	-187.7	
4	C_4H_{10}	butane	-0.5	-138.3	
5	C_5H_{12}	pentane	36.1	-129.8	0.5572
6	C_6H_{14}	hexane	68.7	-95.3	0.6603
7	C_7H_{16}	heptane	98.4	-90.6	0.6837
8	C_8H_{18}	octane	127.7	-56.8	0.7026
9	C_9H_{20}	nonane	150.8	-53.5	0.7177
10	$C_{10}H_{22}$	decane	174.0	-29.7	0.7299
11	$C_{11}H_{24}$	undecane	195.8	-25.6	0.7402
12	$C_{12}H_{26}$	dodecane	216.3	-9.6	0.7487
13	$C_{13}H_{28}$	tridecane	235.4	-5.5	0.7546

| * Density is temperature dependent. The densities given are therefore determined at 20°C

In Figure 1.5, you can see that the melting points of alkanes with even numbers of carbon atoms fall on a smooth curve (the red line). The melting points of alkanes with odd numbers of carbon atoms also fall on a smooth curve (the green line). The two curves do not overlap, however, because alkanes with an odd number of carbon atoms pack less tightly than alkanes with an even number of carbon atoms. Alkanes with an odd number of carbon atoms pack less tightly because the methyl groups at the ends of their chains can avoid those of another chain only by increasing the distance between their chains. Consequently, alkane molecules with odd numbers of carbon atoms have lower intermolecular attractions and correspondingly lower melting points.

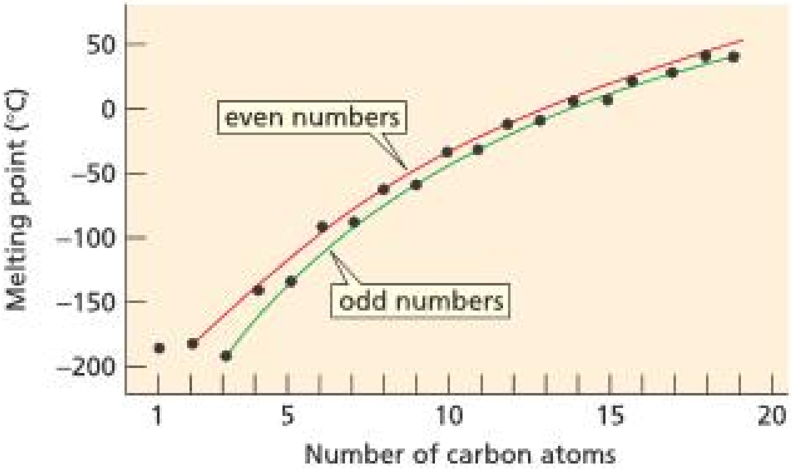
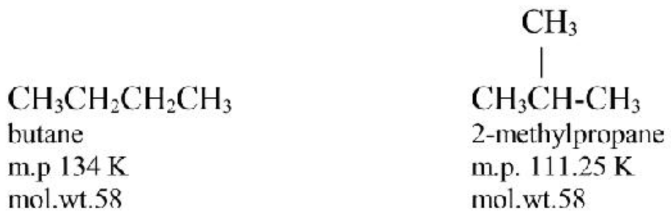


Fig. 1.5: Plot of melting points of straight-chain alkanes. Alkanes with even numbers of carbon atoms fall on a melting-point curve that is higher than the melting point curve for alkanes with odd numbers of carbon atoms.

You can see in the figure that the melting point increases with the increase in the molecular weight. This can also be explained due to increase in the London forces between the larger molecules of higher molecular weight. Thus, each additional methylene ($-CH_2$) unit contributes to the increase in melting point.

In a homologous series, the higher the molecular weight, the larger will be the molecules and the greater will be the ‘area of contact’ between the two molecules and hence the greater will be the London forces.

You must have noticed in Fig. 1.5, the alternating pattern of melting points for the alkanes having odd and even number of carbon atoms. It is also evident from the figure that the compounds having even number of carbon atoms lie on a higher curve as compared to the compounds having odd number of carbon atoms. This can be explained on the basis that in solid state, the London forces among the molecules having odd number of carbon atoms are weaker than those in the molecules having even number of carbon atoms. This is because the molecules of alkanes having odd number of carbon atoms do not fit well in the crystal lattice as compare to those of the alkanes having even number of carbon atoms. After studying the effect of molecular weight on melting point, let us now see how the isomeric compounds having the same molecular weight, show different melting points. The melting points of straight chain and branched chain isomers of butane are given below:

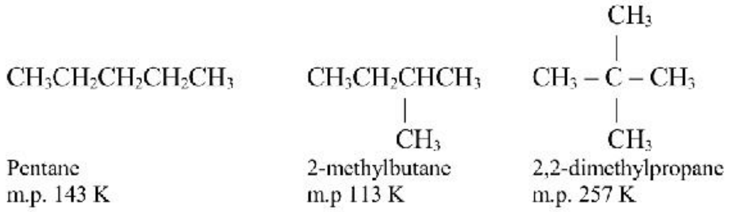


$CH_3CH_2CH_2CH_3$ — butane, m.p 134 K, mol.wt.58

$CH_3CH(CH_3)CH_3$ — 2-methylpropane, m.p. 111.25 K, mol.wt.58

The branching of the carbon chain interferes with the regular packing of the molecules in the crystal; branched chain hydrocarbons tend to have lower melting points than their straight chain isomers.

But, in case, the branched molecule has a substantial symmetry, then its melting point is relatively high. This is clearly evident when we compare the melting points of isomeric pentanes which are as given below:



$CH_3CH_2CH_2CH_2CH_3$ — Pentane, m.p. 143 K

$CH_3CH_2CH(CH_3)CH_3$ — 2-methylbutane, m.p 113 K

$CH_3-C(CH_3)_2-CH_3$ — 2,2-dimethylpropane, m.p. 257 K

The branching from pentane to 2-methylbutane lowers the melting point but further branching in 2,2-dimethylpropane increases the melting point. This can be explained by the fact that the symmetrical molecules fit together more easily in the crystal lattice and hence have higher melting points as compared to the less symmetrical molecules. Hence, higher melting point for 2,2-dimethylpropane is justified.

This is also reflected when we analyse the melting points of *cis*- and *trans*-isomers. The *trans*- isomer being more symmetrical, fits better in the crystal lattice than the less symmetrical *cis*- isomer. Hence, the *trans*- isomers generally have higher melting points.

The nature of the functional groups present in a molecule also affects its physical properties. For example, when the functional group is such that it introduces polarity, and hence leads to a permanent dipole moment in the molecule; then, due to the dipole-dipole forces of attraction between the polar molecules, they show higher melting points than the nonpolar molecules of comparable molecular weights. For example, the melting point of propanone, a polar molecule having molecular weight of 58, is 178 K. You can compare it with the melting points of isomers of nonpolar butane (mol. Wt. = 58) you have just studied above. This leads to the conclusion that the polar propanone has higher melting point than the nonpolar isomeric butanes.

The effect of hydrogen bonding on melting point is small. But, the hydrogen bonding has significant effect on the boiling point, about which you will study in the next subsection.

In-Text Question 4
Which compound has the highest melting point? A. decane B. 2,2,3,3-tetramethylbutane C. 2,2,3-trimethylpentane D. 4-methylnonane

3.1.3 Boiling Point

The boiling point of a substance is the temperature at which it changes (vapourizes) from the liquid to the gaseous state. At the boiling point the vapour pressure of a liquid is equal to the external pressure. Thus, the boiling point depends on the external pressure and it increases with increase in the external pressure. Hence, while reporting the boiling point of a substance, external pressure must be specified.

Similar to the case of melting points, the boiling points are also used as constants for identification and characterization of liquid substances. The knowledge of boiling points is also important in the purification of liquids.

Let us now study some of the factors affecting the boiling point.

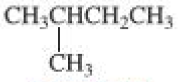
The boiling point of a substance depends on its molecular structure. In order for a compound to vapourize, the forces that hold the individual molecules close to each other in the liquid must be overcome. This means that the boiling point of a compound depends on the strength of the attractive forces between the individual molecules. If the molecules are held together by strong forces, it will take a lot of energy to pull the molecules away from each other and the compound will have a high boiling point. In contrast, if the molecules are held together by weak forces, only a small amount of energy will be needed to pull the molecules away from each other and the compound will have a low boiling point. For example, relatively weak forces hold alkane molecules together. Alkanes contain only carbon and hydrogen atoms. Because the electronegativities of carbon and hydrogen are similar, the bonds in alkanes are nonpolar. Consequently, there are no significant partial charges on any of the atoms in an alkane.

The molecules of an alkane are held together by these induced-dipole–induced-dipole interactions, which are known as van der Waals forces. Van der Waals forces are the weakest of all the intermolecular attractions. In order for an alkane to boil, the van der Waals forces must be overcome. The magnitude of the van der Waals forces that hold alkane molecules together depends on the area of contact between the molecules. The greater the area of contact, the stronger are the van der Waals (London) forces and the greater is the amount of energy needed to overcome those forces. If you look at the homologous series of alkanes in Table 1.1, you will see that the boiling points of alkanes increase as their size increases. Generally, this increase in boiling point amounts to 20-30^o for the addition of each carbon atom in the molecule. This relationship holds because each additional methylene group increases the area of contact between the molecules. The four smallest alkanes have boiling points below room temperature (room temperature is about 25 °C), so they exist as gases at room temperature. Pentane (bp = 36.1^{o}C) is the smallest alkane that is a liquid at room temperature. The boiling points of the compounds in any homologous series increase as their molecular weights increase because of the increase in van der Waals forces. So the boiling points of the compounds in a homologous series of ethers, alkyl halides, alcohols, and amines increase with increasing molecular weight.

Among isomeric molecules, since the unbranched isomer is linear and hence extended in shape, it has larger surface area as compared to the branched isomers. Therefore, the London forces are stronger in the unbranched isomer leading to higher boiling point for this isomer. Thus, if two alkanes have the same molecular weight, the more highly branched alkane will have a lower boiling point This is illustrated in the structures below for the isomers of pentane.

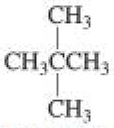
$CH_3CH_2CH_2CH_2CH_3$

pentane
bp = 36.1 °C



$CH_3CH(CH_3)CH_2CH_3$

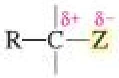
isopentane
bp = 27.9 °C



$CH_3C(CH_3)_2CH_3$

neopentane
bp = 9.5 °C

The boiling points of these compounds, however, are also affected by the polar character of the bond (where Z denotes N, O, F, Cl, or Br) because nitrogen, oxygen, and the halogens are more electronegative than the carbon to which they are attached.



$R{-}\overset{\delta+}{C}{-}\overset{\delta-}{Z}$

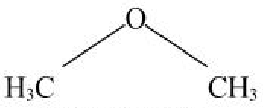
Z = N, O, F, Cl, or Br

The magnitude of the charge differential between the two bonded atoms is indicated by the bond dipole moment. The dipole moment of a bond is equal to the magnitude of the charge on one of the bonded atoms times the distance between the bonded atoms.

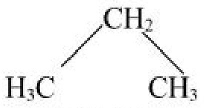
$H_3C{-}NH_2$	$H_3C{-}O{-}CH_3$	$H_3C{-}I$	$H_3C{-}OH$
0.2 D	0.7 D	1.2 D	0.7 D

$H_3C{-}F$	$H_3C{-}Br$	$H_3C{-}Cl$
1.6 D	1.4 D	1.5 D

When we compare molecules having the same shape and size, the more polar molecule has the higher boiling point. Examples are:



Dimethyl ether



propane

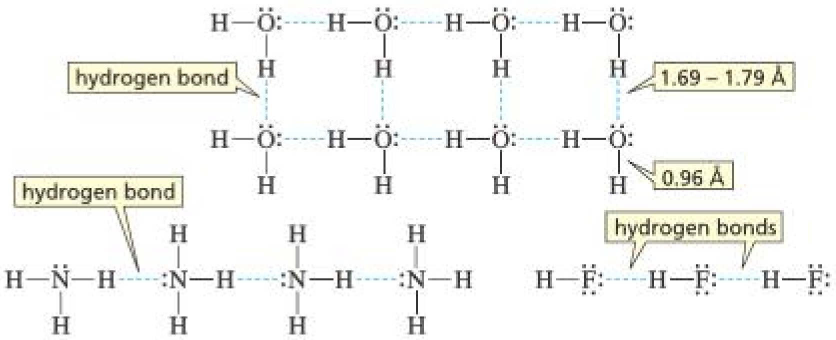
Dipole moment	20.98×10^{-30}cm	-0
Boiling point	249.4 K	231 K
Molecular weight	46	44

Alcohols have much higher boiling points than alkanes or ethers of comparable molecular weight (Table 1.2) because, in addition to London forces and the dipole–dipole interactions of the bond, alcohols can form hydrogen bonds. A hydrogen bond is a special kind of dipole–dipole interaction that occurs between a hydrogen that is bonded to an oxygen, a nitrogen, or a halogen and the lone-pair electrons of an oxygen, nitrogen, or halogen in another molecule (see subsection 3.1.1 of this unit). Thus, to vaporize such a compound, hydrogen bonds between the molecules must be broken. This requires energy, which is manifested as the unusually high boiling point for such compounds.

Table 1.2: Comparative Boiling Points (°C)

Alkanes	Ethers	Alcohols	Amines
$CH_3CH_2CH_3$	CH_3OCH_3	CH_3CH_2OH	$CH_3CH_2NH_2$
-42.1	-23.7	73	16.6
$CH_3CH_2CH_2CH_3$	$CH_3OCH_2CH_3$	$CH_3CH_2CH_2OH$	$CH_3CH_2CH_2NH_2$
-0.5	10.8	97.4	47.8
$CH_3CH_2CH_2CH_2$	$CH_3CH_2OCH_2C$	$CH_3CH_2CH_2CH_2$	$CH_3CH_2CH_2CH_2$
36.1	34.5	117.3	77.8

The length of the covalent bond between oxygen and hydrogen is 0.96 Å. The hydrogen bond between an oxygen of one molecule and a hydrogen of another molecule is almost twice as long (1.69–1.79 Å), which means that a hydrogen bond is not as strong as an O-H covalent bond. A hydrogen bond, however, is stronger than other dipole–dipole interactions. The strongest hydrogen bonds are linear—the two electronegative atoms and the hydrogen between them lie on a straight line. Although each individual hydrogen bond is weak—requiring about 21 kJ/mol (5 kcal/mol) to break—there are many such bonds holding alcohol molecules together. The extra energy required to break these hydrogen bonds is the reason alcohols have much higher boiling points than either alkanes or ethers with similar molecular weights.



The boiling point of water illustrates the dramatic effect hydrogen bonding has on boiling points. Water has a molecular weight of 18 and a boiling point of 100 °C. The alkane nearest in size is methane, with a molecular weight of 16. Methane boils at -167.7^{o}C.

Primary and secondary amines also form hydrogen bonds, so these amines have higher boiling points than alkanes with similar molecular weights. Nitrogen is not as electronegative as oxygen, however, which means that the hydrogen bonds between amine molecules are weaker than the hydrogen bonds between alcohol molecules. An amine, therefore, has a lower boiling point than an alcohol with a similar molecular weight (Table 1.2).

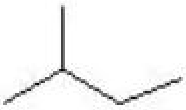
Because primary amines have two bonds, hydrogen bonding is more significant in primary amines than in secondary amines. Tertiary amines cannot form hydrogen bonds between their own molecules because they do not have a hydrogen attached to the nitrogen. Consequently, if you compare amines with the same molecular weight and similar structures, you will find that primary amines have higher boiling points than secondary amines and secondary amines have higher boiling points than tertiary amines.

Hydrogen bonding is also important in other ways. As we shall see in the next subsection, hydrogen bonding plays an important role in the solubility of organic compounds.

In-Text Question 5
Which of the following alkanes will have the lowest boiling point?

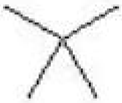
3.1.4 Solubility

a.



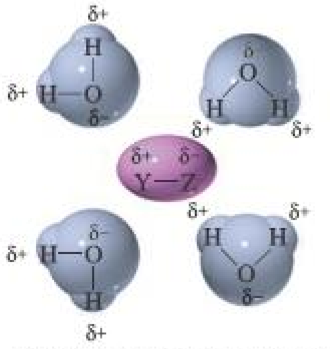
b.

c.



d.

When any substance dissolves in a solvent, its constituent ions or molecules get separated from each other and the space between them is filled by solvent molecules. This is known a *solvation* and the amount of substance dissolved in a certain amount of solvent is referred to as its *solubility* in that solvent. Solubility thus depends on the interactions between solute-solute, solute-solvent and solvent-solvent molecules. The general rule that explains solubility on the basis of the polarity of molecules is that "like dissolves like". In other words, polar compounds dissolve in polar solvents, and nonpolar compounds dissolve in nonpolar solvents. This is because a polar solvent such as water has partial charges that can interact with the partial charges on a polar compound. The negative poles of the solvent molecules surround the positive pole of the polar solute, and the positive poles of the solvent molecules surround the negative pole of the polar solute. Clustering of the solvent molecules around the solute molecules separates solute molecules from each other, which is what makes them dissolve. Clearly strong solute-solvent molecular interactions as compare to those of solute-solute or solvent – solvent molecules will lead to dissolution of the solute.



solvation of a polar compound $\overset{\delta+}{Y}—\overset{\delta-}{Z}$ by water

Similar to the processes of melting or boiling, dissolution of a substance also requires that the interionic or intermolecular forces of attraction between the ions or molecules must be overcome. The strong electrostatic forces between the ions of an ionic compound can be overcome by the solvents which have high dielectric constant. Thus, water which has a high dielectric constant (ϵ) of 80, dissolves ionic compounds readily whereas solvents like carbon tetrachloride (ϵ =1.2) or ether (ϵ = 4.4) are extremely poor solvents for such compounds. Hence, ionic compounds have greater solubility in polar solvents.

The dielectric constant ϵ, of a solvent measures its ability to separate the ions of the solute.

The term polar has double usage in organic chemistry. When we refer that it has a significant dipole moment, μ. But, when we talk about a polar solvent, we understand that it has a high dielectric constant, ϵ. Thus, the dipole moment is the property of individual molecules whereas solvent polarity or dielectric constant is a property of many molecules acting together.

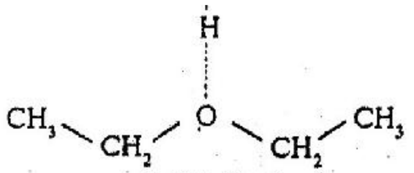
In determining the solubility of covalent compounds, the rule of thumb is like-dissolves-like. Since water is a polar compound, it is a good solvent for polar compounds, but is a poor solvent for hydrocarbon which are nonpolar in nature. Thus, the hydrocarbons readily dissolve in other hydrocarbons or in nonpolar solvents such as benzene, ether or tetrahydrofuran. This is because the van der Waals interactions between solvent and solute molecules are about the same as between solvent–solvent and solute–solute molecules.

Alkanes are nonpolar, which causes them to be soluble in nonpolar solvents and insoluble in polar solvents such as water. The densities of alkanes (Table 1.1) increase with increasing molecular weight, but even a 30-carbon alkane such as triacontane (density at 20 ^{o}C = 0.8097 g/mL) is less dense than water (density at 20 ^{o}C = 0.9982 g/mL). This means that a mixture of an alkane and water will separate into two distinct layers, with the less dense alkane floating on top.

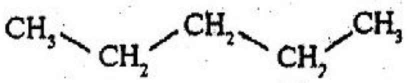
An alcohol has both a nonpolar alkyl group and a polar OH group. So, is an alcohol molecule nonpolar or polar? Is it soluble in a nonpolar solvent, or is it soluble in water? The answer depends on the size of the alkyl group. As the alkyl group increases in size, it becomes a more significant fraction of the alcohol molecule and the compound becomes less and less soluble in water. In other words, the molecule becomes more and more like an alkane. Four carbons tend to be the dividing line at room temperature. Alcohols with fewer than four carbons are soluble in water, but alcohols with more than four carbons are insoluble in water. In other words, an OH group can drag about three or four carbons into solution in water.

The four-carbon dividing line is only an approximate guide because the solubility of an alcohol also depends on the structure of the alkyl group. Alcohols with branched alkyl groups are more soluble in water than alcohols with non-branched alkyl groups with the same number of carbons, because branching minimizes the contact surface of
the nonpolar portion of the molecule. So tert-butyl alcohol is more soluble than n-butyl alcohol in water.

The solubility of organic compounds in water also depends on the extent of hydrogen bonding possible between the solute and the solvent (water) molecules. For example, the greater solubility of ether in water as compared to that of pentane (in water can be accounted on the basis of hydrogen bonding present in the former case.



diethyl ether
solubility : 75 g in 1 dm^3
of water



pentane
0.36 g in 1 dm^3
of water

Since the olefinic, acetylenic or benzenoid character does not affect the polarity much, the solubility of unsaturated and aromatic hydrocarbons in water is similar to that of alkanes. In compounds like ethers, esters, aldehydes, ketones, alcohols, amides, acids and amines, solubility in water depends on the length of the alkyl chain and the members containing less than five carbon atoms in the molecules are soluble in water.

Increase in the intermolecular forces in a solute, as a result of increase in the molecular weight, is also reflected in the low solubility of compounds having high molecular weight. For example, glucose is soluble in water but its polymer, starch is insoluble in water. This is because polymers have high molecular weight. Thus, in a homologous series, the solubility of the members decreases with the increase in molecular weight. However, branching of the carbon chain leads to a decrease in the intermolecular forces. Hence, the branched chain isomer is more soluble as compared to the straight chain isomer.

Apart from other factors discussed above, solubility of a compound in a given solvent generally increases with temperature.

Sometimes high solubility of a compound is observed due to a chemical reaction which acts as a driving force. One such category of reactions is acid-base reactions. For example, the higher solubility of aniline in aqueous acid is due to the formation of anilinium ion.

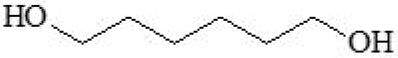
$$H_3O^+ + \underset{\text{aniline}}{C_6H_5NH_2} \longrightarrow \underset{\text{anilinium ion}}{C_6H_5NH_3^+} + H_2O$$

Although determination of the physical properties such as those discussed above helps in the identification of organic compounds, physical methods involving the use of spectroscopy allow determination of the molecular structure much more rapidly and nondestructively using small quantities of material.

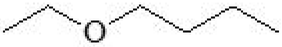
In-Text Question 6
Which of the following compounds is expected to have the greatest solubility in water?


(A)


(B)


(C)


(D)


(E)

SELF ASSESSMENT EXERCISE

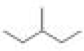
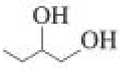
i. Which of the following compounds will form hydrogen bonds between its molecules?

1. $CH_3CH_2CH_2OH$ 2. $CH_3CH_2CH_2SH$ 3. $CH_3OCH_2CH_3$

ii. Which of the compounds in SAQ 4.1 above will form hydrogen bonds with a solvent such as ethanol?

iii. List the following compounds in order of decreasing boiling point:

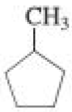


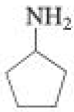




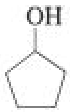

iv Rank the following groups of compounds in order of decreasing solubility in water:

a. $CH_3CH_2CH_2OH$ $CH_3CH_2CH_2CH_2Cl$ $CH_3CH_2CH_2CH_2OH$
$HOCH_2CH_2CH_2OH$

b.



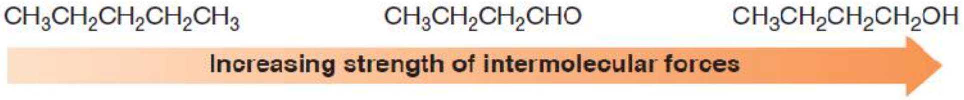




v. In which of the following solvents would cyclohexane have the lowest solubility: pentanol, diethyl ether, ethanol, or hexane?

vi. Rank the following compounds in order of increasing strength of intermolecular forces: $CH_3CH_2CH_2CH_2CH_3$ (pentane), $CH_3CH_2CH_2CH_2OH$ (1-butanol), and $CH_3CH_2CH_2CHO$ (butanal).

- Pentane has only nonpolar C-C and C-H bonds, so its molecules are held together by only **van der Waals** forces.
- 1-Butanol is a polar bent molecule, so it can have **dipole-dipole** interactions in addition to **van der Waals** forces. Because it has an O-H bond, 1-butanol molecules are held together by intermolecular **hydrogen bonds** as well.
- Butanal has a trigonal planar carbon with a polar C=O bond, so it exhibits **dipole-dipole** interactions in addition to **van der Waals** forces. There is *no* H atom bonded to O, so two butanal molecules *cannot* hydrogen bond to each other.

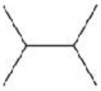


vii Which compound in each pair has the higher boiling point?

a.

A

or

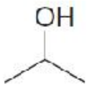


B

b.

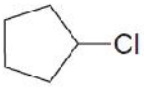
C

or

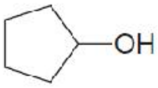


D

viii Which compound is water soluble?



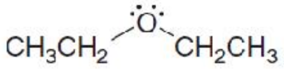
chlorocyclopentane
A



cyclopentanol
B

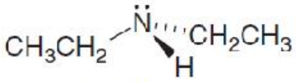
ix Which of the following molecules can hydrogen bond to another molecule like itself?

- Which of the following molecules can hydrogen bond with water?



diethyl ether

A



diethylamine

B

4.0 CONCLUSION

We can safely conclude that a good knowledge of the physical and chemical properties of organic compounds is paramount in the identification of such compounds.

5.0 SUMMARY

During the course of this unit, we have learnt about the relationship between molecular architecture and physical properties of organic compounds. We have also learnt about the interrelationship between intermolecular forces, melting and boiling points and the solubility of organic compounds. The greater the attractive forces between molecules—London (van der Waals) forces, dipole–dipole interactions, hydrogen bonds—the higher is the boiling point of the compound. A hydrogen bond is an interaction between a hydrogen bonded to an O, N, or F and the lone pair of an O, N, or F in another molecule. The boiling point increases with increasing molecular weight of the homolog. Branching lowers the boiling point. Polar compounds dissolve in polar solvents, and nonpolar compounds dissolve in nonpolar solvents. The interaction between a solvent and a molecule or an ion dissolved in that solvent is called solvation. The oxygen of an alcohol or an ether can drag about three or four carbons into solution in water.

6.0 TUTOR MARK ASSIGNMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry*, 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

UNIT 2 FACTORS AFFECTING AVAILABILITY OF ELECTRONS

CONTENTS

1.0 INTRODUCTION

In this unit, you will study about the factors that affect the availability of electrons in organic compounds. These factors are known to affect the reactivity of organic molecules. The reactivity of one substance towards another is measured by the rate at which the two substances react and the amount of the products formed. These effects which are associated with the change in molecular structure are called **structural effects** which includes: *inductive effect, resonance effect* and *steric effect.*

Not all molecules are equally reactive. But, what make some organic molecules more reactive than others? To find an answer to this question, we should have some idea of the nature of reactions that the organic molecules undergo. A large number of reactions that the organic molecules undergo can be readily understood as simple analogies of *acid-base reactions.* Therefore, it is important for us to know the basic features of acid-base reactions. We will familiarize ourselves with the concept of acid-base equilibrium in this unit. Here, you will also study that the position of the acid-base equilibrium is a measure of molecular reactivity; further it is influenced by many factors. Although, the functional groups present in a molecule are of key importance in determining the molecular reactivity, it has been observed that various compounds containing the same functional groups differ in their reactivity. Thus, in addition to the presence of the functional groups, structural effects vis-a-vis the nature and arrangement of atoms attached to the functional groups also control the molecular reactivity. We will also discuss solvent effects and hydrogen bonding which are also important factors affecting the rate and the extent of such reactions. Finally, you will study an interesting equilibrium involving a proton shift from one atom of a molecule to another, called **tautomerism.**

2.0 OBJECTIVES

By the end of this unit, you should be able to:

- understand some of the factors affecting electron availability in organic molecules, along with their consequences.
- apply these factors on organic substrates to locate electron deficient and electron rich sites.
- define acids and bases and be able to classify given compounds as acids or bases according to Bronsted – Lowry and Lewis definitions.
- define pK_a of an acid and predict the relative acidities and basicities of compounds.
- explain the effect of structural changes on the acidic and basic behaviour of organic molecules.
- define tautomerism and give examples of various kinds of tautomerism.

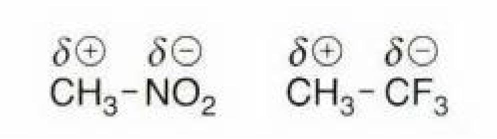
3.0 MAIN CONTENT

3.1 Factors Affecting Availability of Electrons in Organic Compounds

Electronic factors that influence organic reactions include the inductive effect, electromeric effect, resonance (mesomeric) effects, and hyperconjugation. These electronic factors involve organic molecules, most of which are made from a combination of the following six elements: carbon, hydrogen, nitrogen, oxygen, phosphorus, and sulfur (known collectively as CHNOPS). Yet, the limited number of building blocks does not prevent organic compounds from taking on diverse properties in their physical characteristics and chemical reactivity. The subtle differentiation of various compounds in organic chemistry is essential for the biological functions of the molecules and creates a wide variety of reactions. Let us now discuss these factors one after the other.

3.1.1 Inductive Effect

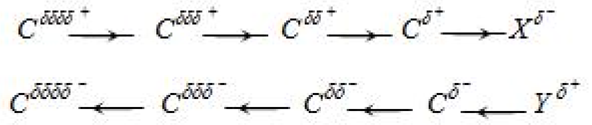
We have seen that when carbon bonds to an electronegative element like O, N, CI, or F, a bond polarization develops, making the C δ+ and the heteroatom or halogen δ-. The phenomenon of withdrawing electrons through sigma (σ) bonds to the more electronegative atom or group is called an inductive effect. The inductive effect is a permanent state of polarization. The electron density in a σ bond between two unlike atoms is not uniform and denser toward the more electronegative of the two atoms. The inductive effect is what gives rise to bond polarizations, polarizations within molecules, and bond and molecular dipole moments.



$\overset{\delta\oplus}{CH_3}-\overset{\delta\ominus}{NO_2}$ $\overset{\delta\oplus}{CH_3}-\overset{\delta\ominus}{CF_3}$

Partial charges due to induction

The inductive effect is a distance-dependent phenomenon:



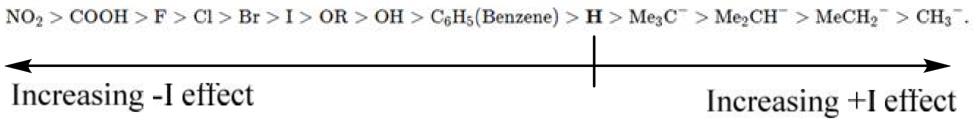
$C^{\delta\delta\delta\delta+} \longrightarrow C^{\delta\delta\delta+} \longrightarrow C^{\delta\delta+} \longrightarrow C^{\delta+} \longrightarrow X^{\delta-}$

$C^{\delta\delta\delta\delta-} \longleftarrow C^{\delta\delta\delta-} \longleftarrow C^{\delta\delta-} \longleftarrow C^{\delta-} \longleftarrow Y^{\delta+}$

If the electronegative atom X is connected to a chain of carbon atoms, then the positive charge is relayed to the other carbon atoms. C_1, with its positive δ charge, exerts a pull on the electrons of C_2, but the pull is weaker than it is between X on C_1. The effect rapidly dies out and is usually not significant after the 2nd carbon atom, or at most the 3rd.

There are two categories of inductive effects: the **electron-withdrawing** (-I) effect and the **electron-donating** (+I) effect. In the figure above, X is electron-withdrawing and Y is electron-donating.

These relative inductive effects are measured with reference to hydrogen: The -I effect is seen around a more electronegative atom or group, and electron density is higher there than elsewhere in the molecule. Electron-withdrawing groups include halogen, nitro (−NO_2), cyano (−CN), carboxyl (−COOH), ester (−COOR), and aryloxy (−OAr). On the other hand, the +I effect is observed among the less electronegative atoms of the molecule by electron-releasing (or electron-donating) groups. The alkyl groups are usually considered electron-releasing (or electron-donating) groups.



$NO_2 > COOH > F > Cl > Br > I > OR > OH > C_6H_5(\text{Benzene}) > \mathbf{H} > Me_3C^- > Me_2CH^- > MeCH_2^- > CH_3^-.$

Inductive effect generally influences both physical and chemical properties of organic compounds as seen in the strength of organic acids (to be discussed in later section of this unit), basic strength of amines and amides, ease of substitution reactions of haloalkanes (dipole moment and bond length), the ease of addition reactions of unsaturated hydrocarbons, and so on.

In-Text Question 1

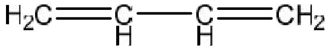
a. State whether the following statements or True or False? Explain your choice: Inductive effect is the ability of an atom or a group of atoms to cause polarization of electron density along the covalent bond so that the atom of higher electronegativity becomes electron deficient.

b. Explain the comparative stability of primary, secondary and tertiary carbocations using Inductive effect.

3.1.2 Resonance (Mesomeric) Effect

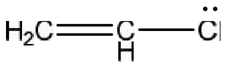
Whilst inductive effects pull electrons through the σ-bond framework, electrons can also move through the π-bond network. A π-bond can stabilize a negative charge, a positive charge, a lone pair of electrons or an adjacent bond by resonance (i.e. delocalisation or ‘spreading out’ of the electrons). A resonance effect reflects the ability of an atom or group of atoms to withdraw or donate electrons through π-bonds. This is also sometimes referred to as a mesomeric effect.

In a normal π bond, the π electrons are localized between the constituent atoms. However, if double and single bonds are present alternately in a molecule, it is called conjugation e.g. in 1,3-butadiene, the double bonds are conjugated.



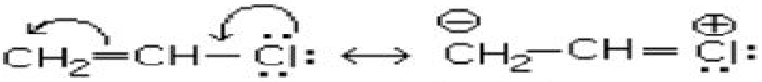
$$H_2C{=}\underset{H}{C}{-}\underset{H}{C}{=}CH_2$$

Similarly, if the double, single and a lone pair are present, alternatively, it is also called conjugation e.g. vinyl chloride.



$$H_2C{=}\underset{H}{C}{-}\ddot{Cl}$$

The presence of conjugation alters the properties of the compound and there is a difference in the actual and expected properties. The theory of resonance explains the anomalous properties of such conjugated compounds. This theory states that when a molecule can be represented by two or more classical structural (or electronic) formula, all of which can explain some but not all the properties, then the molecule has neither of these structures (called contributing or canonical or limiting structures) but is a hybrid of all these contributing structures. For example:



Vinyl chloride

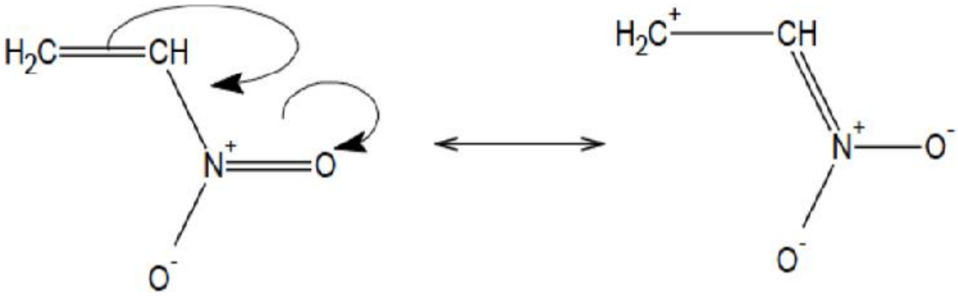
Note that the π electrons are not necessarily present where one would expect them, but are rather delocalised over the entire molecule which gives it extra stability expressed in terms of delocalisation energy or resonance energy. Also, normally, we find chlorine withdrawing electrons towards itself by -I effect but here we find that the same chlorine has got a positive charge and is involved in a double bond. Does this mean that chlorine has lost its -I effect? No, this is not true as -I effect is a permanent effect. In fact, in addition to the –I effect, it now also has an electron donating mesomeric or resonance effect (called +M or +R effect).

Since the two effects are operating in opposite directions, one of them will overwhelm the other. Remember there was no such possibility if halogen's lone pair was not conjugated. For example, in the following case, the Cl is not conjugated to the double bond and hence Cl is only exerting its –I effect.

$H_2C=CH-CH_2-Cl$

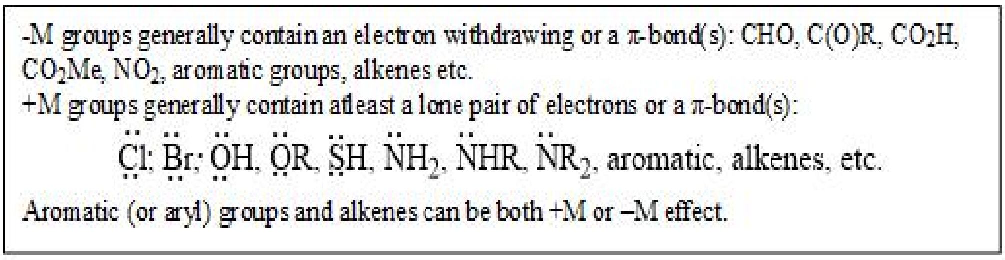
The atoms/groups like Cl in which lone pair (or electrons of negative charge) is in conjugation with double or triple bond are electron donating and gain a formal positive charge in the resonating structure in the process and are known to exert +M/+R Effect.

Consider the case of $-NO_2$ joined to a conjugated system, where the nitro withdraws the conjugated electrons and gives rise to polarization as shown below:



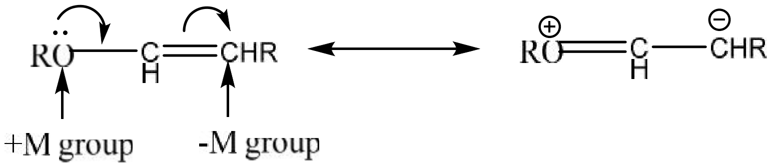
The atoms/groups like $-NO_2$ which are in conjugation with double or triple bond and are electron withdrawing and gain a formal negative charge in the resonating structure in the process and are known to exert -M/-R Effect.

The resonance effect also alters the electron density distribution in the molecule significantly and its direction may be different from the normal inductive effect. In case the two effects are operating in opposite directions, the relative strengths of the two effects will determine which will dominate. Mesomeric/resonance effect introduces total delocalization of charges while inductive effect introduces partial polarization, hence, in general M > I. But there are exceptions to it like when halogens are attached to a conjugated system like benzene, -I > +R (negative inductive effect is greater than resonance effect).

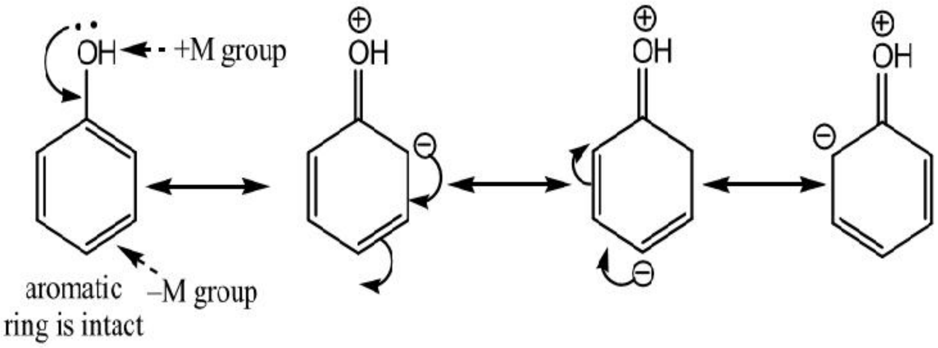


-M groups generally contain an electron withdrawing or a π-bond(s): CHO, C(O)R, CO_2H, CO_2Me, NO_2, aromatic groups, alkenes etc.
+M groups generally contain atleast a lone pair of electrons or a π-bond(s):
$\underset{\cdot\cdot}{\ddot{\mathrm{Cl}}}$: $\underset{\cdot\cdot}{\ddot{\mathrm{Br}}}$: $\ddot{\mathrm{O}}$H, $\ddot{\mathrm{O}}$R, $\ddot{\mathrm{S}}$H, $\ddot{\mathrm{N}}\mathrm{H}_2$, $\ddot{\mathrm{N}}$HR, $\ddot{\mathrm{N}}\mathrm{R}_2$, aromatic, alkenes, etc.
Aromatic (or aryl) groups and alkenes can be both +M or –M effect.

In neutral compounds, therewill always be a +M and –M group(s): One group donates (+M) the electrons and the other group(s) accepts the electrons (–M).



All resonance forms are not of the same energy. In phenol, for example, the resonance form with the intact aromatic benzene ring is expected to predominate.

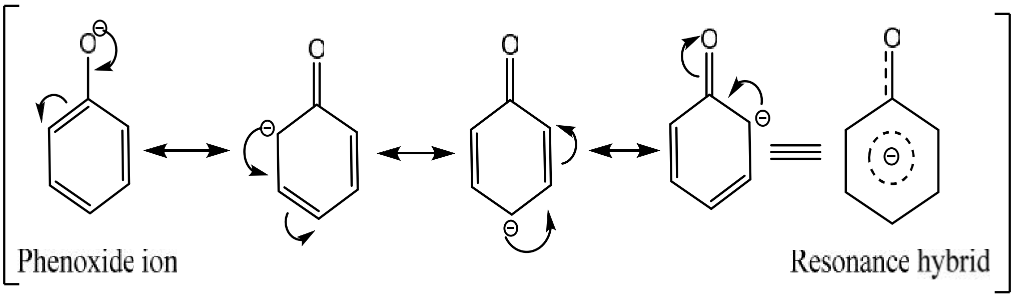


As a rule of thumb, themore resonance structures an anion, cation or neutral π-system can have, the more stable it is.

Key point about resonance:

(i) Resonating/canonical structure are maginary hypothetical, while resonance hybrid is the true strucure.
(ii) Resonance involve the delocalization of lone pair and π-electrons.
(iii) Resonance is an intramolecular process.
(iv) Resonance must follow the Lewis octet rule, i.e. C-atom, N-atom are never pentavalent and O-atom never tetravalent.
(v) In the resonating structure arrangement of atoms remain same, they should differ only with respect to arrangement of electrons.

(vi) The energy difference in between resonance hybrid and most stable resonating structure is called resonance energy.
(vii) Resonance work only at ortho and para position with equal intensity, it never work at meta position.
(viii) Resonance proceeds in the system via π-electrons.



Inductive versus mesomeric effects:

- Mesomeric effects are generally stronger than inductive effects. A+M group is likely to stabilise an anion more effectively than a +I group.
- Mesomeric effects can be effective over much longer distances than inductive effects, provided that conjugation is present (i.e. alternating single and double bonds).Whereas inductive effects are determined by distance, mesomeric effects are determined by the relative positions of +M and –M groups in a molecule.

In-Text Question 2

a. Mesomeric effect involves delocalisation of __________.
b. State whether the following statements or True or False? Explain your choice: The –OH group cannot exhibit Inductive effect.

3.1.3 Hyperconjugation

A σ-bond can stabilize a neighbouring carbocation (or positively charged carbon) by donating electrons to the vacant p-orbital. The positive charge is delocalized or 'spread out', and this stabilizing effect is known as "no-bond resonance". Hyperconjugation helps explain the stability of alkyl radicals. It involves the delocalization of σ-electrons belonging to the C-H bond of the alkyl group attaching to an atom with an unshared p-orbital. The more the hyperconjugative hydrogen, the more is the stability.

Why are more highly substituted alkenes more stable? One explanation involves hyperconjugation: hyper meaning above/beyond and conjugation meaning getting together. Figure 1.6 shows the overlapping of the sp^3-s orbitals of a C-H bond with an empty antibonding π orbital of an adjacent alkene carbon atom. This overlapping of orbitals and sharing of the C-H bonding electrons, called hyperconjugation, increases the stability of the molecule.

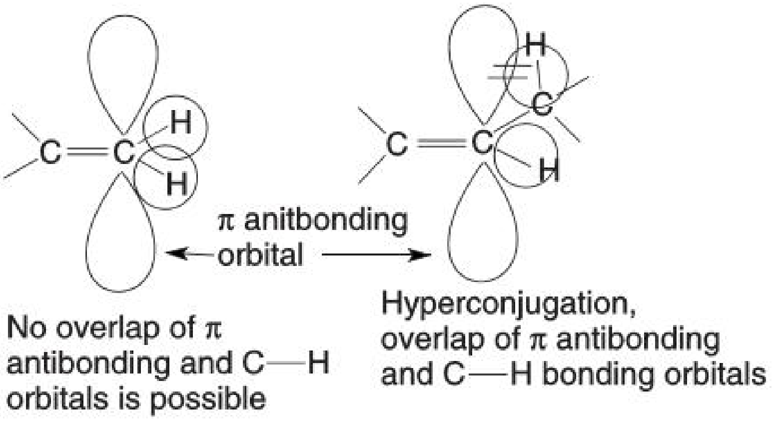
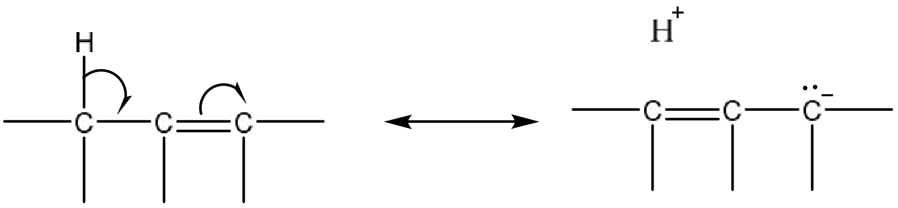


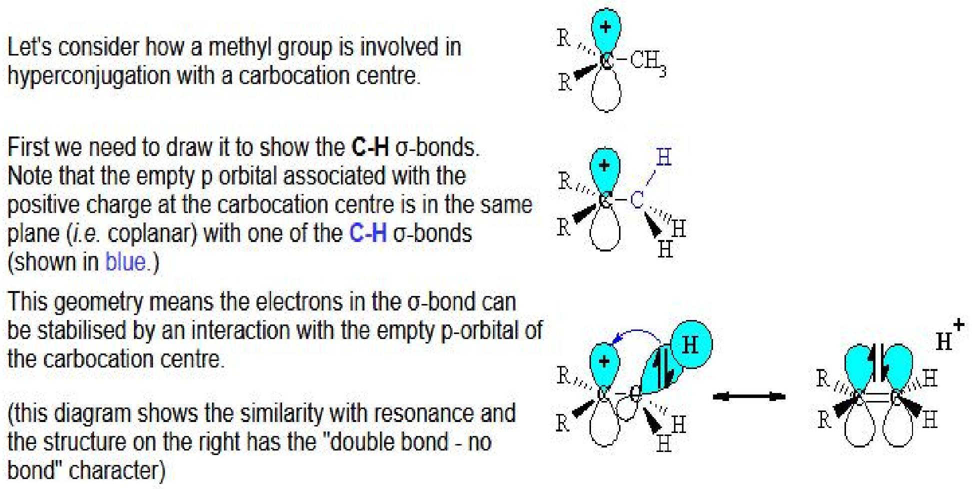
Fig. 1.6: Hyperconjugation stabilization.

Hyperconjugation involves the conjugation of sigma-electrons with adjacent *pi* electrons, as shown below:



This interaction is also known as conjugation. This type of delocalization leads to a situation where there is no bond between the hydrogen and the carbon atom of the molecule. Therefore, it is also known as hydrogen **no-bond resonance.** Remember that the proton does not leave its position and since the nuclei or the atoms do not change their positions, therefore, the hyperconjugation becomes similar to resonance. Hyperconjugation also results in the delocalization of charge, as you will now study in case of carbocations. Hyperconjugation involving hydrogens is the most common.

The stability of carbocations has been earlier explained on the basis of inductive effect of the alkyl groups. Let us consider again a primary carbocation, such as the one shown below in Fig. 1.7 below:



Let's consider how a methyl group is involved in hyperconjugation with a carbocation centre.

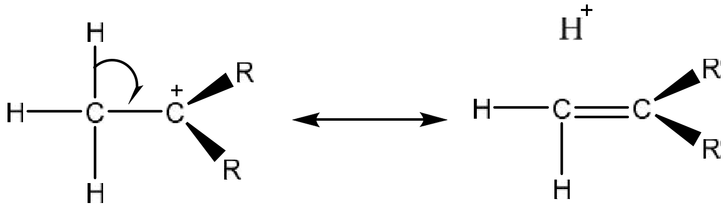
First we need to draw it to show the **C-H** σ-bonds. Note that the empty p orbital associated with the positive charge at the carbocation centre is in the same plane (*i.e.* coplanar) with one of the **C-H** σ-bonds (shown in blue.)

This geometry means the electrons in the σ-bond can be stabilised by an interaction with the empty p-orbital of the carbocation centre.

(this diagram shows the similarity with resonance and the structure on the right has the "double bond - no bond" character)

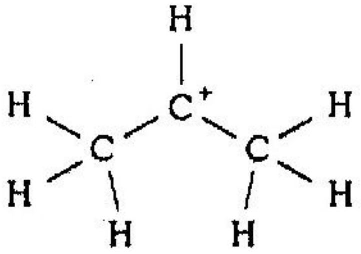
Fig 1.7: the hyperconjugation in a carbocation

It is clear from the above structure that the electrons forming the -C–H bond can overlap, into the empty p orbital of the carbon atom carrying the positive charge. The C–H bond adjacent to the >C = C< or carbonation is referred here as -C-H bond. The resulting hyperconjugation can be represented as illustrated below:

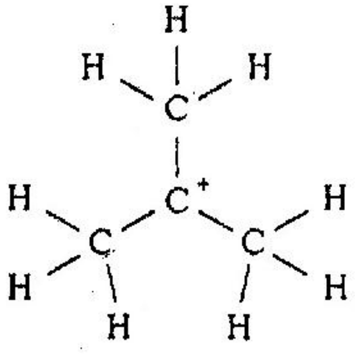


Note that hyperconjugation produces some additional bonding between the electron-deficient carbon and the adjacent carbon atom. Hence, hyperconjugation results in the stabilization of carbocation by delocalizing the positive charge. Obviously, the more the number -C–H bonds which can participate in hyperconjugation, the more stable will be the carbocation. You can see that in case of the primary carbocation shown above, there are three such -C–H bonds. Let us now examine the secondary and the tertiary carbocations.

For hyperconjugation to occur, the substituent next to the positively charged carbon must have a filled σ-orbital available to overlap with vacant p-orbital of the carbon atom carrying the positive charge.

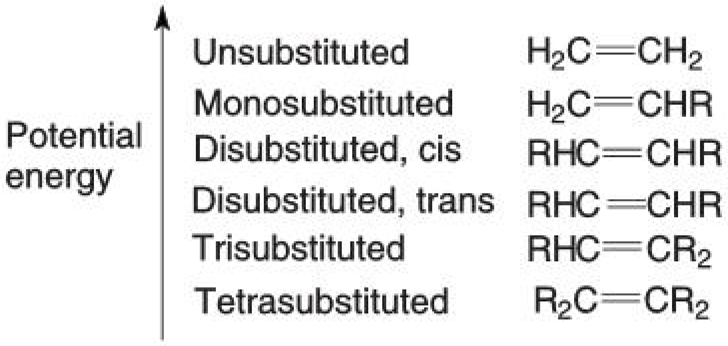


secondary carbocation
6 α – C – H bonds

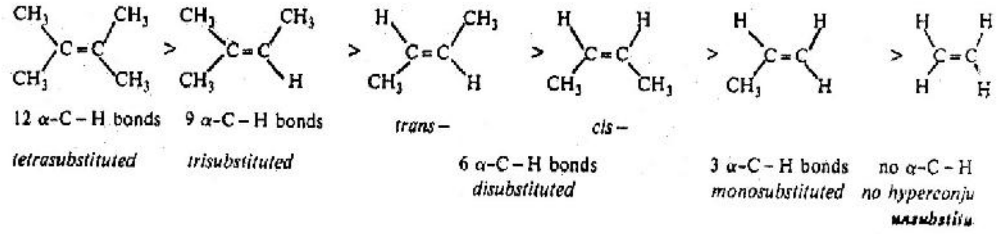


tertiary carbocation
9 α – C – H bonds

The secondary carbocation has 6 α-C–H bonds which can participate in hyperconjugation whereas the tertiary carbocation has 9 α-C–H bonds. Certainly, more delocalization of charge is possible in case of a tertiary carbocation than in a secondary carbocation which is in turn more than the possibility in a primary carbocation. Therefore, the tertiary carbocation is more stable than the secondary carbocation which is more stable-than the primary carbocation. Highly alkyl substituted alkenes have more opportunities to undergo hyperconjugation and therefore have increased stability.



Hyperconjugation has therefore been used to explain the relative stabilities of substituted alkenes. Consider the following order of stability of some alkenes.



You can see that in an alkene, the more the number of α-C-H bonds which can participate in hyperconjugation, the higher is its stability.

In spite of the fact that hyperconjugation can be used to explain many otherwise unconnected phenomena, it is controversial as it involves the formation of a weaker pi bond at the expense of a strong sigma bond.

In-Text Question 3

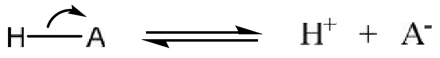
a. Hyperconjugation involves the delocalisation of __________

b. The larger the number of hyperconjugation structures, the stability of free radicals will __________

3.2 Application of Inductive Effect, Hyperconjugation and Mesomeric Effect: Acidity and Basicity

What are Acids and Bases?

There are various ways of defining acids and bases. According to Arrhenius (1884), a Swedish chemist, an acid is a substance which ionizes in aqueous solution to produce hydrogen ions (H^+), also known as protons. And, a base is a substance which ionizes to produce hydroxide (OH) ions. Thus, Arrhenius theory assumes a simple dissociation such as,



$$H{-}A \rightleftharpoons H^+ + A^-$$

Arrhenius acid

and

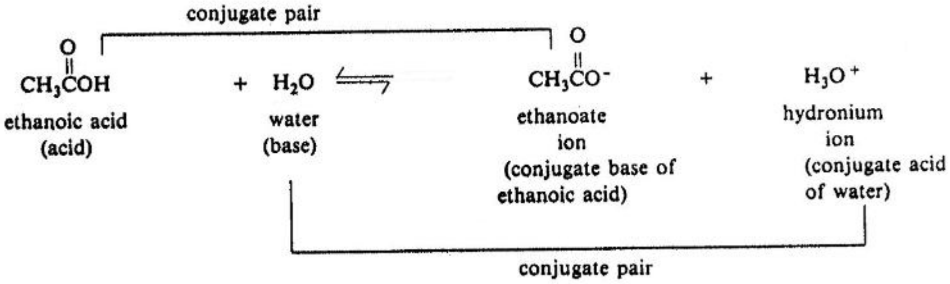
$$M{-}OH \rightleftharpoons M^+ + {}^-OH$$

Arrhenius base

Note that during dissociation, the covalent bond between H–A is broken and the electrons forming this bond shift on A as shown by the curved arrow.

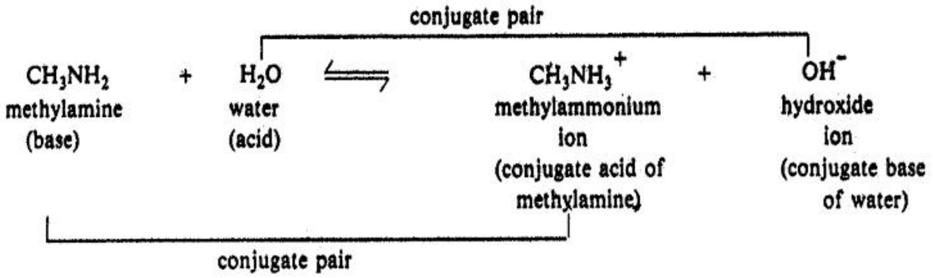
Thus, HCl is an acid and NaOH is a base because on dissociation they yield H^+ and OH^- ions, respectively. Thus, the strength of these acids and bases is related to the degree of their dissociation. The mineral acids such as HCl, HI, HBr, H_2SO_4 and HNO_3 are strong acids because they are almost completely dissociated in aqueous solutions. Similarly, the strength of a base will also depend upon its degree of dissociation.

An alternative theory of acids and bases was devised independently by Bronsted and Lowry in 1922. According to the Bronsted-Lowry approach, an acid is a proton donor and a base is a proton acceptor. Since under ordinary reaction conditions a free proton cannot exist as a separate entity, when an acid in the Bronsted-Lowry sense is considered, a base must be present to accept the proton from the acid. The Bronsted acids are also called protic acids because they react by the transfer of a proton. Consider the following example,



Here, the ethanoic acid is an acid because it donates a proton to water which is a base because it accepts the proton. Similarly, the ethanoate ion, which is formed by the loss of a proton from ethanoic acid, functions as a base because it can accept a proton to become ethanoic acid again. Thus, ethanoate ion is called the conjugate base of ethanoic acid. Similarly, the hydronium ion is the conjugate acid of the base, water. This pair of a base and its conjugate acid or an acid and its conjugate base is also called conjugate acid-base pair.

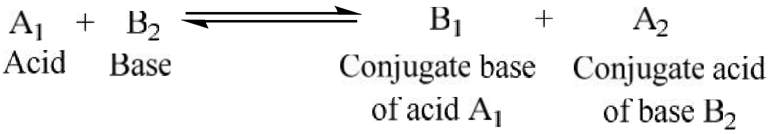
Let us now consider an acid-base reaction involving methylamine which acts as a base and water which acts as an acid in this case, as shown below:



Note that water can act both as an acid as well as a base. It acts as an acid by donating a proton to yield the OH^- ion which is its conjugate base. It can also act as a base by accepting a proton to yield a hydronium ion which is its conjugate acid.

Although, we have illustrated both the above examples using water as one of the components, the scope of Bronsted-Lowry definition of acids and bases is not limited to aqueous solutions as is the case in Arrhenius definition. The Bronsted-Lowry concept of acids and bases is more general and applies to any type of solvent.

Thus, according to this concept the general form of an acid-base reaction can be written as;



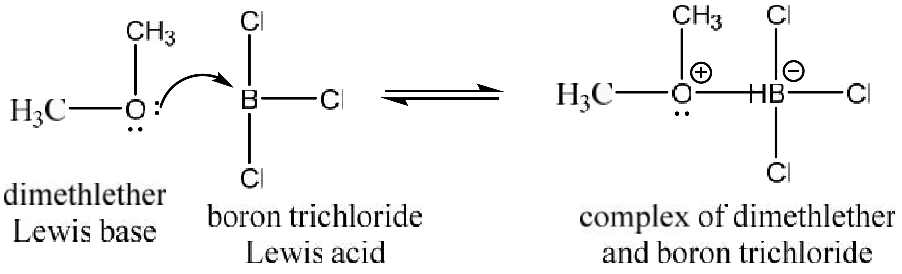
where $A_1 - B_1$ and $A_2 - B_2$ are conjugate acid-base pairs.

The acid-base theory was further broadened by Lewis in 1934. He proposed that the *acids are the electron-pair acceptors and the bases are the electron-pair donors.*

Hence, according to this idea any molecule or ion which can accommodate an electron pair is an acid. For example, a proton, H^+, is a Lewis acid because it can accept an electron pair.

A proton is only one of a large number of species that may act as a Lewis acid. The electron deficient species such as $AlCl_3$, BF_3, BCl_3, $ZnCl_2$, Mg^{2+} and carbocations are also Lewis acids. The electron deficient atoms in these species accept the electrons to complete their valence shell octets.

Similarly, any molecule or ion which has an unshared pair of electrons to donate can act as a base. Thus, dimethyl ether acts as a Lewis base towards boron trichloride which acts as a Lewis acid. This acid-base reaction is represented below:



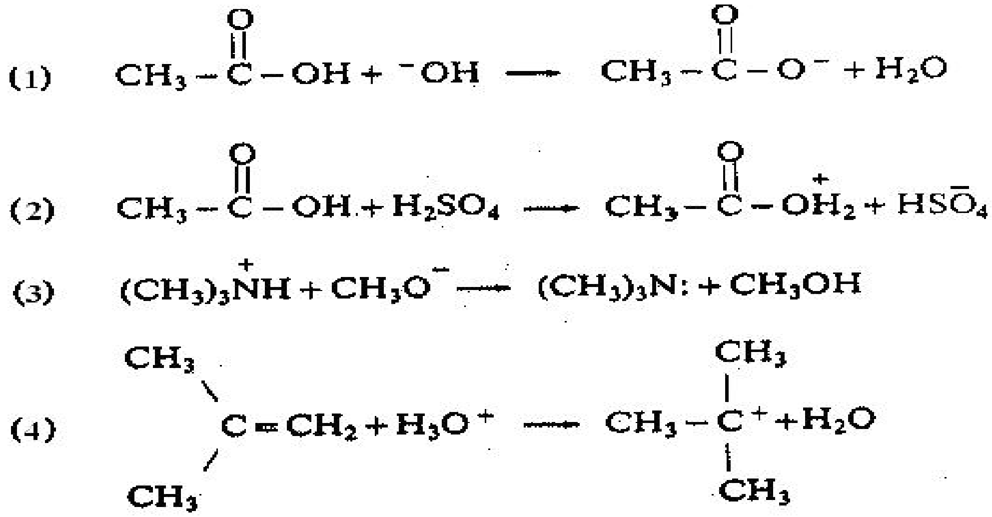
Note that the curved arrow shows the movement of a pair of electrons from their source to their destination.

You will agree that the bases are much the same in both the Lewis and the Bronsted-Lowry definitions because a Bronsted-Lowry base must possess a pair of electrons in order to accept a proton.

Having identified a substance as an acid or a base according to the above criteria, let us study how to determine the strength of an acid or a base using the electronic factors discussed previously in section 3.1 of this unit.

In-Text Question 4

Label the conjugate acid and the conjugate base in each of the following reactions.



(1) $CH_3-\overset{\overset{O}{||}}{C}-OH + {}^{-}OH \longrightarrow CH_3-\overset{\overset{O}{||}}{C}-O^{-} + H_2O$

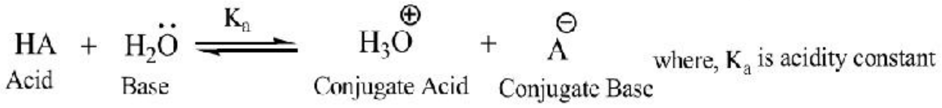
(2) $CH_3-\overset{\overset{O}{||}}{C}-OH + H_2SO_4 \longrightarrow CH_3-\overset{\overset{O}{||}}{C}-\overset{+}{O}H_2 + HS\bar{O}_4$

(3) $(CH_3)_3\overset{+}{N}H + CH_3O^{-} \longrightarrow (CH_3)_3N: + CH_3OH$

(4) $(CH_3)_2C=CH_2 + H_3O^{+} \longrightarrow CH_3-\overset{CH_3}{\underset{CH_3}{C^{+}}} + H_2O$

3.2.1 Strengths of Acids and Bases

It is not possible to determine the strength of an acid or a base in absolute terms. Therefore, these strengths are always expressed in relative terms. The *relative strengths* of acids are determined by the extent to which they transfer a proton to a standard base. The standard base which is commonly used for such comparisons is water. Hence, for an acid HA, the proton transfer can be represented by the following equilibrium;



$$\underset{\text{Acid}}{HA} + \underset{\text{Base}}{H_2\ddot{O}} \overset{K_a}{\rightleftharpoons} \underset{\text{Conjugate Acid}}{H_3\overset{\oplus}{O}} + \underset{\text{Conjugate Base}}{\overset{\ominus}{A}}$$

where, K_a is acidity constant

The equilibrium constant, K_a, for the above equilibrium can be written as,

$$K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

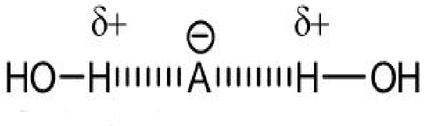
As H_2O is in excess

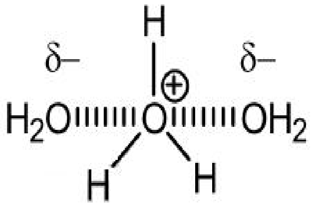
$$pK_a = -\log_{10} K_a$$

The higher the value of K_a, the lower the pK_a value and the more acidic is HA where the quantities in square brackets are the molar concentrations (expressed as moles dm^{-3}) of the species at equilibrium. For dilute solutions, the concentration of water is large and is almost constant.

The pKa value equals the pH of the acid when it is half dissociated. At pH above the pKa the acid exists predominantly as the conjugate base in water. At pH below the pKa, it exists predominantly as HA.

The pKa values are influenced by the solvent. Polar solvents will stabilize cations and/or anions by solvation, in which the charge is delocalized over the solvent (e.g. by hydrogen-bonding in water).





The dissociation of acid HA in solvents other than water can be generalized as,

$$\text{HA} + \text{solvent} \rightleftharpoons \text{H}^{+}\text{-solvent} + :\text{A}$$

The more electronegative the atom bearing the negative charge, the more stable the conjugate base (which is negatively charged).

pKa	3		16		33		48
Most acidic	HF	>	H_2O	>	NH_3	>	CH_4

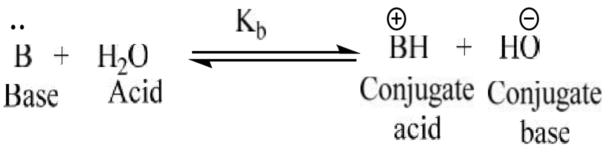
$\xleftarrow[\text{increasing electronegativity}]{}$

Therefore, F$^-$ is more stable than H_3C^-.

The conjugate base can also be stabilised by –I and –M groups which can delocalize the negative charge (the more spread out the negative charge, the more stable it is). While the cation can be stabilised by +I and +M groups, which can delocalize the positive charge. (The more ‘spread out’ the positive charge, the more stable it is).

–I and –M groups therefore lower the pKa, while +I and +M groups raise the pKa

On the other hand, basic compounds have high pKa values and are good proton acceptors, as the cations (or conjugate acids), formed on protonation, are relatively stable. Similar to acids, an equilibrium for bases in water can be written as,



$$\underset{\text{Base}}{\ddot{B}} + \underset{\text{Acid}}{H_2O} \xrightleftharpoons{K_b} \underset{\text{Conjugate acid}}{\overset{\oplus}{BH}} + \underset{\text{Conjugate base}}{\overset{\ominus}{HO}}$$

where, K_b is basicity constant

The strength of bases are usually described by the Ka and pKa values of the conjugate acid.

$$\overset{\oplus}{BH} + H_2O \xrightleftharpoons{Ka} \ddot{B} + \overset{\oplus}{H_3O}$$

where Ka is acidity constant.

$$K_a = \frac{[B]\left[H_3O^{'}\right]}{\left[{}^{+}BH\right]} \qquad \left[\text{As } H_2O \text{ is in excess}\right]$$

Since the reaction is carried out in aqueous solution, water is acting both as a solvent as well as an acid; hence, its concentration can be taken as almost constant.

- If B is a strong base, then BH^+ will be relatively stable and not easily deprotonated. BH^+ will therefore have a high pKa value.
- If B is a weak base, then BH will be relatively unstable and easily deprotonated. BH^+ will therefore have a low pKa value.

It is customary to express the strengths of organic bases not as K_b values but in terms of the Ka and pKa values because it allows a single continuous scale for both acids and bases. As has been stated above the stronger the acid, the weaker will be its conjugate base and vice versa. In other words, the stronger the acid, the lower the pKa, but, the stronger the base, the higher is the pKa.

A comparison of the pKa values shows the following order of the basicities for some of the bases.

$$-CH_3 > NH_2^- > RO^- > OH^- > RCOO^-$$

Note that the organic compounds which act as bases can be regarded as alkyl derivatives of either water or ammonia; for example, alcohols (R – O – H), ethers (R – O – R-) and amines RNH_2, R_2NH and R_3N. The basic character of these compounds can be attributed to atoms such as nitrogen and oxygen which contain at least one lone pair of electrons.

The strengths of acids and bases depend upon many factors. Apart from the presence of functional groups; structural variations in molecules also influence their acidic or basic properties. We will now focus our attention on some effects which arise due to structural changes in the molecule. A change in molecular structure can affect the reactivity of the molecule by changing the electron distribution of the system, in which case it is called an **electronic effect**. Another possibility is that two or more groups or atoms may come close enough in space so that the London interactions between them become significant. The effects arising from such interactions are called **steric effects**.

Before proceeding to the study of the lists which deals with these factors, answer the following ITQ 5.

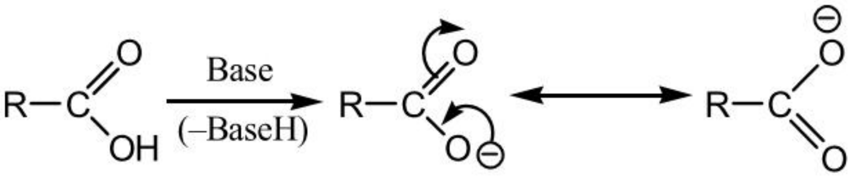
In-Text Question 5

An acid HA_1 has pK_a = 20 and another acid HA_2 has pK_a = 10.

1. Which of these two acids is stronger?
2. If $Na^+ A_1$ salt is added to acid HA_2, does any acid-base reaction take place? Explain.

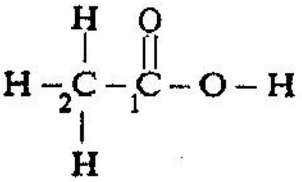
a) Inductive effects in carboxylic acids and aliphatic (or alkyl) amines:

The carboxylate anion is formed on deprotonation of carboxylic acids. The anion is stabilised by resonance (i.e. the charge is spread over both oxygen atoms) but can also be stablised by the R group if this has a –I effect.

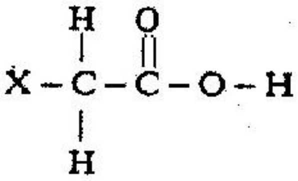


Note that the inductive effect is a permanent effect.

Let us now analyse how inductive effect causes a change in the acidity or basicity of a molecule. Let us take the example of ethanoic acid whose structure is shown below:



ethanoic acid
pK_a 4.76

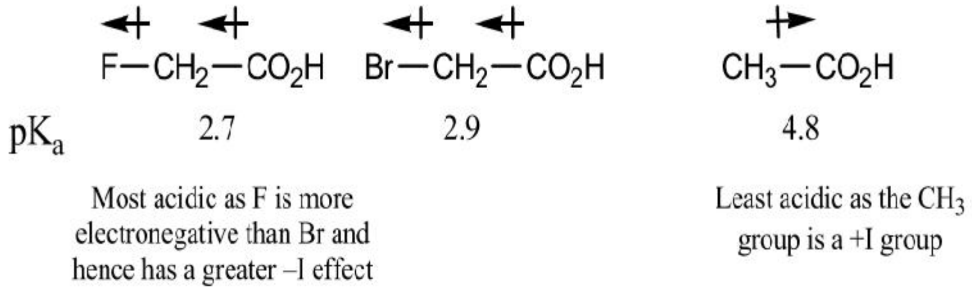


substituted ethanoic acid

If we substitute one of the hydrogen atoms on the C_2 carbon atom with a substituent X, then, the nature of the substituent group may affect the electron density of the O–H bond resulting in a change in the acidity of the molecule.

Depending upon whether the substituent X is electron-withdrawing or electron donating, the electron density will decrease or increase, respectively. If the electron density between the bond formed by O and H atoms *decreases*, then, the loss of H as H^+ ion is facilitated resulting in the *increased acidity* of the molecule. On the other hand, an *increase* in the election density at the bond between O and H atoms will make the proton release difficult, thereby, *decreasing* the acidity.

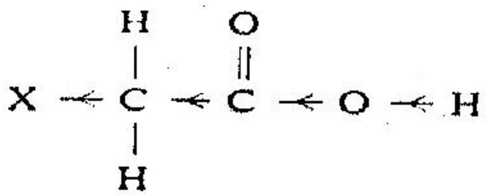
The greater the -I effect, the more stable the carboxylate anion and the more acidic is carboxylic acid.



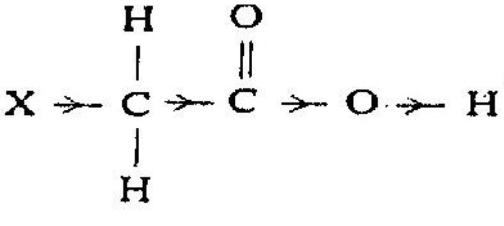
Most acidic as F is more electronegative than Br and hence has a greater –I effect

Least acidic as the CH_3 group is a +I group

(i) When the substitution X is electron withdrawing, it decreases the electron density at H as shown below:



(ii) When the substituent X is electron donating, it increases the electron density at H as represented below:



-I effect of some groups is in the order

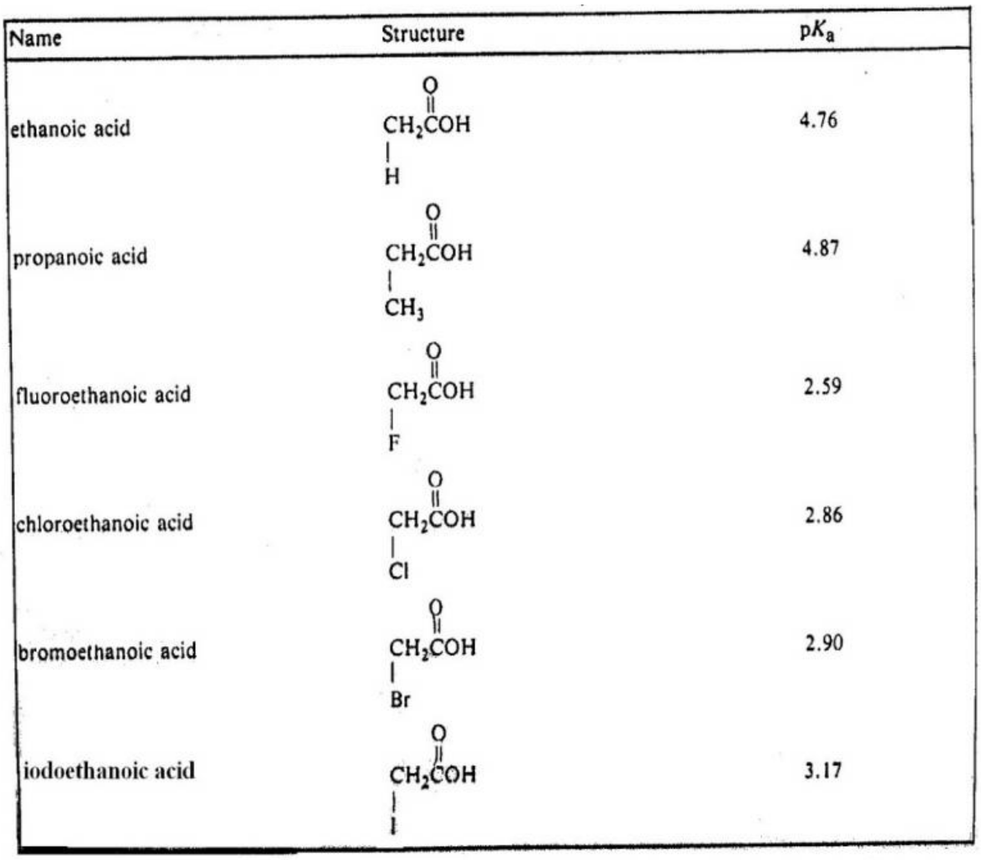
$-H < -C_6H_5 < -OCH_3 < -OH < -I < -Br < -Cl < -F < -COOH < -CN < -NO_2 < -N^+(CH_3)_3$

+I effect of some of the groups is in the following order:

$-H < -D < -CH_3 < -CH_2R < -CHR_2 < -CR_3 < -COO^-$

The effect of some of these substituents on the acidity of the substituted acids in terms of their p*K*a values is shown in Table 1.3 below:

Table 1.3: p*K*a values for some substituted acids determine in water at 298 *K*.

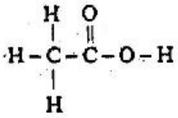
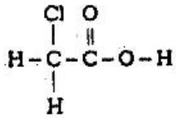
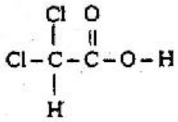
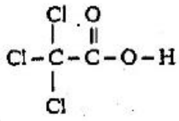


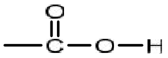
Name	Structure	pK_a
ethanoic acid	$\underset{\mathrm{H}}{\underset{\vert}{\mathrm{CH_2}}}\overset{\overset{\mathrm{O}}{\parallel}}{\mathrm{C}}\mathrm{OH}$	4.76
propanoic acid	$\underset{\mathrm{CH_3}}{\underset{\vert}{\mathrm{CH_2}}}\overset{\overset{\mathrm{O}}{\parallel}}{\mathrm{C}}\mathrm{OH}$	4.87
fluoroethanoic acid	$\underset{\mathrm{F}}{\underset{\vert}{\mathrm{CH_2}}}\overset{\overset{\mathrm{O}}{\parallel}}{\mathrm{C}}\mathrm{OH}$	2.59
chloroethanoic acid	$\underset{\mathrm{Cl}}{\underset{\vert}{\mathrm{CH_2}}}\overset{\overset{\mathrm{O}}{\parallel}}{\mathrm{C}}\mathrm{OH}$	2.86
bromoethanoic acid	$\underset{\mathrm{Br}}{\underset{\vert}{\mathrm{CH_2}}}\overset{\overset{\mathrm{O}}{\parallel}}{\mathrm{C}}\mathrm{OH}$	2.90
iodoethanoic acid	$\underset{\mathrm{I}}{\underset{\vert}{\mathrm{CH_2}}}\overset{\overset{\mathrm{O}}{\parallel}}{\mathrm{C}}\mathrm{OH}$	3.17

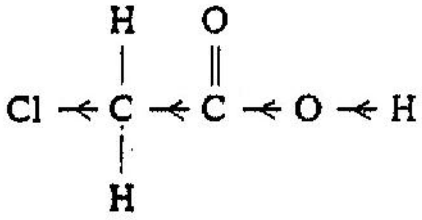
Table 1.3 shows the decreased acidity for propanoic acid (larger p*K*a value) as compared to the ethanoic acid. Note that the propanoic acid has a methyl group in place of H in ethanoic acid. The methyl group is electron-donating in nature and therefore, has a +I effect which results in the decrease in the acidity. But the acidity increases when the electron-withdrawing substituents such as F, Cl, Br and l are present. Note that the increase in acidity is in accordance with the electronegativity of these elements.

The inductive effect of these substituents is further enhanced with the increase in the number of these substituents. This is represented in Table 1.4.

Table 1.4: Effect of increase in the number of chlorine substituents on acidity of ethanoic acid

Acid	Structure	pK_a
Ethanoic acid	 $H-\overset{H}{\underset{H}{C}}-\overset{O}{\overset{\|}{C}}-O-H$	4.76
Monochloroethanoic acid	 $H-\overset{Cl}{\underset{H}{C}}-\overset{O}{\overset{\|}{C}}-O-H$	2.86
Dichloroethanoic acid	 $Cl-\overset{Cl}{\underset{H}{C}}-\overset{O}{\overset{\|}{C}}-O-H$	1.30
Trichloroethanoic acid	 $Cl-\overset{Cl}{\underset{Cl}{C}}-\overset{O}{\overset{\|}{C}}-O-H$	0.65

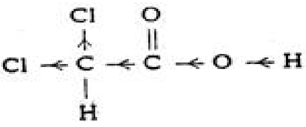
In monochloroethanoic acid, one of the three hydrogen atoms in ethanoic acid has been replaced by an electron withdrawing chlorine atom. Hence, the electron pair constituting the C–Cl bond is drawn closer to the chlorine atom. This effect is transmitted through other atoms forming σ-bonds to the OH bond of the  $-\overset{O}{\overset{\|}{C}}-O-H$ group. This results in a shift of the electrons constituting the O–H bond towards oxygen as shown below:



monochloroethanoic acid

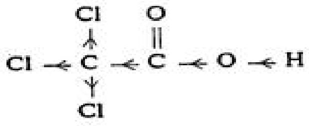
Such an electron withdrawal by chlorine atom, thus, facilities the department of the proton and hence, increases the acidic character of monochloroethanoic acid as compared to ethanoic acids, the presence of second and third chlorine.

In the di- and trichloroethanoic acids, the presence of second and third chlorine.



$Cl \leftarrow \overset{\overset{Cl}{\uparrow}}{\underset{\underset{H}{|}}{C}} \leftarrow \overset{\overset{O}{\|}}{C} \leftarrow O \leftarrow H$

dichloroethanoic acid



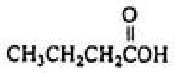
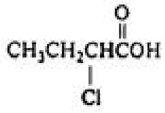
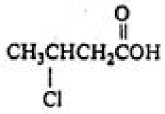
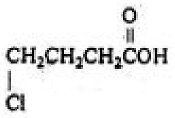
$Cl \leftarrow \overset{\overset{Cl}{\uparrow}}{\underset{\underset{Cl}{\downarrow}}{C}} \leftarrow \overset{\overset{O}{\|}}{C} \leftarrow O \leftarrow H$

trichloroethanoic acid

Atoms results in more electron withdrawal away from hydrogen of the O–H bond and would, therefore, further increases the acidity of the compounds as compared to ethanoic acid or chloroethanoic acid. Therefore, we can arrange these acids in the increasing order of their acidities as ethanoic acid < chloroethanoic acid < dichloroethanoic acid < trichloroethanoic acid.

The position of electron-withdrawing substituents in a molecule also influences its acidic character. This is shown by the pKa values of isomeric monochlorobutanoic acids given in Table 1.5.

Table 1.5: Effect of position of substituent on acidity

Name	Structure	pK_a
butanoic acid	 $CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}OH$	4.82
2-chlorobutanoic acid	 $CH_3CH_2\underset{\underset{Cl}{\vert}}{C}H\overset{\overset{O}{\|}}{C}OH$	2.86
3-chlorobutanoic acid	 $CH_3\underset{\underset{Cl}{\vert}}{C}HCH_2\overset{\overset{O}{\|}}{C}OH$	4.05
4-chlorobutanoic acid	 $\underset{\underset{Cl}{\vert}}{C}H_2CH_2CH_2\overset{\overset{O}{\|}}{C}OH$	4.52

It can be seen that although in each of these acids a chlorine atom has replaced a hydrogen atom but they show different acidities. Note that as the distance of the electron withdrawing chlorine atom from the reaction site (i.e., O–H of the COOH group) increases, the acid strength decreases. Thus, the influence of the inductive effect on acid strength is greatest when the electron withdrawing chlorine atom is present on the carbon next to the carboxylic group and it diminishes quickly with increase in the distance. This effect is almost negligible after the fourth carbon atom in the chain.

A similar electron withdrawal occurs when a positively charged group is present in a molecule. A positive centre such as $(CH_3)_3N^+$- (trimethyl ammonium) or $^+NH_3$ (ammonium), eases the departure of proton by withdrawing electrons and hence, increases the acid character of the molecule. This is illustrated in the example given below:

CH_3COOH	$(CH_3)_3\overset{+}{N}-CH_2COOH$	$(CH_3)_3\overset{+}{N}CH_2CH_2CH_2CH_2COOH$
pK_a 4.76	pK_a 1.83	pK_a 4.27

Note that here also with the increase in the distance between the positively charged group and the carboxyl group, the inductive effect decreases.
If the presence of a positively charged group increases the acidity of a molecule, then a negatively charged group should decrease the acidity. Consider the dissociation of propanedioic acid, as given below:

$$COOHCH_2COOH \xrightleftharpoons{K_{a_1}} HOOCCH_2COO^- + H^+$$

propanedioic acid
$pK_{a_1} = 2.83$

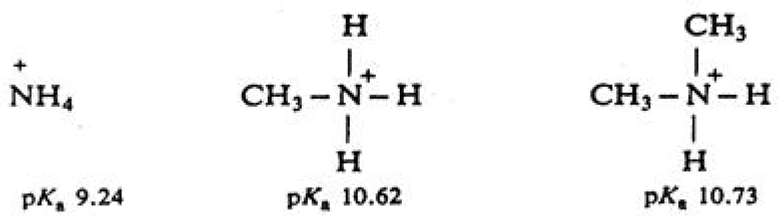
where Ka_1 is the dissociation constant.

Here, a proton is lost from one of the two carboxyl groups of the molecule. The dissociation constant for this dissociation is called the first dissociation constant and is represented by Ka_1. Further dissociation of the anion obtained in the above dissociation is difficult because it involves the removal of the proton from a negatively charged species. Therefore, this step has a pKa value equal to 5.69. This is called pKa_2 because Ka_2 represents the second dissociation constant.

Always remember that Ka_1 is larger than Ka_2 for a dicarboxylic acid. Therefore, for these acids pKa_1 is lower than pKa_2.

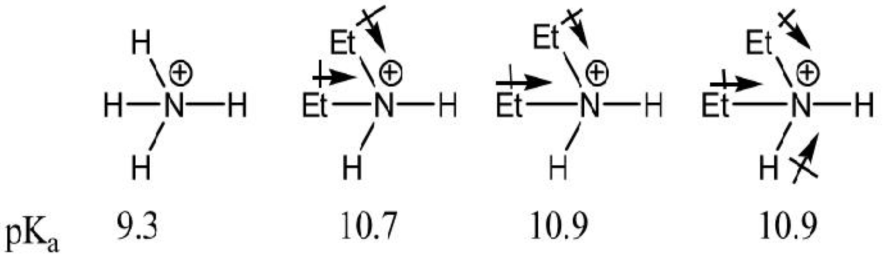
From the above discussion, we can say that the substituents having –I effect increase the acidity while the substituents having +I effect decrease the acidity.

In a similar way, since the substitution having +I effect decrease the acidity, their presence should also increase the basicity. This is what is actually observed when the hydrogen atoms of ammonia are successively replaced by methyl groups to give methylamine and dimethylamine whose basicities increase with the increase in the number of methyl groups, as shown below by the pKa values of their conjugate acids.



On protonation of amines, ammonium salts are formed.

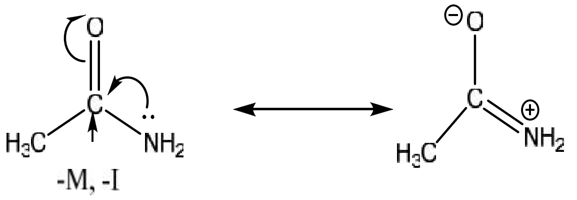
The greater the +I effect of the R group, the greater the electron density at nitrogen and the more basic the amine. The greater the +I effect, the more stable the ammonium cation and the more basic the amine.



The pKa values should increase steadily as more +I alkyl groups are introduced on nitrogen. However, the pKa values are determined in water, and the more hydrogen atoms on the positively charged nitrogen, the greater the extent of hydrogen-bonding between water and the cation. This solvation leads to the stabilization of the cations containing N–H bonds. However, in organic solvents (which cannot solvate the cation), the order of pKas is expected to be as follows:

R_3N > R_2NH > RNH_2 > NH_3 (R= +I alkyl group)
most basic least basic

The presence of –I and /or –M groups on nitrogen reduces the basicity, and hence, for example, amides are poor bases. Ethanamide has a pKa of –0.5.



The C=O group stabilises the lone pair on nitrogen by resonance. This reduces the electron density on nitrogen.

At this stage, it would be helpful to answer the following ITQ.

In-Text Question 6

1. Arrange the following compounds in the decreasing order of their acid strengths. Also, give reasons in support of your answer.

(i) CH_3COOH, $NCCH_2COOH$, $NCCH_2CH_2CH_2COOH$
(ii) CH_3NO_2, $CH_2(NO_2)_2$ $CH(NO_2)_3$
(iii) CH_3COOH, HOOCCOOH, $^-OOCCOOH$

2. Arrange the following compounds in the decreasing order of their base strength. Support your answer with reasons.

(i) aniline, *N*-methylaniline, *N*, *N*-dimethylaniline

(ii) NH_3, NH_2CH_3, NH_2OH

The COOH group is –I type. Hence, it increases the acidity in case of HOOCCOOH as compared to CH_3COOH. But, in case of $^-OOCCOOH$, the removal of a proton is different because it is a negatively charged species. Hence, it is less acidic as compared to CH_3COOH.

i) The basicities decrease in the following order:

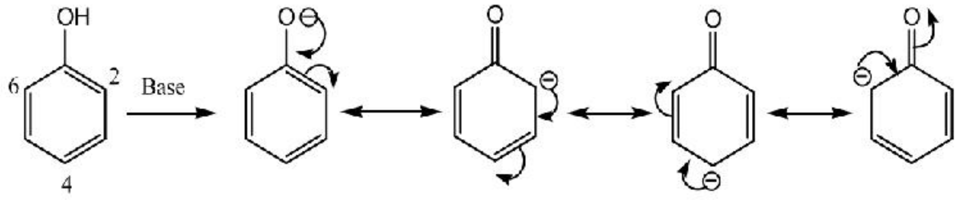
N,*N*-dimethylaniline > *N*-methylaniline > aniline

As the methyl group is electron donating, it increases the basicity in case of *N*-methylaniline as compared to aniline. The basicity further increases in *N*, *N*-dimethylaniline due to the increase in the number of methyl groups.

ii) The decreasing order of basicities is as shown below: $CH_3NH_2 > NH_3 > NH_2OH$
Since the methyl group has +I effect, it increases the basicity of CH_3NH_2 as compared to NH_2. But, the substitution of an –OH group in NH_3 decreases its basicity because it has –I effect.

b) Mesomeric effects in phenols and aryl (or aromatic) amines:

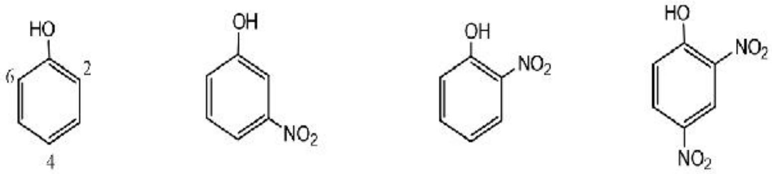
Mesomeric effects can also stabilise positive and negative charges. In this case, The negative charge needs to be on adjacent carbon atom for a –M group to stabilise it while the positive charge needs to be on adjacent carbon atom for a +M group to stabilise it. On deprotonation of phenol the phenoxide anion is formed. This stabilised by delocalisation of the negative charge at the 2-, 4- and 6-positions of the benzene ring.



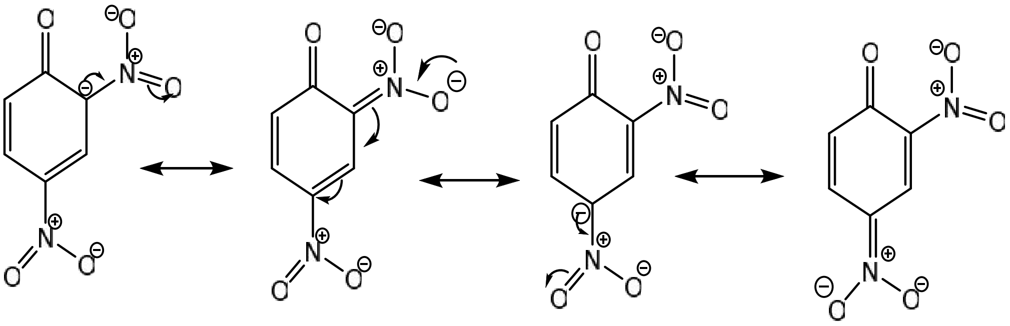
Keynotes in mesomeric effects

- If –M groups are introduced at 2-, 4- and/or 6-positions, the anion can be further stabilised by delocalization through the π-system, as the negative charge can be spread onto the –M group. We can use double-headed curly arrows to show this process.
- If –M groups are introduced at the 3- and/or 5-positions, the anion cannot be stabilised by delocalization, as the negative charge cannot be spread onto the –M group. There is no way of using curly arrows to delocalize the charge onto the –M groups.
- If –I groups are introduced on the benzene ring, the effect will depend on their distance from the negative charge. The closer the –I group is to the negative charge, the greater will be the stabilising effect. The order of –I stabilisation is therefore 2-position > 3-position >4-position.
- The –M effects are much stronger than –I effects.

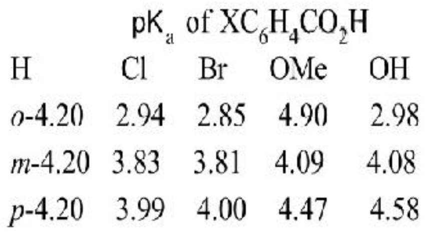
Example: The NO_2 group is strongly electron-withdrawing; –I and –M.



pK_a	9.9	8.4	7.2	4.0
	Least acidic as no -I or -M groups on the ring	The NO_2 can only stabilise the anion inductively	The NO_2 can only stabilise the anion inductively and by resonance	Most acidic as both NO_2 groups can stabilise the anion inductively and by resonance

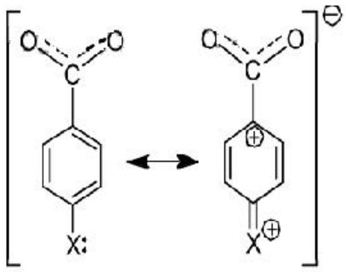


The presence of groups such as OH, OMe, or halogen an electron-withdrawing inductive effect, but an electron-donating mesomeric effect when in the o- and p- positions, may, however, cause the p- substituted acids to be weaker than the m- and, on occasion, weaker even than the unsubstituted acid itself, e.g. p-hydroxybenzoic acid:

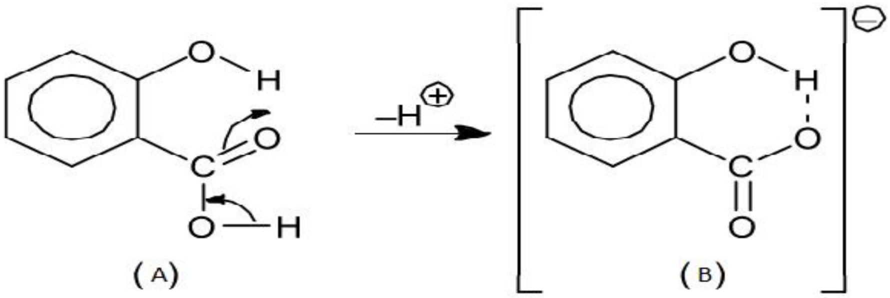


pK$_a$ of $XC_6H_4CO_2H$

H	Cl	Br	OMe	OH
o-4.20	2.94	2.85	4.90	2.98
m-4.20	3.83	3.81	4.09	4.08
p-4.20	3.99	4.00	4.47	4.58



It will be noticed that this compensating effect becomes more pronounced in going Cl ≈ Br → OH, i.e. in increasing order of readiness with which the atom attached to the nucleus will part with its electron pairs. The behaviour of o- substituted acids is, as seen above, often anomalous. Their strength is sometimes found to be considerably greater than expected due to direct interaction between the adjacent groups. Thus intramolecular hydrogen bonding stabilises the anion **(B)** from o-hydroxybenzoic (salicyclic) acid **(A)** by delocalising its charge, an advantage not shared by its m- and p- isomers, nor by o- methoxy benzoic acid:

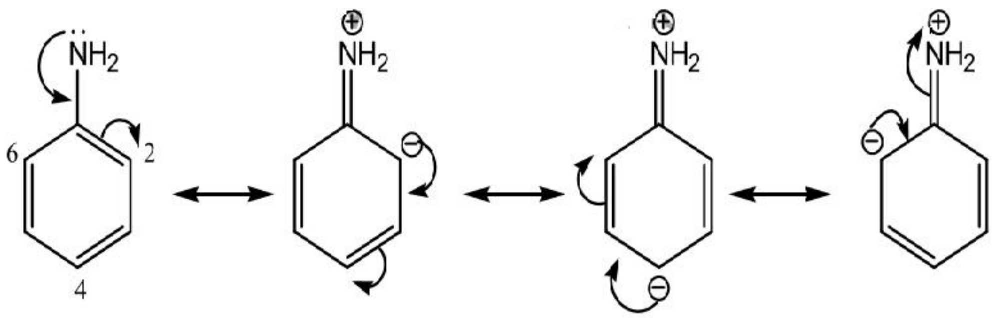


Intramolecular hydrogen bonding can, of course, operate in the undissociated acid as well as in the anion, but it is likely to be considerably more effective in the latter than in the former - with consequent relative stabilisation - because the negative charge on oxygen in the anion will lead to stronger hydrogen bonding. The effect is even more pronounced where hydrogen bonding can occur with hydroxyl groups in both o-position, and 2, 6-dihydroxybenzoic acid is found to have pKa = 1.30. The below table shows different carboxylic acids and their respective pKa values.

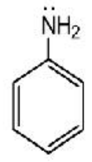
Table 1.6: Different carboxylic acids and their respective pKa values

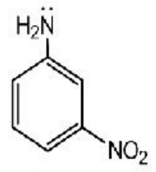
Acid	pKa Value	Acid	pKa Value
HCO_2H	3.77	HO_2CCO_2H	1.23
CH_3CO_2H	4.76	$HO_2CCH_2CO_2H$	2.83
$CH_3CH_2CO_2H$	4.88	$HO_2CCH_2CH_2CO_2H$	4.19
$C_6H_5CO_2H$	4.17	$HO_2CC_6H_4CO_2H$	*o*- 2.98; *m*- 3.46; *p*- 3.51

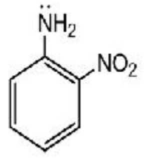
Similar to acidity, the basicity of compounds is also affected by the resonance. For example, in case aminobenzene (aniline), the lone pair of electrons on the nitrogen atom of the aminobenzene can be stabilized by the delocalization of the electrons onto the 2-, 4-and 6-positions of the benzene ring. Aromatic amines are therefore less basic than aliphatic amines.



- If –M groups are introduced at the 2-, 4-and/or 6-positions (but not at the 3- or 5-position), the anion can be further stabilised by delocalization, as the negative charge can be spread onto the –M group. This reduces the basicity of the amine.
- If –I groups are introduced on the benzene ring, the order of –I stabilisation is 2-position > 3-position > 4-position. This reduces the basicity of the amine.



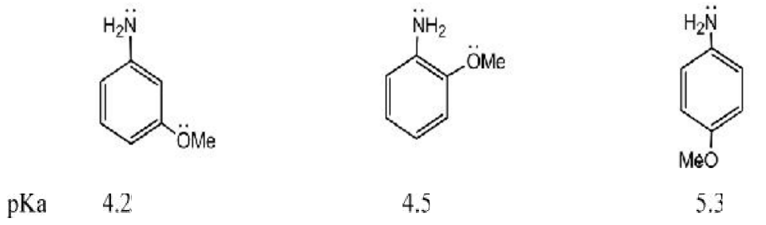




pK_a	4.6	2.45	−0.28
	Most basic as no-I or M groups on the ring	The NO_2 group can stabilise the lone pair inductively	Least basic: The NO_2 group can stabilise the lone pair inductively and by resonance

- If +M group (e.g. OMe) are introduced at the 2-, 4- or 6-position of aminobenzene, then the basicity is increased. This is because the

+M group donates electron density to the carbon atom bearing the amine group.

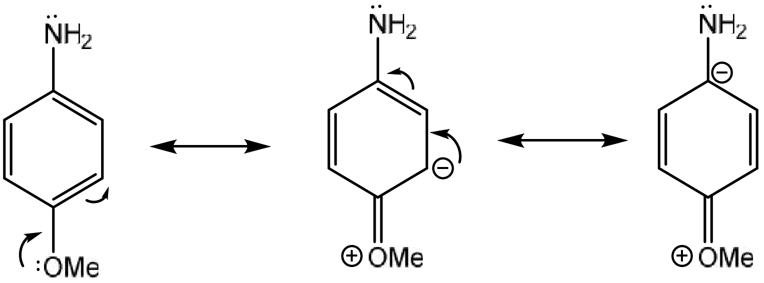


Least basic: The OMe group cannot donate electron density to the carbon atom bearing the nitrongen

The OMe group can donate electron density to the nitrogen but it has a strong –I effect as it is in the 2-position

Most basic: The OMe group can donate electron density to the nitrogen and it has a weak –I effect (as well apart from the nitrogen)

This trend can be illustrated using the scheme below:



electron density adjacent to the nitrogen increases the basicity

Resonance structures discussed in this section involve π - electrons and in some cases non-bonded electrons. These resonance structures clearly show that the nonbonding electrons of the nitrogen atom are delocalized over the aromatic ring. Thus, the electron density at the nitrogen atom increases which results in the higher basicity of *p*-substituted aniline.

You can test your knowledge of resonance by answering the following **ITQ.**

In-Text Question vii

Draw resonance structures for the following species to rationalize the facts given with them.

a. $H_2C = :O^+–H$ is the conjugate acid of methanal (formaldehyde) and has a substantial positive charge on carbon.

b. In acetonitrile oxide. $H_3C – C = N^+–O:$ -, the inner carbon can act as a Lewis acid.

So far we have been discussing factors that may influence the relative availability of electrons in bonds, or at particular atoms, in a compound, and hence affect that compound’s reactivity. The operation of these factors may, however, be modified or even be nullified by the influence of steric factors; thus effective delocalization via π-orbitals can only take place if the p or π-orbitals on the atoms involved in the delocalization, can become parallel or fairly nearly so. If this is prevented, significant overlapping cannot take place and delocalization may be inhibited. In the next section, you will study the steric effect on molecular reactivity.

3.3 Steric Effect

The effect arising from the spatial interactions between the substituent groups is called the **steric effect**. Resonance ability of an atom is lost if it loses planarity with the other part of the system due to steric crowding by bulky group in adjacent positions. In a way, you have already studied the effect of such interactions on the stability of geometrical isomers (where you studied that the trans-isomer is more stable than the cis-isomers) and conformational isomers (where you studied that the staggered conformation is more stable than the eclipsed conformation). As the acid-base behaviour or the molecular reactivity is related to the availability of the electrons, steric factors may also influence the molecular reactivity. For example, they can inhibit the delocalization of charge, as observed in case of N,N-dimethyl-o-toluidine. The delocalization of the non-bonded electron pair on nitrogen, as shown in the structure of N,N-dimethylaniline in Fig 1.8 (a).

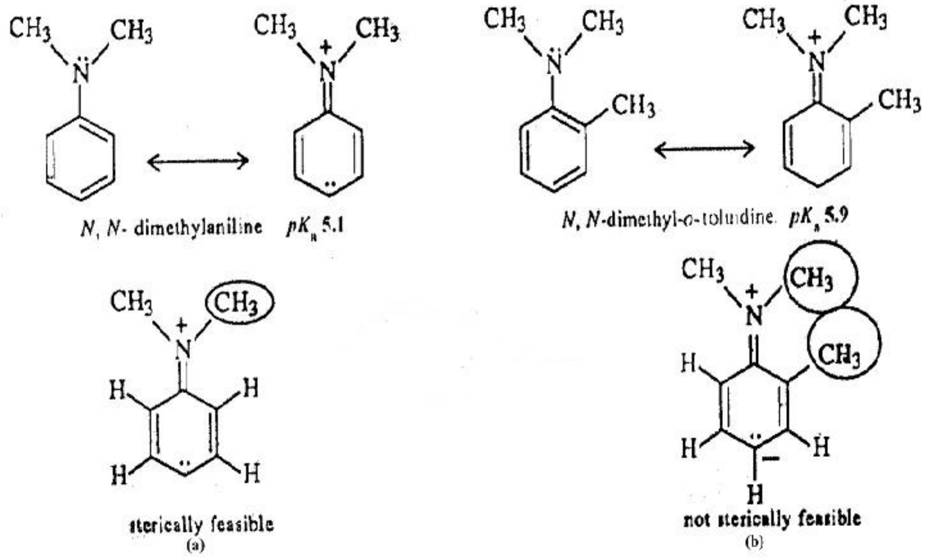


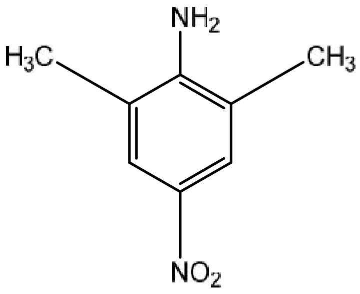
Fig 1.8: (a) Delocalization of non-bonded electrons on nitrogen into aromatic ring in N,N-dimethylaniline (b) Such a delocalization in not possible in N,N-dimethyl-o-toluidine requires that the p-orbital of nitrogen and those of the aromatic ring should be coplanar. Such coplanarity is inhibited in the case N,N-dimethyl-o-toluidine due to the presence of the *ortho* methyl group, as shown in Fig. 1.8 (b). Therefore, in this molecule the electron pair is not delocalized but is available for bonding with the proton which makes this molecule more basic than

N,N-dimethylaniline. This type of steric effect is known as steric, inhibition of resonance.

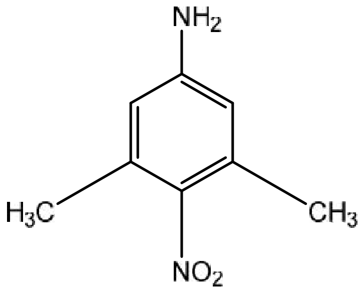
The most common steric effect is, however, the *steric hindrance* where the presence of the bulky groups makes the approach of the reagent to the reaction site difficult. Such steric hindrance can account for the lower basicity of tertiary amines as compared to secondary amines.

Remember that the steric hindrance affects the molecular reactivity not by increasing or decreasing the electron availability but due to spatial congestion. Therefore, it is different from electronic effects.

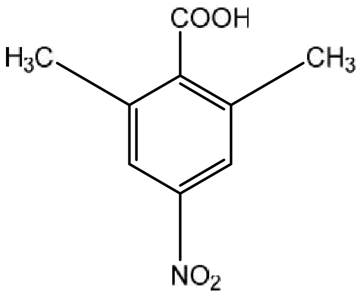
Let’s look at some other acid and base examples below:



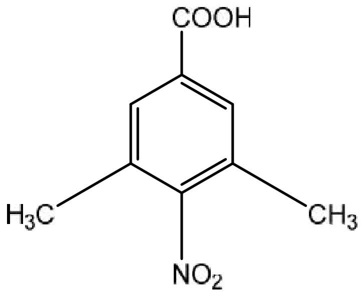
(A)



(B)



(C)

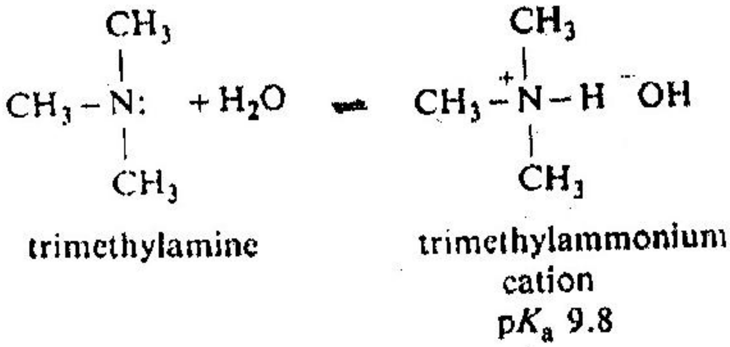


(D)

In the above compounds, A and B have everything identical except position of the two methyl group. It is expected that A should be stronger base than B due to closeness of two electron donating methyl group to –NH_2. The fact is opposite to this. In compound B –NO_2 is surrounded by two bulky methyl group and they sterically repel the –NO_2 group. In order to minimize the steric repulsion by the two adjacent methyl group, the nitro group loses planarity with the benzene ring. Therefore, –NO_2 due to lack of planarity-weigh ring is not able to resonate. This is known as steric inhibition of resonance. Thus in B, –NO_2 is not decreasing basic strength by resonance. In A –NO_2 lies in the plane of the ring, it is in resonance with the ring, decreases basic strength of –NH_2 by resonance, hence weaker base.

Using same analogy, we can explain the acidic strength of C and D. C is stronger acid in spite of closeness of two electron donating methyl group to –COOH.

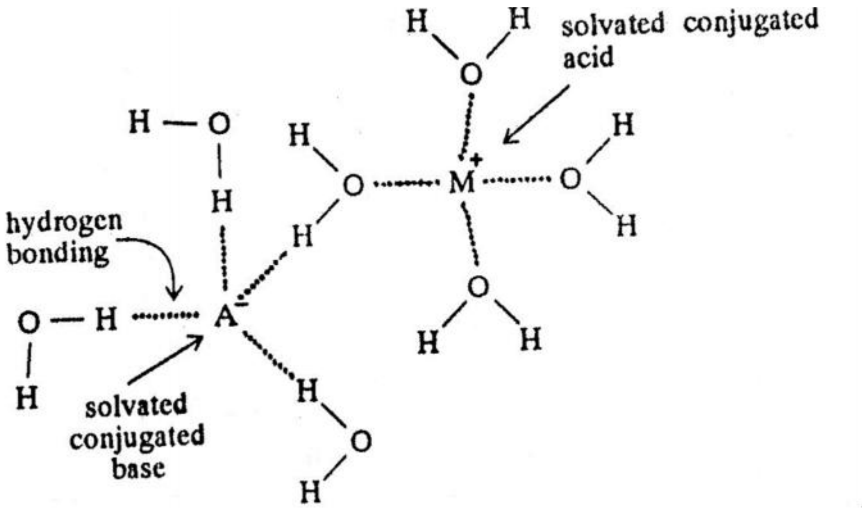
Activity 3.1:
Make models of primary, secondary and tertiary amines and compare the steric hindrance observed in these molecules.



Trimethylamine is thus least stabilized by solvation, leading to the lower basicity of trimethylamine in water as compared to dimethylamine and methylamine. However, in the gas phase or non-aqueous media, the electron-donating inductive effect of a methyl group makes trimethylamine the most basic among the methylamines.

Let us now study what is solvation and the role of solvent on the reactivity of the molecules.

The presence of a solvent in acid-base reactions leads to the solvation of the ionized species which are the conjugate acid and the conjugate base when we are dealing with Bronsted acids and bases. **Solvation** refers to the interaction of the dissolved species and solvent molecules wherein several solvent molecules surround the dissolved species by forming a **solvent shell** or **solvent cage** around it, as shown below:



The greater the solvation, the greater is the delocalization of the charge on the species. Thus, increased solvation increases the dissociation of an acid or a base by increasing the stability of the ions. These interactions are particularly important when water is used as a solvent where the hydrogen bonding plays an important role in solvating the anions. The high dielectric constant of water also helps in the dissociation of the acids. Thus, the ionization and the acidity of a substance increases with the increase in the dielectric constant of the solvent. This is illustrated in Table 1.7.

Table 1.7: Effect of solvent on p*K*a of ethanoic acid at 298 *K*

Solvent	p*K*a
Benzene	Almost unionized
82% Dioxane – 18% Water	10.14
70% Dioxane – 30% Water	4.32
45% Dioxane – 55% Water	6.31
20% Dioxane – 80% Water	5.29
Water	4.76

Thus, as the percentage of water in the solvent system increases, p*K*a value of the acid decreases. Water is peculiar solvent as it can behave both as an acid as well as a base. But its use has a limitation in the sense that some organic compounds are not soluble in it.

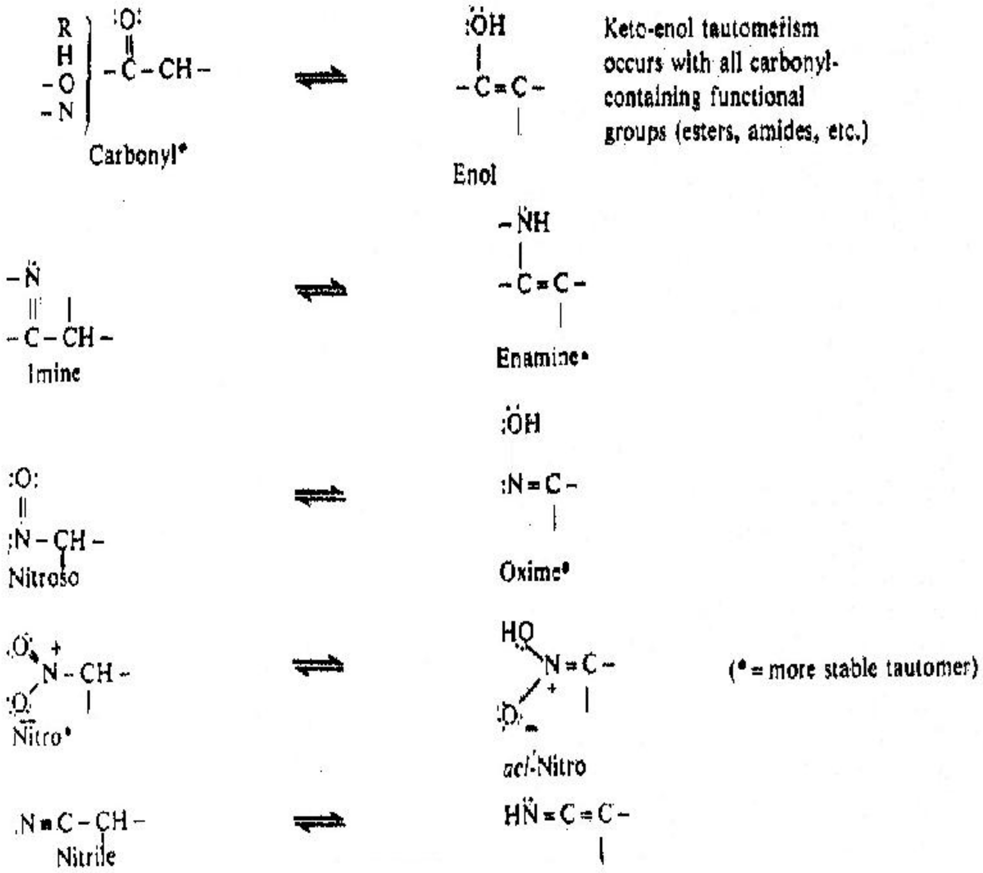
Having discussed the various aspects of acids and bases, let us now focus our attention on an internal acid-base process called *tautomerism.*

In-Text Question viii
What is a steric effect in organic chemistry?

3.4 Tautomerism

The term *tautomerism* designates a rapid and reversible interconversion of isomers which are related to each other with the actual movement of electrons as well as of one or more atoms. Such isomers are called **tautomers.** Thus, tautomerism is a chemical reaction and is to be differentiated from resonance in which the nuclei do not move. It is, therefore, represented by the equilibrium sign ($\rightleftharpoons$) between the tautomers. Tautomers which differ from each other only in the location of a hydrogen atom and a double bond are called **proton tautomers.** Table 1.8 shows some examples of proton tautomers. In contrast to resonance structure, tautomers are real compounds and are capable of independent existence.

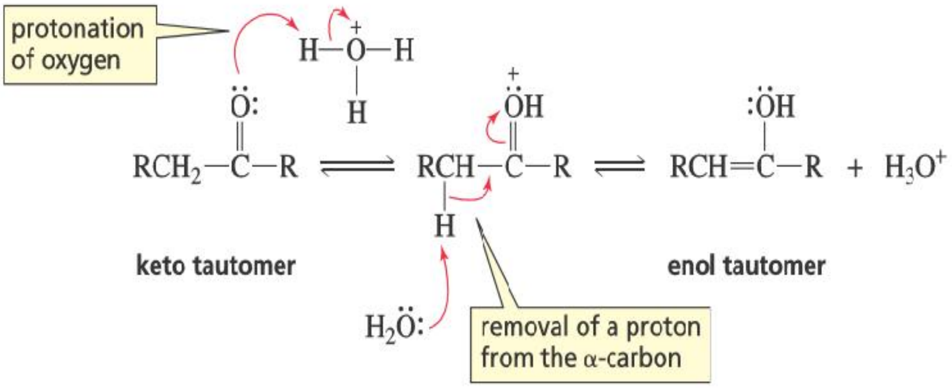
Table 1.8: Some examples of proton tautomers



Keto-enol tautomerism occurs with all carbonyl-containing functional groups (esters, amides, etc.)

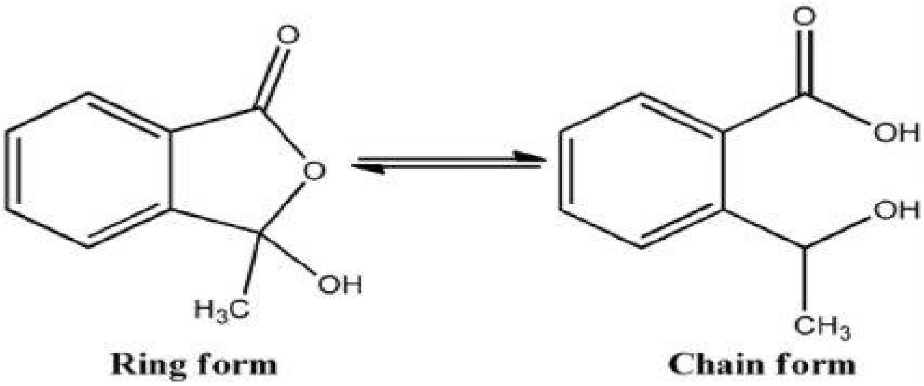
(* = more stable tautomer)

A particular example of tautomerism involving the ketones as carbonyl compounds is called **keto-enol** tautomerism and is represented below:

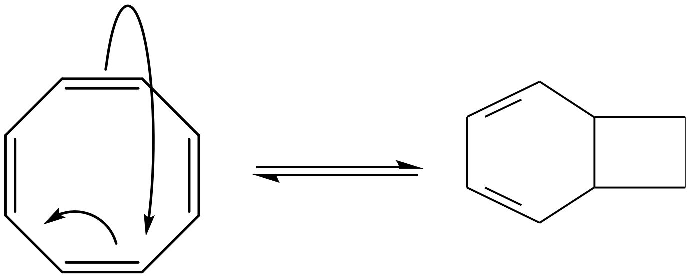


The keto-enol tautorism is enormous importance as you will study later in this course and also in the Organic Reactions Mechanism course. In keto-enol tautomers, the keto form is usually the more stable form and, therefore, it predominates at equilibrium.

The mechanism of enolisation involves solvent mediated proton transfer steps rather than a direct intramolecular jump of the proton from carbon to oxygen. Proton tautomerism in some cases leads to the formation of a ring in one of the tautomers. Such a tautomerism is known as **ring-chain tautomerism** and is illustrated below for 2-acetylbenzoic acid:



Another kind of tautomerism, known as **valence tautomerism** involves a shift in interatomic distance within a molecule, without the separation of any atom from the rest of the molecule, as an intermediate stage. This kind of tautomerism occurs as a result of movement of valence electrons of the molecule. An example of valence tautomerism is shown below:



cyclooctatetraene

The valence tautomerism may appear similar to resonance but remember that the two are different. The difference is that the valence tautomerism involves making and breaking of σ and π electrons or the nonbonding electrons shift and the σ framework of the molecule is not disturbed. Some other differences between tautomerism and resonance are as follows:

ii) Tautomerism may involve a change in the hybridization of atoms which may result in a change in the shape of the molecule. While in resonance there is no such change in the hybridization and geometry of the molecule.
iii) The tautomers have a physical reality while the resonance structures are imaginery.
iv) Tautomerism involves an equilibrium between two or more tautomers. On the other hand, the resonance implies that the actual structure of the molecule in the *weighted averaged* of various resonance contributors and not a mixture on them.

SELF ASSESSMENT EXERCISE

i. Explain the acidic nature of 2,2,2-trifluoroethanol as compared to ethanol.

ii. Explain the difference between pK_{a1} (4.16) and pK_{a2} (5.61) of butanedioic acid.

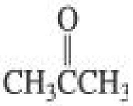
iii. Draw resonance structures for the following:

i) chlorobenzene ii) acetonitrile iii) pyrrole

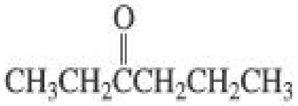
Pyrrole is less resonance stabilized than benzene, as can be seen from the above resonance structure of pyrrole that in four out of the five structures an electronegative nitrogen atom has a positive charge over it.

iv. Ethylamine and aniline react with aq. HCl. Write the equation for these reactions.

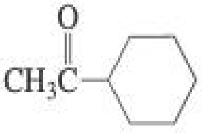
v. Draw all the enol tautomers for each of the following ketones.

a. 

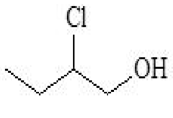
$CH_3\overset{\overset{O}{\|}}{C}CH_3$

b. 

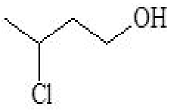
$CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2CH_3$

c. 

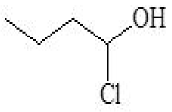
vi Which of the following alcoholic proton (O**H**) is expected to be the most acidic?



(A)



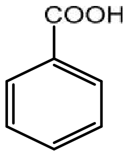
(B)



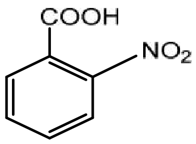
(C)

(D)

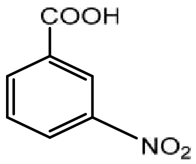
vii Deduce the correct order of acidity among the following compound I-IV.



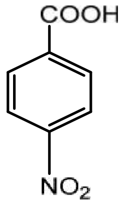
I



II



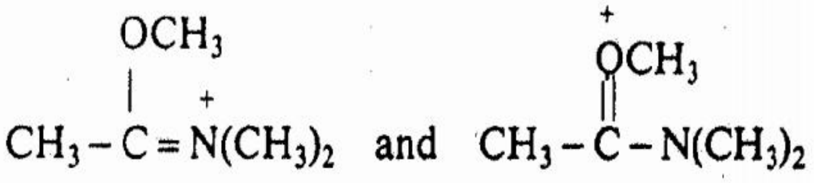
III



IV

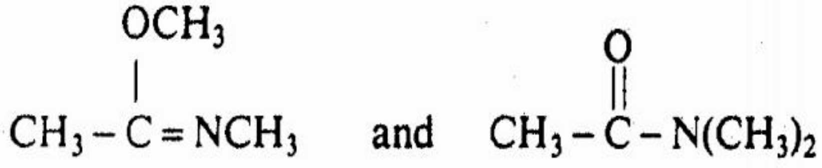
viii Are the following pairs of compounds tautomers or resonance forms?

(a)



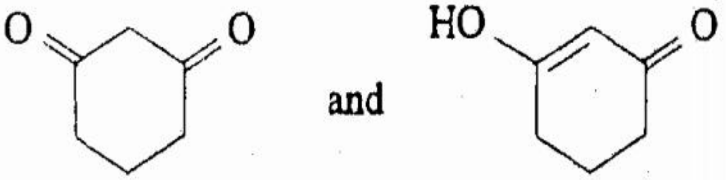
$CH_3-\overset{\overset{OCH_3}{|}}{C}=\overset{+}{N}(CH_3)_2$ and $CH_3-\overset{\overset{\overset{+}{O}CH_3}{||}}{C}-N(CH_3)_2$

(b)

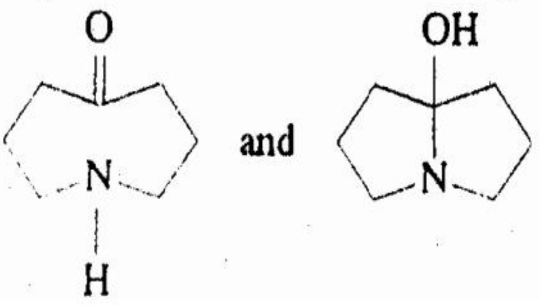


$CH_3-\overset{\overset{OCH_3}{|}}{C}=NCH_3$ and $CH_3-\overset{\overset{O}{||}}{C}-N(CH_3)_2$

(c)



(d)



4.0 CONCLUSION

Electronic effects are the effects originating or present in the organic molecules due to which the reactivity at one part of a molecule is affected by electron attraction or repulsion originating in another part of a molecule. These electronic effects are of three types mainly, inductive effect, mesomeric (or resonance) effect, and hyperconjugative effect. They are all permanent effects that stability and reactivity of organic molecules and also determines the strength of an organic acid or base.

5.0 SUMMARY

In this unit, you studied that:

- Many reactions of organic compounds can be classified as acid-base reactions. Therefore, the study of acids and bases is important for understanding the organic reactions.
- According to Bronsted-Lowry definition, an acid is a proton donor and a base is proton acceptor.
- Lewis definition classifies acids as electron pair acceptors and bases as electric pair donors.
- The acidities of Bronsted acids can be expressed in terms of their pKa values
- A strong acid has a weak conjugate base and a weak acid has a strong conjugate base and vice versa.
- Structural changes can bring about marked differences in the acidic and basic behaviour of a molecule which can be explained on the basis of inductive, resonance and steric effects and on the basis of hydrogen bonding.
- The inductive effects operate through sigma bonds and decrease rapidly with increase in the distance between the substituent and the reaction site. As a consequence of the fact that inductive effect increases with the number of substituents present, a tertiary carbocation is more stable than a secondary carbocation which is more stable than a primary carbocation.
- Resonance stabilization of an anion (or the conjugate base) favours dissociation of the acid.
- The steric effect operates due to the presence of the bulky groups near the reaction site which prevent the approach of the reagent to the reaction site. The steric requirements for Bronsted acids are usually negligible because of the small size of the proton but are important in case of Lewis acids.

- In addition to the structural changes mentioned above, the nature of the solvent also plays an important role in the acid-base equilibrium.

6.0 TUTOR MARK ASSIGNMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry*, 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

UNIT 3 STEREOCHEMISTRY

CONTENTS

1.0 INTRODUCTION

Compounds that have the same molecular formula but are not identical in structure are called isomers. Isomers fall into two main classes: constitutional isomers and stereoisomers. Constitutional isomers differ in the way their atoms are connected (revised your introduction to organic chemistry course). For example, ethanol and dimethyl ether are constitutional isomers because they have the same molecular formula, C_2H_6O, but the atoms in each compound are connected differently. While the oxygen in ethanol is bonded to a carbon and to a hydrogen, the oxygen in dimethyl ether is bonded to two carbons.

CH_3CH_2OH and CH_3OCH_3

ethanol **dimethyl ether**

Unlike the atoms in constitutional isomers, the atoms in stereoisomers are connected in the same way. Stereoisomers (also called configurational isomers) differ in the way their atoms are arranged in space. Stereoisomers are different compounds that do not readily interconvert. Therefore, they can be separated. There are two kinds of stereoisomers: cis–trans isomers and isomers that contain chirality centers.

This unit is all about stereochemistry which deals with the arrangement of atoms in space. Here, you will learn about the different kinds of stereoisomers that are possible for organic compounds.

2.0 OBJECTIVES

At the end of this unit, you should be able to:

- Understand the concept of stereochemistry.
- differentiate chiral and achiral molecules.
- recognize and draw structural isomers (constitutional isomers), stereoisomers including enantiomers and diastereomers and racemic mixture.
- identify the stereocenters in a molecule and assign the configuration as R or S.
- know the relationship between enantiomers and their specific rotations.

3.0 MAIN CONTENT

3.1 Definition of Isomers

If two or more different compounds have the same molecular formula we call them isomers. This is the general definition of isomer. Isomers are the compounds with the same composition of elements, therefore their relative molecular weights and general formulas are identical, but their structures – including in the 3D arrangement – are different. There are two major classes of isomers, and under these major classes there are further classifications of isomers as in Fig 1.9.

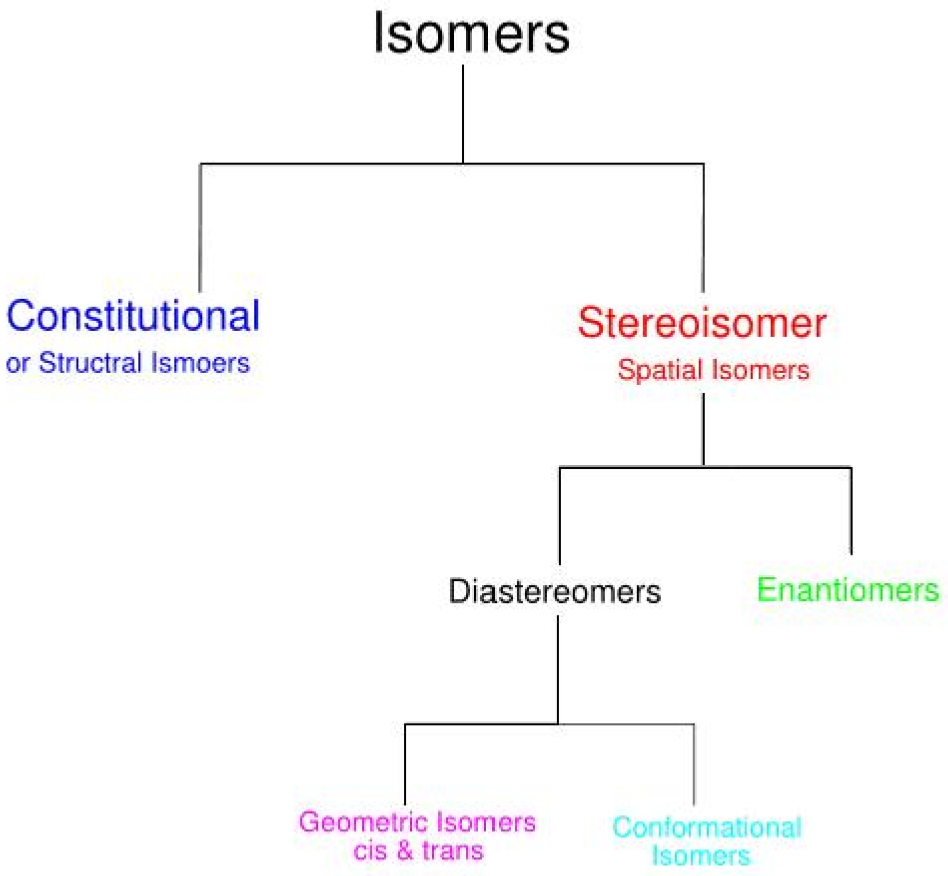


Fig 1.9: Types of Isomers

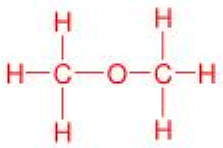
Now let us look individually at the different types of isomer and see some examples for each type.

3.1.1 Constitutional Isomers (Structural Isomers)

Different compounds that have the same molecular formula are called isomers and when they have different connectivity (i.e. which atom is bonded to which) we call them constitutional isomer or structural isomers. Examples are as shown below:

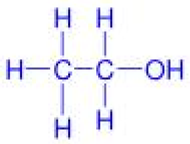
C_2H_6O

This compound has a molecular formula of C_2H_6O. Now we can draw two structures **1** & **2** for this molecular formula:



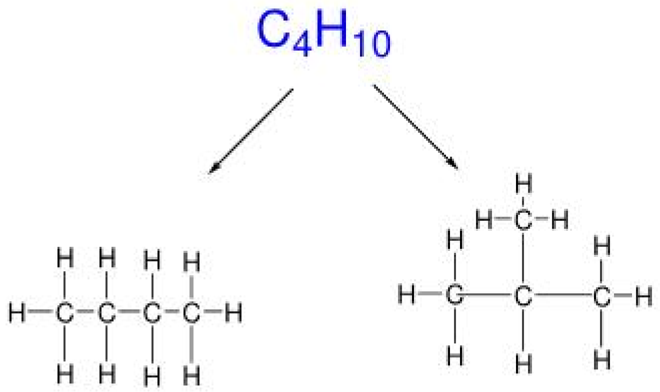
1

Dimethylether



2

Methanol



n-Butane
3

isoButane
4

Dimethyl ether **1** and Methanol **2** are constitutional isomers (or structural isomers) because both of them have the same molecular formula C_2H_6O but they have different structures due to the difference in the bond connectivity of the atoms to each other. In **1** the bonds are C-O-C and each C atom has 3 H atoms. In structure **2** the bonds are C-C-O and each carbon has 2 H and there is a one H bonded to O atom.

Similarly, the molecular formula of butane is C_4H_{10}. Two structures can be drawn for butane in order to obtain a saturated hydrocarbon with molecular formula C_4H_{10}. The two structures have the same molecular formula but they have different bond connectivity so they are constitutional isomers. Note that structure **1 & 2** are completely two different compounds, they have different physical (boiling and melting point etc.) and chemical properties. The second example is however chemically active and both isomer **3 & 4** can react with carboxylic acid to form ester while 1 will not react.
Now if you try to convert **1** to **2** or vice versa, you will never be able to do so without breaking the bonds and then re-building the molecules. The same thing is applicable in the case of structures **3 & 4**. We will never be able to interconvert from one structural isomer to another by rotation about bonds. We only can do that via only breaking bonds.

In-Text Question 1

a. Draw three constitutional isomers with molecular formula C_3H_8O.

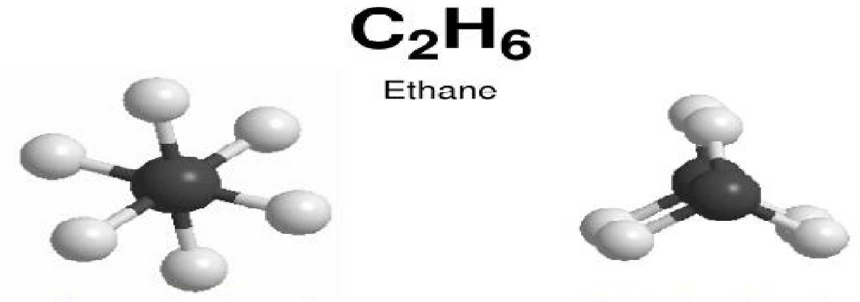
b. How many constitutional isomers can you draw for $C_4H_{10}O$?

3.1.2 Stereoisomers (Spatial Isomers)

In stereoisomers (spatial isomers), different compounds that have the same molecular formula and the same bonds connectivity but they have different arranging (orientation) in the space. There are two types of stereoisomers which are:

Conformational isomers
1) Configurational isomers

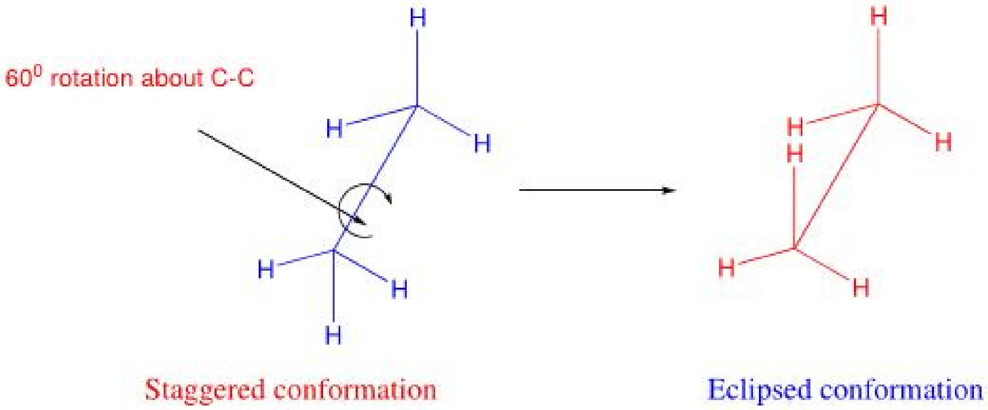
Both types are stereoisomers that have the same molecular formula and the same connectivity and both of them have different arrangement in the space. However, in Conformational isomers we can convert from one isomer to another isomer by just rotation about a C-C bond. Ethane is good and simple example on conformational isomers. Let us look at the most two important conformations of ethane staggered and eclipsed conformations.



Staggered conformation **Eclipsed conformation**

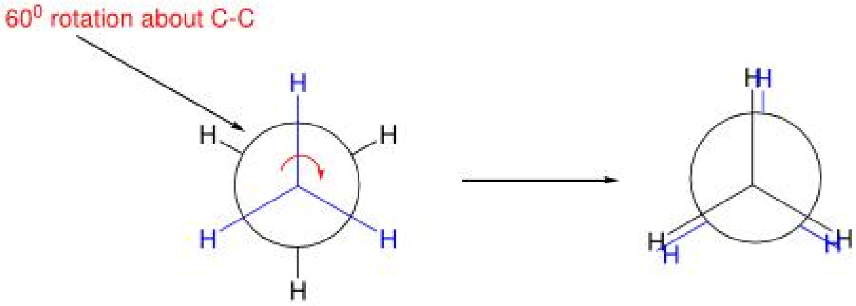
Now apply the definition of stereoisomers on the two isomers and see what you will find out?

The two structures have the same molecular formula that means they are isomers, they have the same bond connectivity that mean they are stereoisomers, they have different bonds arrangement in the space and so they may be either conformational isomers or configurational isomers. For sure now we can say they are conformational isomers because we can convert from staggered conformation to the eclipsed one via rotation about the C-C bonds. Let us look at, respectively, the chair conformers and Newman projection representation of the same example.



Chair conformers of ethane

Another view



Newman projection of the chair conformers of ethane

Hence, conformational isomers are stereoisomers that can be converted from one isomer to other isomers by rotation about C-C bond. The conformations of propane, butane and all other conformations have the same property as the ethane so they all are conformational isomers.

In-Text Question 2

Using Newman projections, draw the most stable conformer for the following:
a. 3-methylpentane, considering rotation about the bond
b. 3-methylhexane, considering rotation about the bond
c. 3,3-dimethylhexane, considering rotation about the bond

Now let us look at the second type of stereoisomers; Configurational isomers.

In the Configurational isomers we cannot convert from one isomer to other isomers by rotation about bonds. We can only convert from one isomer to other isomers via bond breaking. There are two major types of Configurational isomers which are:

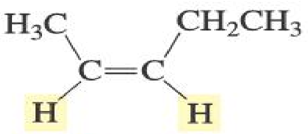
1) Geometrical isomers
2) Optical isomers

Geometrical isomers (cis-trans isomers) are isomers that have the same molecular formula, the same bond connectivity but the atoms are in different non-equivalent positions to one another. Geometrical isomers occur as a result of restricted rotation about a carbon-carbon bond. Restricted rotation about C-C bond can arise in two different situations:

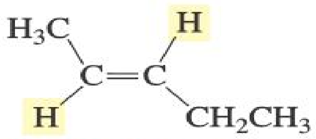
(a) In a double bond
(b) In a cyclic compound

That means geometrical isomers can arise only if we have a double bonds and/or cyclic structures.

As a result of the restricted rotation about a carbon–carbon double bond, an alkene such as 2-pentene can exist as cis and trans isomers. The cis isomer has the hydrogens on the same side of the double bond, whereas the trans isomer has the hydrogens on opposite sides of the double bond.

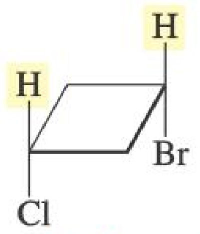


cis-2-pentene

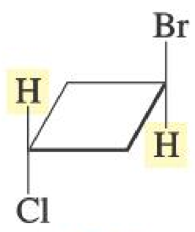


trans-2-pentene

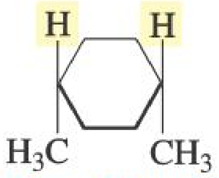
Cyclic compounds can also have cis and trans isomers. The cis isomer has the hydrogens on the same side of the ring, whereas the trans isomer has the hydrogens on opposite sides of the ring.



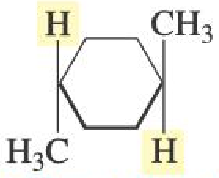
cis-1-bromo-3-chlorocyclobutane



trans-1-bromo-3-chlorocyclobutane



cis-1,4-dimethylcyclohexane



trans-1,4-dimethylcyclohexane

In-Text Question 3

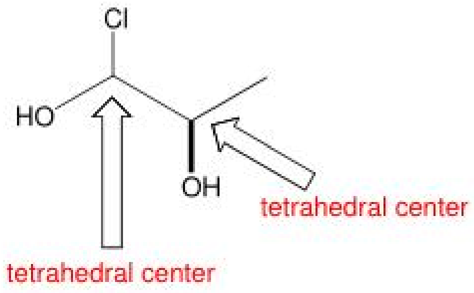
Draw the cis and trans isomers for the following compounds:

a. 3-hexene c. 1-bromo-4-chlorocyclohexane
b. 3-methyl-2-pentene d. 1-ethyl-3-methylcyclobutane

Now we will study the second type of configurational isomers which is the **optical isomers.**

3.1.3 Optical Isomerism

Optical isomerism is one form of stereoisomerism. In optical isomerism there is presence of a tetrahedral center. By tetrahedral center we mean that a C atom is attached to four other atoms or group with single bonds (sp^3 hybridization). We have the name optical isomers because of their effect on plane polarized light (reacts with light) as we will see later.



There are two major types of optical isomers

1) Enantiomers
2) Diastereomers

Before we start studying the optical isomers in details we need to learn some definition of terms related to the stereochemistry.

3.1.3.1 Chirality

Chirality means "handedness". Chiral objects (molecules) are those objects (molecules) which are not superimposable on (cannot be made to coincide with) their mirror image. In other words, its mirror image is not the same as itself. A hand is chiral because if you look at your left hand in a mirror, you do not see your left hand; you see your right hand (Figure 1.10). In contrast, a chair is not chiral—it looks the same in the mirror. Objects that are not chiral are said to be achiral. An achiral object has a superimposable mirror image. Some other achiral objects would be a table, a fork, and a glass.

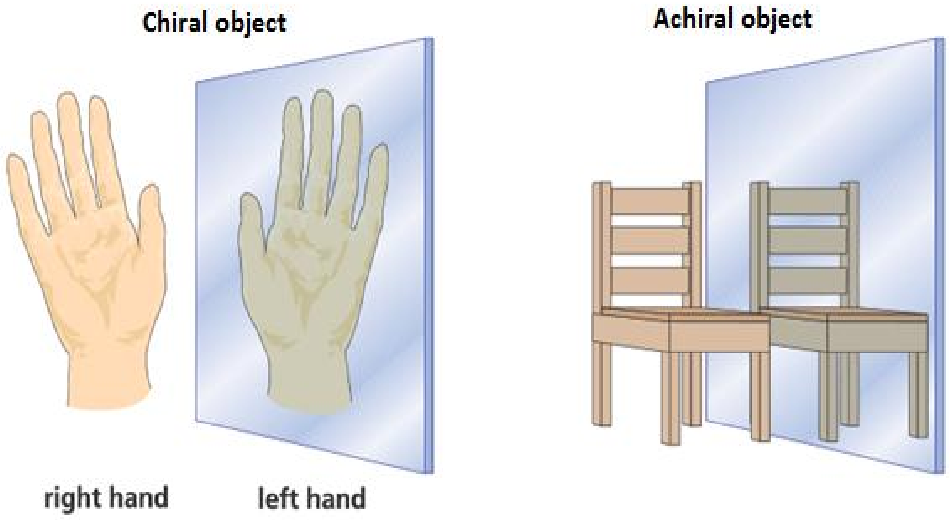
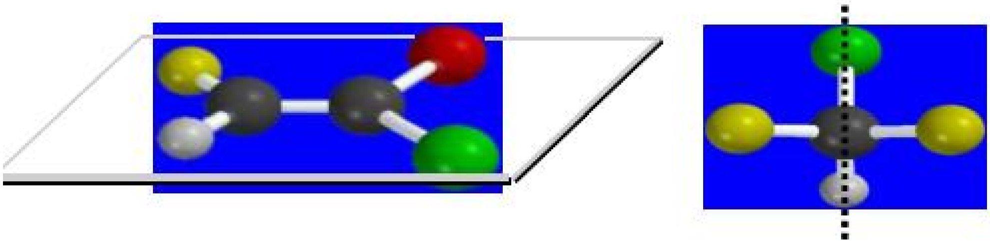
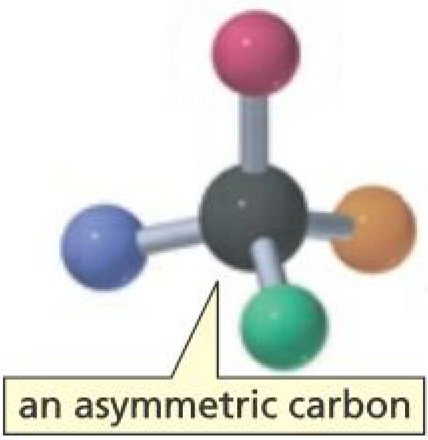


Figure 1.10: Using a mirror to test for chirality. A chiral object, right hand, is not the same as its mirror image - they are non-superimposable. An achiral object, chair, is the same as its mirror image - they are superimposable.

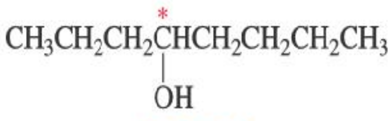
An object will exhibit handedness if it has no plane of symmetry. Plane of symmetry is a position where an object can be cut in half and each half is identical. In other words, a plane of symmetry bisects a molecule into two mirror images halves.



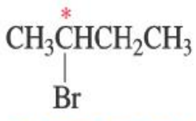
Not only objects can be chiral, molecules can be chiral, too. The feature that most often is the cause of chirality in a molecule is an asymmetric carbon.



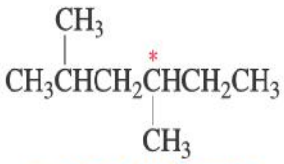
An asymmetric carbon is a carbon atom that is bonded to four different groups. The asymmetric carbon in each of the following compounds is indicated by an asterisk. For example, the starred carbon in 4-octanol is an asymmetric carbon because it is bonded to four different groups (H, OH, $CH_2CH_2CH_3$ and $CH_2CH_2CH_2CH_3$). The starred carbon in 2,4-dimethylhexane is an asymmetric carbon because it is bonded to four different groups—methyl, ethyl, isobutyl, and hydrogen.


$\mathrm{CH_3CH_2CH_2}\underset{\mathrm{OH}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CH_2CH_2CH_3}$

4-octanol

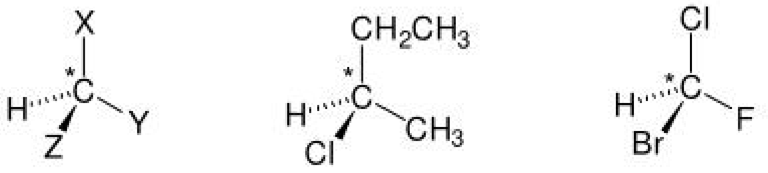

$\mathrm{CH_3}\underset{\mathrm{Br}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CH_3}$

2-bromobutane


$\mathrm{CH_3}\overset{\mathrm{CH_3}}{\mathrm{C}}\mathrm{HCH_2}\underset{\mathrm{CH_3}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CH_3}$

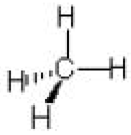
2,4-dimethylhexane

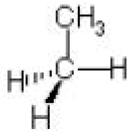
An asymmetric carbon is also known as a chirality center. The hybridization on the chiral carbon must be sp^3. Examples:

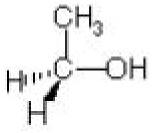


4-different atoms or groups attached to the C atom

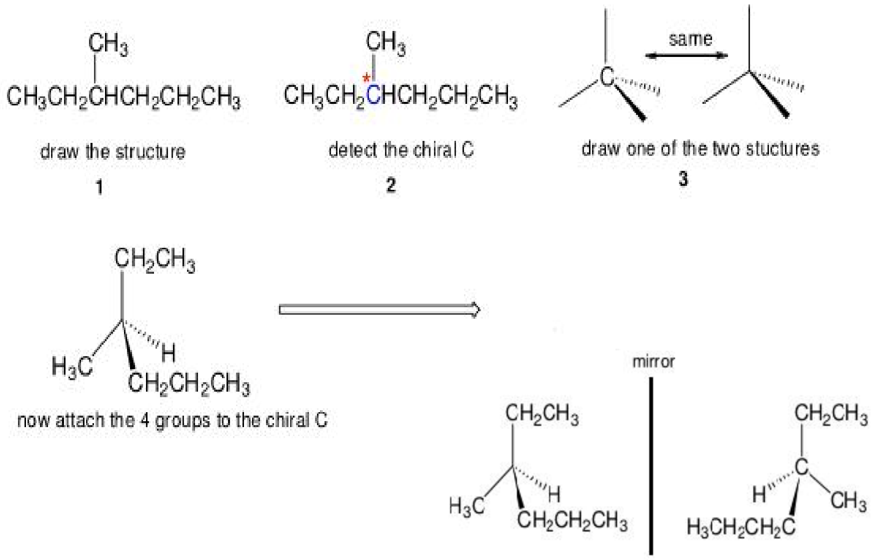
An sp^3 hybridized carbon with 1, 2, or 3 different atoms or groups attached can be superimposed on its mirror image and is, therefore achiral. None of the following three compounds (a, b, c) is chiral because they do not have 4 different atoms or groups on the sp^3 central C atom. Each of them are superimpose on its mirror image.


a

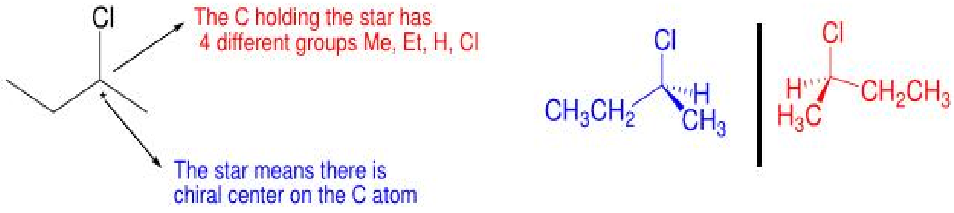

b


c

Now it is important to learn how to draw the mirror image of the structure. All what you need to do is to imagine that you have a mirror and draw what you will see. Let us take 3-methylhexane for example:



Another example using 2-chlorobutane can be shown as,



In-Text Question 4

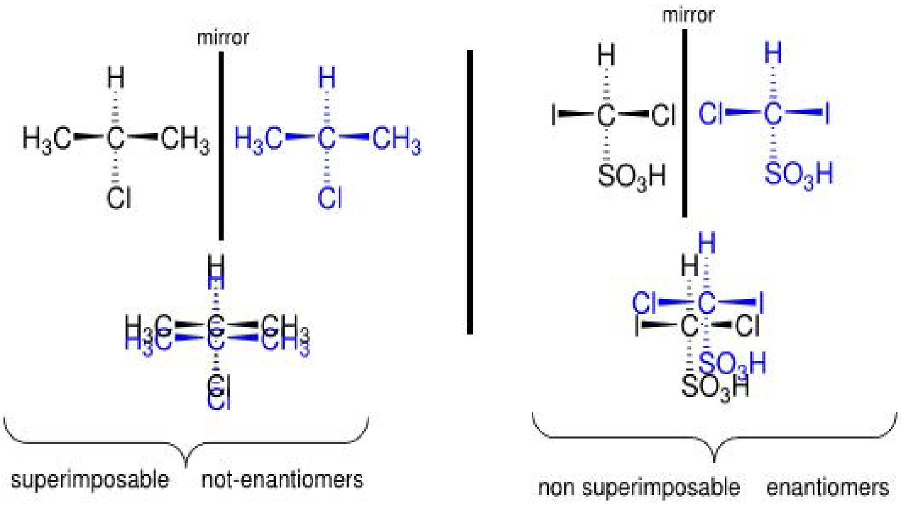
a. Name five capital letters that are chiral.

b. Name five capital letters that are achiral.

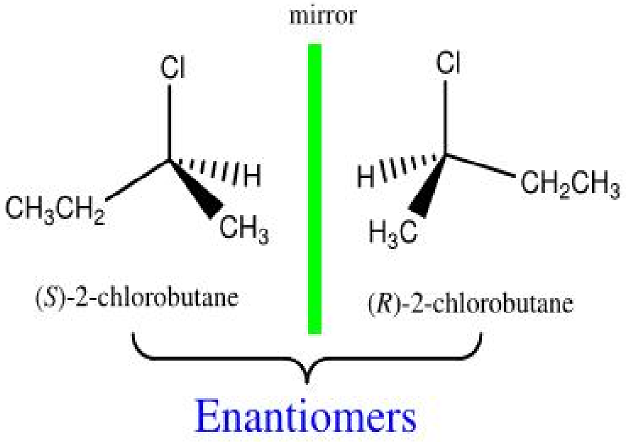
3.1.3.2 Enantiomers

Molecules that are not superimposable on their mirror images are chiral. The existence of chirality is necessary and sufficient condition for the existence of enantiomers i.e. if a compound is chiral; it can exist as enantiomers and if it is achiral it cannot exist as enantiomers.

Enantiomers (from the Greek *enantion*, which means “opposite”) are stereoisomers that are mirror image of each other and they are non-superimposable on their mirror images. In other words, two isomers (the original molecule and its mirror image) have a different spatial arrangement, and so cannot be superimposed on each other. All enantiomers are chiral (we will study them in more details soon).



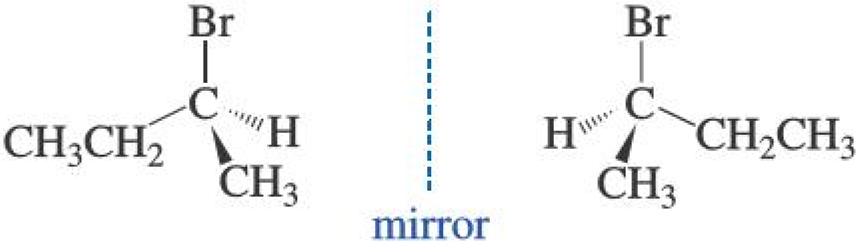
Example:



2-bromobutane can also be presented in a similar manner.

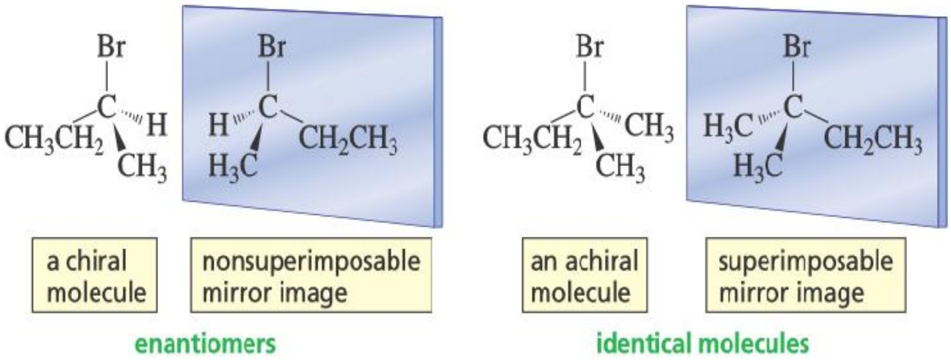
$CH_3\underset{\underset{Br}{|}}{\overset{*}{C}}HCH_2CH_3$

2-bromobutane



the two isomers of 2-bromobutane

enantiomers



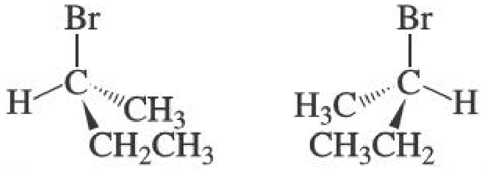
The two stereoisomers of 2-bromobutane are enantiomers. A molecule that has a non-superimposable mirror image, like an object that has a non-superimposable mirror image, is chiral. Each of the enantiomers is chiral. A molecule that has a superimposable mirror image, like an object that has a superimposable mirror image, is achiral.

To see that the achiral molecule is superimposable on its mirror image (i.e., they are identical molecules), mentally rotate the achiral molecule clockwise.

Now let us look at how chemists draw Enantiomers.

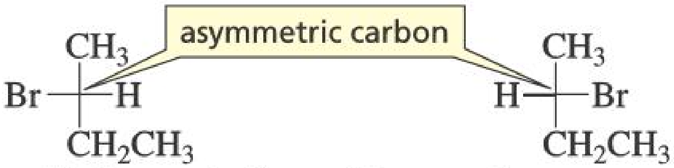
Chemists draw enantiomers using either perspective formulas or Fischer projections.

Perspective formulas show two of the bonds to the asymmetric carbon in the plane of the paper, one bond as a solid wedge protruding out of the paper, and the fourth bond as a hatched wedge extending behind the paper. You can draw the first enantiomer by putting the four groups bonded to the asymmetric carbon in any order. Draw the second enantiomer by drawing the mirror image of the first enantiomer.



perspective formulas of the enantiomers of 2-bromobutane

A shortcut—called a **Fischer projection**—for showing the three-dimensional arrangement of groups bonded to an asymmetric carbon was devised in the late 1800s by Emil Fischer. A Fischer projection represents an asymmetric carbon as the point of intersection of two perpendicular lines; horizontal lines represent the bonds that project out of the plane of the paper toward the viewer, and vertical lines represent the bonds that extend back from the plane of the paper away from the viewer. The carbon chain always is drawn vertically with C-1 at the top of the chain.



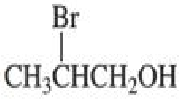
Fischer projections of the enantiomers of 2-bromobutane

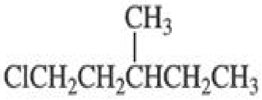
To draw enantiomers using a Fischer projection, draw the first enantiomer by arranging the four atoms or groups bonded to the asymmetric carbon in any order. Draw the second enantiomer by interchanging two of the atoms or groups. It does not matter which two you interchange. It is best to interchange the groups on the two horizontal bonds because the enantiomers then look like mirror images on paper.

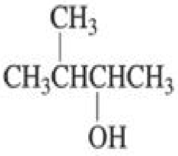
Physical properties including melting point, boiling point, colour, hardness, density, etc. All physical properties of pair of enantiomers are the same except for one propriety which is optical activity (we will discuss this in the next subsection). However, enantiomers have identical chemical properties, except toward chiral substances where they will behave differently. That mean a pair of enantiomers react in different way with external chiral molecule.

In-Text Question 5

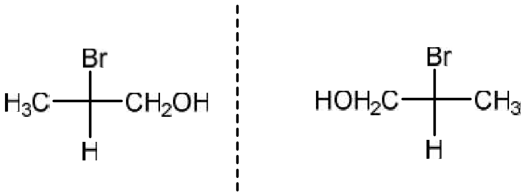
Using Fischer projections, draw enantiomers for each of the following compounds:

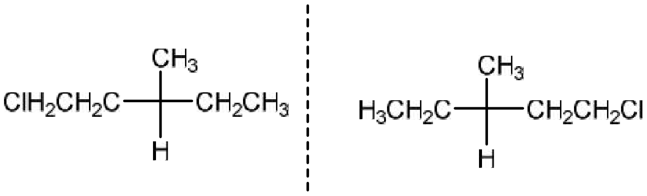
a.

$CH_3\overset{Br}{C}HCH_2OH$

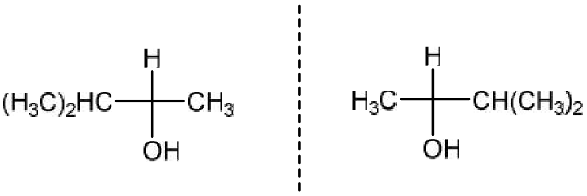
b.

$ClCH_2CH_2\overset{CH_3}{C}HCH_2CH_3$

c.

$CH_3\overset{CH_3}{C}H\underset{OH}{C}HCH_3$

In-Text Answer 5

a.


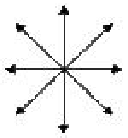
b.


c.


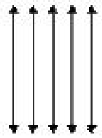
3.1.3.3 Optical Activity

Enantiomers share many of the same properties—they have the same boiling points, the same melting points, and the same solubility. In fact, all the physical properties of enantiomers are the same except those that stem from how groups bonded to the asymmetric carbon are arranged in space. One of the properties that enantiomers do not share is the way they interact with polarized light.

What is polarized light? Normal light consists of electromagnetic waves that oscillate in all directions. Plane-polarized light (or simply polarized light), in contrast, oscillates only in a single plane passing through the path of propagation. Polarized light is produced by passing normal light through a polarizer such as a polarized lens or a Nicol prism or other polarizing medium so that all of the vibrations are in the same plane.

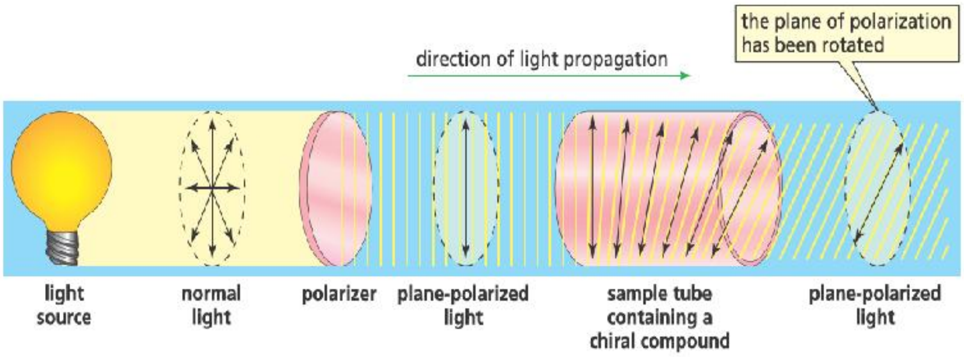


non-polarized



polarized

However, when polarized light passes through a solution of a chiral compound, the light emerges with its plane of polarization changed. Thus, a chiral compound rotates the plane of polarization. A chiral compound will rotate the plane of polarization clockwise or counterclockwise. If one enantiomer rotates the plane of polarization clockwise, its mirror image will rotate the plane of polarization exactly the same amount counterclockwise. Therefore, enantiomers rotate a plane polarized light in different direction.



A compound that rotates the plane of polarization is said to be optically active. In other words, chiral compounds are optically active and achiral compounds are optically inactive. If an optically active compound rotates the plane of polarization clockwise, it is called **dextrorotatory**, indicated by (+). If an optically active compound rotates the plane of polarization counterclockwise, it is called **levorotatory**, indicated by (-). *Dextro* and *levo* are Latin prefixes for “to the right” and “to the left,” respectively. Sometimes lowercase *d* and *l* are used instead of (+) and (-). The degree to which an optically active compound rotates the plane of polarization can be measured with an instrument called a **polarimeter**.

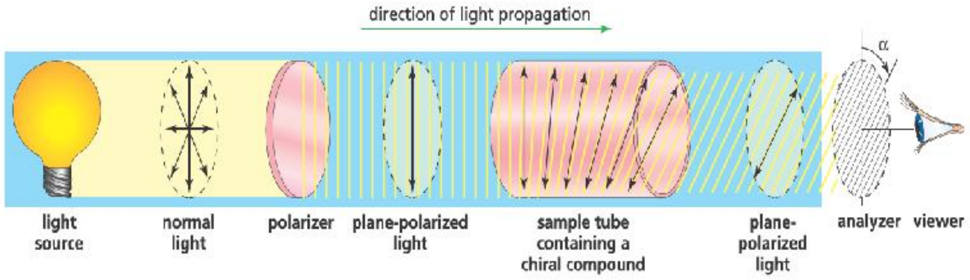


Fig 1.11: Schematic representation of polarimeter

Now when a polarized light pass through a sample in the polarimeter there are two possibilities:

1) The polarized light will pass straight without any reflection, that means either the substance in the polarimeter is achiral.
OR
The substance in the polarimeter is an equal mixture of two enantiomers. In this cases we say the substance is optically inactive. Optically inactive substances are those substances which do not rotate the polarized light. An equal mixture of enantiomers is called **Racemic mixture**. This is a mixture containing equal quantities of enantiomers (50:50) (i.e. a chiral molecule and its mirror image). The racemic mixture is optically inactive because one molecule will rotate the
polarized light for example by 50^o to the right, the other enantiomers will rotate the polarized light by 50^o to the left so they cancel each other and the resultant rotation is zero.

2) The second possibility is when the polarized light of a polarimeter pass through a sample and there is a rotation of the polarized light either to the left or to the right depending on the nature of the substance. If such a rotation takes place, we say the substance is optically active. For a substance to be optically active it must be chiral and it should be either single enantiomers or unequal mixture of enantiomers (one of them present in excess).

The amount of rotation is called the observed optical rotation, α, this value is obtained directly from the polarimeter and it depends on:

1. Concentration
2. length of the cell
3. the wavelength
4. solvent
5. temperature

To compare samples, a quantity called the **specific rotation**, $[\alpha]$, is measured. The specific rotation is the number of degrees of rotation caused by a solution of 1.0 g of the compound per mL of solution in a sample tube 1.0 dm long at a specified temperature and wavelength. The specific rotation can be calculated from the observed rotation using the following formula:

$$[\alpha]^{T}_{\lambda} = \frac{\alpha}{l \times c}$$

Where, $[\alpha]$ = specific rotation
T = temperature in °C
λ = wavelength
α = observed rotation
l = length of sample container in decimeters
c = concentration in g/mL

Example: The observed rotation of 2.0 g of a compound in 50 mL of solution in a polarimeter tube 20-cm long is $+13.4^{o}$. What is the specific rotation of the compound?

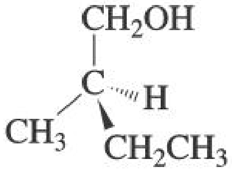
$$[\alpha]^{T}_{\lambda} = \frac{\alpha}{l \times c}$$

l in decimeter = 20/10 = 2 dm (10cm = 1 dm)

c in g/mL = 2/ 50 = 0.04 g/mL

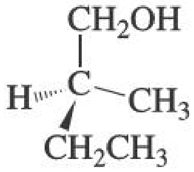
Therefore, specific rotation, $[\alpha]^{T}{}_{\lambda} = \frac{+13.4}{2 \, x \, 0.04} = +167.5^{o}$

For example, one enantiomer of 2-methyl-1-butanol has been found to have a specific rotation of $+5.75^{o}$. Because its mirror image rotates the plane of polarization the same amount but in the opposite direction, the specific rotation of the other enantiomer must be -5.75^{o}.



(*R*)-2-methyl-1-butanol

$$[\alpha]^{20\,°C}_{D} = +5.75°$$



(*S*)-2-methyl-1-butanol

$$[\alpha]^{20\,°C}_{D} = -5.75°$$

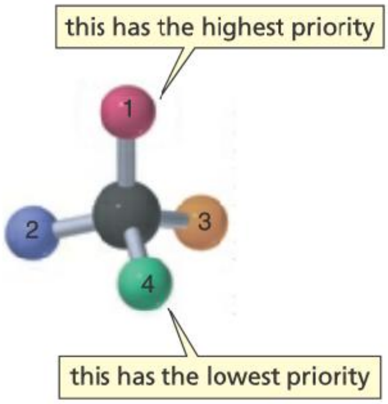
Note: when the sodium D-line is used, λ is indicated as D.

3.1.3.4 Naming of Enantiomers: The *R* and *S* System of Nomenclature

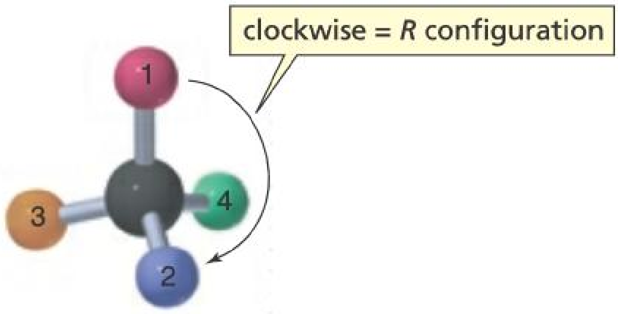
We need a way to name the individual stereoisomers of a compound such as 2-bromobutane so that we know which stereoisomer we are talking about. In other words, we need a system of nomenclature that indicates the configuration (arrangement) of the atoms or groups about the asymmetric carbon. Chemists use the letters R and S to indicate the configuration about an asymmetric carbon. For any pair of enantiomers with one asymmetric carbon, one will have the *R* configuration and the other will have the *S* configuration. The *R*,*S* system was devised by Cahn, Ingold, and Prelog.

Let us now look at the Cahn-Ingold-Prelog (CIP) sequence rules in naming enantiomers.

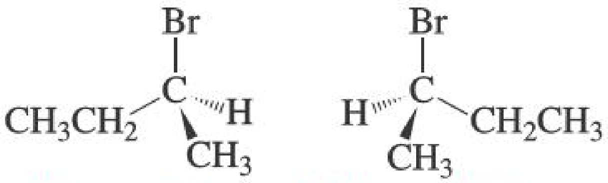
1. Rank the groups (or atoms) bonded to the asymmetric carbon in order of priority. The atomic numbers of the atoms directly attached to the asymmetric carbon determine the relative priorities. The higher the atomic number, the higher the priority.



2. Orient the molecule so that the group (or atom) with the lowest priority (4) is directed away from you. Then draw an imaginary arrow from the group (or atom) with the highest priority (1) to the group (or atom) with the next highest priority (2). If the arrow points clockwise, the asymmetric carbon has the R configuration (R is for *rectus*, which is Latin for “right”). If the arrow points counterclockwise, the asymmetric carbon has the S configuration (S is for *sinister*, which is Latin for “left”).

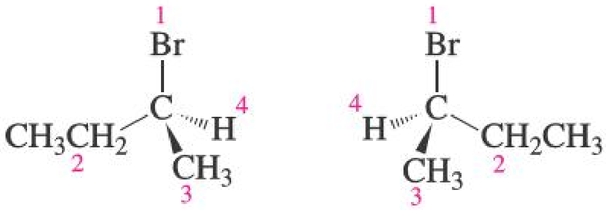


As an example, we will determine which of the enantiomers of 2-bromobutane has the R configuration and which has the S configuration.

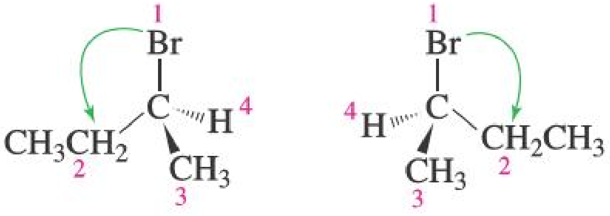


the enantiomers of 2-bromobutane

From step 1 above, we have:

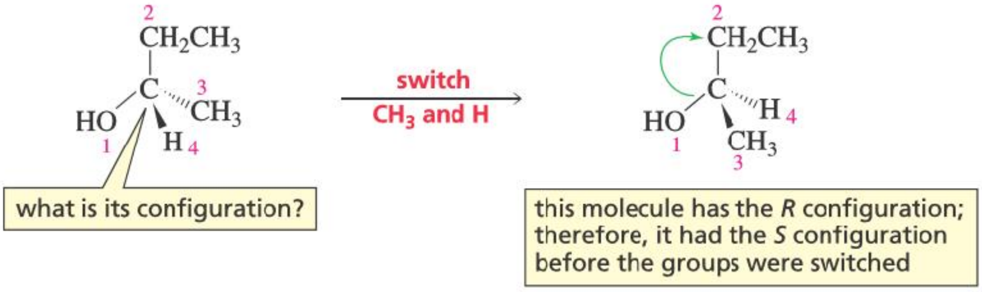


From step 2, if the group (or atom) with the lowest priority is bonded by a hatched wedge, draw an arrow from the group (or atom) with the highest priority (1) to the group (or atom) with the second highest priority (2). If the arrow points clockwise, the compound has the R configuration, and if it points counterclockwise, the compound has the S configuration.

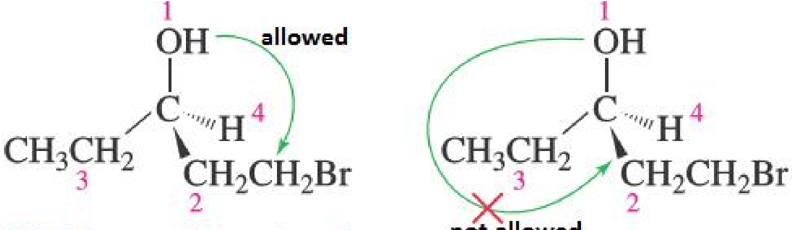


(*S*)-2-bromobutane **(*R*)-2-bromobutane**

If the group with the lowest priority (4) is not bonded by a hatched wedge, then switch two groups so group 4 is bonded by a hatched wedge. Then proceed as in step 2 (above): Draw an arrow from the group (or atom) with the highest priority (1) to the group (or atom) with the second highest priority (2). So if the arrow for the enantiomer with the switched groups points clockwise, the molecule has the R configuration. This means the original molecule before the switch has the S configuration. In contrast, if the arrow points counterclockwise, the enantiomer (with the switched groups) has the S configuration, which means the original molecule has the R configuration.



3. In drawing the arrow from group 1 to group 2, you can draw past the group with the lowest priority (4), but never draw past the group with the next lowest priority (3).

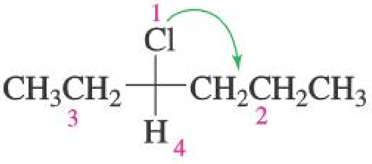


(*R*)-1-bromo-3-pentanol

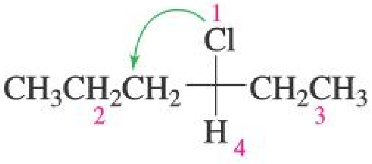
Now let's see how to determine the configuration of a compound drawn as a Fischer projection.

1. Rank the groups (or atoms) that are bonded to the asymmetric carbon in order of priority.

2. Draw an arrow from the group (or atom) with the highest priority (1) to the group (or atom) with the next highest priority (2). If the arrow points clockwise, the enantiomer has the R configuration; if it points counterclockwise, the enantiomer has the S configuration, provided that the group with the lowest priority (4) is on a vertical bond.

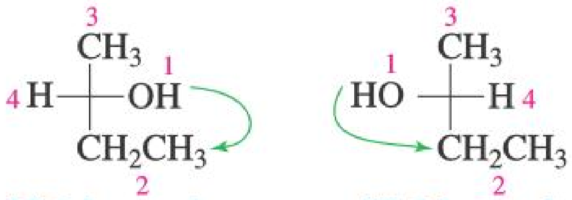


(*R*)-3-chlorohexane



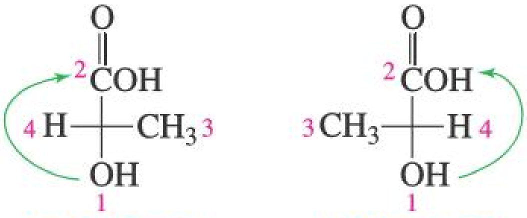
(*S*)-3-chlorohexane

3. If the group (or atom) with the lowest priority is on a horizontal bond, the answer you get from the direction of the arrow will be the opposite of the correct answer. For example, if the arrow points clockwise, suggesting that the asymmetric carbon has the R configuration, it actually has the S configuration; if the arrow points counterclockwise, suggesting that the asymmetric carbon has the S configuration, it actually has the R configuration. In the following example, the group with the lowest priority is on a horizontal bond, so clockwise signifies the S configuration, not the R configuration.



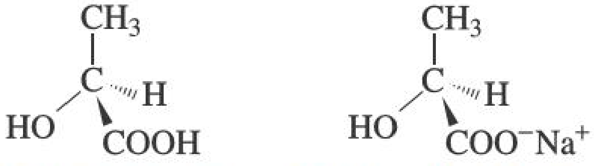
(*S*)-2-butanol (*R*)-2-butanol

4. In drawing the arrow from group 1 to group 2, you can draw past the group (or atom) with the lowest priority (4), but never draw past the group (or atom) with the next lowest priority (3).



(*S*)-lactic acid (*R*)-lactic acid

Knowing whether a chiral molecule has the R or the S configuration does not tell us the direction the compound rotates the plane of polarization, because some compounds with the R configuration rotate the plane to the right (+) and some rotate the plane to the left (-). We can tell by looking at the structure of a compound whether it has the R or the S configuration, but the only way we can tell whether a compound is dextrorotatory (+) or levorotatory (-) is to put the compound in a polarimeter. For example, (S)-lactic acid and (S)-sodium lactate have the same configuration, but (S)-lactic acid is dextrorotatory whereas (S)-sodium lactate is levorotatory. When we know the direction an optically active compound rotates the plane of polarization, we can incorporate (+) or (-) into its name.



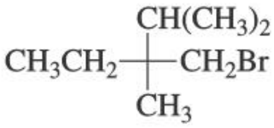
(*S*)-(+)-lactic acid (*S*)-(−)-sodium lactate

Note: When comparing two Fischer projections to see if they are the same or different, never rotate one 90° or turn one over, because this is a quick way to get a wrong answer. A Fischer projection can be rotated 180° in the plane of the paper, but this is the only way to move it without risking an incorrect answer.

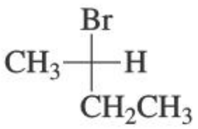
Now answer the following ITQ to check your understanding.

In-Text Question 6

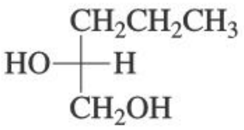
Indicate whether each of the following structures has the R or the S configuration:

a.


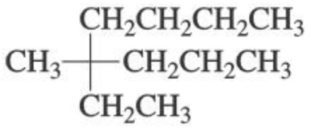
$$\begin{array}{c} CH(CH_3)_2 \\ CH_3CH_2-\!+\!-CH_2Br \\ CH_3 \end{array}$$

c.


$$\begin{array}{c} Br \\ CH_3-\!+\!-H \\ CH_2CH_3 \end{array}$$

b.


$$\begin{array}{c} CH_2CH_2CH_3 \\ HO-\!+\!-H \\ CH_2OH \end{array}$$

d.


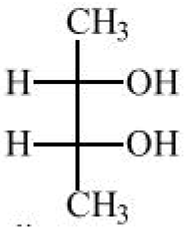
$$\begin{array}{c} CH_2CH_2CH_2CH_3 \\ CH_3-\!+\!-CH_2CH_2CH_3 \\ CH_2CH_3 \end{array}$$

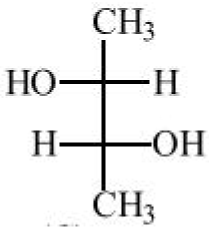
SELF ASSESSMENT EXERCISE

i. 20 mg mandelic acid was dissolved in 1 cm^3 of ethanol and the solution placed in a 10 cm long polarimeter cell. An optical rotation of –4.35ºC was measured (that is, 4.35º to the left) at 20ºC with light of wavelength 589 nm. What is the specific rotation of the acid?

ii. Neglecting stereoisomers, give the structures of all compounds with molecular formula C_5H_{10}. Which ones can exist as cis-trans isomers?

iii. The relationship between the following two structures is:





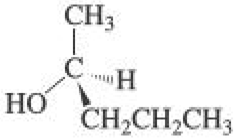
(A) enantiomers (B) diastereomers (C) structural isomers (D) identical

iv The specific rotation of pure (R)-2-butanol is -13.5°. What % of a mixture of the two enantiomeric forms is (S)-2-butanol if the specific rotation of this mixture is -5.4°? (A) 40%(B) 30%(C) 60%(D) 70%(E) None of the above

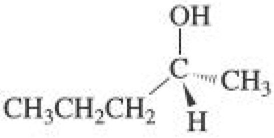
v Which of the following objects are chiral?

a. A mug with DAD written on one side of the handle.
b. A mug with MOM written on one side of the handle.
c. A mug with DAD written opposite the handle.
d. A mug with MOM written opposite the handle.
e. A wheelbarrow.
f. A remote control device.
g. A nail.
h. A screw.

vi Do the following structures represent identical molecules or a pair of enantiomers?



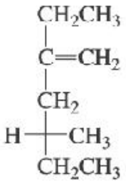
and



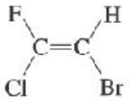
SAQ 4.7

Name each of the following compounds using R,S and E,Z designations where necessary:

a.

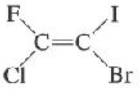


c.

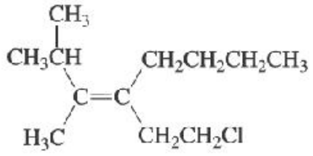


e.

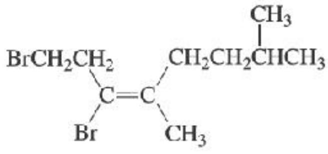
b.



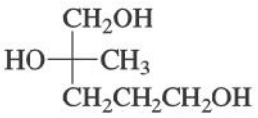
d.



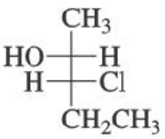
f.



g.



h.



4.0 CONCLUSION

The excitement that chemists feel for the area of stereochemistry has hopefully rubbed off during your reading of this unit. From simple structural isomers to geometric isomers and then optical isomers where we mentioned enantiomers and diastereomers, stereochemistry continues to challenge organic chemists to create molecules of increasing complexity, which inevitably leads to molecules with intriguing properties and simple aesthetic beauty. Furthermore, stereochemical concepts shed important light on the study of reaction mechanisms. It is this topic that we still need to develop further. In our analyses of reaction mechanisms, we will rely heavily upon the concepts and terminology introduced in this unit. All introductory organic chemistry courses teach the fundamentals of stereoisomerism, and we have only briefly review that information here.

5.0 SUMMARY

- Stereochemistry is the field of chemistry that deals with the structures of molecules in three dimensions.
- Compounds that have the same molecular formula but are not identical are called isomers; they fall into two classes: constitutional isomers and stereoisomers. Constitutional isomers differ in the way their atoms are connected. Stereoisomers differ in the way their atoms are arranged in space. There are two kinds of stereoisomers: cis–trans isomers and isomers that contain chirality centers.
- A chiral molecule has a nonsuperimposable mirror image. An achiral molecule has a superimposable mirror image. The feature that is most often the cause of chirality is an asymmetric carbon.
- Nonsuperimposable mirror-image molecules are called enantiomers. Diastereomers are stereoisomers that are not enantiomers.
- The letters R and S indicate the configuration about an asymmetric carbon. If one molecule has the R and the other has the S configuration, they are enantiomers; if they both have the R or both have the S configuration, they are identical.
- Chiral compounds are optically active-they rotate the plane of polarized light; achiral compounds are optically inactive. If one enantiomer rotates the plane of polarization clockwise (+), its mirror image will rotate the plane of polarization the same amount counterclockwise (-).
- A racemic mixture (recemate) is optically inactive.

6.0 TUTOR MARK ASSIGMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry*, 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry,* vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

MODULE 2 FUNCTIONAL GROUPS AND REACTIVITY IN ORGANIC CHEMISTRY

INTRODUCTION

The main classes of compounds you will study in organic chemistry are alkanes, alkenes, alkynes, alkyl halides, ethers, alcohols, and amines. As you learn various properties and reactivity of compounds, you will need to be able to refer to them by name. So you will begin your study of this module by learning how to identify and name some of these main classes of organic compounds. First you will learn how to name alkanes and the way they react because they form the basis for the names of almost all organic compounds. Subsequently you will study the various organic reactions. It is important that you are conversant with the names and formula of at least the first 10 members of each functional group in organic chemistry. The following units will be discussed in this module:

UNIT 1 FUNCTIONAL GROUP CHEMISTRY OF MAIN CLASS ORGANIC COMPOUNDS

CONTENTS

7.0 References/Further Readings

1.0 NTRODUCTION

Chemists have learned through years of experience that organic compounds can be classified into families according to their structural features and that the members of a given family often have similar chemical behaviour. Instead of 40 million compounds with random reactivity, there are a few dozen families of organic compounds whose chemistry is reasonably predictable. We'll study the chemistry of the specific families throughout much of this unit, beginning in this module with a look at the simplest family, the *hydrocarbons.*

The structural features that make it possible to classify compounds into families are called *functional groups.* A functional group is a group of atoms within a molecule that has a characteristic chemical behaviour. Chemically, a given functional group behaves in nearly the same way in every molecule it is a part of. For example, compare ethylene, a plant hormone that causes fruit to ripen, with menthene, a much more complicated molecule found in peppermint oil. Both substances contain a carbon–carbon double-bond functional group, and both therefore react with Br_2 in the same way to give a product in which a Br atom has added to each of the double-bond carbons. This example is typical: *the chemistry of every organic molecule, regardless of size and complexity, is determined by the functional groups it contains.*

2.0 OBJECTIVES

When you have studied this unit, you should be able to:

- know the major classes of organic compounds and identify important functional groups.
- understand the factors that determine the properties of organic compounds.
- have a better understanding of functional groups and reactivity of organic compounds.
- describe the importance and purpose of functional groups in organic reactions.

3.0 MAIN CONTENT

3.1 Functional Groups in Organic Chemistry

What are the characteristic features of an organic compound? Most organic molecules have C-C and C-H σ bonds. These bonds are strong, nonpolar, and are not readily broken. Organic molecules may have the following structural features as well:

- **Heteroatoms -** atoms other than carbon or hydrogen. Common heteroatoms are nitrogen, oxygen, sulfur, phosphorus, and the halogens.
- **π Bonds.** The most common π bonds occur in C-C and C-O double bonds.

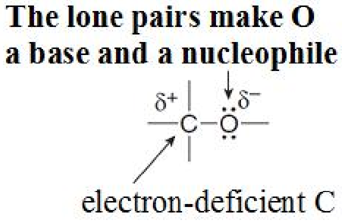
These structural features distinguish one organic molecule from another. They determine a molecule's geometry, physical properties, and reactivity, and comprise what is called a **functional group.**

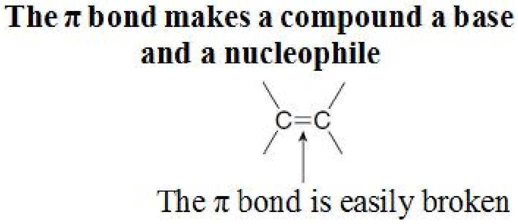
- **A *functional group* is an atom or a group of atoms with characteristic chemical and physical properties. It is the *reactive part* of the molecule.**

Why do heteroatoms and π bonds confer reactivity on a particular molecule?

- Heteroatoms have lone pairs and create electron-deficient sites on carbon.

- π Bonds are easily broken in chemical reactions. A π bond makes a molecule a base and a nucleophile.



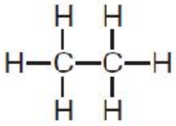


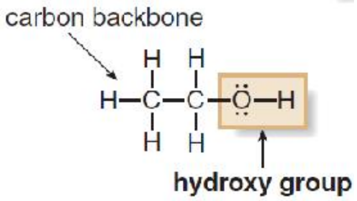
Don't think, though, that the C-C and C-H σ bonds are unimportant. They form the **carbon backbone** or **skeleton** to which the functional groups are bonded. A functional group usually behaves the same whether it is bonded to a carbon skeleton having as few as two or as many as 20 carbons. For this reason, we often abbreviate the carbon and hydrogen portion of the molecule by a capital letter **R,** and draw the **R** bonded to a particular functional group.

Ethane, for example, has only C-C and C-H σ bonds, so it has *no* functional group. Ethane has no polar bonds, no lone pairs, and no π bonds, so it has **no reactive sites.** Because of this, ethane and molecules like it are very unreactive.

Ethanol, on the other hand, has two carbons and five hydrogens in its carbon backbone, as well as an OH group, a functional group called a **hydroxyl** group. Ethanol has lone pairs and polar bonds that makes it reactive with a variety of reagents, including the acids and bases.

The hydroxyl group makes the properties of ethanol very different from the properties of ethane. Moreover, any organic molecule containing a hydroxyl group has properties similar to ethanol.





Ethane

All C-C and C-H σ bonds Polar C-O and O-H bonds

No functional group Two lone pairs

Most organic compounds can be grouped into a relatively small number of categories, based on the structure of their functional group. Ethane, for example, is an **alkane,** whereas ethanol is a simple **alcohol.**

3.2 An Overview of Functional Groups

We can subdivide the most common functional groups into several types.

- Hydrocarbons
- Compounds containing a C-Z σ bond where Z = an electronegative element
- Compounds containing a C=O group
- Others.

In-Text Question 1
What is a functional group? Give at least two examples of functional groups.

3.2.1 Hydrocarbons

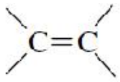
Hydrocarbons are compounds made up of only the elements carbon and hydrogen. They may be aliphatic or aromatic.

1. **Aliphatic hydrocarbons** can be divided into three subgroups.

- **Alkanes** have only C-C σ bonds and no functional group. Ethane, CH_3CH_3, is a simple alkane.

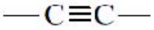
alkane

- **Alkenes** are hydrocarbons that contain one or more double bonds between neighboring carbon atoms. They have a C-C double bond as a functional group. Ethylene, $CH_2=CH_2$, is a simple alkene.



alkene

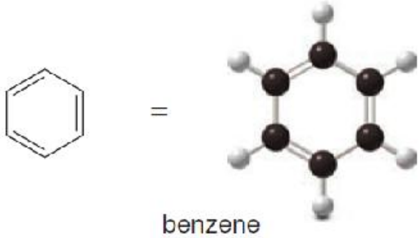
- **Alkynes** contain one or more triple bonds between neighboring carbon atoms. They have a C-C triple bond as a functional group. Acetylene, HC≡CH, is a simple alkyne.



alkyne

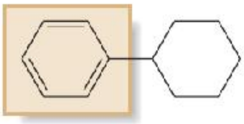
2. **Aromatic hydrocarbons.** The additional functional group that contains only carbon and hydrogen is an aromatic ring which is a six-carbon ring with alternating double bonds. The aromatic ring can also be shown as a ring with a circle in the middle representing the double bonds. Aromatic rings are found in many compounds including steroids and medications. This class of hydrocarbons was so named because many of the earliest known aromatic compounds had strong, characteristic odours.

The simplest aromatic hydrocarbon is **benzene.** The six-membered ring and three π bonds of benzene comprise a *single* functional group.



benzene

molecular formula C_6H_6



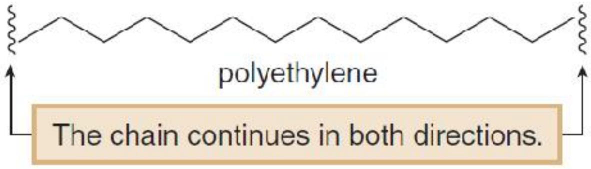
phenyl group

C_6H_5-

phenylcyclohexane

When a benzene ring is bonded to another group, it is called a **phenyl group.** In phenylcyclohexane, for example, a phenyl group is bonded to the six-membered cyclohexane ring.

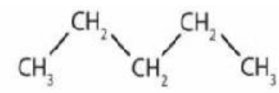
Alkanes, which have no functional groups, are notoriously unreactive except under very drastic conditions. For example, **polyethylene** is a synthetic plastic and high molecular weight alkane, consisting of chains of $-CH_2-$ groups bonded together, hundreds or even thousands of atoms long. Because it is an alkane with no reactive sites, it is a very stable compound that does not readily degrade and thus persists for years in landfills.



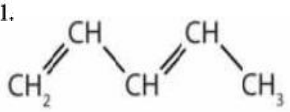
In-Text Question 2

a. Identify the type of hydrocarbon in each structure.

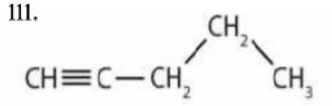
i.



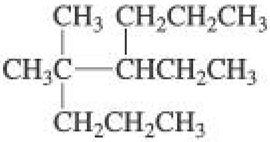
ii.



iii.



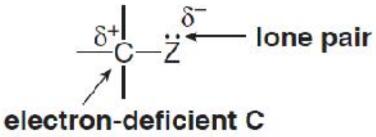
b. Give the systematic name of the following compound:



$$\begin{array}{l} \quad \mathrm{CH_3}\ \ \mathrm{CH_2CH_2CH_3} \\ \quad\ |\qquad\ | \\ \mathrm{CH_3C{-}CHCH_2CH_3} \\ \quad\ | \\ \quad \mathrm{CH_2CH_2CH_3} \end{array}$$

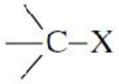
3.2.2 Compounds Containing C-Z σ Bonds

The electronegative heteroatom Z creates a polar bond, making carbon electron deficient. The lone pairs on Z are available for reaction with protons and other electrophiles, especially when Z = N or O.



Several simple compounds in this category are widely used.

1. Alkyl halides: The haloalkanes, also known as alkyl halides, are a group of chemical compounds that comprised of an alkane with one or more hydrogens replaced by a halogen atom (Group 17 atom). There is a fairly large distinction between the structural and physical properties of haloalkanes and the structural and physical properties of alkanes.

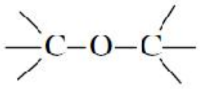


alkyl halide (1°, 2°, 3°)

As an example, chloroethane (CH_3CH_2Cl, commonly called ethyl chloride) is an alkyl halide used as a local anesthetic. Chloroethane quickly evaporates when sprayed on a wound, causing a cooling sensation that numbs the site of an injury.

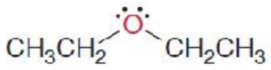
Haloalkanes are found in fire extinguishers, refrigerants, propellants, solvents, and medications. They are also a significant source of pollution and their use has been reduced or eliminated in some products. Chlorofluorocarbons (CFCs) were used as refrigerants in air-conditioners but were found to be a major cause of the depletion of the ozone layer. Research and development of alternatives began in the 1970s. Hydrochlorofluorocarbons (HCFCs) have been used for many years since they cause less damage to the ozone layer, but many countries agreed to eliminate HCFCs by the year 2020.

2. Ethers: The ether functional group consists of an oxygen atom that forms single bonds with two carbon atoms. Molecules containing these functional groups may be simple or very complex.



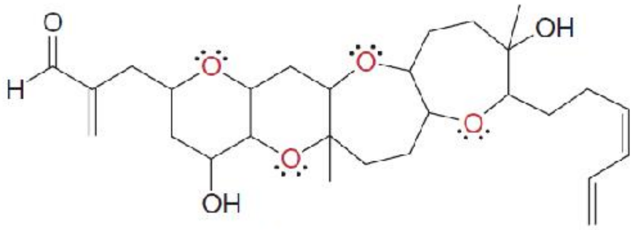
ether

Diethyl ether, the first common general anesthetic, is a simple ether because it contains a single O atom, depicted in red, bonded to two C atoms. Hemibrevetoxin B, on the other hand, contains four ether groups, in addition to other functional groups.



$CH_3CH_2\ddot{O}CH_2CH_3$

Diethyl ether



hemibrevetoxin B

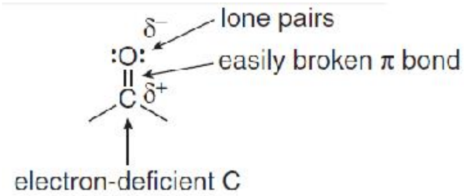
Although ethers themselves are relatively unreactive, they can be converted to peroxides after prolonged exposure to oxygen. Peroxides are very reactive and are often explosive at elevated temperatures. Many commercially available ethers come with a small amount of a peroxide scavenger dissolved in them to help prevent this type of safety hazard.

In-Text Question 3

Determine the molecular formula of a 5-carbon hydrocarbon with one bond and one ring

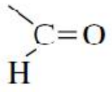
3.2.3 Compounds Containing C=O Group

Many different types of functional groups possess a C-O double bond (a **carbonyl group**). The polar C-O bond makes the carbonyl carbon an electrophile, while the lone pairs on O allow it to react as a nucleophile and base. The carbonyl group also contains a π bond that is more easily broken than a C-O σ bond.



Reactive features of a carbonyl group

1. **Aldehyde:** A very common structural component of organic structures is the **carbonyl**, which is simply a carbon atom and an oxygen atom connected by a double bond. The reactivity of carbonyls is primarily dictated by the polarization of the C=O bond, but the surrounding atoms also play a role in its specific reaction pathways.



aldehyde

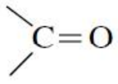
The other group attached to the carbonyl may be an R-group or a hydrogen atom. Because the hydrogen atom is so small, the partial positive charge on the carbonyl carbon is very easy for other molecules to approach, making aldehydes a particularly reactive type of carbonyl.

Aldehydes are versatile reactants for a wide variety of organic syntheses. Many aldehydes also have distinctive flavours and aromas. For example, the flavour of cinnamon is primarily due to the molecule cinnamaldehyde, and vanillin is the Aldehyde most responsible for the smell and taste of vanilla extract.

A special aldehyde is the molecule in which the carbonyl is bonded to two hydrogen atoms. This molecule, called formaldehyde, has a wide variety of uses. By itself, it can be used as a tissue preservative or as a very harsh disinfectant. It is also used as a precursor to various materials, including plastics, resins, and other polymers.

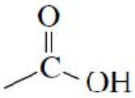
2. **Ketone:** A **ketone** involves a carbonyl in which the carbon atom makes single bonds with two R-groups. Ketones undergo most of the same reactions as aldehydes, but they tend to be slightly less reactive. The

simplest ketone is acetone, in which the carbonyl carbon is bonded to two CH_2 groups. This ketone is commonly used to remove fingernail polish and serves as an industrial solvent. Methyl ethyl ketone is used as a paint stripper and a solvent. Ketones are also used in the production of various polymers, either as a building block or as a solvent. The R-group in a ketone can be the same or different as seen in the example.



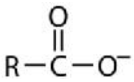
ketone

3. Carboxylic acids: are another carbonyl-containing functional group, in which the carbon atom is bonded to a hydroxyl group on one side and either a carbon or hydrogen atom on the other.



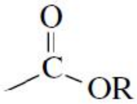
carboxylic acid

As the name implies, carboxylic acids are weak acids. An OH group that is directly connected to a carbonyl will ionize to a small extent when dissolved in water. The reason for this is the relative stability of the resulting anion. A carboxylate ion, in which the negative charge is spread over two different oxygen atoms through resonance structures, is more stable than an isolated oxygen-centered anion. The carboxylic acid and carboxylate ion are interchangeable. Carboxylate ions are often present in amino acids.



Carboxylate ion

4. Ester: An ester is similar to a carboxylic acid, in that it contains a carbonyl where the carbon is bonded to one additional oxygen atom and one carbon or hydrogen atom. However, the second oxygen atom is bonded to another carbon instead of to an acidic hydrogen atom. Structurally, carboxylic acids and esters are related to one another in the same way as alcohols and ethers.

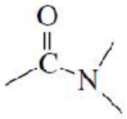


ester

Esters can be formed by heating carboxylic acids and alcohols in the presence of an acid catalyst. This process is reversible, and the starting materials can be regenerated by reacting an ester with water in the presence of a weak base.

Some esters have very pleasant odours, so they are used in the manufacture of many perfumes. Propyl acetate contributes to the odour of pears, while isoamyl acetate gives bananas their smell. This ester also serves as an alarm signal for honeybees. Esters are employed in the manufacture of fabrics (polyesters) and Plexiglass. Anesthetics such as procaine and benzocaine also contain esters.

5. Amides: An amide is a carbonyl in which the carbon is attached to one nitrogen atom and one carbon or hydrogen atom. Alternatively, we could define an amide as an **amine** in which one of the carbon atoms attached to the nitrogen is part of a carbonyl.

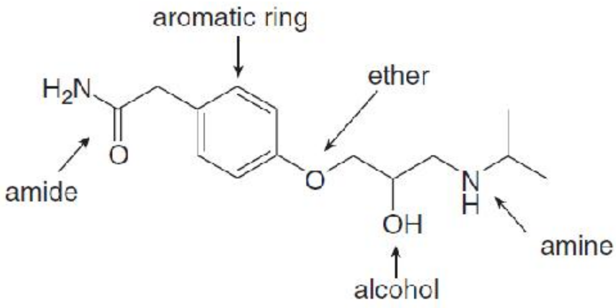


amide (1°, 2°, 3°)

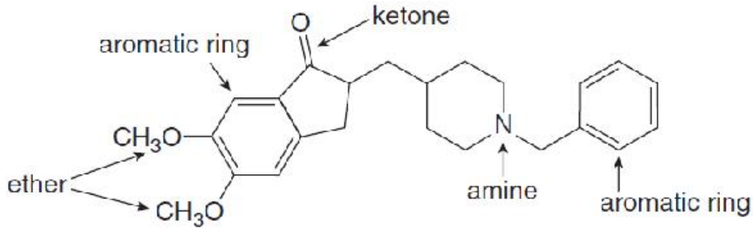
An amide can be formed by combining a carboxylic acid and an amine. Only primary and secondary amines can be sued to form amides, since they have a hydrogen that can be replaced with the carbonyl carbon; tertiary amines will not form amides.

Amides are used as colouring agents in crayons, pencils, and ink. They are employed in the paper, plastic, and rubber industries. Polyacrylamide is a very widely used amide; it is involved in the treatment of drinking water and sewage, and in plastics manufacture. The amide Kevlar is widely employed for the production of body armor, and nylon is another type of amide-based polymer.

Atenolol and donepezil are examples of useful drugs that contain a variety of functional groups. **Atenolol is a β blocker,** a group of drugs used to treat hypertension. Donepezil, sold under the trade name Aricept, is used to treat mild to moderate dementia associated with Alzheimer's disease.



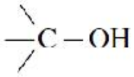
atenolol
(used to treat high blood pressure)



donepezil
(used to treat Alzheimer's disease)

3.2.4 Alcohols

The **alcohol** functional group involves an oxygen atom that is bonded to one hydrogen atom and one carbon atom. The carbon atom will be part of a larger organic structure. One way to indicate a generic alcohol would be with the formula R-OH. R represents any organic fragment in which a carbon atom is directly bonded to the explicitly indicated functional group (in this case, OH). The R group is typically a chain of carbon atoms.



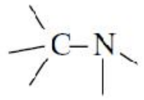
alcohol (1°, 2°, 3°)

Alcohols can be classified as primary, secondary, or tertiary based on the characteristics of the carbon to which it is attached. In a primary alcohol, the carbon bonded directly to the oxygen atom is also bonded to exactly one carbon atom, with the other bonds generally going to hydrogen atoms. In a secondary alcohol, the carbon is attached to two other carbon atoms, and in a tertiary alcohol, the carbon is bonded to three other carbon atoms. The type of alcohol being used will determine the product of certain reactions.

We are already familiar with several common alcohols. For example, ethanol is the alcohol present in alcoholic beverages. It is also widely used in the industrial manufacture of other chemicals. Methanol is used as a gasoline additive or alternative. Additionally, methanol can be used to manufacture formaldehyde, which is employed in the production of plastics, paints, and other useful substances. Isopropanol is commonly known as rubbing alcohol. In addition to its industrial uses, isopropanol is used to clean various surfaces, including computer monitors, whiteboards, and even skin (e.g., before getting blood drawn).

3.2.5 Amines

An **amine** consists of a nitrogen atom bonded to some combination of carbons and hydrogens.



amine (1°, 2°, 3°)

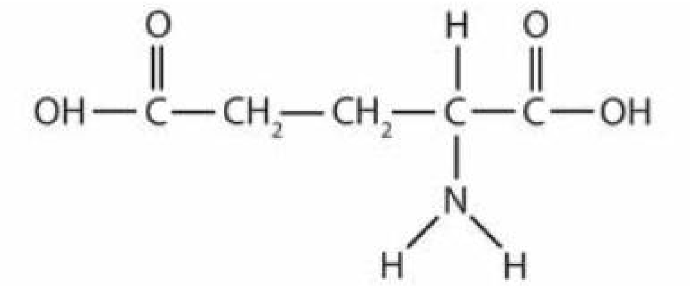
Like alcohols, amines can be classified as primary, secondary, or tertiary. However, the rules for assigning these categories are slightly different. In an alcohol, the oxygen atom is always bonded to exactly one carbon atom, so we look at the branching on the adjacent carbon, not the oxygen atom itself. In a neutral amine, the nitrogen can be bonded to one, two, or three carbon atoms, and this is how we decide whether it is called a primary, secondary, or tertiary amine.

Neutral amines are weak bases, because the lone pair on nitrogen can act as a proton acceptor. Many smaller amines have very strong and offensive odors. For example, the aptly-named compounds cadaverine and putrescine are foul-smelling amines, formed as a part of the decay process after death.

Amines serve a wide variety of uses. Diphenylamine acts as a stabilizer for certain types of explosives. Amines are found as components in some lubricating materials, in developers, and are a part of waterproofing textiles. Some amines, such as Novocain, are used as anesthetics. Many pharmaceutical compounds contain amines, including 8 of the 10 most prescribed medications in 2012.

In-Text Question 4

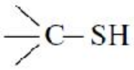
1. The general formula for amines is __________.
   A. $R\text{-}CH_2$ B. R_2CH C. $R\text{-}NH_2$ D. $R\text{-}COOH$
2. Glutamic acid is the parent compound of monosodium glutamate (known as MSG), which is used as a flavor enhancer. Glutamic acid has the following structure:



Name the functional groups you recognize in this molecule. Do you think there are other groups of atoms in this molecule that might qualify as functional groups?

3.2.6 Thiol

The **thiol** functional group contains a sulphur atom bonded to a hydrogen atom. It is very similar to an alcohol functional group with the sulphur replacing the O.



mercaptan, thiol

Thiols are also called mercaptans which are derived from the Latin phrase for "capturing mercury" because of the strong bonds it forms with mercury-containing compounds. Some thiol compounds have a distinctive smell similar to rotten eggs. They are often added to natural gas, which itself has no odor, as a way to detect leaks since its odor can be detected by humans in very small amounts. A thiol group is also present in the amino acid cysteine.

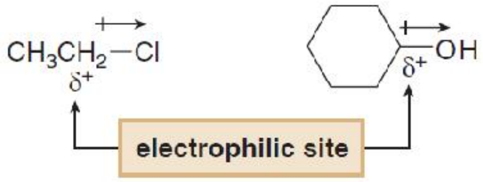
3.3 Functional Groups and Reactivity

A functional group also determines reactivity. What type of reaction does a particular kind of organic compound undergo? Begin by recalling two fundamental concepts.

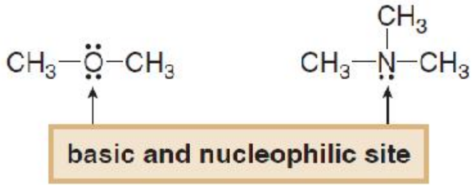
- Functional groups create reactive sites in molecules.
- Electron-rich sites react with electron-poor sites.

All functional groups contain a heteroatom, a π bond, or both, and these features make electron-deficient (or electrophilic) sites and electron-rich (or nucleophilic) sites in a molecule. Molecules react at these sites. To predict reactivity, first locate the functional group and then determine the resulting electron-rich or electron-deficient sites it creates. Keep three guidelines in mind.

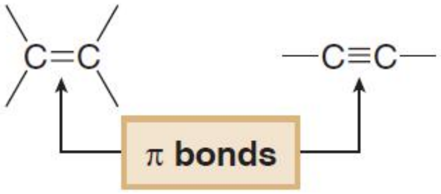
- An electronegative heteroatom like N, O, or halogens makes a carbon atom electrophilic.



- A lone pair on a heteroatom makes it basic and nucleophilic.



- π Bonds create *nucleophilic* sites and are more easily broken than r bonds.



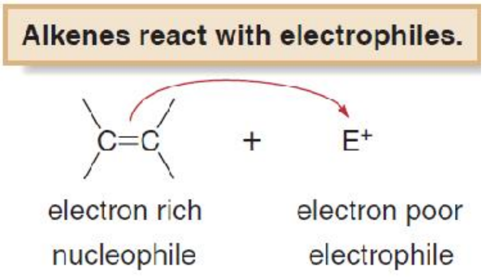
By identifying the nucleophilic and electrophilic sites in a compound you can begin to understand how it will react. In general, electron-rich sites react with electron-deficient sites:

- An electron-deficient carbon atom reacts with a nucleophile, symbolized as $:Nu^-$.

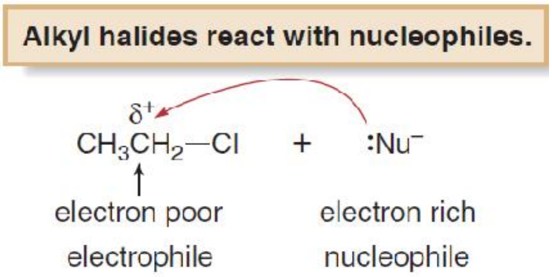
- An electron-rich carbon reacts with an electrophile, symbolized as E^+.

At this point we don't know enough organic chemistry to draw the products of many reactions with confidence. We do know enough, however, to begin to predict if two compounds might react together based solely on electron density arguments, and at what atoms that reaction is most likely to occur.

For example, alkenes contain an electron-rich C–C double bond and so they react with electrophiles, E^+. On the other hand, alkyl halides possess an electrophilic carbon atom, so they react with electron-rich nucleophiles.



Alkenes react with electrophiles.



Alkyl halides react with nucleophiles.

In-Text Question 5

1. Why are alkanes sometimes called paraffins?
2. What is the principal difference in properties between alkenes and alkanes? How are they alike?

4.0 CONCLUSION

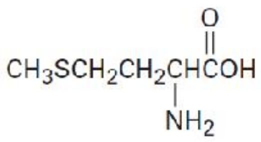
Propose structures for simple molecules that contain the following functional groups:

(a) Alcohol
(b) Aromatic ring
(c) Carboxylic acid
(d) Amine
(e) Both ketone and amine
(f) Two double bonds

SAQ 4.2

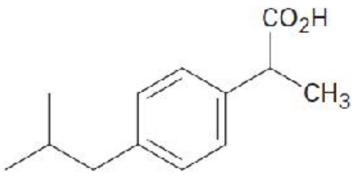
Identify the functional groups in each of the following molecules:

(a) Methionine, an amino acid:

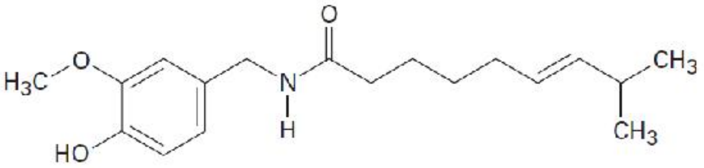


$CH_3SCH_2CH_2CH(NH_2)C(=O)OH$

(b) Ibuprofen, a pain reliever:



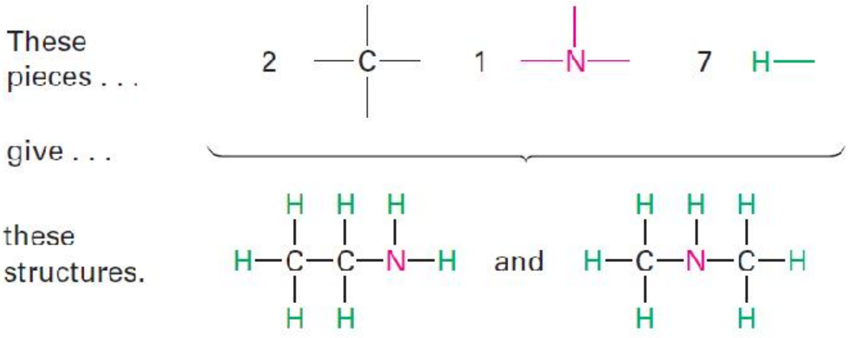
(c) Capsaicin, the pungent substance in chili peppers:



SAQ 4.3

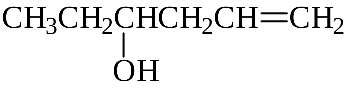
Propose structures for two isomers with the formula C_2H_7N.

There are two isomeric structures. One has the connection C-C-N, and the other has the connection C-N-C.



SAQ 4.4

The correct IUPAC name for the following structure is.



$$\underset{\displaystyle OH}{CH_3CH_2\overset{}{C}HCH_2CH{=}CH_2}$$

(A) 5-hexen-3-ol
(B) 1-hexen-4-ol
(C) 3-hydroxy-5-hexene
(D) Isohexen-3-ol
(E) 4-hydroxy-1-hexene

SAQ 4.5

Write a structure for each of the following compounds:

a. isopropyl alcohol
b. isopentyl fluoride
c. sec-butyl iodide
d. neopentyl chloride
e. tert-butylamine
f. n-octyl bromide

4.0 CONCLUSION

In this unit, we have been able to classify the numerous organic compounds into several major categories based on the functional groups they contain. We also explained how functional groups present in organic molecules determine the chemical reactivity of those molecules.

5.0 SUMMARY

With over twenty million known organic compounds in existence, it would be very challenging to memorize chemical reactions for each one. Fortunately, molecules with similar functional groups tend to undergo similar reactions. A **functional group** is defined as an atom or group of atoms within a molecule that has similar chemical properties whenever it appears in various compounds. Even if other parts of the molecule are quite different, certain functional groups tend to react in certain ways.

Organic molecules vary greatly in size and when focusing on functional groups, we direct our attention to the atoms involved in the functional group. As a result, the abbreviation R is used in some examples. The letter R is used in molecular structures to represent the "**R**est of the molecule". It consists of a group of carbon and hydrogen atoms of any size. It is used as an abbreviation since a group of carbon and hydrogen atoms does not affect the functionality of the compound. In some molecules, you will see R, R', or R'' which indicates that the R groups in the molecule can be different from one another. For example, R might be $–CH_2CH_3$ while R' is $–CH_2CH_2CH_2CH_3$.

6.0 TUTOR MARK ASSIGMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry*, 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

UNIT 2 ALKANES, FREE RADICAL SUBSTITUTION REACTIONS IN ALKANES AND THE REACTIVITY-SELECTIVITY PRINCIPLE

CONTENTS

1.0 INTRODUCTION

It will be well to reiterate what an alkane is, lest you be confused as to the difference between alkanes and alkenes. Alkanes are compounds of carbon and hydrogen only, without double bonds, triple bonds, or rings. They all conform to the general formula C_nH_{2n+2} and sometimes are called paraffin hydrocarbons, open-chain saturated hydrocarbons, or acyclic hydrocarbons. The nomenclature of alkanes has been discussed in the previous units, and you may find it well to review Module 1-unit 1 and Module 2-unit 1 before proceeding.

This unit is concerned with the chemistry of only one class of compounds, saturated hydrocarbons or alkanes, several fundamental reaction principles are developed that we shall discussed extensively in later units. The study of some of these principles such as activation energy of a reaction has been associated traditionally more with physical chemistry than with organic chemistry. We include them here because they provide a sound basis for understanding the key questions concerning the practical use of organic reactions. Is the equilibrium point of a given reaction far enough toward the desired products to be useful? Can conditions be found in which the reaction will take place at a practical rate? How can unwanted side reactions be suppressed?

Initially, we will be concerned with the physical properties of alkanes and how these properties can be correlated by the important concept of homology. This will be followed by a brief survey of the occurrence and uses of hydrocarbons, with special reference to the petroleum industry. Chemical reactions of alkanes then will be discussed, with special emphasis on free radical substitution reaction. These reactions are employed to illustrate how we can predict and use energy changes-particularly ΔH, the heat evolved or absorbed by a reacting system, which often can be estimated from bond energies. Then we consider some of the problems involved in predicting reaction rates in the context of a specific reaction, the chlorination of methane. The example is complex, but it has the virtue that we are able to break the overall reaction into quite simple steps.

2.0 LEARNING OBJECTIVES

By the end of this unit, you should be able to:

- understand the chemistry of alkanes.
- know the characteristic physical properties of alkanes.
- describe the chemical reactions alkanes undergo.
- understand the concept of free radical substitution reactions in alkanes.
- use the reactivity-selectivity principle and activation energy to predict expected products yield in a radical substitution reaction.

3.0 MAIN CONTENT

3.1 Physical Properties of Alkanes

The series of straight-chain alkanes, in which *n* is the number of carbons in the chain, shows a remarkably smooth gradation of physical properties (see Table 2.1). As *n* increases, each additional CH_2 group contributes a fairly constant increment to the boiling point and density, and to a lesser extent to the melting point. This makes it possible to estimate the properties of an unknown member of the series from those of its neighbors. For example, the boiling points of hexane and heptane are 69^o and 98^o, respectively. Thus a difference in structure of one CH_2 group for these compounds makes a difference in boiling point of 29^o; we would predict the boiling point of the next higher member, octane, to be $98^o + 29^o = 127^o$, which is close to the actual boiling point of 126^o.

Table 2.1: Physical Properties of Alkanes, $CH_3(CH_2)_{n-1}H$

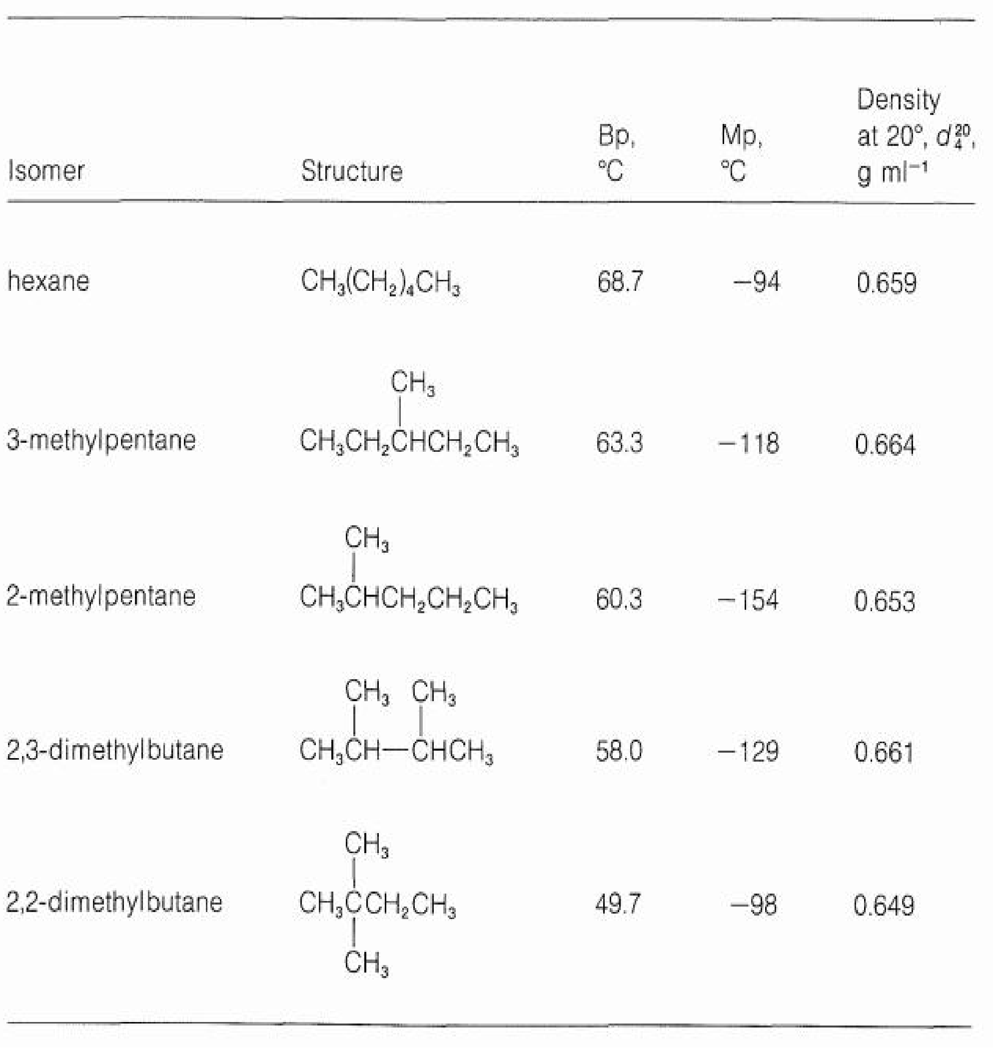
n	Name	Bp, °C (760 mm)	Mp, °C	Density at 20°, d_4^{20}, g ml^{-1}
1	methane	−161.5	−183	0.424[a]
2	ethane	−88.6	−172	0.546[a]
3	propane	−42.1	−188	0.501[b]
4	butane	−0.5	−135	0.579[b]
5	pentane	36.1	−130	0.626
6	hexane	68.7	−95	0.659
7	heptane	98.4	−91	0.684
8	octane	125.7	−57	0.703
9	nonane	150.8	−54	0.718
10	decane	174.1	−30	0.730
11	undecane	195.9	−26	0.740
12	dodecane	216.3	−10	0.749
15	pentadecane	270.6	10	0.769
20	eicosane	342.7	37	0.786[c]
30	triacontane	446.4	66	0.810[c]

[a] At the boiling point. [b] Under pressure. [c] For the supercooled liquid.

Members of a group of compounds, such as the alkanes, that have similar chemical structures and graded physical properties, and which differ from one another by the number of atoms in the structural backbone, are said to constitute a **homologous series**. When used to forecast the properties of unknown members of the series, the concept of homology works most satisfactorily for the higher-molecular-weight members because the introduction of additional CH_2 groups makes a smaller relative change in the overall composition of such molecules.

Branched-chain alkanes do not exhibit the same smooth gradation of physical properties as do the continuous-chain alkanes. Usually there is too great a variation in molecular structure for regularities to be apparent. Nevertheless, in any one set of isomeric hydrocarbons, volatility increases with increased branching. This can be seen from the data in Table 2.2 and Figure 2.1, which lists the physical properties of the five hexane isomers. The most striking feature of the data is the 19^o difference between the boiling points of hexane and 2,2-dimethylbutane.

Table 2.2: Physical Properties of Hexane Isomers



Isomer	Structure	Bp, °C	Mp, °C	Density at 20°, d_4^{20}, g ml^{-1}
hexane	$CH_3(CH_2)_4CH_3$	68.7	−94	0.659
3-methylpentane	$CH_3CH_2\overset{CH_3}{\overset{\vert}{C}}HCH_2CH_3$	63.3	−118	0.664
2-methylpentane	$CH_3\overset{CH_3}{\overset{\vert}{C}}HCH_2CH_2CH_3$	60.3	−154	0.653
2,3-dimethylbutane	$CH_3\overset{CH_3}{\overset{\vert}{C}}H—\overset{CH_3}{\overset{\vert}{C}}HCH_3$	58.0	−129	0.661
2,2-dimethylbutane	$CH_3\underset{CH_3}{\underset{\vert}{\overset{CH_3}{\overset{\vert}{C}}}}CH_2CH_3$	49.7	−98	0.649

Activity 3.1

Use the data of Tables 2.1 and 2.2 to estimate the boiling points of tetradecane, heptadecane, 2-methylhexane, and 2,2-dimethylpentane.

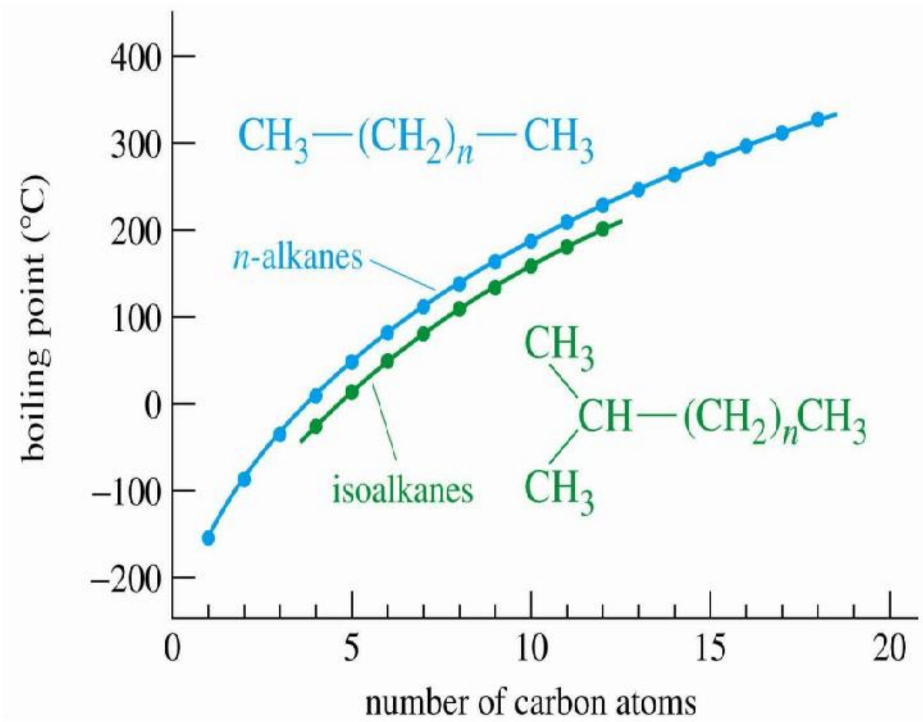


Fig 2.1: Graph of Boiling Points of Alkanes

Straight chain alkanes have a higher boiling point than branched alkanes due to the greater surface area in contact and therefore greater van der Waals interactions.

Since alkanes are hydrocarbons and there is no significant difference in electronegativity between carbon and hydrogen, they are nonpolar. In being nonpolar, alkanes dissolve in nonpolar solvents because the van der Waals interactions between nonpolar alkane molecules and nonpolar solvent molecules are similar to the alkane-alkane and nonpolar solvent-nonpolar solvent molecule interactions.

Alkanes are thus soluble in nonpolar solvents (i.e. other alkanes) and insoluble in polar solvents (such as water). The liquid alkanes are therefore good solvents for
nonpolar covalent compounds.

In-Text Question 1
For each of the following pairs of compounds, select the substance you expect to have the higher boiling point.

1. octane and nonane.
2. octane and 2,2,3,3-tetramethylbutane.

Note: The actual boiling points are nonane = 150.8°C, octane = 125.7°C, 2,2,3,3-tetramethylbutane = 106.5°C

3.3 Chemical Reactions of Alkanes

Alkanes have only strong σ bonds. Because the carbon and hydrogen atoms of an alkane have approximately the same electronegativity, the electrons in the C-H and C-C σ bonds are shared equally by the bonding atoms. Consequently, none of the atoms in an alkane have any significant charge. This means that neither nucleophiles (electron pair donors) nor electrophiles (electron pair acceptors) are attracted to them. Alkanes, therefore, are relatively unreactive compounds. Their failure to undergo reactions prompted early organic chemists to call them paraffins, from the Latin *parum affinis*, which means “little affinity” (for other compounds). Thus none of the C-H or C-C bonds in a typical saturated hydrocarbon, for example ethane, are attacked at ordinary temperatures by a strong acid, such as sulfuric acid (H_2SO_4), or by an oxidizing agent, such as bromine (in the dark), oxygen, or potassium permanganate ($KMnO_4$). Under ordinary conditions, ethane is similarly stable to reducing agents such as hydrogen, even in the presence of catalysts such as platinum, palladium, or nickel.

However, all saturated hydrocarbons are attacked by oxygen at elevated temperatures and, if oxygen is in excess, complete combustion to carbon dioxide and water occurs.

$$CH_4 + 2O_2 \longrightarrow CO_2 + 2H_2O$$

Vast quantities of hydrocarbons from petroleum are utilized as fuels for the production of heat and power by combustion. Natural gas consists of about 75% methane. The remaining 25% is composed of small alkanes such as ethane, propane, and butane.

Petroleum is a complex mixture of alkanes and cycloalkanes that can be separated into fractions by distillation. The fraction that boils at the lowest temperature (hydrocarbons containing three and four carbons) is natural gas that can be liquefied under pressure. This gas is used as a fuel for cigarette lighters, camp stoves, and barbecues. The fraction that boils at somewhat higher temperatures (hydrocarbons containing 5 to 11 carbons) is gasoline; the next fraction (9 to 16 carbons) includes kerosene and jet fuel. The fraction with 15 to 25 carbons is used for heating oil and diesel oil, and the highest-boiling fraction is used for lubricants and greases. The nonpolar nature of these compounds is what gives them their oily feel. After distillation, a nonvolatile residue called asphalt or tar is left behind.

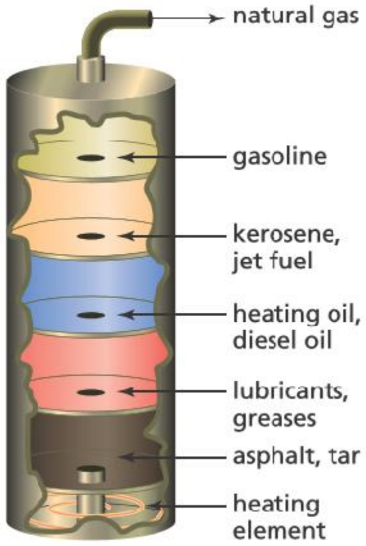


Fig 2.2: Different fractions of petroleum

Alkanes (the most basic of all organic compounds) undergo very few reactions. The two reactions of more importance are combustion and halogenation (i.e., substitution of a single hydrogen on the alkane for a single halogen to form a haloalkane). The halogen reaction is very important in organic chemistry because it opens a gateway to further chemical reactions.

In-Text Question 2

1. Liquefied petroleum gas is mainly composed of _____________
   a) Methane and ethane b) Ethane and propane c) Propane and butane
   d) Butane and hexane
2. If you drop a lighted match onto some petrol (gasoline), it ignites almost explosively. If you drop a lighted match onto some tar on the road, almost certainly nothing will happen. Both contain alkanes, Explain the difference.

3.3.6 Combustion of Alkanes

In general, the formula for complete combustion of alkanes is:

$$C_xH_{y(g)} + (x + y/4)\,O_{2(g)} \longrightarrow xCO_{2(g)} + y/2\,H_2O_{(g)}$$

When there is sufficient oxygen, alkanes will burn and form water and carbon dioxide as products:

$$CH_{4(g)} + 2O_{2(g)} \longrightarrow CO_{2(g)} + 2H_2O_{(g)}$$

It is quite important that you can write properly balanced equations for these reactions, because they often come up as a part of thermochemistry calculations. Some are easier than others. For example, with alkanes, the ones with an even number of carbon atoms are marginally harder than those with an odd number.

For example, with propane (C_3H_8), you can balance the carbons and hydrogens as you write the equation down. Your first draft would be:

$C_3H_8 + O_2 \rightarrow 3CO_2 + 4H_2O$

Counting the oxygens leads directly to the final version:

$$C_3H_{8(g)} + 5O_{2(g)} \longrightarrow 3CO_{2(g)} + 4H_2O_{(g)}$$

With butane (C_4H_{10}), you can again balance the carbons and hydrogens as you write the equation down.
$C_4H_{10} + O_2 \rightarrow 4CO_2 + 5H_2O$

Counting the oxygens leads to a slight problem - with 13 on the right-hand side. The simple trick is to allow yourself to have "six-and-a-half" O molecules on the left.

$$C_4H_{10(g)} + 6\frac{1}{2}O_{2(g)} \longrightarrow 4CO_{2(g)} + 5H_2O_{(g)}$$

If you are not comfortable with that, double everything:

$$2C_4H_{10(g)} + 13O_{2(g)} \longrightarrow 8CO_{2(g)} + 10H_2O_{(g)}$$

The hydrocarbons become harder to ignite as the molecules get bigger. This is because the bigger molecules do not vaporize so easily - the reaction is much better if the oxygen and the hydrocarbon are well mixed as gases. If the liquid is not very volatile, only those molecules on the surface can react with the oxygen. Bigger molecules have greater Van der Waals attractions which makes it more difficult for them to break away from their neighbors and turn to a gas.

Provided the combustion is complete, all the hydrocarbons will burn with a blue flame. However, combustion tends to be less complete as the number of carbon atoms in the molecules rises. That means that the bigger the hydrocarbon, the more likely you are to get a yellow, smoky flame. Incomplete combustion (where there is not enough oxygen present) can lead to the formation of carbon or carbon monoxide. As a simple way of thinking about it, the hydrogen in the hydrocarbon gets the first chance at the oxygen, and the carbon gets whatever is left over. The presence of glowing carbon particles in a flame turns it yellow, and black carbon is often visible in the smoke. Carbon monoxide is produced as a colourless poisonous gas.

For example, incomplete combustion of octane can be represented as:

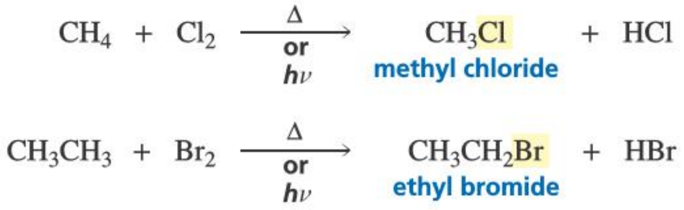
$$2C_8H_{18(g)} + 17O_{2(g)} \longrightarrow 16CO_{(g)} + 18H_2O_{(g)}$$

Note: Why is carbon monoxide said to be poisonous?
Oxygen is carried around the blood by haemoglobin. Carbon monoxide unfortunately binds to exactly the same site on the haemoglobin that oxygen does. The difference is that carbon monoxide binds irreversibly (or very strongly) - making that particular molecule of haemoglobin useless for carrying oxygen. Hence, if you breath in enough carbon monoxide you will die from a sort of internal suffocation.

In-Text Question 3
Write equations for the complete combustion of
a) pentane, C_5H_{12} b) ethane, C_2H_6 c) decane, $C_{10}H_{22}$ d) cyclohexane, C_6H_{12}

3.2.2 Halogenation of Alkanes (Free Radical Substitution Reaction)

Alkanes do react with chlorine (Cl_2) or bromine (Br_2) to form alkyl chlorides or alkyl bromides. These halogenation reactions take place only at high temperatures or in the presence of light (symbolized by hv). They are the only reactions that alkanes undergo—with the exception of combustion (burning), a reaction with oxygen. Unlike the complex transformations of combustion, the halogenation of an alkane appears to be a simple **substitution reaction** in which a C-H bond is broken and a new C-X bond is formed.

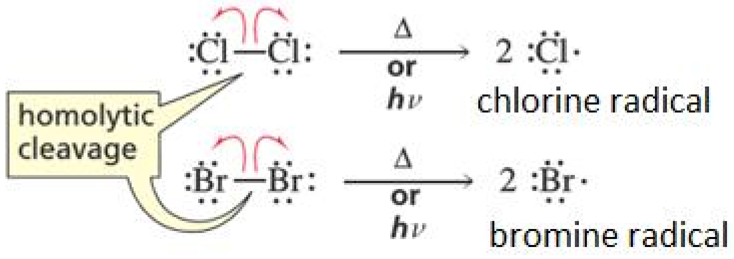


$$CH_4 + Cl_2 \xrightarrow[h\nu]{\Delta \text{ or}} CH_3Cl + HCl$$

$$CH_3CH_3 + Br_2 \xrightarrow[h\nu]{\Delta \text{ or}} CH_3CH_2Br + HBr$$

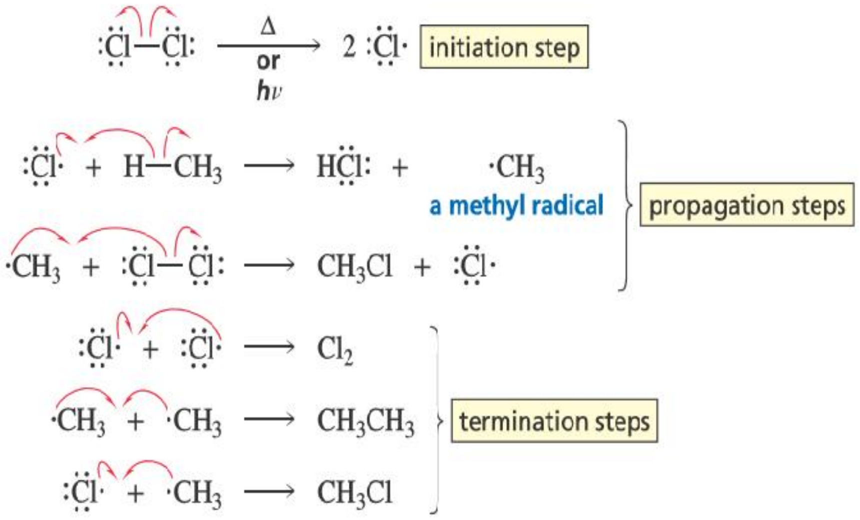
When a bond breaks so that both of its electrons stay with one of the atoms, the process is called **heterolytic bond cleavage** or **heterolysis**. When a bond breaks so that each of the atoms retains one of the bonding electrons, the process is called **homolytic bond cleavage** or **homolysis**.

The mechanism for the halogenation of an alkane is well understood. The high temperature (or light) supplies the energy required to break the or bond homolytically. Homolytic bond cleavage is the **initiation step** of the reaction because it creates the radical that is used in the first propagation step.



A radical (often called a free radical) is a species containing an atom with an unpaired electron. A radical is highly reactive because it wants to acquire an electron to complete its octet. As an example, in the mechanism for the monochlorination of methane, the chlorine radical formed in the initiation step abstracts a hydrogen atom from methane, forming HCl and a methyl radical. The methyl radical abstracts a chlorine atom from Cl_2, forming methyl chloride and another chlorine radical, which can abstract a hydrogen atom from another molecule of methane. These two steps are called **propagation steps** because the radical created in the first propagation step reacts in the second propagation step to produce a radical that can repeat the first propagation step. Thus, the two propagation steps are repeated over and over. The first propagation step is the rate-determining step of the overall reaction. Because the reaction has radical intermediates and repeating propagation steps, it is called a **radical chain reaction**.

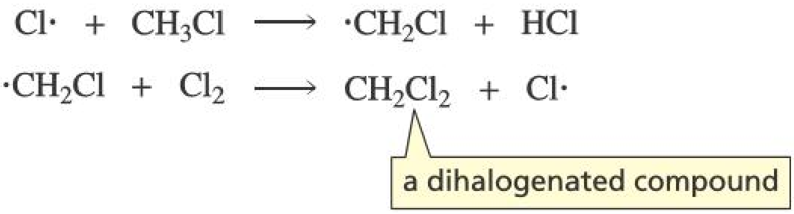
mechanism for the monochlorination of methane



Any two radicals in the reaction mixture can combine to form a molecule in which all the electrons are paired. The combination of two radicals is called a **termination step** because it helps bring the reaction to an end by decreasing the number of radicals available to propagate the reaction. Any two radicals present in the reaction mixture can combine in a termination step, so radical reactions produce a mixture of products.

The radical chlorination of alkanes other than methane follows the same mechanism. The reaction of an alkane with chlorine or bromine to form an alkyl halide is called a **radical substitution reaction** because radicals are involved as intermediates and the end result is the substitution of a halogen atom for one of the hydrogen atoms of the alkane.

In order to maximize the amount of monohalogenated product obtained, a radical substitution reaction should be carried out in the presence of excess alkane. Excess alkane in the reaction mixture increases the probability that the halogen radical will collide with a molecule of alkane rather than with a molecule of alkyl halide —even toward the end of the reaction, by which time a considerable amount of alkyl halide will have been formed. If the halogen radical abstracts a hydrogen from a molecule of alkyl halide rather than from a molecule of alkane, a dihalogenated product will be obtained.



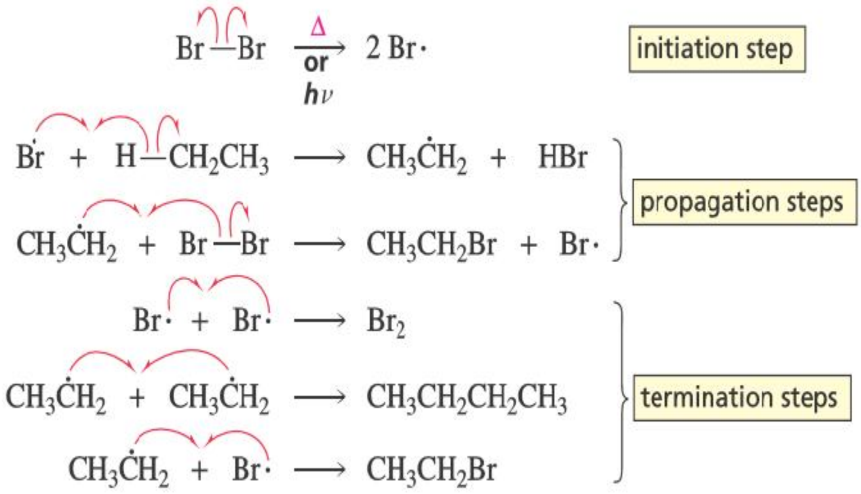
$$Cl\cdot + CH_3Cl \longrightarrow \cdot CH_2Cl + HCl$$

$$\cdot CH_2Cl + Cl_2 \longrightarrow CH_2Cl_2 + Cl\cdot$$

a dihalogenated compound

Bromination of alkanes follows the same mechanism as chlorination.

mechanism for the monobromination of ethane



$$Br{-}Br \xrightarrow[h\nu]{\Delta \text{ or}} 2\,Br\cdot$$

initiation step

$$Br\cdot + H{-}CH_2CH_3 \longrightarrow CH_3\dot{C}H_2 + HBr$$

$$CH_3\dot{C}H_2 + Br{-}Br \longrightarrow CH_3CH_2Br + Br\cdot$$

propagation steps

$$Br\cdot + Br\cdot \longrightarrow Br_2$$

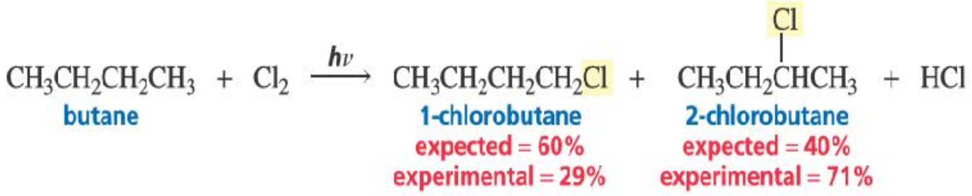
$$CH_3\dot{C}H_2 + CH_3\dot{C}H_2 \longrightarrow CH_3CH_2CH_2CH_3$$

$$CH_3\dot{C}H_2 + Br\cdot \longrightarrow CH_3CH_2Br$$

termination steps

3.2.2.1 Factors that Determine Product Distribution

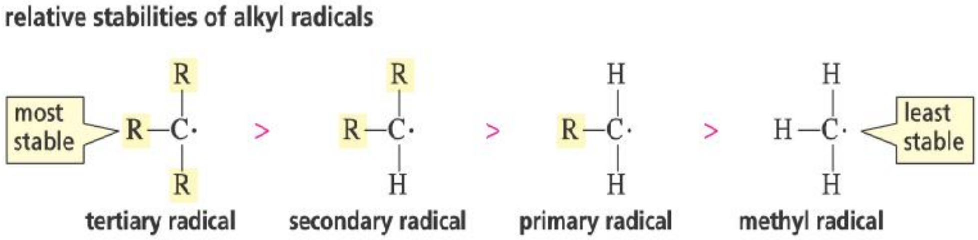
The distribution of products depends on probability and reactivity. Two different alkyl halides are obtained from the monochlorination of butane. Substitution of a hydrogen bonded to one of the terminal carbons produces 1-chlorobutane, whereas substitution of a hydrogen bonded to one of the internal carbons forms 2-chlorobutane.



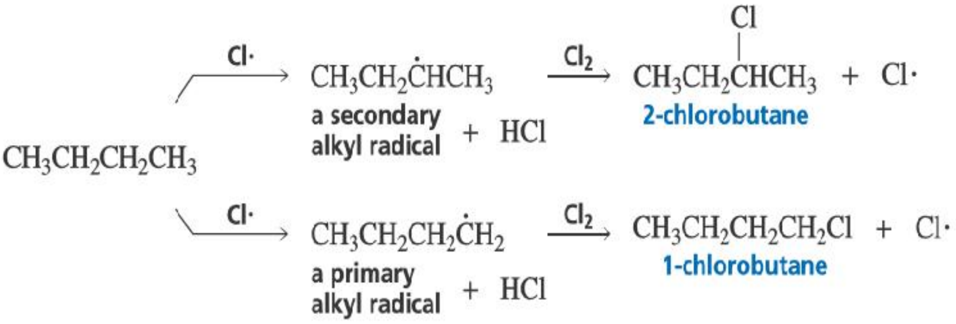
The expected (statistical) distribution of products is 60% 1-chlorobutane and 40% 2-chlorobutane because six of butane’s 10 hydrogens can be substituted to form 1-chlorobutane, whereas only four can be substituted to form 2-chlorobutane. This assumes, however, that all of the bonds in butane are equally easy to break. Then, the relative amounts of the two products would depend only on the probability of a chlorine radical colliding with a primary hydrogen, compared with its colliding with a secondary hydrogen. When we carry out the reaction in the laboratory and analyze the product, however, we find that it is 29% 1-chlorobutane and 71% 2-chlorobutane.

Therefore, probability alone does not explain the regioselectivity of the reaction. Because more 2-chlorobutane is obtained than expected and the rate-determining step of the overall reaction is hydrogen atom abstraction, we conclude that it must be easier to abstract a hydrogen atom from a secondary carbon than from a primary carbon.

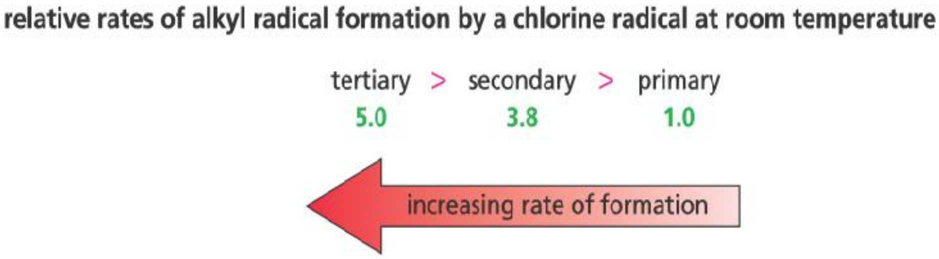
Alkyl radicals have different stabilities, and the more stable the radical, the more easily it is formed because the stability of the radical is reflected in the stability of the transition state leading to its formation. Consequently, it is easier to remove a hydrogen atom from a secondary carbon to form a secondary radical than it is to remove a hydrogen atom from a primary carbon to form a primary radical.



When a chlorine radical reacts with butane, it can abstract a hydrogen atom from an internal carbon, thereby forming a secondary alkyl radical, or it can abstract a hydrogen atom from a terminal carbon, thereby forming a primary alkyl radical. Because it is easier to form the more stable secondary alkyl radical, 2-chlorobutane is formed faster than 1-chlorobutane.



After experimentally determining the amount of each chlorination product obtained from various hydrocarbons, chemists were able to conclude that at room temperature it is 5.0 times easier for a chlorine radical to abstract a hydrogen atom from a tertiary carbon than from a primary carbon, and it is 3.8 times easier to abstract a hydrogen atom from a secondary carbon than from a primary carbon. The precise ratios differ at different temperatures.



To determine the relative amounts of products obtained from radical chlorination of an alkane, both probability (the number of hydrogens that can be abstracted that will lead to the formation of the particular product) and reactivity (the relative rate at which a particular hydrogen is abstracted) must be taken into account. When both factors are considered, the calculated amounts of 1-chlorobutane and 2-chlorobutane agree with the amounts obtained experimentally.

relative amount of 1-chlorobutane

number of hydrogens × reactivity

$$6 \times 1.0 = 6.0$$

$$\text{percent yield} = \frac{6.0}{21} = 29\%$$

relative amount of 2-chlorobutane

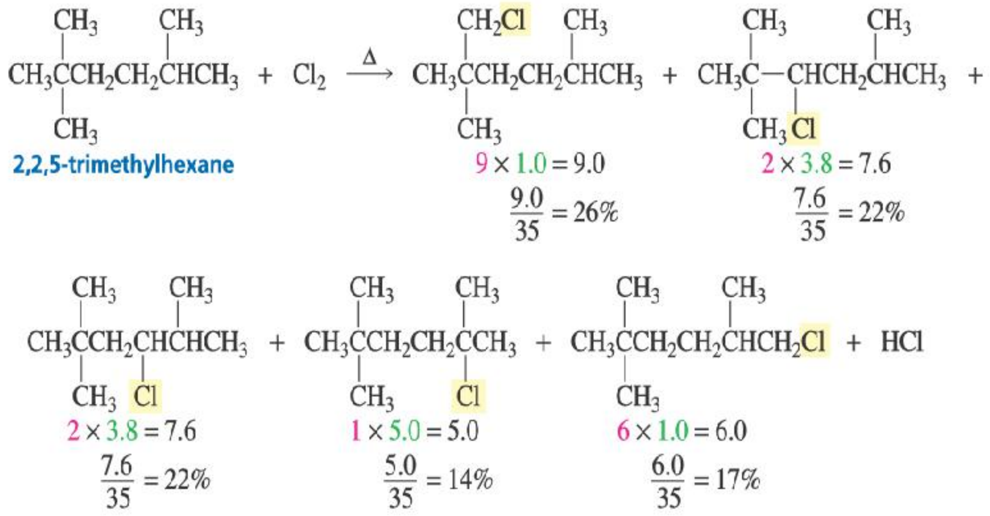
number of hydrogens × reactivity

$$4 \times 3.8 = 15$$

$$\text{percent yield} = \frac{15}{21} = 71\%$$

The percent yield of each alkyl halide is calculated by dividing the relative amount of the particular product by the sum of the relative amounts of all the alkyl halide products (16 + 15 = 21).

Radical monochlorination of 2,2,5-trimethylhexane results in the formation of five monochlorination products. Because the relative amounts of the five alkyl halides total 35 (19.0 + 7.6 + 7.6 + 5.0 + 6.0 = 35), the percent yield of each product can be calculated as follows:

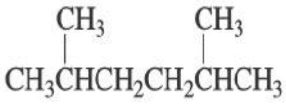


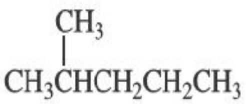
Because radical chlorination of an alkane can yield several different monosubstitution products as well as products that contain more than one chlorine atom, it is not the best method for synthesizing an alkyl halide. Addition of a hydrogen halide to an alkene or conversion of an alcohol to an alkyl halide is a much better way to make an alkyl halide. Radical halogenation of an alkane is nevertheless still a useful reaction because it is the only way to convert an unreactive alkane into a reactive compound. Once the halogen is introduced into the alkane, it can be replaced by a variety of other substituents.

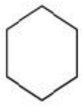
In-Text Question 4

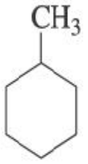
How many alkyl halides can be obtained from monochlorination of the following alkanes? Neglect stereoisomers.

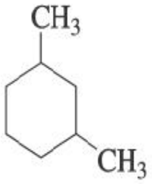
a. $CH_3CH_2CH_2CH_2CH_3$

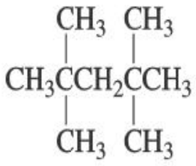
b.

$CH_3\overset{CH_3}{C}HCH_2CH_2\overset{CH_3}{C}HCH_3$

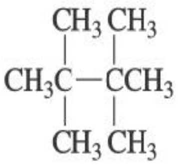
c.

$CH_3\overset{CH_3}{C}HCH_2CH_2CH_3$

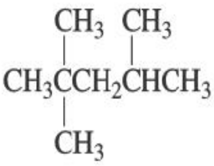
d.


e.


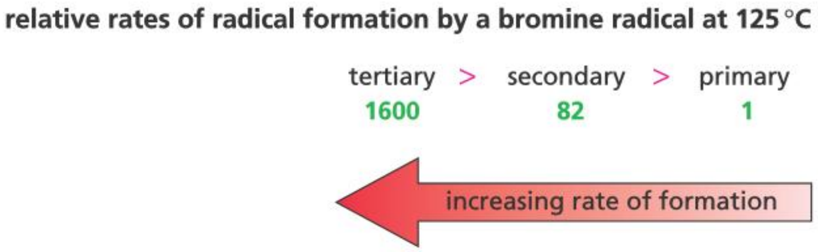
f.


g.

$CH_3\underset{CH_3}{\overset{CH_3}{C}}CH_2\underset{CH_3}{\overset{CH_3}{C}}CH_3$

h.

$CH_3\underset{CH_3}{\overset{CH_3}{C}}-\underset{CH_3}{\overset{CH_3}{C}}CH_3$

i.

$CH_3\underset{CH_3}{\overset{CH_3}{C}}CH_2\overset{CH_3}{C}HCH_3$

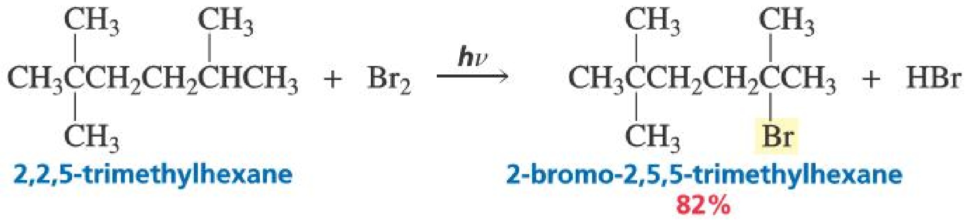
The relative rates of radical formation when a bromine radical abstracts a hydrogen atom are different from the relative rates of radical formation when a chlorine radical abstracts a hydrogen atom. At 125 °C, a bromine radical abstracts a hydrogen atom from a tertiary carbon 1600 times faster than from a primary carbon and abstracts a hydrogen atom from a secondary carbon 82 times faster than from a primary carbon.



When a bromine radical is the hydrogen-abstracting agent, the differences in reactivity are so great that the reactivity factor is vastly more important than the probability factor. For example, radical bromination of butane gives a 98% yield of 2-bromobutane, compared with the 71% yield of 2-chlorobutane obtained when butane is chlorinated. A bromine radical is less reactive and more selective than a chlorine radical. In other words, bromination is more highly regioselective than chlorination.


$CH_3CH_2CH_2CH_3 + Br_2 \xrightarrow{h\nu} CH_3CH_2CH_2CH_2Br + CH_3CH_2\overset{Br}{C}HCH_3 + HBr$

Similarly, bromination of 2,2,5-trimethylhexane gives an 82% yield of the product in which bromine replaces the tertiary hydrogen. Chlorination of the same alkane results in a 14% yield of the tertiary alkyl chloride.



$$CH_3CCH_2CH_2CHCH_3 + Br_2 \xrightarrow{h\nu} CH_3CCH_2CH_2CCH_3 + HBr$$

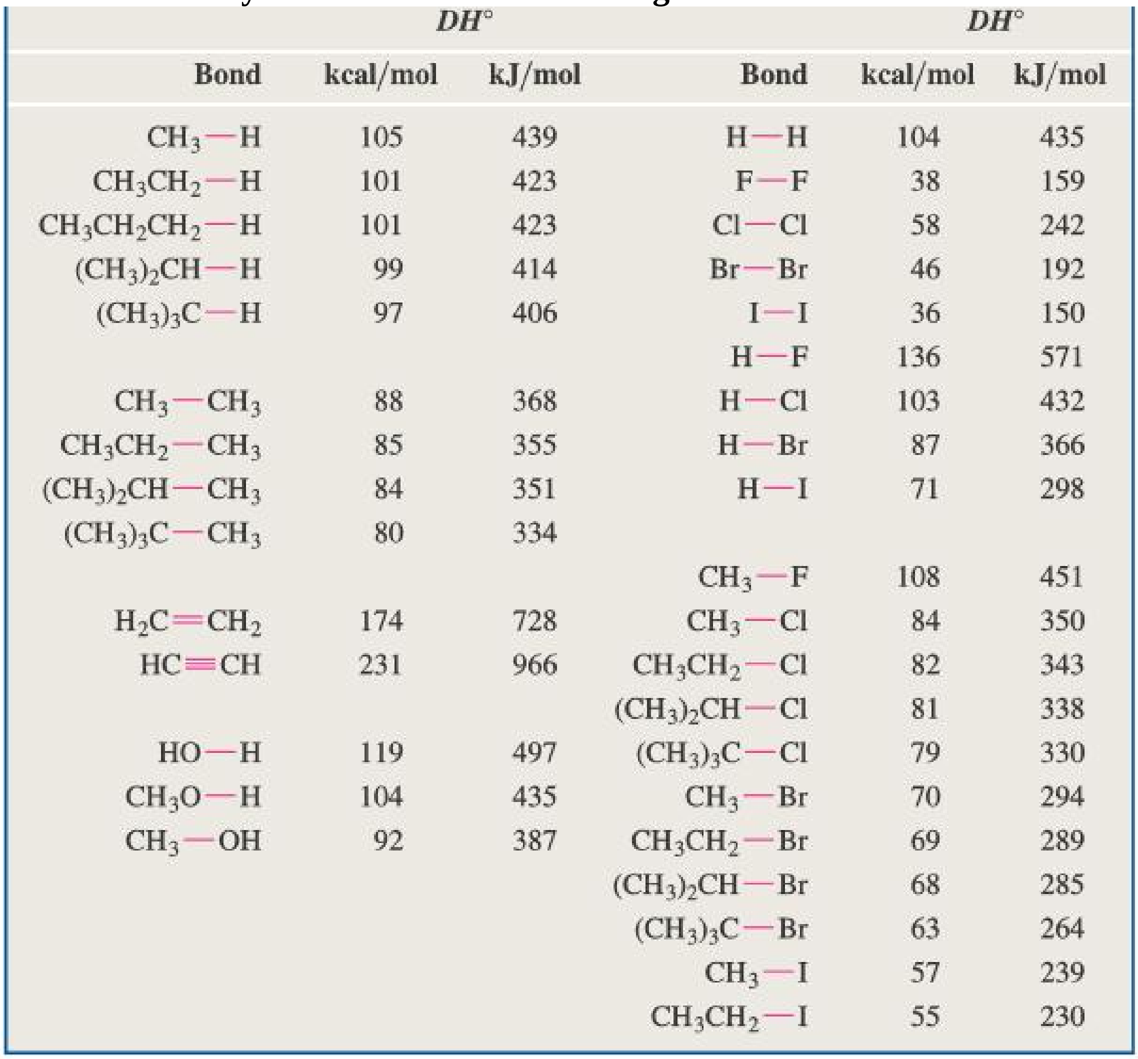
In-Text Question 5

Calculate the percent yield of each product obtained in Problems 1a and b above if chlorination is carried out in the presence of light at room temperature.

3.2.2.2 The Reactivity–Selectivity Principle

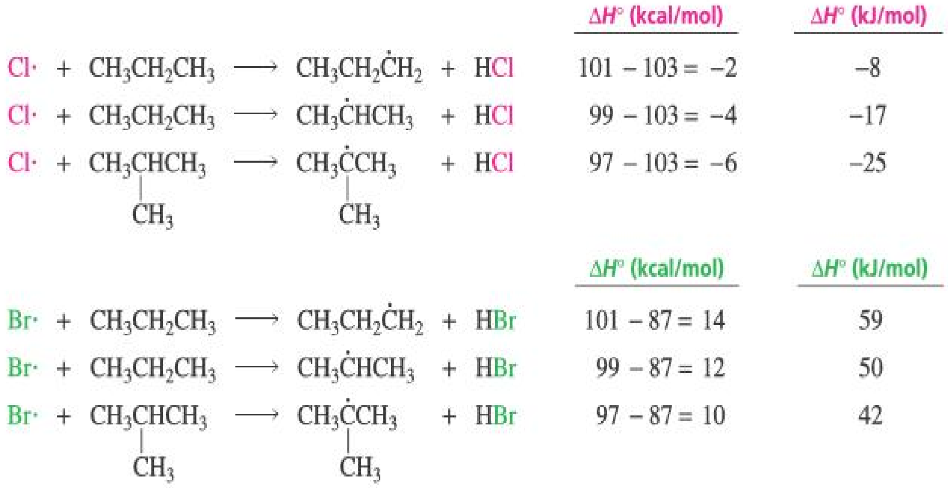
Why are the relative rates of radical formation so different when a bromine radical rather than a chlorine radical is used as the hydrogen-abstracting reagent? To answer this question, we must compare the ΔH^o values for the formation of primary, secondary, and tertiary radicals when a chlorine radical is used, as opposed to when a bromine radical is used. These ΔH^o values can be calculated using the bond dissociation energies in Table 2.3 below. Remember that ΔH^o is equal to the energy of the bond being broken minus the energy of the bond being formed.

Table 2.3: Homolytic Bond Dissociation Energies Y-Z → $Y^{\cdot}$ + $Z^{\cdot}$



	$DH°$			$DH°$	
Bond	kcal/mol	kJ/mol	Bond	kcal/mol	kJ/mol
$CH_3—H$	105	439	$H—H$	104	435
$CH_3CH_2—H$	101	423	$F—F$	38	159
$CH_3CH_2CH_2—H$	101	423	$Cl—Cl$	58	242
$(CH_3)_2CH—H$	99	414	$Br—Br$	46	192
$(CH_3)_3C—H$	97	406	$I—I$	36	150
			$H—F$	136	571
$CH_3—CH_3$	88	368	$H—Cl$	103	432
$CH_3CH_2—CH_3$	85	355	$H—Br$	87	366
$(CH_3)_2CH—CH_3$	84	351	$H—I$	71	298
$(CH_3)_3C—CH_3$	80	334			
			$CH_3—F$	108	451
$H_2C=CH_2$	174	728	$CH_3—Cl$	84	350
$HC\equiv CH$	231	966	$CH_3CH_2—Cl$	82	343
			$(CH_3)_2CH—Cl$	81	338
$HO—H$	119	497	$(CH_3)_3C—Cl$	79	330
$CH_3O—H$	104	435	$CH_3—Br$	70	294
$CH_3—OH$	92	387	$CH_3CH_2—Br$	69	289
			$(CH_3)_2CH—Br$	68	285
			$(CH_3)_3C—Br$	63	264
			$CH_3—I$	57	239
			$CH_3CH_2—I$	55	230

J. Berkowitz, G.B. Ellison, D. Gutman, *J. Phys. Chem.*, **1994**, *98*, 2744.



	$\Delta H°$ (kcal/mol)	$\Delta H°$ (kJ/mol)
$Cl\cdot + CH_3CH_2CH_3 \longrightarrow CH_3CH_2\dot{C}H_2 + HCl$	101 − 103 = −2	−8
$Cl\cdot + CH_3CH_2CH_3 \longrightarrow CH_3\dot{C}HCH_3 + HCl$	99 − 103 = −4	−17
$Cl\cdot + CH_3\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_3 \longrightarrow CH_3\underset{\displaystyle CH_3}{\underset{\vert}{\dot{C}}}CH_3 + HCl$	97 − 103 = −6	−25

	$\Delta H°$ (kcal/mol)	$\Delta H°$ (kJ/mol)
$Br\cdot + CH_3CH_2CH_3 \longrightarrow CH_3CH_2\dot{C}H_2 + HBr$	101 − 87 = 14	59
$Br\cdot + CH_3CH_2CH_3 \longrightarrow CH_3\dot{C}HCH_3 + HBr$	99 − 87 = 12	50
$Br\cdot + CH_3\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_3 \longrightarrow CH_3\underset{\displaystyle CH_3}{\underset{\vert}{\dot{C}}}CH_3 + HBr$	97 − 87 = 10	42

We must also be aware that bromination is a much slower reaction than chlorination. The activation energy for abstraction of a hydrogen atom by a bromine radical has been found experimentally to be about 4.5 times greater than that for abstraction of a hydrogen atom by a chlorine radical.

Using the calculated values and the experimental activation energies, we can draw reaction coordinate diagrams for the formation of primary, secondary, and tertiary radicals by chlorine radical abstraction (Figure 2.3a) and by bromine radical abstraction (Figure 2.3b).

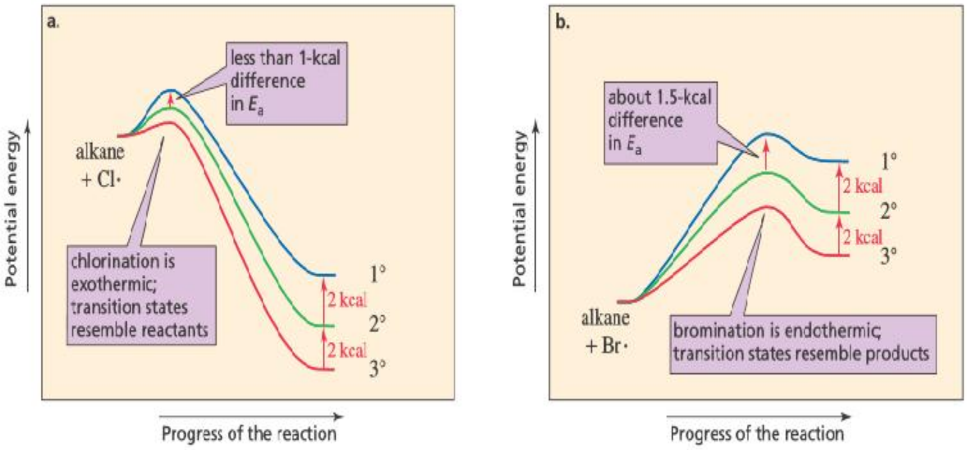
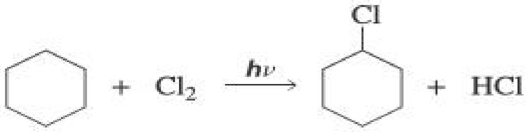


Figure 2.3: (a) Reaction coordinate diagrams for the formation of primary, secondary, and tertiary alkyl radicals as a result of abstraction of a hydrogen atom by a chlorine radical. The transition states have relatively little radical character because they resemble the reactants. (b) Reaction coordinate diagrams for the formation of primary, secondary, and tertiary alkyl radicals as a result of abstraction of a hydrogen atom by a bromine radical. The transition states have a relatively high degree of radical character because they resemble the products.

Because the reaction of a chlorine radical with an alkane to form a primary, secondary, or tertiary radical is exothermic, the transition states resemble the reactants more than they resemble the products. The reactants all have approximately the same energy, so there will be only a small difference in the activation energies for removal of a hydrogen atom from a primary, secondary, or tertiary carbon. In contrast, the reaction of a bromine radical with an alkane is endothermic, so the transition states resemble the products more than they resemble the reactants. Because there is a significant difference in the energies of the product radicals—depending on whether they are primary, secondary, or tertiary—there is a significant difference in the activation energies. Therefore, a chlorine radical makes primary, secondary, and tertiary radicals with almost equal ease, whereas a bromine radical has a clear preference for formation of the easiest-to-form tertiary radical (Figure 2.3). In other words, because a bromine radical is relatively unreactive, it is highly selective about which hydrogen atom it abstracts. In contrast, the much more reactive chlorine radical is considerably less selective. These observations illustrate the **reactivity–selectivity principle**, which states that the greater the reactivity of a species, the less selective it will be.

Because chlorination is relatively nonselective, it is a useful reaction only when there is just one kind of hydrogen in the molecule.



By comparing the values for the sum of the two propagating steps for the monohalogenation of methane, we can understand why alkanes undergo chlorination

and bromination but not iodination and why fluorination is too violent a reaction to be useful. The fluorine radical is the most reactive of the halogen radicals, and it reacts violently with alkanes (ΔH^o = -31 kcal/mol). In contrast, the iodine radical is the least reactive of the halogen radicals. In fact, it is so unreactive (ΔH^o = 34 kcal/mol) that it is unable to abstract a hydrogen atom from an alkane. Consequently, it reacts with another iodine radical and reforms I_2.

$$\begin{array}{ll} F\cdot + CH_4 \longrightarrow \cdot CH_3 + HF & 105 - 136 = -31 \\ \cdot CH_3 + F_2 \longrightarrow CH_3F + F\cdot & 38 - 108 = -70 \\ \hline & \Delta H^\circ = -101 \text{ kcal/mol} \quad (\text{or } -423 \text{ kJ/mol}) \end{array}$$

$$\begin{array}{ll} Cl\cdot + CH_4 \longrightarrow \cdot CH_3 + HCl & 105 - 103 = 2 \\ \cdot CH_3 + Cl_2 \longrightarrow CH_3Cl + Cl\cdot & 58 - 84 = -26 \\ \hline & \Delta H^\circ = -24 \text{ kcal/mol} \quad (\text{or } -100 \text{ kJ/mol}) \end{array}$$

$$\begin{array}{ll} Br\cdot + CH_4 \longrightarrow \cdot CH_3 + HBr & 105 - 87 = 18 \\ \cdot CH_3 + Br_2 \longrightarrow CH_3Br + Br\cdot & 46 - 70 = -24 \\ \hline & \Delta H^\circ = -6 \text{ kcal/mol} \quad (\text{or } -25 \text{ kJ/mol}) \end{array}$$

$$\begin{array}{ll} I\cdot + CH_4 \longrightarrow \cdot CH_3 + HI & 105 - 71 = 34 \\ \cdot CH_3 + I_2 \longrightarrow CH_3I + I\cdot & 36 - 57 = -21 \\ \hline & \Delta H^\circ = 13 \text{ kcal/mol} \quad (\text{or } 54 \text{ kJ/mol}) \end{array}$$

In-Text Question 6

Carry out the calculations that predict that

a. 2-bromobutane will be obtained in 98% yield.

b. 2-bromo-2,5,5,-trimethylhexane will be obtained in 82% yield.

SELF-ASSESSMENT EXERCISE

i. Explain why chlorination or bromination of methylcyclohexane will produce a greater yield of 1-halo-1-methylcyclohexane.

a. Would chlorination or bromination produce a greater yield of 1-halo-2,3 dimethylbutane?

b. Would chlorination or bromination produce a greater yield of 2-halo-2,3-dimethylbutane?

c. Would chlorination or bromination be a better way to make 1-halo-2,2-dimethylpropane?

ii Iodine does not react with ethane even though I_2 is more easily cleaved homolytically than the other halogens. Explain.

iii When 2-methylpropane is monochlorinated in the presence of light at room temperature, 36% of the product is 2-chloro-2-methylpropane and 64% is 1-chloro-2-methylpropane. From these data, calculate how much easier it is to abstract a hydrogen atom from a tertiary carbon than from a primary carbon under these conditions.

Let total amount of product = 100
The relative amount of 1-chloro-2-methylpropane = number of primary hydrogen x ease of the primary hydrogen removal (X)
i.e. $64 = 9 \times X$
$X = 7.11$
Similarly,
The relative amount of 2-chloro-2-methylpropane = number of tertiary hydrogen x ease of the tertiary hydrogen removal (Y)
i.e. $36 = 1 \times Y$
$Y = 36$
Relative ease of removal of hydrogen atom from a tertiary carbon than from a primary carbon are Y : X i.e. 36 : 7.11
= 5 : 1
Hence, it is five times easier to abstract a hydrogen atom from a tertiary carbon than from a primary carbon under the given conditions.
iv If 2-methylpropane is brominated at 125 °C in the presence of light, what percent of the product will be 2-bromo-2-methylpropane? Compare your answer with the percent given in Problem 2 above for chlorination.
v. a) Why does a bunsen burner with the air-hole closed produce a yellow flame?
b) Explain why carbon monoxide, formed by incomplete combustion of hydrocarbons, is poisonous.

4.0 CONCLUSION

Alkanes (the most basic of all organic compounds) undergo very few reactions. The two reactions of more importance are combustion and halogenation. Halogenation is the replacement of one or more hydrogen atoms in an organic compound by a halogen (fluorine, chlorine, bromine or iodine). Unlike the complex transformations of combustion, the halogenation of an alkane appears to be a simple substitution reaction in which a C-H bond is broken and a new C-X bond is formed.

5.0 SUMMARY

- Alkanes are called saturated hydrocarbons because they do not contain any double or triple bonds. Since they also have only strong σ bonds and atoms with no partial charges, alkanes are very unreactive.
- Alkanes do undergo radical substitution reactions with chlorine (Cl_2) or bromine (Br_2) at high temperatures or in the presence of light, to form alkyl chlorides or alkyl bromides. The substitution reaction is a radical chain reaction with initiation, propagation, and termination steps.
- Unwanted radical reactions are prevented by radical inhibitors—compounds that destroy reactive radicals by creating unreactive radicals or compounds with only paired electrons.
- The rate-determining step of the radical substitution reaction is hydrogen atom abstraction to form a radical.
- The relative rates of radical formation are $3^o > 2^o > 1^o >$ methyl.
- To determine the relative amounts of products obtained from the radical halogenation of an alkane, both probability and the relative rate at which a particular hydrogen is abstracted must be taken into account.
- The reactivity–selectivity principle states that the more reactive a species is, the less selective it will be.
- A bromine radical is less reactive than a chlorine radical, so a bromine radical is more selective about which hydrogen atom it abstracts.
- Fluorine radicals ($F^{\cdot}$) are the most reactive of all of the halogen atoms and iodine radicals ($I^{\cdot}$) are the least reactive. $I^{\cdot}$ is so unreactive that it does not abstract H from most alkanes. The overall reactivity trend for halogen atoms is F > Cl > Br > I and this is the same order as they appear in the next to the last column of a periodic table.

6.0 TUTOR MARK ASSIGMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry,* 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

UNIT 3 VARIOUS ORGANIC REACTIONS

CONTENTS

1.0 INTRODUCTION

An understanding of chemical processes has made possible the conversion of natural substances into new compounds with different, and sometimes superior, properties. Aspirin, ibuprofen, nylon, and polyethylene are all products of chemical reactions between substances derived from petroleum.

Reactions are difficult to learn when each reaction is considered a unique and isolated event.

Virtually all chemical reactions are woven together by a few basic themes. In this unit, we shall be looking at the equations for organic reactions, reaction mechanisms, various organic reactions, how a reaction occurs, and types of reagents. Understanding the details of an organic reaction allows us to determine when it might be used in preparing interesting and useful organic compounds.

A chemical reaction is the transformation of one chemical or collection of chemicals into another chemical or collection of chemicals. This involves the making of new chemical bonds and the breaking of old chemical bonds. Organic reactions are the chemical reactions that are undergone by organic compounds. Reactions of organic compounds can be organized broadly by the types of reactions and how these reactions occur. The types of reactions organic compounds undergo are divided into substitution reactions, elimination reactions, addition reactions, redox reactions, rearrangement reactions, pericyclic reactions and free radical reactions.

2.0 OBJECTIVES

When you have studied this unit, you should be able to:

- understand how equations for organic reactions are written.
- have a better understanding of reaction mechanisms.
- become familiar with the various classes of organic reactions.

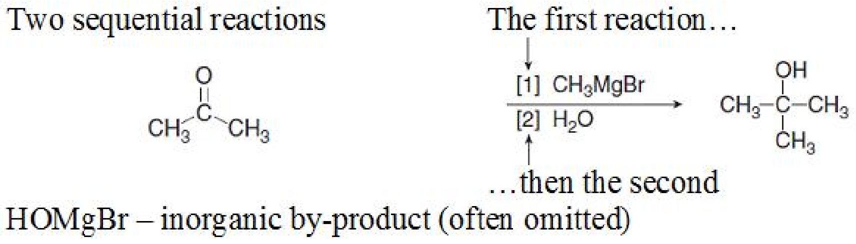
3.0 MAIN CONTENT

3.1 Writing Equations for Organic Reactions

Like other reactions, equations for organic reactions are usually drawn with a single reaction arrow (→) between the starting material and product, but other conventions make these equations look different from those encountered in general chemistry.

The **reagent,** the chemical substance with which an organic compound reacts, is sometimes drawn on the left side of the equation with the other reactants. At other times, the reagent is drawn above the reaction arrow itself, to focus attention on the organic starting material by itself on the left side. The solvent and temperature of a reaction may be added above or below the arrow. **The symbols "*hv*" and "Δ" are used for reactions that require *light* or *heat,* respectively.** Figure 3.1 presents an organic reaction in different ways.

When two sequential reactions are carried out without drawing any intermediate compound, the steps are usually numbered above or below the reaction arrow. This convention signifies that the first step occurs *before* the second, and the reagents are added *in sequence*, not at the same time.



In this equation only the organic product is drawn on the right side of the arrow. Although the reagent CH_3MgBr contains both Mg and Br, these elements do not appear in the organic product, and they are often omitted on the product side of the equation. These elements have not disappeared. They are part of an inorganic by-product (HOMgBr in this case), and are often of little interest to an organic chemist.

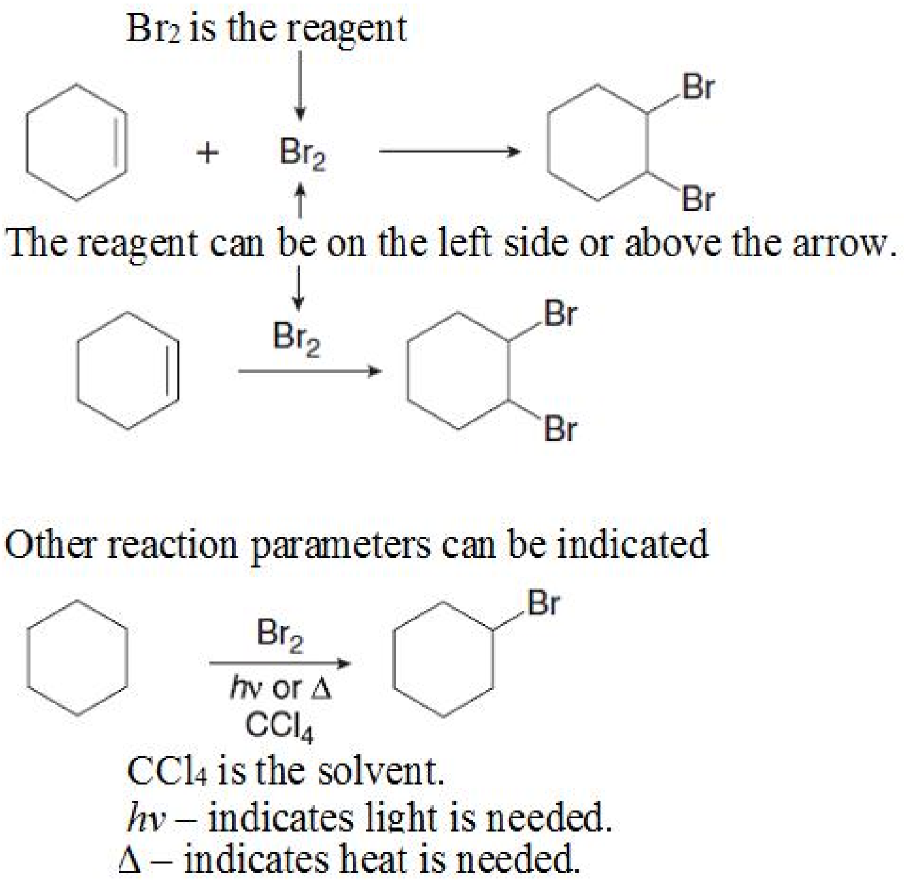


Figure 2.4: Different ways of writing organic reactions

3.2 Reaction Mechanisms

Having now learned how to write and identify some common kinds of organic reactions, we can turn to a discussion of **reaction mechanism.** Due to the unique properties of carbon, namely, its ability to catenate, form chains and rings, and form multiple bonds with itself or other atoms, an enormous number of organic compounds are possible. Moreover, an organic compound can undergo many different reactions. For example, ethanol may react to form acetaldehyde, acetic acid, ethylene, formic acid, carbon dioxide, and so on. So, it may appear that studying organic reactions should be a very difficult and almost futile exercise. But, fortunately, closer studies have revealed that the reactions of enormously large number of organic compounds actually take place in such ways that these may be classified into a few groups of reactions. In most cases, the organic reactions are brought about with inorganic compounds like acids, bases, oxidizing agents, reducing agents and so on. The inorganic compounds that bring about the organic reactions are termed as *reagents*, and the organic compounds undergoing the chemical transformations are termed as *substrates.*

A *reaction mechanism* is a detailed description of how bonds are broken and formed as a starting material is converted to a product. A reaction mechanism describes the relative order and rate of bond cleavage and formation. It explains all the known facts about a reaction and accounts for all products formed, and it is subject to modification or refinement as new details are discovered.

A reaction can occur either in one step or in a series of steps. **A one-step reaction is called a *concerted reaction.*** No matter how many bonds are broken or formed, a starting material is converted *directly* to a product.

A → B

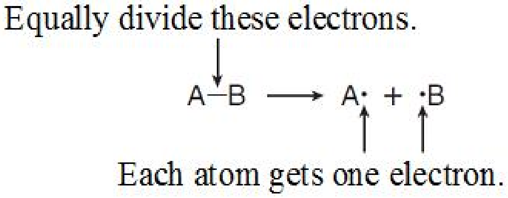
A stepwise reaction involves more than one step. A starting material is first converted to an unstable intermediate, called a *reactive intermediate,* which then goes on to form the product.

A → reactive intermediate → B

3.2.1 Bond Cleavage

Bonds are broken and formed in all chemical reactions. No matter how many steps there are in the reaction, however, there are only two ways to break (cleave) a bond: the electrons in the bond can be divided *equally or unequally* between the two atoms of the bond.

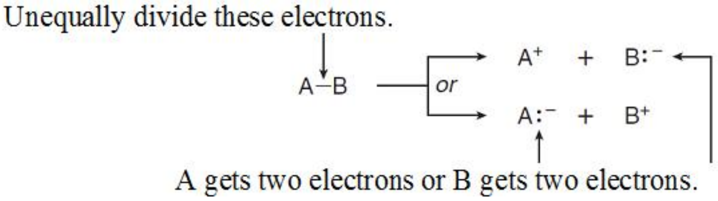
- Breaking a bond by *equally dividing the electrons* between the two atoms in the bond is called *homolysis or homolytic cleavage.*



Homolysis or homolytic cleavage

- Breaking a bond by *unequally dividing the electrons* between the two atoms in the bond is called *heterolysis* or *heterolytic cleavage.*

Heterolysis of a bond between **A** and **B** can give either **A** or **B** the two electrons in the bond. When **A** and **B** have different electronegativities, the *electrons normally end up on the more electronegative atom.*



Heterolysis or heterolytic cleavage

Homolysis and heterolysis require energy. Both processes generate reactive intermediates, but the products are different in each case.

- *Homolysis generates uncharged reactive intermediates with unpaired electrons.*
- *Heterolysis generates charged intermediates.*

Each of these reactive intermediates has a very short lifetime, and each reacts quickly to form a stable organic product.

3.2.2 Radicals, Carbocations, and Carbanions

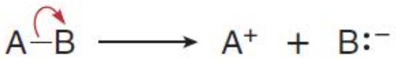
The curved arrow notation works fine for heterolytic bond cleavage because it illustrates the movement of an *electron pair*. For homolytic cleavage, however, one electron moves to one atom in the bond and one electron moves to the other, so a different kind of curved arrow is needed.

- *To illustrate the movement of a single electron, use a half-headed curved arrow, sometimes called a fishhook.*

Homolysis

Two **half-headed** curved arrows are needed for **two single electrons**.

Heterolysis



One **full-headed** curved arrow is needed for **one electron pair**.

A full-headed curved arrow shows the movement of an electron *pair*. **A half headed curved arrow** shows the movement of a *single* electron.

Homolysis of the C–Z bond generates two uncharged products with unpaired electrons.

- *A reactive intermediate with a single unpaired electron is called a radical.*

Most radicals are highly unstable because they contain an atom that does not have an octet of electrons. Radicals typically have no charge. They are intermediates in a group of reactions called *radical reactions*.

Heterolysis of the C–Z bond can generate a carbocation or a carbanion.

- *Giving two electrons to Z and none to carbon generates a positively charged carbon intermediate called a carbocation.*

- *Giving two electrons to C and none to Z generates a negatively charged carbon species called a carbanion.*

Both carbocations and carbanions are unstable reactive intermediates: A carbocation contains a carbon atom surrounded by only six electrons. A carbanion has a negative charge on carbon, which is not a very electronegative atom. Carbocations (electrophiles) and carbanions (nucleophiles) can be intermediates in ***polar reactions*** - reactions in which a nucleophile reacts with an electrophile.

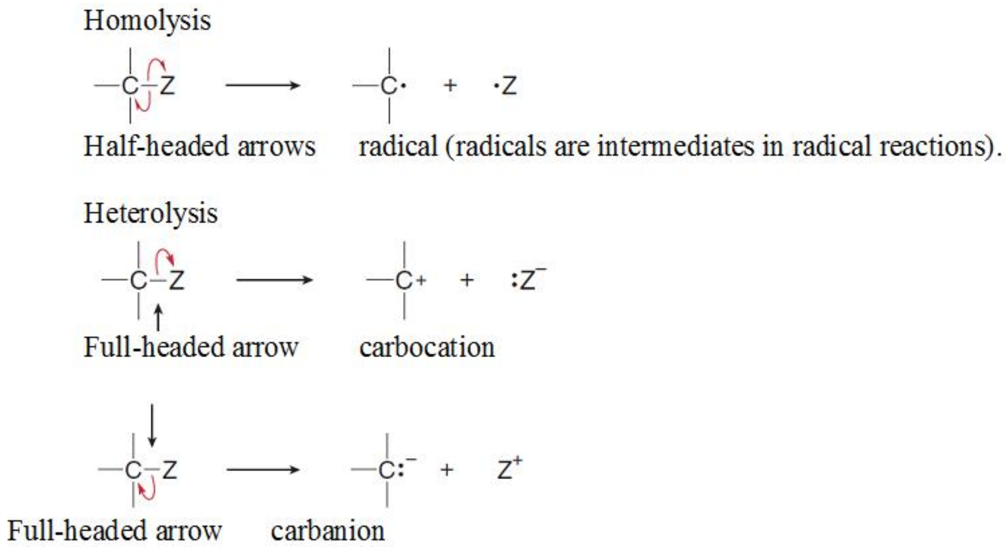
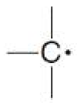
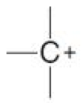
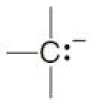


Figure 2.5: Three reactive intermediates resulting from homolysis and heterolysis of a C–Z bond

Thus, homolysis and heterolysis generate radicals, carbocations, and carbanions, the three most common reactive intermediates in organic chemistry.


radical


carbocation


carbanion

- *Radicals and carbocations are electrophiles because they contain an electron-deficient carbon.*

- *Carbanions are nucleophiles because they contain a carbon with a lone pair.*

In-Text Question 1

1. Select the correct statement on carbanion from the following option.

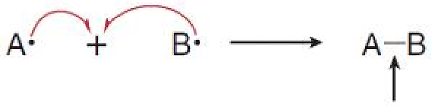
a) Carbanion is an intermediate compound
b) In carbanion, central carbon atom carries negative charge
c) It possess an unshared pair of electron
d) All of the mentioned

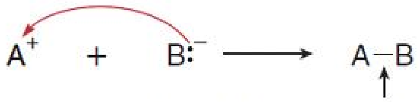
2. Carbonium ions are the intermediates in which the positive charge is carried by the carbon atom with ___________ electrons in the valence shell.

a) 6 b) 5 c) 4 d) 3

3.2.3 Bond Formation

Like bond cleavage, bond formation occurs in two different ways. Two radicals can each donate *one electron* to form a two-electron bond. Alternatively, two ions with unlike charges can come together, with the negatively charged ion donating *both electrons* to form the resulting two electron bond. *Bond formation always releases energy.*


One electron comes from each atom.
Forming a bond from two radicals.


Both electrons come from one atom
Forming a bond from two ions.

3.2.4 Kinds of Arrows

Table 3.1 below summarizes the many kinds of arrows used in describing organic reactions. Curved arrows are especially important because they explicitly show what electrons are involved in a reaction, how these electrons move in forming and breaking bonds, and if a reaction proceeds via a radical or polar pathway.

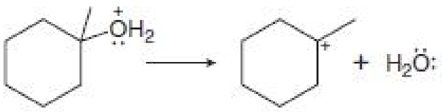
Table 2.4: A Summary of Arrow Types in Chemical Reactions

Arrow	Name	Use
→	Reactive arrow	Drawn between the starting materials and products in an equation
⇌	Double reaction arrows (equilibrium arrows)	Drawn between the starting materials and products in an equilibrium equation
↔	Double-headed arrow	Drawn between resonance structures
	Full-headed curved arrow	Shows movement of an electron pair
	Half-headed curved arrow (fishhook)	Shows movement of a single electron

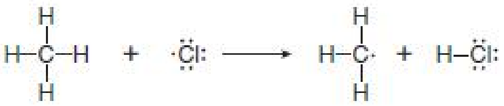
In-Text Question 2

Use full-headed or half-headed curved arrows to show the movement of electrons in the following equations.

a.



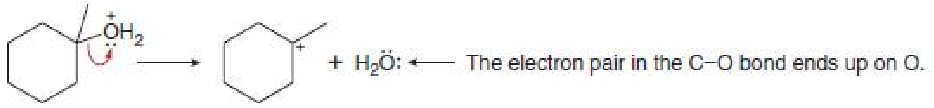
b.



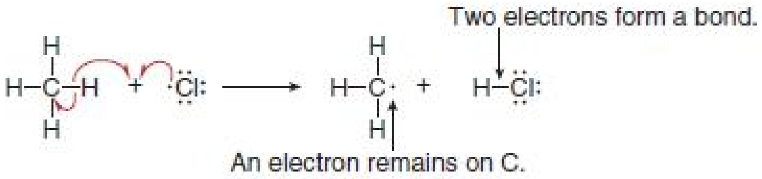
$$H-\underset{H}{\overset{H}{C}}-H + \cdot\ddot{\underset{..}{Cl}}: \longrightarrow H-\underset{H}{\overset{H}{C}}\cdot + H-\ddot{\underset{..}{Cl}}:$$

In-Text Answer 2

a. In this reaction, the C–O bond is broken heterolytically. Because only one electron pair is involved, one full-headed curved arrow is needed.



b. This reaction involves radicals, so half-headed curved arrows are needed to show the movement of single electrons. One new two-electron bond is formed between H and Cl, and an unpaired electron is left on C. Because a total of three electrons are involved, three half headed curved arrows are needed.



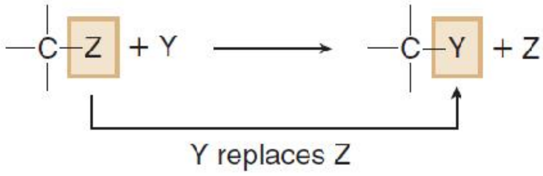
3.3 Various Organic Reactions

Like other compounds, organic molecules undergo the following reactions:

3.3.1 Substitution Reactions

A substitution reaction is that in which an atom or a group of atoms is replaced by another atom or group of atoms.

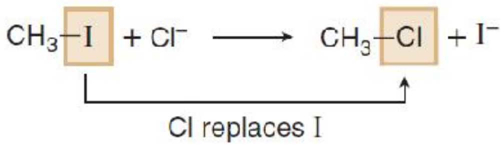
A general substitution reaction:

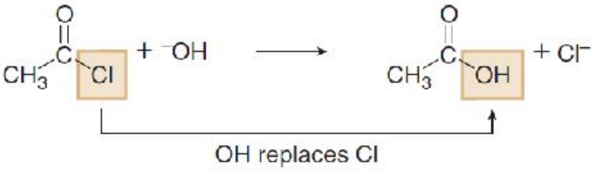


(Z = H or heteroatom).

In a general substitution reaction, Y **replaces** Z on a carbon atom. **Substitution reactions involve σ bonds: one σ bond breaks and another form at the same carbon atom.** The most common examples of substitution occur when Z is hydrogen or a heteroatom that is more electronegative than carbon.

Examples:

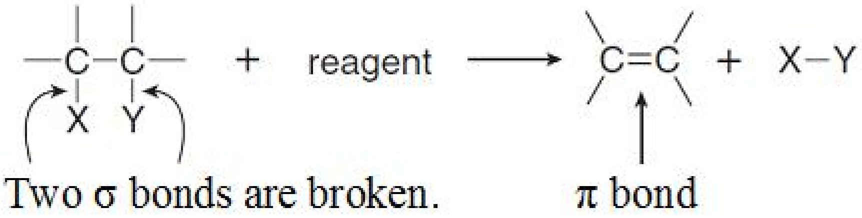




3.3.2 Elimination Reactions

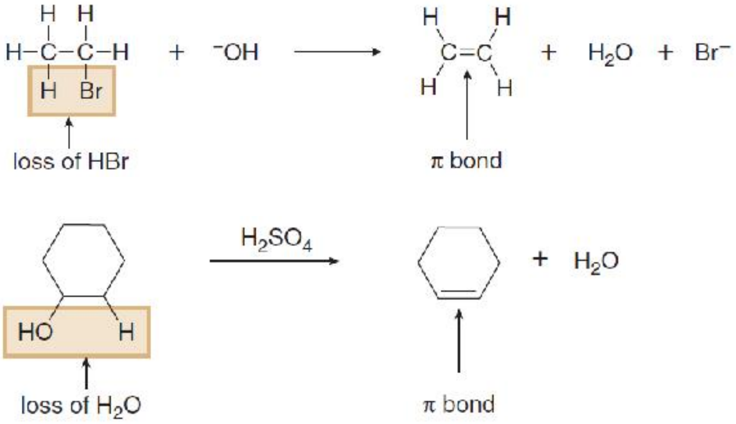
An elimination reaction is one in which elements of the starting material are "lost" and a π bond is formed.

A general elimination reaction can be represented as below:



In an elimination reaction, two groups X and Y are removed from a starting material. **Two σ bonds are broken, and a π bond is formed between adjacent atoms.** The most common examples of elimination occur when X=H and Y is a heteroatom more electronegative than carbon.

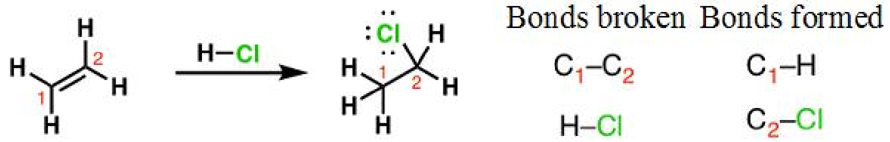
Examples:



3.3.3 Addition Reactions

Addition reactions occur when one or two molecules of the reagent are added to a multiple bond or a small ring of the substrate. The two starting materials add together to form only one product with no atoms left over.
A + B → A-B
In an addition all parts of the adding reagent appear in the product; two molecules become one.
When you take an alkene (or alkyne) and add certain types of reagents to them, you get results like this. In this reaction, $C_1 - C_2$ *and* $H - Cl$ are broken and $C_1 - H$ *and* $C_2 - Cl$ bonds are formed.

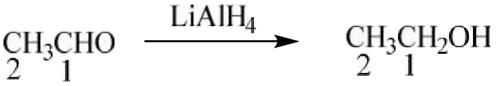
A typical addition reaction:



All addition reactions follow the same pattern (break a π bond, form two single bonds). However, these do not always proceed through the same mechanism. One of the challenges with learning addition reactions is in keeping track of which kinds of reagents lead to “regioisomers” (i.e. constitutional isomers) and which lead to “stereoisomers” as some even lead to both!

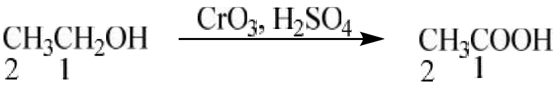
3.3.4 Redox Reactions

In these reactions, the reagents bring about a change in the oxidation number of the C-atom of the substrate molecule. A reduction reaction is that in which the oxidation number of the C-atom in the molecule decreases to form the product, while in an oxidation reaction, oxidation number increases. For example,



$$\underset{2\ \ 1}{CH_3CHO} \xrightarrow{LiAlH_4} \underset{2\ \ 1}{CH_3CH_2OH}$$

It is a reduction reaction as the oxidation number of the C_1-atom of the substrate decreases from 0 to -2.

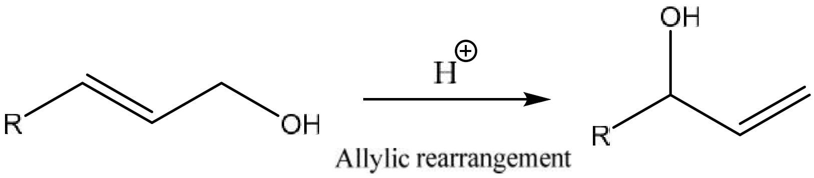


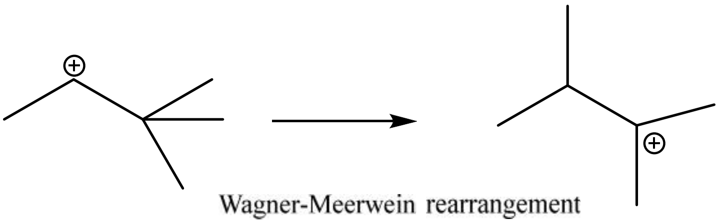
$$\underset{2\ \ 1}{CH_3CH_2OH} \xrightarrow{CrO_3,\ H_2SO_4} \underset{2\ \ 1}{CH_3COOH}$$

It is an oxidation reaction as the oxidation number of the C_1-atom of the substrate increases from -2 to +2.

3.3.5 Rearrangement Reactions

In these reactions, the bond connectivity within the molecule changes to give a different compound having same molecular formula. Such a change in the bond connectivity takes place due to the migration of an atom or a group from one location to a new location within the molecule. Such a migration of an atom or a group may take place within the same molecule in Intramolecular processes or may involve two different molecules of the same species in intermolecular processes. For example,





Wagner-Meerwein rearrangement

In-Text Question 3

Classify each reaction as addition, elimination, substitution, or rearrangement.

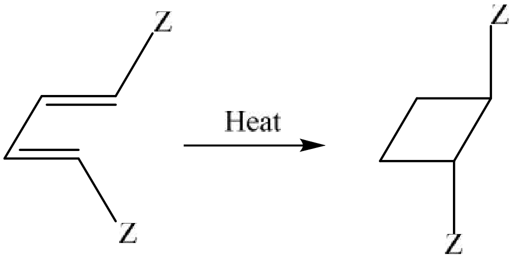
(a) $CH_3CH_2Br + LiOH \rightarrow CH_3CH_2OH + LiBr$

(b) $CH_3CH_2CH_2Cl \rightarrow CH_3CH{=}CH_2 + HCl$

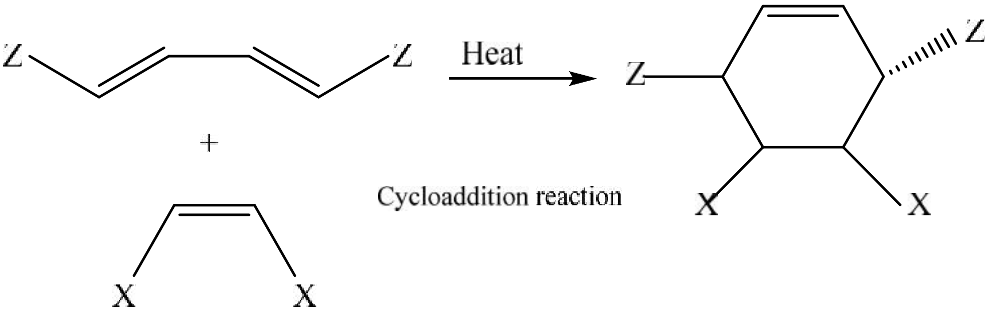
(c) $CH_3CH{=}CH_2 + H_2 \rightarrow CH_3CH_2CH_3$

3.3.6 Pericyclic Reactions

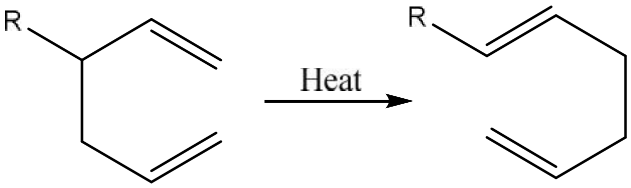
In these reactions, the electron reorganization of the substrate molecule takes place through a cyclic transition state in a single-step reaction, giving stereo specific products under the influence of either heat or light. For example,



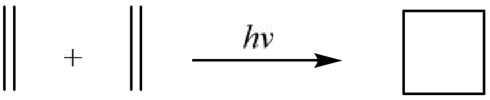
Electrocyclic reaction



Cycloaddition reaction



Sigmatropic reaction



Cycloaddition reaction

In these reactions, the products that are obtained by heating the substrate cannot be formed by irradiation with light and vice versa. The mechanism of a reaction of any one of the above types consists of everything that happens as the starting materials are converted to the products.

The reactions may take place in a single step or in a multiple step. In a multiple-step reaction, the product of a step that takes part in the successive step is considered as an intermediate in the overall reaction. For example,

$$\underset{\text{Reactant}}{A} \longrightarrow B \longrightarrow C \longrightarrow \underset{\text{Product}}{D}$$

B and C are intermediates for the overall reaction:

$$A \longrightarrow D$$

The reactions take place due to electron reorganization in the reactant molecule.

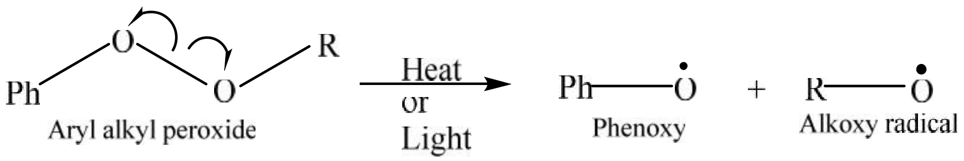
3.3.7 Free Radical Reactions

As discussed earlier in unit 2 of this module, free radicals are chemical species having one or more unpaired electrons in their valence shells. Homolytic bond fission leads to the formation of free radicals. Thus, free radicals are odd electron molecules, e.g. $\bullet CH_3$, $\bullet C_2H_5$, $\bullet C_6H_5$, $(C_6H_5)_3\bullet C$, etc., and are highly reactive. Free radicals are paramagnetic, that is, they possess a small permanent magnetic moment, due to the presence of unpaired electron(s). This property is used for the detection of the presence of free radicals.

Formation of Free Radicals

Free radicals are formed by homolytic fission of a covalent bond, when a molecule is supplied with sufficient energy – thermal or photochemical.

(i) *Thermal Cleavage* – Most of the covalent bonds are thermally stable up to a temperature of 200°C . However, there are a few group of compounds (peroxy and azo) which undergo homolytic cleavage at temperatures below 200°C. These are designated as initiators.



$$H_3C-N=N-CH_3 \xrightarrow[\text{or Light}]{\text{Heat}} 2CH_3 + N_2$$

(ii) *Photochemical Cleavage* – A second general method of obtaining radicals is through irradiation with either UV or visible light. The energy transferred to the molecule by the interaction must be of the order of bond dissociation energy or grater to produce homolysis.

Alkanes undergo substitution reaction with halogens. The hydrogen atom of the alkane is substituted with a halogen atom to give an alkyl halide in the presence of light or heating at 250℃ - 400℃.

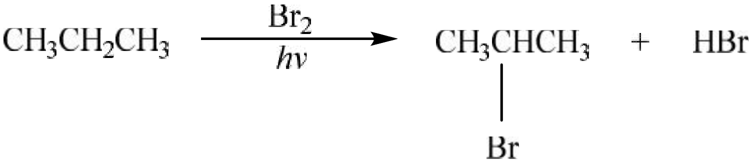
$$CH_4 + Cl_2 \xrightarrow{hv} CH_3Cl + HCl$$

$$CH_3Cl + Cl_2 \xrightarrow{hv} CH_2Cl_2 + HCl$$

$$CH_2Cl_2 + Cl_2 \xrightarrow{hv} CHCl_3 + HCl$$

$$CHCl_3 + Cl_2 \xrightarrow{hv} CCl_4 + HCl$$

This free radical reaction is less vigorous in bromine and more discriminatory. Bromine radical will prefer secondary carbon to the primary.



$$CH_3CH_2CH_3 \xrightarrow[hv]{Br_2} CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 + HBr$$

This reaction proceeds via a free radical mechanism.

Mechanism of Free Radical Reaction

(i) ***Chain Initiation Step:*** This is the step in which energy is absorbed and reactive particles are generated. Here the chlorine molecule is broken into chlorine radicals. This cleavage is homolytic.

$$Cl_2 \xrightarrow[\Delta]{uv} Cl^{\bullet} + Cl^{\bullet} \quad \text{(chain initiation step)}$$

(ii) ***Chain Propagation Step:*** Here, a reactive particle (free radical) is consumed and another reactive particle is generated.

$$CH_4 + Cl^{\bullet} \longrightarrow CH_3^{\bullet} + HCl$$

$$CH_3^{\bullet} + Cl_2 \longrightarrow CH_3Cl + Cl^{\bullet}$$

(chain propagation steps)

(iii) Chain Termination Step: Here, the reactive particles are consumed but no new particles are generated.

$$Cl^{\bullet} + Cl^{\bullet} \longrightarrow Cl_2$$

$$CH_3^{\bullet} + CH_3^{\bullet} \longrightarrow CH_3CH_3 \qquad \text{(chain termination step)}$$

$$CH_3^{\bullet} + Cl^{\bullet} \longrightarrow CH_3Cl$$

In-Text Question 4
Radical chlorination of alkanes is not generally useful because mixtures of products often result when more than one kind of C-H bond is present in the substrate. Draw and name all mono-chloro substitution products $C_6H_{13}Cl$ you might obtain by reaction of 2-methylpentane with Cl_2.

3.4 Types of Reagents

Many reagents that bring about numerous organic reactions can be classified into two main groups. This classification is done on the basis of the ability of the reagents to accept or donate electrons to the substrate molecule.

The reagent that accept electrons are termed as ***Electrophiles*** (philic meaning loving, that is, electron loving) and often abbreviated by the symbol $E^{\oplus}$. The reagents that donate electrons to the electron-deficient species are called ***Nucleophiles*** (nucleus or positive centre loving) and often abbreviated by the symbol$Nu^{\ominus}$.
Electrophiles are electron-deficient species. All positively charged species are electrophilic in nature, for example, $H^{\oplus}, CH_3^{\oplus}, \bullet$ $Cl^{\oplus}, NO_2^{\oplus}$, and so on.

Neutral molecules or species where the central atom is unsaturated with respect to electrons also behave as electrophiles. For example, $AlCl_3$, BF_3, and $\ddot{C}H_2$, where the central atom contains the sextet of electrons. Other neutral molecules where the central atom can expand its octet to decet or dodecet also behave as electrophiles. For instance, SF_4 can form species like SF_6^{2-}, and $SiCl_4$and form $SiCl_6^{2\ominus}$,so, SF_4 and $SiCl_4$ behave as electrophiles. Transition metal compounds that act as Lewis acids due to the ability of the metal ions to accommodate electrons in the *d*-AOs also behave as electrophile, for example, $ZnCl_2$, $SnCl_4$, $FeCl_3$, and so on. Odd electron species like free radicals where the unpaired electron is accommodated in a low energy. Singly Occupied Molecular Orbital (SOMO) also act as electrophiles, for example, CH_3O.
Nucleophiles, on the other hand, are electron-rich species.

All negatively charged species by nature are Nucleophilic, for example, $H^{\ominus}$, $CH_3^{\ominus}$, $Cl^{\ominus}$, $HO^{\ominus}$, $HS^{\ominus}$, and so on. Neutral species that have loosely held electrons as in π-bonds, act as nucleophiles. For example, alkenes, alkynes, and so on, are Nucleophilic in nature. Neutral molecules that have one or more lone pairs on an atom, usually a heteroatom, behave as the nucleophiles. For example, $H_2\ddot{O}:$, $\ddot{N}H_3$, and so on.

Odd electron species where the unpaired electron is accommodated in a high-energy SOMO also behave as nucleophiles, for example, $\dot{C}H_3$.

In-Text Question 5

1. Which of the following is not an electrophile?
   a) $(CH_3)_4N^+$ b) Cl_2 c) HBr d) Br_2
2. Which reagent is a good nucleophile?
   a) NH_3 b) BH_3 c) Br_2 d) HBr

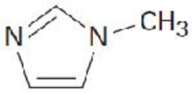
SELF-ASSESSMENT EXERCISE

i. Classify each of the following reactions as an addition, elimination, substitution, or rearrangement:

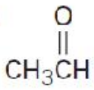
(a) $CH_3Br + KOH \rightarrow CH_3OH + KBr$
(b) $CH_3CH_2Br \rightarrow H_2C{=}CH_2 + HBr$
(c) $H_2C{=}CH_2 + H_2 \rightarrow CH_3CH_3$

ii Which of the following species are likely to be nucleophiles and which electrophiles? Which might be both?

(a) CH_3Cl **(b)** CH_3S^- **(c)**

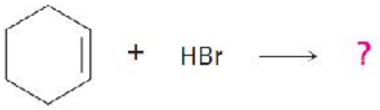


(d)

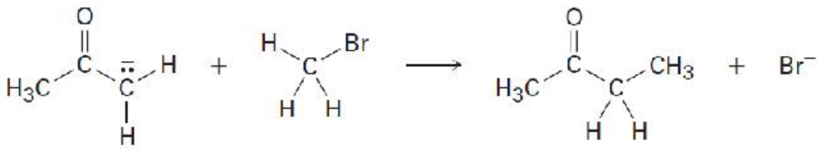


$CH_3\overset{O}{\overset{\|}{C}}H$

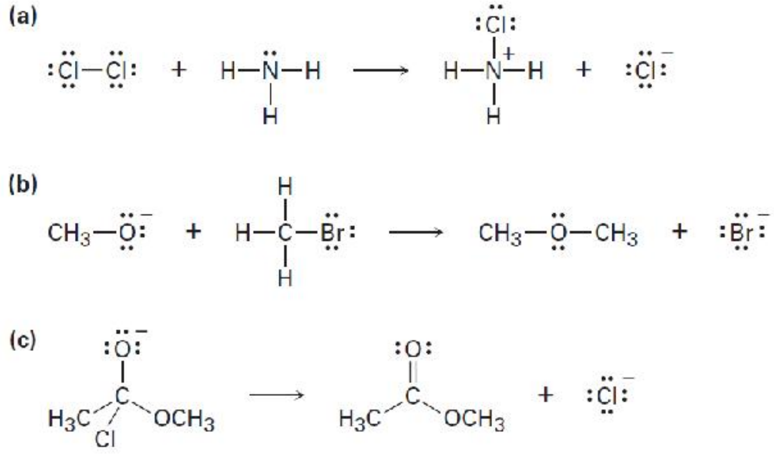
iii What product would you expect from reaction of cyclohexene with HBr? With HCl?



iv Add curved arrows to the following polar reaction to show the flow of electrons:



v. Add curved arrows to the following polar reactions to indicate the flow of electrons in each:



4.0 CONCLUSION

We have been able to explain how equations for organic reaction are written; the reaction mechanism involving bond cleavage, radicals, carbocation and carbonions, bond formation and kind of arrows. Also the various types of organic reactions with examples and lastly the types of reagents used in organic reactions.

5.0 SUMMARY

There are common patterns to how organic reactions occur. In a substitution reaction, one atom or a group of atoms in a substance is replaced by another atom or group of atoms from another substance. Bulky groups that prevent attack cause the reaction to be sterically hindered. In an elimination reaction, adjacent atoms are removed with subsequent formation of a multiple bond and a small molecule. An addition reaction is the reverse of an elimination reaction. Radical reactions are not very selective and occur in three stages: initiation, propagation, and termination. Oxidation-reduction reactions in organic chemistry are identified by the change in the number of oxygen in the hydrocarbon skeleton or the number of bonds between carbon and oxygen or carbon and nitrogen.

6.0 TUTOR MARK ASSIGNMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry*, 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

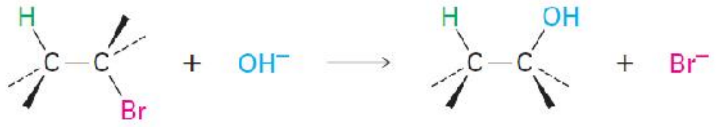
Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

UNIT 4 NUCLEOPHILIC SUBSTITUTION AND ELIMINATION REACTIONS

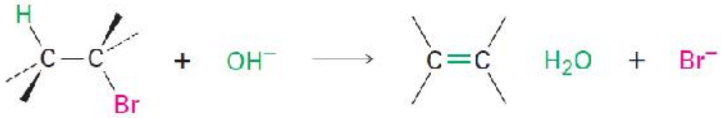
CONTENTS

1.0 INTRODUCTION

The carbon-halogen bond in an alkyl halide is polar and the carbon atom is electron-poor. Thus, alkyl halides are electrophiles, and much of their chemistry involves polar reactions with nucleophiles and bases. Alkyl halides do one of two things when they react with a nucleophile/base, such as hydroxide ion: either they undergo *substitution* of the X group by the nucleophile, or they undergo *elimination* of HX to yield an alkene.



Substitution



Elimination

Nucleophilic substitution and base-induced elimination are two of the most widely occurring and versatile reaction types in organic chemistry, both in the laboratory and in biological pathways. We'll look at them closely in this unit to see how they occur, what their characteristics are, and how they can be used. We'll begin with nucleophilic substitution reactions.

2.0 OBJECTIVES

By the end of this session, you should be able to:

- have a better understanding of nucleophilic substitution and elimination reactions.
- have a better understanding of the types of nucleophilic substitution and elimination reactions.
- understand the characteristics of nucleophilic substitution and elimination reactions.
- become familiar with biological nucleophilic substitution and elimination reactions

3.0 MAIN CONTENT

3.1 The Discovery of Nucleophilic Substitution Reactions

The discovery of the nucleophilic substitution reaction of alkyl halides dates back to work carried out in 1896 by the German chemist Paul Walden. Walden found that the pure enantiomeric (+)- and (-)-malic acids could be interconverted through a series of simple substitution reactions. When Walden treated (-)-malic acid with PCl_5, he isolated (+)-chlorosuccinic acid. This, on treatment with wet Ag_2O, gave (+)-malic acid. Similarly, reaction of (+)-malic acid with PCl_5 gave (-)-chlorosuccinic acid, which was converted into (-)-malic acid when treated with wet Ag_2O. The full cycle of reactions is shown in **Figure 2.6** below.

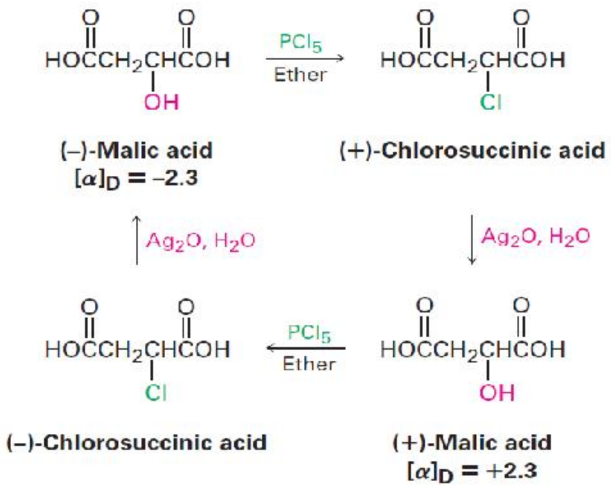


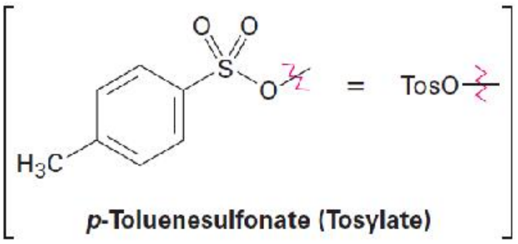
Figure 2.6: Walden's cycle of reactions interconverting (+)- and (-)-malic acids.

At the time, the results were astonishing. The eminent chemist Emil Fischer called Walden's discovery "the most remarkable observation made in the field of optical activity since the fundamental observations of Pasteur." Because (-)-malic acid was converted into (+)-malic acid, *some reactions in the cycle must have occurred with a change, or inversion, in configuration at the chirality center*.

Today, we refer to the transformations taking place in Walden's cycle as nucleophilic substitution reactions because each step involves the substitution of one nucleophile (chloride ion, Cl^-, or hydroxide ion, HO^-) by another. Nucleophilic substitution reactions are one of the most common and versatile reaction types in organic chemistry.

$$R{-}X \quad + \quad Nu{:}^- \quad \longrightarrow \quad R{-}Nu \quad + \quad X{:}^-$$

Following the work of Walden, further investigations were undertaken during the 1920s and 1930s to clarify the mechanism of nucleophilic substitution reactions and to find out how inversions of configuration occur. Among the first series studied was one that interconverted the two enantiomers of 1-phenyl-2-propanol **(Figure 2.7).** Although this particular series of reactions involves nucleophilic substitution of an alkyl *p*-toluenesulfonate (called a *tosylate*) rather than an alkyl halide, exactly the same type of reaction is involved as that studied by Walden. For all practical purposes, the entire tosylate group acts as if it were simply a halogen substituent. (In fact, when you see a tosylate substituent in a molecule, do a mental substitution and tell yourself that you're dealing with an alkyl halide.)



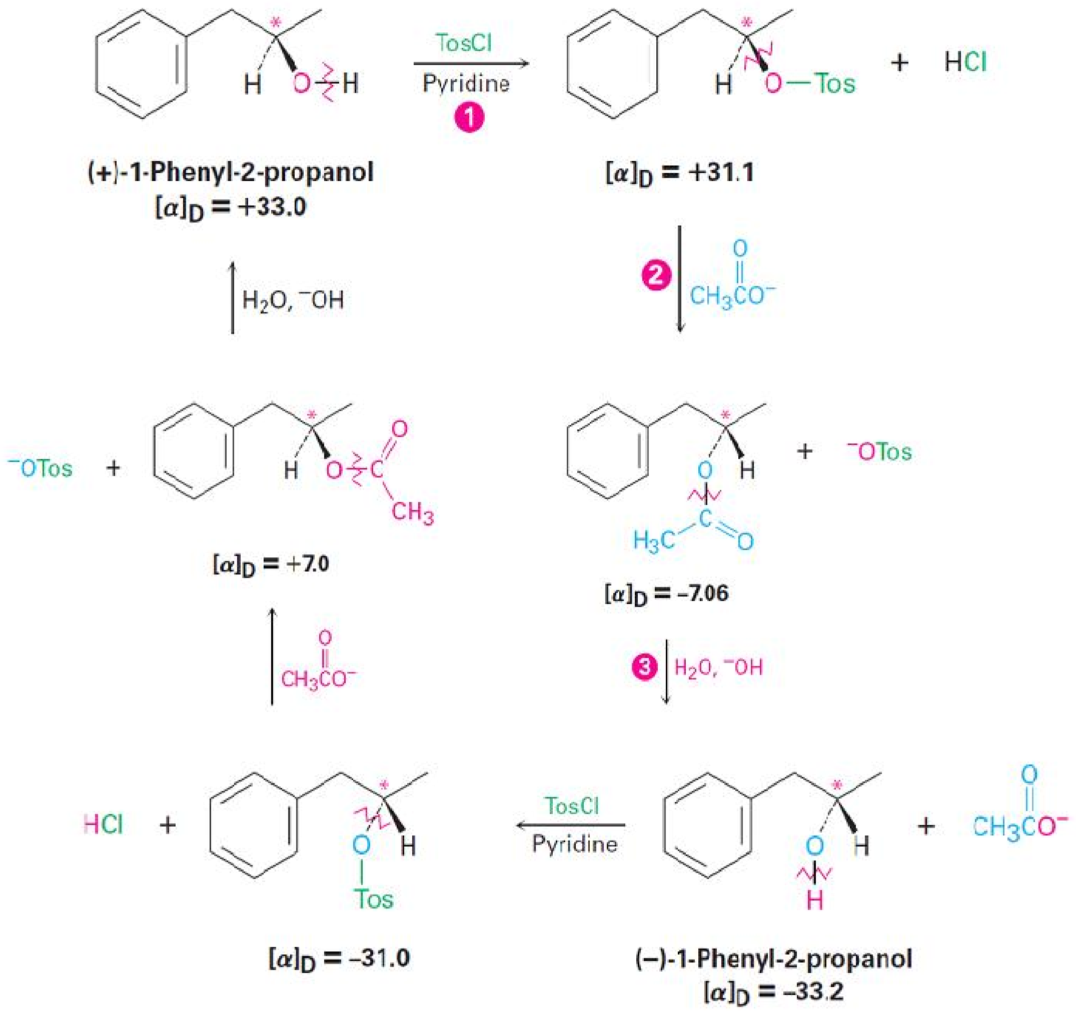
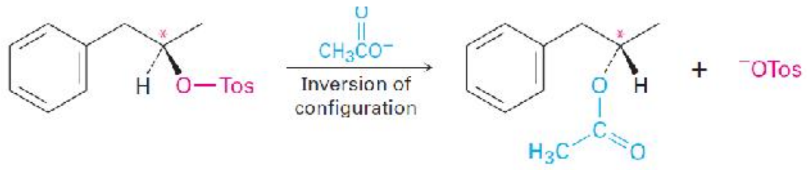


Figure 2.7: A Walden cycle interconverting (+) and (-) enantiomers of 1-phenyl-2-propanol.

In the three-step reaction sequence shown in **Figure 2.7**, (+)-1-phenyl-2-propanol is interconverted with its (-) enantiomer, so at least one of the three steps must involve an inversion of configuration at the chirality center. Step 1, formation of a tosylate, occurs by breaking the O-H bond of the alcohol rather than the C-O bond to the chiral carbon, so the configuration around carbon is unchanged. Similarly, step 3, hydroxide-ion cleavage of the acetate, takes place without breaking the C-O bond at the chirality center. *The inversion of stereo chemical configuration must* *therefore take place in step 2, the nucleophilic substitution of tosylate ion by acetate ion.*



From this and nearly a dozen other series of similar reactions, workers concluded that the nucleophilic substitution reaction of a primary or secondary alkyl halide or tosylate always proceeds with inversion of configuration.

In-Text Question 1

What product would you expect from a nucleophilic substitution reaction of (*R*)-1-bromo-1-phenylethane with cyanide ion, $-C \equiv N$, as nucleophile? Show the stereochemistry of both reactant and product, assuming that inversion of configuration occurs.

?

3.2 The S_N2 Reaction

In every chemical reaction, there is a direct relationship between the rate at which the reaction occurs and the concentrations of the reactants. When we measure this relationship, we measure the kinetics of the reaction. For example, let’s look at the kinetics of a simple nucleophilic substitution—the reaction of CH_3Br with OH^- to yield CH_3OH plus Br^-.

At a given temperature, solvent, and concentration of reactants, the substitution occurs at a certain rate. If we double the concentration of OH^-, the frequency of encounter between the reaction partners doubles and we find that the reaction rate also doubles. Similarly, if we double the concentration of CH_3Br, the reaction rate again doubles. We call such a reaction, in which the rate is linearly dependent on the concentrations of two species, a second-order reaction. Mathematically, we can express this second-order dependence of the nucleophilic substitution reaction by setting up a *rate equation.* As either [RX] or [$^-$OH] changes, the rate of the reaction changes proportionately.

Reaction rate = Rate of disappearance of reactant

= *k* x [RX] x [$^-$OH]
Where [RX] = CH_3Br concentration in molarity
[$^-$OH] = $^-$OH concentration in molarity
k = A Constant value (the rate constant).

The essential feature of the S_N2 mechanism is that it takes place in a single step without intermediates when the incoming nucleophile reacts with the alkyl halide or tosylate (the *substrate*) from a direction opposite the group that is displaced (the *leaving group*). As the nucleophile comes in on one side of the substrate and bonds to the carbon, the halide or tosylate departs from the other side, thereby inverting the stereo chemical configuration. The process is shown in **Figure 2.8** for the reaction of (*S*)-2-bromobutane with HO^- to give (*R*)-2-butanol.

Mechanism

The mechanism of the S_N2 reaction takes place in a single step when the incoming nucleophile approaches from a direction 180° away from the leaving halide ion, thereby inverting the stereochemistry at carbon.

Step 1: The nucleophile –OH uses its lone-pair electrons to attack the alkyl halide carbon 180° away from the departing halogen. This leads to a transition state with a partially formed C–OH bond and a partially broken C–Br bond.

Step 2: The stereochemistry at carbon is inverted as the C–OH bond forms fully and the bromide ion departs with the electron pair from the former C–Br bond.

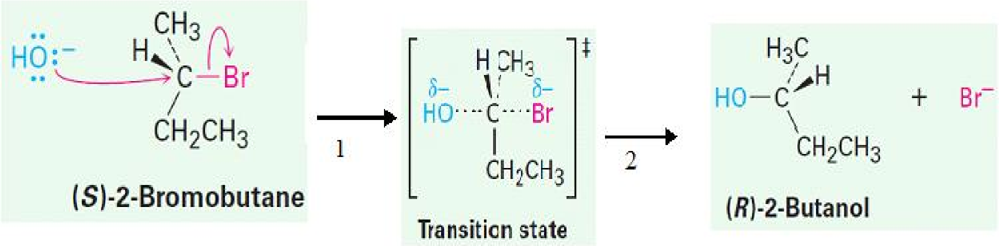


Figure 2.8: Mechanism of S_N2 reaction

As shown in the mechanism above, the S_N2 reaction occurs when an electron pair on the nucleophile Nu**:**$^-$ forces out the group X**:**$^-$, which takes with it the electron pair from the former C-X bond. This occurs through a transition state in which the new Nu-C bond is partially forming at the same time that the old C-X bond is partially breaking and in which the negative charge is shared by both the incoming nucleophile and the outgoing halide ion. The transition state for this inversion has the remaining three bonds to carbon in a planar arrangement **(Figure 2.9)**.

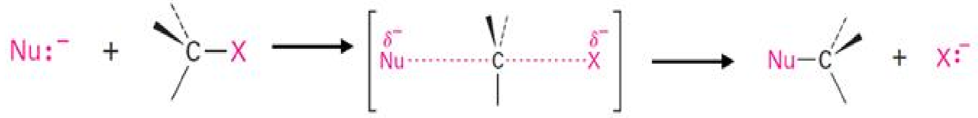


Figure 2.9: The transition state of an S$_N$**2 reaction has a planar arrangement of the carbon atom and the remaining three groups. Electrostatic potential maps show that negative charge is delocalized in the transition state.**

The mechanism proposed by Hughes and Ingold is fully consistent with experimental results, explaining both stereo chemical and kinetic data. Thus, the requirement for backside approach of the entering nucleophile from a direction 180° away from the departing X group causes the stereochemistry of the substrate to invert, much like an umbrella turning inside out in the wind. The Hughes–Ingold mechanism also explains why second-order kinetics are found: the S$_N$2 reaction occurs in a single step that involves both alkyl halide and nucleophile. Two molecules are involved in the step whose rate is measured.

3.3 Characteristics of the S$_N$2 Reaction

Now that we know how S$_N$2 reactions occur, we need to see how they can be used and what variables affect them. Some S$_N$2 reactions are fast, and some are slow; some take place in high yield and others in low yield. Understanding the factors involved can be of tremendous value. Let’s begin by recalling a few things about reaction rates in general.

The rate of a chemical reaction is determined by the activation energy $\Delta G^‡$, the energy difference between reactant ground state and transition state. A change in reaction conditions can affect $\Delta G^‡$ either by changing the reactant energy level or by changing the transition-state energy level. Lowering the reactant energy or raising the transition-state energy increases $\Delta G^‡$ and decreases the reaction rate; raising the reactant energy or decreasing the transition-state energy decreases $\Delta G^‡$ and increases the reaction rate **(Figure 2.10)**. We’ll see examples of all these effects as we look at S$_N$2 reaction variables.

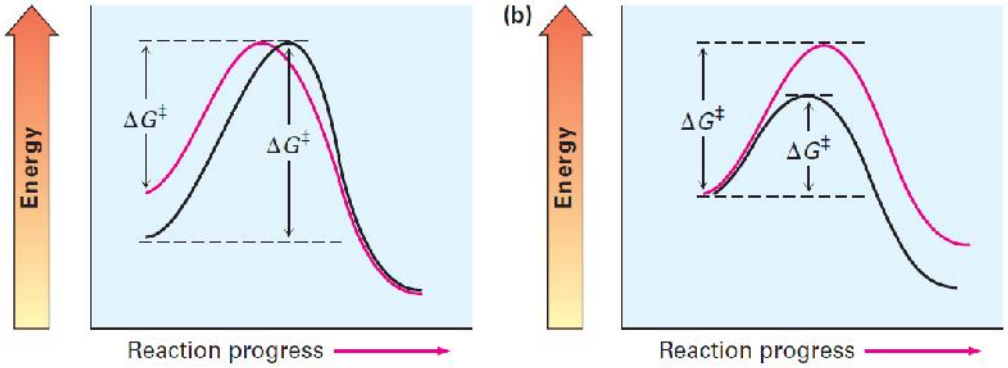


Figure 2.10: The effects of changes in reactant and transition-state energy levels on reaction rate. (a) A higher reactant energy level (red curve) corresponds to a faster reaction (smaller Δ*G*‡). (b) A higher transition state energy level (red curve) corresponds to a slower reaction (larger Δ*G*‡).

3.3.1 The Substrate: Steric Effects in the S_N2 Reaction

The first S_N2 reaction variable to look at is the structure of the substrate. Because the S_N2 transition state involves partial bond formation between the incoming nucleophile and the alkyl halide carbon atom, it seems reasonable that a hindered, bulky substrate should prevent easy approach of the nucleophile, making bond formation difficult. In other words, the transition state for reaction of a sterically hindered substrate, whose carbon atom is "shielded" from approach of the incoming nucleophile, is higher in energy and forms more slowly than the corresponding transition state for a less hindered substrate **(Figure 2.11)**.

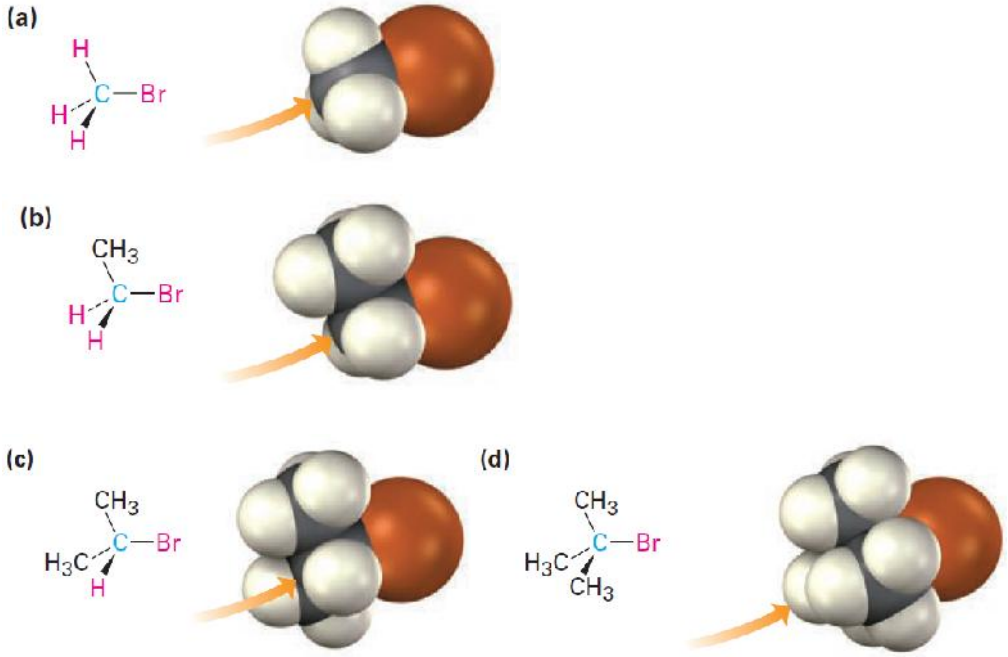
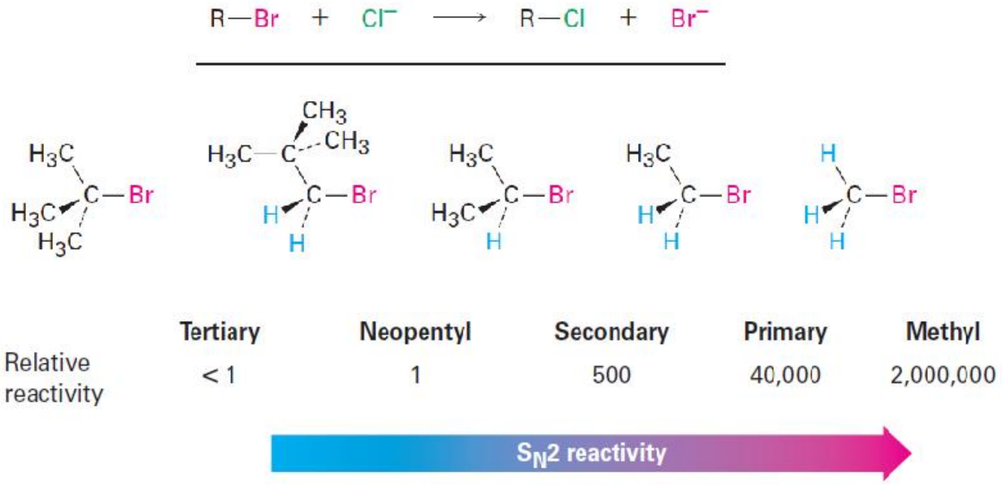


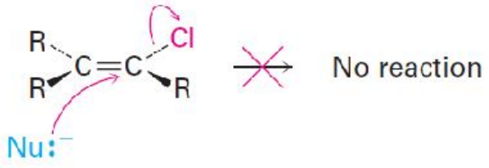
Figure 2.11: Steric hindrance to the S_N2 reaction. As the models indicate, the carbon atom in (a) bromomethane is readily accessible, resulting in a fast S_N2 reaction. The carbon atoms in (b) bromoethane (primary), (c) 2-bromopropane (secondary), and (d) 2-bromo-2-methylpropane (tertiary) are successively more hindered, resulting in successively slower S_N2 reactions.

As **Figure 2.11** shows, the difficulty of nucleophile approach increases as the three substituents bonded to the halo-substituted carbon atom increase in size. Methyl halides are by far the most reactive substrates in S_N2

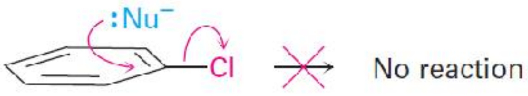
reactions, followed by primary alkyl halides such as ethyl and propyl. Alkyl branching at the reacting center, as in isopropyl halides (2°), slows the reaction greatly, and further branching, as in *tert*-butyl halides (3°), effectively halts the reaction. Even branching one carbon removed from the reacting center, as in 2,2-dimethylpropyl *(neopentyl)* halides, greatly slows nucleophilic displacement. As a result, S_N2 reactions occur only at relatively unhindered sites and are normally useful only with methyl halides, primary halides, and a few simple secondary halides. Relative reactivities for some different substrates are as follows:



Vinylic halides ($R_2C=CRX$) and aryl halides are not shown on this reactivity list because they are unreactive toward S_N2 displacement. This lack of reactivity is due to steric factors: the incoming nucleophile would have to approach in the plane of the carbon–carbon double bond and burrow through part of the molecule to carry out a backside displacement.



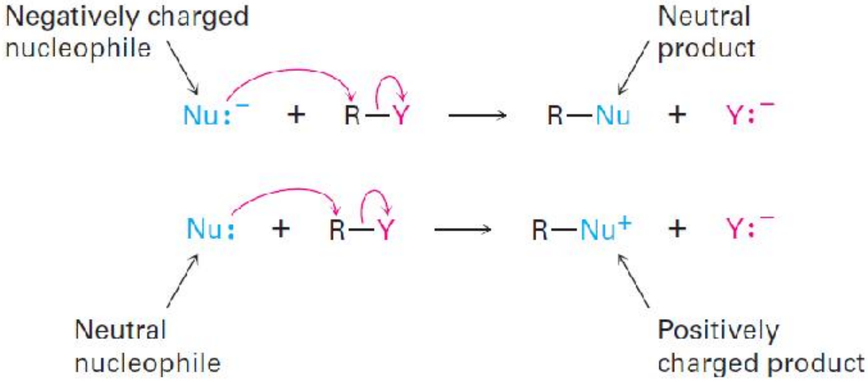
Vinylic halide



Aryl halide

3.3.2 The Nucleophile

Another variable that has a major effect on the S_N2 reaction is the nature of the nucleophile. Any species, either neutral or negatively charged, can act as a nucleophile as long as it has an unshared pair of electrons; that is, as long as it is a Lewis base. If the nucleophile is negatively charged, the product is neutral; if the nucleophile is neutral, the product is positively charged.



A wide array of substances can be prepared using nucleophilic substitution reactions.

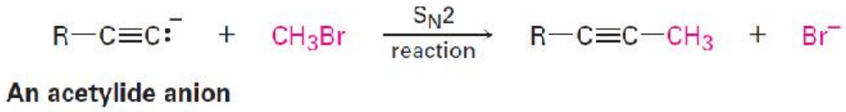
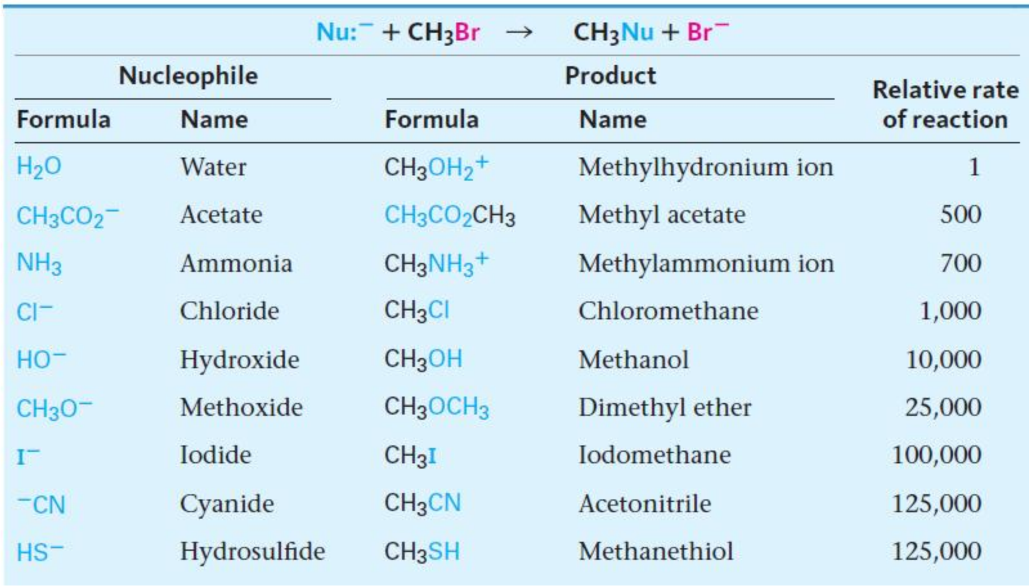


Table 2.5 lists some nucleophiles in the order of their reactivity, shows the products of their reactions with bromomethane, and gives the relative rates of their reactions. Clearly, there are large differences in the rates at which various nucleophiles react.

What are the reasons for the reactivity differences observed in **Table 2.5**? Why do some reactants appear to be much more “nucleophilic” than others? The answers to these questions aren’t straightforward. Part of the problem is that the term *nucleophilicity* is imprecise. The term is usually taken to be a measure of the affinity of a nucleophile for a carbon atom in the S_N2 reaction, but the reactivity of a given nucleophile can change from one reaction to the next. The exact nucleophilicity of a species in a given reaction depends on the substrate, the solvent, and even the reactant concentrations. Detailed explanations for the observed nucleophilicities aren’t always simple, but some trends can be detected in the data of **Table 2.5**.

Table 2.5: Some S_N2 Reactions with Bromomethane



$Nu:^- + CH_3Br \rightarrow CH_3Nu + Br^-$

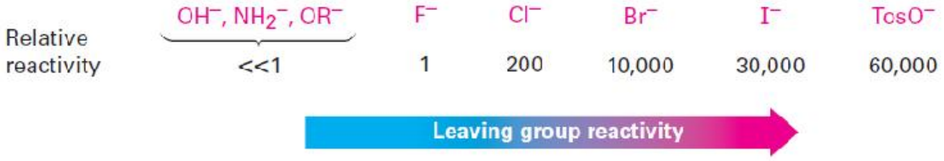
Nucleophile		Product		Relative rate of reaction
Formula	Name	Formula	Name	
H_2O	Water	$CH_3OH_2^+$	Methylhydronium ion	1
$CH_3CO_2^-$	Acetate	$CH_3CO_2CH_3$	Methyl acetate	500
NH_3	Ammonia	$CH_3NH_3^+$	Methylammonium ion	700
Cl^-	Chloride	CH_3Cl	Chloromethane	1,000
HO^-	Hydroxide	CH_3OH	Methanol	10,000
CH_3O^-	Methoxide	CH_3OCH_3	Dimethyl ether	25,000
I^-	Iodide	CH_3I	Iodomethane	100,000
^-CN	Cyanide	CH_3CN	Acetonitrile	125,000
HS^-	Hydrosulfide	CH_3SH	Methanethiol	125,000

- Nucleophilicity roughly parallels basicity when comparing nucleophiles that have the same reacting atom. Thus, OH^- is both more basic and more nucleophilic than acetate ion, $CH_3CO_2^-$, which in turn is more basic and more nucleophilic than H_2O. Since "nucleophilicity" is usually taken as the affinity of a Lewis base for a carbon atom in the S_N2 reaction and "basicity" is the affinity of a base for a proton, it's easy to see why there might be a correlation between the two kinds of behavior.
- Nucleophilicity usually increases going down a column of the periodic table. Thus, HS^- is more nucleophilic than HO^-, and the halide reactivity order is I^-. Br^-. Cl^-. Going down the periodic table, elements have their valence electrons in successively larger shells where they are successively farther from the nucleus, less tightly held, and consequently more reactive. The matter is complex, though, and the nucleophilicity order can change depending on the solvent.
- Negatively charged nucleophiles are usually more reactive than neutral ones. As a result, S_N2 reactions are often carried out under basic conditions rather than neutral or acidic conditions.

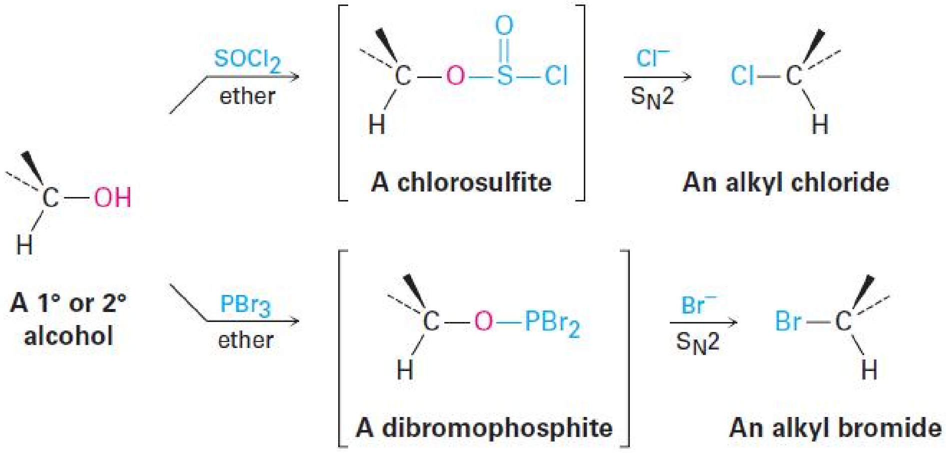
3.3.3 The Leaving Group

Still another variable that can affect the S_N2 reaction is the nature of the group displaced by the incoming nucleophile. Because the leaving group is expelled with a negative charge in most S_N2 reactions, the best leaving groups are those that best stabilize the negative charge in the transition state. The greater the extent of charge stabilization by the leaving group, the lower the energy of the transition state and the more rapid the reaction.

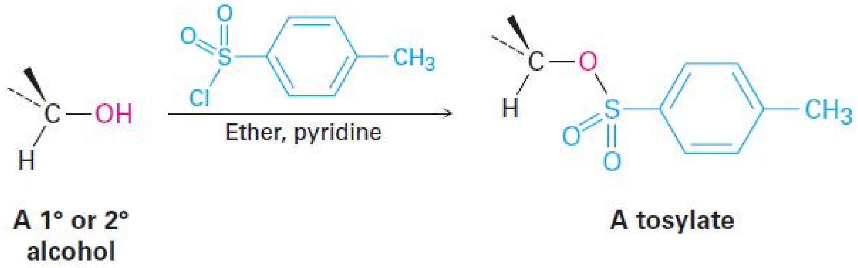
Thus, weak bases such as Cl^-, Br^-, and tosylate ion make good leaving groups, while strong bases such as OH^- and NH_2^- make poor leaving groups.



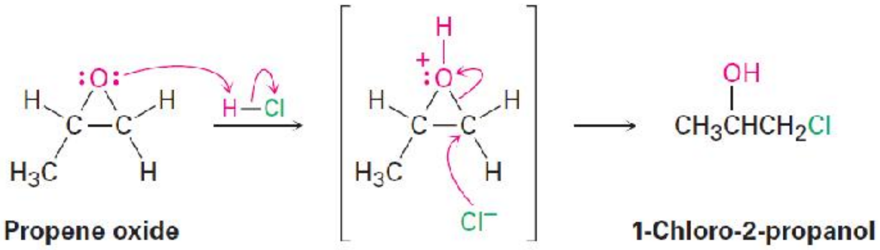
It's just as important to know which are poor leaving groups as to know which are good, and the preceding data clearly indicate that F^-, HO^-, RO^-, and H_2N^- are not displaced by nucleophiles. In other words, alkyl fluorides, alcohols, ethers, and amines do not typically undergo S_N2 reactions. To carry out an S_N2 reaction with an alcohol, it's necessary to convert the ^-OH into a better leaving group. This, in fact, is just what happens when a primary or secondary alcohol is converted into either an alkyl chloride by reaction with $SOCl_2$ or an alkyl bromide by reaction with PBr_3.



Alternatively, an alcohol can be made more reactive toward nucleophilic substitution by treating it with *para*-toluenesulfonyl chloride to form a tosylate. As noted previously, tosylates are even more reactive than halides in nucleophilic substitutions. Note that tosylate formation does not change the configuration of the oxygen-bearing carbon because the C-O bond is not broken.

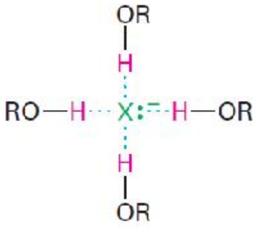


The one general exception to the rule that ethers don't typically undergo S_N2 reactions occurs with epoxides and the three-membered cyclic ethers. Epoxides, because of the angle strain in the three membered rings, are much more reactive than other ethers. They react with aqueous acid to give 1,2-diols, and they react readily with many other nucleophiles as well. Propene oxide, for instance, reacts with HCl to give 1-chloro-2-propanol by S_N2 backside attack on the less hindered primary carbon atom.



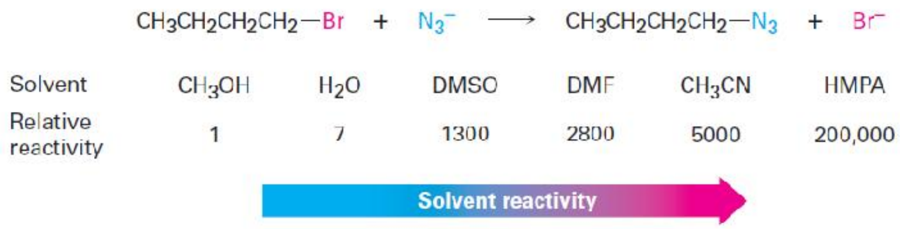
3.3.4 The Solvent

The rates of S_N2 reactions are strongly affected by the solvent. Protic solvents—those that contain an -OH or -NH group - are generally the worst for S_N2 reactions, while polar aprotic solvents, which are polar but don't have an –OH or -NH group, are the best.
Protic solvents, such as methanol and ethanol, slow down S_N2 reactions by solvation of the reactant nucleophile. The solvent molecules hydrogen bond to the nucleophile and form a cage around it, thereby lowering its energy and reactivity.



A solvated anion (reduced nucleophilicity due to enhanced ground-state stability).

In contrast with protic solvents, which decrease the rates of S_N2 reactions by lowering the ground-state energy of the nucleophile, polar aprotic solvents increase the rates of S_N2 reactions by raising the ground-state energy of the nucleophile. Acetonitrile (CH_3CN), dimethylformamide [$(CH_3)_2NCHO$, abbreviated DMF], dimethyl sulfoxide [$(CH_3)_2SO$, abbreviated DMSO], and hexamethylphosphoramide {$[(CH_3)_2N]_3PO$, abbreviated HMPA} are particularly useful. These solvents can dissolve many salts because of their high polarity, but they tend to solvate metal cations rather than nucleophilic anions. As a result, the bare unsolvated anions have a greater nucleophilicity and S_N2 reactions take place at correspondingly faster rates. For instance, a rate increase of 200,000 has been observed on changing from methanol to HMPA for the reaction of azide ion with 1-bromobutane.

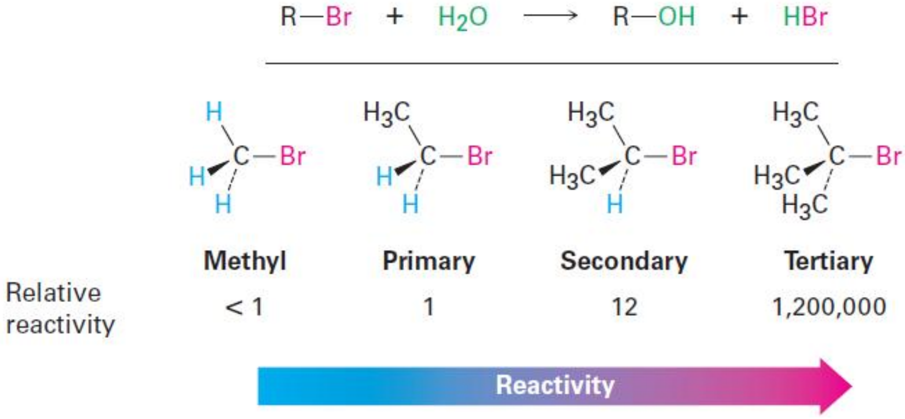


$$CH_3CH_2CH_2CH_2{-}Br + N_3^- \longrightarrow CH_3CH_2CH_2CH_2{-}N_3 + Br^-$$

Solvent	CH_3OH	H_2O	DMSO	DMF	CH_3CN	HMPA
Relative reactivity	1	7	1300	2800	5000	200,000

3.4 The S_N1 Reaction

Most nucleophilic substitutions take place by the S_N2 pathway just discussed. The reaction is favoured when carried out with an unhindered substrate and a negatively charged nucleophile in a polar aprotic solvent, but is disfavoured when carried out with a hindered substrate and a neutral nucleophile in a protic solvent. You might therefore expect the reaction of a tertiary substrate (hindered) with water (neutral, protic) to be among the slowest of substitution reactions. Remarkably, however, the opposite is true. The reaction of the tertiary halide $(CH_3)_3CBr$ with H_2O to give the alcohol 2-methyl-2-propanol is more than *1 million times* as fast as the corresponding reaction of CH_3Br to give methanol.



$$R{-}Br + H_2O \longrightarrow R{-}OH + HBr$$

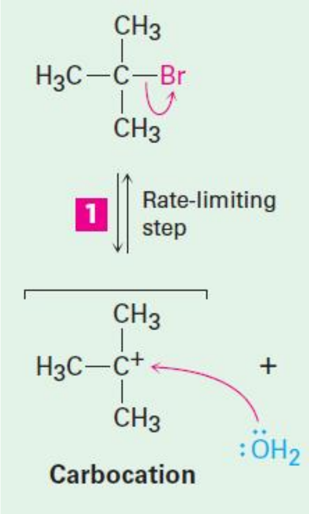
	Methyl	Primary	Secondary	Tertiary
Relative reactivity	< 1	1	12	1,200,000

A nucleophilic substitution reaction is occurring - a halogen is replacing a hydroxyl group - yet the reactivity order seems backward. These reactions can’t be taking place by the S_N2 mechanism we’ve been discussing, and we must therefore conclude that they are occurring by an alternative substitution mechanism. This alternative mechanism is called the S_N1 reaction, for *substitution, nucleophilic, unimolecular*.

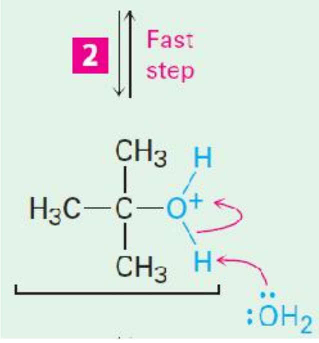
In contrast to the S_N2 reaction of CH_3Br with OH^-, the S_N1 reaction of $(CH_3)_3CBr$ with H_2O has a rate that depends only on the alkyl halide concentration and is independent of the H_2O concentration. In other words, the reaction is a first-order process; the concentration of the nucleophile does not appear in the rate equation.

Reaction rate = Rate of disappearance of alkyl halide
$= k \times [RX]$
Many organic reactions occur in several steps, one of which usually has a higher-energy transition state than the others and is therefore slower. We call this step with the highest transition-state energy the *rate-limiting step,* or *rate determining step.* No reaction can proceed faster than its rate-limiting step, which acts as a kind of traffic jam, or bottleneck. In the S_N1 reaction of $(CH_3)_3CBr$ with H_2O, the fact that the nucleophile concentration does not appear in the first-order rate equation means that it is not involved in the rate limiting step and must therefore be involved in some other, non–rate-limiting step.

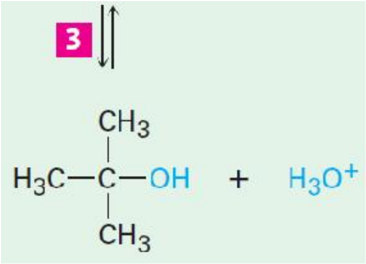
Mechanism
Step 1: Spontaneous dissociation of the alkyl bromide occurs in a slow, rate-limiting step to generate a carbocation intermediate plus bromide ion.



Step 2: The carbocation intermediate reacts with water as nucleophile in a fast step to yield protonated alcohol as product.



Step 3: Loss of a proton from the protonated alcohol intermediate then gives the neutral alcohol product.



The mechanism of the S_N1 reaction of 2-bromo-2-methylpropane with H_2O involves three steps. Step - the spontaneous, unimolecular dissociation of the alkyl bromide to yield a carbocation - is rate-limiting. Unlike what happens in an S_N2 reaction, where the leaving group is displaced at the same time the incoming nucleophile approaches, an S_N1 reaction takes place by loss of the leaving group *before* the nucleophile approaches. 2-Bromo-2-methylpropane spontaneously dissociates to the *tert*-butyl carbocation plus Br^- in a slow rate-limiting step, and the intermediate carbocation is then immediately trapped by the nucleophile water in a faster second step. Water is not a reactant in the step whose rate is measured. The energy diagram is shown in **Figure 2.12**.

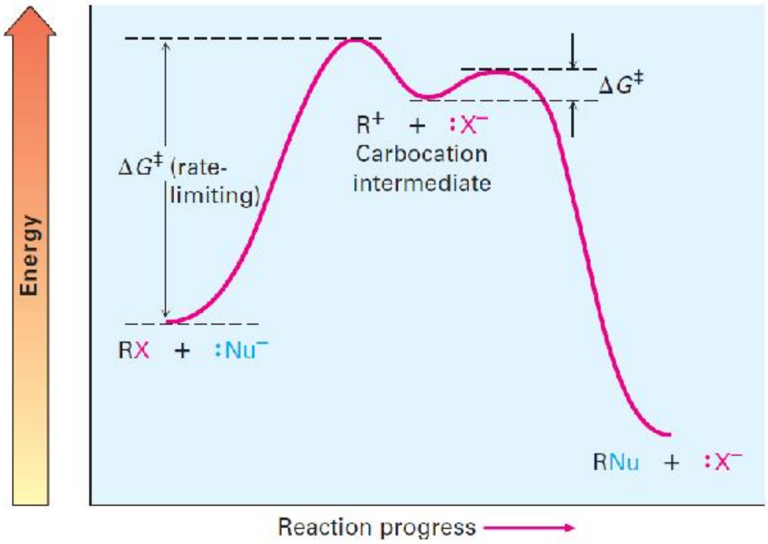
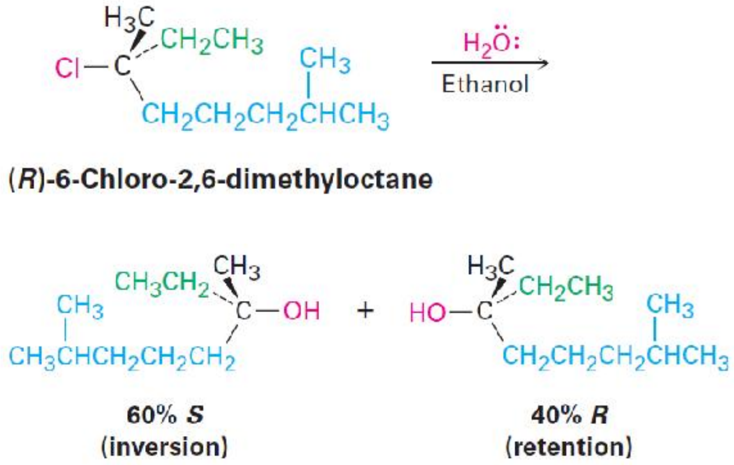


Figure 2.12: An energy diagram for an S_N1 reaction. The rate-limiting step is the spontaneous dissociation of the alkyl halide to give a carbocation intermediate. Reaction of the carbocation with a nucleophile then occurs in a second, faster step

Because an S_N1 reaction occurs through a carbocation intermediate, its stereo chemical outcome is different from that of an S_N2 reaction. Carbocations, as we've seen, are planar, *sp*2-hybridized, and achiral. Thus, if we carry out an S_N1 reaction on one enantiomer of a chiral reactant and go through an achiral carbocation intermediate, the product must lose its optically activity. That is, the symmetrical intermediate carbocation can react with a nucleophile equally well from either side, leading to a racemic, 50;50 mixture of enantiomers.

The conclusion that SN1 reactions on enantiomerically pure substrates should give racemic products is nearly, but not exactly, what is found. In fact, few SN1 displacements occur with complete racemization. Most give a minor (0–20%) excess of inversion. The reaction of (*R*)-6-chloro-2,6-dimethyloctane with H_2O, for example, leads to an alcohol product that is approximately 80% racemized and 20% inverted (80% *R*,*S*+20% *S* is equivalent to 40% *R*+60% S).



This lack of complete racemization in SN1 reactions is due to the fact that *ion pairs* are involved. If a certain amount of substitution occurs before the two ions fully diffuse apart, then a net inversion of configuration will be observed.

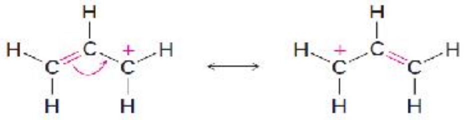
3.5 Characteristics of the SN1 Reaction

Just as the SN2 reaction is strongly influenced by the structure of the substrate, the leaving group, the nucleophile, and the solvent, the SN1 reaction is similarly influenced. Factors that lower $\Delta G‡$, either by lowering the energy level of the transition state or by raising the energy level of the ground state, favor faster SN1 reactions. Conversely, factors that raise $\Delta G‡$, either by raising the energy level of the transition state or by lowering the energy level of the reactant, slow down the SN1 reaction.

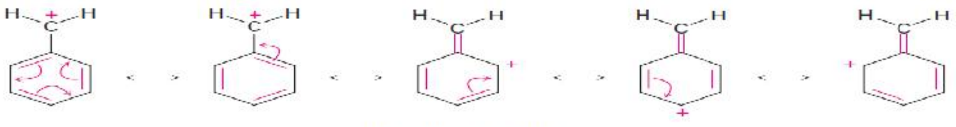
3.5.1 The Substrate

According to the Hammond postulate, any factor that stabilizes a high-energy intermediate also stabilizes the transition state leading to that intermediate. Since the rate-limiting step in an SN1 reaction is the spontaneous, unimolecular dissociation of the substrate to yield a carbocation, the reaction is favored whenever a stabilized carbocation intermediate is formed. The more stable the carbocation intermediate, the faster the SN1 reaction.

The stability order of alkyl carbocations is 3° > 2° > 1° > $-CH_3$. To this list we must also add the resonance-stabilized allyl and benzyl cations. Just as allylic radicals are unusually stable because the unpaired electron can be delocalized over an extended *p* orbital system, so allylic and benzylic carbocations are unusually stable. An allylic cation has two resonance forms. In one form the double bond is on the "left"; in the other form it's on the "right." A benzylic cation has five resonance forms, all of which contribute to the overall resonance hybrid.



Allyl carbocation



Benzyl carbocation

Figure 2.13: Resonance forms of allylic and benzylic carbocations. The positive charge is delocalized over the *p* system in both

Because of resonance stabilization, a primary allylic or benzylic carbocation is about as stable as a secondary alkyl carbocation and a secondary allylic or benzylic carbocation is about as stable as a tertiary alkyl carbocation. This stability order of carbocations is the same as the order of S_N1 reactivity for alkyl halides and tosylates.

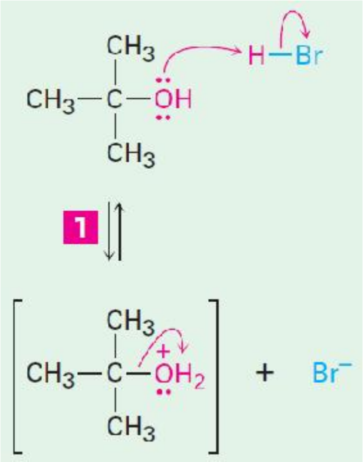
3.5.2 The Leaving Group

We said during the discussion of S_N2 reactivity that the best leaving groups are those that are most stable; that is, those that are the conjugate bases of strong acids. An identical reactivity order is found for the S_N1 reaction because the leaving group is directly involved in the rate-limiting step. Thus, the S_N1 reactivity order is

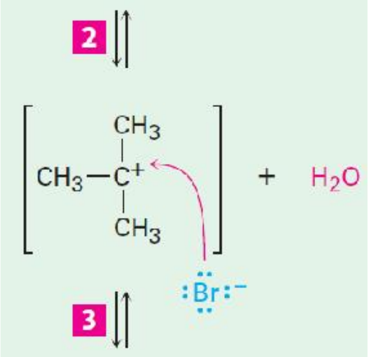
Note that in the S_N1 reaction, which is often carried out under acidic conditions, neutral water is sometimes the leaving group. This occurs, for example, when an alkyl halide is prepared from a tertiary alcohol by reaction with HBr or HCl. The alcohol is first protonated and then spontaneously loses H_2O to generate a carbocation, which reacts with halide ion to give the alkyl halide. Knowing that an S_N1 reaction is involved in the conversion of alcohols to alkyl halides explains why the reaction works well only for tertiary alcohols. Tertiary alcohols react fastest because they give the most stable carbocation intermediates.

Mechanism

Step 1: The –OH group is first protonated by HBr.



Step 2: Spontaneous dissociation of the protonated alcohol occurs in a slow, rate limiting step to yield a carbocation intermediate plus water.



Step 3: The carbocation intermediate reacts with bromide ion in a fast step to yield the neutral substitution product.

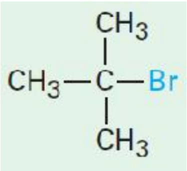
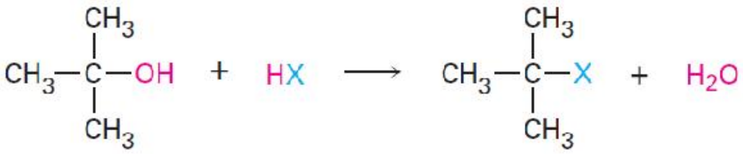


Figure 2.14: The mechanism of the S_N1 reaction of a tertiary alcohol with HBr to yield an alkyl halide. Neutral water is the leaving group (step).

3.5.3 The Nucleophile

The nature of the nucleophile plays a major role in the S$_N$2 reaction but does not affect an S$_N$1 reaction. Because the S$_N$1 reaction occurs through a rate-limiting step in which the added nucleophile has no part, the nucleophile can't affect the reaction rate. The reaction of 2-methyl-2-propanol with HX, for instance, occurs at the same rate regardless of whether X is Cl, Br, or I. Furthermore, neutral nucleophiles are just as effective as negatively charged ones, so S$_N$1 reactions frequently occur under neutral or acidic conditions.



$$(CH_3)_3C{-}OH + HX \longrightarrow (CH_3)_3C{-}X + H_2O$$

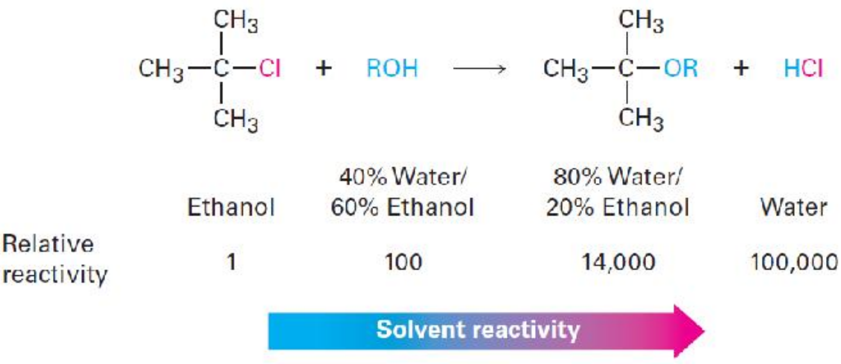
2-Methyl-2-propanol

(Same rate for X = Cl, Br, I)

3.5.4 The Solvent

What about the solvent? Do solvents have the same effect in S$_N$1 reactions that they have in S$_N$2 reactions? The answer is both yes and no. Yes, solvents have a large effect on S$_N$1 reactions, but no, the reasons for the effects on S$_N$1 and S$_N$2 reactions are not the same. Solvent effects in the S$_N$2 reaction are due largely to stabilization or destabilization of the nucleophile *reactant,* while solvent effects in the S$_N$1 reaction are due largely to stabilization or destabilization of the *transition state.*

The properties of a solvent that contribute to its ability to stabilize ions by solvation are related to the solvent's polarity. S$_N$1 reactions take place much more rapidly in strongly polar solvents, such as water and methanol, than in less polar solvents, such as ether and chloroform. In the reaction of 2-chloro-2-methylpropane, for example, a rate increase of 100,000 is observed on going from ethanol (less polar) to water (more polar). The rate increases on going from a hydrocarbon solvent to water are so large they can't be measured accurately.



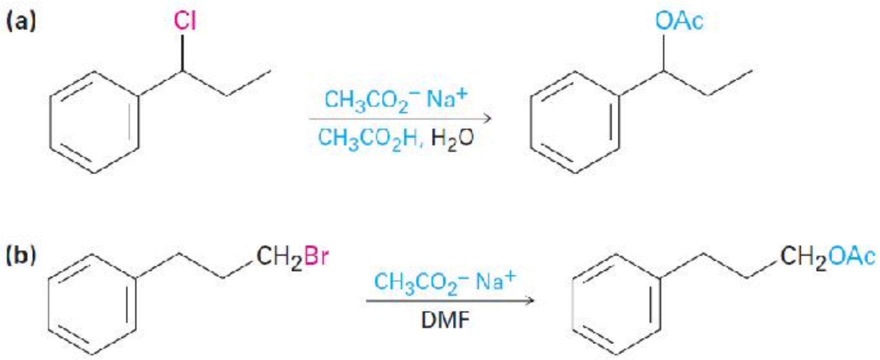
$$(CH_3)_3C{-}Cl + ROH \longrightarrow (CH_3)_3C{-}OR + HCl$$

	Ethanol	40% Water/ 60% Ethanol	80% Water/ 20% Ethanol	Water
Relative reactivity	1	100	14,000	100,000

Both the S_N1 and the S_N2 reaction show solvent effects, but they do so for different reasons. S_N2 reactions are *disfavoured* in protic solvents because the *ground-state energy* of the nucleophile is lowered by solvation. S_N1 reactions are *favoured* in protic solvents because the *transition-state energy* leading to carbocation intermediate is lowered by solvation.

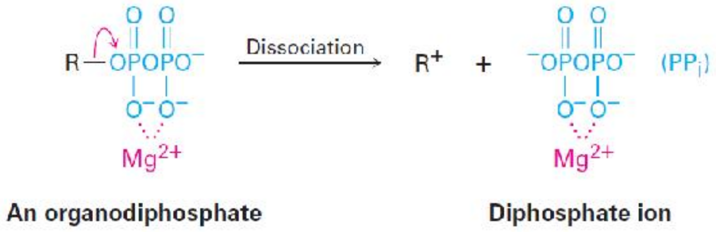
In-Text Question 2

Predict whether each of the following substitution reactions is likely to be S_N1 or S_N2:



3.6 Biological Substitution Reactions

Both S_N1 and S_N2 reactions are well-known in biological chemistry, particularly in the pathways for biosynthesis of the many thousands of plant-derived substances called *terpenoids*. Unlike what typically happens in the laboratory, however, the substrate in a biological substitution reaction is usually an organodiphosphate rather than an alkyl halide. Thus, the leaving group is the diphosphate ion, abbreviated PPi, rather than a halide ion. In fact, it's useful to think of the diphosphate group as the "biological equivalent" of a halogen. The dissociation of an organodiphosphate in a biological reaction is typically assisted by complexation to a divalent metal cation such as Mg^{2+} to help neutralize charge and make the diphosphate a better leaving group.

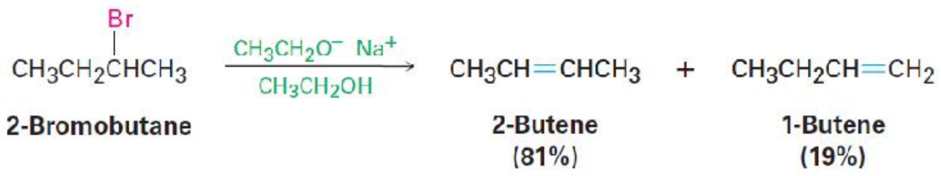


3.7 Elimination Reactions: Zaitsev's Rule

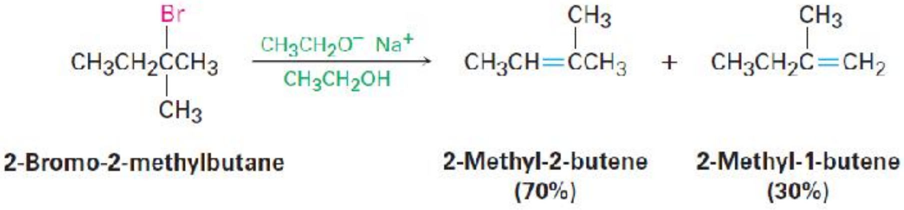
We said at the beginning of this unit that two kinds of reactions can take place when a nucleophile/Lewis base reacts with an alkyl halide. The nucleophile can either substitute for the halide by reaction at carbon or can cause elimination of HX by reaction at neighbouring hydrogen.
Elimination reactions are more complex than substitution reactions for several reasons. One is the problem of regiochemistry. What products result by loss of HX from an unsymmetrical halide? In fact, elimination reactions almost always give mixtures of alkene products, and the best we can usually do is to predict which will be the major product.

According to Zaitsev's rule, formulated in 1875 by the Russian chemist Alexander Zaitsev, base-induced elimination reactions generally (although not always) give the more stable alkene product - that is, the alkene with more alkyl substituents on the double-bond carbons. In the following two cases, for example, the more highly substituted alkene product predominates.

Zaitsev's Rule
In the elimination of HX from an alkyl halide, the more highly substituted alkene product predominates.



$$CH_3CH_2CH(Br)CH_3 \xrightarrow[CH_3CH_2OH]{CH_3CH_2O^-\ Na^+} CH_3CH{=}CHCH_3 + CH_3CH_2CH{=}CH_2$$

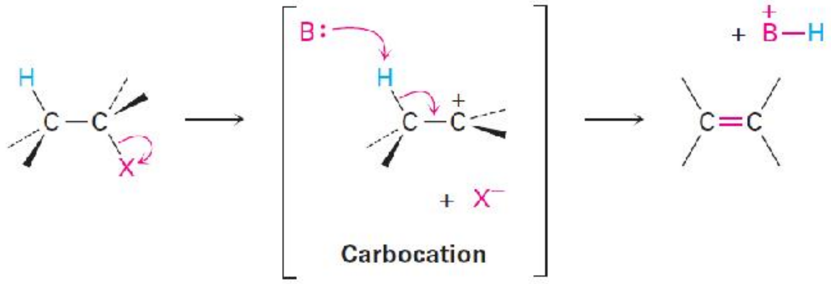


$$CH_3CH_2CBr(CH_3)CH_3 \xrightarrow[CH_3CH_2OH]{CH_3CH_2O^-\ Na^+} CH_3CH{=}C(CH_3)CH_3 + CH_3CH_2C(CH_3){=}CH_2$$

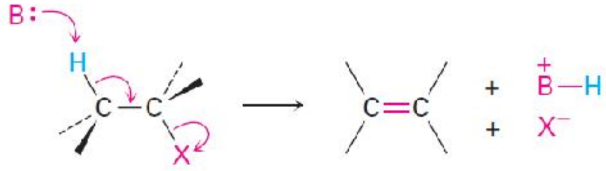
Another factor that complicates a study of elimination reactions is that they can take place by different mechanisms, just as substitutions can. We'll consider three of the most common mechanisms - the E1, E2, and

E1cB reactions - which differ in the timing of C-H and C-X bond-breaking.

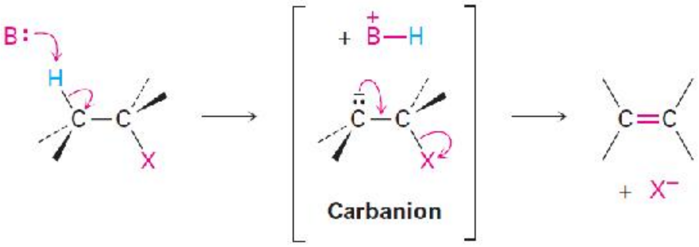
In the E1 reaction, the C-X bond breaks first to give a carbocation intermediate that undergoes subsequent base abstraction of H^+ to yield the alkene. In the E2 reaction, base-induced C-H bond cleavage is simultaneous with C-X bond cleavage, giving the alkene in a single step. In the E1cB reaction (cB for “conjugate base”), base abstraction of the proton occurs first, giving a carbanion ($R:^-$) intermediate. This anion, the conjugate base of the reactant “acid,” then undergoes loss of X^- in a subsequent step to give the alkene. All three mechanisms occur frequently in the laboratory, but the E1cB mechanism predominates in biological pathways.



E1 Reaction: C–X bond breaks first to give a carbocation intermediate, followed by base removal of a proton to yield the alkene.



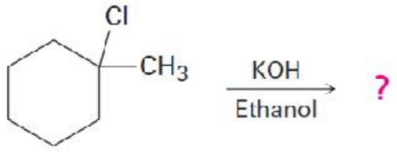
E2 Reaction: C–H and C–X bonds break simultaneously, giving the alkene in a single step without intermediates.



E1cB Reaction: C–H bond breaks first, giving a carbanion intermediate that loses X– to form the alkene.

In-Text Question 3

What product would you expect from reaction of 1-chloro-1-methylcyclohexane with KOH in ethanol?

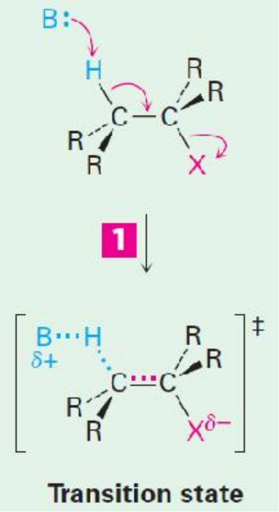


3.8 The E2 Reaction and the Deuterium Isotope Effect

The E2 reaction (for *elimination*, *bimolecular*) occurs when an alkyl halide is treated with a strong base, such as hydroxide ion or alkoxide ion (RO$^-$). It is the most commonly occurring pathway for elimination.

Mechanism

Step 1: Base (B:) attacks a neighboring hydrogen and begins to remove the H at the same time as the alkene double bond starts to form and the X group starts to leave.



Step 2: Neutral alkene is produced when the C–H bond is fully broken and the X group has departed with the C–X bond electron pair.

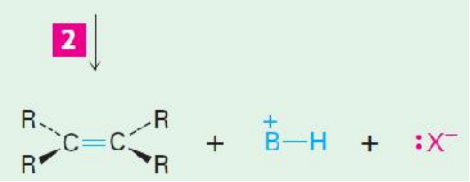
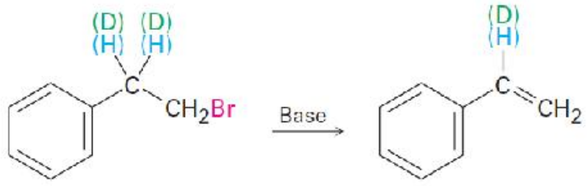


Figure 2.15: Mechanism of the E2 reaction of an alkyl halide. The reaction takes place in a single step through a transition state in which the double bond begins to form at the same time the H and X groups are leaving.

Like the S$_N$2 reaction, the E2 reaction takes place in one step without intermediates. As the base begins to abstract H$^+$ from a carbon next to the leaving group, the C-H bond begins to break, a C=C bond begins to form, and the leaving group begins to depart, taking with it the electron pair from the C-X bond. Among the pieces of evidence supporting this mechanism is that E2 reactions show second-order kinetics and follow the rate law: rate = k x [RX] x [Base]. That is, both base and alkyl halide takes part in the rate-limiting step.

A second piece of evidence in support of the E2 mechanism is provided by a phenomenon known as the deuterium isotope effect. For reasons that we won't go into, a carbon–hydrogen bond is weaker by about 5 kJ/mol (1.2 kcal/mol) than the corresponding carbon–deuterium bond. Thus, a C-H bond is more easily broken than an equivalent C-D bond, and the rate of C-H bond cleavage is faster. For instance, the base-induced elimination of HBr from 1-bromo-2-phenylethane proceeds 7.11 times as fast as the corresponding elimination of DBr from 1-bromo-2,2-dideuterio-2-phenylethane. This result tells us that the C-H (or C-D) bond is broken in the rate-limiting step, consistent with our picture of the E2 reaction as a one-step process. If it were otherwise, we couldn't measure a rate difference.



(H)—Faster reaction
(D)—Slower reaction

Yet a third piece of mechanistic evidence involves the stereochemistry of E2 eliminations. As shown by a large number of experiments, E2 reactions occur with *periplanar* geometry, meaning that all four reacting atoms—the hydrogen, the two carbons, and the leaving group—lie in the same plane. Two such geometries are possible: syn periplanar geometry, in which the H and the X are on the same side of the molecule, and anti periplanar geometry, in which the H and the X are on opposite sides of the molecule. Of the two, anti periplanar geometry is energetically preferred because it allows the substituents on the two carbons to adopt a staggered relationship, whereas syn geometry requires that the substituents be eclipsed.

In-Text Question 4

What stereochemistry do you expect for the alkene obtained by E2 elimination of (1*S*,2*S*)-1,2-dibromo-1,2-diphenylethane?

3.9 The E2 Reaction and Cyclohexane Conformation

Anti periplanar geometry for E2 reactions is particularly important in cyclohexane rings, where chair geometry forces a rigid relationship between the substituents on neighboring carbon atoms. The anti periplanar requirement for E2 reactions overrides Zaitsev's rule and can be met in cyclohexanes only if the hydrogen and the leaving group are trans diaxial. If either the leaving group or the hydrogen is equatorial, E2 elimination can't occur.

The difference in reactivity between the isomeric methyl chlorides is due to the difference in their conformations. Neomethyl chloride has a conformation with the methyl and isopropyl groups equatorial and the chlorine axial - a perfect geometry for E2 elimination. Loss of the hydrogen atom at C4 occurs easily to yield the more substituted alkene product, 3-menthene, as predicted by Zaitsev's rule.

Methyl chloride, by contrast, has a conformation in which all three substituents are equatorial. To achieve the necessary geometry for elimination, methyl chloride must first ring-flip to a higher-energy chair conformation, in which all three substituents are axial. E2 elimination then occurs with loss of the only trans-diaxial hydrogen available, leading to the non-Zaitsev product 2-methene. The net effect of the simple change in chlorine stereochemistry is a 200-fold change in reaction rate and a complete change of product. The chemistry of the molecule is controlled by its conformation.

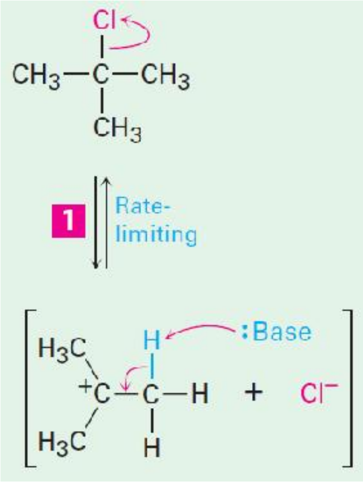
3.10 The E1 and E1cB Reactions

3.10.1 The E1 Reaction

Just as the E2 reaction is analogous to the S_N2 reaction, the S_N1 reaction has a close analog called the E1 reaction (for *elimination, unimolecular*). The E1 reaction can be formulated for the elimination of HCl from 2-chloro-2-methylpropane.

Mechanism

Step 1: Spontaneous dissociation of the tertiary alkyl chloride yields an intermediate carbocation in a slow, rate-limiting step.



Step 2: Loss of a neighboring H^+ in a fast step yields the neutral alkene product. The electron pair from the C–H bond goes to form the alkene *π* bond.

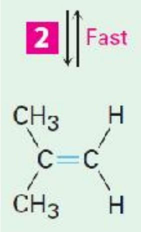
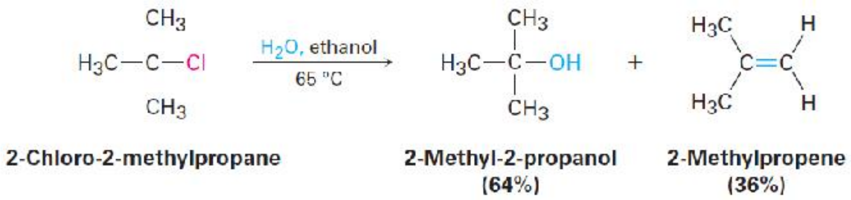


Figure 2.16: Mechanism of the E1 reaction. Two steps are involved, the first of which is rate-limiting, and a carbocation intermediate is present.

E1 eliminations begin with the same unimolecular dissociation to give a carbocation that we saw in the S_N1 reaction, but the dissociation is followed by loss of H^+ from the adjacent carbon rather than by substitution. In fact, the E1 and S_N1 reactions normally occur together whenever an alkyl halide is treated in a protic solvent with a nonbasic nucleophile. Thus, the best E1 substrates are also the best S_N1 substrates, and mixtures of substitution and elimination products are usually obtained. For example, when 2-chloro-2-methylpropane is warmed to 65°C in 80% aqueous ethanol, a 64;36 mixture of 2-methyl-2-propanol (S_N1) and 2-methylpropene (E1) results.

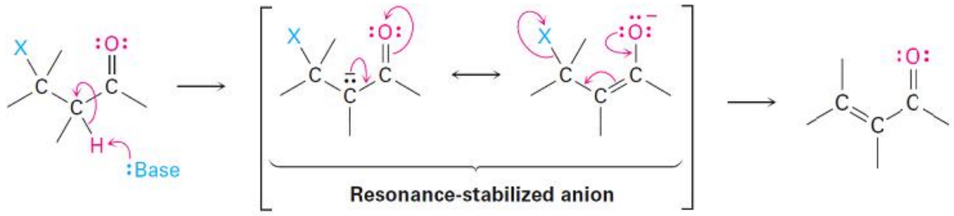


Much evidence has been obtained in support of the E1 mechanism. For example, E1 reactions show first-order kinetics, consistent with a rate-limiting, unimolecular dissociation process. Furthermore, E1 reactions show no deuterium isotope effect because rupture of the C-H (or C-D) bond occurs after the rate-limiting step rather than during it. Thus, we can't measure a rate difference between a deuterated and nondeuterated substrate.

A final piece of evidence involves the stereochemistry of elimination. Unlike the E2 reaction, where anti periplanar geometry is required, there is no geometric requirement on the E1 reaction because the halide and the hydrogen are lost in separate steps. We might therefore expect to obtain the more stable (Zaitsev's rule) product from E1 reaction, which is just what we find. To return to a familiar example, methyl chloride loses HCl under E1 conditions in a polar solvent to give a mixture of alkenes in which the Zaitsev product, 3-menthene, predominates.

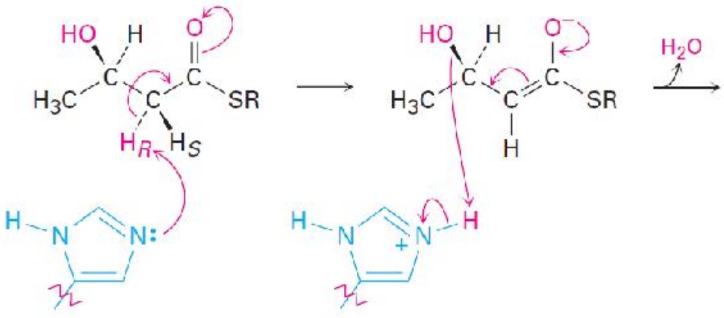
3.10.2 The E1cB Reaction

In contrast to the E1 reaction, which involves a carbocation intermediate, the E1cB reaction takes place through a carbanion intermediate. Base-induced abstraction of a proton in a slow, rate-limiting step gives an anion, which expels a leaving group on the adjacent carbon. The reaction is particularly common in substrates that have a poor leaving group, such as -OH, two carbons removed from a carbonyl group, HO-C-CH-C=O. The poor leaving group disfavors the alternative E1 and E2 possibilities, and the carbonyl group makes the adjacent hydrogen unusually acidic by resonance stabilization of the anion intermediate.

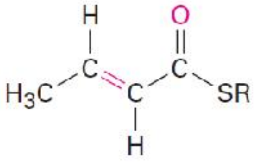


3.11 Biological Elimination Reactions

All three elimination reactions - E2, E1, and E1cB - occur in biological pathways, but the E1cB mechanism is particularly common. The substrate is usually an alcohol rather than an alkyl halide, and the H atom removed is usually adjacent to a carbonyl group, just as in laboratory reactions. Thus, 3-hydroxy carbonyl compounds are frequently converted to unsaturated carbonyl compounds by elimination reactions. A typical example occurs during the biosynthesis of fats when a 3-hydroxybutyryl thioester is dehydrated to the corresponding unsaturated (crotonyl) thioester. The base in this reaction is a histidine amino acid in the enzyme, and loss of the -OH group is assisted by simultaneous protonation.



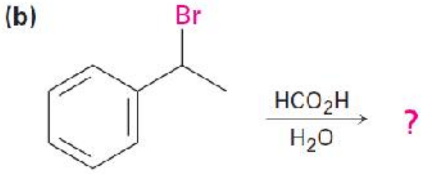
3-Hydroxybutyryl thioester



Crotonyl thioester

In-Text Question 5

Tell whether each of the following reactions is likely to be SN1, SN2, E1, E1cB, or E2, and predict the product of each:



SELF-ASSESSMENT EXERCISE

i. What product would you expect to obtain from a nucleophilic substitution reaction of (*S*)-2-bromohexane with acetate ion, $CH_3CO_2^-$?

ii. What product would you expect to obtain from S_N2 reaction of OH^- with (*R*)-2-bromobutane? Show the stereochemistry of both reactant and product.

iii What product would you expect from S_N2 reaction of 1-bromobutane with each of the following?

(a) NaI **(b)** KOH **(c)** $H - C \equiv C - Li$ **(d)** NH_3

iv Which substance in each of the following pairs is more reactive as a nucleophile? Explain.

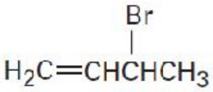
(a) $(CH_3)_2N^-$ or $(CH_3)_2NH$ **(b)** $(CH_3)_3B$ or $(CH_3)_3N$ **(c)** H_2O or H_2S

v. Rank the following compounds in order of their expected reactivity toward SN2 reaction: CH_3Br, CH_3OTos, $(CH_3)_3CCl$, $(CH_3)_2CHCl$

vi What product(s) would you expect from reaction of (*S*)-3-chloro-3-methyloctane with acetic acid? Show the stereochemistry of both reactant and product.

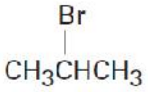
Vii Rank the following substances in order of their expected SN1 reactivity:

CH_3CH_2Br



$H_2C{=}CH\overset{Br}{C}HCH_3$

$H_2C{=}CHBr$



$CH_3\overset{Br}{C}HCH_3$

4.0 CONCLUSION

In this unit, we have succeeded in explaining that nucleophilic substitution and base-induced elimination are two of the most widely occurring and versatile reaction types in organic chemistry, both in the laboratory and in biological pathways.

5.0 SUMMARY

The effects on S_N1 reactions of the four variables - substrate, leaving group, nucleophile, and solvent - are summarized in the following statements:

Substrate: The best substrates yield the most stable carbocations. As a result, S_N1 reactions are best for tertiary, allylic, and benzylic halides.

Leaving group: Good leaving groups increase the reaction rate by lowering the energy level of the transition state for carbocation formation.

Nucleophile: The nucleophile must be nonbasic to prevent a competitive elimination of HX, but otherwise does not affect the reaction rate. Neutral nucleophiles work well.

Solvent: Polar solvents stabilize the carbocation intermediate by solvation, thereby increasing the reaction rate.

S_N1, S_N2, E1, E1cB, E2—how can you keep it all straight and predict what will happen in any given case? Will substitution or elimination occur? Will the reaction be bimolecular or unimolecular? There are no rigid answers to these questions, but it’s possible to recognize some trends and make some generalizations.

- *Primary alkyl halides*: S_N2 substitution occurs if a good nucleophile is used, E2 elimination occurs if a strong, sterically hindered base is used, and E1cB elimination occurs if the leaving group is two carbons away from a carbonyl group.

- *Secondary alkyl halides*: S_N2 substitution occurs if a weakly basic nucleophile is used in a polar aprotic solvent, E2 elimination predominates if a strong base is used, and E1cB elimination takes place if the leaving group is two carbons away from a carbonyl group. Secondary allylic and benzylic alkyl halides can also undergo S_N1 and E1 reactions if a weakly basic nucleophile is used in a protic solvent.

- *Tertiary alkyl halides*: E2 elimination occurs when a base is used, but S_N1 substitution and E1 elimination occur together under neutral conditions, such as in pure ethanol or water. E1cB elimination takes place if the leaving group is two carbons away from a carbonyl group.

6.0 TUTOR MARK ASSIGNMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry*, 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

MODULE 3 AROMATIC COMPOUNDS

INTRODUCTION

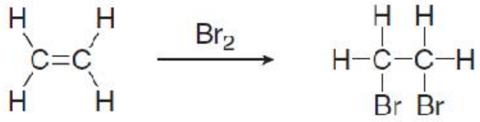
Compounds which have relatively few hydrogens in relation to the number of carbons, such as benzene, are typically found in oils produced by trees and other plants. Early chemists called such compounds **aromatic** compounds because of their pleasing fragrances. In this way, they were distinguished from aliphatic compounds, with higher hydrogen-to-carbon ratios, that were obtained from the chemical degradation of fats. The chemical meaning of the word “aromatic” now signifies certain kinds of chemical structures. This module will lead us to the discussion of two units where we will examine the criteria that a compound must satisfy to be classified as aromatic and their reaction types. These units are:

UNIT 1 BENZENE AND OTHER AROMATIC COMPOUNDS

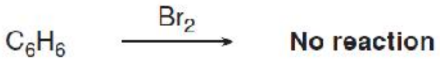
CONTENTS

1.0 INTRODUCTION

Benzene (C_6H_6) is the simplest aromatic hydrocarbon (or arene). Since its isolation by Michael Faraday from the oily residue remaining in the illuminating gas lines in London in 1825, it has been recognized as an unusual compound. Benzene has four degrees of unsaturation, making it a highly unsaturated hydrocarbon. But, whereas unsaturated hydrocarbons such as alkenes, alkynes, and dienes readily undergo addition reactions, *benzene does not.* For example, bromine adds to ethylene to form a dibromide, but benzene is inert under similar conditions.



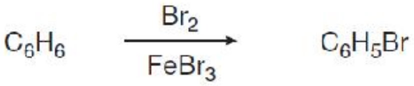
Ethylene addition product



$$C_6H_6 \xrightarrow{Br_2} \text{No reaction}$$

Benzene

Benzene *does* react with bromine, but only in the presence of $FeBr_3$ (a Lewis acid), and the reaction is a **substitution,** *not* an addition.



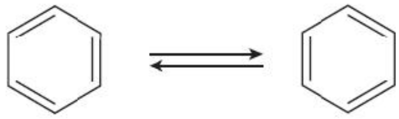
$$C_6H_6 \xrightarrow[FeBr_3]{Br_2} C_6H_5Br$$

Substitution: Br replaces H

Thus, any structure proposed for benzene must account for its high degree of unsaturation and its lack of reactivity towards electrophilic addition.

For 6C's, the maximum number of H's = 2n + 2 = 2(6) + 2 = 14. Because benzene contains only 6H's, it has 14 – 6 = 8 H's fewer than the maximum number. This corresponds to $\frac{8\ H's}{2\ H's}$ for each degree of unsaturation = **four degrees of unsaturation in benzene.**

In the last half of the nineteenth century August Kekulé proposed structures that were close to the modern description of benzene. In the Kekulé model, benzene was thought to be a rapidly equilibrating mixture of two compounds, each containing a six-membered ring with three alternating π bonds. These structures are now called **Kekulé structures.** In the Kekulé description, the bond between any two carbon atoms is sometimes a single bond and sometimes a double bond.



Kekulé description: An equilibrium

Although benzene is still drawn as a six-membered ring with three alternating π bonds, in reality **there is no equilibrium between two different kinds of benzene molecules.** Instead, current descriptions of benzene are based on resonance and electron delocalization due to orbital overlap.

In the nineteenth century, many other compounds having properties similar to those of benzene were isolated from natural sources. Because these compounds possessed strong and characteristic odours, they were called ***aromatic compounds.*** It is their chemical properties, though, not their odour that make these compounds special.

- *Aromatic compounds resemble benzene - they are unsaturated compounds that do not undergo the addition reactions characteristic of alkenes.*

2.0 OBJECTIVES

When you have studied this session, you should be able to:

- understand the processes of benzene isolation.
- get acquainted with the nomenclature of benzene and benzene derivatives.
- understand the stability of benzene and the criteria for Aromaticity.

3.0 MAIN CONTENT

3.1 Isolation of Benzene

Benzene and other arenes can be obtained by distilling coal. This is a particular messy process in the laboratory, and requires a lengthy business of separating the products from one another. However, in industry it is an economic way of isolating benzene. There is strong demand for coke, which is produced by heating coal in the absence of air. For every tone of coal turned into coal, about 70 dm^3 of coal tar is made. This is an oily liquid, which contains a variety of products. If the coal tar is separated by fractional distillation, around 30 dm^3 of benzene can be collected. Methylbenzene, naphthalene and anthracene are also obtained in smaller quantities.

In the laboratory a quicker way to make benzene is to heat the calcium salt of benzoic acid, $(C_6H_5COOH)_2Ca$, with soda lime (soda lime contains calcium hydroxide together with sodium hydroxide):

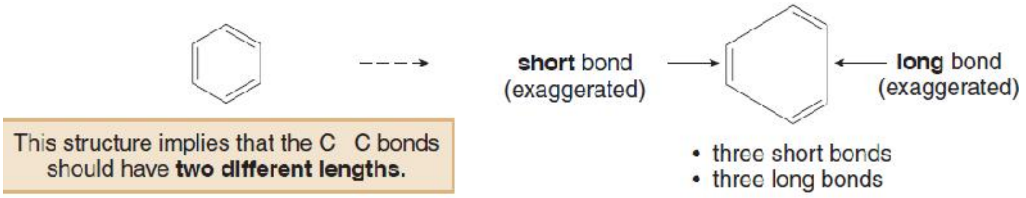
$$(C_6H_5COO)_2Ca(s) + Ca(OH)_2(s) \rightarrow 2C_6H_6(l) + 2CaCO_3(s)$$

3.2 The Structure of Benzene

Any structure for benzene must account for the following:

- *It contains a six-membered ring and three additional degrees of unsaturation.*
- *It is planar.*
- *All C - C bond lengths are equal.*

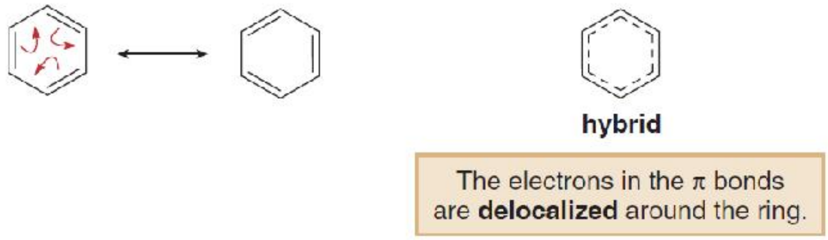
Although the Kekulé structures satisfy the first two criteria, they break down with the third, because having three alternating π bonds means that benzene should have three short double bonds alternating with three longer single bonds.



3.2.1 Resonance

Benzene is conjugated, so we must use resonance and orbitals to describe its structure. The resonance description of benzene consists of two equivalent

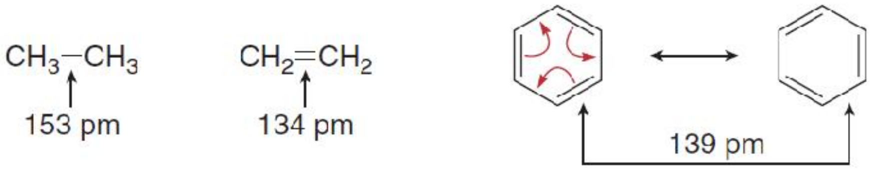
Lewis structures, each with three double bonds that alternate with three single bonds.



The electrons in the π bonds are **delocalized** around the ring.

The resonance description of benzene matches the Kekulé description with one important exception. The two Kekulé representations are *not* in equilibrium with each other. Instead, the true structure of benzene is a resonance hybrid of the two Lewis structures, with the dashed lines of the hybrid indicating the position of the π bonds.

The resonance hybrid of benzene explains why all C – C bond lengths are the same. Each C– C bond is single in one resonance structure and double in the other, so the actual bond length (139 pm) is intermediate between a carbon–carbon single bond (153 pm) and a carbon– carbon double bond (134 pm).



The C–C bonds in benzene are equal and intermediate in length.

3.2.2 Hybridization and Orbitals

Each carbon atom in a benzene ring is surrounded by three atoms and no lone pairs of electrons, making it *sp*2 hybridized and trigonal planar with all bond angles 120°**.** Each carbon also has a *p* orbital with one electron that extends above and below the plane of the molecule.

The six adjacent *p* orbitals overlap, delocalizing the six electrons over the six atoms of the ring and making benzene a conjugated molecule. Because each *p* orbital has two lobes, one above and one below the plane of the benzene ring, the overlap of the *p* orbitals creates two “doughnuts” of electron density.

- *Benzene's six π electrons make it electron rich and so it readily reacts with electrophiles.*

In-Text Question 1
In principle, which of the following is true regarding benzene and 1,3,5-cyclohexatriene?

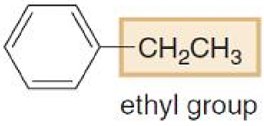
a. Theoretically they are the same molecules
b. Both have same length of all their C-C bonds
c. Both have same enthalpy of hydrogenation
d. Cyclohexatriene has three different C-C bond lengths while benzene has only one type of C-C bond length whose value is between those of cyclohexatriene

3.3 Nomenclature of Benzene Derivatives

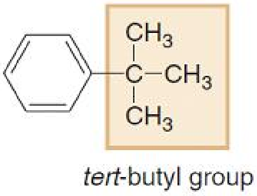
Many organic molecules contain a benzene ring with one or more substituents, so we must learn how to name them. Many common names are recognized by the IUPAC system, however, so this complicates the nomenclature of benzene derivatives somewhat.

3.3.1 Monosubstituted Benzenes

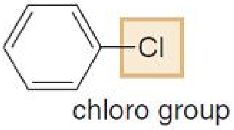
To name a benzene ring with one substituent, name the substituent and add the word benzene. Carbon substituents are named as alkyl groups.



ethylbenzene

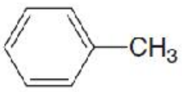


tert-butylbenzene

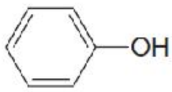


chlorobenzene

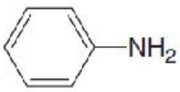
Many monosubstituted benzenes, such as those with methyl (CH_3–), hydroxy (–OH), and amino (–NH_2) groups, have common names.



toluene
(methylbenzene)



phenol
(hydroxybenzene)



aniline
(aminobenzene)

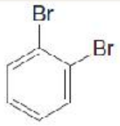
In-Text Question 2

Draw the structure of each of the following compounds:
a. 2-phenylhexane
b. benzyl alcohol
c. 3-benzylpentane
d. bromomethylbenzene

3.3.2 Disubstituted Benzenes

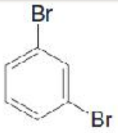
There are three different ways that two groups can be attached to a benzene ring, so a prefix **- ortho, meta,** or **para -** can be used to designate the relative position of the two substituents. Ortho, meta, and para are also abbreviated as ***o, m,*** and ***p,*** respectively.

1,2-Disubstituted benzene
ortho isomer



ortho-dibromobenzene
or
o-dibromobenzene
or
1,2-dibromobenzene

1,3-Disubstituted benzene
meta isomer



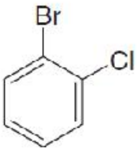
meta-dibromobenzene
or
m-dibromobenzene
or
1,3-dibromobenzene

1,4-Disubstituted benzene
para isomer

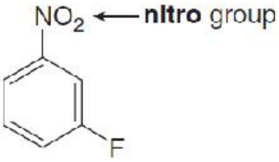
para-dibromobenzene
or
p-dibromobenzene
or
1,4-dibromobenzene

If the two groups on the benzene ring are different, alphabetize the names of the substituents preceding the word benzene. If one of the substituents is part of a common root, name the molecule as a derivative of that monosubstituted benzene.

Alphabetize two different substituent names:

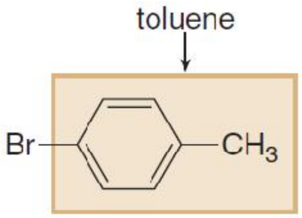


o-**bromochloro**-
benzene

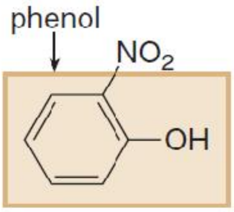


m-**fluoronitro**-
benzene

Use a common root name:



p-bromo**toluene**



o-nitro**phenol**

3.3.3 Polysubstituted Benzenes

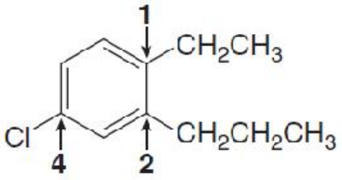
For three or more substituents on a benzene ring:

- Number to give the lowest possible numbers around the ring.

- Alphabetize the substituent names.

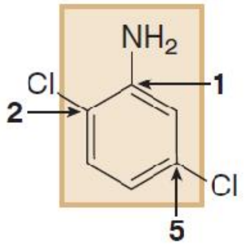
- When substituents are part of common roots, name the molecule as a derivative of that monosubstituted benzene. The substituent that comprises the common root is located at C_1.

Examples of naming polysubstituted benzenes



4-chloro-1-ethyl-2-propylbenzene

- Assign the lowest set of numbers.
- Alphabetize the names of all the substituents.



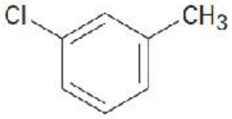
2,5-dichloroaniline

- Name the molecule as a derivative of the common root ***aniline.***
- Designate the position of the NH_2 group as "1" and then assign the lowest possible set of numbers to the other substituents.

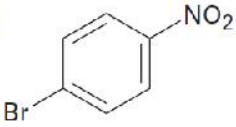
In-Text Question 3

Tell whether the following compounds are ortho-, meta-, or para-disubstituted:

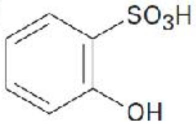
(a)



(b)

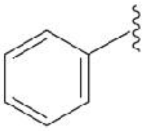


(c)



3.3.4 Naming Aromatic Rings as Substituents

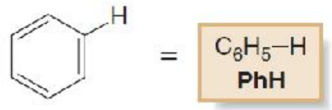
A benzene substituent (C_6H_5–) is called a phenyl group, and it can be abbreviated in a structure as Ph**–.**



phenyl group
C_6H_5

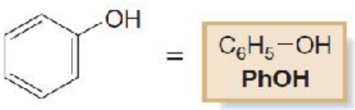
- *A phenyl group (C_6H_5–) is formed by removing one hydrogen from benzene (C_6H_6).*

Benzene, therefore, can be represented as PhH, and phenol would be PhOH.



C_6H_5–H
PhH

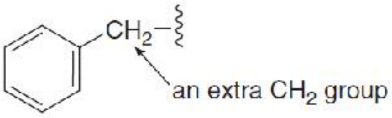
benzene



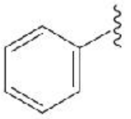
C_6H_5–OH
PhOH

phenol

The benzyl group, another common substituent that contains a benzene ring, differs from a phenyl group.



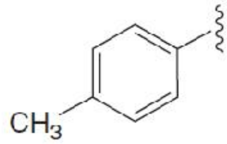
benzyl group
$C_6H_5CH_2$–

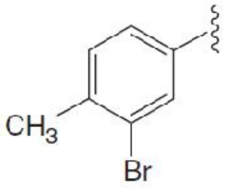


phenyl group
C_6H_5–

Finally, substituents derived from other substituted aromatic rings are collectively called **aryl groups.**

Examples of aryl groups:

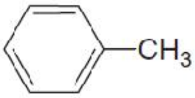




3.4 Interesting Aromatic Compounds

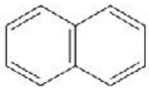
Benzene and toluene, the simplest aromatic hydrocarbons obtained from petroleum refining, are useful starting materials for synthetic polymers. They are two components of the aromatic compound mixture added to gasoline to boost octane ratings.


benzene



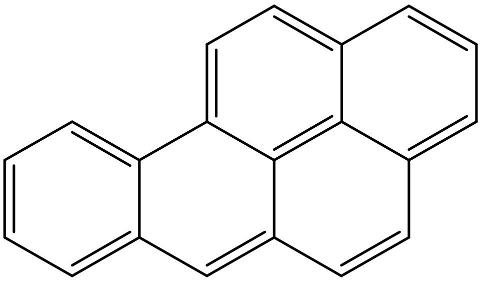
toluene

p-xylene


naphthalene
(used in mothballs)

Polycyclic aromatic hydrocarbons (PAHs). Naphthalene, the simplest PAH, is the active ingredient in mothballs.

Benzo[*a*]pyrene, a more complicated PAH is formed by the incomplete combustion of organic materials. It is found in cigarette smoke, automobile exhaust, and the fumes from charcoal grills. When ingested or inhaled, benzo[*a*]pyrene and other similar PAHs are oxidized to carcinogenic products.


Benzo[a]pyrene

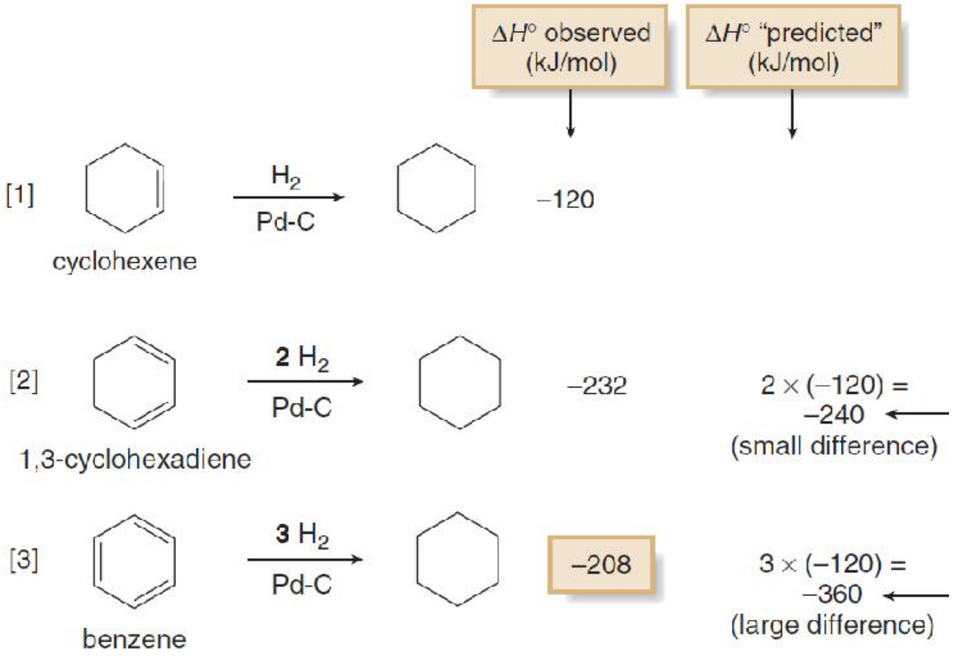
Helicene and **twistoflex** are two synthetic PAHs. Helicene consists of six benzene rings. Because the rings at both ends are not bonded to each other, all of the rings twist slightly, creating a rigid helical shape that prevents the hydrogen atoms on both ends from crashing into each other. Similarly, to reduce steric hindrance between the hydrogen atoms on nearby benzene rings, twistoflex is also nonplanar.

- *Benzo[a]pyrene, produced by the incomplete oxidation of organic compounds in tobacco, is found in cigarette smoke.*

3.5 Stability of Benzene

Considering benzene as the hybrid of two resonance structures adequately explains its equal C-C bond lengths, but does not account for its unusual stability and lack of reactivity towards addition.

Heats of hydrogenation, used to show that conjugated dienes are more stable than isolated dienes, can also be used to estimate the stability of benzene. Equations (1) - (3) compare the heats of hydrogenation of cyclohexene, 1,3-cyclohexadiene, and benzene, all of which give cyclohexane when treated with excess hydrogen in the presence of a metal catalyst.



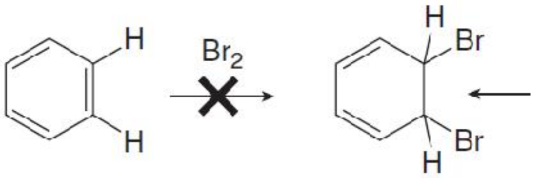
The addition of one mole of H_2 to cyclohexene releases -120 kJ/mol of energy. If each double bond is worth -120 kJ/mol of energy, then the addition of two moles of H_2 to 1,3-cyclohexadiene should release 2 × -120 kJ/mol = -240 kJ/mol of energy. The observed value, however, is -232 kJ/mol. This is slightly smaller than expected because 1,3-cyclohexadiene is a conjugated diene, and conjugated dienes are more stable than two isolated carbon-carbon double bonds.

The hydrogenations of cyclohexene and 1,3-cyclohexadiene occur readily at room temperature, but benzene can be hydrogenated only under forcing conditions, and even then the reaction is extremely slow. If each double bond is worth -120 kJ/mol of energy, then the addition of three moles of H_2 to benzene should release 3 × -120 kJ/mol = -360 kJ/mol of energy. In fact, the observed heat of hydrogenation is only -208 kJ/mol, which is 152 kJ/mol less than predicted and even lower than the observed value for 1,3-cyclohexadiene.

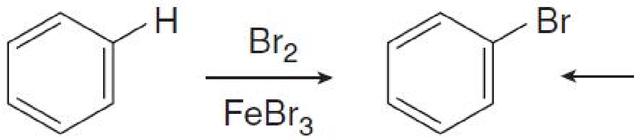
The huge difference between the hypothetical and observed heats of hydrogenation for benzene cannot be explained solely on the basis of resonance and conjugation.

- *The low heat of hydrogenation of benzene means that benzene is especially stable, even more so than the conjugated. This unusual stability is characteristic of aromatic compounds.*

Benzene's unusual behaviour in chemical reactions is not limited to hydrogenation. Benzene does not undergo addition reactions typical of other highly unsaturated compounds, including conjugated dienes. Benzene does not react with Br_2 to yield an addition product. Instead, in the presence of a Lewis acid, bromine *substitutes* for a hydrogen atom, thus yielding a product that retains the benzene ring.



Addition does not occur. An addition product would no longer contain a benzene ring.



Addition occurs. A substitution product still contains a benzene ring

This behavior is characteristic of aromatic compounds.

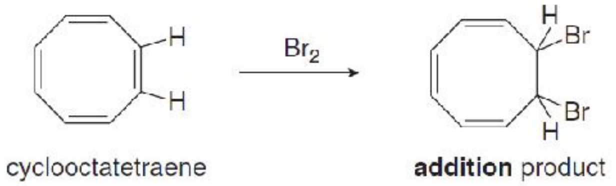
3.6 The Criteria for Aromaticity - Hückel’s Rule

Four structural criteria must be satisfied for a compound to be aromatic:
A molecule must be cyclic.

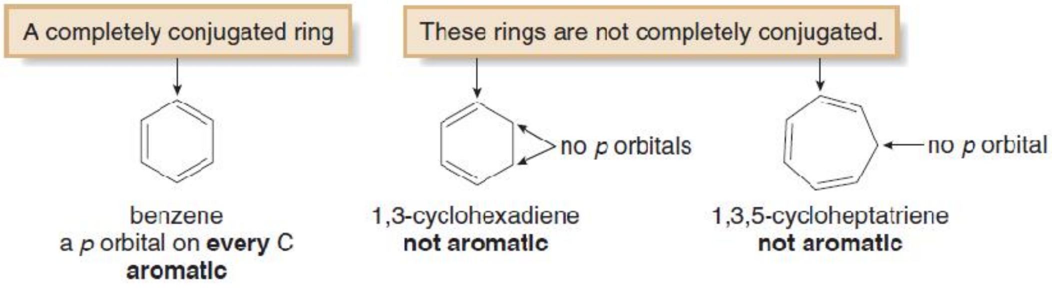
- *To be aromatic, each p orbital must overlap with p orbitals on two adjacent atoms.*
  The *p* orbitals on all six carbons of benzene continuously overlap, so benzene is aromatic. 1,3,5-Hexatriene has six *p* orbitals, too, but the two on the terminal carbons cannot overlap with each other, so **1,3,5-hexatriene is not aromatic.**
  A molecule must be planar.

- *All adjacent p orbitals must be aligned so that the o electron density can be delocalized.*

For example, cyclooctatetraene resembles benzene in that it is a cyclic molecule with alternating double and single bonds. Cyclooctatetraene is tub shaped, however, **not planar,** so overlap between adjacent π bonds is impossible. **Cyclooctatetraene, therefore, is *not* aromatic,** so it undergoes addition reactions like those of other alkenes.



A molecule must be completely conjugated.



Both 1,3-cyclohexadiene and 1,3,5-cycloheptatriene contain at least one carbon atom that does not have a *p* orbital, and so they are not completely conjugated and therefore ***not* aromatic.**

A molecule must satisfy Hückel's rule, and contain a particular number of π electrons.

Some compounds satisfy the first three criteria for aromaticity, but still they show none of the stability typical of aromatic compounds. For example, **cyclobutadiene** is so highly reactive that it can only be prepared at extremely low temperatures.

- *Aromatic compounds must have a p orbital on every atom.*

It turns out that in addition to being cyclic, planar, and completely conjugated; a compound needs a particular number of π electrons to be aromatic. Erich Hückel first recognized in 1931 that the following criterion, expressed in two parts and now known as **Hückel's rule,** had to be satisfied, as well:

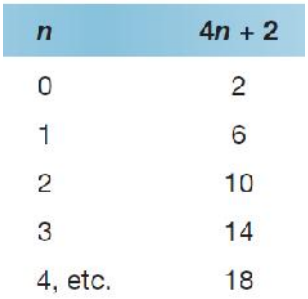
- *An aromatic compound must contain* $4n + 2$ π *electrons* ($n = 0, 1, 2$, *and so forth).*
- *Cyclic, planar, and completely conjugated compounds that contain* $4n$ π *electrons are especially unstable, and are said to be antiaromatic.*

Thus, compounds that contain 2, 6, 10, 14, 18, and so forth π electrons are aromatic. Benzene is aromatic and especially stable because it contains 6 π electrons. Cyclobutadiene is antiaromatic and especially unstable because it contains 4 π electrons.

$4n + 2 = 4(1) + 2 =$
6 π electrons
aromatic

$4n = 4(1) =$
4 π electrons
antiaromatic

Table 3.1: The Number of π Electrons That Satisfy Hückel's Rule



n	4*n* + 2
0	2
1	6
2	10
3	14
4, etc.	18

Considering aromaticity, all compounds can be classified in one of three ways:

Aromatic - A cyclic, planar, completely conjugated compound with 4*n* + 2 π electrons.

Antiaromatic - A cyclic, planar, completely conjugated compound with 4*n* π electrons.

Not aromatic - A compound that lacks one (or more) of the four requirements (or nonaromatic) to be aromatic or antiaromatic.

Note:

- *An aromatic compound is more stable than a similar acyclic compound having the same number of* π *electrons. Benzene is more stable than 1,3,5-hexatriene.*
- *An antiaromatic compound is less stable than an acyclic compound having the same number of* π *electrons. Cyclobutadiene is less stable than 1,3-butadiene.*
- *A compound that is not aromatic is similar in stability to an acyclic compound having the same number of* π *electrons. 1,3-Cyclohexadiene is similar in stability to cis, cis-2,4- hexadiene, so it is not aromatic.*

In-Text Question 4

a. What is the value of n in Hückel's rule when a compound has nine pairs of π-electrons?

b. Is such a compound aromatic?

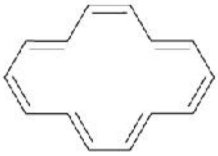
3.7 Examples of Aromatic Compounds

3.7.1 Aromatic Compounds with a Single Ring

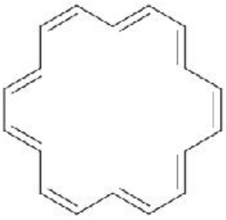
Benzene is the most common aromatic compound having a single ring. Completely conjugated rings larger than benzene are also aromatic if they are planar and have 4*n* + 2 π electrons.

- Hydrocarbons containing a single ring with alternating double and single bonds are called *annulenes.*

To name an annulene, indicate the number of atoms in the ring in brackets and add the word *annulene.* Thus, benzene is [6]-annulene. Both **[14]-annulene** and **[18]-annulene** are cyclic, planar, completely conjugated molecules that follow Hückel's rule, and so they are aromatic.



[14]-annulene
$4n + 2 = 4(3) + 2 =$
14 π electrons
aromatic

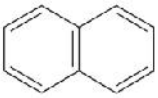


[18]-annulene
$4n + 2 = 4(4) + 2 =$
18 π electrons
aromatic

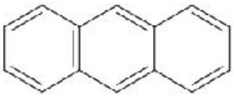
[10]-Annulene has 10 π electrons, which satisfies Hückel's rule, but a planar molecule would place the two H atoms inside the ring too close to each other, so the ring puckers to relieve this strain. Because **[10]-annulene is not planar,** the 10 π electrons can't delocalize over the entire ring and it is **not aromatic.**

3.7.2 Aromatic Compounds with More Than One Ring

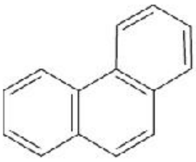
Hückel's rule for determining aromaticity can be applied only to monocyclic systems, but many aromatic compounds containing several benzene rings joined together are also known. Two or more six-membered rings with alternating double and single bonds can be fused together to form **polycyclic aromatic hydrocarbons (PAHs).** Joining two benzene rings together forms **naphthalene.** There are two different ways to join three rings together; forming **anthracene** and **phenanthrene,** and many more complex hydrocarbons are known.



naphthalene
10 π **electrons**

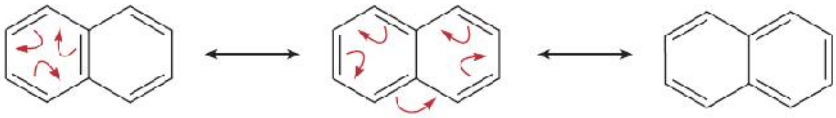


anthracene
14 π electrons



phenanthrene
14 π electrons

As the number of fused benzene rings increases, the number of resonance structures increases as well. Although two resonance structures can be drawn for benzene, naphthalene is a hybrid of three resonance structures.



Three resonance structures for naphthalene

3.7.3 Aromatic Heterocycles

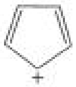
Heterocycles containing oxygen, nitrogen, or sulphur - atoms that also have at least one lone pair of electrons - can also be aromatic. With heteroatoms, we must always determine whether the lone pair is localized on the heteroatom or part of the delocalized π system. Two examples, **pyridine** and **pyrrole,** illustrate these different possibilities.

3.7.4 Charged Aromatic Compounds

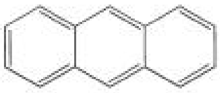
Both negatively and positively charged ions can also be aromatic if they possess all the necessary elements. These charged aromatic compounds include: cyclopentadienyl anion and tropylium cation.

In-Text Question 5
Which of the following compounds are aromatic?

a.

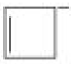


b.

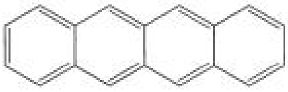


c. cycloheptatrienyl cation

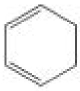
d.



e.



f.



g. cyclononatetraenyl anion

h. $CH_2{=}CHCH{=}CHCH{=}CH_2$

3.8 Basis of Hückel's Rule?

Why does the number of π electrons determine whether a compound is aromatic? Cyclobutadiene is cyclic, planar, and completely conjugated, just like benzene, but why is benzene aromatic and cyclobutadiene antiaromatic?

A complete explanation is beyond the scope of an introductory organic chemistry text, but nevertheless, you can better understand the basis of aromaticity by learning more about orbitals and bonding.

3.8.1 Bonding and Antibonding Orbitals

So far we have used the following basic concepts to describe how bonds are formed:

- Hydrogen uses its 1*s* orbital to form σ bonds with other elements.
- Second-row elements use hybrid orbitals (*sp*, sp^2, or sp^3) to form σ bonds.
- Second-row elements use *p* orbitals to form π bonds.

This description of bonding is called **valence bond theory.** In valence bond theory, a covalent bond is formed by the overlap of two atomic orbitals, and the electron pair in the resulting bond is shared by both atoms. Thus, a carbon–carbon double bond consists of a σ bond, formed by overlap of two sp^2 hybrid orbitals, each containing one electron, and a π bond, formed by overlap of two *p* orbitals, each containing one electron.

This description of bonding works well for most of the organic molecules we have encountered thus far. Unfortunately, it is inadequate for describing systems with many adjacent *p* orbitals that overlap, as there are in aromatic compounds. To more fully explain the bonding in these systems, we must utilize **molecular orbital (MO) theory.**

MO theory describes bonds as the mathematical combination of atomic orbitals that form a new set of orbitals called **molecular orbitals (MOs).** A molecular orbital occupies a region of space *in a molecule* where electrons are likely to be found. When forming molecular orbitals from atomic orbitals, keep in mind:

- A set of *n* atomic orbitals forms *n* molecular orbitals.
- When two *p* orbitals of similar phase overlap side-by-side, a π bonding molecular orbital results.
- When two *p* orbitals of opposite phase overlap side-by-side, a π* antibonding molecular orbital results.

A π bonding MO is lower in energy than the two atomic *p* orbitals from which it is formed because a stable bonding interaction results when orbitals of similar phase combine. A bonding interaction holds nuclei together. Similarly, a π* antibonding MO is higher in energy because a destabilizing node results when orbitals of opposite phase combine. A destabilizing interaction pushes nuclei apart.

If two atomic *p* orbitals each have one electron and then combine to form MOs, the two electrons will occupy the lower energy π bonding MO.

3.8.2 Molecular Orbitals Formed When More Than Two *p* Orbitals Combine

The molecular orbital description of benzene is much more complex than the two MOs formed. Because each of the six carbon atoms of benzene has a *p* orbital, six atomic *p* orbitals combine to form six π molecular orbitals. A description of the exact appearance and energies of these six MOs requires more sophisticated mathematics and understanding of MO theory than is presented in this unit. Nevertheless, note that the six MOs are labeled ψ1–ψ6, with ψ1 being the lowest in energy and ψ6 the highest.

The most important features of the six benzene MOs are as follows:

- The larger the number of bonding interactions, the lower in energy the MO. The lowest energy molecular orbital (ψ1) has all bonding interactions between the *p* orbitals.
- The larger the number of nodes, the higher in energy the MO. The highest energy MO (ψ6*) has all nodes between the *p* orbitals.
- Three MOs are lower in energy than the starting *p* orbitals, making them bonding MOs (ψ1, ψ2, ψ3), whereas three MOs are higher in energy than the starting *p* orbitals, making them antibonding MOs (ψ4*, ψ5*, ψ6*).
- The two pairs of MOs (ψ2 and ψ3; ψ4* and ψ5*) with the same energy are called degenerate orbitals.
- The highest energy orbital that contains electrons is called the *highest occupied molecular orbital* (HOMO). For benzene, the degenerate orbitals ψ2 and ψ3 are the HOMOs.
- The lowest energy orbital that does *not* contain electrons is called the *lowest unoccupied molecular orbital* (LUMO). For benzene, the degenerate orbitals ψ4* and ψ5* are the LUMOs.

To fill the MOs, the six electrons are added, two to an orbital, beginning with the lowest energy orbital. As a result, the six electrons completely fill the bonding MOs, leaving the antibonding MOs empty. This is what gives benzene and other aromatic compounds their special stability and this is why six π electrons satisfy Hückel's $4n + 2$ rule.

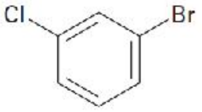
- All bonding MOs (and HOMOs) are completely filled in aromatic compounds. No π electrons occupy antibonding **MOs.**

- Depicted in this diagram are the interactions of the six atomic *p* orbitals of benzene, which form six molecular orbitals. When orbitals of like phase combine, a bonding interaction results. When orbitals of opposite phase combine, a destabilizing node results.

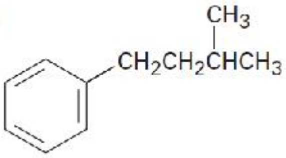
SELF-ASSESSMENT EXERCISE

i. Give IUPAC names for the following compounds:

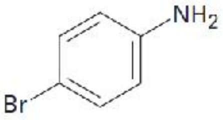
(a)



(b)



(c)



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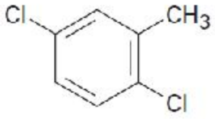
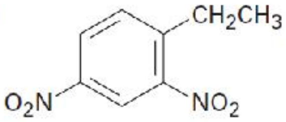
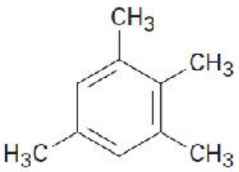


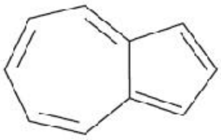
(e)



(f)

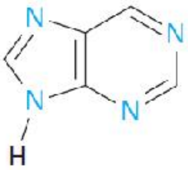


ii. Azulene, a beautiful blue hydrocarbon, is an isomer of naphthalene. Is azulene aromatic? Draw a second resonance form of azulene in addition to that shown.



Azulene

iii. How many electrons does each of the four nitrogen atoms in purine contribute to the aromatic *p* system?



Purine

iv The [10]- and [12]-annulenes have been synthesized, and neither has been found to be aromatic. Explain.

v. How many bonding, nonbonding, and antibonding molecular orbitals does cyclobutadiene have? In which molecular orbitals are the electrons?

4.0 CONCLUSION

In this unit, we have been able to explain the concept of aromaticity, isolation of benzene, structure of benzene, nomenclature of benzene and spectroscopic properties of aromatic compounds. Also, we were able to give examples of aromatic compound, explain why benzene is exceptionally stable, and criteria and basis for Hückel's rule.

5.0 SUMMARY

Aromatic rings are a common part of many biological structures and are particularly important in nucleic acid chemistry and in the chemistry of several amino acids. In this unit, we've seen how and why aromatic compounds are different from such apparently related compounds as cycloalkenes.

The word aromatic is used for historical reasons to refer to the class of compounds related structurally to benzene. Aromatic compounds are systematically named according to IUPAC rules, but many common names are also used. Disubstituted benzenes are named as ortho (1,2 disubstituted), meta (1,3 disubstituted), or para (1,4 disubstituted) derivatives. The $C_6H_5^-$ unit itself is referred to as a phenyl group, and the $C_6H_5CH_2^-$ unit is a benzyl group.

Benzene is described by valence-bond theory as a resonance hybrid of two equivalent structures and is described by molecular orbital theory as a planar, cyclic, conjugated molecule with six π electrons. According to the Hückel rule, a molecule must have $4n + 2$ π electrons, where n = 0, 1, 2, 3, and so on, to be aromatic. Planar, cyclic, conjugated molecules with other numbers of π electrons are antiaromatic.

Other kinds of substances besides benzene-like compounds can also be aromatic. The cyclopentadienyl anion and the cycloheptatrienyl cation, for instance, are aromatic ions. Pyridine and pyrimidine are six-membered, nitrogen-containing, aromatic heterocycles. Pyrrole and imidazole are five-membered, nitrogen-containing heterocycles. Naphthalene, quinoline, indole, and many others are polycyclic aromatic compounds.

Aromatic compounds have the following characteristics:

- Aromatic compounds are cyclic, planar, and conjugated.

- Aromatic compounds are unusually stable. Benzene, for instance, has a heat of hydrogenation 150 kJ/mol less than we might expect for a cyclic triene.
- Aromatic compounds react with electrophiles to give substitution products, in which cyclic conjugation is retained, rather than addition products, in which conjugation is destroyed.
- Aromatic compounds have $4n + 2$ π electrons, which are delocalized over the ring.

6.0 TUTOR MARK ASSIGNMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry,* 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book,* 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.

UNIT 2 REACTIONS OF AROMATIC COMPOUNDS

CONTENTS

1.0 INTRODUCTION

In this unit, we shall look at the chemical reactions of benzene and other aromatic compounds. Although aromatic rings are unusually stable, benzene acts as a nucleophile with certain electrophiles, yielding substitution products with an intact aromatic ring.

We begin this unit with the basic features and mechanism of electrophilic aromatic substitution, the basic reaction of benzene. Next, we will discuss the electrophilic aromatic substitution of substituted benzenes, and conclude with other useful reactions of benzene derivatives. The ability to interconvert resonance structures and evaluate their relative stabilities is crucial to understanding this unit.

2.0 OBJECTIVES

By the end of this session, you should be able to:

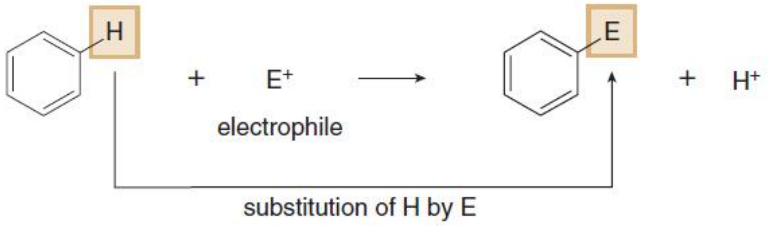
- understand the concept of electrophilic aromatic substitution reaction.
- understand the general mechanism of electrophilic aromatic substitution reaction.
- get acquainted with the chemistry of substituted benzenes and their electrophilic substitution reaction.
- understand how benzene can be activated and deactivated.
- understand the orientation effects in substituted benzene.

3.0 MAIN CONTENT

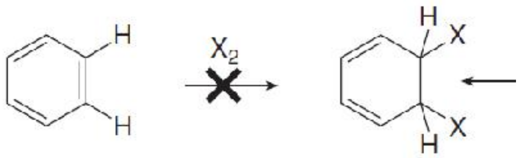
3.1 Electrophilic Aromatic Substitution

Based on its structure and properties, what kinds of reactions should benzene undergo? Are any of its bonds particularly weak? Does it have electron-rich or electron-deficient atoms?
Benzene has six o electrons delocalized in six *p* orbitals that overlap above and below the plane of the ring. These loosely held π electrons make the benzene ring electron rich, and so it reacts with electrophiles.

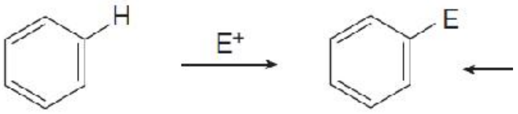
Because benzene's six π electrons satisfy Hückel's rule, benzene is especially stable.
Reactions that keep the aromatic ring intact are therefore favored.
As a result, the characteristic reaction of benzene is electrophilic aromatic substitution - a hydrogen atom is replaced by an electrophile.



Benzene does *not* undergo addition reactions like other unsaturated hydrocarbons, because addition would yield a product that is not aromatic. Substitution of hydrogen, on the other hand, keeps the aromatic ring intact.



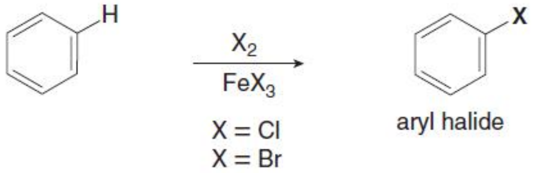
Addition (The product is not aromatic)



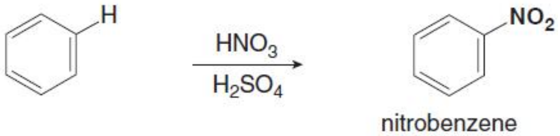
Substitution (The product is aromatic)

3.1.1 The General Mechanism

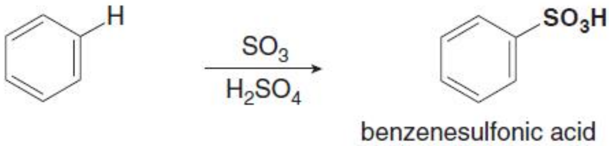
No matter what electrophile is used, all electrophilic aromatic substitution reactions occur via a **two-step mechanism:** addition of the electrophile E^+ to form a resonance-stabilized carbocation, followed by deprotonation with base, as shown in the mechanism below.



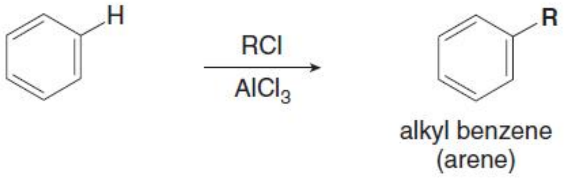
1. Halogenation - Replacement of H by X (Cl or Br).



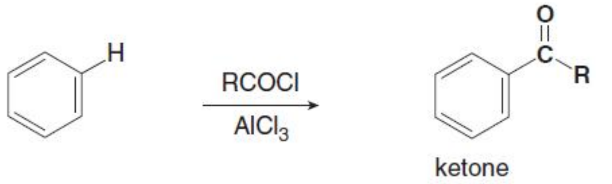
2. Nitration - Replacement of H by NO_2.



3. Sulfonation - Replacement of H by SO_3H



4. Friedel - Crafts alkylation - Replacement of H by R

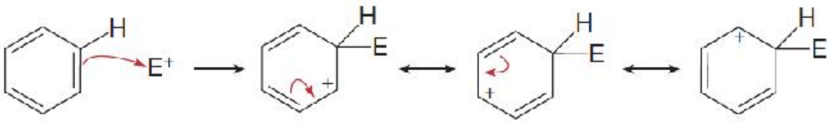


5. Friedel - Crafts acylation - Replacement of H by RCO

Mechanism

General Mechanism of Electrophilic Aromatic Substitution

Step 1: Addition of the electrophile (E^+) to form a carbocation.

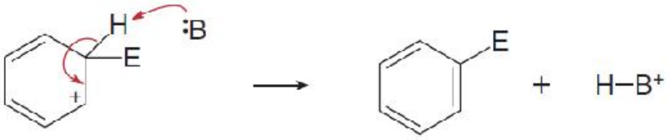


Resonance-stabilized carbocation

- Addition of the electrophile (E^+) forms a new C - E bond using two π electrons from the benzene ring, and generating a carbocation. This carbocation intermediate is not aromatic, but it is resonance stabilized - three resonance structures can be drawn.

- Step 1 is rate-determining because the aromaticity of the benzene ring is lost.

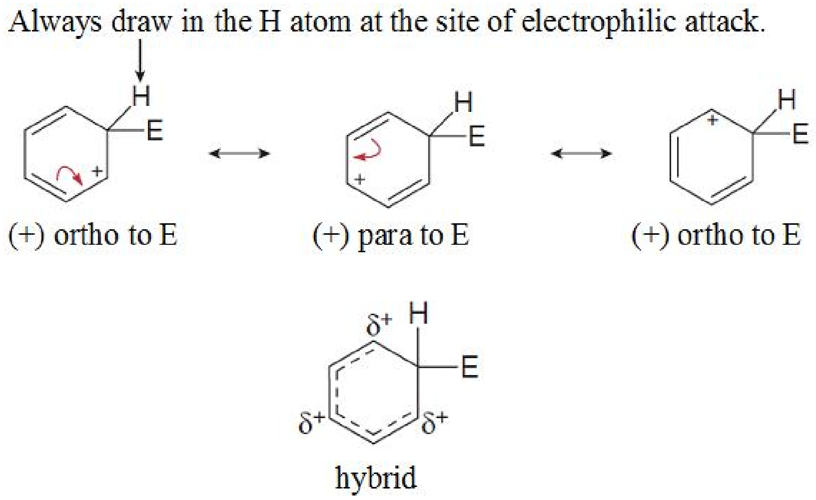
Step 2: Loss of a proton to re-form the aromatic ring.



- In Step 2, a base (B:) removes the proton from the carbon bearing the electrophile, thus re-forming the aromatic ring. This step is fast because the aromaticity of the benzene ring is restored.

- Any of the three resonance structures of the carbocation intermediate can be used to draw the product. The choice of resonance structure affects how curved arrows are drawn, but not the identity of the product.

The first step in electrophilic aromatic substitution forms a carbocation, for which three resonance structures can be drawn.



This two-step mechanism for electrophilic aromatic substitution applies to all electrophiles. The net result of addition of an electrophile (E^+) followed by elimination of a proton (H^+) is substitution of E for H.

3.2 Halogenation

The general mechanism outlined above can now be applied to each of the five specific examples of electrophilic aromatic substitution. For each mechanism we must learn how to generate a specific electrophile. This step is *different* with each electrophile. Then, the electrophile reacts with benzene by the two-step process of the mechanism outlined above. These two steps are the *same* for all five reactions.

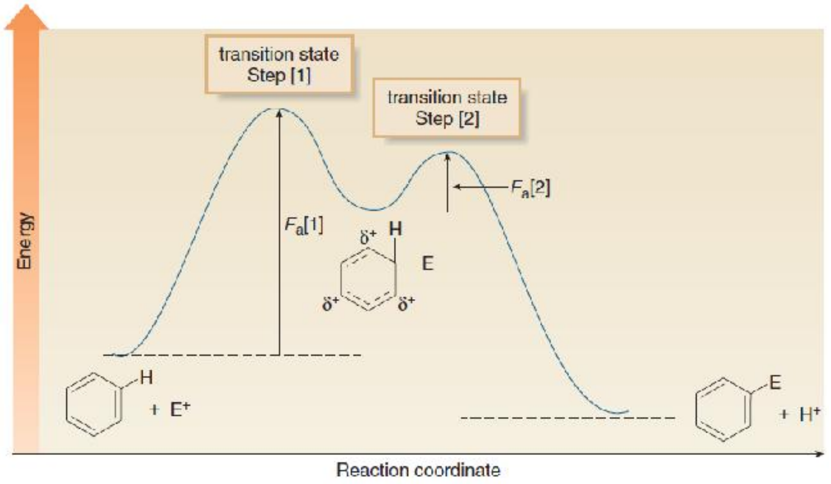
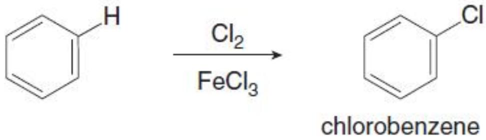


Figure 3.1: Energy diagram for electrophilic aromatic substitution: $PhH + E^+ \rightarrow PhE + H^+$

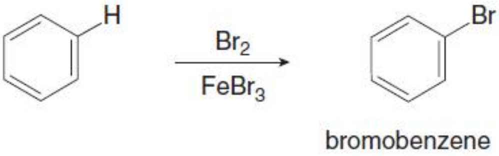
- The mechanism has two steps, so there are two energy barriers.

- Step 1 is rate-determining; its transition state is at higher energy.

In **halogenation,** benzene reacts with Cl_2 or Br_2 in the presence of a Lewis acid catalyst, such as $FeCl_3$ or $FeBr_3$, to give the aryl halides chlorobenzene or bromobenzene, respectively. Analogous reactions with I_2 and F_2 are not synthetically useful because I_2 is too unreactive and F_2 reacts too violently.



Chlorination

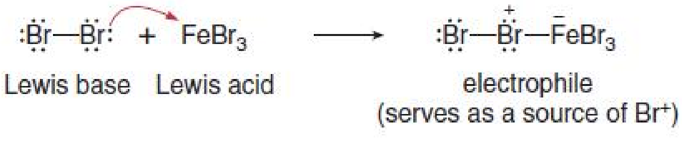


Bromination

In bromination, the Lewis acid $FeBr_3$ reacts with Br_2 to form a Lewis acid - base complex that weakens and polarizes the Br–Br bond, making it more electrophilic. This reaction is Step 1 of the mechanism for the bromination of benzene. The remaining two steps follow directly from the general mechanism for electrophilic aromatic substitution: addition of the electrophile (Br^+ in this case) forms a resonance-stabilized carbocation, and loss of a proton regenerates the aromatic ring.

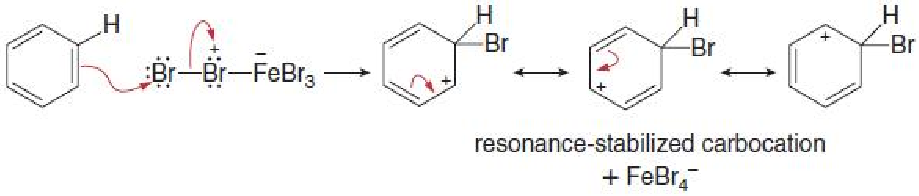
Mechanism for the Bromination of Benzene

Step 1: Generation of the electrophiles



- Lewis acid–base reaction of Br_2 with $FeBr_3$ forms a species with a weakened and polarized Br – Br bond. This adduct serves as a source of Br^+ in the next step.

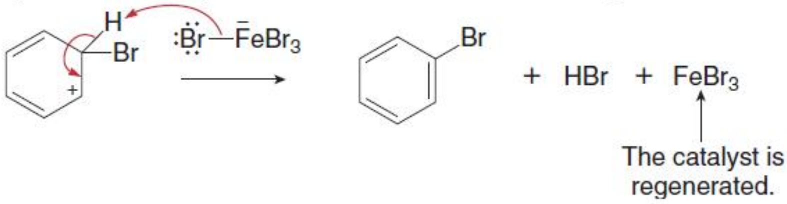
Step 2: Addition of the electrophile to form a carbocation



- Addition of the electrophile forms a new C-Br bond and generates a carbocation. This carbocation intermediate is resonance stabilized - three resonance structures can be drawn.

- The FeBr$_4$ – also formed in this reaction is the base used in Step 3.

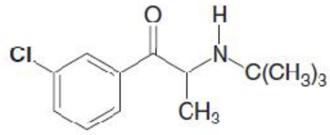
Step 3: Loss of a proton to re-form the aromatic ring.



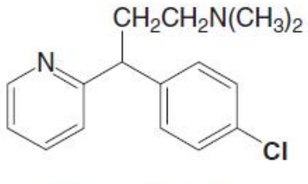
- FeBr$_4$ – removes the proton from the carbon bearing the Br, thus re-forming the aromatic ring.

- FeBr$_3$, a catalyst, is also regenerated for another reaction cycle.

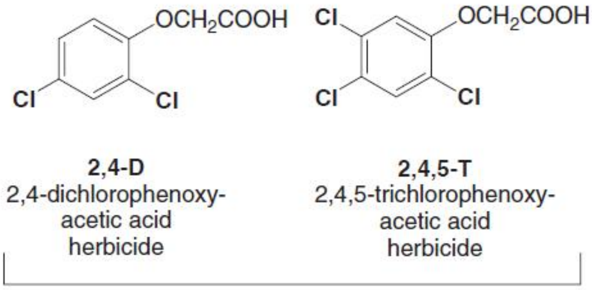
Chlorination proceeds by a similar mechanism. Reactions that introduce a halogen substituent on a benzene ring are widely used, and many halogenated aromatic compounds with a range of biological activity have been synthesized, as shown in Figure 3.2.



Generic name: **bupropion**
Trade names: **Wellbutrin, Zyban**
antidepressant,
also used to reduce nicotine cravings



chlorpheniramine
antihistamine

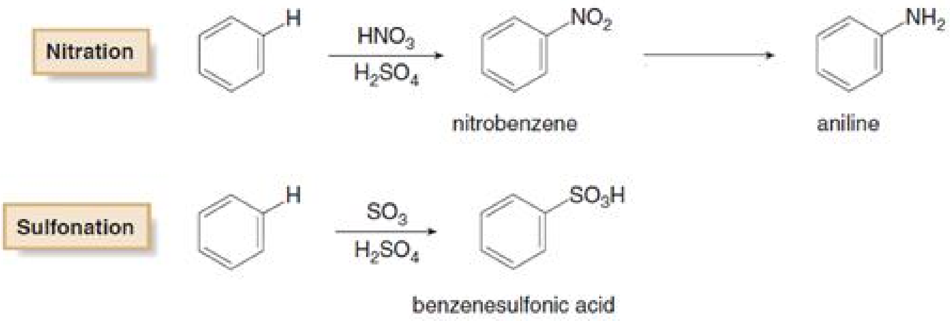


the active components in **Agent Orange**,
a defoliant used in the Vietnam War

Figure 3.2: Examples of biologically active aryl chlorides

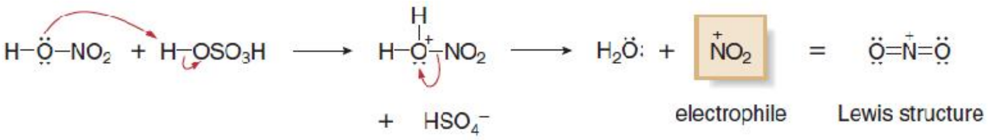
3.3 Nitration and Sulphonation

Nitration and sulphonation of benzene introduce two different functional groups on an aromatic ring. Nitration is an especially useful reaction because a nitro group can then be reduced to an NH_2 group, a common benzene substituent.

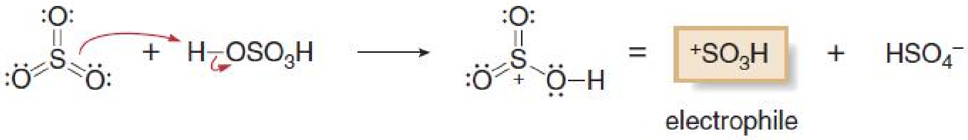


Generation of the electrophile in both nitration and sulphonation requires strong acid. In **nitration,** the electrophile is $^+NO_2$ (the **nitronium ion**), formed by protonation of HNO_3 followed by loss of water.

Mechanism for Formation of the Nitronium Ion ($^+NO_2$) for Nitration.



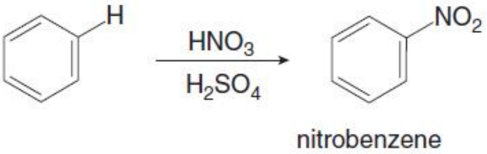
In **sulphonation,** protonation of sulfur trioxide, SO_3, forms a positively charged sulfur species ($^+SO_3H$) that acts as an electrophile.



These steps illustrate how to generate the electrophile E^+ for nitration and sulphonation, the process that begins any mechanism for electrophilic aromatic substitution. To complete either of these mechanisms, you must replace the electrophile E^+ by either $^+NO_2$ or $^+SO_3H$ in the general mechanism. Thus, **the two-step sequence that replaces H by E is the same regardless of E^+.**

In-Text Question 1

Draw a stepwise mechanism for the nitration of a benzene ring.

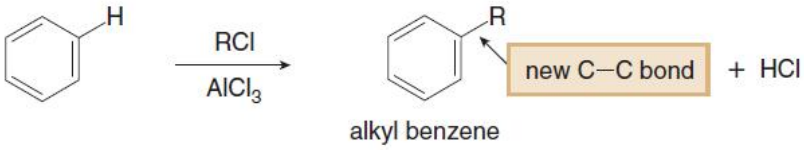


3.4 Friedel - Crafts Alkylation and Friedel - Crafts Acylation

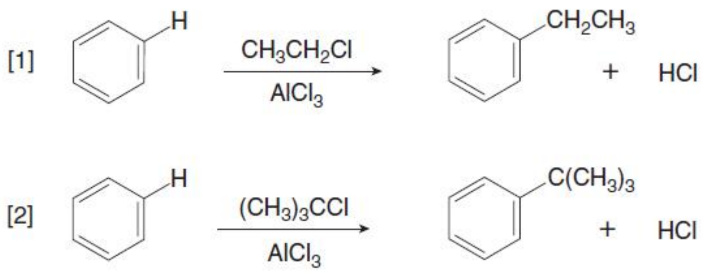
Friedel - Crafts alkylation and Friedel - Crafts acylation form new carbon-carbon bonds.

3.4.1 General Features

In Friedel - Crafts alkylation, treatment of benzene with an alkyl halide and a Lewis acid ($AlCl_3$) forms an alkyl benzene. This reaction is an alkylation because it results in transfer of an alkyl group from one atom to another (from Cl to benzene).

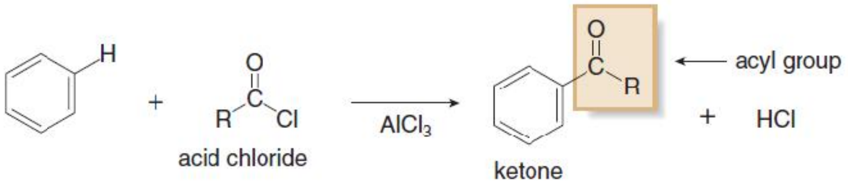


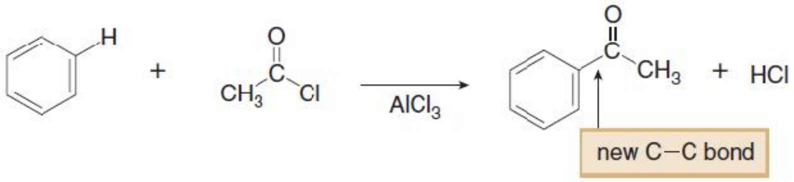
Friedel-Crafts alkylation – General reaction



Examples of Friedel-Crafts alkylation

In Friedel - Crafts acylation, a benzene ring is treated with an acid chloride (RCOCl) and $AlCl_3$ to form a ketone. Because the new group bonded to the benzene ring is called an acyl group, the transfer of an acyl group from one atom to another is an acylation.



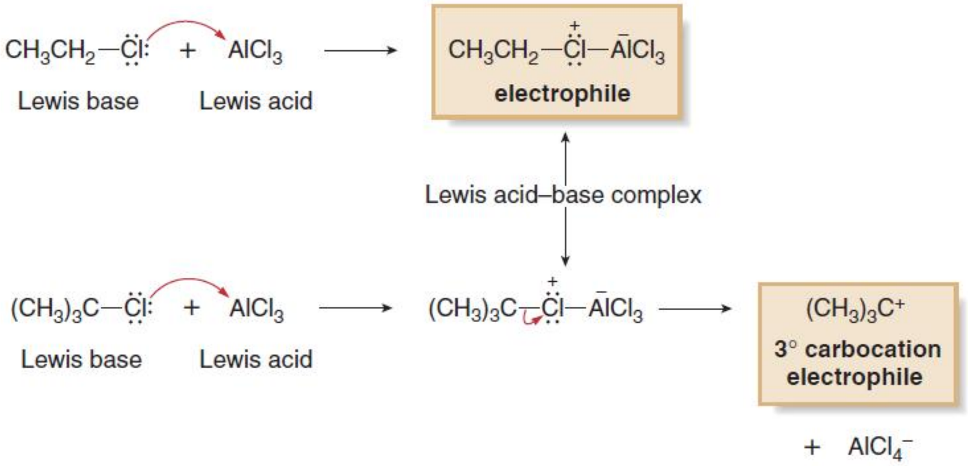


Acid chlorides are also called **acyl chlorides.**

Mechanism

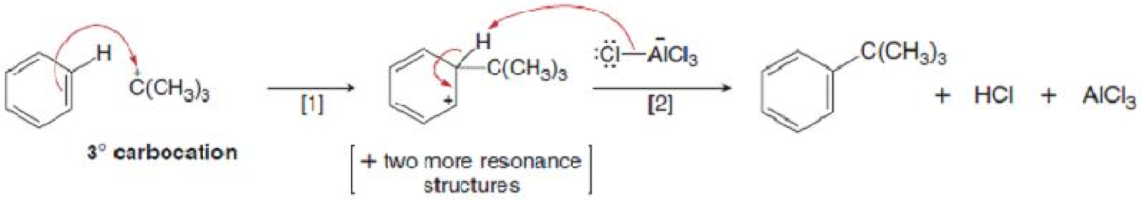
The mechanisms of alkylation and acylation proceed in a manner analogous to those for halogenation, nitration, and sulphonation. The unique feature in each reaction is how the electrophile is generated.

In Friedel–Crafts alkylation, the Lewis acid $AlCl_3$ reacts with the alkyl chloride to form a Lewis acid–base complex, illustrated with CH_3CH_2Cl and $(CH_3)_3CCl$ as alkyl chlorides. The identity of the alkyl chloride determines the exact course of the reaction.



- For CH_3Cl and 1° RCl, the Lewis acid–base complex itself serves as the electrophile for electrophilic aromatic substitution.
- With 2° and 3° RCl, the Lewis acid–base complex reacts further to give a 2° or 3° carbocation, which serves as the electrophile. Carbocation formation occurs only with 2° and 3° alkyl chlorides, because they afford more stable carbocations.

In either case, the electrophile goes on to react with benzene in the two-step mechanism characteristic of electrophilic aromatic substitution, illustrated in Mechanism 18.6 using the 3° carbocation, $(CH_3)_3C^+$.

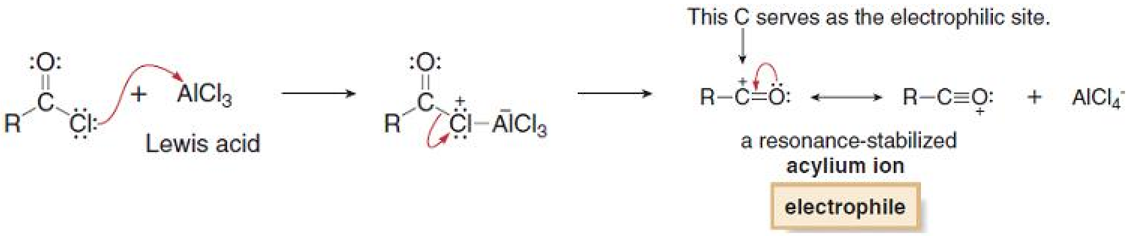


Mechanism of Friedel - Crafts Alkylation Using a 3° Carbocation.

- Addition of the electrophile (a 3° carbocation) forms a new carbon–carbon bond in Step (1).

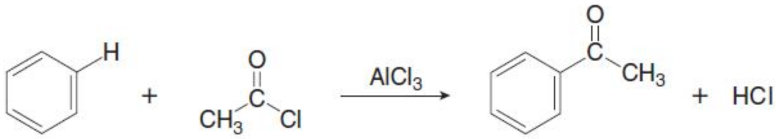
- $AlCl_4^-$ removes a proton on the carbon bearing the new substituent, thus re-forming the aromatic ring in Step (2).

In Friedel - Crafts acylation, the Lewis acid $AlCl_3$ ionizes the carbon - halogen bond of the acid chloride, thus forming a positively charged carbon electrophile called an acylium ion, which is resonance stabilized. The positively charged carbon atom of the acylium ion then goes on to react with benzene in the two-step mechanism of Electrophilic aromatic substitution.



To complete the mechanism for acylation, insert the electrophile into the general mechanism and draw the last two steps, as illustrated in the ITQ 2 below.

In-Text Question 2
Draw a stepwise mechanism for the following Friedel–Crafts acylation.



3.4.2 Other Facts about Friedel - Crafts Alkylation

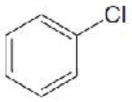
Three additional facts about Friedel - Crafts alkylations must be kept in mind.

1. Vinyl halides and aryl halides do *not* react in Friedel–Crafts alkylation

Most Friedel - Crafts reactions involve carbocation electrophiles. Because the carbocations derived from vinyl halides and aryl halides are highly unstable and do not readily form, these organic halides do *not* undergo Friedel–Crafts alkylation.

CH_2—CHCl

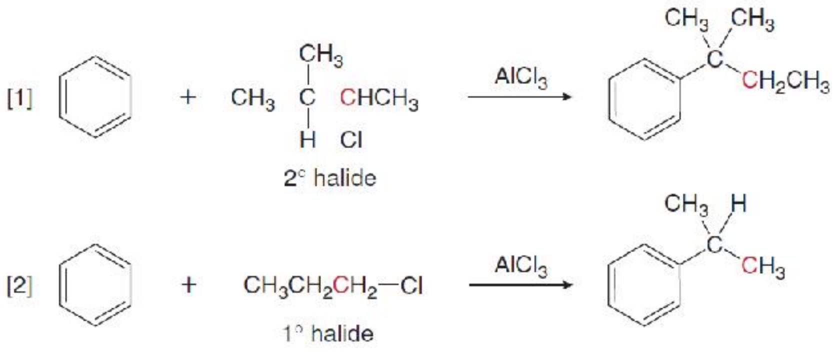
vinyl halide



aryl halide

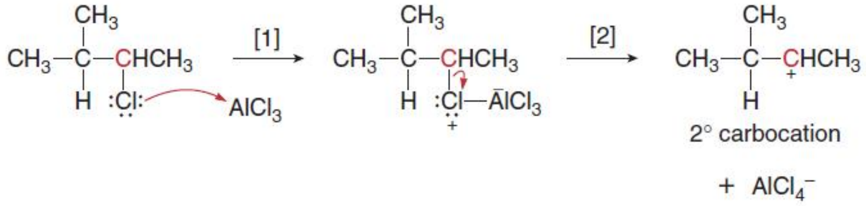
2. Rearrangements can occur

The Friedel - Crafts reaction can yield products having rearranged carbon skeletons when 1° and 2° alkyl halides are used as starting materials, as shown in Equations (1) and (2). In both reactions, the carbon atom bonded to the halogen in the starting material (labeled in red) is not bonded to the benzene ring in the product, thus indicating that a rearrangement has occurred.



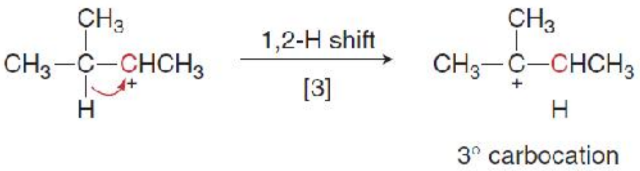
The result in Equation (1) is explained by a carbocation rearrangement involving a 1,2-hydride shift: **the less stable 2° carbocation (formed from the 2° halide) rearranges to a more stable 3° carbocation,** as illustrated below.

Steps (1) and (2) Formation of a 2° carbocation



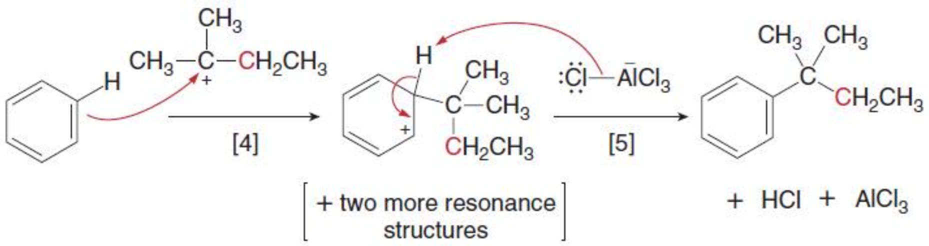
- Reaction of the alkyl chloride with $AlCl_3$ forms a complex that decomposes in Step (2) to form a **2° carbocation.**

Step [3] Carbocation rearrangement

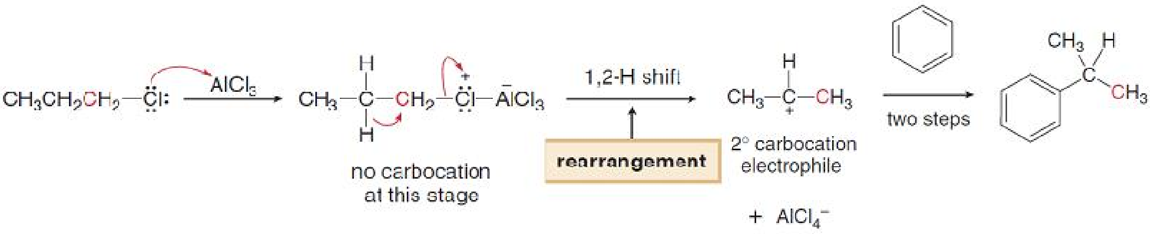


- **1,2-Hydride shift** converts the less stable 2° carbocation to a more stable 3° carbocation.

Steps (4) and (5) Addition of the carbocation and loss of a proton



- Friedel–Crafts alkylation occurs by the usual two-step process: **addition of the carbocation** followed by **loss of a proton** to form the alkylated product.



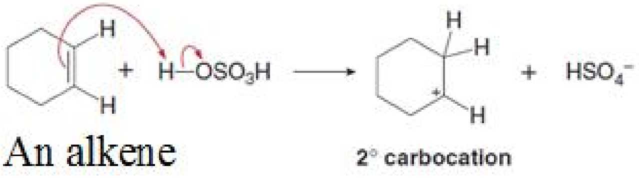
A Rearrangement Reaction Beginning with a 1° Alkyl Chloride

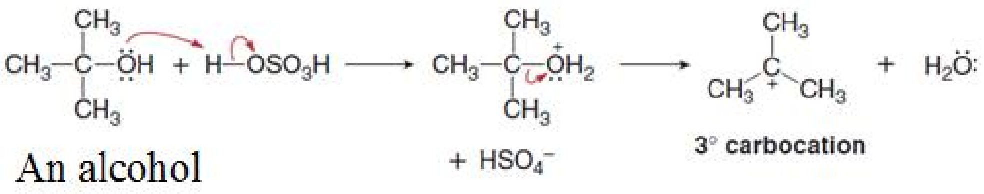
Other functional groups that form carbocations can also be used as starting materials

Although Friedel - Crafts alkylation works well with alkyl halides, any compound that readily forms a carbocation can be used instead. The two most common alternatives are alkenes and alcohols, both of which afford carbocations in the presence of strong acid.

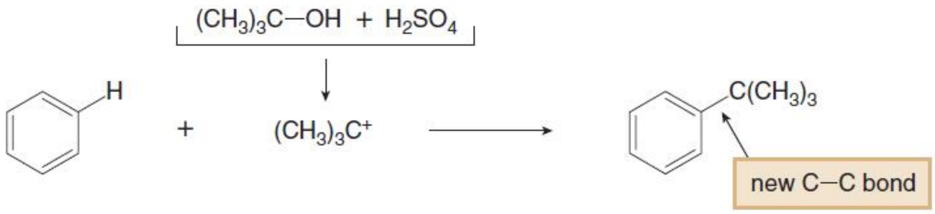
- Protonation of an alkene forms a carbocation, which can then act as an electrophile in a Friedel - Crafts alkylation.

- Protonation of an alcohol, followed by loss of water, likewise forms a carbocation.



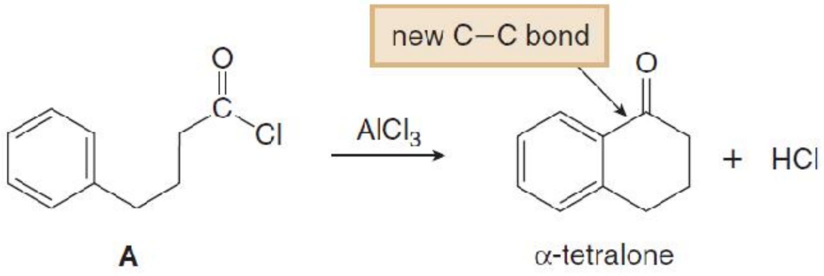


Each carbocation can then go on to react with benzene to form a product of electrophilic aromatic substitution. For example:



3.4.3 Intramolecular Friedel–Crafts Reactions

All of the Friedel–Crafts reactions discussed thus far have resulted from intermolecular reaction of a benzene ring with an electrophile. Starting materials that contain both units are capable of **intramolecular reaction,** and this forms a new ring. For example, treatment of compound **A,** which contains both a benzene ring and an acid chloride, with $AlCl_3$, forms α-tetralone by an intramolecular Friedel - Crafts acylation reaction.



3.5 Substituted Benzenes

Many substituted benzene rings undergo electrophilic aromatic substitution. Common substituents include halogens, OH, NH_2, alkyl, and many functional groups that contain a carbonyl. Each substituent either increases or decreases the electron density in the benzene ring, and this affects the course of electrophilic aromatic substitution.

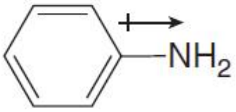
What makes a substituent on a benzene ring electron donating or electron withdrawing? The answer is **inductive effects** and **resonance effects,** both of which can add or remove electron density.

3.5.1 Inductive Effects

Inductive effects stem from the **electronegativity** of the atoms in the substituent and the **polarizability** of the substituent group.

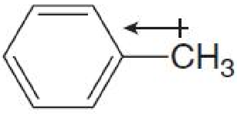
- Atoms more electronegative than carbon - including N, O, and X - pull electron density away from carbon and thus exhibit an electron-withdrawing inductive effect.
- Polarizable alkyl groups donate electron density, and thus exhibit an electron-donating inductive effect.

  Considering inductive effects *only*, an NH_2 group withdraws electron density and CH_3 donates electron density.



Electron-withdrawing inductive effect

- N is more electronegative than C.
- N inductively withdraws electron density.



Electron-donating inductive effect

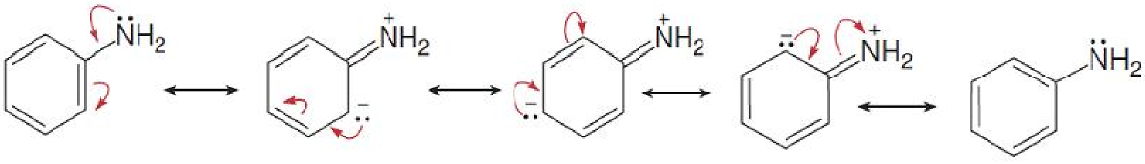
- Alkyl groups are Polarizable, making them electron-donating groups.

3.5.2 Resonance Effects

Resonance effects can either donate or withdraw electron density, depending on whether they place a positive or negative charge on the benzene ring.

- A resonance effect is electron donating when resonance structures place a negative charge on carbons of the benzene ring.
- A resonance effect is electron withdrawing when resonance structures place a positive charge on carbons of the benzene ring.

An electron-donating resonance effect is observed whenever an atom Z having a lone pair of electrons is directly bonded to a benzene ring (general structure - $C_6H_5{}^{-}Z:$). Common examples of Z include N, O, and halogen. For example, five resonance structures can be drawn for aniline ($C_6H_5NH_2$). Because three of them place a negative charge on a carbon atom of the benzene ring, an NH_2 group donates electron density to a benzene ring by a resonance effect.

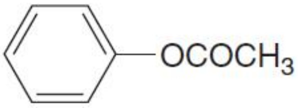


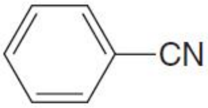
Aniline A B C

Three resonance structures A, B, and C place a (-) charge on atoms in the ring.

In contrast, an electron-withdrawing resonance effect is observed in substituted benzenes having the general structure $C_6H_5{}^{-}Y=Z$, where Z is more electronegative than Y.

In-Text Question 3
Classify each substituent as electron donating or electron withdrawing.

a. 

b. 

3.6 Electrophilic Aromatic Substitution of Substituted Benzenes

Electrophilic aromatic substitution is a general reaction of *all* aromatic compounds, including polycyclic aromatic hydrocarbons, heterocycles, and substituted benzene derivatives. A substituent affects two aspects of electrophilic aromatic substitution:

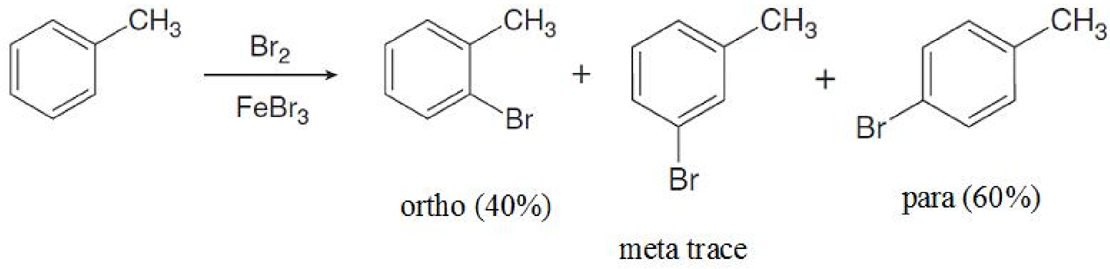
- **The rate of reaction:** A substituted benzene reacts faster or slower than benzene itself.

- **The orientation:** The new group is located either ortho, meta, or para to the existing substituent. The identity of the first substituent determines the position of the second substituent.

Toluene ($C_6H_5CH_3$) and nitrobenzene ($C_6H_5NO_2$) illustrate two possible outcomes.

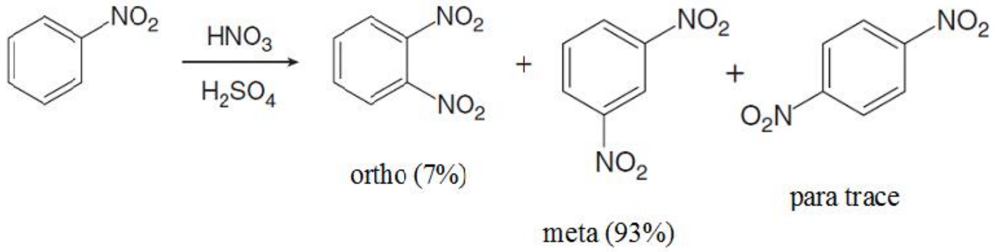
1. Toluene

Toluene reacts **faster** than benzene in all substitution reactions. Thus, its electron-donating CH_3 group activates the benzene ring to electrophilic attack. Although three products are possible, compounds with the new group ortho or para to the CH_3 group predominate. The CH_3 group is therefore called an ortho, para director.



2. Nitrobenzene

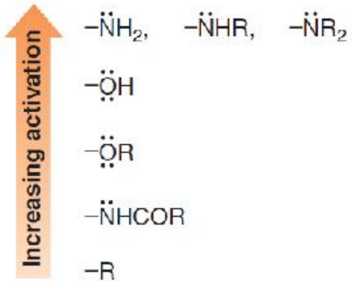
Nitrobenzene reacts **more slowly** than benzene in all substitution reactions. Thus, its electron withdrawing NO_2 group deactivates the benzene ring to electrophilic attack. Although three products are possible, the compound with the new group meta to the NO_2 group predominates. The NO_2 group is called a meta director.



Substituents either activate or deactivate a benzene ring towards electrophiles, and direct selective substitution at specific sites on the ring. All substituents can be divided into three general types.

Ortho, para directors and activators

- Substituents that *activate* a benzene ring and direct substitution ortho and para.



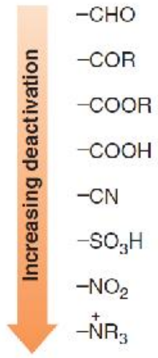
General structure

Ortho, para deactivators

- Substituents that *deactivate* a benzene ring and direct substitution ortho and para.

Meta directors

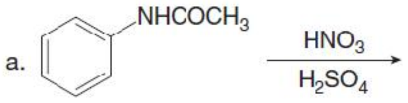
- Substituents that direct substitution meta.
- All meta directors *deactivate* the ring.

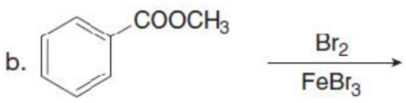


General structure –Y(δ^+ or +)

In-Text Question 4

Draw the products of each reaction and state whether the reaction is faster or slower than a similar reaction with benzene.





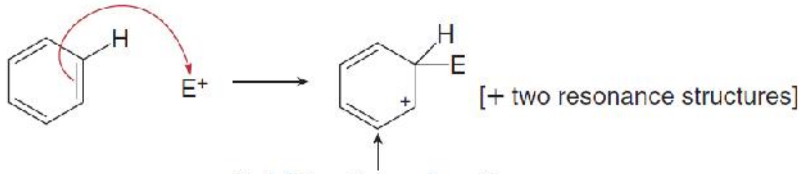
3.7 Activation and Deactivation of Benzene Ring

- Why do substituents activate or deactivate a benzene ring?

- Why are particular orientation effects observed? Why are some groups ortho, para directors and some groups meta directors?

To understand why some substituents make a benzene ring react faster than benzene itself (activators), whereas others make it react slower (deactivators), we must evaluate the rate-determining step (the first step) of the mechanism. Recall the first step in Electrophilic aromatic substitution is the addition of an electrophile (E^+) to form a resonance-stabilized carbocation. The Hammond postulate makes it possible to predict the relative rate of the reaction by looking at the stability of the carbocation intermediate.

- The more stable the carbocation, the lower in energy the transition state that forms it, and the faster the reaction.



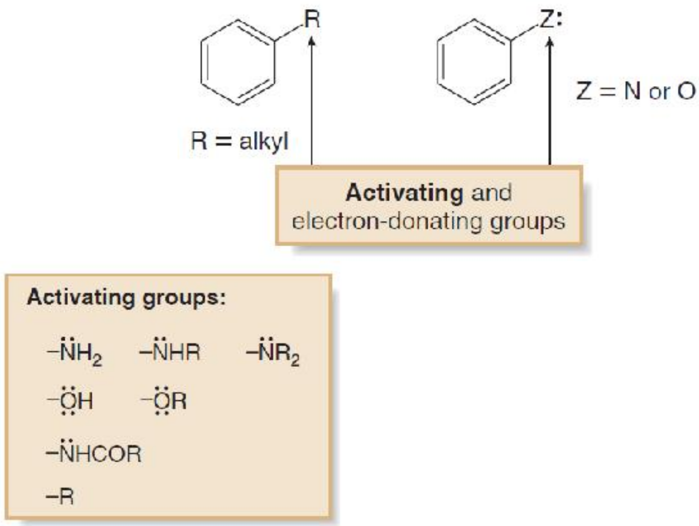
Stabilizing the carbocation makes the reaction faster.

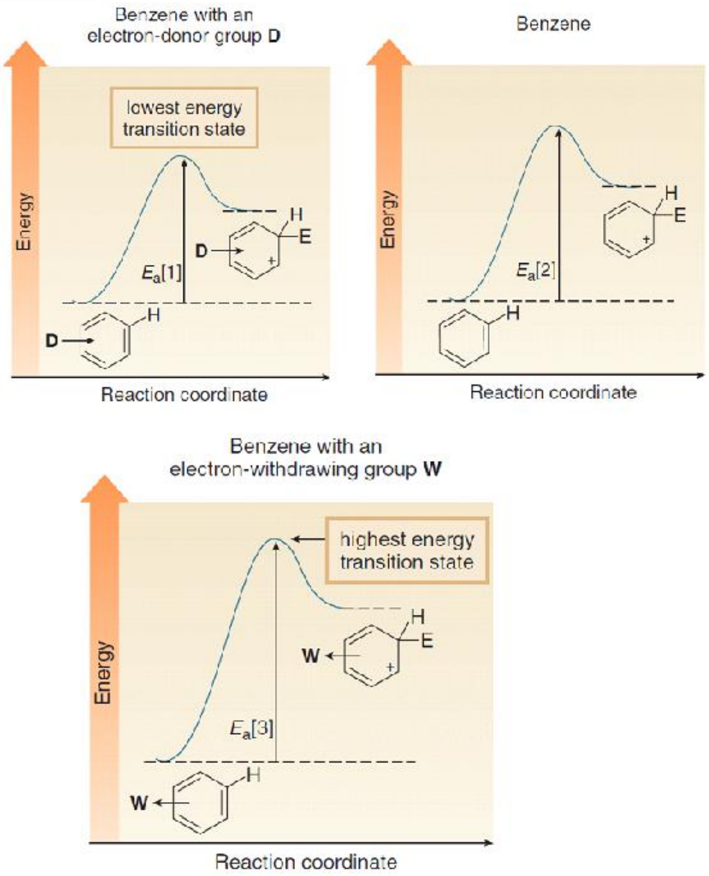
The principles of inductive effects and resonance effects can now be used to predict carbocation stability.

- Electron-donating groups stabilize the carbocation and activate a benzene ring towards electrophilic attack.
- Electron-withdrawing groups destabilize the carbocation and deactivate a benzene ring towards electrophilic attack.

The energy diagrams in Figure 3.3 illustrate the effect of electron-donating and electron withdrawing groups on the energy of the transition state of the rate-determining step in Electrophilic aromatic substitution.

- All activators are either R groups or they have an N or O atom with a lone pair bonded directly to the benzene ring.

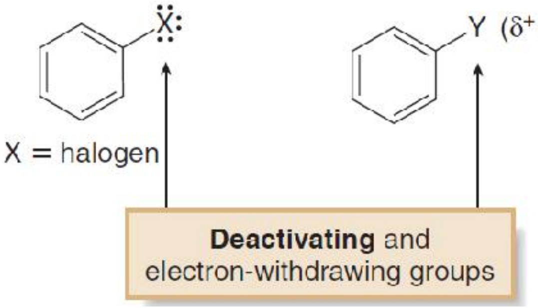




Figures 3.3: Energy diagrams comparing the rate of electrophilic aromatic substitution of substituted benzenes

- Electron-donor groups **D** stabilize the carbocation intermediate, lower the energy of the transition state, and increase the rate of reaction.

- Electron-withdrawing groups **W** destabilize the carbocation intermediate, raise the energy of the transition state, and decrease the rate of reaction.
- All deactivators are either halogens or they have an atom with a partial or full positive charge bonded directly to the benzene ring.



3.8 Orientation Effects in Substituted Benzenes

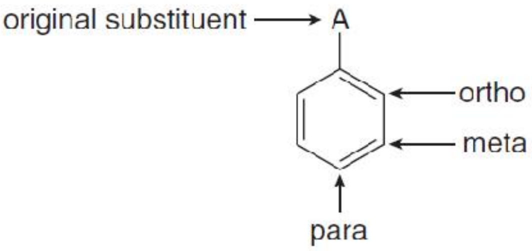
To understand why particular orientation effects arise, you must keep in mind the general structures for ortho, para directors and for meta directors. There are two general types of ortho, para directors and one general type of meta director:

- All ortho, para directors are R groups or have a nonbonded electron pair on the atom bonded to the benzene ring.
- All meta directors have a full or partial positive charge on the atom bonded to the benzene ring.

To evaluate the directing effects of a given substituent, we can follow a stepwise procedure.

How to Determine the Directing Effects of a Particular Substituent

Step 1: Draw all resonance structures for the carbocation formed from attack of an electrophile E^+ at the ortho, meta, and para positions of a substituted benzene (C_6H_5-A).



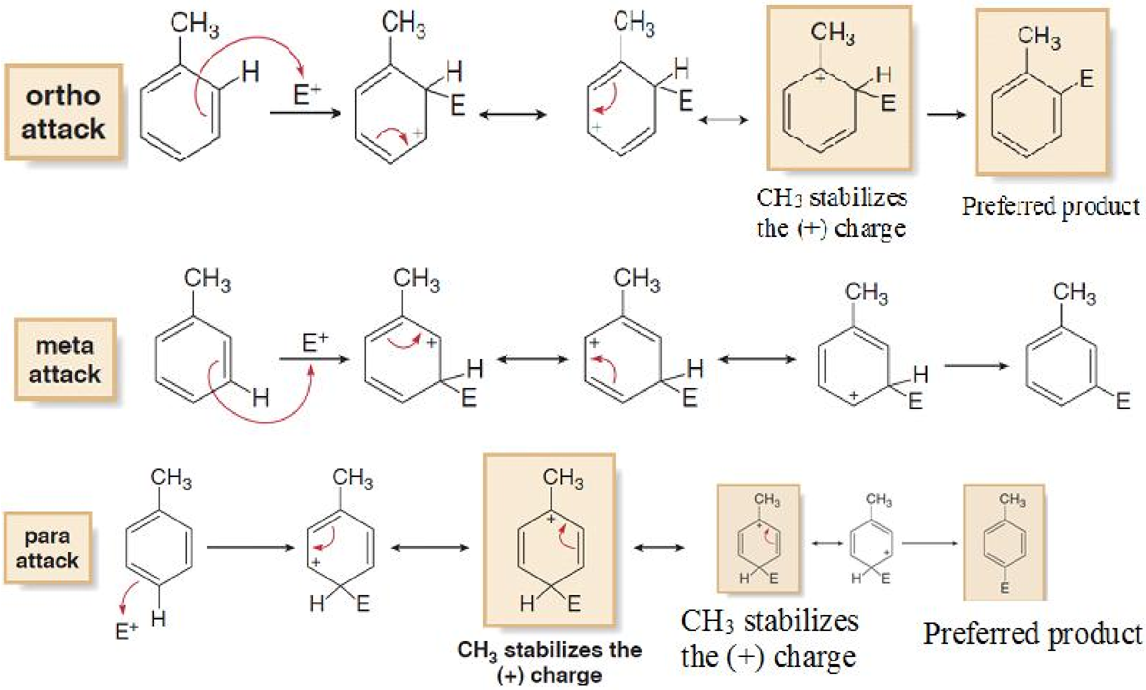
- There are at least three resonance structures for each site of reaction.

- Each resonance structure places a positive charge *ortho* or *para* to the new C–E bond.

Step 2: Evaluate the stability of the intermediate resonance structures. The electrophile attacks at those positions that give the most stable carbocation.

3.8.1 The CH_3 Group - An *ortho, para* Director

To determine why a CH_3 group directs electrophilic aromatic substitution to the ortho and para positions, first draw all resonance structures that result from electrophilic attack at the ortho, meta, and para positions to the CH_3 group.

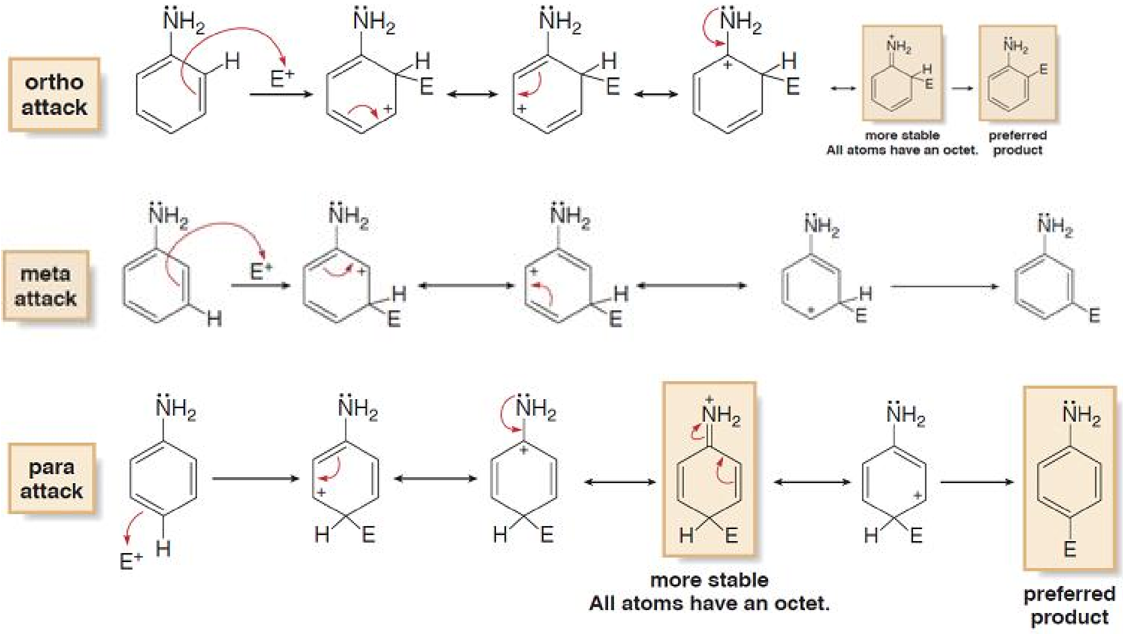


To evaluate the stability of the resonance structures, determine whether any are especially stable or unstable. In this example, attack ortho or para to CH_3 generates a resonance structure that places a positive charge on a carbon atom with the CH_3 group. The electron-donating CH_3 group *stabilizes* the adjacent positive charge. In contrast, attack meta to the CH_3 group does *not* generate any resonance structure stabilized by electron donation. Other alkyl groups are ortho, para directors for the same reason.

The CH_3 group directs electrophilic attack ortho and para to itself because an electron-donating inductive effect stabilizes the carbocation intermediate.

3.8.2 The NH_2 Group - An ortho, para Director

To determine why an amino group (NH_2) directs electrophilic aromatic substitution to the ortho and para positions, follow the same procedure.

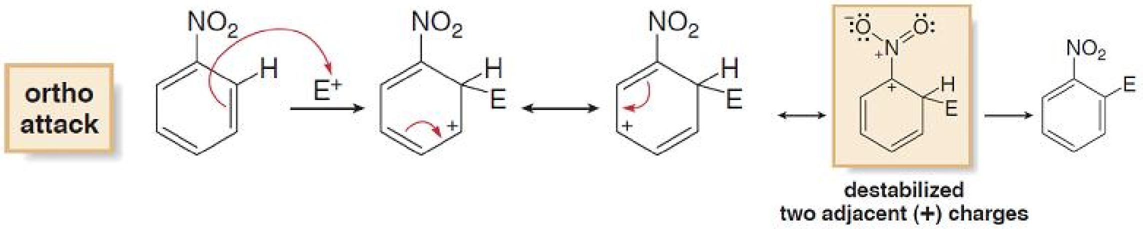


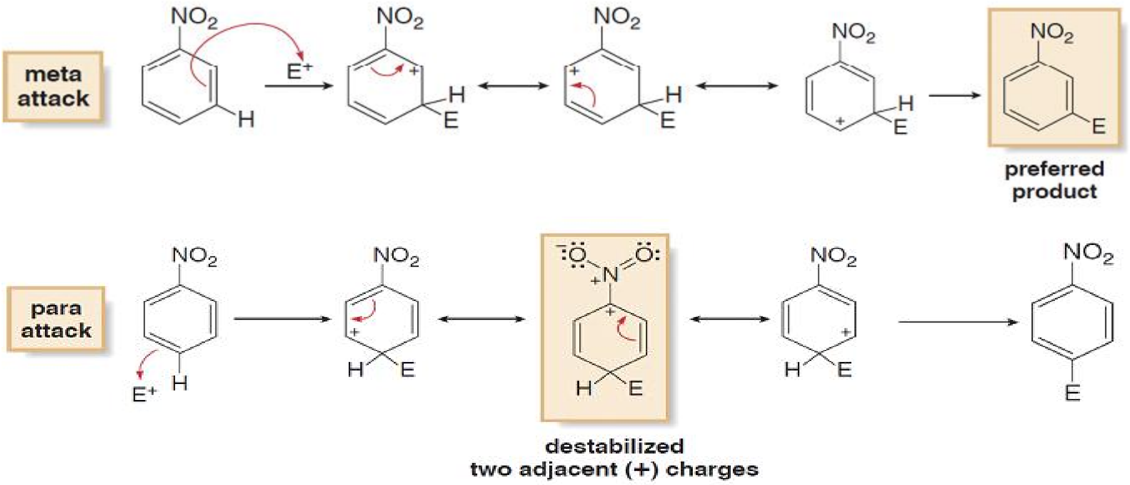
Attack at the meta position generates the usual three resonance structures. Because of the lone pair on the N atom, attack at the ortho and para positions generates a fourth resonance structure, which is stabilized because every atom has an octet of electrons. This additional resonance structure can be drawn for all substituents that have an N, O, or halogen atom bonded directly to the benzene ring.

The NH_2 group directs electrophilic attack ortho and para to itself because the carbocation intermediate has additional resonance stabilization.

3.8.3 The NO_2 Group - A meta Director

To determine why a nitro group (NO_2) directs electrophilic aromatic substitution to the meta position, follow the same procedure.





Attack at each position generates three resonance structures. One resonance structure resulting from attack at the ortho and para positions is especially *destabilized,* because it contains a positive charge on two adjacent atoms. Attack at the meta position does not generate any particularly unstable resonance structures.

With the NO_2 group (and all meta directors), meta attack occurs because attack at the ortho or para position gives a destabilized carbocation intermediate.

In-Text Question 5

The Friedel - Crafts reaction of benzene with 2-chloro-3-methylbutane in the presence of $AlCl_3$ occurs with a carbocation rearrangement. What is the structure of the product?

SELF-ASSESSMENT EXERCISE)

i. Predict the major product of the sulphonation of toluene.

ii Rank the compounds in each of the following groups in order of their reactivity to electrophilic substitution:

  (a) Nitrobenzene, phenol, toluene, benzene
  (b) Phenol, benzene, chlorobenzene, benzoic acid
  (c) Benzene, bromobenzene, benzaldehyde, aniline

iii Predict the major products of the following reactions:

  (a) Nitration of bromobenzene
  (b) Bromination of nitrobenzene

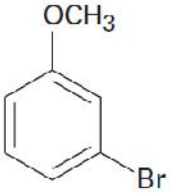
(c) Chlorination of phenol
(d) Bromination of aniline

iv Draw resonance structures for the intermediates from reaction of an electrophile at the ortho, meta, and para positions of nitrobenzene. Which intermediates are most stable?

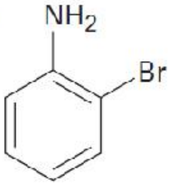
v. What product would you expect from bromination of *p*-methylbenzoic acid?

vi At what position would you expect electrophilic substitution to occur in each of the following substances?

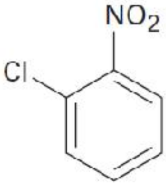
(a)



(b)



(c)



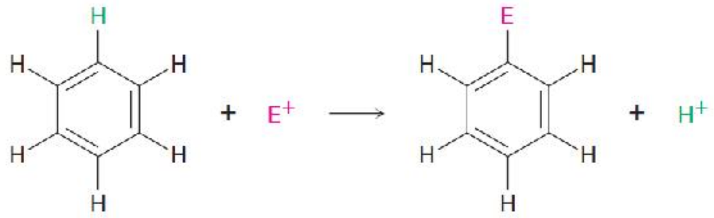
4.0 CONCLUSION

In this unit, we looked at some of the unique reactions that aromatic molecules undergo and their mechanisms. These reactions include halogenation, nitration and sulphonation, Friedel-Crafts Alkylation and Friedel-Crafts Acylation. We also looked at the chemistry of substituted benzene, activation and deactivation of benzene and lastly orientation effects in substituted benzenes.

5.0 SUMMARY

In the preceding chapter, we looked at *aromaticity* - the stability associated with benzene and related compounds that contain a cyclic conjugated system of $4n + 2\ \pi$ electrons.

The most common reaction of aromatic compounds is electrophilic aromatic substitution, in which an electrophile (E^+) reacts with an aromatic ring and substitutes for one of the hydrogens. The reaction is characteristic of all aromatic rings, not just benzene and substituted benzenes. In fact, the ability of a compound to undergo electrophilic substitution is a good test of aromaticity.



Many different substituents can be introduced onto an aromatic ring through electrophilic substitution reactions. To list some possibilities, an aromatic ring can be substituted by a halogen (-Cl, -Br, I), a nitro group ($-NO_2$), a sulphonic acid group ($-SO_3H$), a hydroxyl group (-OH), an alkyl group (-R), or an acyl group (-COR). Starting from only a few simple materials, it's possible to prepare many thousands of substituted aromatic compounds.

6.0 TUTOR MARK ASSIGNMENT

7.0 REFERENCES/FURTHER READINGS

Bruice, P. Y. (2004). *Organic Chemistry*, 7th Edition. Pearson Education: London.

Dewick, P. M. (2006). *Essentials of organic chemistry: for students of pharmacy, medicinal chemistry and biological chemistry*. John Wiley & Sons.

Morrison, R. T., & Boyd, R. N. (2007). *Organic Chemistry text book*, 6th editions. Prentice-Hall of India Pvt. Ltd.

Brown, T. L. (2009). Chemistry: the central science. Pearson Education.

Mukherji, S. M., Singh, S. P., Kapoor, R. P., & Dass, R. (2010). *Organic Chemistry*, vol. I. New Age International.

Okuyama, T., & Maskill, H. (2013). Organic Chemistry: a mechanistic approach. Oxford University Press.

Ghatak, K. L. (2014). *A Textbook of Organic Chemistry and Problem Analysis*. PHI Learning Pvt. Ltd.

Brown, W. H., & Poon, T. (2016). *Introduction to organic chemistry*. John Wiley & Sons.